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Testing the effectiveness of a new type of spacers for local antibiotic therapy

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Abstract

Introduction The established treatments for purulent infection in the bone and joint involve one- or two-stage local effect on the biofilm with use of bone cement and an active substance including an antibiotic in addition to systemic therapy.

The **objective** was to evaluate experimental qualitative and quantitative antibiotic release from bone cement introduced into a new type of lattice-structured spacer.

Material and methods A new type of lattice-structured implant/spacer manufactured using additive technologies and a comparison sample simulating a traditional reinforced spacer made of bone cement + antibiotic were used. Vancomycin release was measured by spectrophotometry for periods of 30 days. A regression line was used to plot calibration curves based on data obtained from mother solutions.

Results An effective profile of antibiotic release from bone cement was obtained in the first days of the experiment, followed by a decrease at the end of the first week and an exit to a uniform plateau. The amount of fixed antibiotic in solutions did not exceed 1 % of the total mass of bone cement and active substance. The amount of antibiotic released from the lattice-structured samples was higher than that in the comparison samples.

Discussion Antibiotic release is a superficial process and is not dependent on the total volume of bone cement. A possible increase in the volume of the medicinal composition does not lead to a proportional increase in the amount of the active substance released. The findings showed that the antibiotic release is more intense even with a smaller volume of material in the lattice structures compared to the control samples, which emphasizes the importance of optimizing the geometry and structure of the material to achieve maximum efficiency of the release of active substances.

Conclusion The lattice structure of implants quantitatively affects the release of antibiotic from bone cement into the environment.

Keywords: bone infection, bone cement, implant, antibiotic elution, additive technologies

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INTRODUCTION

Purulent infection is one of the most formidable complications in surgery of the musculoskeletal system [1–3]. Conventional systemic therapy is effectively accompanied by a local effect on the pathological focus [4–7]. Infection can be arrested with a two-stage revision surgery: placement of a spacer made of bone cement (BC) with an active substance (selected antibiotic) followed by implantation of a revision construct. The technique can be applied to joint and long bone conditions [8].

Many technologies have been developed to increase the time and amount of antibiotic release into the environment. It is a known fact that the elution of the active substance occurs from the superficial layer of the spacer (within 2–3 mm). This predetermines the possibility of increasing the degree of elution by increasing the contact area of the therapeutic composite layer (bone cement + antibiotic) and the environment [9]. The antibiotic (AB) effect on the surrounding tissue extends to a maximum of 20–25 mm. Technologically, the distribution of the therapeutic composite layer (TCL) over the surface of the spacer is limited by the location of the infectious focus and is costly in terms of the use and redistribution of large volumes of AB [10]. The strength characteristics of the formed spacer are supposed to facilitate functional capabilities of the patient and serve as the basis for osteosynthesis if needed [11, 12].

The use of lattice structures in the manufacture of basic implants could increase the contact area of the composite layer and the environment and improve the elution of AB from the BC. Preliminary calculation of strength characteristics allows to minimize changes in the implant design specified by the manufacturer. The combination of a volumetric lattice structure with TCL forms the so-called metamaterial, which could become one of the options for solving the problem [13]. A volumetric lattice structure as part of an implant/spacer is produced using additive technologies. This is achieved with the design of elementary cells that fill the volume of the product. The distribution of the elementary cell has an impact on the strength of the structure [14]. Topological or structural optimization is another method to be used. N. Kladovasilakis et al. [15] optimized the designs for hip implants achieving 50% porosity and maintaining strength requirements. Lattice-based implants can act as a preformed base with predetermined parameters to reduce or eliminate the need for handicraft production of reinforced spacers.

The **objective** was to evaluate experimental qualitative and quantitative antibiotic release from bone cement introduced into a new type of lattice-structured spacer.

MATERIAL AND METHODS

A lattice-structured cylinder (Fig. 1 a) was selected as a base for antibiotic loaded bone cement, copying a fragment of the proposed implant number I and comparison sample II (Fig. 1 b), that is, a fragment of a pin with a 2 mm mantle of BC applied on the surface as a continuous layer.

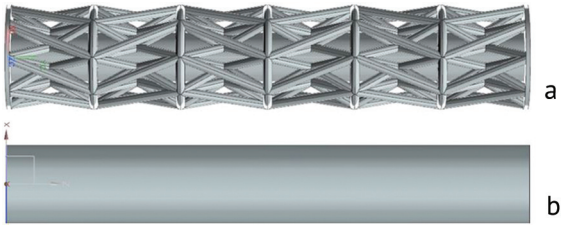


Fig. 1 Types of the samples: (a) lattice-structured implant I; (b) comparison sample II

Sample I is a composition of an inner rod with a diameter of 6 mm and a layer of outer ribs at an angle of 45° with an outer diameter of 12 mm. A cylinder with an outer diameter of 8 mm serves as a comparison sample. The characteristics of the samples are presented in Table 1.

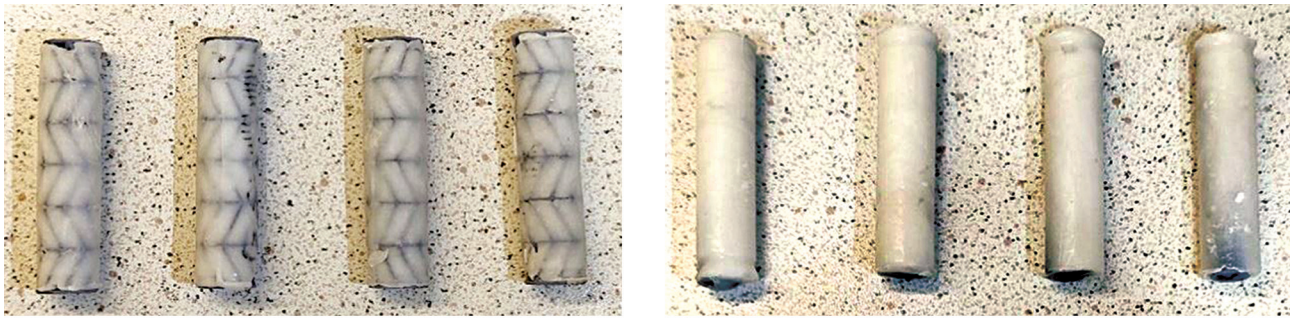
Table 1

Comparative parameters of the samples

№	Diameter, mm	Length, mm	Diameter of the pin, mm	Diameter of the rib, mm	Porosity, %	Cement volume, mm^3	Surface area, mm^2
I	12	60	6	1	61.9	3702	2261
II	8	60	–	–	0	3769	2261

The study samples

The antibiotic release from the TCL was explored using four samples of each structure produced with laser stereolithography and strengthened using ultraviolet light. A photopolymer printer with photopolymer resin was selected for the sample production. Synycem bone cement (France) was used for the study. TCL of each test sample was prepared with 4.0 g of the dry bone cement and 0.2 g of Vancomycin. AB was chosen with regard to the thermal stability, active use in clinical practice and research on the problem. The powdered component of the BC was homogeneously mixed with the antibiotic, then 2 ml of monomer was added to the mixture, and homogeneously mixed to a plastic condition. The TCL was applied to the samples using a disposable 5 ml syringe and an internal diameter of 12 mm which served as a mold. The samples are shown in Fig. 2.



a b

Fig. 2 Appearance of the manufactured samples: (a) samples I; (b) samples II

The lattice structures were coated with TCL so that it did not protrude beyond the ends o the sample. The outer diameter of the samples was 12 mm. Each sample was placed in a Falcon tube filled with 30 mL of Dulbecco's phosphate-buffered saline (DPBS) without Ca^{2+} and Mg2+ at 37 °C. The samples were immersed to ensure complete contact with DPBS.

Evaluation of antibiotic release from the medicinal composite

Quantification of the antibiotic in solutions was produced using the spectrophotometric method and a BioMate 3S UV-Visible spectrophotometer (USA) to identify the dependence of the optical density of solutions and the concentration of the AB. Measurements were performed in the wavelength range from 190 to 230 nm. The peak of measurements corresponding to the antibiotic was assessed in the spectra. Several stock solutions of AB were used as calibration standards: Vancomycin at concentrations of 0, 0.00005, 0.0001, 0.00025, 0.0005, 0.00075, 0.001, 0.002, 0.003, 0.004 mg/ml. The sample volume in the cuvette measured was 1000 µl. Vancomycin in a volume of 0.5 g was dissolved in 5 ml of DPBS to obtain a concentration of 1 mg/ml.

To construct calibration curves, a regression line was used based on data obtained from mother solutions. The nonparametric Mann – Whitney test was used to assess the reliability of differences in AB release between the structures and compare two independent samples and determine statistically significant differences between them.

Table 2

Concentration calculated for constructing Vancomycin calibration curves using stock solutions

Amount of stock solution, µl	Amount of DPBS, µl	Concentration, mg/ml
400 from a concentration of 0.01	600	0.004
300 from a concentration of 0.01	700	0.003
200 from a concentration of 0.01	800	0.002
500 from a concentration of 0.01	4500	0.001
750 from a concentration of 0.001	250	0.00075
500 from a concentration of 0.001	500	0.0005
250 from a concentration of 0.001	750	0.00025
200 from a concentration of 0.001	1800	0.0001
500 from a concentration of 0.0001	500	0.00005

Measurement of antibiotic elution kinetics

The AB elution was measureed after 1, 3, 7, 15 and 29 days, respectively. The total amount of Vancomycin in the solution was determined at each measurement point according to the schedule. For each day, the concentration was estimated using the following formula:

$$C_a(d) = \frac{p(d)}{k} \cdot c(d),$$

where p is the spectrometer value in the sample taken on a given day, k is the regression coefficient, c is the coefficient associated with the dilution of the sample in the cuvette, d is the exposure length in days.

The coefficient associated with sample dilution in the cuvette depended on the day of measurement. This was due to the fact that the concentration increased over time. To determine the kinetics of the antibiotic, the time derivative was used and the rate of the antibiotic release was calculated with the formula:

$$U(d_i) = \frac{C_a(d_i) - C_a(d_{i-1})}{d_i - d_{i-1}},$$

where d_i is the exposure duration of the i-th shot.

The mass of the extracted antibiotic at a given exposure time (d) was calculated by multiplying the corresponding concentration of the antibiotic in the sample by the total volume in the vial V:

$$m_a(d) = C_a(d) \cdot V.$$

RESULTS

Analysis of the peaks for the absorption spectra showed that the wavelength for Vancomycin was 271–280 nm, which is consistent with the drug's pharmacopoeia data.

The regression coefficient was measured and the regression curve plotted (0). The value of the regression coefficient k was 405.9 for Vancomycin. The linear dependence for AB showed a high determination coefficient $R^2 \geqslant 0.986$ (Fig. 3). Based on the concentration measured within one day of shooting, the average values were calculated for both structures. The average elution values for the experimental sample I were higher than those for the comparison sample II at all stages of exposure (Fig. 4). The pairwise reliability of differences in mean values was assessed.

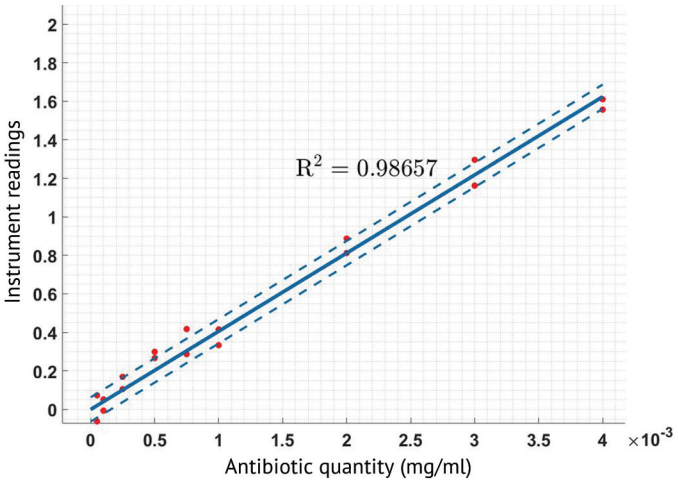


Fig. 3 Vancomycin regression curve: solid line is the regression curve, dash-dotted line is the confidence interval, red dots are the spectrophotometer values

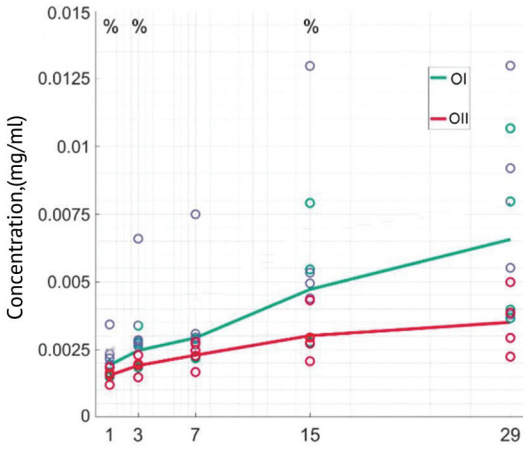


Fig. 4 Comparative curve of antibiotic concentration

No significant difference in the average values of Vancomycin concentration was found between the samples. Control sample II showed the lowest rate of antibiotic release and the smallest spread (Fig. 5). The total mass of the isolated AB Vancomycin was calculated separately and measured 0.1969 mg in sample I and 0.1051 mg in sample II, respectively (Fig. 6). The average value of AB release in experimental sample II was 97% better than in the control.

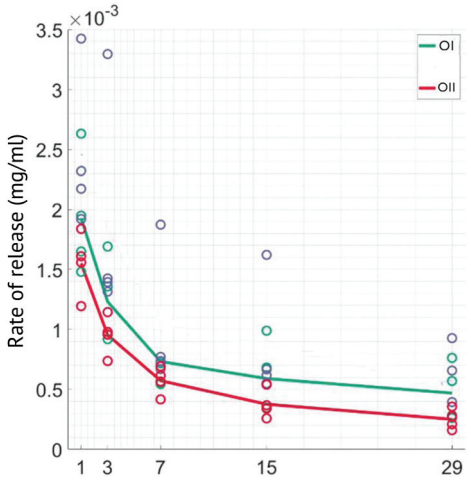


Fig. 5 Kinetics of Vancomycin

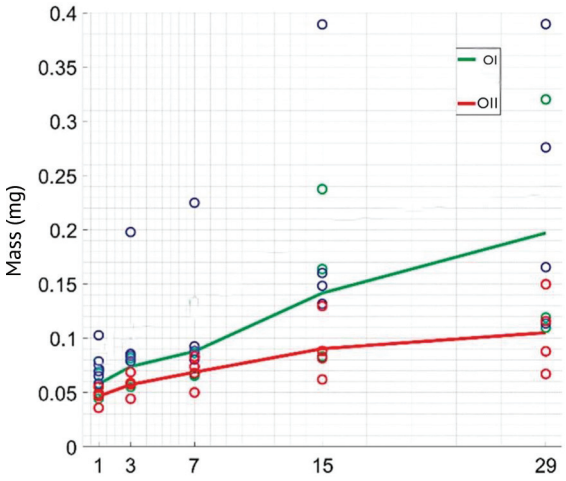


Fig. 6 Mass of isolated antibiotic

The results of a multi-day experiment showed changes in the mass of the isolated AB obtained depending on the control periods (Table 3).

Table 3

Antibiotic release from TCL

No	Amount of Vancomycin, mcg				
	1	3	7	15	29
I	57.8 ± 15.2	73.8 ± 21.9	87.8 ± 31.6	141.5 ± 74.4	196.9 ± 101
II	46.5 ± 8.0	57.2 ± 10.0	68.6 ± 13.9	90.3 ± 28.4	105.1 ± 35.8

A coefficient was introduced as the ratio of the free surface of the sample to the volume of the TCL to describe the comparative characteristics of the samples. The parameter allowed us to evaluate the efficiency of AB release depending on the geometric features of each sample. The percentage of the released AB to the initially set was calculated to quantitatively evaluate the elution process (Table 4).

The introduced coefficient as the ratio of the free surface of the sample to the volume of the BC showed the dependence on the released amount of AB.

Table 6

Relative characteristics of samples

No	Area / Volume	Vancomycin, %
I	0.61	0.07 ± 0.05
II	0.6	0.05 ± 0.0179

DISCUSSION

The study was conducted to determine the effect of a lattice structure on the antibiotic eluted from the drug composite layer, i.e. antibiotic-loaded bone cement. A characteristic profile of AB elution from the BC was obtained in all samples with a significant release in the first days of the experiment, followed by fading after seven days and reaching a uniform plateau after 15 days, which is consistent with the results of similar studies [16–20]. The amount of released AB measured to a maximum of 1% of the mass of the impregnated preparation.

A significant difference in the amount of isolated Vancomycin was noted between the samples. Lattice-structured samples showed higher amount of AB isolated despite the relatively higher initial content of TCL in the comparison samples.

The main part of the antibiotic is eluted from micropores and cracks of the surface layer of bone cement [21–25], which is confirmed by our results. The higher level of Vancomycin release can be explained by the presence of lattice-structured ribs. The single TCL structure divided into small areas increases the contact zone with the washing solution and increases the diffusion of AB compared to the control sample. This phenomenon is important for local antibiotic therapy with controlled and prolonged release of active substances being a key factor in the effectiveness [26].

The antibiotic release is considered as a surface process and does not depend on the total volume of the BC [27, 28]. A possible increase in the volume of the TCL does not lead to a proportional increase in the amount of AB released. In this series, this is confirmed by the fact that even with a smaller volume of material in the lattice structures, the release of the antibiotic is more intense compared to the control samples. Optimizing the geometry and structure of the material is essential for achieving maximum efficiency in the release of active substances [29, 30].

The limitation of the study include investigation of one type of a common antibiotic only. A comparative analysis of combinations of active substances eluted from the TCL, lattice variants, studies on metal samples, that is, a large volume of experiments, is required.

CONCLUSION

The study showed that the use of lattice structures for the fabrication of spacer implants allowed for an increase in the rate and amount of AB eluted from the TCL compared to conventional reinforcement with bone cement.

Conflict of interest *The authors declare that there is no conflict of interest.*

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Ethical review *Not applicable.*

Informed consent for publication *Not required.*

REFERENCES

1. Morcos MW, Kooner P, Marsh J, et al. The economic impact of periprosthetic infection in total knee arthroplasty. *Can J Surg*. 2021;64(2):E144-E148. doi: 10.1503/cjs.012519.
2. Murylev VYu, Rudnev AI, Kukovenko GA, et al. Diagnosis of Deep Periprosthetic Infection of the Hip. *Traumatology and Orthopedics of Russia*. 2022;28(3):123-135. (In Russ.) doi: 10.17816/2311-2905-1797.
3. Bozhkova SA, Kasimova FR, Tikhilov RM, et al. Adverse trends in the etiology of orthopedic Infection: Results of 6-year monitoring of the structure and resistance of leading pathogens. *Traumatology and Orthopedics of Russia*. 2018;24(4):20-31. doI: 10.21823/2311-2905-2018-24-4-20-31.
4. Afinogenova AG, Darovskaya EN. Microbial biofilms of wounds: status of the issuea. *Traumatology and Orthopedics of Russia*. 2011;17(3):119-125. (In Russ.) doi: 10.21823/2311-2905-2011-0-3-119-125.
5. Adams K, Couch L, Cierny G, et al. In vitro and in vivo evaluation of antibiotic diffusion from antibiotic-impregnated polymethylmethacrylate beads. *Clin Orthop Relat Res*. 1992;(278):244-252.
6. Ermakov AM, Kliushin NM, Ababkov IV, et al. Efficiency of two-stage revision arthroplasty in management of periprosthetic knee and hip joint infection. *Genij Ortopedii*. 2018;24(3):321-326. doi: 10.18019/1028-4427-2018-24-3-321-326.
7. Ermakov A., Kliushin N., Ababkov I., et al. One-stage revision arthroplasty for management of periprosthetic hip infection. *Genij Ortopedii*. 2019;25(2):172-179. doi: 10.18019/1028-4427-2019-25-2-172-179.
8. Sereda AP, Bogdan VN, Andrianova MA, Berenstein M. Treatment of Periprosthetic Infection: Where and Who? *Traumatology and Orthopedics of Russia*. 2019;25(4):33-55. (In Russ.) doi: 10.21823/2311-2905-2019-25-4-33-55.
9. Bozhkova SA, Novokshonova AA, Konev VA. Current trends in loCal antibaCterial therapy of periprosthetic infection and osteomyelitis. *Traumatology and Orthopedics of Russia*. 2015; (3):92-107. (In Russ.) doi: 10.21823/2311-2905-2015-0-3-92-107.
10. Murylev VYu, Parvizi J, Rudnev AI, et al. Results of the intraoperative alpha defensin lateral flow test in the second stage of revision hip arthroplasty. *Genij Ortopedii*. 2024;30(6):811-821. doi: 10.18019/1028-4427-2024-30-6-811-821.
11. Williams DF, Rouf R. *Implants in surgery* [Russian translation]. Moscow: Medicina; 1978:552. (In Russ.)
12. Prokhorenko VM, Pavlov VV. *Infectious complication in hip joint endoprosthetics*. Novosibirsk: Nauka; 2010:179. (In Russ.)
13. Abdullah NN, Abdullah H, Ramlee MH. Current trend of lattice structures designed and analysis for porous hip implants: A short review. *Materials Today Proceedings*. 2023. doi: 10.1016/j.matpr.2023.09.199.
14. Kharin N, Bolshakov P, Kuchumov AG. Numerical and Experimental Study of a Lattice Structure for Orthopedic Applications. *Materials (Basel)*. 2023;16(2):744. doi: 10.3390/ma16020744.
15. Kladovasilakis N, Tsongas K, Tzetzis D. Finite Element Analysis of Orthopedic Hip Implant with Functionally Graded Bioinspired Lattice Structures. *Biomimetics (Basel)*. 2020;5(3):44. doi: 10.3390/biomimetics5030044.
16. Luo S, Jiang T, Long L, et al. A dual PMMA/calcium sulfate carrier of vancomycin is more effective than PMMA-vancomycin at inhibiting Staphylococcus aureus growth in vitro. *FEBS Open Bio*. 2020;10(4):552-560. doi: 10.1002/2211-5463.12809.
17. Wall V, Nguyen TH, Nguyen N, Tran PA. Controlling Antibiotic Release from Polymethylmethacrylate Bone Cement. *Biomedicines*. 2021;9(1):26. doi: 10.3390/biomedicines9010026.
18. Mensah LM, Love BJ. A meta-analysis of bone cement mediated antibiotic release: Overkill, but a viable approach to eradicate osteomyelitis and other infections tied to open procedures. *Mater Sci Eng C Mater Biol Appl*. 2021;123:111999. doi: 10.1016/j.msec.2021.111999.
19. Paz E, Sanz-Ruiz P, Abenojar J, et al. Evaluation of Elution and Mechanical Properties of High-Dose Antibiotic-Loaded Bone Cement: Comparative "In Vitro" Study of the Influence of Vancomycin and Cefazolin. *J Arthroplasty*. 2015;30(8):1423-1429. doi: 10.1016/j.arth.2015.02.040.
20. Melikova RE, Tsiskarashvili AV, Artyukhov AA, Sokorova NV. In vitro study of the dynamics in elution of antibacterial drugs impregnated into matrices based on polymer hydrogel. *Genij Ortopedii*. 2023;29(1):64-70. doi: 10.18019/1028-4427-2023-29-1-64-70.
21. Miller R, McLaren A, Leon C, McLemore R. Mixing method affects elution and strength of high-dose ALBC: a pilot study. *Clin Orthop Relat Res*. 2012;470(10):2677-2683. doi: 10.1007/s11999-012-2351-2.
22. Samelis PV, Papagrigorakis E, Sameli E, et al. Current Concepts on the Application, Pharmacokinetics and Complications of Antibiotic-Loaded Cement Spacers in the Treatment of Prosthetic Joint Infections. *Cureus*. 2022;14(1):e20968. doi: 10.7759/cureus.20968.
23. Wu K, Chen YC, Hsu YM, Chang CH. Enhancing Drug Release From Antibiotic-loaded Bone Cement Using Porogens. *J Am Acad Orthop Surg*. 2016;24(3):188-195. doi: 10.5435/JAAOS-D-15-00469.
24. Shi M, Kretlow JD, Spicer PP, et al. Antibiotic-releasing porous polymethylmethacrylate/gelatin/antibiotic constructs for craniofacial tissue engineering. *J Control Release*. 2011;152(1):196-205. doi: 10.1016/j.jconrel.2011.01.029.
25. Spicer PP, Shah SR, Henslee AM, et al. Evaluation of antibiotic releasing porous polymethylmethacrylate space maintainers in an infected composite tissue defect model. *Acta Biomater*. 2013;9(11):8832-8839. doi: 10.1016/j.actbio.2013.07.018.

26. Mironov SP, Tsiskarashvili AV, Gorbatiuk DS. Chronic post-traumatic osteomyelitis as a problem of contemporary traumatology and orthopedics (literature review). *Genij Ortopedii*. 2019;25(4):610-621. doi: 10.18019/1028-4427-2019-25-4-610-621.
27. Samelis PV, Papagrigorakis E, Sameli E, et al. Current Concepts on the Application, Pharmacokinetics and Complications of Antibiotic-Loaded Cement Spacers in the Treatment of Prosthetic Joint Infections. *Cureus*. 2022;14(1):e20968. doi: 10.7759/cureus.20968.
28. Perry NPJ, Tucker NJ, Hadeed MM, et al. The Antibiotic Cement Bead Rouleaux: A Technical Trick to Maximize the Surface Area to Volume Ratio of Cement Beads to Improve the Elution of Antibiotics. *J Orthop Trauma*. 2022;36(9):369-373. doi: 10.1097/BOT.0000000000002335.
29. Kuropatkin GV, Akhtiamov IF. *Bone cement in traumotology and orthopaedic*. Kazan: Tagraf Publ.; 2014:188. (In Russ.)
30. 30. Stogov MV, Shastov AL, Kireeva EA, Tushina NV. Release of antibiotics from the materials for postosteomyelitic bone defect filling. *Genij Ortopedii*. 2024;30(6):873-880 doi: 10.18019/1028-4427-2024-30-6-873-880.

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