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Remodeling of articular cartilage and subchondral zone of the tibia in exo-prosthetics of the limb

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Abstract

Introduction Exo-prosthetics of limbs through osseointegration opens up new possibilities in prosthetics. Modern prostheses are becoming more high-tech, which requires deep understanding of the anatomical and functional features of the bone-joint system.

Aim To identify features of structural reorganization of articular cartilage and subchondral zone of the tibia in lower leg prosthetics using an implant with calcium phosphate coating and an implant without additional coating.

Materials and methods The study was performed on 5 intact (control) and 6 experimental dogs (age 1.8 ± 0.5 years, weight 19 ± 1.2 kg). A tibial stump was modeled in the animals at the border of the middle and upper third of the diaphysis. After 2.5 months a PressFit type implant was installed. Depending on the Press-Fit type, the animals were divided into groups: group 1 made of Ti6Al4V alloy ($n = 3$); group 2 of Ti6Al4V alloy with calcium phosphate coating ($n = 3$). Duration of the experiment was 180 days after prosthesis fitting. Histomorphometric study of the articular cartilage and subchondral zone was performed on paraffin sections using an AxioScope.A1 microscope supplied with AxioCam camera and Zenblue software (CarlZeissMicroImagingGmbH, Germany).

Results Bone tissue remodeling was expressed by thinning of the subchondral bone plate, osteolysis, changes in the architecture of bone trabeculae in the subchondral trabecular bone, and a decrease in bone tissue mineralization. These signs were more intense in group 1. Signs of reparative osteogenesis with osteoblasts on the surface of bone trabeculae were noted in group 2. Subchondral bone plate thickness reduced twofold in group 1, and by 1.5 times in group 2 relative to the control. The values of the parameter of trabecular area were reduced in group 1 by 17 % and in group 2 by 10 %. Statistically significant decrease in the values of articular cartilage thickness was recorded in group 1 and was accompanied by a higher (by 1.8 times) frequency of vessels been found in the deep zone of cartilage compared to group 2.

Discussion The identified changes in the subchondral zone corresponded to stage 0 (according to the O-M classification. Aho et al., 2017): very early signs of osteoarthritis, when subchondral sclerosis is not pronounced, the subchondral bone plate is thin. Structural changes in articular cartilage corresponded to grade 0–1 according to the histological classification of the International Society for the Study of Osteoarthritis OARSI.

Conclusion Histomorphometric changes in the osteochondral component of the tibial plateau during lower leg prosthetics (thinning of the subchondral bone plate, rarefaction of the subchondral trabecular bone, penetration of vessels into non-calcified cartilage) are predictors of arthrosis. The use of implants made of Ti6Al4V alloy coated with a calcium phosphate provides reduction of bone resoption intensity and activates reparative osteogenesis.

Keywords: exo-prosthetics, titanium implant, calcium phosphate coating, articular cartilage, subchondral bone, histomorphometry

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INTRODUCTION

Exoprosthetics of limbs via osseointegration provides physiological weight-bearing, osteoperceptual sensory feedback, improved range of motion in the proximal joint, which contributes to the creation of a fully functional artificial limb and opens up new possibilities for prosthetics [1–3]. Modern prostheses are becoming increasingly complex and high-tech, requiring a deep understanding of the anatomical and functional features of the musculoskeletal system [4–6]. The study of the structural reorganization of the main elements of the adjacent joint due to prosthetics is of great importance for the development of rehabilitation programs aimed at improving the quality of life of patients.

Previous studies on a single-stage technology for lower leg prosthetics showed stability and survival of the Press-Fit implant and bone formation along the entire length [7], while structural changes in the femoral condyles in the area of contact between the hyaline cartilage and the subchondral bone were detected in the adjacent joint [8]. Numerous recent studies demonstrated increasing evidence of pathological changes in the subchondral bone during the development of arthrosis [9–11]. Today, there is an urgent need to develop methods for visualization and histological quantitative assessment of the processes of subchondral bone remodeling [12, 13].

The study of the processes of implant osseointegration is aimed at improving the contact between bone tissue and the implant by acting on the composition of the implant and the microstructure of its surface [14, 15], the bone tissue regenerating on the surface of the implant [16], and also by applying medicinal and biologically active substances to the surface of the implant [17, 18].

Studies of the structural reorganization of the articular cartilage of the adjacent joint in prosthetic care are few in number; the features of the reorganization of the subchondral bone and histological predictors of arthrosis have not been studied. These facts determined the purpose of the study.

The **purpose** of the study was to identify features of structural reorganization of articular cartilage and subchondral bone of the tibia in lower leg prosthetic fitting using a calcium-phosphate coated implant and an implant without any coating.

MATERIALS AND METHODS

Study design

The study was conducted on six mongrel male dogs (age: (1.8 ± 0.5) g; body weight: (19.0 ± 1.2) kg). A tibial stump was modeled at the border of the middle and upper thirds of the diaphysis.

After 2.5 months, a Press-Fit implant was installed in the animals [19]. Then the implant was fixed and a compression load on the bone $F_Н$ = 20 N was performed using a special device (Fig. 1) [20] for 35 days, followed by an exoprosthesis attachment. The animals were divided into two equal groups depending on the implant material: group 1 with an implant made of Ti6Al4V alloy (*n* = 3); group 2 with an implant made of Ti6Al4V alloy coated with calcium (*n* = 3). The experiment period was 180 days after prosthesis fitting.

Object of study: articular cartilage and subchondral plate of the tibia

As a control, the articular cartilage and subchondral bone of the tibia of three intact dogs were examined.

Ethical approval

The study was conducted in accordance with the principles of the European Convention ETS No. 123 for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (with the appendix of 15.06.2006, Strasbourg) and the rules of good laboratory practice (GOST 33044-2014). The protocol of the institutional ethics committee dated 29.11.2024 No. 1 (76).

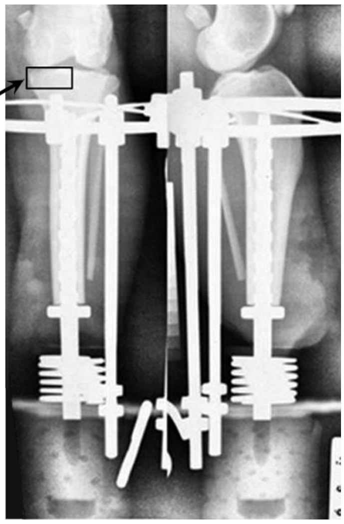


Fig. 1 Radiographs of the tibia with a prosthetic fitting using a Press-Fit implant and the installation of a compression device; the rectangle shows

Euthanasia

The animals were withdrawn from the experiment after muscle relaxation with a solution of 1 diphenhydramine (0.02 mg/kg) and 2 rometar (5 mg/kg), followed by a lethal dose of barbiturates.

Histomorphometric study

For histomorphometric study, the articular end of the tibia was exposed; soft tissues were removed, and the bone-cartilage fragments were fixed in a 10 solution of neutral formalin (pH 7.4). Then the bone-cartilage fragments were placed in a decalcifying solution consisting of a mixture of formic and hydrochloric acid solutions. After the decalcification stage, the material was washed in running water and subjected to histological processing, including the stages of dehydration, impregnation, and embedding in paraffin.

By embedding, the pieces were oriented considering the zonal structure of the articular cartilage; paraffin sections of adequate thickness [21] were used perpendicular to the articular surface and were prepared using a Thermo Scientific HM 450 microtome (USA). The main method of staining histological preparations was used: hematoxylin and eosin staining and a special method of three-color staining according to Masson with aniline blue.

Light-optical study of the preparations and digitalization of the images were performed on an AxioScope.A1 microscope with an AxioCam digital camera (CarlZeissMicroImagingGmbH, Germany). Describing the subchondral bone based on the definition of its two structural units: the subchondral bone plate and the subchondral trabecular bone [9].

For the quantitative study, Zenblue software (CarlZeissMicroImagingGmbH, Germany) was used. The following parameters were measured: thickness of non-calcified cartilage ($h_{uncal.cr}$, mm), thickness of calcified cartilage ($h_{cal.cr}$, μm), thickness of subchondral bone plate ($h_{s.b.pl}$, μm). In the subchondral trabecular bone, the area of bone trabeculae (S_{Tr}, %,) and their thickness (h_{Tr}, μm) were calculated. In the deep zone of the cartilage, the frequency of vessel was determined; this parameter was calculated as the sum of vessels in the visual fields divided by the number of all visual fields studied (an average of 20 fields were analyzed in each animal at 400-fold magnification).

Statistical methods

Quantitative data were processed in Microsoft Excel spreadsheets. Samples were assessed for normal distribution using the Kolmogorov criterion. The measure of the central tendency of morphometric parameters was presented as a median and quartiles, minimum and maximum values (*Me* (p25–p75) [min–max]) and as the mean and error of the mean (M ± m). The Mann – Whitney criterion was used to assess differences in the compared groups, and the Barnard criterion for the frequency indicator; differences were considered significant at $p < 0.05$.

RESULTS

Articular cartilage histopathology

The light-optical study of histological preparations showed that the articular cartilage of the lateral condyle of the tibia in the experimental and control groups retained its zonal structure (Fig. 2).

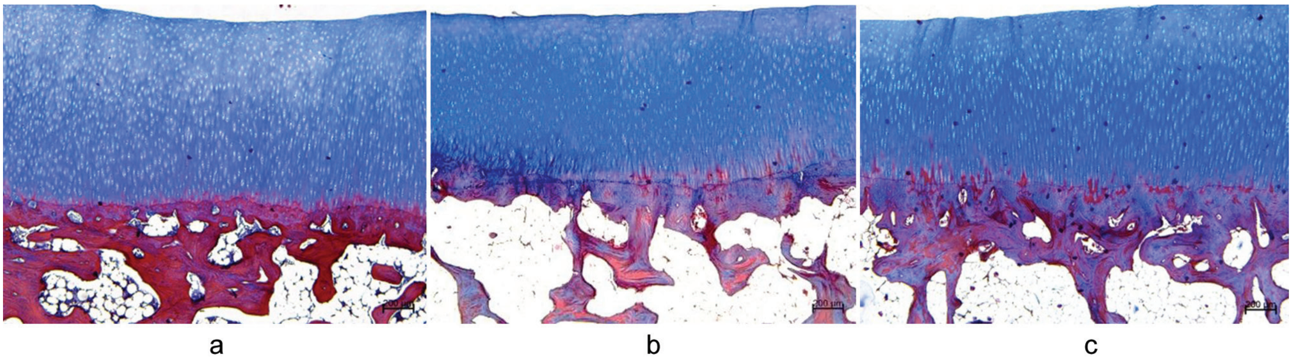


Fig. 2 Articular lining of the lateral condyle of the tibia: (a) control (intact norm); (b) group 1; (c) group 2. Paraffin sections, stained with the three-color method according to Masson, ×40

In most experimental cases, there was no tangential arrangement of cells in the superficial zone; empty cellular lacunae and acellular fields were noted; the intercellular substance of the superficial zone was unevenly stained (Fig. 3 a); difibering foci were not detected; in group 1, synovial pannus was noted in one case (Fig. 3 c).

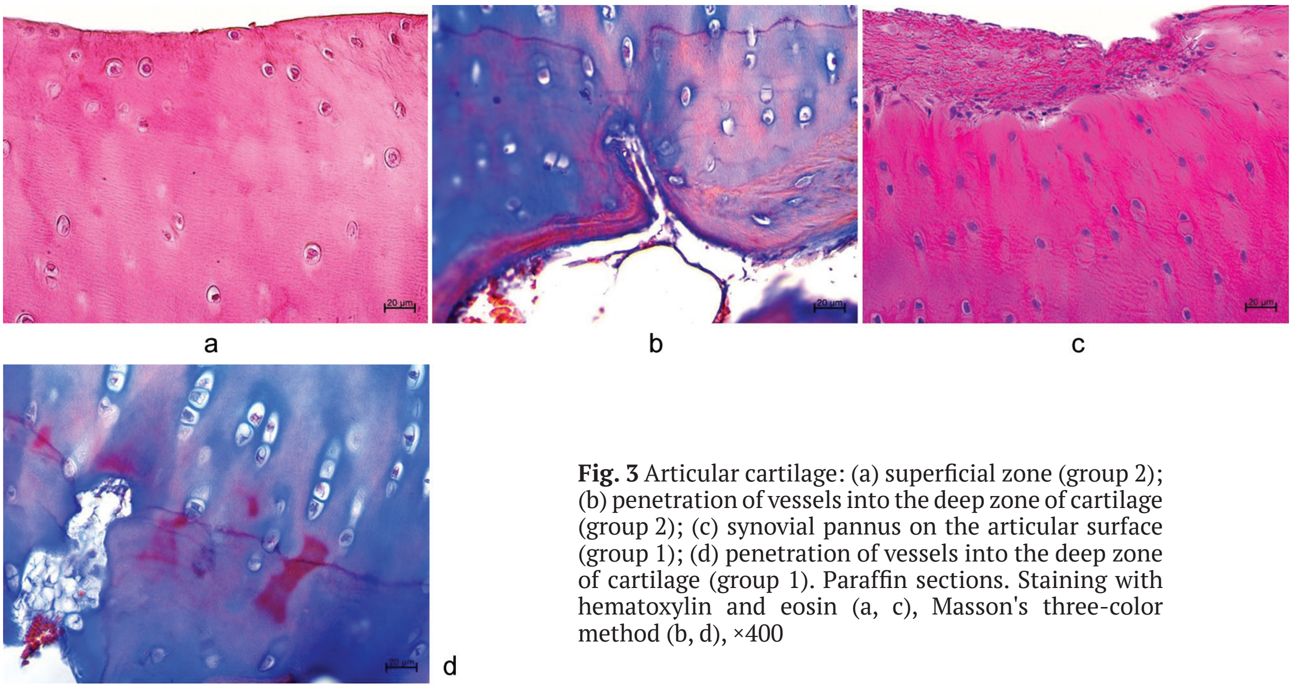


Fig. 3 Articular cartilage: (a) superficial zone (group 2); (b) penetration of vessels into the deep zone of cartilage (group 2); (c) synovial pannus on the articular surface (group 1); (d) penetration of vessels into the deep zone of cartilage (group 1). Paraffin sections. Staining with hematoxylin and eosin (a, c), Masson's three-color method (b, d), ×400

In the intermediate zone, chondrocytes were located more solely and in the form of isogenic groups consisting of two cells. In the deep zone, there was a columnar arrangement of cartilaginous cells; hypertrophied chondrocytes prevailed, some cells had signs of chondroptosis.

In both groups, areas of basophilic line disruption, penetration of vessels and bone marrow pannus into the deep zone of non-calcified cartilage were revealed (Fig. 3 b, d).

The frequency of vessels in the deep zone in group 1 was (0.65 ± 0.06), which is statistically significantly (p = 0.0148) higher than in group 2 (0.35 ± 0.02).

The thickness of non-calcified cartilage in group 1 was statistically significantly lower than in the controls; in group 2 it was comparable to the controls; the differences between the groups are statistically significant (Table 1). The values of the parameter "calcified cartilage thickness" in groups 1 and 2 are comparable with the controls (Table 1).

Table 1

Quantitative characteristics of articular cartilage and subchondral zone of the tibia in experimental groups and in controls

Groups		Parameters				
		$h_{uncal.cr}$, (mm)	$h_{cal.cr.}$(µm)	$h_{s.b.pl}$ (µm)	h_{Tr} (µm)	S_{Tr} (%)
Control	*Me*	1,28	125,93	144,11	156,47	45,21
	(Q1; Q3)	(1,21; 1,33)	(104,68; 135,66)	(87,55; 205,31)	(81,95; 234,91)	(24,73; 49,15)
	[min–max]	[1,16–1,66]	[95,98–173,84]	[60,92–223,87]	[28,23–281,94]	[20,31–51,01]
Group 1	*Me*	1,09	132,64	67,95	107,93	30,81
	(Q1; Q3)	(1,06; 1,13)	(79,92; 154,41)	(87,55; 205,31)	(59,05; 124,93)	(20,11; 35,49)
	[min–max]	[1,01–1,15]	[60,14–194,82]	[40,02–203,86]	[21,06–293,71]	[11,79–38,51]
	p	0,0001	0,3263	0,0218	0,0071	0,0102
Group 2	*Me*	1,24	120,34	97,44	112,91	37,04
	(Q1; Q3)	(1,18; 1,32)	(105,43; 129,24)	(87,97; 172,96)	(70,35; 140,54)	(28,72; 37,69)
	[min–max]	[1,15–1,79]	[75,36–189,76]	[60,92–167,86]	[56,82–195,12]	[18,28–49,01]
	p	0,5823	0,9081	0,0105	0,2801	0,0126
	p^1	0,0124	0,9528	0,001	0,0129	0,0268

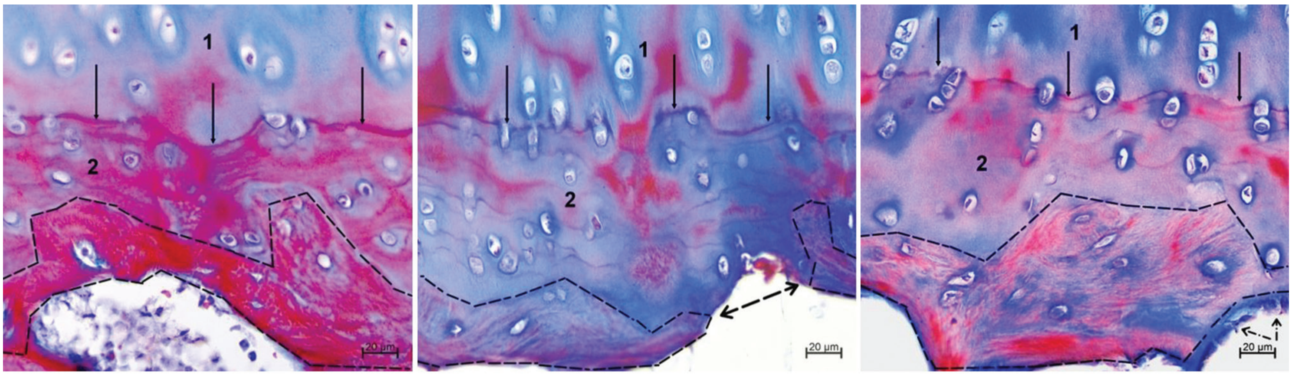
Note: p level of difference as compared with the controls; p^1 level of significance of differences between groups according to the Mann-Whitney criterion, at $p \leqslant 0.05$

Subchondral bone plate histopathology

The subchondral bone plate in the control group was of uneven thickness and continuous throughout (Fig. 4 a). In the experimental groups, the subchondral bone plate was thinned; in group 1 it was absent in some places (Fig. 4 b); in group 2, areas lined with osteoblasts were seen (Fig. 4 c). The values of the parameter "thickness of the subchondral bone plate" in both groups were statistically significantly lower than the norm; the minimum values were recorded in group 1 (Table 1).

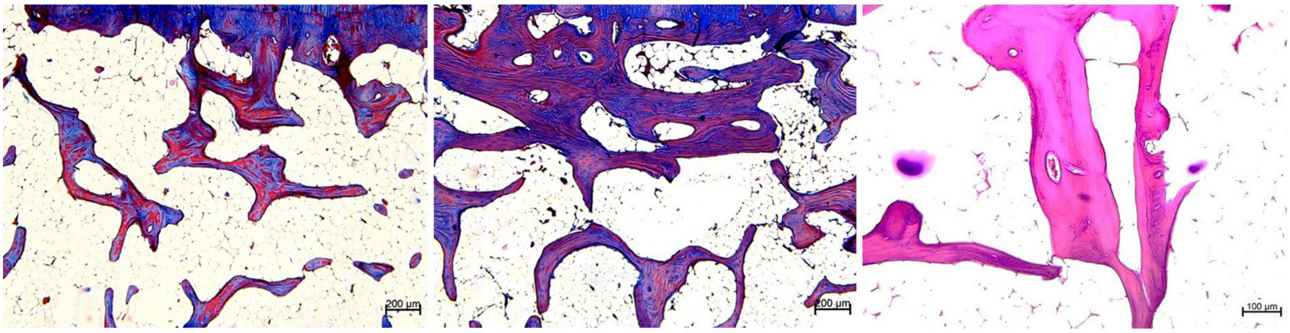
Staining histological sections with the three-color method according to Masson showed that the subchondral bone plate in the control was stained mainly red; in group 2 a decrease in the proportion of fuchsinophilic structures was noted, and in group 1, anilinophilic structures predominated (Fig. 4), which indirectly indicated a decrease in bone matrix mineralization.

In the experimental groups, rarefaction of the subchondral trabecular bone was revealed; the most pronounced signs of resorption were noted in group 1 (Fig. 5 a, b). Histomorphometric study revealed a statistically significant decrease in the values of the parameters of the area and thickness of the trabeculae in group 1 relative to the controls (Table 1), in group 2 the parameter "thickness of the trabeculae" did not have statistically significant differences with the controls, the differences between the groups were statistically significant (Table 1).



a b c

Fig. 4 Contact of the articular cartilage and subchondral bone: (a) control; (b) group 1; (c) group 2. Designations: 1 — deep zone of articular cartilage; 2 — zone of calcified cartilage; solid arrows — basophilic line; dotted line — borders of subchondral bone plate; double-edged dotted arrow — subchondral bone plate is absent; dotted arrows — osteoblasts lining the subchondral bone plate. Paraffin sections. Staining by Masson's three-color method, ×400



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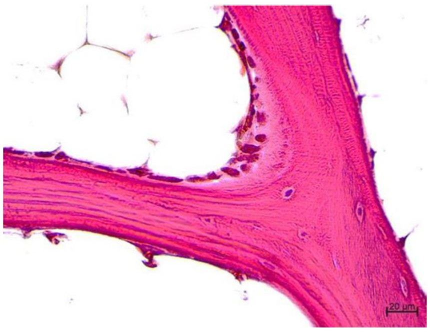

d

Fig. 5 Subchondral trabecular bone: (a) group 1; (b) group 2; (c) autolysis of bone matrix (group 1); (d) osteoblasts on the surface of the trabecula (group 2). Paraffin sections, stained with Masson's three-color method (a, b), hematoxylin and eosin (c, d). Magnification: ×40 (a, b), ×100 (c), ×400 (d)

In group 1, osteolytic phenomena were more frequent: autolysis of the bone matrix, splitting of the basic substance of the trabeculae along the adhesion lines (Fig. 5 c); the surfaces of the bone trabeculae did not contain cells. In group 2, there were trabecular surfaces lined with active osteoblasts producing the basic substance (Fig. 5 d).

DISCUSSION

The condition of the adjacent joint is of great importance for the restoration of the function of the prosthetic limb. Prosthetics of the lower limbs in both children and adult patients may result in contractures and deforming arthrosis in the joints located above [22]. It is known that surgical intervention on bone structures is accompanied by compensatory changes in bone tissue metabolism, the development of stress remodeling, which ensures the adaptive restructuring of bone tissue after surgery [23]. Thereby, destructive changes in the articular cartilage are noted in the adjacent joint [24, 25].

In this study, the features of subchondral zone remodeling in the tibia during exoprosthetics of the limb were studied for the first time on an experimental model using histomorphometry methods. The processes of bone tissue remodeling include thinning of the subchondral bone plate, osteolysis and changes in the architectonics of bone trabeculae in the subchondral trabecular bone, a decrease in bone tissue mineralization that was more intensely expressed in group 1, and signs of reparative osteogenesis expressed by active osteoblasts lining the surfaces of bone trabeculae in group 2. Histomorphometrically, a twofold decrease in the values of the parameter "thickness of the subchondral bone plate" in group 1 and by 1.5 times in group 2, compared to the controls, can be attributed to the processes of bone tissue remodeling. The values of the parameter “trabecular area” were reduced on average by 17 in group 1, by 10 in group 2, and the minimum values of the parameter “trabecular thickness” were recorded in group 1.

According to the classification of Aho et al. [26], the changes in the subchondral zone observed in our study corresponded to stage 0 (very early signs of osteoarthritis), when subchondral sclerosis is not expressed but the subchondral bone plate is thin.

The initiating role of the subchondral bone in the degradation of the articular cartilage was confirmed by numerous studies [27–29]. The subchondral bone, together with the articular cartilage, forms an “osteochondral” functional unit and is a mechanical basis for the articular cartilage, supporting its structure and trophism, protecting it from excessive loads [30–32].

The pathological changes in the contact zone between cartilage and subchondral bone provoke significant structural changes in the entire joint. Thinning of the subchondral bone plate and rarefaction of the subchondral trabecular bone lead to an increased load on the articular cartilage and disruption of its structure [29]. Remodeling of subchondral bone tissue is accompanied by vascular invasion into the area of calcified cartilage. The combination of vascular invasion into the articular cartilage and an increased influx of catabolic factors without inhibition of metalloproteinases ensures the progression of cartilage tissue destruction [33, 34].

The observed structural changes in the articular cartilage of the tibial plateau in lower leg prosthetic applicatoion (thinning, death of some chondrocytes in the superficial zone, uneven staining of the intercellular matrix) corresponded to grade 0–1 according to the histological classification of the International Osteoarthritis Society OARSI [35].

A statistically significant decrease in the articular cartilage thickness was observed in group 1 and was accompanied by a higher (1.8 times) of occurrence of vessels in the deep zone of non-calcified cartilage compared to group 2. The use of group 2 implants contributed to less pronounced changes in the subchondral zone.

The knowledge gained about the features of structural reorganization of the articular cartilage and the subchondral zone of the adjacent joint in the conditions of limb prosthetics is of great importance. Therapeutic strategies aimed at stimulating reparative osteogenesis can prevent joint destruction.

CONCLUSION

Histomorphometric changes in the osteochondral component of the tibial plateau in lower leg prosthetic care (thinning of the subchondral bone plate, rarefaction of the subchondral trabecular bone, penetration of vessels into non-calcified cartilage) are predictors of arthrosis. The use of implants made of Ti6Al4V alloy coated with a calcium phosphate provides reduction of bone resoption intensity and activates reparative osteogenesis.

Conflict of interests *Not declared.*

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Ethical approval *The study was conducted in accordance with the principles of the European Convention ETS No. 123 for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (with the appendix of 15.06.2006, Strasbourg) and the rules of good laboratory practice (GOST 33044-2014). Protocol of the institutional ethics board dated 29.11.2024 No. 1 (76).*

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