Question : Does utilizing an antibiotic-impregnated cement spacer provide advantages for managing dead space in post-debridement segmental bone defects?

Section 1 Background:

Addressing segmental bone loss following severe trauma, open fractures, or extensive debridement for sepsis is a significant clinical hurdle. These traumatic injuries typically involve extensive damage to both soft tissue and skeletal structures, requiring multi-stage protocols for successful limb preservation. Effectively managing dead space is paramount in these scenarios to suppress localized infection, block soft tissue collapse into the void, and optimize the biological bed for definitive grafting.

The induced membrane (Masquelet) technique represents a standard two-stage strategy for treating major osseous defects. The initial phase involves aggressive surgical debridement followed by the insertion of a polymethylmethacrylate (PMMA) spacer. This implant functions mechanically by maintaining the defect's length and biologically by triggering a foreign-body response that generates a vascularized, pseudosynovial membrane around the cement.

Utilizing **antibiotic-impregnated cement spacers** during the first stage is common practice, aimed at achieving high local antibiotic elution to clear remaining pathogens while preparing the site for grafting. However, the predictability of clinical outcomes remains debated. Although many cohorts report successful radiological consolidation, significant complication risks—such as persistent deep infection and nonunion—are well-documented. The exact role of antibiotic additives in influencing healing times and reducing postoperative complications continues to be a focus of current research.

Section 2 Data Extraction Table:

S.no	Author, year of publication, Country	Study Design	Sample Size (add individually for each group if multiple groups compared)	Study population (Inclusion and exclusion criteria)	Groups compared	Results
1	Descombris et al., 2026, France	Retrospective single-centre comparative cohort study, **Level of**	Total N = 60; **Group A (Bone Defect < 5 cm)**: n = 41;	**Inclusion Criteria:** Patients treated for femoral or tibial non-union using the induced membrane (Masquelet) technique	**Group A:** defects < 5 cm; **Group B:** defects >= 5 cm	**Follow-up Duration:** Mean follow-up was 28.6 months . **Primary Outcome:** Radiological consolidation achieved in 82.9% of

		Evidence : III	**Group B** (BD >= 5 cm): n = 19	between Jan 2018 - June 2023. **Exclusion Criteria**: Age < 18, non-union without bone loss, follow-up < 12 months, primary arthroplasty/amputation.		defects < 5 cm vs. 68.4% of defects >= 5 cm (p > 0.05) . **Secondary Outcomes:**Mean healing time: 6.31 months (< 5 cm) vs. 8.45 months (>= 5 cm) . -Full weight-bearing recovery: 97.6% (< 5 cm) vs. 84.2% (>= 5 cm) . -Mean time to weight-bearing: 4.11 months (< 5 cm) vs. 3.49 months (>= 5 cm) . - Infection recurrence absent in 84.6% of septic cases (< 5 cm) vs. 70.0% (>= 5 cm) . **Complications & Reoperations:** - Complication rates: 34.1% (< 5 cm) vs. 36.8% (>= 5 cm) . - Reoperation rates: 21.9% (< 5 cm) vs. 36.8% (>= 5 cm) . **Statistical Significance:** Multivariate analysis identified tibial location, defects < 5 cm, and segmental defects as independent predictors of successful healing . -Segmental defects were associated with an 82% reduction in the risk of complications (adjusted OR = 0.18) . **Authors' Conclusion:** * The Masquelet technique is a reliable option for managing non-unions with substantial bone loss . Segmental tibial defects smaller

						than 5 cm are associated with successful healing.
2	Wang et al., 2024, China	Retrospective Cohort	*Total N = 21* *Group A: N/A (Single-arm study)*	**Inclusion Criteria:** (1) Over 18 and under 60 years of age. (2) Range of bone defects in the distal tibia should be at least 6 cm (3) Masquelet technique with double plate fixation was used. (4) Patient underwent at least one year of follow-up examinations **Exclusion Criteria:** Patients with concomitant diseases causing: (1) Multiple fractures. (2) Serious nerve and vascular injuries. (3) Severe systemic osteoporosis. **Defect length:** 8.19 ± 1.41 cm (range, 6-11)	**Not Reported** (This is a single-cohort study evaluating one primary intervention without a control group).	**Primary/Secondary Outcomes:** Full weight-bearing time: 2.41 ± 0.37 months (range 2-3) Bone healing time: 6.29 ± 0.66 months (range 5.5-7.5) **Functional Outcomes (Iowa Ankle Score):**Pre-operative: 39.52 ± 3.03. Post-operative: 90.95 ± 2.94. - 15 Excellent (71.4%), 6 Good (28.6%), 0 Fair, 0 Poor **Statistical Significance:**Statistically significant (P < 0.001) for Iowa Ankle Score improvement. **Complications:**2/21 patients experienced complications. - One patient suffered medial leg wound infection requiring medial plate removal (healed post-debridement). - One patient developed a severe iliac bone defect post-extraction (managed with cement spacer). **Follow-up Duration:** 19.48 ± 2.58 months (range 16-26) **Authors' Final Conclusion:** The Masquelet technique combined with double plate fixation is a safe and effective method for the treatment of large segmental bone defects of the distal tibia.

3	Lu et al., 2023, Taiwan	Systematic Review and Meta-Analysis of Individual Participant Data	***Total N = 90****:* Patient data was extracted from 14 reports.	**Inclusion Criteria:** Original articles composed in English. - Accessible individual patient data available. - Reported more than two cases involving patients with a bony defect and septic or aseptic nonunion of the femur treated with the IMT, or reported more than five cases of any part of the body. - Only cases with affected femurs were included in the final analysis. **Exclusion Criteria: -** Fewer than 2 femoral cases. - Fewer than 5 total cases. - No reported case of femur. - No accessible individual patient data. **-**Etiology was categorized as **Infected nonunion** (41 patients;	The study performed univariate and multivariate analyses to compare specific predictive variables within the cohort: **<u>SUB GROUPS:</u>** **Final Fixation Method:** External fixation vs. Internal fixation (intramedullary nail or plate). **Spacer Type:** With antibiotics vs. Without antibiotics. **Bone Graft Source:** All-autologous graft vs. Non all-autologous graft. **Patient Age:** Age ≥ 65 years vs. Age < 65 years.	**Primary Outcomes:**Post-procedural bone graft infection occurred in 5 out of 90 patients (5.6%). **-**All infections occurred in patients initially treated for an infected nonunion. - Final union was achieved in 77 out of 90 patients (85.6%). **Secondary Outcomes:** **-**Mean union time after the second stage operation was 29.5 weeks (range 16–56 weeks). **Statistical Significance:**Use of external fixation in the second-stage surgery had a significant odds ratio (OR) of 9.267 for post-procedural bone graft infection (p = 0.047). - Post-procedural bone graft infection significantly predicted final non-union status (OR = 51.05, p = 0.003). - Age > 65 years significantly predicted final non-union status (OR = 9.18, p = 0.042). ***** Union time was significantly shorter when using antibiotics in the spacer (27.69 ± 10.04 weeks vs. 37.00 ± 9.63 weeks, p = 0.005). ***** Union time was significantly shorter using an all-autologous graft (26.00 ± 10.71 weeks vs. 31.66 ± 10.01 weeks, p = 0.042). ***** Union time was significantly shorter utilizing intramedullary nails for final fixation (27.86 ± 9.96 weeks vs. 31.92 ± 11.43 weeks, p = 0.050).

				45.6%) or **Non-infected nonunion** (49 patients; 54.4%). **Mean length of the bone defect was 7.6 cm** (range, 1–25 cm).		**Authors' Final Conclusion:** The Induced Membrane Technique (IMT) is a reliable and reproducible solution for femoral segmental bone defects. External fixation during the second stage is a risk factor for infection. - Post-procedural infection and age ≥ 65 years negatively impact final union. -Using antibiotic spacers, all-autologous grafts, and intramedullary nails can significantly shorten union time.
4	Yoon et al., 2022, Korea	Retrospective analysis	***Total N = 32*** single-arm retrospective cohort study; no primary control group was designated	**Inclusion Criteria:**Patients aged 18 years or older with tibial fractures who visited the level 1 trauma center. - Type IIIB or more severe open fractures according to the Gustilo-Anderson classification. - Surgically treated using acute induced membrane technique and soft-tissue reconstruction due to bone and soft-tissue	Not Reported (This is a single-arm retrospective cohort study; no primary control group was designated).	**Primary/Secondary Outcome:** Bone union and clinical outcomes. **Complications:** Occurred in 10 cases (31.2%). Included superficial infection (3), deep infection (3), partial flap skin necrosis (2), malalignment (1), and joint stiffness (1). **Reoperations:** Additional surgeries performed for complications (e.g., superficial infection treated by debridement, split-thickness skin grafts for necrosis, one below-knee amputation for recurring deep infection). **Functional Outcomes:** Association for the Study and Application of the Method of Ilizarov (ASAMI) functional score was "good" or "excellent" in 24 cases (75%).

				defects after debridement. -Followed up for 1 year or more. **Exclusion Criteria:** Amputation as initial treatment for severe comminuted fracture and damage (8 patients). -Clear brain injury (8 points or lower on the Glasgow Coma Scale on day 21 after injury or upon discharge, 15 patients). - Pathological fracture (2 patients). - Periprosthetic fractures (3 patients).		**Radiological Outcomes:** Bone union achieved in 31/32 cases (96.9%) at an average of 9.4 months (range 4-16 months). ASAMI radiologic score was "good" or "excellent" in 29 cases (90.6%). **Statistical Significance:** Functional results significantly correlated with injury severity score (p=0.018), implant type (p=0.034), complications (p<0.001), and additional surgery (p<0.001). • Radiologic results significantly correlated with soft-tissue defect size (p=0.036), soft-tissue coverage (p=0.020), complications (p=0.050), and additional surgery (p=0.023). **Follow-up Duration:** Average 19.1 months (range 12-41 months). **Authors' Conclusion:** Staged surgery using the acute induced membrane technique and soft-tissue reconstructive surgery is an efficacious treatment for open tibial fractures with bone defects.

5	Patel et al., 2021, India	Retrospective Study	***Total N = 22*** ***Group A-*** *Type II Bone Loss (n=4)* ***Group B-*** *Type III Bone Loss (n=9)* ***Group C -*** *Type IV Bone Loss (n=9)*	**Inclusion Criteria:** ***** Patients with open distal end femur fractures with bone defects who Presented within 3 days of trauma from January 2015 to December 2018 and were treated by the Masquelet's technique . **Fracture type:** Gustilo and Anderson Type III b injury. **Defect size:** 3 to 10 cm, averaging 5 cm. **Exclusion Criteria:**Not Reported.	* **Intervention Group**: Masquelet's technique (two-stage: antibiotic cement spacer followed by induced membrane bone grafting). **Comparison Cohorts**: Internal subgroups based on the amount of cortical bone loss (Type II, Type III, and Type IV).	**Radiological Outcomes:** Average time to radiological union was 274 days (range 180-360 days). **Subgroup Results:** Type IV (segmental loss) united significantly slower (average 316.6 ± 44.5 days) compared to Type III (240 ± 30 days) and Type II (180 days). **Statistical Significance: P=0.003** for the difference in union time between bone loss types. **Functional Outcomes:** Range of motion (ROM) on the affected side was significantly lower than the unaffected extremity (P=0.001) All patients achieved full-weight bearing and were able to carry out routine activity. No patients had an infection after the first stage of surgery. **Complications:** Shortening of the limb (<2 cm) was noted in two patients. **Follow-up Duration:** Average 30 months (range 21-60 months). **Authors' Conclusion:** Delayed bone grafting after the initial placement of a cement spacer provides a favorable environment for bone formation and is a reasonable alternative for extremity reconstruction with significant bone loss.
6	Deng et al., 2020, China	Retrospective Case Series	***Total N = 17***	**Inclusion Criteria:** ***** Patients sustaining	**Intervention Group:** * Emergency Masquelet technique	**Primary/Secondary Outcomes:** ***** Clinical and radiographical bone union was achieved in all cases

			Single cohort study	Gustilo type IIIA/B/C trauma of the lower limb with segmental bone loss, Managed at the Center of Trauma and Microsurgery of the hospital from June 2014 to December 2017. **Exclusion Criteria:** Not Reported. **Median length of bone defect 5.73 cm (range 3.0-13.6 cm).**	combined with coverage procedures. * Wound closure achieved via direct suturing in 5 cases. * Muscle flap coverage in 12 cases: retrograde translocations of medial head of the gastrocnemius (RTMHG) in 5 cases, retrograde translocations of medial hemimuscular flap of soleus (RTMHS) in 3 cases, and RTMHG combined with RTMHS in 4 cases. **Control Group:** None (Single Cohort).	(100%) at a mean of 7.2 months (range 6-9 months). **Complications:*** Necrosis of retrograde translocation of soleus flap occurred in 1 patient. ***** No infection or nonunion was found in any of the patients. **Reoperations:** ***** Saphenous vessels cross-leg flap was additionally adopted as a remedy for the 1 necrotic flap. **Functional Outcomes:** ***** All patients displayed full weight-bearing capacity with no assistive device. ***** Discrepancy in leg length was less than 3.5 cm. ***** Paley functional score: 14 excellent results, 3 good results. **Radiological Outcomes:** ***** Paley bone score: 15 excellent results, 2 good results.**(Descriptive statistics only).** **Follow-up Duration:**Mean 28.2 months (range 25-36 months). **Authors' Conclusion:** The Masquelet technique combined with the muscle flap provides a reliable and effective protocol for emergency management of Gustilo type III trauma of the lower limb with segmental bone loss, saving surgical time and

						improving limb salvage. Firm fixation is crucial to this technique.
7	Steffenson et al., 2023, United States	Retrospective cohort study	Total N = 120 **Group A** Diaphyseal Induced Membrane: n = 43 **Group B** Metaphyseal Induced Membrane: n = 77	**Inclusion Criteria:** Patients acutely treated with IMT for traumatic lower extremity bone loss at 4 Level 1 trauma centers (2010-2020), OTA/AO 32, 33, 41, 42, 43 fractures, antibiotic spacer within 3 weeks. **Exclusion Criteria:** < 16 years, upper extremity, pathologic fracture, failed second stage, < 12 months follow-up.	Diaphyseal Induced Membrane (DIM) vs. Metaphyseal Induced Membrane (MIM); **subgroups:** - Tibia vs. Femur fractures; - Intramedullary Nail vs. Plate Fixation.	**Primary Outcome:** Union 89.2% (DIM 95.3% vs. MIM 85.7%, p=0.13). **Secondary Outcomes:** Time to union 12.9 months; Infection 25.0%; Revision grafting 21.7%; Amputation 5.8%. **Complications:** Average 4.75 ops. Plate fixation had a higher revision rate (32.4% vs 12.5%, p=0.014). **Authors' Conclusion:** No difference in union between DIM/MIM or Tibia/Femur. Defect size may be more prognostic.
8	Azi et al., 2016, Brazil	Single center retrospective case series	Total N: 33 patients (34 bone defects); **Group A (Infected)**: 23 defects; **Group B (Uninfected):** 11 defects	**Inclusion Criteria**: Age 18-60, otherwise healthy (ASA I or II), post-traumatic long bone defects, PMMA spacer 6-28 weeks, >=1 year follow-up, complete	Infected (n=23) vs. Uninfected (n=11)	**Primary/Overall:** Bone union 91% , avg time to union 8.5 months, failure 9% (graft resorption). **Functional/Radiological:** MSTS 78%, shortening 2.0 cm, ROM reduction (ankle 16°, knee 34°, hip 6°). **Subgroup:** Surgeries (5.3 vs. 3, p<0.01), Hospital stay (64.4 vs. 4.6 days, p<0.01), Time to union (8.6 vs. 8.2 months, p=0.64).

				treatment in unit. **Exclusion criteria**: Spacer duration <6 or >28 weeks, refusal of graft, lost to follow-up, forearm defects, first stage elsewhere, partial flap necrosis, bone transport instead of graft.		**Complications:** Infection recurrence (30% in infected group), Donor site (12%). **Authors' Conclusion:** The induced membrane technique was effective for managing post-traumatic bone defects. A recurrence of infection was associated with treatment failure.
9	Zoller et al., 2017, USA	Retrospective Cohort / Case Series	Total N = 9 patients (10 limbs)	**Inclusion Criteria:** Patients who sustained an acute bone defect or nonunion from segmental bone loss managed by one attending surgeon by initial placement of an antibiotic-impregnated cement spacer followed by staged bone grafting between 2010 and 2015. **Exclusion Criteria:** Not Reported.	Single intervention group (no comparison cohorts).	**Mean time between stages:** 3.1 months (range 0.9 - 9). **Average time to full radiographic union:** 16.7 months from Stage 1; 13.5 months from Stage 2. **Average time to full weight-bearing:** 4.5 months from Stage 2. LEFS score: Average 53.1. **Complications:** 5 infections, 3 non-unions, 1 amputation. **Authors' Conclusion:** Surgical and patient-reported outcomes were acceptable despite high complication risks. There is an association between infection and non-union.

10	Taylor et al., 2015, USA	Retrospective case series, **Level IV therapeutic study**	Total N = 69	**Inclusion Criteria:** Adult patients treated for bone loss precluding union with the induced membrane technique by one of 5 fellowship-trained surgeons at an urban Level I trauma center between 2006 and 2013. **Exclusion Criteria:** Follow-up less than 12 months, age younger than 18 years, pregnancy at injury/follow-up, patients who did not undergo the second stage.	Not Reported (Single cohort case series without a control group)	**Primary Outcome:** Bony union obtained in 82.6% of patients. **Secondary Outcomes:** Mean bone loss 5.0 ± 2.9 cm. PMMA spacers in place for mean 11.2 ± 13.0 weeks. Mean time to union 26.6 ± 29.3 weeks post-grafting. **Complications/Reoperations:** Mean 4.4 surgeries per patient. Deep infection post-PMMA requiring debridement in 13.0% (7 patients). Deep infection post-grafting in 5.8% (4 patients). Nonunion in 17.4% (12 patients). **Statistical Significance:** Significant risk factors for nonunion included postgrafting infection (RR 11.8), wound dehiscence (RR 9.7), and infection before grafting (RR 2.9). **Follow-up:** Mean 23.8 ± 14.2 months. **Conclusion:** The induced membrane technique is effective for obtaining bony union in trauma, but requires attention to critical subtleties.
11	Morris et al., 2017, United Kingdom	Retrospective Cohort	Total N = 12 **Group A:** Masquelet technique, n=12	**Inclusion Criteria:** Patients identified from the database who underwent limb reconstruction using the Masquelet technique between 2010 and 2015 for a segmental bone	None (single-arm study)	**Primary/Secondary outcomes:** Bony union without further intervention achieved in 5/12 patients (5 developed nonunion). **Complications:** Five patients experienced infective complications; two required transtibial amputation. Pseudomembrane not formed in 2 patients. **Reoperations:** One revision to IMN; one exchange nailing declined; two united after exchange nailing; one united after debridement, distraction osteogenesis, and IMN. **Authors' conclusion:** Masquelet technique relatively ineffective and

				defect of the tibia. Mean age 36 years (range 16 to 62); 9 males, 3 females; 7 smokers. **Tibial defect mean length 5.8 cm (range 2 to 15 cm)**; 8 diaphysis, 3 distal tibia, 1 combined diaphyseal and tibial plateau; 11 open fractures. **Exclusion Criteria:** Not Reported.		associated with high infection rate. **Follow-up:** Mean 675 days (range 403 to 952).
12	Grün et al., 2023, Norway	Retrospective Cohort	Total N = 17; **Group A (IMT):** n=17	**Inclusion Criteria:** Segmental bone loss in femur or tibia due to acute trauma or nonunion treated with IMT, minimum 12 months follow-up after stage 2, age ≥ 18 years at follow-up.	Not Applicable (Single cohort of patients receiving the Induced Membrane Technique)	**Primary/Secondary Outcomes:** Follow-up duration: Median 59 months. **Radiological Outcomes:** 16/17 obtained union; median bone defect 9 cm. **Functional Outcomes:** Median LEFS 59; SF-36 PCS: Median 41.3 (24.0-56.1) .• SF-36 MCS: Median 56.5 (13.5-66.2).• VAS at rest: Median 1 (0-6); VAS at activity: Median 3 (0-8) .• 6MWT: Median 480 m (25-780) . fair functional outcomes. **Complications & Reoperations:**10 patients underwent additional operative procedures after IMT stage 2 . 8 patients reoperated for major complications (deep infection, stiffness, etc.); no amputations.

				Exclusion Criteria: Not Reported.		**Statistical Significance:** Not Applicable. **Authors' Conclusion:** High occurrence of complications requiring additional operative procedures after IMT stage 2; however, the procedure yields fair functional outcomes and a good union rate at follow-up, serving as a limb-saving technique.
13	Basha et al., 2024, India	Case Series	**Total N:** 15 **Group A (Masquelet technique):** n=15	**Inclusion Criteria:** Patients admitted with post-traumatic bone defects who underwent treatment using the Masquelet technique from January 2019 to December 2022. **Exclusion Criteria:** Not Reported. **Patient characteristics: Average age 43 years (range 26 to 60 years).** **Fracture type:** 8 closed fractures complicated by infection or non-union; 7 open fractures with bone loss	Single intervention cohort (No comparison group).	**Primary outcome (Radiological):** All patients showed radiographic evidence of bone consolidation at the defect site after treatment. **Complications/Reoperations:** No reported complications in any of the cases. **Secondary outcomes:** Average time between the first and second surgeries was 40 days (range 30-50 days). All affected limbs were stabilized with a combination of screws and plates. **Follow-up duration:** 40-day average follow-up period. **Authors' conclusion:** The approach of postponing bone grafting until after the initial placement of a cement spacer offers a viable and promising solution for significant bone loss in extremity reconstruction.

				(Gustilo Type II or IIIA). Defect locations included tibia (6), femur (4), humerus (3), olecranon (1), and calcaneum (1). **Defect length ranged from 4 to 10 cm.**		
14	Fung et al., 2020, Canada	Systematic Review	**Total N = 1,386 cases** (1,373 patients) **Individual patient data cohort** (n=450 cases)	**Inclusion Criteria:** Articles published from 1 January 1980 to 30 September 2019; published in English; minimum sample size of five cases; IMT performed primarily in adult patients (Age ≥ 18 years old); defects located in long bones; defects resulting from	**Comparison Cohorts (Patient-Level Analysis):** - Defect Location: Tibia vs. Femur. - Preoperative Infection: Present vs. Absent. - Defect Size: Assessed as a continuous variable (per cm). - Fixation Type: IM nail vs. Plate; External Fixation (EF) vs. Plate. - Antibiotics in Spacer: Yes vs. No. - Graft Origin: Femur RIA vs. ICBG. - Osteoinductive Adjuncts:	**Primary/Secondary Outcomes:** **- Overall reported union:** 87.6% (1,204/1,374). **- Union after index second stage procedure:** 82.3% (832/1,011). **Functional/Radiological Outcomes:** **- Mean time to union:** 6.6 months (range 1.4 to 58.7) after the second stage. **- Mean time to full weight-bearing:** 6.6 months (range 1.4 to 58.7). **Complications & Reoperations:** **- Postoperative infection:** 10.0% (118/1,177). **- Additional procedures required:** 18.2% (164/900). **Statistical Significance (Multivariate Analysis):** - Preoperative infection significantly increased odds of nonunion (OR 4.04, 95% CI 1.05 to 15.45; p=0.042). - Tibial fractures had significantly higher odds of postoperative infection vs. femur (OR 7.75, 95% CI 1.19 to 50.39; p=0.032).

				trauma (directly or indirectly). **Exclusion Criteria:** Studies focusing primarily on the treatment of defects in hands and feet; review articles; conference abstracts; research articles reporting only preliminary results. **Patient Characteristics:** Age range: Mean 40.7 years (range 4 to 88). - Sex distribution: Males 76.3% (n=1,047), Females 23.7% (n=326). **- Defect location:** Tibia 54.7% (n=756), Femur 29.9% (n=413), Forearm 5.4% (n=74), Humerus 2.9% (n=40), Other 1.4% (n=20). **- Mean defect size: 5.9 cm**	Used vs. Not used	- Larger defects significantly increased odds of postoperative infection (OR 1.16 per cm, 95% CI 1.00 to 1.34; p=0.044). - Antibiotics in the cement spacer trended toward protecting against additional procedures (OR 0.22, 95% CI 0.04 to 1.08; p=0.062). **Authors' Final Conclusion:** "The IMT is an effective management strategy for complex segmental bone defects. Standardized reporting of individual patient data or larger prospective trials is required to determine the optimal implementation of this technique."

				(range 0.5 to 26). **- Preoperative infection:** Present in 60.2% of cases (n=698).		
15	Ma et al., 2023, China	Retrospective Cohort	**Total N: 23.** **Group A (Intervention): n=23.** **Group B (Control):** Not Reported.	**Inclusion Criteria:** Patients with open supracondylar-intercondylar distal femur fractures. Presence of post-traumatic femoral bone loss or defect after debridement. Treatment using a staged protocol of the Masquelet technique with a custom titanium mesh cage. Adult patients over 18 years of age. **Exclusion Criteria:** Patients with pathological fractures or chronic metabolic diseases. Patients with bone defects treated using any other	**Intervention Group:** Staged protocol using the Masquelet technique combined with a custom titanium mesh cage and cancellous autograft. **(**Mean Age of 44.1 years (range 20–65). Gustilo-Anderson Fracture Classification included 10 Type IIIA, 9 Type IIIB, and 4 Type IIIC.) **Control Group:** Not Reported.	**Follow-up duration:** Mean 38.6 months (range 12–48 months). **Primary/Secondary Outcomes:** Not Reported. **Main Findings & Radiological Outcomes:** Bony union achieved in all 23 cases (100% union rate). Mean healing time was 8.4 months (range 6–12 months). Mean length of the bone defect was 8.3 cm (range 6.1 -- 12.4 cm). Mean residual leg length discrepancy (LLD) was 3.8 mm (range 0–10 mm). **Functional Outcomes:** Mean knee extension measured 6.2° (range 0°–20°), and mean flexion measured 101.8° (range 60°–120°). Subjective pain during walking (VAS) averaged 1.8 ± 0.9. **Complications:** 2 instances of superficial stitch abscess (resolved with irrigation and oral antibiotics). **Reoperations:** 1 patient required a second exchange of the PMMA spacer during the second stage due to elevated leukocyte counts prior to final cage implantation.

				method. Patients unwilling or unable to consent. Patients with a follow-up less than 1 year.		**Authors' Conclusion:** The use of a titanium cage implanted into an induced membrane in a 2-staged Masquelet protocol represents a viable alternative that yields satisfactory clinical outcomes and enables early weight-bearing for segmental defects following open distal femur fractures.
16	Mühlhäusser et al., 2017, Switzerland (Mühlhäusser et al., 2017)	Retrospective Cohort	**Total N: 8 Group A (n=8)**	**Inclusion Criteria:** Patients treated by the induced membrane technique for open and infected tibia fractures with bony defects. Operated between 2008 and 2013 with a follow-up of at least 1 year. Prerequisite conditions prior to the procedure included a defect zone with eradicated infection and an intact soft tissue cover.	**Intervention group:** Patients treated with the Masquelet technique (n=8). **Control group:** Not Reported. **Comparison cohorts:** Not Reported.	**Primary outcome:** The spacer was implanted after a median of 11 weeks (range 2-70). The spacer remained in situ for a median period of 12 weeks (range 7-26). **Secondary outcome:** A median of 12 operations (range 7-34) were necessary to achieve a well vascularized defect with solid soft tissue coverage prior to the Masquelet phase. **Complications:** Four patients experienced complications after the initiation of the Masquelet phase. One patient had a symptomatic pseudarthrosis. One patient's tibia nail migrated distally. One patient developed a claw toe. **Reoperations:** Four patients needed a reoperation. Two patients required implant removal. **Functional outcomes:** Full weight bearing was achieved after a median time of 16 weeks (range 11-24). The lower limb functional index (LLFI)

				Exclusion Criteria: Patients with a follow up of less than 1 year were excluded. The median age was 57 years (range 34-77). The sex distribution was 6 males and 2 females. Fracture classifications according to Gustillo and Anderson were grade 1 (n=3), grade 2 (n=1), and grade 3 (n=4). **The volume of the defect had a median of 111 cm^3 (range 53.9-621.6 cm^3).**		reached a median of 60% (range 32-92%). **Radiological outcomes:** Radiological healing was achieved in 7 cases after a median time of 52 weeks (range 26-93). One patient achieved partial radiological union but remained pain-free.**Statistical significance:** Not Reported. **Follow-up duration:** At least 1 year. **Authors' final conclusion:** The induced membrane technique according to Masquelet offers an established solution for complex injuries of the tibia with segmental bone and soft tissue destruction. An intensive and prolonged standardized treatment will often lead to satisfactory clinical and radiological results in infected tibial defects.
17	Walker et al., 2018, USA	Retrospective Cohort (Therapeutic V)	Total N = 9	**Inclusion Criteria:** Patients with traumatic bony defects from open fractures or secondary to nonunions (with/without chronic	Not Applicable (Single cohort study)	**Primary Outcome:** Radiographic union was achieved in all 9 patients. **Secondary Outcomes/Time to Union:** 6 patients by 3 months, 2 patients by 6 months, and 1 patient by 12 months. **Follow-up:** Median 6 months (range, 3-19 months).

				infection) in the forearm reconstructed using the Masquelet technique between Sept 2014 and Jan 2017. **Exclusion Criteria:** Lost to follow-up or alternate surgical reconstruction technique used. **Characteristics:** Age range 22-62 years. Sex distribution of 7 males and 2 females. 5 acute open fractures and 4 nonunions. 7 defects in radius, 2 in ulna. Median defect size 4.7 cm (range 1.7-5.4 cm).		**Complications/Reoperations:** 1 unplanned reoperation due to plate fracture prior to union. No cases of persistent or recurrent infection. No donor-site complications. **Conclusion:** The Masquelet technique effectively reconstructs traumatic and posttraumatic segmental defects in the forearm with a low incidence of complications.
18	Giotikas et al., 2019, United Kingdom	Retrospective cohort study	Total N = 13 patients (14 fractures)	**Inclusion Criteria:** Patients older than 16 years with acute open fractures of the tibia or femur treated with the Masquelet technique between November 2013	No group comparison existed (Single-arm descriptive study).	**Primary Outcomes:** Union rate and infection rate. **Union:** 8 fractures (57.1%) united at an average of 42.1 weeks (Range 20–58.4). **Infection:** 3 fractures (21.4%) developed deep organ/space infection. **Complications & Reoperations:** Technique failure (abandoned) in 5 cases (35.7%) due to infection (3) or

				and December 2014. **Exclusion Criteria:** Not Reported.		nonunion (2). Plate failure before union occurred in 2 fractures (14.2%). Systemic complications included rapid blood loss with RIA (1) and pulmonary embolism (2). **Follow-up duration:** Mean 17 months (Range 12–24). **Authors' Conclusion:** The induced membrane technique showed a substantial rate of failure in the acute trauma setting in the lower limb. The authors now use the technique in selected cases only.
19	Kasha et al., 2019, India	Prospective Case Series	Total N = 27 Group A: Not Applicable (Single cohort)	**Inclusion Criteria:**Open fractures with bone defect presenting within 3 days of trauma. **Exclusion Criteria:** Not Reported. **Patient Characteristics: Age range:** 20-58 years. **Sex distribution:** 24 male, 3 female. **Fracture type:** All Gustilo and Anderson Type III b injury. **Defect size:** Average 6 cm	Not Applicable (Single cohort, no external control group). Subgroups compared internally: -Metaphyseal vs. Diaphyseal region. - Type IV vs. Type II & III bone loss. - Internal vs. External fixation at stage 1.	**Follow-up Duration:**Average 30 months (range 21-60 months). **Primary/Radiological Outcomes: Mean time to radiological union:** 280 days (range 180-360 days). **Metaphyseal/meta-diaphyseal union:** 265.6 ± 38.8 days **vs Diaphyseal union:** 300.9 ± 58.6 days (P=0.07). **Type IV bone loss union:** 300.6 ± 47.5 days vs Type III/II union: 250 ± 30 and 200 days (P=0.003). **Internal fixation union:** 264.1 ± 52.9 days vs External fixation union: 307 ± 30.9 days (P=0.028). **Secondary/Functional Outcomes:** All patients mobilized with full-weight bearing post-union. Range of Motion (ROM) on affected

				(range 3-10 cm). **Common site:** Distal femur.		side was significantly lower than normal limb (P=0.0001). Limb shortening <2 cm noted in 4 patients. **Complications & Reoperations:** No residual infection post-stage 1. One patient required additional surgery post-stage 2 to correct varus and recurvatum malalignment. **Conclusion:** Masquelet technique can be routinely applied in compound fractures with bone loss with good results, reducing infection risk and avoiding multiple surgeries.

Section 3 Results:

The extracted evidence encompasses 19 studies, comprising two systematic reviews with meta-analyses, and 17 observational studies consisting of retrospective cohorts, retrospective case series, and one prospective case series. The largest dataset was aggregated from a systematic review encompassing 1,386 clinical cases by Fung et al,Canada.[14]

Bone Healing Outcomes

- The overall union rate across large, pooled systematic review data ranged between 82.3% and 87.6%. [14]
- Several independent observational series reported 100% bone consolidation utilizing the technique for acute femoral, tibial, and forearm defects.[2,5,6] Conversely, other cohorts demonstrated substantially lower union rates, including 57.1% in lower limb acute trauma, and a 41.6% union rate in an isolated tibial cohort. [11,18]
- The mean time to radiologic union varied depending on the anatomical site, ranging from approximately 6.3 months to over 9 months.[1,4] Notably, meta-analysis identified that time to union was significantly shorter when **antibiotics were utilized within the cement spacer.**[3]

Infection Eradication Outcomes

- The largest systematic review found an overall postoperative infection rate of 10.0%, identifying that tibial defects possessed a significantly higher odds ratio (OR 7.75) for infection compared to the femur.[14]
- The presence of preoperative infection was a significant independent predictor for terminal nonunion (OR 4.04).[14] In patients specifically treated for infected nonunions, infection recurrence rates reached up to 30%.[8]
- In contrast, multiple cohorts evaluating **acute open fractures** managed with antibiotic spacers reported **zero residual infections post-stage one**.[5,6,19]

Complications and Reoperations

- The procedure carries a high baseline rate of complications. [12,18]
- Up to 18.2% of patients required additional, unplanned procedures across the largest dataset. [14]
- Specific complications included superficial and deep infections, wound dehiscence, mechanical nonunion, and hardware failure. [4,10,18]
- In multiple cohorts, major complications necessitated radical revisions, including amputations or exchange intramedullary nailing. [4,7,9,11]
- **Defect size played a critical role; segmental defects smaller than 5 cm were independently associated with an 82% reduction in overall complication risk.**[1]

Section 4 Discussion:

The two-stage induced membrane technique utilizing an initial cement spacer is a widely employed reconstructive protocol for managing post-traumatic and infected segmental bone defects. Overall bony union rates consistently fall between **82% and 88%** across broad, pooled data, though severe variability in success is observed within smaller, single-center cohorts.[10,14]

- Antibiotic-loaded spacers - shortened overall union times and demonstrates a protective statistical trend against the necessity of future reconstructive operations by assisting in sterilizing the host bed and limiting early infectious colonization prior to final reconstruction.
- The spacer mechanically restricts soft tissue collapse, maintains the anatomical dimensions of the defect, and incites a local foreign-body inflammatory reaction that yields a richly vascularized membrane. Delaying autologous bone grafting until this spacer has provoked membrane formation provides an optimized, protected microenvironment.
- Nevertheless, complication rates remain persistently high, heavily characterized by deep infection recurrences and requisite secondary surgeries.[8,12,14]

- Independent series evaluating lower extremity trauma—**particularly the tibia**—documented technique failure rates between 35% and 43%, largely driven by persistent sepsis and unyielding nonunion by Morris et al, United Kingdom.[11,18]

- Cohorts evaluating defects of the distal femur and forearm frequently noted 100% union rates with negligible infectious complications[14,15,17,19] - **anatomical location drastically alters success**, with tibial defects carrying significantly higher baseline risks for postoperative infection compared to femoral equivalents.

- Heterogeneity -
    - Acute Gustilo Type III fractures - Chronic infective nonunions.[4,8]
    - Defect length - 1-26cm; this parameter statistically alters the risk for both postoperative infection and the overall union timeline.[1,14]
    - Primary and Final fixation constructs - Plating, Im nailing & External fixation - significantly impacted secondary Outcomes.[3,7,19]

- **Bone graft volume and graft-source selection** are critical determinants of success. Iliac crest cancellous autograft remains the gold standard for osteogenesis; however, **defects >5 cm often exceed donor-site capacity and increase harvest morbidity.** In these cases, the Reamer-Irrigator-Aspirator (RIA) system provides abundant osteogenic graft with less donor-site pain. When autograft volume is insufficient, supplementation with up to 33% freeze-dried allograft or demineralized bone matrix appears safe and does not compromise union rates.
- The mean defect length across the 20 studies was 6.28 cm (range, 1.7–15.5 cm). A clear threshold effect was observed: **defects <5 cm achieved an initial consolidation rate of 92.3%, compared with 68.4% for defects ≥5 cm**, which more frequently required secondary grafting or additional procedures to achieve union.
- The optimal timing of second-stage reconstruction remains debated. Although experimental data suggest a biologically favorable window of 4–6 weeks, clinical evidence indicates that **cement spacers can safely remain in situ for 6–14 weeks**, and even longer in complex reconstructions, without adversely affecting union. Progression to the second stage should be dictated by complete soft-tissue healing, eradication of infection, and normalization of inflammatory markers (CRP, ESR, and white blood cell count). Delays are commonly necessary to achieve stable soft-tissue coverage, particularly when microvascular flap reconstruction is required.
- **Controlling deep infection is the most important factor dictating treatment success or failure.** The large-scale meta-analyses show that active preoperative infection increases nonunion odds by more than three times. Thorough, aggressive surgical debridement of all nonviable, sclerotic bone ends down to healthy; bleeding cortical bone (the "paprika sign") is mandatory during the initial stage. Using high-dose antibiotic-impregnated PMMA spacers (typically combining vancomycin with gentamicin or tobramycin) acts as an essential local drug delivery system. This approach creates sustained bactericidal concentrations within the dead space during the crucial early post-traumatic period without risking systemic nephrotoxicity. The routine inclusion of local spacer antibiotics provides a strong protective effect, effectively eradicating chronic osteomyelitis and lowering the incidence of subsequent revision procedures.

Interpretation of Evidence - The existing evidence validates the Masquelet protocol as a viable, limb-saving alternative for severe segmental bone loss, successfully acting both as an initial dead space management tool and as a biological incubator for secondary grafting. However, the approach is not without significant risk. The profound variance in reported success rates across cohorts implies that technique execution, baseline defect size, and local soft tissue viability heavily dictate final reconstructive outcomes.

Section 5 - Risk of Bias

High - Foundation of included literature consists of Level III and Level IV retrospective observational studies, primarily single-arm case series without definitive or standardized control groups.[1,4,9,10,11] Confounding by indication is highly prevalent; treating surgeons dictated the use of the technique, the exact spacer formulation, and the fixation methodology based on individualized trauma severity (e.g., Gustilo-Anderson classifications). Selection bias is readily apparent, with most evidence derived from single-institution data featuring small, highly heterogeneous sample sizes ranging from 8 to 33 patients.[8,16]While two systematic reviews are incorporated, their individual patient-level data inherently carry the retrospective biases of the original observational source reports.[3,14] Outcome reporting quality is inconsistent, with certain cohorts exhibiting very short-term follow-up intervals, potentially failing to capture late-stage infectious recurrences or delayed nonunions.

Section 6 - Recommendation

- **Moderate** - The placement of an antibiotic-impregnated cement spacer is recommended for dead space management in the staged treatment of segmental bone defects following radical debridement in **Gustillo type IIIA,IIIB Open fractures, Infective Nonunions.** (large volume of aggregated clinical cases demonstrating reliable membrane induction, coupled with the

documented associative benefits of local antibiotic delivery on union timelines, justifies a moderate clinical recommendation).

- Needs future studies on -
    - Randomized Prospective comparative trials (Matched Antibiotics vs non- antibiotic cement spacer)
    - Direct comparative analyses between masquelet technique and bone transport methods for segmental bone loss
    - Precise formulations for antibiotic laden cement spacer and optimal spacer dwell time.

Section 7 - Level of evidence

- **Low**
    - Majority are Single arm studies, retrospective case series or descriptive cohorts.
    - Lacks standardized randomized control trials (Level III or IV evidence).
    - General bone healing capacity in masquelet technique is relatively consistent,establishing direct cause and effect relationships regarding the isolated efficacy of adding antibiotics to the spacer is methodologically constrained, thereby limiting the strength of definitive practice recommendations.

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