

# MULTICENTRE EVALUATION OF RAPID MOLECULAR SYNDROMIC APPROACH IN JOINT INFECTIONS USING A NEW DEDICATED PANEL : FILMARRAY® BIOFIRE® JOINT INFECTION

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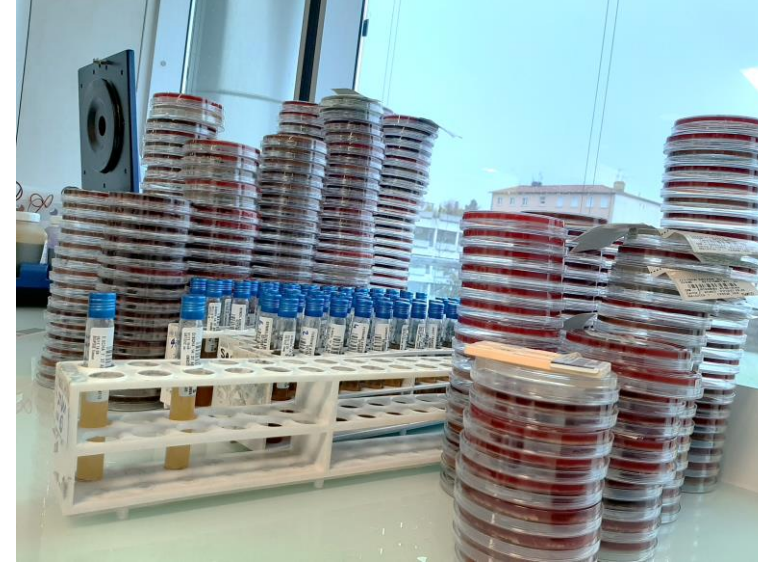
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## CONTEXT : DIAGNOSING JOINT INFECTIONS IS CHALLENGING

- Gold standard : microbiological cultures
- **Diagnosis** sometimes **difficult**:
- **Lack of standardization**



- Potential contaminants
- Slow-growing/ Fastidious / non cultivable pathogens
- False negative Cultures due to prior antibiotic therapy
- Polymicrobial infections (10-15% of chronic infections)



### Clinical specimens

Synovial fluid specimens for patients with acute arthritis

#### Criteria in adults

⇒ Combination of criteria from ICM Philly 2018 and EBJS 2021

- Acute arthritis on native joint or on prosthesis
- Elevated synovial WBC > 1500 cells/μl with ≥ 65 % PMN
- Or sinus tract with evidence of communication to the joint or visualization / prosthesis

#### Criteria in children

⇒ Functional impairment (pain, effusion) with clinical or biological signs of infection

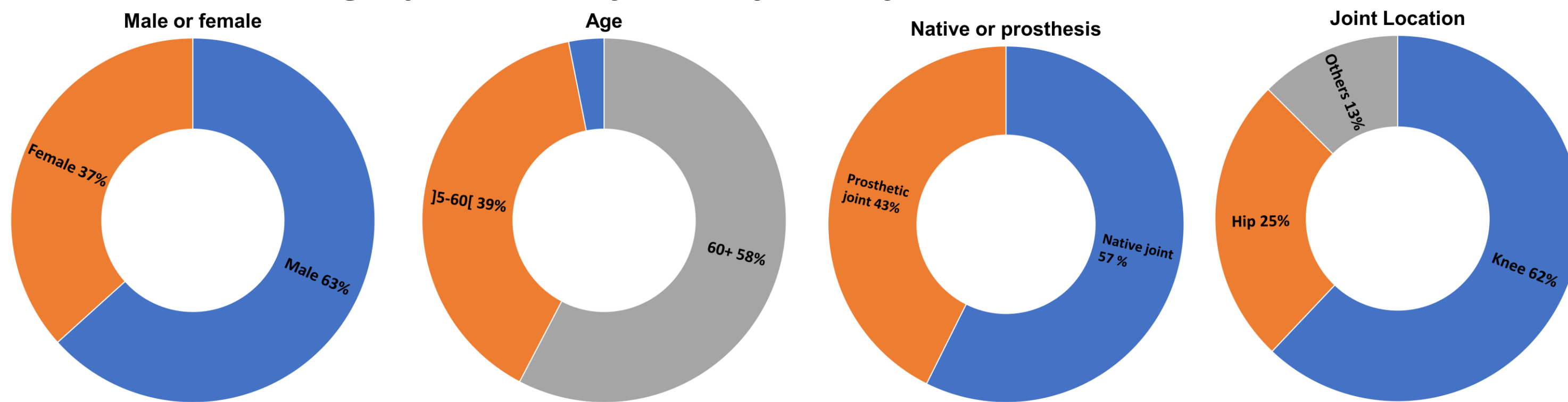
## MATERIAL AND METHOD

### Study design and clinical specimens

- July 2021-May 2022 (FDA-cleared), in collaboration with bioMérieux
- 6 French sites, 5 laboratories from public hospitals and 1 private laboratory
- Leftover synovial fluid specimens from patients with acute arthritis

**319 specimens from unique patients → 312 results**

### Enrollment demographics and synovial fluid information



### Microbiological molecular techniques in case of discrepancies

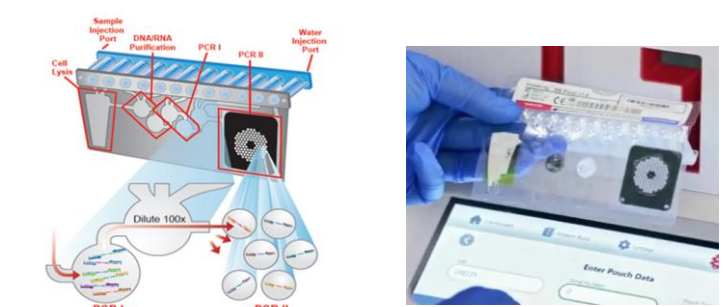
- In-house 16S rRNA gene amplification (480-bp amplification product) followed by Sanger sequencing + 16S rRNA-targeted metagenomics sequencing using Minlon technology (Oxford Nanopore Technologies)
- Specific PCR (if applicable) :
  - *S. aureus* : MRSA/SA ELITE MGB® Assay (Elitech, France)
  - *Staphylococcus spp* : in-house *tuf* gene amplification (380-bp amplification product)
  - *Streptococcus spp* : in-house *tuf* gene amplification (500-bp amplification product)
  - Enterobacteria: in-house *tuf* gene amplification (400-bp amplification product).
  - *K. kingae* : RealCycler® KING-UX / KING-GX kit (Progenie Molecular, Valencia, Spain)
  - *N. gonorrhoeae* : Aptima Combo 2™ assay (Hologic, Marlborough, MA, USA)

### Conventional microbiological techniques

- Routine culture on synovial fluid specimen in each laboratory / Standard of care
- Leftover synovial fluid specimen (≥ 200 μl) → FilmArray BioFire JI testing
- In case of discrepancies ⇒ comparator testing

### FilmArray® BioFire® Joint Infection (FA-JI)

- Syndromic approach
- Disposable cassette “pouch” with easy sample preparation (<5 minutes)
- Automated testing
- Ready to use results



### FilmArray® BioFire® Joint Infection Panel



#### Missing targets !

***Staphylococcus epidermidis* / *S. capitis***  
***Staphylococcus warneri***  
***Cutibacterium acnes***  
***Corynebacterium spp***

### Data analysis

- Bacteriological results considered positive if at least one culture yielded a strict pathogen or two cultures yielded a pathogen from the skin flora (such as CNS or *Cutibacterium acnes*), in accordance with guidelines
- Performance metrics defined :

True Positive TP	FA-JI + / Culture or additional method +
True Negative TN	FA-JI - / Culture -
False Positive FP	FA-JI + / Culture or additional method -
False Negative FN	FA-JI - / Culture +

## RESULTS

319 specimens from unique patients → **312 results** (1 invalid, 6 with insufficient volume for further investigations)

True Positive	True Negative	False Positive	False Negative
155	130	0	27 (9%)

**Overall agreement 285/312 (91%)**

**No False Positive result obtained**



### 25 diagnosis carried out thanks to FA-JI :

- **20/149 (13%)** were confirmed after investigation
  - 11 patients under **previous antibiotic treatment**
    - 7 *S. aureus*, 1 *P. aeruginosa*, 2 *S. agalactiae*, 1 *Streptococcus spp*
  - 8 specimens with **fastidious microorganisms**
    - 5 *K. kingae*, 1 *S. pneumoniae*, 2 *N. gonorrhoeae*
- **6 codetections / 12** included in the study
  - Including 2 specimens with 5 microorganisms !

- 18 (6%): not detectable = Results from the « **missing target** »
  - 10 *S. epidermidis*, 2 *S. capitis*, 2 *C. acnes*, 4 others)
- 9 (3%): False Negative results due to a **lack of sensitivity** of the panel ?
  - Very low inoculum = sampling effect ?
  - 8 *S. aureus*, 4 *P. aeruginosa*, 1 *E. coli*, 1 *N. gonorrhoeae*, 1 *P. micra*

## CONCLUSION

- **High performance** of the FilmArray® JI panel
- **AMR genes** : the results were consistent with the resistance phenotype obtained
- Need to define **indications** of such a panel **with the physicians** (acute vs chronic arthritis ?)
  - Missing targets !

- Influence of the early results on the **antibiotic treatment**:

- Medico-economic studies needed

⇒ To evaluate the added medical value

⇒ To rationalize the place of this new technique +++

