**Review article**
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# Elution of antibiotics from bone cement: problems and ways to solution

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**Abstract**

**Introduction** The widespread use of bone cement in the treatment of patients with orthopedic infections can be associated with limited elution of antibiotics with use of local spacers.

The **objective** was to determine problems of elution of antibiotics from bone cement and ways to solve them based on literature data.

**Material and methods** The original literature search was conducted on key resources including Scientific Electronic Library (www.elibrary.ru) and the National Library of Medicine (www.pubmed.org) (1994 to 2024) and using keywords: bone cement, PMMA, polymethylmethacrylate, antibiotic elution, bone cement, antibiotic elution, additive manufacturing, porous constructions, lattice structures. The sources were included based on the hypothesis that preformed implants based on a lattice structure could be used in combinations with bone cement.

**Results and discussion** The elution of antibiotics from bone cement can be improved through examination of the cement type, the porosity, the implant/spacer shape, the type of antibiotics, quantities and combinations administered that pose a difficult scientific problem in the absence of an acceptable solution along with the variety of publications. However, research in this area has not led to any complete solution.

**Conclusion** A paradigm has been developed for improving the elution of antibiotics from polymethyl methacrylate (PMMA) to include working with the cement: its composition, geometry and pyrogenicity. Solutions offered for improving the elution of antibiotics from PMMA are often impracticable and can deteriorate the performance properties of cement. Another approach can involve a research aimed at studying the effectiveness of spacers with a preformed base and bone cement coating, without or with minimal interference with the properties specified by the manufacturer.

**Keywords**: bone cement, polymethyl methacrylate, antibiotic elution, additive manufacturing, lattice structures

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## INTRODUCTION

Discovered in the 30s of the last century, bone cement (BC) based on polymethyl methacrylate (PMMA) has become an integral part of joint replacement due to its mechanical properties, commercial availability, the ability to release antibiotics, and greater knowledge compared to other transport systems. Since its introduction in 1970, antibiotic-impregnated cement has been used for the prevention and treatment of orthopedic infections [1, 2]. Despite the current use of other depot systems that are potentially superior to BC in the elution properties of antibiotics, as shown by *in vitro* and *in vivo* studies, BC will be in demand in clinical practice for many years to come [3, 4]. However, the study of the characteristics of antibiotic-impregnated cement has revealed a number of problems including the control of the antibiotic elution.

Despite the large number of publications on to the topic, there seems to be no confidence that the problem has been solved [5–11]. The elution of antibiotics from bone cement can be improved through examination of the cement type, the porosity, the implant/spacer shape, the type of antibiotics, quantities and combinations administered that pose a difficult scientific problem.

The **objective** was to determine problems of elution of antibiotics from bone cement and ways to solve them based on literature data.

## MATERIAL AND METHODS

The original literature search was conducted on key resources including Scientific Electronic Library (www.elibrary.ru) and the National Library of Medicine (www.pubmed.org) (1994 to 2024) and using keywords: bone cement, PMMA, polymethylmethacrylate, antibiotic elution, bone cement, antibiotic elution. The review included articles that contained information about elution of antibiotics from bone cement and/or ways to improve it. The sources included in the Discussion were selected based on the hypothesis that preformed lattice-based implants can be used with bone cement. Search words in the “Discussion” section included additive manufacturing, porous constructions, lattice structures, additive manufacturing, lattice structures.

## RESULTS

### *Elution depending on the type of cement*

BCs vary depending on the manufacturer, viscosity, duration of polymerization, intended use, the presence of additional inclusions and, accordingly, have different antibiotic release abilities. For example, comparison of antibiotic elution from medium- and high-viscosity cement illustrates the specific release for each species. Although both cements contain the same amount of antibiotic, it is Palacos® R+G that releases more gentamicin [9].

Ensig et al. [12] reported the release of gentamicin and clindamycin from Copal bone cement (Biomet Merck, Darmstadt, Germany) over 28 days with long-lasting inhibition of *S. aureus* GS and coagulase-negative *S. aureus* GR. However, Palacos R-G bone cement (Schering-Plough, Maarssen, the Netherlands) failed to provide a continuous significant release of gentamicin after the first 24 hours [13].

### *Antibiotic elution depending on the shape of the bone cement implant*

Although the shape of the implanted bone cement component depends on anatomical features, there is a proven correlation between shape and antibiotic elution. Duey et al. [14] were unable to detect a difference between the volumes of implanted BCs, and reported a direct relationship between the implant area and antibiotic release.

The larger the area, the higher the release of the antibiotic, as reported by Masri et al. [15]. Their study revealed an increase in antibiotic elution with increased antibiotic area and constant cement volume. This circumstance is explained by the fact that the release of the antibiotic occurs from the most superficial layers of cement. The overwhelming amount of antibiotic was eluted from the 100-μm-thick superficial layer, whereas only 19 % was eluted from the deeper 700-μm-thick layer [9].

***Antibiotic elution depending on bone cement porosity***

The porous structure of bone cement increases the surface area of the release (due to contact with the environment), hence the release of the antibiotic. Miller et al. [16] created highly porous bone cement by adding vancomycin pieces. A significantly higher elution of the antibiotic was observed with the antibiotic being thoroughly ground before adding it to the BC [16]. The nonhomogeneous distribution of the antibiotic in the BC can lead to uneven release of the antibiotic. McLaren et al. [17] compared different methods for manual homogenization of cement and antibiotic and did not find that manual mixing resulted in uneven release of the antibiotic. Lewis et al. [18] analyzed manually loaded and premixed Cemex (Tecres, Sommacampagna, Italy). Although similar cement structures were reported in the series after polymerization, the elution rate of the artisanal antibiotic was on average 36 % lower [18]. Because of these rather contradictory results, some authors would not recommend the use of artisanal addition of antibiotics to BC, arguing that industrially produced BC with antibiotic ensure a uniform release of the latter [18].

Regardless of the method used to add antibiotic to bone cement, porosity can be altered using a vacuum mixing system that is designed to reduce air entrapment into the cement. However, the effect of vacuum method on antibiotic elution would depend on factors such as the solubility of the antibiotic in water, the diffusion gradient and the type of cement [19, 20].

Meyer et al. compared the effect of a vacuum mixing system on various commercially available BCs containing gentamicin. Antibiotic elution was increased using a vacuum mixer for Palacos® R+G and Cobalt® G-HV (Biomet, Warsaw, IN, USA), and was decreased for Cemex® Genta (Exactech, Gainesville, FL, USA), SmartSet® GMV (DePuy, Warsaw, IN, USA) and VersaBond® AB (Smith & Nephew, London, UK) [21].

Porosity can be further modified *in vitro* using special additives [22]. Shi et al. found that gelatin promoted the formation of pores in bone cement [23]. Chen et al. explored the correlation of PMMA porosity, the particle size and gelatin mass fraction [24]. Other components that can increase bone cement porosity include calcium phosphate (CaP) compounds, thereby increasing drug elution [25]. Calcium carbonate is another porogenic compound, which is a component of the commercially available Copal® spacem bone cement, specifically designed for use as a spacer base. Bitsch et al. [26] reported the microporous structure of the cement, in contrast to the dense structure of Palacos® R+G, several antibiotics showed better washing out with Copal® spacem. However, another study was unable to confirm the claimed antibiotic elution characteristics of Copal® spacem and Palacos® R+G cements with a combination of vancomycin and gentamicin loaded into the two cements [27]. Biodegradable polymers based on polylactic-glycolic acid (PLGA) can be used to increase the porosity of the BC controlling the elution of antibiotics [28–30]. Large crystals of table salt can be optionally used in the outer layers of the BC implant. The dissolved salt leaves voluminous lacunae in the superficial layers of the implant increasing the antibiotic volume releasing into the environment [31]. Perforation of the implant at the stage of manufacturing from BC is a simple way to increase the effectiveness of the antibiotic [32].

***Elution of antibiotics and combinations depending on the type, quantity and technology of inclusion into the BC***

Antibiotics added to BC reduces the mechanical characteristics due to changes in the cement polymerization with antibiotic molecules. Hsieh et al. reported a 37 % reduction in compressive strength with a gentamicin solution added to Simplex CC (Stryker, Kalamazoo, MI, USA) [33]. The current consensus is that only crystalline antibiotics that have been found to be suitable for inclusion in BC *in vitro* should be added to BC [34, 35]. The mechanical properties of BC can be affected by the shape and the type. Some antibiotics can impair BC polymerization to a greater extent. For example, rifampicin, which has a crystalline structure, can completely suppress the BC polymerization processes [36].

The temperature stability of antibiotic is to be evaluated prior to the use since BC can heat up above 50–60° Celsius during polymerization. A short-term heating to 80° during polymerization did not lead to the destruction of anti-tuberculosis drugs [37]. The quantity of antibiotic to be added has not yet been definitively established. The BC Palacos® R+G and Copal® spacem added as a 2.5 % antibiotic fraction reduced the compressive strength of bone cement to a value close to the required 70 MPa [27].

Lilikakis et al. reported the effect of vancomycin added to BC Palamed® (Haereus, Hanau, Germany) and Copal® G+C (Haereus, Hanau, Germany) and found that the addition of 5 % vancomycin maintained the compressive strength of BC well above the required 70 MPa for both cements. Addition of 10 % vancomycin decreased the compressive strength by 18.15 and 17.48 %, respectively, and the compressive strength of both cements remained above the threshold value of 70 MPa [38]. A 5–10 % antibiotic concentration in BC is considered sufficient for a temporary spacer [34, 35, 38, 39]. Since the mechanical load on the temporary spacer can be controlled by limiting the weight, some authors allow an increase in the proportion of antibiotic to 20 % during its manufacture [40], but the dose of antibiotic increased above 5 % can lead to a slowdown polymerization of bone cement [37].

The technique of adding antibiotics to BC raises questions. Kuhn et al. reported the need for careful homogenization of the antibiotic crystals and the dry BC when adding the antibiotic in fractions [34]. Parvizi et al. offered the immediate addition of an antibiotic to the cement powder leading to “rough” homogenization. The technique facilitates maximum washing out of the antibiotic after the solidification of the BC due to the formation of conglomerates of the added drug [41]. Laine et al. compared the effects of different methods of adding antibiotics and confirmed the effect of the difference in the degree of homogenization of BC and antibiotic. Failed homogenization can result in the formation of pores in the BC. Subsequent mechanical tests revealed no significant difference in its strength [42].

Thus, the choice of an antibiotic for inclusion in the BC is determined by its availability, sterility, thermal stability, the presence or absence of a crystalline powder form, and sufficient elution kinetics.

The release of antibiotics occurs either continuously or in an “explosive” manner. Gentamicin is a typical representative of elution with continuous kinetics [9]. Vancomycin is usually released explosively with a high initial release rate followed by a sharp decline. Galvez-Lopez et al. compared the elution kinetics of 11 different antibiotics and concluded that each antibiotic exhibited its own release pattern. For example, moxifloxacin showed a longer release than vancomycin, meropenem showed continuously decreasing elution kinetics over a long period of time [36].

The combination of antibiotics affects differently on elution. The synergistic and antagonistic effects of antibiotics included in BC have been described. Hsieh et al. studied the elution of gentamicin and vancomycin from Simplex® BC. This combination increased the release of vancomycin by 145 % and gentamicin by 45 %, respectively [33]. Paz et al. explored combinations of more than two antibiotics: the addition of cefazolin significantly increased the elution of vancomycin from BC, which also contained gentamicin [43]. However, the kinetics of elution can be changed by the combination of antibiotics and by their relative mass in the BC. The significant increase in the kinetics of gentamicin elution with an increase in the proportion of vancomycin in cement is an example [20]. Kaplan et al. studied the combination of daptomycin and tobramycin and found an increase in the release kinetics of daptomycin with an initial increase in the amount of tobramycin [44].

An increased proportion of antibiotic in the cement is a simple way to increase the kinetics of antibiotic elution for a local effect on the microflora with use of the BC spacer in a number of combinations. An increased amount of vancomycin led to an increase in the elution of the antibiotic from cement [27].

A combination of silver preparations with various antibiotics can be used to increase the activity of antibiotics against pathogenic microflora [45–47]. A summary of factors affecting antibiotic elution and ways to improve it is given in Table 1.

Table 1

Factors affecting the elution of antibiotics

| Author, year | Type of BC used | Antibiotics used (AB) | Factor influencing AB elution | Result |
|---|---|---|---|---|
| Ensing et al., 2014 [12] | Copal, Palacos R-G | Gentamicin, Clindamycin | Depending on the type of BC | BC Copal outperforms Palacos R-G |
| Duey et al., 2012 [14] | Simplex P | Tobramycin, Vancomycin | Increased BC area | An increased area leads to an increase in AB elution |
| Masri et al., 1995 [15] | Simplex P | Gentamicin | Increased BC area | An increased area leads to an increase in AB elution |
| Miller et al., 2012 [16] | Simplex P | Vancomycin | Increasing the porosity of BC during mixing due to the inclusion of greater volume of AB | An increase in BC porosity led to an increase in AB elution |
| McLaren et al., 2009 [17] | Cemex G, Cobalt G-HV, Palacos G, Simplex P, Smart Set G HV | Gentamicin | Method of BC mixing | There was no difference between “handicraft” and factory mixing of BC and AB |
| Lewis et al., 2005 [18] | Cemex G | Gentamicin | Method of BC mixing | Artisanal mixing of CC with AB reduces the elution rate |
| Meyer et al., 2011 [21] | Palacos R+G, Cobalt G-HV, Cemex Genta | Gentamicin | Using Vacuum Mixing | AB elution is increased in Palacos R+G and Cobalt G-HV, and decreased in Cemex Genta |
| Wu et al., 2016 [22] | Osteobond copolymer bone cement, Zimmer | Gentamicin | Increasing the porosity of BC by adding gelatin and ceramic granules | The addition of porogens increased AB elution. AB elution was higher with the addition of gelatin |
| Shi et al., 2011 [23] | SmartSet | Colistin | Increasing the porosity of BC by adding gelatin | Addition of gelatin increases the porosity of BC |
| Chen et al., 2019 [24] | Mendec Spine Resin and Kit | Gentamicin | Increasing the porosity of BC by adding gelatin | An increase in the mass fraction of gelatin correlates with an increase in AB elution |

Table 1 (continued)

Factors affecting the elution of antibiotics

| Author, year | Type of BC used | Antibiotics used (AB) | Factor influencing AB elution | Result |
|---|---|---|---|---|
| Bitsch et al., 2015 [26] | Copal, Palacos R+G | Gentamicin | Increasing the porosity of BC by adding $CaCO_3$ to Copal BC | Addition of $CaCO_3$ increases AB elution |
| Boelch et al., 2018 [27] | Copal, Palacos R+G | Gentamicin | Increasing the porosity of BC by adding $CaCO_3$ to Copal BC | No difference in elution detected |
| Spicer et al., 2013 [30] | | Colistin | Increasing the porosity of BC by adding polylactic-co-glycolic acid (PGLA) | Addition of PGLA increases elution |
| Akhtyamov et al., 2015 [31] | Not specified | Not specified | Adding table salt crystals to the solidifying BC | When dissolved, table salt increases the area of AB release |
| Kuropatkin, Akhtyamov, 2014 [32] | Not specified | Not specified | Increasing the area of the BC due to the perforation | Increased BC area increases AB elution |
| Zahar, Hannah, 2016 [40] | Not specified | Not specified | Increasing the mass fraction of AB up to 20 % | An increase in the AB mass fraction leads to an increase in AB elution |
| Laine et al., 2011 [42] | DePuy SmartSet MV Bone Cement | Vancomycin | Elimination of homogenization process during mixing | Increase in pores in the BC with homogenization failure during mixing |
| Galvez-Lopez et al., 2014 [36] | Medium viscosity bone cement DePuy | Vancomycin Gentamicin Daptomycin Moxifloxacin, Rifampicin, Cefotaxime, Cefepime, Amoxicillin clavulanate, Ampicillin, Meropenem Ertapenem | Type of AB | Elution varies depending on the type of AB |
| Hsieh et al., 2009 [33] | Simplex | Vancomycin Gentamicin | Combined AB | Both ABs potentiated an increase in each other's elution |
| Paz et al., 2015 [43] | Palacos R + G | Cefazolin Vancomycin | Combined AB | The addition of cefazolin significantly increased the elution of vancomycin from bone cement also containing gentamicin |
| Kaplan et al., 2012 [44] | Not specified | Daptomycin Tobramycin | Combined AB | Increasing the initial concentration of tobramycin increases the elution of daptomycin |
| Peretsmanas et al., 2021 [37] | Cemex | Isoniazid Cycloserine, Rifampicin Amikacin, Kanamycin, Ethambutol | Type of AB | Different types of anti-tuberculosis drugs showed different elution dynamics |
| Gordina et al., 2024 [45] | Depuy CMW 1 Gentamicin | Ceftazidime Vancomycin Poviargol | Adding silver preparations | Increasing silver preparations increased the AB efficiency of the samples |
| Bozhkova et al., 2023 [46] | Depuy CMW 1 Gentamicin | Vancomycin Poviargol | Adding silver preparations | The addition of silver preparations increased the AB efficiency of the samples |
| Bozhkova et al., 2021 [47] | Depuy CMW 1 Gentamicin | Vancomycin Poviargol | Adding silver preparations | The combination of vancomycin with highly dispersed silver prolonged the antimicrobial activity of the samples |

## DISCUSSION

Publications indicated a paradigm that emerged to improve the elution of antibiotics from PMMA involving the quality of the cement: the composition, geometry and structure. However, the investigation did not lead to any complete solution, being often impracticable/cannot be implemented, and sometimes neglecting the costs and quality properties of BC.

Hypothetically, an increase in cement surface area, porosity, and therefore antibiotic release could be achieved through customized design. In this case, the structure of the implant should allow to place the cement inside the product and form a contact area of the implant with cement and the bone, allowing the antibiotic to elute from the deeper layers of the BC. An implant with a lattice structure can be one of the solutions to allow the antibiotic loaded cement be placed inside the product, increasing the contact area and porosity maintaining the quality and performance properties.

Bolshakov et al. [48] reported the results of the design and optimization of a lattice implant for a rabbit leg; a morphological study indicates maintained diffusion of substances and cell migration through the latticed implant. Cement can be placed inside the latticed implant using a special silicone matrix, similar to the one used for casting spacers. Eminences are essential for the silicone matrix to form a contact area and increase the free surface area of the cement.

Latticed implants are commonly manufactured using additive technologies [49–51]. The technology facilitate production of customized products for the patient and a complex irregular three-dimensional geometry [52, 53]. Products manufactured with additive technologies provide the strength, biocompatibility, biodegradability and sterilizability [54, 55]. With SLM metal printing, medical device manufacturers can produce patient-specific implants and prosthetics with exact dimensions and optimal surface finishes, ensuring perfect compatibility and function. SLM metal printing supports the incorporation of porous structures into implants, promoting osseointegration [56, 57]. With advances in personalized medicine, organs to be replaced can be scanned preoperatively. Computed tomography is one of the methods for obtaining a digital image of an organ [58–61]. This solution allows for numerical calculations to assess the stress-strain state of implants and bone organs [57].

The most common are Two methods are common to design products manufactured with additive technologies [62]. The first method suggests the use of elementary cells for design, they are also the basic elements that fill the volume of the product [63]. Kharin et al. [64] report the influence of the distribution of the unit cell on the strength of the construct. The second method suggests topological or structural optimization. Bolshakov et al. [65] explored optimization methods for hip implants and reported 11 % porosity of the implants achieved without compromising the strength characteristics.

Therefore, lattice implants in conjunction with BC and antibiotics could improve the elution of the antibiotic from BC without interfering or minimally interfering with the parameters specified by the manufacturer and could be one of the options for solving the problem. With the paucity of publications on this issue, the hypothesis requires confirmation.

## CONCLUSION

The disadvantages of PMMA-based BC can be leveled up by its obvious advantages in the treatment and prevention of orthopedic infections, which will remain relevant for many years with the advances of antibiotic-resistant microflora.

Numerous publications on experimental and clinical use of BC demonstrate a striking contradiction in approaches to the use of PMMA-based BC. Local control of the infectious process, control of the elution of antibiotics with use of BC spacers are essential.

A paradigm has been developed for improving the elution of antibiotics from PMMA to include the cement parameters: its composition, geometry and structure. However, adherence to the paradigm demonstrated no complete solution, and was shown to be impracticable reducing the performance of the BC.

Another approach suggests a research aimed at exploring the efficacy of preformed bone cement spacers, without or with minimal interference with the characteristics specified by the manufacturer.

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REFERENCES

1. Romanò CL, Scarponi S, Gallazzi E, et al. Antibacterial coating of implants in orthopaedics and trauma: a classification proposal in an evolving panorama. *J Orthop Surg Res*. 2015;10:157. doi: 10.1186/s13018-015-0294-5.
2. Winkler H, Haiden P. Allograft Bone as Antibiotic Carrier. *J Bone Jt Infect*. 2017;2(1):52-62. doi: 10.7150/jbji.17466.
3. 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.
4. Tsiskarashvili AV, Melikova RE, Volkov AV, et al. In vivo effectiveness of polymer hydrogels impregnated with an antibacterial drug in chronic osteomyelitis. *Genij Ortopedii*. 2023;29(5):535-545. doi: 10.18019/1028-4427-2023-29-5-535-545.
5. Amin TJ, Lamping JW, Hendricks KJ, McIff TE. Increasing the elution of vancomycin from high-dose antibiotic-loaded bone cement: a novel preparation technique. *J Bone Joint Surg Am*. 2012;94(21):1946-1951. doi: 10.2106/JBJS.L.00014.
6. Anagnostakos K, Kelm J, Regitz T, et al. In vitro evaluation of antibiotic release from and bacteria growth inhibition by antibiotic-loaded acrylic bone cement spacers. *J Biomed Mater Res B Appl Biomater*. 2005;72(2):373-378. doi: 10.1002/jbm.b.30171.
7. Ensing GT, Hendriks JG, Jongsma JE, et al. The influence of ultrasound on the release of gentamicin from antibiotic-loaded acrylic beads and bone cements. *J Biomed Mater Res B Appl Biomater*. 2005;75(1):1-5. doi: 10.1002/jbm.b.30140.
8. Frutos G, Pastor JY, Martínez N, et al. Influence of lactose addition to gentamicin-loaded acrylic bone cement on the kinetics of release of the antibiotic and the cement properties. *Acta Biomater*. 2010;6(3):804-811. doi: 10.1016/j.actbio.2009.08.028.
9. von Hertzberg-Boelch SP, Luedemann M, Rudert M, Steinert AF. PMMA Bone Cement: Antibiotic Elution and Mechanical Properties in the Context of Clinical Use. *Biomedicines*. 2022;10(8):1830. doi: 10.3390/biomedicines10081830.
10. Wall V, Nguyen TH, Nguyen N, Tran PA. Controlling Antibiotic Release from Polymethylmethacrylate Bone Cement. *Biomedicines*. 2021;9(1):26. doi: 10.3390/biomedicines9010026.
11. Bozhkova SA, Novokshonova AA, Konev VA. Modern possibilities of local antibiotic therapy for periprosthetic infection and osteomyelitis (literature review). *Traumatology and orthopedics of Russia*. 2015;21(3):92-107. (In Russ.) doi: 10.21823/2311-2905-2015-0-3-92-107.
12. Ensing GT, van Horn JR, van der Mei HC, et al. Copal bone cement is more effective in preventing biofilm formation than Palacos R-G. *Clin Orthop Relat Res*. 2008;466(6):1492-1498. doi: 10.1007/s11999-008-0203-x.
13. Kendall RW, Duncan CP, Smith JA, Ngui-Yen JH. Persistence of bacteria on antibiotic loaded acrylic depots. A reason for caution. *Clin Orthop Relat Res*. 1996;(329):273-280. doi: 10.1097/00003086-199608000-00034.
14. Duey RE, Chong AC, McQueen DA, et al. Mechanical properties and elution characteristics of polymethylmethacrylate bone cement impregnated with antibiotics for various surface area and volume constructs. *Iowa Orthop J*. 2012;32:104-115.
15. Masri BA, Duncan CP, Beauchamp CP, et al. Effect of varying surface patterns on antibiotic elution from antibiotic-loaded bone cement. *J Arthroplasty*. 1995;10(4):453-459. doi: 10.1016/s0883-5403(05)80145-7.
16. 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.
17. McLaren AC, Nugent M, Economopoulos K, et al. Hand-mixed and premixed antibiotic-loaded bone cement have similar homogeneity. *Clin Orthop Relat Res*. 2009;467(7):1693-1698. doi: 10.1007/s11999-009-0847-1.
18. Lewis G, Janna S, Bhattaram A. Influence of the method of blending an antibiotic powder with an acrylic bone cement powder on physical, mechanical, and thermal properties of the cured cement. *Biomaterials*. 2005;26(20):4317-4325. doi: 10.1016/j.biomaterials.2004.11.003.
19. 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.
20. Kuhn KD. *PMMA Cements*. Berlin: Springer; 2014:303.

21. Meyer J, Piller G, Spiegel CA, et al. Vacuum-mixing significantly changes antibiotic elution characteristics of commercially available antibiotic-impregnated bone cements. *J Bone Joint Surg Am*. 2011;93(22):2049-2056. doi: 10.2106/JBJS.J.01777.
22. 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.
23. 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.
24. Chen L, Tang Y, Zhao K, et al. Fabrication of the antibiotic-releasing gelatin/PMMA bone cement. *Colloids Surf B Biointerfaces*. 2019;183:110448. doi: 10.1016/j.colsurfb.2019.110448.
25. Fini M, Giavaresi G, Aldini NN, et al. A bone substitute composed of polymethylmethacrylate and alpha-tricalcium phosphate: results in terms of osteoblast function and bone tissue formation. *Biomaterials*. 2002;23(23):4523-4531. doi: 10.1016/s0142-9612(02)00196-5.
26. Bitsch RG, Kretzer JP, Vogt S, et al. Increased antibiotic release and equivalent biomechanics of a spacer cement without hard radio contrast agents. *Diagn Microbiol Infect Dis*. 2015;83(2):203-209. doi: 10.1016/j.diagmicrobio.2015.06.019.
27. Boelch SP, Rueckl K, Fuchs C, et al. Comparison of Elution Characteristics and Compressive Strength of Biantibiotic-Loaded PMMA Bone Cement for Spacers: Copal® Spacem with Gentamicin and Vancomycin versus Palacos® R+G with Vancomycin. *Biomed Res Int*. 2018;2018:4323518. doi: 10.1155/2018/4323518.
28. Gentile P, Chiono V, Carmagnola I, Hatton PV. An overview of poly(lactic-co-glycolic) acid (PLGA)-based biomaterials for bone tissue engineering. *Int J Mol Sci*. 2014;15(3):3640-3659. doi: 10.3390/ijms15033640.
29. Mader JT, Calhoun J, Cobos J. In vitro evaluation of antibiotic diffusion from antibiotic-impregnated biodegradable beads and polymethylmethacrylate beads. *Antimicrob Agents Chemother*. 1997;41(2):415-418. doi: 10.1128/AAC.41.2.415.
30. 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.
31. Akhtyamov IF, Kaminskiy AV, Pollyak LN, et al. *Method for manufacturing a spacer from bone cement*. Patent RF, no. 2542510, 2015. Available at: https://www.fips.ru/registers-doc-view/fips_servlet?DB=RUPAT&rn=9871&DocNumber=2542510&TypeFile=html. Accessed Oct 16, 2024.
32. Kuropatkin GV, Akhtyamov IF. *Bone cement in surgery*. Kazan: TaGraf Publ.; 2014:128-131. (In Russ.).
33. Hsieh PH, Tai CL, Lee PC, Chang YH. Liquid gentamicin and vancomycin in bone cement: a potentially more cost-effective regimen. *J Arthroplasty*. 2009;24(1):125-130. doi: 10.1016/j.arth.2008.01.131.
34. Kühn KD, Renz N, Trampuz A. Local antibiotic therapy. *Unfallchirurg*. 2017;120(7):561-572. (In German) doi: 10.1007/s00113-017-0372-8.
35. Anagnostakos K. Therapeutic Use of Antibiotic-loaded Bone Cement in the Treatment of Hip and Knee Joint Infections. *J Bone Jt Infect*. 2017;2(1):29-37. doi: 10.7150/jbji.16067.
36. Gálvez-López R, Peña-Monje A, Antelo-Lorenzo R, et al. Elution kinetics, antimicrobial activity, and mechanical properties of 11 different antibiotic loaded acrylic bone cement. *Diagn Microbiol Infect Dis*. 2014;78(1):70-74. doi: 10.1016/j.diagmicrobio.2013.09.014.
37. Peretsmanas EO, Artyukhov AA, Shtilman MI, et al. Study of elution characteristics of anti-tuberculosis drugs mixed with bone cement. *Tuberculosis and Lung Diseases*. 2021;99(4):30-35. (In Russ.) doi: 10.21292/2075-1230-2021-99-4-30-35.
38. Lilikakis A, Sutcliffe MP. The effect of vancomycin addition to the compression strength of antibiotic-loaded bone cements. *Int Orthop*. 2009;33(3):815-819. doi: 10.1007/s00264-008-0521-3.
39. Lachiewicz PF, Wellman SS, Peterson JR. Antibiotic Cement Spacers for Infected Total Knee Arthroplasties. *J Am Acad Orthop Surg*. 2020;28(5):180-188. doi: 10.5435/JAAOS-D-19-00332.
40. Zahar A, Hannah P. Addition of antibiotics to bone cement for septic prosthesis exchange. *Oper Orthop Traumatol*. 2016;28(2):138-144. (In German) doi: 10.1007/s00064-015-0424-6.
41. Parvizi J. Antibiotic spacers in the infected hip: optimising placement. *Orthop Procs*. 2017;99-B(SUPP_7):126-126. doi: 10.1302/1358-992X.99BSUPP_7.CCJR2016-126.
42. Laine JC, Nguyen TQ, Buckley JM, Kim HT. Effects of mixing techniques on vancomycin-impregnated polymethylmethacrylate. *J Arthroplasty*. 2011;26(8):1562-1566. doi: 10.1016/j.arth.2011.02.011.
43. 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.
44. Kaplan L, Kurdziel M, Baker KC, Verner J. Characterization of daptomycin-loaded antibiotic cement. *Orthopedics*. 2012;35(4):e503-e509. doi: 10.3928/01477447-20120327-19.
45. Gordina EM, Bozhkova SA, Gazhdimagomedov MSh. Antibacterial effect of ceftazidime, vancomycin combinations with silver in bone cement. *Problems in medical mycology*. 2024;26(2):104.
46. Bozhkova SA, Gordina EM, Artyukh VA, Yudin VE. Combined effect of vancomycin and silver in bone cement composition against the main pathogens causing periprosthetic infection. *Siberian Medical Review*. 2023;(1):37-45. (In Russ.) doi: 10.20333/25000136-2023-1-37-45.
47. Bozhkova SA, Gordina EM, Markov MA, et al. he Effect of Vancomycin and Silver Combination on the Duration of Antibacterial Activity of Bone Cement and Methicillin-Resistant Staphylococcus aureusBiofilm Formation. *Traumatology and Orthopedics of Russia*. 2021;27(2):54-64. (In Russ.) doi: 10.21823/2311-2905-2021-27-2-54-64.
48. Bolshakov P, Raginov I, Egorov V, et al. Design and Optimization Lattice Endoprosthesis for Long Bones: Manufacturing and Clinical Experiment. *Materials* (Basel). 2020;13(5):1185. doi: 10.3390/ma13051185.
49. Kilina PN, Sirotenko LD, Kozlov MS, Drozdov AA. Quality assurance thermophysical aspects of highly porous implants with cellular structure obtained by selective laser melting. *Russian Journal of Biomechanics*. 2023;27(4):200-211. (In Russ.) doi: 10.15593/RZhBiomeh/2023.4.16.
50. Borovkov AI, Maslov LB, Zhmaylo MA, et al. Elastic properties of additively produced metamaterials based on lattice structures. *Materials Physics and Mechanics*. 2023;51(7):42-62. doi: 10.18149/MPM.5172023_6.

51. Sushentsov EA, Musaev ER, Maslov LB, et al. Computer simulation, 3D-printing and custom-made prosthetics in treatment of a patient with osteosarcoma of the pelvis. *Bone and soft tissue sarcomas, tumors of the skin*. 2019;11(4):53-61. (In Russ.).
52. Akifyev KN, Kharin NV, Statsenko EO, et al. Pilot study of lattice endoprosthesis buckling by compression in-situ using x-ray tomography. *Russian Journal of Biomechanics*. 2023;27(4):40-49. (In Russ.) doi: 10.15593/RZhBiomeh/2023.4.03.
53. Fedorova NV, Kosinov AM. Determination mechanical properties and permeability of porous titanium alloy bone implants, including under conditions of their interaction with biological fluids. *Russian Journal of Biomechanics*. 2023;28(1):54-66. (In Russ.) doi: 10.15593/RZhBiomeh/2024.1.04.
54. Abdudeen A, Qudeiri JEA, Kareem A, Valappil AK. Latest developments and insights of orthopedic implants in biomaterials using additive manufacturing technologies. *J Manuf Mater Process*. 2022;6(6):162. doi: 10.3390/jmmp6060162.
55. Frazar EM, Shah RA, Dziubla TD, Hilt JZ. Multifunctional temperature-responsive polymers as advanced biomaterials and beyond. *J Appl Polym Sci*. 2020;137(25):48770. doi: 10.1002/app.48770.
56. Sufiiarov VSh, V Borisov EV, Sokolova VO, et al. Structural analysis of an endoprosthesis designed with graded density lattice structures. *Int J Numer Method Biomed Eng*. 2021;37(2):e3420. doi: 10.1002/cnm.3420.
57. Müller P, Gembarski PC, Lachmayer R. Design automation of a patient-specific endoprosthesis with multi- objective optimized lattice structures. In: Lachmayer R, Bode B, Kaierle S. (eds.) *Innovative Product Development by Additive Manufacturing 2021*. Springer International Publ.; 2022:113-128. doi:10.1007/978-3-031-05918-6_8.
58. Gerasimov O, Kharin N, Statsenko E, et al. Patient-Specific Bone Organ Modeling Using CT Based FEM. In: *Lecture Notes in Computational Science and Engineering*. Cham: Springer; 2022;141:125-139. doi: 10.1007/978-3-030-87809-2_10.
59. Gerasimov OV, Kharin NV, Fedyanin AO, et al. Bone Stress-Strain state Evaluation using CT based FEM. *Front. Mech. Eng*. 2021;7:688474. doi: 10.3389/fmech.2021.688474.
60. Gerasimov OV, Rakhmatulin RR, Baltina TV, Sachenkov OA. Determination of the bone tissue mechanical properties by a numerical-digital method using CT data. *Russian Journal of Biomechanics*. 2023;27(3):53-66. (In Russ.) doi: 10.15593/RZhBiomech/2023.3.04.
61. Kharin NV, Gerasimov OV, Bolshakov PV, et al. Technique for determining the orthotropic properties of the bone organ according to computer tomography. *Rus J Biomech*. 2019;23(3):460-468. (In Russ.) doi: 10.15593/RZhBiomeh/2019.3.11.
62. Bolshakov P, Kharin N, Agathonov A, et al. Extension of the Voronoi Diagram Algorithm to Orthotropic Space for Material Structural Design. *Biomimetics* (Basel). 2024;9(3):185. doi: 10.3390/biomimetics9030185.
63. Bolshakov P, Kharin N, Kashapov R, Sachenkov O. Structural Design Method for Constructions: Simulation, Manufacturing and Experiment. *Materials* (Basel). 2021;14(20):6064. doi: 10.3390/ma14206064.
64. 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.
65. Bolshakov P, Kuchumov AG, Kharin N, et al. Method of computational design for additive manufacturing of hip endoprosthesis based on basic-cell concept. *Int J Numer Method Biomed Eng*. 2024;40(3):e3802. doi: 10.1002/cnm.3802.

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