

# Identification of Pathogens in Synovial Fluid Samples with an Automated Multiplexed Molecular Detection System



Pons B.<sup>1</sup>, Jay C.<sup>1</sup>, Martin T.<sup>1</sup>, Sothier I.<sup>1</sup>, Savelli H.<sup>1</sup>, Kensinger B.<sup>2</sup>, Laurent F.<sup>3</sup>, Abad L.<sup>3</sup>, Murphy C.<sup>4</sup>, Craney A.<sup>4</sup>, Schmitt B.<sup>5</sup>, Waggoner A.<sup>5</sup>, Butler-Wu S.<sup>6</sup>, Costales C.<sup>6</sup>, Dien-Bard J.<sup>7</sup>, Mestas J.<sup>7</sup>, Esteban J.<sup>8</sup>, Salar-Vidal L.<sup>8</sup>, Harrington A.<sup>9</sup>, Collier S.<sup>9</sup>, Leber A.<sup>10</sup>, Everhart K.<sup>10</sup>, Balada-Llasat J-M.<sup>12</sup>, Horn J.<sup>12</sup>, Magro S.<sup>1</sup>, Bourzac K.<sup>2</sup>

<sup>1</sup>Molecular Biology R&D, bioMérieux SA, Grenoble, France. <sup>2</sup>BioFire Diagnostics, LLC, Salt Lake City, UT. <sup>3</sup>Hospices Civils De Lyon, French National Reference Center for Staphylococci, Lyon, France. <sup>4</sup>University of Nebraska Medical Center, Omaha, NE. <sup>5</sup>Pathology and Laboratory Medicine, Indiana University, Indianapolis, IN. <sup>6</sup>Keck School of Medicine, Los Angeles, CA. <sup>7</sup>Children's Hospital Los Angeles, Los Angeles, CA. <sup>8</sup>Department of Clinical Microbiology, Foundation Jimenez Diaz, Madrid, Spain. <sup>9</sup>Loyola University Medical Center, Maywood, IL. <sup>10</sup>Department of Laboratory Medicine, Nationwide Children's Hospital, Columbus, OH. <sup>11</sup>Clinical Microbiology, The Ohio State University Wexner Medical Center, Columbus, OH.

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## BACKGROUND/OBJECTIVES

Bone and Joint Infections (BJI) have high morbidity and are difficult to treat. Culture-based diagnosis is limited in its ability to recover fastidious bacteria and because several organisms can be involved. Culture time of up to two weeks may be necessary for certain bacteria. The sensitivity of culture is also negatively impacted by antibiotics received before sample collection. Alternatively, molecular methods offer a promising improvement for the diagnosis of BJI with reduced time to result. The goal of this study was to evaluate a development version of BioFire® FilmArray® Bone and Joint Infection (BJI) Panel (bioMérieux SA, BioFire Diagnostics, LLC) using synovial fluid samples. Time to result for this panel is about 1 hour.

## MATERIALS AND METHODS

- A pilot evaluation was performed at 9 hospitals in the United States and Europe.
- 925 synovial fluid specimens were prospectively collected from patients with suspected BJI infections. Each hospital followed its standard protocol to collect and process the samples.
- All samples were cultured and a residual volume of 200 µl was tested on the BioFire BJI Panel.
- BioFire results were compared to culture and discordant results were investigated using an independent comparator PCR with sequence confirmation.

Sites Location
Indianapolis, IN, USA
Omaha, NE, USA
Lyon, France - Europe
Los Angeles, CA
Madrid, Spain - Europe
Chicago, IL, USA
Columbus, OH, USA
Los Angeles CA, USA
Columbus, OH, USA



## The BioFire BJI Panel

Simultaneous detection of 31 Pathogens and 8 Antimicrobial Resistance Markers

### Gram-negative bacteria

- *Escherichia coli*
- *Proteus* spp.
- *Citrobacter*
- *Enterobacter cloacae* complex
- *Klebsiella aerogenes*
- *Klebsiella pneumoniae* group
- *Morganella morganii*
- *Serratia marcescens*
- *Salmonella* spp.
- *Kingella kingae*
- *Pseudomonas aeruginosa*
- *Haemophilus influenzae*
- *Neisseria gonorrhoeae*
- *Bacteroides fragilis*

### Gram-positive bacteria

- *Staphylococcus aureus*
- *Staphylococcus lugdunensis*
- *Streptococcus* spp.
  - *Streptococcus pyogenes*
  - *Streptococcus agalactiae*
  - *Streptococcus pneumoniae*
- *Enterococcus faecalis*
- *Enterococcus faecium*
- *Anaerococcus prevotii/vaginalis*
- *Peptoniphilus*
- *Clostridium perfringens*
- *Finnegoldia magna*
- *Parvimonas micra*
- *Peptostreptococcus anaerobius*
- *Cutibacterium granulosum/avidum*

### Yeast

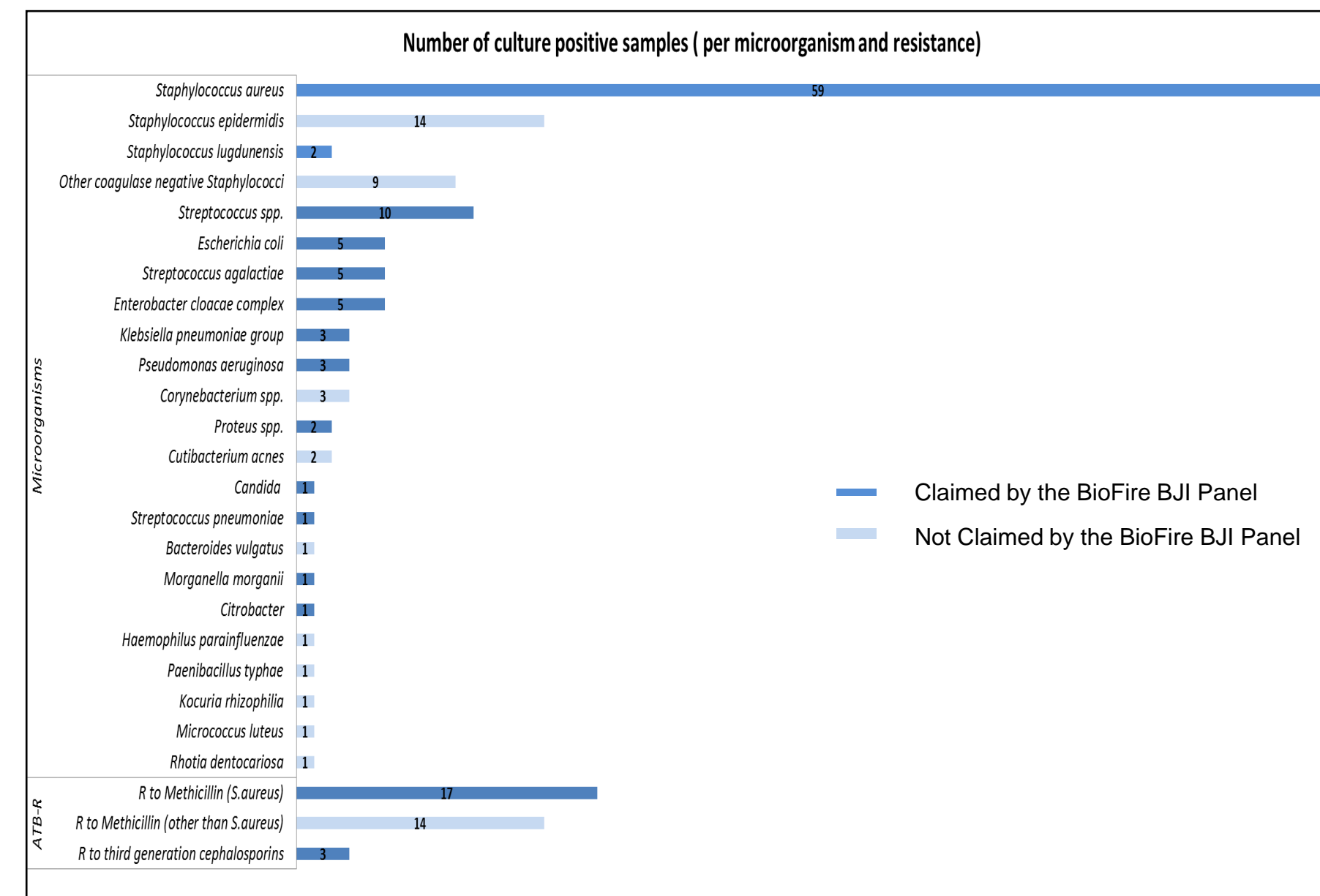
- *Candida*
  - *Candida albicans*

### Antimicrobial Resistance Markers

- *mecA/C* and *MREJ*
- *vanA/B*
- *CTX-M*
- *KPC*, *NDM*, *OXA-48*-like, *VIM*, *IMP*

## RESULTS

### MICROORGANISMS AND RESISTANCE MARKERS IDENTIFIED BY CULTURE



- Out of 925 specimens, 124 (13 %) were positive by culture → 121 samples were monomicrobial and 3 had two organisms (Table 1).

- Resistance to methicillin was reported for :
  - 17 out of 59 *S.aureus* isolates (29 %).
  - 14 out of 25 Staphylococci other than *S.aureus* (56 %).

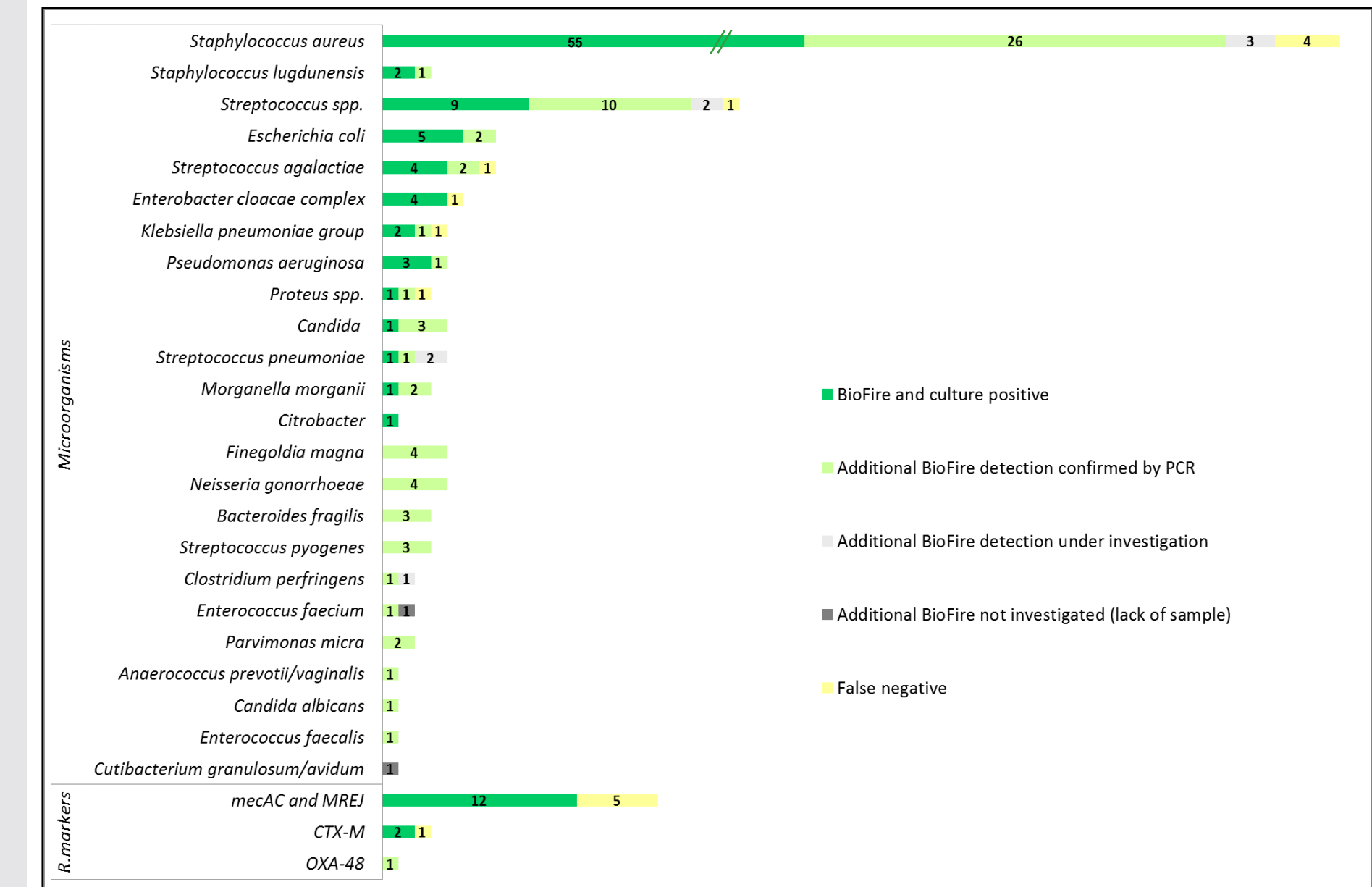
- Resistance to third-generation cephalosporins was reported in 3 isolates (*E.cloacae* complex, *K.pneumoniae* and *M.morganii*).

## CONCLUSION

- These results showed a good correlation between the BioFire BJI Panel and culture. Most of the claimed organisms and resistance markers identified by culture were detected by the BioFire BJI Panel (103/118).
- Moreover, compared to culture, the BioFire BJI Panel allowed the detection of more positive samples and more polymicrobial samples.
- Additional detections were confirmed in majority of cases (90 %) by an independent comparator PCR.
- The test is user-friendly, with 2 min hands-on time and time to result of about 1 hour.
- These data suggest that a multiplexed molecular system such as the BioFire BJI Panel is a good option for the diagnosis of Bone and Joint Infections in synovial fluid samples.

*These data are a preliminary analysis of a « research use only » version of the BioFire BJI Panel and are subject to change before final version. The BioFire BJI Panel has not been evaluated by the FDA or other regulatory agencies for In vitro diagnostic use.*

### MICROORGANISMS IDENTIFIED BY THE BIOFIRE BJI PANEL



- Out of 925 specimens, 145 (16 %) were positive with the BioFire BJI Panel → 135 were monomicrobial and 10 were polymicrobial (Table 1)

Table 1: Number of positive samples with the BioFire BJI Panel and with culture

	BioFire BJI Panel	Culture
<b>Total</b>	<b>145</b>	<b>124</b>
Monomicrobial samples	135	121
Polymicrobial samples	10	3
2 organisms	9	3
5 organisms	1	0

- 185 positive assays with the BioFire BJI Panel were compared to culture results :

- ✓ 103 were concordant
- ✓ 82 additional positive were observed :
  - 72 (90 %) were confirmed positive with a comparator PCR
  - 2 could not be investigated due to lack of sample
  - 8 are still under investigation

- Investigation of the 15 false negative results is described in Table 2.

Table 2: Investigation of false negative results

Reason for false negative	Assay concerned (sample number)
Sample load below BioFire Limit of Detection	<i>Staphylococcus aureus</i> (4 samples), <i>mecA/C</i> and <i>MREJ</i> (1), <i>Streptococcus</i> spp. (1), <i>Enterobacter cloacae</i> complex (1), <i>Klebsiella pneumoniae</i> group (1), <i>Proteus</i> spp. (1)
Culture information questionable	• <i>mecA/C</i> and <i>MREJ</i> (3 samples) : resistance to methicillin was not confirmed on sample by comparator PCR neither on isolates using Vitek2® • <i>mecA/C</i> and <i>MREJ</i> (1) : resistance to methicillin not due to <i>S.aureus</i> • <i>Streptococcus agalactiae</i> (1) : PCR comparator sequencing identified <i>S.galloyticus</i> and not <i>S.agalactiae</i> . This sample was detected positive to <i>Streptococcus</i> spp. with the BioFire BJI Panel
Resistance due to another gene	<i>CTX-M</i> (1) : Reported phenotypic resistance to C3G was due to <i>AmpC</i> and not <i>CTX-M</i> ESBL