

## **Next Generation Sequencing for the Diagnosis of Periprosthetic Knee Infection: A Multicenter Investigation**

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**Introduction:** Identifying the infecting organism in periprosthetic joint infection (PJI) continues to be a challenge, with one-third of PJIs reported to have negative cultures. Recent reports demonstrate that Next-Generation Sequencing (NGS) facilitates pathogen identification in culture-negative PJI (CN-PJI); however, this signal has not been externally corroborated. This multi-institutional study was initiated to examine the ability of NGS to identify the causative organism(s) in patients with PJI of the knee.

**Methods:** In this prospective multicenter study involving 13 academic institutions, samples were collected from 102 revision total knee arthroplasties (TKA). Synovial fluid, deep tissue and swabs were obtained at the time of surgery and shipped to the laboratory for NGS. Deep tissue specimens were also sent to the institutional lab for culture. Sensitivity and specificity were calculated, using the Musculoskeletal Infection Society (MSIS) definition of PJI as standard.

**Results:** In 36 revisions, the cases were considered to be infected; 26 of these were culture-positive (26/36; 72.7%), while NGS was positive in 21 (30/36; 83.3%). Among the positive cultures, complete concordance between NGS and culture was noticed in 19 cases (19/21; 90.4%). Two cases were discordant between NGS and culture. Among the 10 cases of culture-negative PJI, NGS identified an organism in 9 cases (90%). Five patients with negative NGS results had positive cultures, of which two were fungal species. Sixty-six revisions were considered aseptic; NGS identified microbes in 25 of 66 “aseptic” revisions (37.9%) and culture isolated an organism in 4 of 66 cases (6.1%). The remaining cases (41/66; 62.1%) were both NGS and culture-negative.

**Conclusions:** NGS was able to detect a pathogen in the majority (>90%) of culture-negative cases and demonstrated a high rate of concordance with culture in culture-positive cases. Our collaborative findings suggest that NGS is a useful adjunct for identifying the causative organism in PJI, particularly in the setting of CN-PJI.