# Prospective Pilot Evaluation of the BioFire® FilmArray® Bone and Joint Infection (BJI) Panel on Synovial Fluids at a Large County Hospital

Costales C[1], Van T[2], Pons B[3], Martin T[3], Magro S[3], Jay C[3], Bridon I[3], Bourzac K[4], Kensinger B[4] and Butler-Wu SM[5]

[1] Department of Pathology and Laboratory Medicine, Los Angeles County + USC Medical Center, Los Angeles, CA, USA; [2] Department of Pathology, Children's Hospital Los Angeles, Los Angeles, CA, USA ; [3] bioMérieux, Centre Christophe Mérieux, [4] BioFire Diagnostics, LLC, Salt Lake City, UT, USA ; Grenoble, France; [5]Department of Pathology and Laboratory Medicine, Keck School of Medicine of USC, Los Angeles, CA, USA

## ABSTRACT

**Background:** Septic arthritis (SA) is a serious infection associated with significant orthopedic morbidity that requires rapid diagnosis and early initiation of therapy to preserve joint function.[1,2] Accurate diagnosis of SA is challenging because the signs, symptoms and common laboratory findings overlap with other common joint pathologies such as rheumatoid arthritis (RA) and gout.[2,3] The sensitivity of synovial fluid culture for SA is between 60-72%[4]. Thus, there is a need for a rapid molecular test that could accurately rule out joint infection and thus reduce the use of unnecessary antibiotics in patients with non-infectious joint pathologies.

**Methods:** The FilmArray BJI Panel is a research use only (RUO) multiplex PCR panel capable of identifying 32 bacteria, fungi, and antimicrobial resistance markers in approximately 1 hour. We evaluated the performance of a pilot version of the RUO FilmArray BJI Panel on 45 consecutive remnant synovial fluid specimens with bacterial cultures ordered at LAC+USC Medical Center between November 2016 and March 2017. Performance of the Panel was compared to conventional culture and independent PCR analysis was performed for discrepancy investigation.

**Results:** 37.8% of synovial fluid samples were from patients with a previous history of non-infectious joint pathologies. The FilmArray BJI Panel was positive in 4 of the 45 synovial fluids (8.9%); all 45 synovial fluid specimens were negative by culture for an overall specificity of 91.8%. However, three of the four apparent false-positives occurred in patients who were on antibiotics at the time of arthrocentesis and had a history of joint infection. Two of these three specimens had one or more organisms detected by independent molecular assays. One of these patients had subsequent cultures positive for the organisms detected by the BJI Panel. Thus, the Panel had a clinically adjusted specificity of 97.6%. The overall negative predictive value of the Panel was 100%.

**Conclusion:** The FilmArray BJI Panel is a novel method for the rapid detection of microorganisms directly from synovial fluid. The high negative predictive value of the panel (100%) could have utility in facilitating timelier discontinuation of unnecessary empiric therapy.

## OBJECTIVES

- Evaluate the performance and clinical utility of potential targets to be included in the FilmArray BJI Panel on synovial fluid specimens from patients with suspected joint infection.
- Pilot data will be used to optimize a final FilmArray BJI Panel to conduct prospective clinical evaluations.

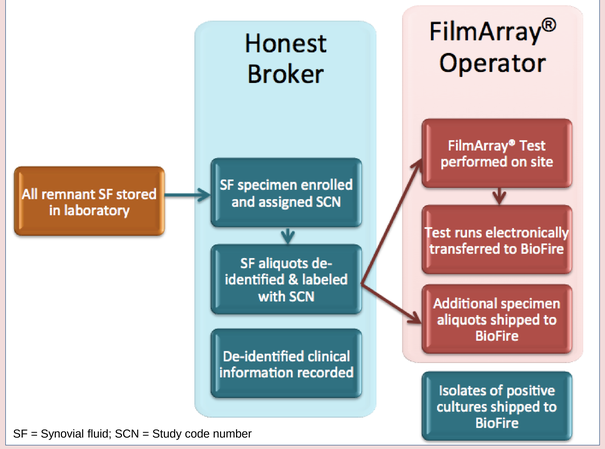
## MATERIALS AND METHODS

- 45 consecutive synovial fluid specimens from LAC + USC Medical Center met inclusion criteria for study enrollment between November 2016 and March 2017.
- LAC+USC Medical Center is a 600-bed tertiary teaching hospital and Level 1 trauma center in central Los Angeles.
- Performance of the FilmArray BJI Panel was compared to conventional culture and discrepancy PCR analysis was performed at bioMérieux.
- Bacterial cultures from synovial fluid were plated directly on aerobic and anaerobic agar plates held for 3 days per the Clinical Microbiology Laboratory standard operating procedure.

## INCLUSION CRITERIA

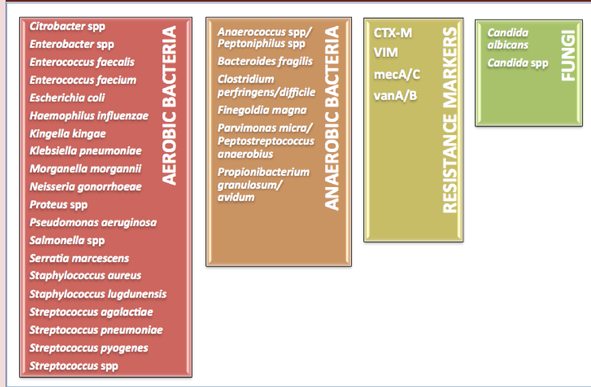
- Synovial fluid specimens left over from standard of care testing for suspected bone or joint infection, as defined by a physician-ordered bacterial or fungal culture on a synovial fluid specimen.
- Specimens consisted of native synovial fluid only (i.e. not diluted in transport media, not collected by swab, etc).
- Specimens held at room temperature for ≤4 hours or refrigerated (4°C) for ≤10 days before enrollment.
- At least 0.5 mL of specimen remained after standard of care testing and available for study use.

## STUDY DESIGN

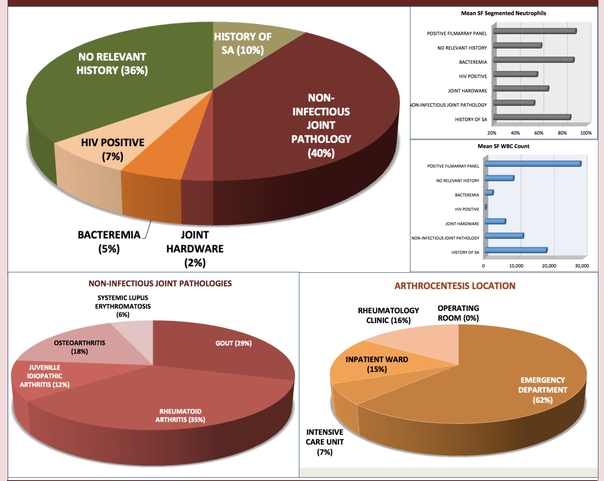



SF = Synovial fluid; SCN = Study code number

## PILOT FILMARRAY BJI PANEL PATHOGENS




## SUBJECT CLINICAL CHARACTERISTICS




## OVERALL BJI PANEL PERFORMANCE

**SEPTIC ARTHRITIS AS DEFINED BY SPECIMEN CULTURE**

| | SF CULTURE POSITIVE | SF CULTURE NEGATIVE | |
|---|---|---|---|
| FILMARRAY PANEL POSITIVE | 0 | 4 | POSITIVE PREDICTIVE VALUE = N/A |
| FILMARRAY PANEL NEGATIVE | 0 | 41 | NEGATIVE PREDICTIVE VALUE = 100% |
| | SENSITIVITY = N/A | SPECIFICITY = 91.5% | |

**SEPTIC ARTHRITIS AS DEFINED CLINICALLY**

| | CULTURE PROVEN SA IN SAME JOINT (DIFFERENT SPECIMEN) | NO CLINICAL EVIDENCE OF ACTIVE SA | |
|---|---|---|---|
| FILMARRAY PANEL POSITIVE | 3 | 1 | POSITIVE PREDICTIVE VALUE =75%* |
| FILMARRAY PANEL NEGATIVE | 0 | 41 | NEGATIVE PREDICTIVE VALUE = 100% |
| | SENSITIVITY = 100%* | SPECIFICITY = 97.6% | |

*Denotes small sample size

## SUBJECTS WITH POSITIVE FILMARRAY BJI PANEL RESULTS

| FILMARRAY POSITIVE RESULTS BY SUBJECT | SF CX RESULTS | SUBJECT CLINICAL CHARACTERISTICS | SUBJECT ON ABX AT COLLECTION | SF WBC COUNT /CUMM | SF SEGMENTED NEUTROPHILS | CLINICALLY ADJUSTED FILMARRAY RESULTS |
|---|---|---|---|---|---|---|
| *Enterococcus faecalis, Finegoldia magna, Staphylococcus lugdunensis* | NEGATIVE | History of gout | NO | 23,750 | 95% | FALSE POSITIVE |
| *Streptococcus* spp | NEGATIVE | History of acute SA status post incision and drainage at OSH; MRI showed synovitis with full thickness cartilage loss in the lateral joint with evidence of osteomyelitis of the distal femur and proximal tibia | YES | 15,505 | 81% | TRUE POSITIVE |
| *Staphylococcus aureus, Streptococcus pyogenes* | NEGATIVE | History of chronic SA; SF culture 18 days prior positive for both pathogens; SF culture collected 13 days later positive for *S. aureus* | YES | N/A | N/A | TRUE POSITIVE |
| *Streptococcus* spp | NEGATIVE | Thigh abscess with extension to knee joint on imaging; subsequent SF gram stain positive for gram positive cocci | YES | 47,100 | 92% | TRUE POSITIVE |

SF= Synovial fluid; CX = Culture; ABX = Antibiotics; WBC = White blood cell; SA = Septic arthritis; OSH = Outside hospital

## CONCLUSIONS

- The FilmArray BJI Panel is a novel method for the rapid detection of microorganisms directly from synovial fluid.
- Testing data collected from this pilot study, along with data from other sites, will be used to optimize the finalized FilmArray BJI reagent pouch for use in a future prospective clinical evaluation.
- The majority of synovial fluids collected for suspected septic arthritis were drawn in the emergency department. The FilmArray BJI Panel may have potential clinical utility in rapidly identifying those patients without joint infection that could be discharged without antibiotics.
- The high negative predictive value of the panel (100%) could also have utility in facilitating more timely discontinuation of unnecessary empiric therapy.
- The subjects with clinical septic arthritis on antibiotics at the time of collection, all had microorganisms detected by the FilmArray BJI Panel. These pathogens were detected by either subsequent culture and/or discrepancy molecular methods.
- Additional studies with larger sample sizes are needed to further characterize the FilmArray BJI Panel sensitivity and positive predictive value.
- The FilmArray BJI Panel is technically simple to perform and with turnaround time averaging approximately one hour.

## ACKNOWLEDGEMENTS

- We would like to acknowledge the staff of the LAC+USC Medical Center Clinical Microbiology Laboratory for their support in identifying and storing remnant synovial fluid specimens.
- Data presented are from assays that have not been cleared or approved for diagnostic use.
- This study was funded by BioFire Diagnostics, LLC/bioMerieux.

## REFERENCES

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