

SH37. How important is positive frozen section for diagnosis of PJI? Should it still be included in the minor criteria? If so, what weighted score should it be given in the diagnostic criteria?

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Methodology: A comprehensive literature review was performed to identify all studies on positive frozen section and its importance in the diagnosis of shoulder PJI. Searches for the terms “(frozen section OR histology OR histologic) AND shoulder AND (arthroplasty OR replacement) AND infection” performed using the search engines PubMed and Google Scholar which were searched through October 2024. Inclusion criteria for systematic review were all English studies (Level I-IV evidence) that reported on the use of the “frozen section” in making a diagnosis of PJI in shoulder arthroplasty. Eight articles met inclusion and exclusion criteria and were reviewed. Four of these articles presented data that supported the response to this query. Additional sources were obtained from the reference lists of these articles as well as from independent query.

Answer: Based on a review of the literature, including both individual studies as well as systematic reviews, a positive intraoperative frozen section (IOFS) may help diagnose shoulder PJI, and should be included in the Minor Criteria. However, a positive IOFS may not appear to be as important as previously thought and consideration should be given to assigning a lower weight. A positive IOFS is most helpful to identify acute inflammation but the benefit of routine IOFS to diagnose shoulder PJI during revision shoulder arthroplasty is less clear for several reasons:

1. Some studies have noted the poor sensitivity of IOFS, especially for low virulence organisms, such as *Cutibacterium acnes* and *Staph epidermidis* [Topolski]. Others have suggested a role for IOFS in equivocal cases but that it may be unnecessary when the diagnosis of shoulder PJI has been established preoperatively [Updegrave]
2. The interpretation of IOFS varies greatly from one institution to the other. Most hospitals, even tertiary care centers, lack access to dedicated musculoskeletal pathologists. Some studies have recommended changing the thresholds for positive frozen section from 5 polymorphonucleocytes (PMNs) to 10 PMNs per high powered field (HPF) [Grosso]. But it is unclear if this strategy is generalizable.
3. IOFS adds cost

Overall, the importance of a positive IOFS appears to be limited relative to other Minor Criteria, because there is only limited and selective evidence supporting its use. Retaining positive IOFS as a high-weight Minor Criterion is questionable if these are not obtained, analyzed and interpreted consistently. Additionally, the value of a positive IOFS is limited by the availability of a dedicated musculoskeletal pathologist. Some revision shoulder arthroplasty surgeons practice at hospitals lacking experienced pathologists. In other instances, the pathologist may be unavailable altogether or available only after a delay that needlessly prolongs the surgery.

Additionally, If IOFS are obtained only selectively then this creates a variable threshold for defining possible or probable (non-definite) shoulder PJI. Centers that routinely employ IOFS, perhaps because of the availability of dedicated musculoskeletal pathologists and timely intraoperative analysis, would maintain a lower effective threshold for shoulder PJI than those that

do not employ IOFS. In turn, this complicates comparative and multicenter study, which remain essential strategies for improving our understanding of the diagnosis and treatment of shoulder PJI.

It follows that a positive IOFS should be assigned a weighted score of 1 or 2, but less than the weighted score of 3 in the Minor Criteria.

Strength of Recommendation: Moderate. Data from a couple of recent high-level studies document the moderate to high specificity of positive IOFS in establishing a diagnosis of shoulder PJI. However, other studies do not support the routine use of IOFS.

Strength of Recommendation: Limited

Rationale:

Multiple studies have reported on the use of IOFS to aid in the diagnosis of shoulder PJI. The best study is the study by Patel et al. that aimed to validate the ICM 2018 criteria. The authors found that a positive IOFS, defined as ≥ 5 PMN in 5 high power fields or greater had a specificity of 100%, a sensitivity of 90%, an accuracy of 95%, as well as a positive predictive value of 92% and a negative predictive value of 50%. Of all the minor criteria, positive frozen section had a highest sensitivity. The addition of 2 positive cultures improved sensitivity and accuracy only marginally, from 90 to 95% and from 95 to 97.5%, respectively. The authors acknowledged the retrospective nature of their study as a limitation. Additionally, the study was performed at a tertiary medical center so that the results may not be generalizable.

The ASES Shoulder PJI Multicenter Research Group analyzed their database and employed receiver operating characteristics curves to evaluate the predictors of definite or non-definite shoulder PJI, according to the ICM 2018 criteria, including a positive IOFS, defined as ≥ 5 PMNs per high-powered field [ASES/Hsu, in preparation]. The authors found that a positive IOFS had a specificity of 78%, a sensitivity of 71%, a positive predictive value of 90% and a negative predictive value of 73% for a definite PJI with ≥ 2 cultures positive for the identical bacterium. Similarly, the authors found that a positive IOFS had a specificity of 50%, a sensitivity of 67%, a positive predictive value of 53% and a negative predictive value of 60% for a definite PJI with ≥ 3 cultures positive for the identical bacterium.

Two studies provided the foundation for the ICM 2018 consensus statement on the role of IOFS in evaluating for shoulder PJI. Topolski et al. also evaluated the value of IOFS and history in diagnosing PJI at the time of revision shoulder arthroplasty [Topolski]. An average of 2.2 biopsy for cultures were obtained along with biopsy for intraoperative frozen shoulder. Only 6 of 73 patients (8.2%) with at least one positive culture had a positive IOFS. The authors question the role for IOFS in diagnosing shoulder PJI.

Grosso et al. evaluated the role of IOFS for identifying shoulder PJI, and specifically infections with *C. acnes* [Grosso]. The authors used traditional thresholds of 5 PMN per HPF in at least 3 HPFs and determined a specificity of 100% for PJI as well as sensitivities of 50% for *C. acnes* and

67% for infection with other organisms. The authors used a receiver operating characteristics (ROC) curve to optimize the threshold of a total of 10 PMNs in the 5 highest density HPFs to increase the sensitivity to 72% for *C. acnes*, while maintaining 100% specificity. The threshold of 10 PMNs per PHF in at least 5 HPFs has been employed previously for hip and knee PJI [Banit].

Mansat opined in a commentary on the study by Grosso et al. that a positive IOFS may guide the surgeon towards bridge antibiotic therapy or away from single stage and towards two-stage revision surgery [Mansat]. Although bridge antibiotics therapy is performed routinely, irrespective of IOFS and good outcomes have been reported for single stage revision surgery a higher Minor Criteria score has been associated with an increased risk of PJI recurrence [Givens].

In contrast, Pottinger et al. found that the odds of a positive culture were not significantly increased by the findings of acute inflammation on histologic analysis of IOFS [Pottinger]. In contrast, the authors found male gender, humeral osteolysis, cloudy fluid at surgery, humeral loosening, and membrane formation were highly associated with the likelihood of obtaining a positive *C. acnes* culture.

References:

1. Banit DM, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. Clin Orthop Relat Res. 2002 Aug;(401):230-8. doi: 10.1097/00003086-200208000-00026. PMID: 12151900.
2. Topolski MS, Chin PY, Sperling JW, Cofield RH. Revision shoulder arthroplasty with positive intraoperative cultures: the value of preoperative studies and intraoperative histology. J Shoulder Elbow Surg. 2006 Jul-Aug;15(4):402-6. doi: 10.1016/j.jse.2005.10.001. PMID: 16831641.
3. Grosso MJ, Frangiamore SJ, Ricchetti ET, Bauer TW, Iannotti JP. Sensitivity of frozen section histology for identifying Propionibacterium acnes infections in revision shoulder arthroplasty. J Bone Joint Surg Am. 2014 Mar 19;96(6):442-7. doi: 10.2106/JBJS.M.00258. PMID: 24647499.
4. Mansat P. Frozen section histology: a new tool to identify Propionibacterium acnes infections in revision shoulder arthroplasty. Commentary on an article by Matthew J. Grosso, BS, et al., "Sensitivity of frozen section histology for identifying Propionibacterium acnes infections in revision shoulder arthroplasty". J Bone Joint Surg Am. 2014 Mar 19;96(6):e49. doi: 10.2106/JBJS.M.01476. PMID: 24647516.
5. Updegrave GF, Armstrong AD, Kim HM. Preoperative and intraoperative infection workup in apparently aseptic revision shoulder arthroplasty. J Shoulder Elbow Surg. 2015 Mar;24(3):491-500. doi: 10.1016/j.jse.2014.10.005. Epub 2014 Dec 2. PMID: 25487903.
6. Patel VV, Ernst SMC, Rangarajan R, Blout CK, Lee BK, Itamura JM. Validation of new shoulder periprosthetic joint infection criteria. J Shoulder Elbow Surg. 2021 Jul;30(7S):S71-S76. doi: 10.1016/j.jse.2021.04.009. Epub 2021 Apr 22. PMID: 33895298.
7. Givens J, Schmidt CM, Patel R, Kucharik M, Grayson W, Chase C, Davis CM, Christmas KN, Simon P, Frankle MA. Factors affecting risk of recurrence with periprosthetic infection in shoulder arthroplasty. J Shoulder Elbow Surg. 2024 Jun;33(6S):S80-S85. doi: 10.1016/j.jse.2023.11.013. Epub 2024 Jan 3. PMID: 38182021.

8. Pottinger P, Butler-Wu S, Neradilek MB, Merritt A, Bertelsen A, Jette JL, Warme WJ, Matsen FA 3rd. Prognostic factors for bacterial cultures positive for *Propionibacterium acnes* and other organisms in a large series of revision shoulder arthroplasties performed for stiffness, pain, or loosening. *J Bone Joint Surg Am*. 2012 Nov 21;94(22):2075-83. doi: 10.2106/JBJS.K.00861. PMID: 23172325.
9. Hsu J, ASES Shoulder PJI Multicenter Research Group, accepted for presentation, AAOS Annual Meeting, 2025.