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BACKGROUND / OBJECTIVES

Bone and Joint Infections (BJI) are severe pathologies which can lead to permanent disability, or in rare cases death, and which have significant economic impact on public health systems.

BJI can be polymicrobial or caused by fastidious bacteria and the patient could have received antibiotics before surgery. Those factors increase the difficulty of culture-based diagnosis. Furthermore, up to two weeks are often needed to detect bacteria by culture. Alternatively, molecular approaches have been developed. A development version of the FilmArray® Bone and Joint Infection Panel (BJI Panel) is available.

This panel detects Gram-positive and -negative bacteria, *Candida* spp., and several antibiotic resistance markers. Utilization of this panel is so far limited to synovial fluids.

The objective of this study is to perform a preliminary evaluation of this panel.

MATERIALS AND METHODS

- A pilot evaluation was performed at 4 hospitals in the United States and France from July 2016 to March 2017.
- Synovial fluid specimen from 235 patients with suspected BJI were prospectively included in the study. Only patients with synovial fluids were included.
- This represents a total of 243 samples (8 patients had 2 samples).
- Each hospital followed its standard protocol to collect and process the samples. All samples were tested in culture, PCR was used by site 3 to detect *Kingella kingae*.
- A residual volume of 200 µl was tested on the BJI panel.
- BJI Panel results were compared to culture and discordant results were investigated using a comparator assay (PCR/sequencing).

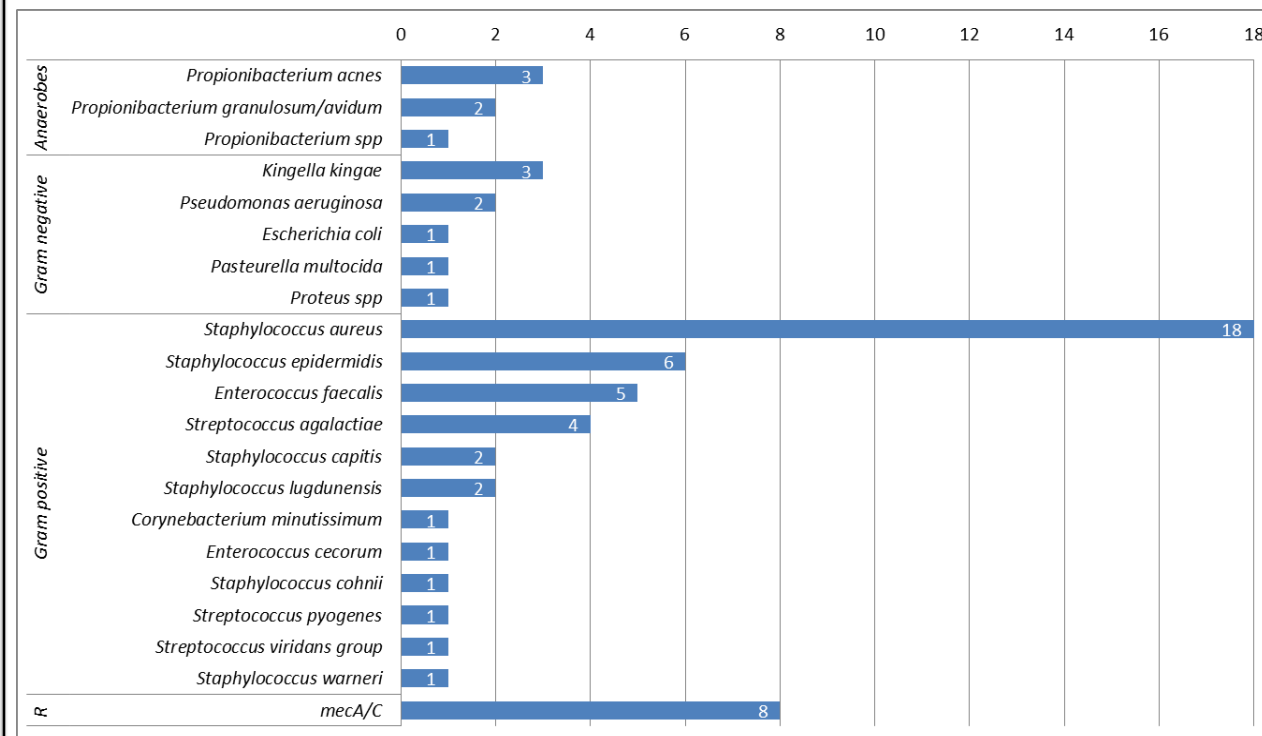


FilmArray® Bone and Joint Infection Panel description

Gram positive	Gram negative	Resistance markers	Yeast
<i>S. aureus</i>	<i>E. coli</i>	vanA/B	<i>Candida</i> spp.
<i>S. lugdunensis</i>	<i>K. pneumoniae</i>	CTX-M	<i>C. albicans</i>
<i>Streptococcus</i> spp.	<i>Enterobacter</i> spp.	mecA/C	
<i>S. pyogenes</i>	<i>Proteus</i> spp	KPC	
<i>S. agalactiae</i>	<i>M. morgannii</i>	NDM	
<i>S. pneumoniae</i>	<i>Citrobacter</i> spp.	OXA-48-like	
<i>E. faecalis</i>	<i>S. marcescens</i>	IMP	
<i>E. faecium</i>	<i>Salmonella</i> spp.	VIM	
<i>F. magna</i> *	<i>P. aeruginosa</i>		
<i>P. granulosum/avidum</i> *	<i>K. kingae</i>		
<i>C. perfringens</i> *	<i>N. gonorrhoeae</i>		
<i>Anaerococcus</i> spp./ <i>Peptoniphilus</i> spp.*	<i>H. influenzae</i>		
<i>P. micra/P. anaerobius</i> *	<i>B. fragilis</i> *		

* Anaerobes

Microorganisms identified using culture



- 55 synovial fluids were positive by culture (23 %).
- A total of 57 isolates were recovered, 2 samples had 2 isolates.
- The *mecA* gene was detected in 4 *S. epidermidis*, 3 *S. aureus* and 1 *S. cohnii*.
- The BJI Panel covers 42 out of 57 strains reported by culture. Species not covered are : *S. epidermidis* (6 isolates), *P. acnes* (3), *S. capitis* (2), *S. warneri* (1), *E. cecorum* (1), *C. minutissimum* (1) and *P. multocida* (1).

FilmArray Bone and Joint Infection Panel preliminary performances

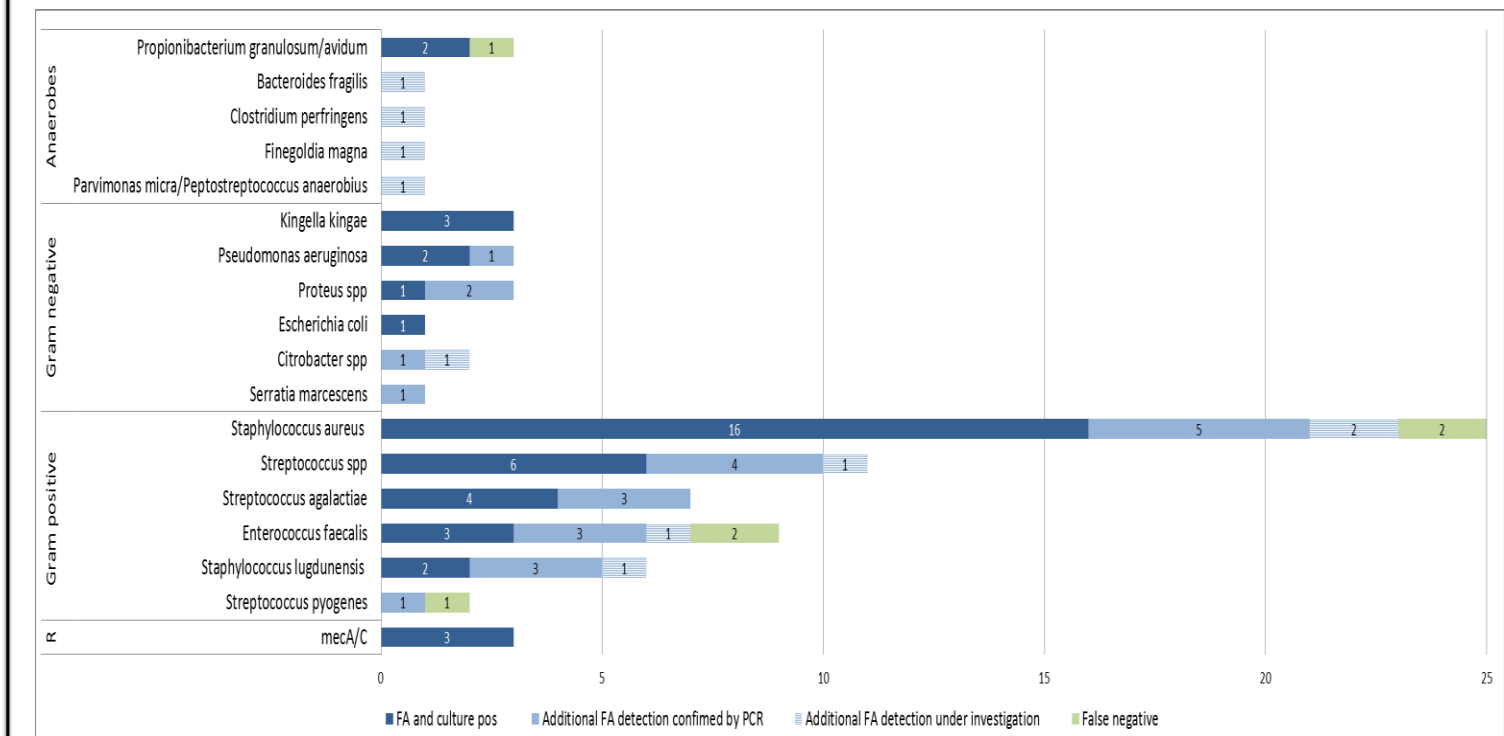
FilmArray® compared to culture						FilmArray® compared to culture and after investigation of discordants							
Target	FN	TP	Sensitivity	TN	FP	Specificity	Target	FN	TP	Sensitivity	TN	FP	Specificity
<i>Escherichia coli</i>	0	1	100	242	0	100	<i>Escherichia coli</i>	0	1	100	242	0	100
<i>Kingella kingae</i>	0	3	100	240	0	100	<i>Kingella kingae</i>	0	3	100	240	0	100
<i>Pseudomonas aeruginosa</i>	0	2	100	240	1	99.6	<i>Pseudomonas aeruginosa</i>	0	3	100	240	0	100
<i>Staphylococcus lugdunensis</i>	0	2	100	237	4	98.3	<i>Staphylococcus lugdunensis</i>	0	5	100	237	1	99.6
<i>Streptococcus agalactiae</i>	0	4	100	236	3	98.7	<i>Streptococcus agalactiae</i>	0	7	100	236	0	100
<i>Streptococcus</i> spp	0	6	100	232	5	97.9	<i>Streptococcus</i> spp	0	10	100	232	1	99.6
<i>Proteus</i> spp	0	1	100	240	2	99.1	<i>Proteus</i> spp	0	3	100	240	0	100
<i>mecA/C</i>	0	3	100	240	0	100	<i>mecA/C</i>	0	3	100	240	0	100
<i>Staphylococcus aureus</i>	2	16	89	218	7	96.8	<i>Staphylococcus aureus</i>	2	21	91.3	218	2	99.1
<i>P. granulosum/avidum</i>	1	2	67	240	0	100	<i>P. granulosum/avidum</i>	0	2	100	241	0	100
<i>Enterococcus faecalis</i>	2	3	60	234	4	98.3	<i>Enterococcus faecalis</i>	2	6	75	234	1	99.6
<i>Streptococcus pyogenes</i>	1	0	0	241	1	99.6	<i>Streptococcus pyogenes</i>	0	1	100	242	0	100
<i>Anaerococcus</i> spp/ <i>Peptoniphilus</i> spp	0	0	NA	243	0	100	<i>Anaerococcus</i> spp/ <i>Peptoniphilus</i> spp	0	0	NA	243	0	100
<i>Bacteroides fragilis</i>	0	0	NA	242	1	99.6	<i>Bacteroides fragilis</i>	0	0	NA	242	1	99.6
<i>Candida albicans</i>	0	0	NA	243	0	100	<i>Candida albicans</i>	0	0	NA	243	0	100
<i>Candida</i> spp*	0	0	NA	231	0	100	<i>Candida</i> spp*	0	0	NA	231	0	100
<i>Citrobacter</i> spp*	0	0	NA	229	2	99.1	<i>Citrobacter</i> spp*	0	1	100	229	1	99.6
<i>Clostridium perfringens</i>	0	0	NA	242	1	99.6	<i>Clostridium perfringens</i>	0	0	NA	242	1	99.6
<i>Enterobacter</i> spp	0	0	NA	243	0	100	<i>Enterobacter</i> spp	0	0	NA	243	0	100
<i>Enterococcus faecium</i>	0	0	NA	243	0	100	<i>Enterococcus faecium</i>	0	0	NA	243	0	100
<i>Finegoldia magna</i>	0	0	NA	242	1	99.5	<i>Finegoldia magna</i>	0	0	NA	242	1	99.5
<i>Haemophilus influenzae</i> *	0	0	NA	231	0	100	<i>Haemophilus influenzae</i> *	0	0	NA	231	0	100
<i>Klebsiella pneumoniae</i>	0	0	NA	243	0	100	<i>Klebsiella pneumoniae</i>	0	0	NA	243	0	100
<i>Morganella morgannii</i> *	0	0	NA	231	0	100	<i>Morganella morgannii</i> *	0	0	NA	231	0	100
<i>Neisseria gonorrhoeae</i>	0	0	NA	243	0	100	<i>Neisseria gonorrhoeae</i>	0	0	NA	243	0	100
<i>P. micra/P. anaerobius</i>	0	0	NA	242	1	99.6	<i>P. micra/P. anaerobius</i>	0	0	NA	242	1	99.6
<i>Salmonella</i> spp	0	0	NA	243	0	100	<i>Salmonella</i> spp	0	0	NA	243	0	100
<i>Serratia marcescens</i> *	0	0	NA	230	1	99.6	<i>Serratia marcescens</i> *	0	1	100	230	0	100
<i>Streptococcus pneumoniae</i>	0	0	NA	243	0	100	<i>Streptococcus pneumoniae</i>	0	0	NA	243	0	100

*targets tested with 231 samples

FN : False Negative ; TP: True Positive; TN : True Negative; FP : False Positive

RESULTS

Microorganisms identified by FilmArray Bone and Joint Infection Panel



- 77 positive detections by BJI panel were compared to culture results:
- 43 were concordant
- 34 additional positive detections by the panel were investigated :
 - 24 were confirmed by a comparator assay (PCR followed by sequencing)
 - 10 are under investigation

Investigation of the 6 false negative results is described in the following table :

False negative	Results of investigation
1 <i>P. granulosum/avidum</i>	<i>Propionibacterium</i> obtained in culture was concluded to be a contaminant by the site, therefore this was a true negative
1 <i>S. pyogenes</i>	This sample was positive on FA BJI Panel for <i>Streptococcus</i> spp and was identified as <i>S. dysgalactiae</i> by comparator assay, this was a true negative
1 <i>S. aureus</i>	FA BJI Panel was positive for <i>S. aureus</i> on a second synovial fluid from the same patient, therefore the patient's infection could have been detected
1 <i>S. aureus</i> 2 <i>E. faecalis</i>	Corresponding samples and strains under investigation

CONCLUSION

- These preliminary results showed overall good correlation between FilmArray BJI Panel and culture.
- Additional detections were confirmed in the majority of cases by a comparator PCR followed by sequencing, suggesting that a multiplexed molecular system such as the BJI Panel may be a more sensitive method than culture to detect pathogens in synovial fluid samples.
- These data confirm the feasibility of a multi-target approach for detection of pathogens and resistance markers in Bone and Joint Infections.

The data presented are a preliminary analysis of a development version of FilmArray BJI Panel and are subject to change upon re-analysis with future versions of the software. At the moment, the FilmArray BJI Panel has not been evaluated by the FDA or other regulatory agencies for In vitro diagnostic use.