Original article
https://doi.org/10.18019/1028-4427-2026-32-2-214-224

Application of platelet-rich plasma in compensating bone defects with ceramic Implants

I.P. Antropova, E.A. Volokitina✉, K.A. Timofeev, R.A. Trufanenko, S.M. Kutepov, L.G. Polushina

Ural State Medical University, Ekaterinburg, Russian Federation

Corresponding author: Elena A. Volokitina, Volokitina_elena@rambler.ru

Abstract

Introduction The use of ceramic materials is a promising approach to bone defect repair. Various orthobiological agents are used to improve their properties and enhance their regenerative potential.

The **aim** of this study was to determine the efficacy of platelet-rich plasma in repairing bone defects with yttria-doped zirconia ceramic implants.

Materials and Methods Bioceramic samples were zirconium dioxide. The ceramic implants measured 0.15 × 0.15 × 1.00 cm. Male Chinchilla rabbits were used in the experiment: Group 1 (n = 10) included animals that underwent bilateral metaphyseal bone defect filling with implantation of ceramic augments; Group 2 (n = 10) included animals that underwent bone defect repair without implantation. Platelet-rich plasma (PRP) was injected into the bone defect in the right femur of rabbits in both groups; PRP was not injected into the defect in the left femur. Blood samples were collected preoperatively and at the end of the experiment, four and eight weeks after surgery. Key blood parameters, including C-reactive protein, and platelet-derived growth factor (PDGF) in PRP were determined. To assess the effect of PRP on the dynamics of osteogenesis, a comparative histological analysis of the tissue structure in the simulated bone defect area was conducted.

Results No significant differences were found between the groups in key parameters of leukocytes, erythrocytes, and platelets, or C-reactive protein levels, either preoperatively or eight weeks after surgery. The concentration of PDGF in the injected PRP did not differ significantly between the groups. Histological analysis showed that injection of PRP increased the number of regenerating bone trabeculae and reduced the number and size of fibrotic foci and osteochondral callus in both groups.

Discussion Autologous PRP has previously been shown to be a simple and effective way to enhance bone regeneration due to the release of multiple growth factors by platelets, which regulate key biological processes, including angiogenesis, inflammation resolution, and tissue regeneration. Our study aimed to investigate whether platelet-rich plasma enhances the osteogenic potential of zirconia ceramic implants in bone defect repair. Our results confirm that PRP, with a platelet concentration of 800 × 10^9/L to 1200 × 10^9/L, a white blood cell count of 4–7 %, and a red blood cell count of no more than 1 % of the baseline blood count, may be a useful tool for bone regeneration.

Conclusion The use of PRP is effective in compensating bone defects using zirconia ceramic implants. However, further rigorous clinical studies are needed to integrate PRP-based methods into evidence-based medical practice.

Keywords: bone tissue, defect repair, implant, zirconium ceramics, platelet-rich plasma, osseointegration, experiment

For citation: Antropova IP, Volokitina EA, Timofeev KA, Trufanenko RA, Kutepov SM, Polushina LG. Application of platelet-rich plasma in compensating bone defects with ceramic Implants. *Genij Ortopedii*. 2026;32(2):214-224. doi: 10.18019/1028-4427-2026-32-2-214-224.

INTRODUCTION

Bone defect repair is a key objective in modern traumatology and orthopedics. Every year, the number of injuries, degenerative diseases, and oncological pathologies involving bone tissue and requiring surgical treatment and, in some cases, defect repair continue to grow. The number of surgical interventions for intra-articular and comminuted fractures with bone defects is increasing every year [1, 2, 3].

Various osteoplastic materials are used to compensate bone defects. Autografts are considered the "gold standard," but their use is associated with potential complications, both at the donor site and at the site of defect 4]. The use of allografts and xenografts also has significant drawbacks [5]. A shortage of natural sources, coupled with the growing demand for implants, has stimulated the search for and development of artificial materials for osteoplasty.

One promising area for bone defect repair is the use of ceramic materials. The broad range of properties of bioceramics and their good compatibility with human tissue make this material potentially suitable for solving a wide range of problems in traumatology and orthopedics [6]. Yttria-stabilized zirconia dioxide bioceramics occupy an important place. This material exhibits exceptional mechanical properties and biocompatibility, and does not cause cytotoxic effects or allergic reactions in surrounding tissues [7, 8].

Due to their physicochemical properties, bioceramics used for bone plasty primarily exhibit osteoconductive properties [9]. To improve the properties of osteoplastic materials and enhance their regenerative potential, various orthobiological preparations are used [10]. Particular attention has been paid in recent years to platelet-based biopreparations [11]. It has been noted that the use of platelet-rich plasma (PRP) not only improves the proliferation of mesenchymal stem cells [12], but also promotes their osteogenic differentiation [13]. Studies show that the use of PRP in combination with ceramic or composite implants can promote osteoinduction [14] and significantly improve treatment outcomes [15]. The results of the combined use of PRP therapy with bone plasty materials are considered promising [16]. At the same time, it was noted that, despite the additional advantages of combining ceramic osteosubstituting materials with platelet-based orthobiological products, further experimental and clinical studies are needed.

The **aim** of this study was to determine the efficacy of platelet-rich plasma in repairing bone defects with yttrium-doped zirconium dioxide ceramic implants.

MATERIALS AND METHODS

Experimental animals

Experimental animals were male chinchilla rabbits kept in the vivarium of the Ural State Medical University at a temperature of 23–25 °C, with a 12-hour day/night lighting cycle, and with access to food and water ad libitum. All experiments were carried out in accordance with the Good Laboratory Practice Rules (Order of the Ministry of Health of the Russian Federation No. 199n dated 01.04.2016), State Standards (GOST 33215-2014, GOST 33216-2014 "Guidelines for the care and maintenance of laboratory animals"), and the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (ETS No. 123, Strasbourg, 18 March 1986 with the appendix dated 15.06.2006). The studies were approved by the institutional ethics committee of the Federal State Budgetary Educational Institution of Higher Education Ural State Medical University of the Ministry of Health of the Russian Federation (protocol No. 4 dated 26.05.23).

All rabbits were divided into two groups: group 1 (n = 10) included animals that underwent modeling of bilateral metaphyseal bone defects in their femurs with implantation of ceramic augments; group 2 (n = 10) included animals that also underwent modeling of bilateral metaphyseal bone defects in their femurs but did not undergo implantation of ceramic augments. Rabbits in both groups received PRP injections into the bone defect in the right femur; PRP was not injected into the defect in the left femur.

Surgical modeling of a bone defect in the distal metaphysis of the femur

To model a bone defect, the experimental animal was placed on their side, the hind limb was treated with antiseptic solutions, and the surgical field was covered with sterile surgical drapes. A 1-cm longitudinal skin incision was made along the lateral surface of the lower third of the thigh in the projection of the femur. Soft tissue along the approach was separated using a blunt dissection. A bone defect was created in the distal metaphysis of the femur parallel to the articular surface of the knee using a 2.0-mm Kirschner wire. The bone defect was modeled bilaterally. PRP was injected into the bone defect in the right limb; no PRP was injected into the bone defect in the left limb.

In group 1, ceramic augments (0.15 × 0.15 × 1 cm) were implanted into the bone defects of both femurs. In group 2, ceramic augments were not implanted into the bone defects of either femur. The wound was sutured layer by layer, the skin was treated with an antiseptic, and an aseptic dressing was applied. In each group, five animals were sacrificed four weeks after surgery, and five animals were sacrificed eight weeks after surgery.

Material for bone defects compensation

Bioceramic implants made of zirconium dioxide (ZrO_2) doped with yttrium oxide (Y_2O_3, 5 wt %) were obtained at the Institute of High-Temperature Electrochemistry, Ural Branch of the Russian Academy of Sciences. The material has closed porosity, with a pore volume fraction of approximately 15 %. Pores range in size from 1–2 to 30 μm and have complex shapes. The ceramic implants measured 0.15 × 0.15 × 1 cm (Fig. 1).

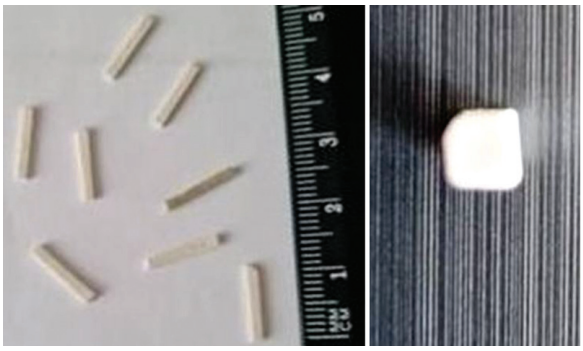

Fig. 1 Ceramic implants made of yttrium oxide-doped zirconium dioxide and a cross-section of the implant

Preparation of plasma, serum, PRP

The procedure for collecting blood in both groups was carried out before surgery and at withdrawal from the experiment four and eight weeks after surgery.

Blood was collected from the marginal vein of the rabbit ear:

— in tubes with EDTA-K2 (ethylenediaminetetraacetate potassium) to determine hematological parameters;

— in tubes without anticoagulant to obtain serum, which was then was frozen and stored at –80 °C until enzyme-linked immunosorbent assay (ELISA);

— in tubes with 3.2 % sodium citrate in a 9:1 ratio.

To obtain PRP, blood with sodium citrate was centrifuged for 7 minutes at 1500 rpm. The resulting plasma was aspirated with a sterile insulin syringe, 200 µl was placed in an Eppendorf tube for platelet count determination using a Cell-70 hematology analyzer (Biocode-Hygel, France) and subsequent freezing. The remaining PRP (1 ml) was injected into the metaphyseal defect of the right femur.

Laboratory tests

Laboratory studies were conducted at the Central Scientific Research Laboratory of the Ural State Medical University. Basic blood parameters were determined using a Cell-70 automated hematology analyzer (Biocode-Hygel, France). Platelet-derived growth factor (PDGF subunit A, rabbit) was determined after the PRP freeze-thaw procedure using ELISA kits (Cloud-Clone Corp., China). C-reactive protein (CRP, rabbit, Cloud-Clone Corp) and osteocalcin (Osteocalcin, rabbit, Cloud-Clone Corp) were also determined using ELISA. The analysis was performed using a system including a Termo Scirntific Multiskan GO plate enzyme immunoassay analyzer (Japan); a Thermo Scientific Wellwash washer (Japan), and an Elmi ST-3L shaker-thermostat (Latvia).

Histological study

After the animal was sacrificed, block-like samples of bone tissue were collected from the distal femoral metaphyses and fixed by immersion in 10 % buffered formaldehyde at room temperature for at least seven days. Following fixation, the samples were decalcified for 48 hours in a solution of hydrochloric (11.5 ± 0.5 %) and formic (5.8 ± 0.3 %) acids, which was replaced every 24 hours. The decalcified samples were sectioned at the bone defect site to form 2- to 4-mm-thick plates. The resulting plates were dehydrated in graded ethanol and embedded in paraffin to form blocks. The paraffin blocks were then sectioned to 3- to 4-µm-thick sections, and the material was stained with hematoxylin and eosin. Ceramic implants were removed during the excision of samples for histological examination after decalcification. Histological sections were prepared using a CUT 4062 mechanical rotary microtome. Histological and morphometric studies were performed using an Olympus CX-31 microscope and an Olympus DP27 camera. The degree of fibrosis, the presence and severity of osteochondral callus, and regenerating bone trabeculae were assessed, and the presence of inflammatory infiltrate was determined.

Statistical protesting of the findings

Variation statistics were used using Statistica 10 software. The Mann-Whitney test was used to compare the groups. A $p < 0.05$ level was considered statistically significant. Data are presented as median [interquartile range].

RESULTS

To assess the impact of the implanted ceramic material on the overall health of the experimental animals, general hematological parameters were determined dynamically (before and after surgery). A complete blood count (Table 1) revealed no significant differences in the key white blood cell, red blood cell, and platelet counts between groups 1 and 2, either before or after surgery.

The analysis of the inflammatory marker C-reactive protein preoperatively showed no significant differences between the groups (Fig. 2). However, four weeks after surgery, CRP levels were significantly higher in the animals of group 1 than in group 2, which could be related to both the body's response to the implant and the implantation technique. Eight weeks after surgery, no differences in inflammatory marker levels were found between the groups.

The concentration of osteogenesis marker osteocalcin four weeks after surgery was significantly higher in group 2. However, after eight weeks, significantly higher osteocalcin levels were observed in group 1 (Fig. 3). These data indicate changes in the dynamics of osteogenesis in the animals with ceramic implant compared to the animals in the control group.

Table 1

Basic hematological parameters before and after modeling of bone defect in rabbits

Параметры и группы		Median [interquartile range]		
		Baseline (*n* = 10)	4 weeks (*n* = 5)	8 weeks (*n* = 5)
Leukocytes (WBC), ×10⁹/l	Group 1	11.4 [10.3; 12.4]	7.8 [7.5; 8.1]	9.4 [9.3; 9.7]
	Group 2	10.4 [9.3; 10.6]	8.2 [7.8; 8.4]	8.5 [7.4; 9.6]
	p	0.109	0.095	0.413
Erythrocytes (RBC), ×10¹²/l	Group 1	5.72 [5.50; 6.10]	6.06 [5.76; 6.23]	5.82 [5.74; 5.84]
	Group 2	6.08 [5.65; 6.23]	5.24 [5.19; 5.51]	5.56 [5.38; 5.97]
	p	0.193	0.056	0.286
Hemoglobin (HGB), (g/l)	Group 1	130 [122; 135]	130 [126; 138]	130 [129; 130]
	Group 2	135 [128; 139]	120 [117; 126]	125 [118; 132]
	p	0.193	0.151	0.556
Hematocrit (HCT), %	Group 1	37.5 [35.8; 38.6]	39.0 [37.0; 39.8]	37.3 [37.0; 37.5]
	Group 2	39.6 [36.7; 40.4]	35.9 [34.8; 38.1]	36.9 [35.1; 38.3]
	p	0.109	0.151	0.730
Platelets (PLT), ×10⁹/l	Group 1	211 [199; 243]	216 [202; 223]	239 [234; 244]
	Group 2	212 [176; 231]	239 [217; 280]	235 [181; 290]
	p	0.669	0.413	0.730
Mean platelets volume (MPV), fl	Group 1	3.7 [3.4; 4.1]	4.1 [3.6; 4.2]	3.5 [3.4; 3.5]
	Group 2	3.4 [3.3; 3.9]	3.8 [3.7; 3.9]	3.8 [3.3; 4.8]
	p	0.417	0.548	0.413
Relative width of platelet distribution by volume PDW	Group 1	19.0 [18.2; 19.9]	19.9 [19.3; 20.7]	17.7 [17.5; 18.3]
	Group 2	18.4 [17.8; 19.0]	19.3 [18.4; 19.3]	18.4 [17.6; 19.0]
	p	0.270	0.310	0.730
Band neutrophils, ×10⁹/l	Group 1	0.21 [0.11; 0.28]	0.22 [0.08; 0.24]	0.19 [0.19; 0.22]
	Group 2	0.09 [0.00; 0.28]	0.11 [0.08; 0.17]	0.26 [0.17; 0.34]
	p	0.364	0.310	0.556
Segmented neutrophils, ×10⁹/l	Group 1	3.30 [2.71; 4.72]	3.55 [2.35; 4.56]	2.88 [2.59; 3.35]
	Group 2	2.88 [2.60; 4.49]	2.81 [2.77; 3.10]	2.85 [2.33; 3.56]
	p	0.475	0.690	0.905
Eosinophils, ×10⁹/l	Group 1	0.32 [0.14; 0.56]	0.13 [0.08; 0.21]	0.09 [0.07; 0.12]
	Group 2	0.20 [0.12; 0.32]	0.25 [0.17; 0.31]	0.12 [0.08; 0.24]
	p	0.613	0.343	0.730
Basophils, ×10⁹/l	Group 1	0.0 [0.0; 0.0]	0.0 [0.0; 0.0]	0.0 [0.0; 0.0]
	Group 2	0.0 [0.0; 0.1]	0.0 [0.0; 0.0]	0.0 [0.0; 0.0]
	p	0.161	0.690	0.556
Lymphocytes, (LYM), ×10⁹/l	Group 1	7.21 [4.62; 7.78]	3.31 [2.64; 4.11]	5.95 [5.12; 6.91]
	Group 2	6.90 [5.58; 7.06]	4.16 [3.90; 4.37]	5.05 [.22; 5.46]
	p	0.475	0.343	0.286
Monocytes (MON), ×10⁹/l	Group 1	0.33 [0.22; 0.79]	0.41[0.30; 0.44]	0.28 [0.23; 0.29]
	Group 2	0.31 [0.20; 0.36]	0.64 [0.46; 0.83]	0.24 [0.15; 0.32]
	p	0.315	0.151	0.730

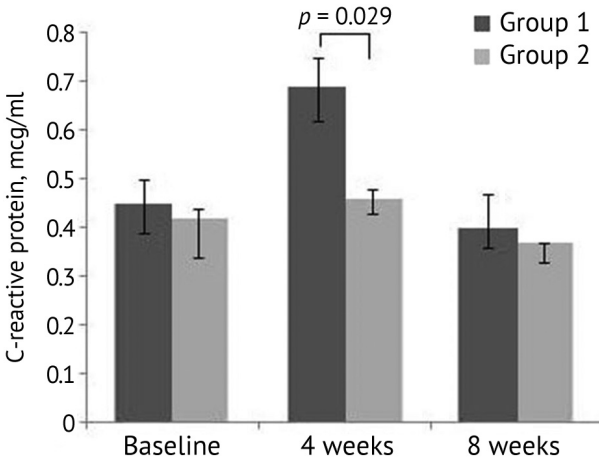

Fig. 2. C-reactive protein levels before and after modeling a bone defect in rabbits that received ceramic implants (group 1) and in the rabbits without implantation (group 2). The results are presented as median and interquartile range

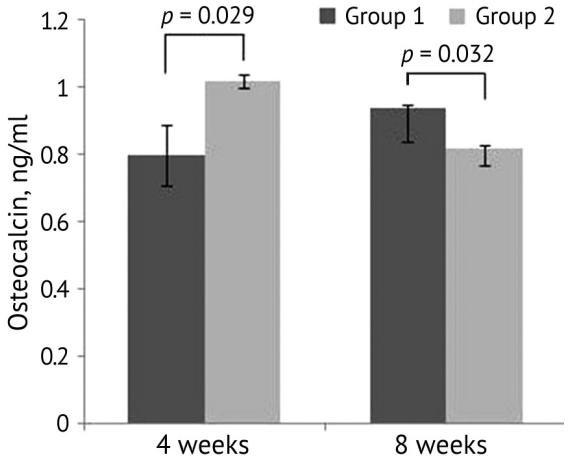

Fig. 3 Osteocalcin concentration after modeling a bone defect in rabbits that received ceramic implants (group 1) and in rabbits without implantation (group 2). The results are presented as median and interquartile range

The resulting PRP was characterized using parameters such as platelet, leukocyte, and erythrocyte concentrations (Table 2). The relative leukocyte count did not exceed 5–8 %, and the erythrocyte count did not exceed 1 % of the baseline blood levels of these cells. The concentration of PDGF, a growth factor released during platelet activation, also showed no significant differences between groups 1 and group 2. Relative to the baseline blood level, the platelet count in the PRP was increased fourfold, and the mean platelet volume was increased 1.4-fold (Fig. 4).

Table 2

Indices of PRP injected in the rabbits of the study groups

Parameters	Median [interquartile range]		
	Group 1	Group 2	*p*
Platelets (PLT), $\times 10^9$/l	846 [837; 1204]	808 [790; 1110]	0.310
Mean platelet volume (MPV), fl	5.0 [5.0; 5.1]	4.8 [4.3; 5.0]	0.421
Leukocytes (WBC), $\times 10^9$/l	0.50 [0.40; 0.70]	0.70 [0.60; 0.90]	0.310
Erythrocytes (RBC), $\times 10^{12}$/l	0.04 [0.03; 0.04]	0.04 [0.04; 0.05]	0.421
PDGF, ng/ml	1.89 [1.88; 2.18]	1.78 [1.75; 2.14]	0.364

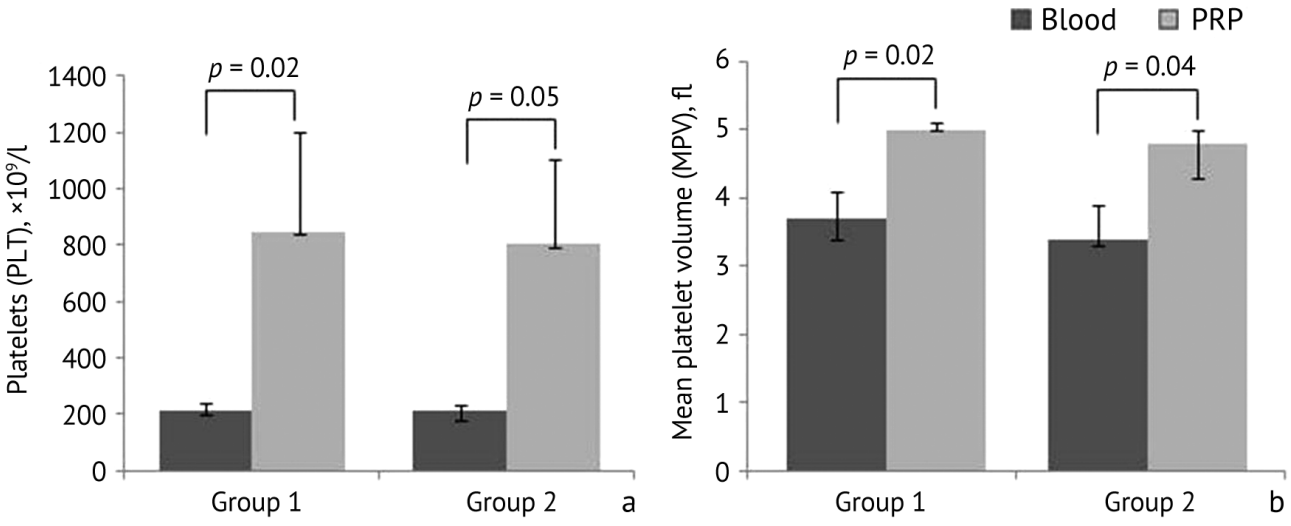

Fig. 4 Comparison of platelet levels (a) and mean platelet volume (b) in blood and PRP obtained from it in the rabbits of the studied groups. The results are presented as median and interquartile range

To assess the effect of PRP on the dynamics of osteogenesis during surgical modeling of a bone defect in the area of the distal metaphysis of the rabbit's femur, a comparative analysis of the histological structure of tissues in the area of the bone defect modeling was carried out.

Histological analysis revealed that four weeks after surgery, large foci of fibrosis (Fig. 5a) and foci of incomplete secondary osteogenesis (Fig. 5b) were observed in the microscopic specimens of group 2 (without implantation) with modeling of the defect without PRP administration. In the case of PRP administration, regenerating bone trabeculae were observed, indicating more effective regeneration under the conditions of the platelet-derived product injection (Fig. 5c).

In group 1 (with ceramic implants), a more active reparative process was also observed with PRP injection into the defect area. However, unlike group 2 and regardless of PRP use, inflammation was observed in the peri-implant area (Fig. 5g). The inflammation may be related to both the reaction to the implant and the implantation technique.

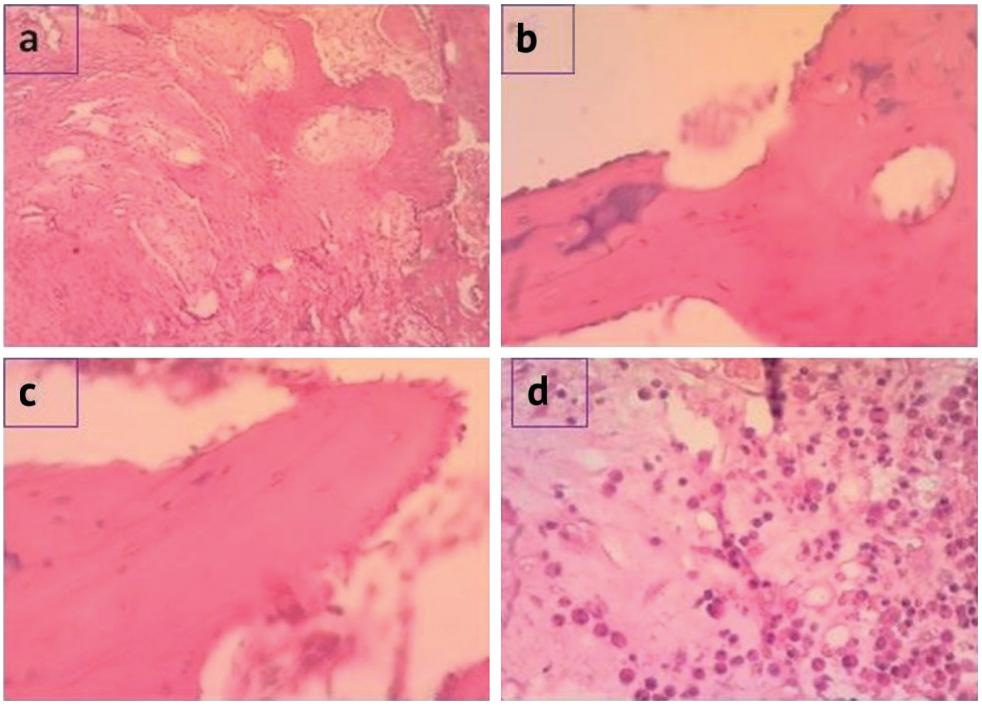

Fig. 5 Features of the histological structure of tissues in the area of modeling a bone defect in rabbits 4 weeks after surgery: (a) a large focus of fibrosis in the animals without implantation and without PRP, ×40, G-E; (b) a small focus of incomplete secondary osteogenesis in animals without implantation, without PRP, ×100, G-E; (c) regenerating bone trabecula, animals with implantation, with PRP, ×100, G-E; (d) inflammation in the implant area, animals with implantation, with PRP, ×100, G-E

Eight weeks after surgery without PRP administration, bone tissue micropreparations from the animals in both groups showed signs of incomplete reparative bone regeneration, including secondary (enchondral) osteogenesis and areas of fibrosis. However, the use of PRP promoted more effective reparative regeneration in both the group that did not undergo bone defect augmentation and the group that received the implant. Regenerating bone trabeculae were detected in both groups. Table 3 presents the comparative results for PRP use in groups 1 and group 2.

Thus, the use of PRP increased the number of regenerating bone trabeculae in both groups 1 and group 2. The use of the platelet-derived product also resulted in a decrease in the number and size of fibrotic foci and osteochondral callus in both groups. The signs of inflammation in the histological samples are likely related to the body's response to the insertion of the artificial implant; the influence of the implantation technique could be ruled out either. However, it should

be noted that by the eighth postoperative week, the level of the biochemical inflammation marker C-reactive protein in the group of animals that received implantation did not differ significantly from the group of animals that did not.

Table 3

Comparison in regard to PRP use in groups

	Focuses			
	Group 1		Group 2	
	PRP (–)	PRP (+)	PRP (–)	PRP (+)
Fibrosis	Multiple large	Solitary small	multiple small, solitary large	Solitary small
Osseo-cartilaginous callus	Multiple small, solitary large	Solitary small	multiple small, solitary large	Solitary small
Regenerating bone trabeculae	Single	Multiple	Not dtected	multiple
Inflammatory infiltration	+	+	–	–

Note: **fibrosis**: *solitary* — no more than one focus in three fields of view at ×40; *small* — fewer than 1 field of view at ×100; *multiple* — two or more focuses in three fields of view at ×40; *large* — more than 1 field of view at ×100. **Osseo-cartilaginous callus**: *solitary* — not more than 1 focus in three fields of view at ×40; *small* — fewer than 1 field of view at ×200; *multiple* — two or more focuses in three fields of view at ×40; *large* — more than one field of view at ×200. **Regenerating bone trabeculae**: *solitary*— not more than three regenerating trabeculae in a sample; *multiple* — more than three regenerating trabeculae in a sample

DISCUSSION

The desire to find optimal treatment strategies for patients with bone injuries has led to the study of the potential use of PRP to accelerate fracture healing [17], since platelet-rich plasma is a cost-effective autologous preparation containing a wide range of growth factors, cytokines, and adhesion molecules [18].

Direct injection of PRP into the injured area provides a high concentration of growth factors at the site of injury, which promotes tissue repair, reduces inflammation, and accelerates the regenerative process [19]. The use of platelet-rich plasma in surgical procedures can be combined with the use of bone grafts; this approach is aimed at optimizing the integration of osteosubstituting materials and at increasing the effectiveness of reparative regeneration [19]. Currently, the efficacy and safety of PRP have been demonstrated in a large number of medical studies [20]. However, the regenerative effects of PRP used along with artificial, particularly ceramic, implants have not yet been fully elucidated [21].

It is known that the effectiveness of PRP depends on the donor's health [22]. A clinical blood test can reflect the general health. Our study showed that the introduction of zirconium dioxide implants to the animals included in the study did not significantly affect red blood cell, white blood cell, or platelet counts during the postoperative period.

Yttria-stabilized zirconia-based bioceramics, in addition to exceptional mechanical properties, also exhibit biocompatibility and do not cause cytotoxic effects or allergic reactions in surrounding tissues [23, 24]. In our study, a highly sensitive analysis of C-reactive protein concentrations revealed that implantation increased the level of this inflammatory marker in rabbits relative to animals that did not receive the implant. However, given that no differences in C-reactive protein levels were detected between the groups by the end of the follow-up, it can be concluded that this reaction was associated not with the physicochemical properties of the ceramic material, but with the body's response to the implant and the surgical technique.

We previously showed that the rate of human fibroblast proliferation in the presence of bioceramic samples is slower than in controls during the initial stages of cell culture growth [25]. In the present study, we used osteocalcin to assess osteogenesis, which is released by osteoblasts

during osteosynthesis and is used as an informative marker of bone formation [26]. We found that the application of the implant slows down the osteogenesis process in the early postoperative period, which can be explained by adaptation processes to the introduction of an artificial bone substitute material.

The PRP obtained in this study was characterized in terms of cell composition and the concentration of platelet-derived growth factor released from alpha granules upon activation. Platelet count is one of the main parameters routinely assessed during PRP preparation, as it is believed to be related to the concentration of biologically active components in the platelet product. Although a clear correlation between platelet count in PRP and clinical response is currently not supported [27], the recommended platelet count in PRP ranges from 800×109 до 1200×109/L [21, 28]. In our study, the platelet count in PRP in both groups complied with these recommendations.

Recent studies have shown that mean platelet volume can be a useful parameter. A higher MPV indicates a higher concentration of bioactive molecules [29]. We found that the MPV in our PRP was significantly higher than that in rabbit whole blood. This may be due to the plasma preparation technique. We observed this finding in both groups of the animals studied.

Leukocytes perform numerous biological functions that typically promote and initiate inflammation. Leukocyte levels should be measured and reported by describing PRP preparation [30]. The benefit of including leukocytes in PRP is controversial, but the release of beneficial cytokines by leukocytes is considered a positive factor, especially in cases where an initial pro-inflammatory process is necessary [31]. At the same time, the presence of erythrocytes in PRP is considered undesirable [32]. In our study, a small number of leukocytes (4–7 % of the initial level) was retained in the PRP product, and the residual number of erythrocytes did not exceed 1 % of their initial content in the blood.

Platelet alpha granules, release numerous growth factors being activated, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), and insulin-like growth factors (IGF-1 and IGF-2). These factors control key biological processes, including angiogenesis induction, inflammation resolution, and tissue regeneration [33]. The level of growth factors in PRP, and consequently its quality, can be determined after the freeze-thaw procedure [34]. We applied this method with subsequent determination of PDGF; the level of platelet-derived growth factor was similar in the PRP products of the studied groups. The work of Pulcini et al. found a direct correlation between the platelet count and the PDGF-AA isoform, but not with the -BB and -AB isoforms. We did not find a correlation between the platelet count and PDGF [21]. This can be explained by the fact that we determined the A subunit, which is present in both the PDGF-AA and PDGF-AB isoforms.

The use of PRP to improve bone tissue regeneration during bone defect reconstruction is varied. In particular, the use of autologous PRP is a simple and effective way to ensure osteoinduction and improve bone regeneration in bone grafting and tissue-engineered bone reconstructions [35, 36].

Our study aimed to investigate whether platelet-rich plasma enhances the osteogenic potential of zirconia ceramic implants in the restoration of bone defects. Histological evaluation of the effectiveness of using PRP for osteogenesis correction in a surgically modeled bone defect in the distal metaphysis of rabbits' femurs was performed four and eight weeks after surgery. The previous study of Saginova et al. showed that the PRP-and-bone graft complex improves bone tissue restoration in a bone defect at the initial stages of bone regeneration [37]. Oktaş et al. also found that the use of PRP can play a role in accelerating fracture healing and eliminating nonunion at very early stages in the restoration of bone defects [38]. Our data are consistent with those studies; we also showed that four weeks after the implantation of the ceramic material a more active reparation process was observed after PRP injection into the defect area. At a later date, eight weeks

after surgery, we found that the use of PRP not only increased the number of regenerating bone trabeculae, but also reduced the number and size of fibrous foci and osteochondral callus.

Platelet concentrates are known to have the ability to control the inflammatory environment due to their anti-inflammatory properties [39]. However, the analysis of histological samples in our study did not find significant reduction in inflammatory infiltration in peri-implant tissue following PRP injection.

Platelet-rich plasma is a useful adjunct in the context of bone reparative regeneration due to its benefits which include stimulation of cell responses, acceleration of tissue repair, and potentially enhanced rehabilitation. However, further rigorous clinical studies are needed to integrate PRP-based methods into evidence-based medical practice. Such studies could deepen our understanding of PRP's role in regenerative medicine and facilitate effective treatment for patients with injuries and musculoskeletal disorders.

CONCLUSION

The use of platelet-rich plasma is effective in compensation of bone defects with ceramic implants made of yttrium oxide-doped zirconium dioxide.

Conflict of interest *Not declared.*

Funding *Not declared.*

REFERENCES

1. *Global status report on road safety 2018*. Geneva: World Health Organization; 2018.
2. Schade AT, Mbowuwa F, Chidothi P, et al. Epidemiology of fractures and their treatment in Malawi: Results of a multicentre prospective registry study to guide orthopaedic care planning. *PLoS One*. 2021;16(8):e0255052. doi: 10.1371/journal.pone.0255052.
3. Fayn AM, Vaza AYu, Gnetetskiy SF, et al. Available methods to enhance regenerative potential of plastic materials for bone defects replacement in orthopedics. Part 1. Autologous platelet rich plasma. *The Russian Journal of Transplantation*. 2022;14(1):79-97. doi: 10.23873/2074-0506-2022-14-1-79-97.
4. Parikh SN. Bone graft substitutes: past, present, future. *J Postgrad Med*. 2002;48(2):142-148.
5. Oryan A, Alidadi S, Moshiri A, Maffulli N. Bone regenerative medicine: classic options, novel strategies, and future directions. *J Orthop Surg Res*. 2014;9(1):18. doi: 10.1186/1749-799X-9-18.
6. Vaiani L, Boccaccio A, Uva AE, et al. Ceramic Materials for Biomedical Applications: An Overview on Properties and Fabrication Processes. *J Funct Biomater*. 2023;14(3):146. doi: 10.3390/jfb14030146.
7. Gahlert M, Roehling S, Sprecher CM, et al. *In vivo* performance of zirconia and titanium implants: a histomorphometric study in mini pig maxillae. *Clin Oral Implants Res*. 2012;23(3):281-286. doi: 10.1111/j.1600-0501.2011.02157.x.
8. Han JM, Hong G, Lin H, et al. Biomechanical and histological evaluation of the osseointegration capacity of two types of zirconia implant. *Int J Nanomedicine*. 2016;11:6507-6516. doi: 10.2147/IJN.S119519.
9. Kirilova IA, Sadovoy MA, Podorozhnaya VT. Comparative characteristics of materials for bone grafting: composition and properties. *Russian Journal of Spine Surgery*. 2012;(3):72–83. (In Russ.) doi: 10.14531/ss2012.3.72-83.
10. Bin Shahri N, Chong AKS, Karjalainen T. The role of orthobiologics in bone healing and joint and tendon degeneration in the upper limb. *J Hand Surg Eur Vol*. 2025;50(6):728-737. doi: 10.1177/17531934251327034.
11. Khandan-Nasab N, Torkamanzadeh B, Abbasi B, et al. Application of Platelet-Rich Plasma-Based Scaffolds in Soft and Hard Tissue Regeneration. *Tissue Eng Part B Rev*. 2025. doi: 10.1089/ten.teb.2024.0285.
12. Mishra A, Tummala P, King A, et al. Buffered platelet-rich plasma enhances mesenchymal stem cell proliferation and chondrogenic differentiation. *Tissue Eng Part C Methods*. 2009;15(3):431-435. doi: 10.1089/ten.tec.2008.0534.
13. Becerra-Bayona SM, Solarte VA, Alviar Rueda JD, et al. Effect of biomolecules derived from human platelet-rich plasma on the ex vivo expansion of human adipose-derived mesenchymal stem cells for clinical applications. *Biologicals*. 2022;75:37-48. doi: 10.1016/j.biologicals.2021.11.001.
14. Teotia AK, Qayoom I, Kumar A. Endogenous Platelet-Rich Plasma Supplements/Augments Growth Factors Delivered via Porous Collagen-Nanohydroxyapatite Bone Substitute for Enhanced Bone Formation. *ACS Biomater Sci Eng*. 2019;5(1):56-69. doi: 10.1021/acsbiomaterials.8b00227.
15. Lyu J, Ma T, Huang X, et al. Core decompression with β-tri-calcium phosphate grafts in combination with platelet-rich plasma for the treatment of avascular necrosis of femoral head. *BMC Musculoskelet Disord*. 2023;24(1):40. doi: 10.1186/s12891-022-06120-z.
16. Borzunov DYu, Gilmanov RT. Promising osteoplastic materials and surgical technologies in reconstructive treatment of patients with bone nonunion and defects. *Genij Ortopedii*. 2024;30(2):263-272. doi: 10.18019/1028-4427-2024-30-2-263-272.
17. Kale P, Shrivastava S, Balusani P, Pundkar A. Therapeutic Potential of Platelet-Rich Plasma in Fracture Healing: A Comprehensive Review. *Cureus*. 2024;16(6):e62271. doi: 10.7759/cureus.62271.
18. Zhang N, Wu YP, Qian SJ, et al. Research progress in the mechanism of effect of PRP in bone deficiency healing. *ScientificWorldJournal*. 2013;2013:134582. doi: 10.1155/2013/134582.

19. Bacevich BM, Smith RDJ, Reihl AM, et al. Advances with Platelet-Rich Plasma for Bone Healing. *Biologics*. 2024;18:29-1859. doi: 10.2147/BTT.S290341
20. Gupta S, Paliczak A, Delgado D. Evidence-based indications of platelet-rich plasma therapy. *Expert Rev Hematol*. 2021;14(1):97-108. doi: 10.1080/17474086.2021.1860002.
21. Pulcini S, Merolle L, Marraccini C, et al. Apheresis Platelet Rich-Plasma for Regenerative Medicine: An *In Vitro* Study on Osteogenic Potential. *Int J Mol Sci*. 2021;22(16):8764. doi: 10.3390/ijms22168764.
22. O'Donnell C, Migliore E, Grandi FC, et al. Platelet-Rich Plasma (PRP) From Older Males With Knee Osteoarthritis Depresses Chondrocyte Metabolism and Upregulates Inflammation. *J Orthop Res*. 2019;37(8):1760-1770. doi: 10.1002/jor.24322
23. Yin L, Nakanishi Y, Alao AR, et al. A review of engineered zirconia surfaces in biomedical applications. *Procedia CIRP*. 2017;65:284-290. doi: 10.1016/j.procir.2017.04.057
24. Ulyanov YuA, Zaripova EM, Mingazova EN. The issue of biocompatibility of ceramic implants in the provision of orthopedic care. *Manager Zdravoohranenia*. 2023;(9):18-22. (In Russ.) doi: 10.21045/1811-0185-2023-9-18-22.
25. Ulitko M, Antonets Y, Antropova I, et al. Ceramic materials based on lanthanum zirconate for the bone augmentation purposes: cytocompatibility in a cell culture model. *Chimica Techno Acta*. 2023;10(4):202310402. doi: 10.15826/chimtech.2023.10.4.02.
26. Drouzhinina TV, Khlousov IA, Karlov AV, Rostovtsev AV. Osteogenesis markers in peripheral blood as pathogenetic factors and predictors of the systemic effects of implants for osteosynthesis. *Genij Ortopedii*. 2007;4:83-88. (In Russ.)
27. Laver L, Filardo G, Sanchez M, et al. ESSKA–ORBIT Group. The use of injectable orthobiologics for knee osteoarthritis: A European ESSKA-ORBIT consensus. Part 1-Blood-derived products (platelet-rich plasma). *Knee Surg Sports Traumatol Arthrosc*. 2024;32(4):783-797. doi: 10.1002/ksa.12077.
28. Aprili G, Gandini G, Guaschino R, et al. SIMTI Working Group. SIMTI recommendations on blood components for non-transfusional use. *Blood Transfus*. 2013;11(4):611-622. doi: 10.2450/2013.0118-13
29. Ozer K, Kankaya Y, Çolak Ö. An important and overlooked parameter in platelet rich plasma preparation: The mean platelet volume. *J Cosmet Dermatol*. 2019;18(2):474-482. doi: 10.1111/jocd.12682.
30. Ragni E, Taiana MM, Čengić T, et al. PRP or not PRP: Is the debate surrounding platelets-based blood-derived products evolving? *Knee Surg Sports Traumatol Arthrosc*. 2025;33(5):1920-1924. doi: 10.1002/ksa.12655.
31. Tischer T, Bode G, Buhs M, et al. Platelet-rich plasma (PRP) as therapy for cartilage, tendon and muscle damage - German working group position statement. *J Exp Orthop*. 2020;7(1):64. doi: 10.1186/s40634-020-00282-2.
32. Zhou JY, Wong JH, Berman ZT, et al. Bleeding with iron deposition and vascular remodelling in subchondral cysts: A newly discovered feature unique to haemophilic arthropathy. *Haemophilia*. 2021;27(6):e730-e738. doi: 10.1111/hae.14417.
33. Kale P, Shrivastava S, Balusani P, Pundkar A. Therapeutic Potential of Platelet-Rich Plasma in Fracture Healing: A Comprehensive Review. *Cureus*. 2024;16(6):e62271. doi: 10.7759/cureus.62271.
34. Tang S, Wang L, Zhang Y, Zhang F. A Biomimetic Platelet-Rich Plasma-Based Interpenetrating Network Printable Hydrogel for Bone Regeneration. *Front Bioeng Biotechnol*. 2022;10:887454. doi: 10.3389/fbioe.2022.887454.
35. Korytkin AA, Zykin AA, Zakharova DV, Novikova YS. Bone grafting enhanced by platelet-rich plasma in treatment of avascular necrosis of femoral head. *Traumatology and Orthopedics of Russia*. 2018;24(1):115-122. (In Russ.) doi: 10.21823/2311-2905-2018-24-1-115-122
36. Guo Y, Yang Y, Peng B, Xing G. Repair of Vertebral Bone Defects with Injectable Calcium Phosphate Bone Cement Reinforced with Autologous Platelet-rich Plasma in Goats. *Tissue Eng Part C Methods*. 2025;31(6):211-220. doi: 10.1089/ten.tec.2025.0021.
37. Saginova D, Tashmetov E, Tuleubaev B, Kamyshanskiy Y. Effect of autologous platelet-rich plasma on new bone formation and viability of a Marburg bone graft. *Open Life Sci*. 2023;18(1):20220761. doi: 10.1515/biol-2022-0761.
38. Oktaş B, Çırpar M, Şanlı E, et al. The effect of the platelet-rich plasma on osteogenic potential of the periosteum in an animal bone defect model. *Jt Dis Relat Surg*. 2021;32(3):668-675. doi: 10.52312/jdrs.2021.199.
39. Salem M, Rizk A, Mosbah E, et al. Reinforcement of osteochondoral defects repair with leukocyte platelet-rich fibrin and bone marrow-derived mononuclear cells in a rabbit model. *BMC Musculoskelet Disord*. 2025;26(1):707. doi: 10.1186/s12891-025-08952-x.

The article was submitted 19.11.2025; approved after reviewing 19.01.2026; accepted for publication 09.02.2026.

Information about futhors:

Irina P. Antropova — Doctor of Biological Sciences, Leading Researcher, aip.hemolab@mail.ru, https://orcid.org/0000-0002-9957-2505;

Elena A. Volokitina — Doctor of Medical Sciences, Professor, Head of Department, Leading Researcher, volokitina_elena@rambler.ru, https://orcid.org/0000-0001-5994-8558;

Kirill A. Timofeev — Postgraduate Student, orthopaedic surgeon, kirilltimofeev64166@gmail.com, https://orcid.org/0000-0003-2208-7154;

Roman A. Trufanenko — Assistant Professor, rtrufanenko@gmail.com, https://orcid.org/0000-0002-9978-4807;

Sergey M. Kutepov — Corresponding Member of the Russian Academy of Sciences, Professor, Doctor of Medical Sciences, Head of the Institute of Traumatology at the Central Research Laboratory, kcm@usma.ru, https://orcid.org/0000-0002-3069-8150;

Larisa G. Polushina — Candidate of Medical Sciences, Senior Researcher, polushina-larisa@bk.ru, https://orcid.org/0000-0002-4921-7222.