

# Utility of Frozen Sections and Sonication in MSIS-Positive, Culture-Negative Periprosthetic Joint Infection

Lawrence E. Garvin II MD, Akeem Williams BS MS, Matthew J. Hadad MD, Nicholas Drain MD, Lauren K. Gross BS, Kyle S. Yoon BS, Alexandra S. Gabrielli MD, Kenneth L. Urish MD PhD, Malcolm E. Dombrowski MD, Michael J. O'Malley MD, Brian A. Klatt MD, Alan E. Wilson. Jr. MD, Johannes F. Plate MD PhD

Department of Orthopaedic Surgery, University of Pittsburgh, Pittsburgh, PA, USA

## Introduction

- Culture-negative periprosthetic joint infection (CN-PJI) remains a persistent diagnostic challenge, with reported rates ranging from 5–45% [1-3].
- Adjunctive diagnostic modalities such as histology and implant sonication may improve diagnostic yield and confidence.

### Aims:

- 1) Evaluate the diagnostic performance and agreement of histology and sonication in MSIS-defined PJI
- 2) Compare clinical characteristics and outcomes between culture-positive (CP-PJI) and culture-negative cases.

## Methods

- A retrospective cohort study was performed on 316 MSIS-positive PJI cases, including 131 CN-PJI and 185 CP-PJI patients.
- Baseline demographics, inflammatory markers, and outcomes were compared.
- Diagnostic performance of histology (>5 PMNs/HPF) and sonication was assessed using sensitivity, specificity, predictive values, and estimated area under the curve (AUC).
- Agreement between modalities was evaluated using Cohen's  $\kappa$ .
- Multivariable logistic regression was performed to assess predictors of subsequent revision.

## Results

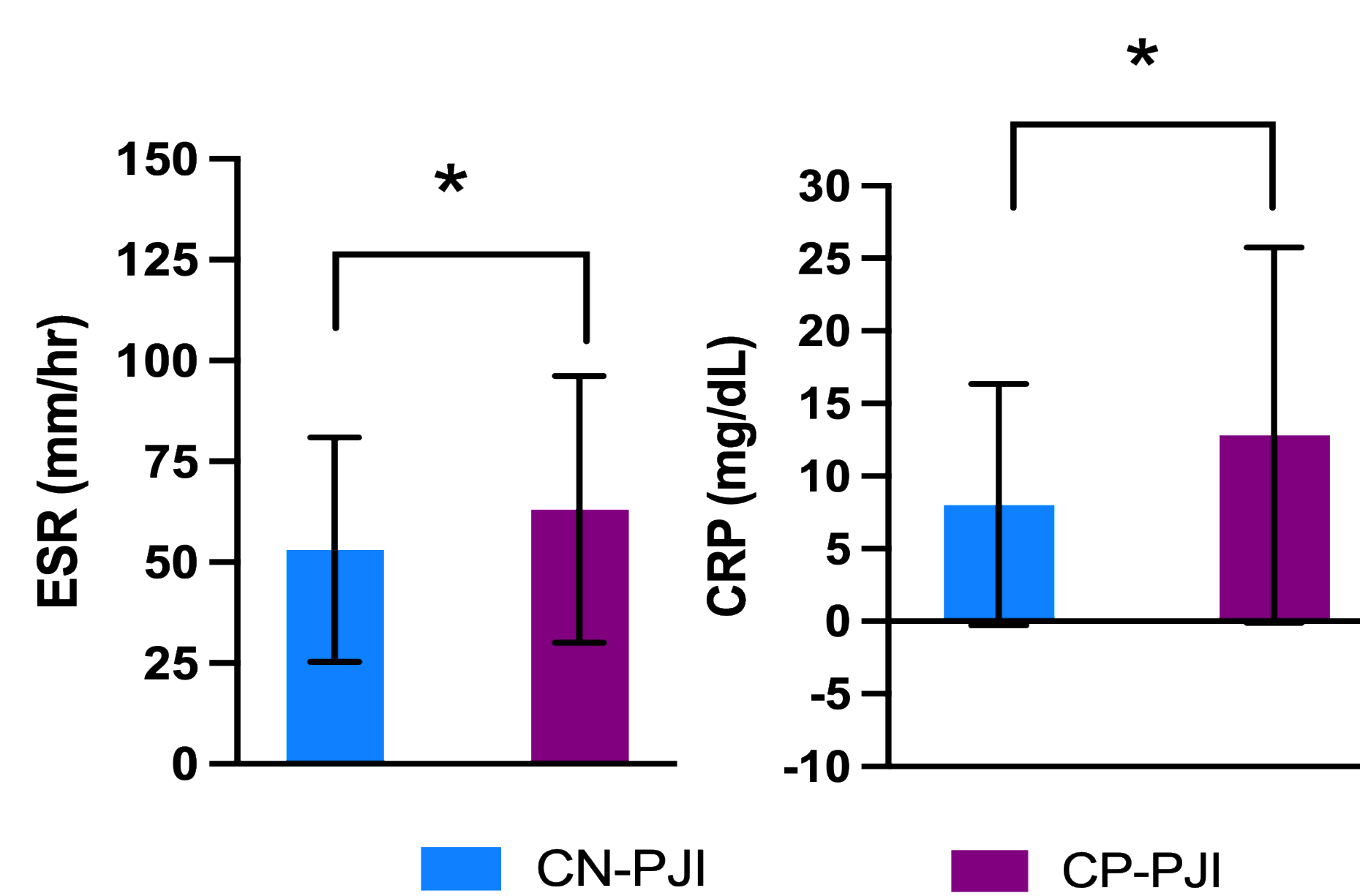
- The overall rate of CN-PJI was 41.5%. CP-PJI demonstrated higher inflammatory markers (**Figure 1**), while demographics, rates of subsequent revision (38.9% vs 41.2%,  $p=0.68$ ), and revision for infection (24.5% vs 26.2%,  $p=0.73$ ) were comparable.

### References

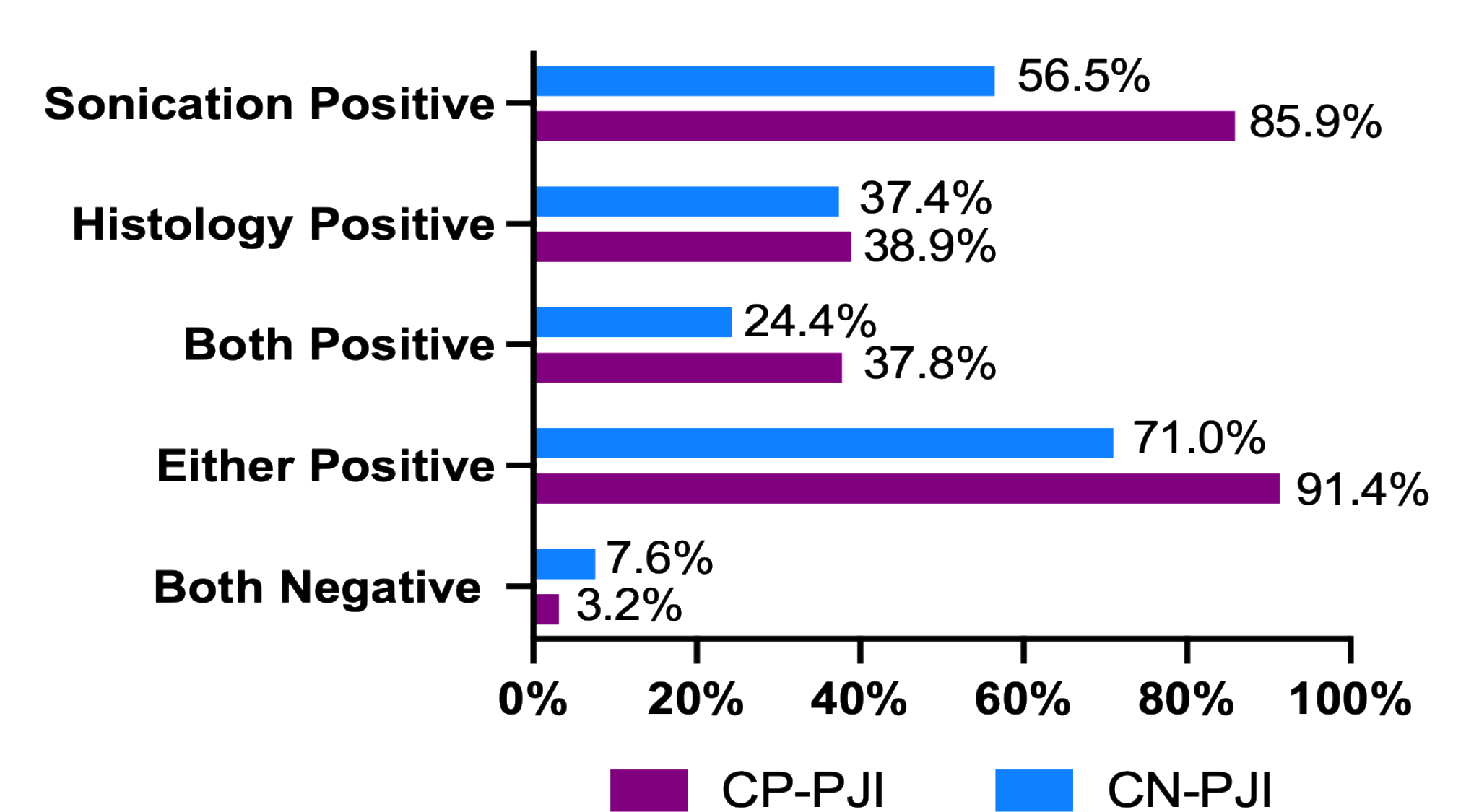
[1] Kalbian et al., Int Orthop, 2020 [2] Reisener et al., Biomed Res Int, 2018 [3] Tai et al., Clin Microbiol Infect, 2022

## Results cont.

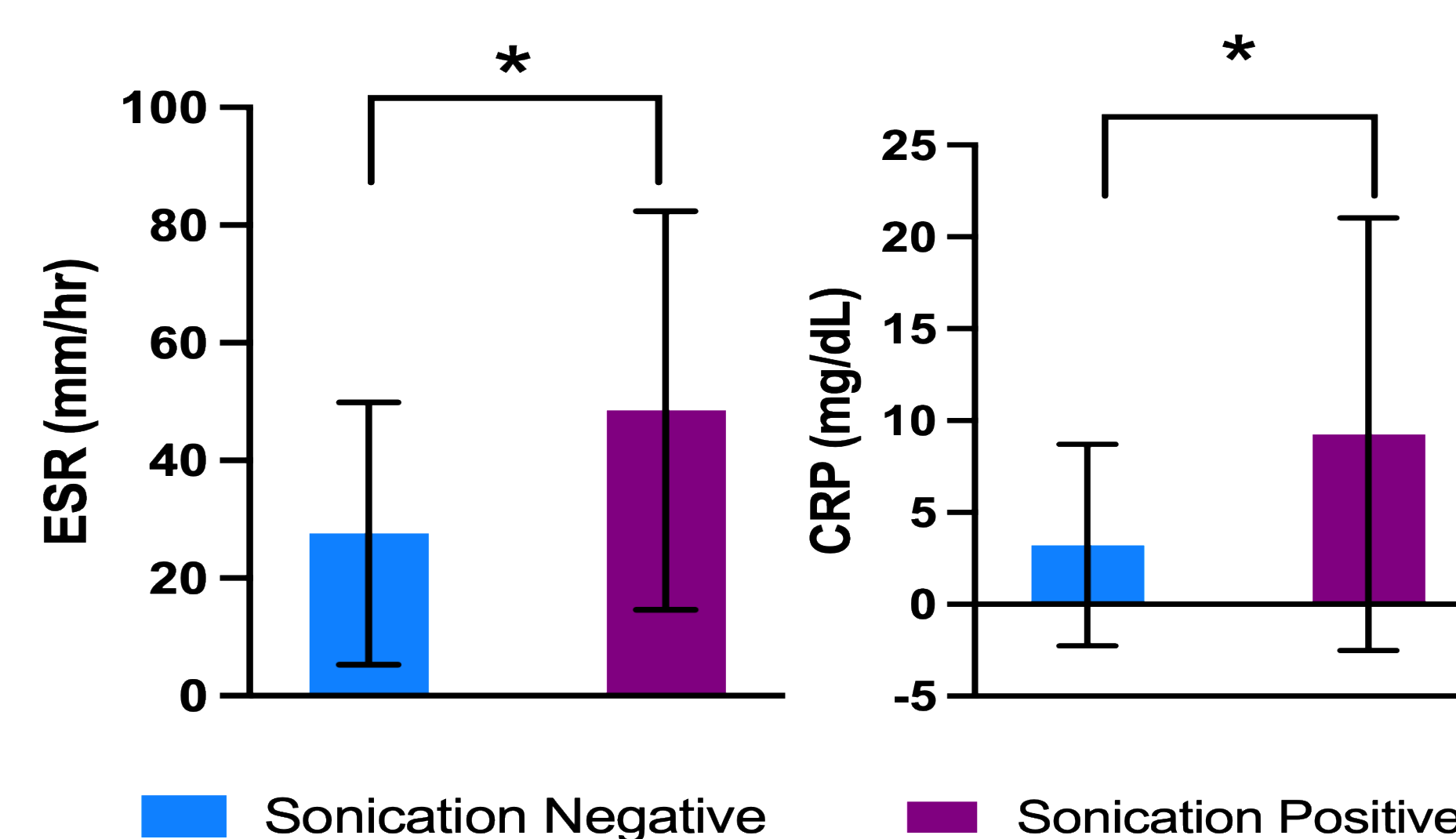
- Sonication positivity was higher in CP-PJI, whereas histology positivity was similar between groups (**Figure 2**). Within CN-PJI, sonication-positive cases demonstrated significantly higher ESR and CRP than sonication-negative cases (**Figure 3**).
- Using culture status as the reference classification, sonication demonstrated the highest overall diagnostic performance (sensitivity 85.9%, specificity 43.5%, AUC 0.65). Histology showed comparable sensitivity (85.7%) but lower specificity (24.6%, AUC 0.55).
- Combining modalities improved diagnostic performance: an "either positive" strategy maximized sensitivity (91.4%, LR+ 0.30), whereas a "both positive" strategy improved specificity (75.2%) with limited rule-in value (LR+ 1.52).
- Agreement between histology and sonication was poor ( $\kappa = 0.04$ ).
- On multivariable analysis, neither histology (OR 1.56, 95% CI 0.60-4.06,  $p=0.359$ ) nor sonication (OR 1.69, 95% CI 0.77-3.71,  $p=0.192$ ) independently predicted subsequent revision.



**Figure 1.** Pre-operative inflammatory markers based on culture status



**Figure 2.** Sonication and Histology results based on culture status



**Figure 3.** Pre-operative inflammatory markers based on sonication results in culture negative PJI patients

## Conclusions

- Sonication demonstrates superior overall diagnostic performance compared to histology and provides complementary diagnostic information, particularly in culture-negative cases. Combining modalities improves sensitivity, supporting an "either positive" strategy for screening. However, overall diagnostic discrimination remains modest, and neither modality predicts clinical outcomes.
- **Clinical Relevance:** These findings support the use of sonication as a valuable adjunct in PJI evaluation while highlighting the need for improved diagnostic and prognostic tools.
- **Limitations:** The sensitivity and specificity analysis uses culture positivity as the reference positive classification. However, culture is an imperfect reference for PJI, as patients may still meet MSIS criteria despite having negative cultures. As a result, these estimates reflect diagnostic performance to culture status rather than presence of PJI.