

Authors: Matthew Abdel, Brian A. Klatt, Shaoqi Tian, C.G. Salib

QUESTION 6: Is there a role for sonication of implants retrieved during explantation?

RECOMMENDATION: Several studies have demonstrated that sonication of explanted orthopaedic prostheses is a viable method for detecting pathogens, particularly in the setting of culture-negative infections.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 88%, Disagree: 8%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

Periprosthetic joint infection (PJI) is an uncommon, but devastating, complication following total joint arthroplasty with serious economic implications [1–3]. Since the management of aseptic implant failure differs from that of PJI, accurate diagnosis is critical [2]. One of the greatest challenges in the treatment of PJI remains the identification of the infective organism. Routine cultures are commonly performed for the microbiological diagnosis of PJI, however, these cultures may be falsely negative, which may complicate management [4]. Prior studies have demonstrated synovial fluid culture sensitivities ranging from 43 to 75% and periprosthetic tissue culture sensitivities ranging from 61 to 73% [5]. Culture sensitivity is dependent upon various variables such as prior use of antibiotics, sampling error, inadequate transport and an insufficient number of viable bacteria retrieved [6].

Investigations have shown that PJI is typically caused by microorganisms forming biofilms on implant surfaces [7,8]. Biofilms are complex bacterial communities capable of self-producing a glycocalyx matrix that protects the cells from environmental and antimicrobial threats [7]. Biofilms can be polymicrobial or possess the ability to recruit other species to allow for permanent attachment to the host tissue and the endoprosthetic surface, thereby increasing antibiotic resistance and metabolic cooperation between all involved bacterial species [8]. Accurate microbiological diagnosis, therefore, depends on the effective disruption of biofilms from implant surface using low-intensity sonication for more sensitive PJI diagnosis than the current conventional methods using a periprosthetic tissue or synovial fluid cultures [9–13]. Sonication before the culture of explanted prostheses has also been shown to enhance bacterial growth in culture by dislodging the sessile organisms [14,15].

Review of available literature shows that sonication fluid cultures (SFC) consistently demonstrates increased sensitivity (78.5% to 97%) in the identification of organism without sacrificing the specificity (81% to 98.8%). [9,10,14,16–19] In a study of 331 patients, Trampuz et al. showed the sensitivity of SFC (78.5%) was significantly superior to tissue culture (60.8%) ($p < 0.001$) [10]. They had also shown that use of SFC (75%) was more sensitive than tissue culture (45%) when the antimicrobial agent was discontinued within 14 days before surgery [10]. In 2017 Rothenberg et al. used MusculoSkeletal Infection Society (MSIS) criteria and found that SFC was more sensitive than synovial fluid or tissue culture (97 vs. 57%) [17]. Janz et al. have also shown that sensitivity and specificity can be further improved to 100% by separating components into multiple sonication fluid cultures [20].

In contrast to the above results, some studies have shown a lower sensitivity with using SFC suggesting the importance of the technique used [21]. It is also suggested that in early PJI cases sonication is not superior to conventional techniques [22]. As with all microbiological diagnostic tests, the sonication procedure could be poten-

tially contaminated during the process and could result in false-positive results [20,23]. Therefore it is essential to define what constitutes positive SFC. Various studies recommended five Colony Forming Units (CFUs) as a cutoff to limit false-positive results [10,17,24].

While positive histology, periprosthetic tissue and SFC are highly predictive of implant failures in patients with PJI, more than 10% of patients with suspected aseptic loosening are misdiagnosed PJI [25]. Unrecognized or occult infection has been implicated in contributing to “aseptic” loosening of joint prostheses [26]. Studies by Holinka et al. and Janz et al. have shown that all endoprosthetic components are colonized in cases of PJI for revision arthroplasties [14,27]. Investigations to optimize pathogen identification are still ongoing. Studies have indicated that polymerase chain reaction (PCR) of sonication fluid is a promising test for microbiological diagnosis of PJI especially in patients who were on antibiotics [22,28–31]. A limitation of PCR is that identification of bacterial DNA does not necessarily confirm the presence of live bacteria [32]. However, the advantage of PCR is its short processing time (<5 hours) and fully automated procedure [33].

Currently, the microbiological diagnosis of PJI remains a challenge because a gold standard protocol has not yet been established. Cultures are commonly performed for the microbiological diagnosis of PJI, but their sensitivity is influenced by various factors as mentioned earlier. Given the overwhelming literature supporting the increased sensitivity of sonicate fluid to identify pathogens relative to conventional methods, and the feasibility of this technique, we conclude that there is a beneficial role regarding the use of sonication for explanted prostheses in the setting of suspected PJI.

REFERENCES

- [1] Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. *J Arthroplasty*. 2012;27:61–65.e1. doi:10.1016/j.arth.2012.02.022.
- [2] Tande AJ, Patel R. Prosthetic Joint Infection. *Clin Microbiol Rev*. 2014;27:302–345. doi:10.1128/CMR.00111-13.
- [3] Ryu SY, Greenwood-Quaintance KE, Hanssen AD, Mandrekar JN, Patel R. Low sensitivity of periprosthetic tissue PCR for prosthetic knee infection diagnosis. *Diagn Microbiol Infect Dis*. 2014;79:448–453. doi:10.1016/j.diagmicrobio.2014.03.021.
- [4] Berbari EF, Marculescu C, Sia I, Lahr BD, Hanssen AD, Steckelberg JM, et al. Culture-negative prosthetic joint infection. *Clin Infect Dis*. 2007;45:1113–1119. doi:10.1086/522184.
- [5] Gallo J, Kolar M, Dendis M, Loveckova Y, Sauer P, Zapletalova J, et al. Culture and PCR analysis of joint fluid in the diagnosis of prosthetic joint infection. *New Microbiol*. 2008;3:1:97–104.
- [6] De Vecchi E, Bortolin M, Signori V, Romanò CL, Drago L. Treatment with dithiothreitol improves bacterial recovery from tissue samples in osteoarticular and joint infections. *J Arthroplasty*. 2016;31:2867–2870. doi:10.1016/j.arth.2016.05.008.
- [7] Singh G, Hameister R, Feuerstein B, Awiszus F, Meyer H, Lohmann CH. Low-frequency sonication may alter surface topography of endoprosthetic components and damage articular cartilage without eradicating biofilms completely. *J Biomed Mater Res Part B Appl Biomater*. 2014;102:1835–1846. doi:10.1002/jbm.b.33163.

- [8] Janz V, Wassilew GI, Kribus M, Trampuz A, Perka C. Improved identification of polymicrobial infection in total knee arthroplasty through sonicate fluid cultures. *Arch Orthop Trauma Surg.* 2015;135:1453–1457. doi:10.1007/s00402-015-2317-4.
- [9] Tunney MM, Patrick S, Gorman SP, Nixon JR, Anderson N, Davis RI, et al. Improved detection of infection in hip replacements. A currently underestimated problem. *J Bone Joint Surg Br.* 1998;80:568–572.
- [10] Trampuz A, Piper KE, Jacobson MJ, Hanssen AD, Unni KK, Osmon DR, et al. Sonication of removed hip and knee prostheses for diagnosis of infection. *New Eng J Med.* 2007;357:654–663. doi:10.1056/NEJMoa061588.
- [11] Hischebeth GTR, Randau TM, Molitor E, Wimmer MD, Hoerauf A, Bekeredjian-Ding I, et al. Comparison of bacterial growth in sonication fluid cultures with periprosthetic membranes and with cultures of biopsies for diagnosing periprosthetic joint infection. *Diagn Microbiol Infect Dis.* 2016;84:112–115. doi:10.1016/j.diagmicrobio.2015.09.007.
- [12] Shen H, Tang J, Wang Q, Jiang Y, Zhang X. Sonication of explanted prosthesis combined with incubation in BD bactec bottles for pathogen-based diagnosis of prosthetic joint infection. *J Clin Microbiol.* 2015;53:777–781. doi:10.1128/JCM.02863-14.
- [13] Nguyen LL, Nelson CL, Saccente M, Smeltzer MS, Wassell DL, McLaren SG. Detecting bacterial colonization of implanted orthopaedic devices by ultrasonication. *Clin Orthop Relat Res.* 2002;29:37.
- [14] Holinka J, Bauer L, Hirschl AM, Graninger W, Windhager R, Prestler E. Sonication cultures of explanted components as an add-on test to routinely conducted microbiological diagnostics improve pathogen detection. *J Orthop Res.* 2011;29:617–622. doi:10.1002/jor.21286.
- [15] Scorzoloni L, Lichtner M, Iannetta M, Mengoni F, Russo G, Panni AS, et al. Sonication technique improves microbiological diagnosis in patients treated with antibiotics before surgery for prosthetic joint infections. *New Microbiol.* 2014;37:321–328.
- [16] Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, et al. Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. *J Clin Microbiol.* 2009;47:1878–1884. doi:10.1128/JCM.01686-08.
- [17] Rothenberg AC, Wilson AE, Hayes JP, O'Malley MJ, Klatt BA. Sonication of arthroplasty implants improves accuracy of periprosthetic joint infection cultures. *Clin Orthop Relat Res.* 2017;475:1827–1836. doi:10.1007/s11999-017-5315-8.
- [18] Puig-Verdié L, Alentorn-Geli E, González-Cuevas A, Sorlí L, Salvadó M, Alier A, et al. Implant sonication increases the diagnostic accuracy of infection in patients with delayed, but not early, orthopaedic implant failure. *Bone Joint J.* 2013;95-B:244–249. doi:10.1302/0301-620X.95B2.30486.
- [19] Janz V, Wassilew GI, Hasart O, Matziolis G, Tohtz S, Perka C. Evaluation of sonicate fluid cultures in comparison to histological analysis of the periprosthetic membrane for the detection of periprosthetic joint infection. *Int Orthop.* 2013;37:931–936. doi:10.1007/s00264-013-1853-1.
- [20] Janz V, Wassilew GI, Hasart O, Tohtz S, Perka C. Improvement in the detection rate of PJI in total hip arthroplasty through multiple sonicate fluid cultures. *J Orthop Res.* 2013;31:2021–2024. doi:10.1002/jor.22451.
- [21] Van Diek FM, Albers CGM, Van Hooff ML, Meis JF, Goosen JHM. Low sensitivity of implant sonication when screening for infection in revision surgery. *Acta Orthop.* 2017;88:294–299. doi:10.1080/17453674.2017.1300021.
- [22] Prieto-Borja L, Auñón Á, Blanco A, Fernández-Roblas R, Gadea I, García-Cañete J, et al. Evaluation of the use of sonication of retrieved implants for the diagnosis of prosthetic joint infection in a routine setting. *Eur J Clin Microbiol Infect Dis.* 2018;37:715–722. doi:10.1007/s10096-017-3164-8.
- [23] Trampuz A, Piper KE, Hanssen AD, Osmon DR, Cockerill FR, Steckelberg JM, et al. Sonication of explanted prosthetic components in bags for diagnosis of prosthetic joint infection is associated with risk of contamination. *J Clin Microbiol.* 2006;44:628–631. doi:10.1128/JCM.44.2.628-631.2006.
- [24] Zhai Z, Li H, Qin A, Liu G, Liu X, Wu C, et al. Meta-analysis of sonication fluid samples from prosthetic components for diagnosis of infection after total joint arthroplasty. *J Clin Microbiol.* 2014;52:1730–1736. doi:10.1128/JCM.03138-13.
- [25] Fernandez-Sampedro M, Salas-Venero C, Fariñas-Álvarez C, Sumillera M, Pérez-Carro L, Fakkas-Fernandez M, et al. 26 Postoperative diagnosis and outcome in patients with revision arthroplasty for aseptic loosening. *BMC Infect Dis.* 2015;15. doi:10.1186/s12879-015-0976-y.
- [26] Kempthorne JT, Ailabouni R, Raniga S, Hammer D, Hooper G. Occult infection in aseptic joint loosening and the diagnostic role of implant sonication. *Biomed Res Int.* 2015;2015:946215. doi:10.1155/2015/946215.
- [27] Janz V, Wassilew GI, Perka CF, Bartek B. Increased rate of bacterial colonization on PE-components in total joint arthroplasty: an evaluation through sonication. *Technol Health Care.* 2017;25:137–142. doi:10.3233/THC-161257.
- [28] Portillo ME, Salvadó M, Sorlí L, Alier A, Martínez S, Trampuz A, et al. Multiplex PCR of sonication fluid accurately differentiates between prosthetic joint infection and aseptic failure. *J Infect.* 2012;65:541–548. doi:10.1016/j.jinf.2012.08.018.
- [29] Gomez E, Cazanave C, Cunningham SA, Greenwood-Quaintance KE, Steckelberg JM, Uhl JR, et al. Prosthetic joint infection diagnosis using broad-range PCR of biofilms dislodged from knee and hip arthroplasty surfaces using sonication. *J Clin Microbiol.* 2012;50:3501–3508. doi:10.1128/JCM.00834-12.
- [30] Achermann Y, Vogt M, Leunig M, Wüst J, Trampuz A. Improved diagnosis of periprosthetic joint infection by multiplex PCR of sonication fluid from removed implants. *J Clin Microbiol.* 2010;48:1208–1214. doi:10.1128/JCM.00006-10.
- [31] Esteban J, Alonso-Rodríguez N, del-Prado G, Ortiz-Pérez A, Molina-Manso D, Cordero-Ampuero J, et al. PCR-hybridization after sonication improves diagnosis of implant-related infection. *Acta Orthop.* 2012;83:299–304. doi:10.3109/17453674.2012.693019.
- [32] Bereza P, Ekiel A, Auguściak-Duma A, Aptekorz M, Wilk I, Kusz D, et al. Comparison of cultures and 16S rRNA sequencing for identification of bacteria in two-stage revision arthroplasties: preliminary report. *BMC Musculoskelet Dis.* 2016;17:138. doi:10.1186/s12891-016-0991-1.
- [33] Renz N, Feihl S, Cabric S, Trampuz A. Performance of automated multiplex PCR using sonication fluid for diagnosis of periprosthetic joint infection: a prospective cohort. *Infection* 2017;45:877–884. doi:10.1007/s15010-017-1073-5.



2.5. DIAGNOSIS: REIMPLANTATION

Authors: Carlos A. Higuera, AliSina Shahi

QUESTION 1: Are the MusculoSkeletal Infection Society (MSIS) and Interntional Consensus Meeting (ICM) criteria valid for decision-making before reimplantation?

RECOMMENDATION: The validity of the MSIS and ICM criteria for determination of the timing of reimplantation is unclear.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 90%, Disagree: 7%, Abstain: 3% (Super Majority, Strong Consensus)

RATIONALE

George et al. [1] studied 79 patients undergoing reimplantation and found that MSIS criteria had a high specificity (96%) in predicting persistent infection, though the sensitivity was low (26%). They also found that patients who had positive MSIS criteria were at increased risk for reinfection after reimplantation. Kheir et al. [2] also investigated the MSIS criteria in patients who were undergoing two-stage

exchange for periprosthetic joint infection (PJI) and reported a sensitivity of 25% and a specificity of 87% for detecting persistent infection. The authors further investigated the utility of the leucocyte esterase (LE) strip test and found that the LE strip test was positive in 22.2% of culture-positive and 4.4% of culture-negative cases. The LE test was negative in all patients who had not failed at their latest follow-