

ORIGINAL ARTICLE

EXPERIMENTAL STUDY OF BONE DENSITY IN PATIENTS WITH CONGENITAL PSEUDOARTHROSIS OF THE TIBIA BEFORE AND AFTER SURGERY

DOI: 10.36740/WLek202209112

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ABSTRACT

The aim: Determine the changes in bone density that occur in the cortical layer of the tibia in patients with CPT after surgical treatment due to radiography data.

Materials and methods: The study was performed on X-rays of the tibia of three patients with CPT, aged 5 to 7 years. X-rays were taken before surgery and 1 year after surgery. The optical density of the cortical layer of both tibia bones was determined, for which they were conditionally divided into 7 zones.

Results: In all patients with CPT before treatment, there is significant decrease in the optical density of cortical bone tissue of the damaged tibia compared with contralateral. One year after surgery, there was an increase in the optical density of the cortical layer of both tibia of the studied patients. The increase in the density of the nonoperated tibia can be attributed to the active growth of patients. On the operated limb, the increase in the density of the cortical layer became statistically significant in all studied areas, which can be attributed not only to the growth of patients, but also to the possibility of active loading of the operated limb.

Conclusions: In all patients with CPT before treatment, a statistically significant decrease in the density of cortical bone tissue of the damaged tibia was observed.

As a result of the treatment there is an approximation of the bone density of the operated limb to the indicators of intact contralateral bone.

KEY WORDS: pediatric orthopedics, tibia, radiography, comparative analysis, fibula

Wiad Lek. 2022;75(9 p1):2112-2120

INTRODUCTION

Congenital pseudoarthrosis of the tibia (CPT) remains a complex and unresolved disease of pediatric orthopedics. CPT leads to shortening and deformation of the lower leg and ankle joint with limb dysfunction [1,2].

Surgical treatment of CPT is accompanied by a significant number of reoperations, a high percentage of complications and refractures [3].

There are ongoing studies and development of new technique in treatment of CPT with metal fixator. [4]. One of the features of CPT is a violation of the quality of bone tissue in the area of pseudoarthrosis, and pathological tissue (hamartoma) and pathology of periosteum [1,5].

Currently, there are not many studies in which changes in bone quality parameters before and after surgical treatment of CPT have been compared.

THE AIM

The goal was to determine the changes in bone density that occur in the cortical layer of the tibia in patients with CPT after surgical treatment due to radiography data.

MATERIALS AND METHODS

In the laboratory of biomechanics of the Sytenko Institute of Spine and Joint Pathology National Academy of Med-

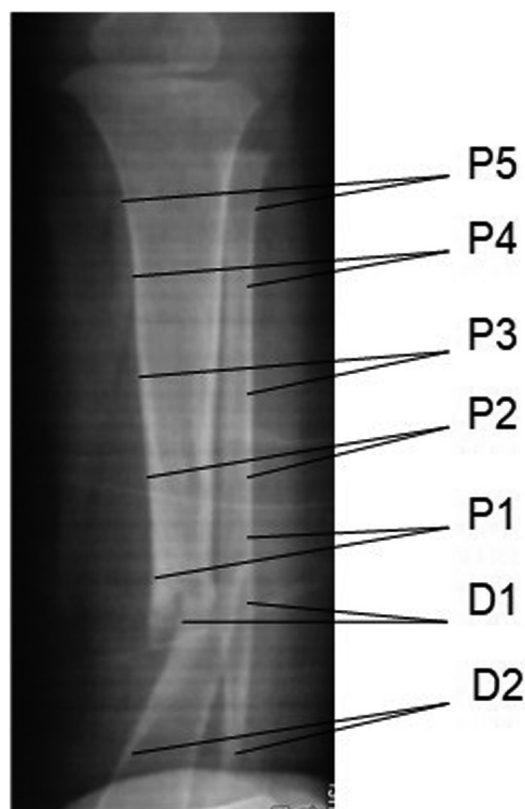


Fig. 1. Scheme of areas of measurement of cortical bone density.

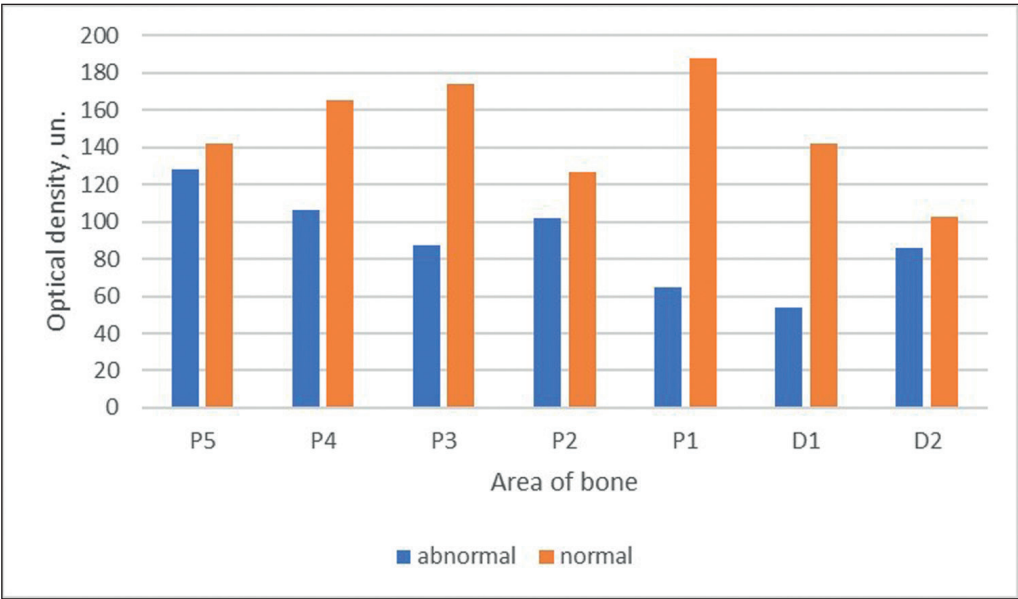


Fig. 2. Diagram of the optical density of the tibia in patients with CPT before surgery.

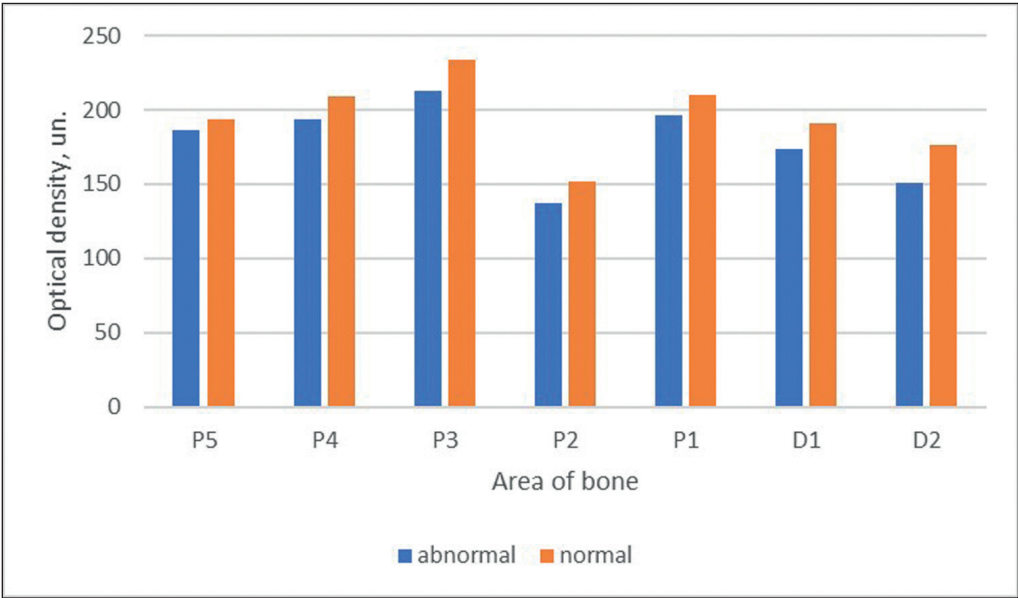


Fig. 3. Diagram of the optical density of the tibia in patients with CPT after surgery.

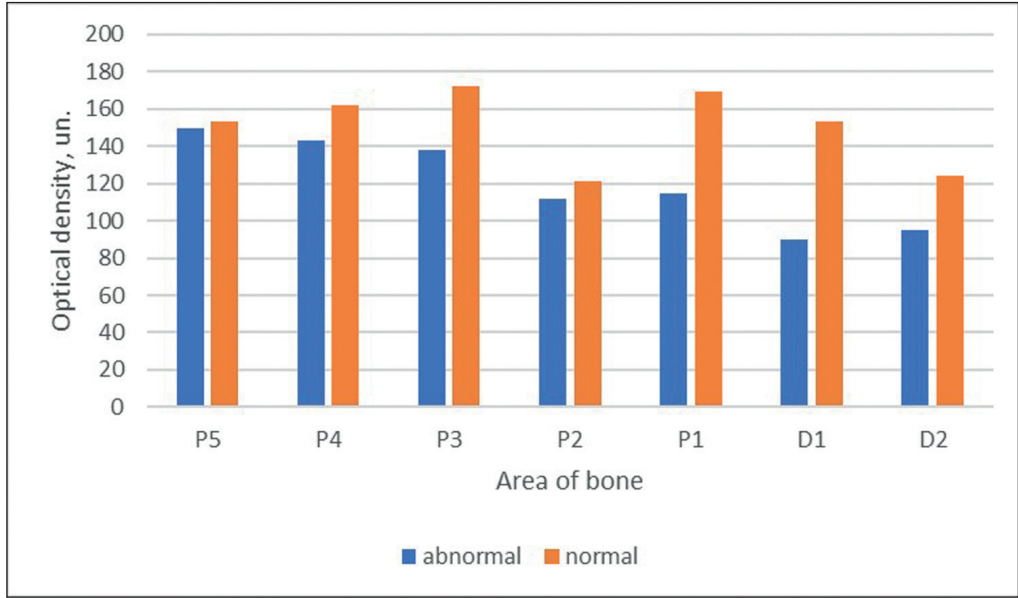


Fig. 4. Diagram of the optical density of the fibula in patients with CPT before surgery.

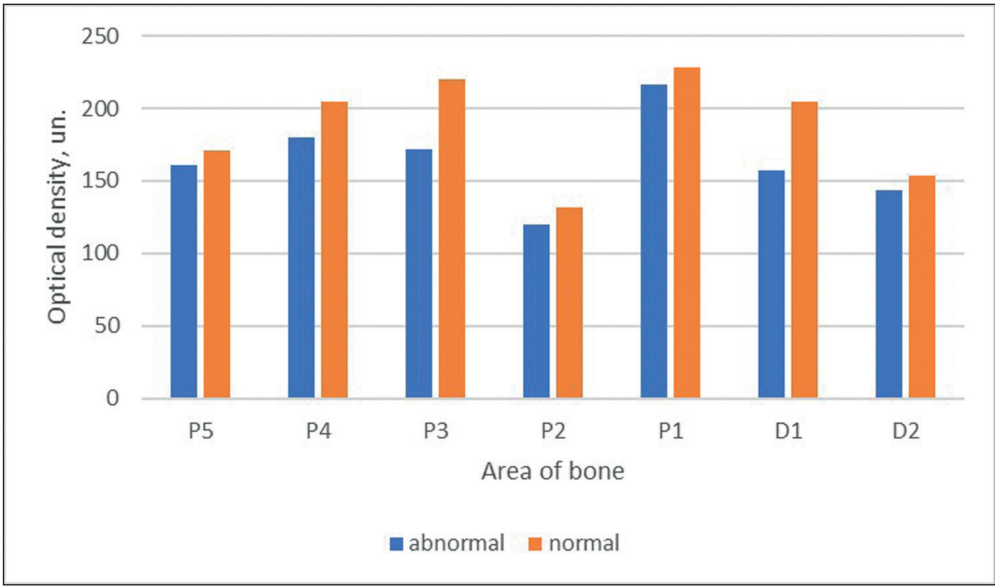


Fig. 5. Diagram of the optical density of the fibula in patients with CPT after surgery.

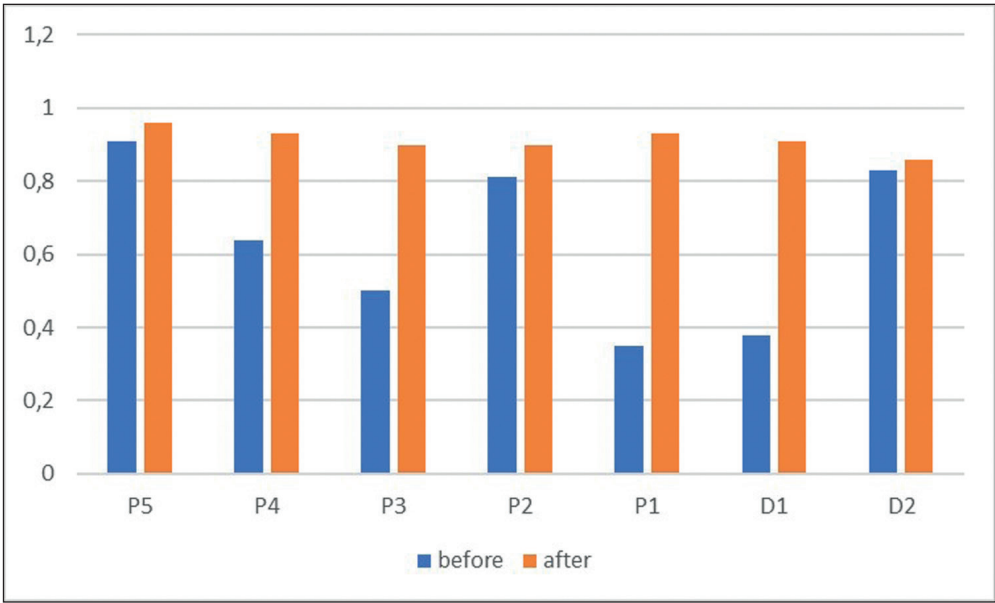


Fig. 6. Diagram of the ratio of the density of the patient abnormal/normal tibia in patients with CPT before and after surgery.

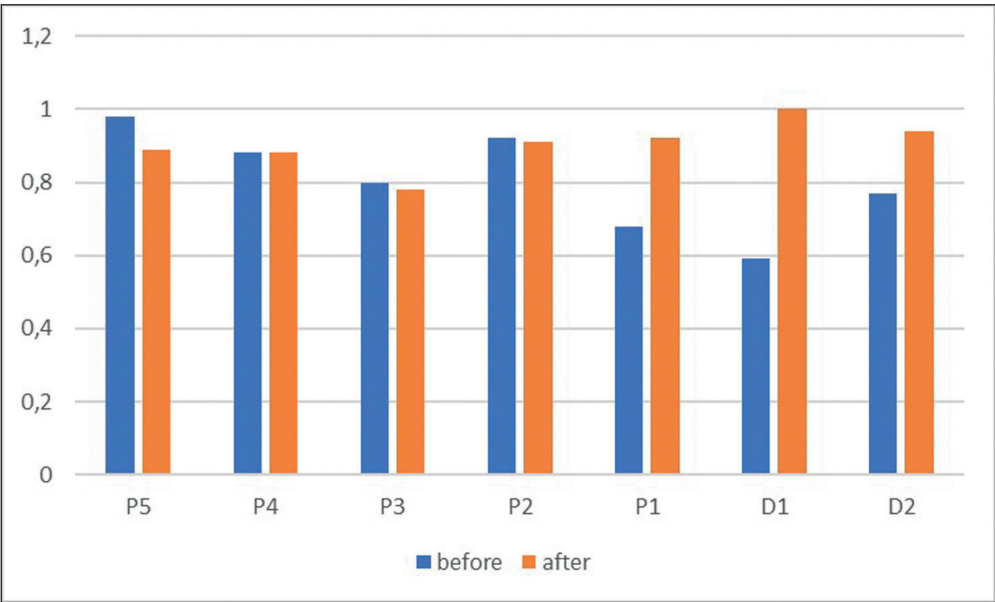


Fig. 7. Diagram of patient / healthy fibula density ratios in patients with CPT before and after surgery.

Table I. The density of the tibia in patients with CPT before surgery.

Area	Index	Optical density, un.		T_test
		Normal	Abnormal	
P5	M±SD	128±8	142±6	t=-5,547; p=0,031
P4	M±SD	106±5	165±3	t=-13,084; p=0,006
P3	M±SD	87±5	174±9	t=-11,111; p=0,008
P2	M±SD	102±6	127±7	t=-4,536; p=0,045
P1	M±SD	65±7	188±4	t=-20,524; p=0,002
D1	M±SD	54±6	142±7	t=-17,600; p=0,003
D2	M±SD	86±3	103±2	t=-14,422; p=0,005

Table II. The optical density of the tibia in patients with CPT after surgery.

Area	Index	Optical density, un.		T_test
		Abnormal	Normal	
P5	M±SD	186±10	194±12	t=-2,538; p=0,126
P4	M±SD	194±8	209±3	t=-2,887; p=0,102
P3	M±SD	213±10	234±11	t=-1,698; p=0,232
P2	M±SD	137±2	152±2	t=-8,693; p=0,013

Table III. Comparative analysis of tibia density in patients with CPT before and after surgery.

Area	Period	Optical density, Un.			
		Abnormal	T_test	Normal	T_test
P5	before	128±8	t=-11,995	142±6	t=-0,100
	after	186±10	p=0,007	194±12	p=0,930
P4	before	106±5	t=-21,774	165±3	t=-3,393
	after	194±8	p=0,002	209±3	p=0,077
P3	before	87±5	t=-20,464	174±9	t=-4,504
	after	213±10	p=0,002	234±11	p=0,046
P2	before	102±6	t=-7,142	127±7	t=-1,310
	after	137±2	p=0,019	152±2	p=0,320
P1	before	65±7	t=-50,190	188±4	t=-10,865
	after	196±8	p=0,000	210±11	p=0,008
D1	before	534±6	t=-27,602	142±7	t=-12,217
	after	174±7	p=0,001	191±2	p=0,007
D2	before	86±3	t=-34,843	103±2	t=-7,318
	after	151±3	p=0,001	176±4	p=0,018

ical Sciences of Ukraine” an X-ray study of the density of cortical bone tissue of the tibia in patients with congenital pseudoarthrosis was performed.

The research was performed based on X-rays of the tibia of three patients with congenital pseudoarthrosis, aged 5 to 7 years. All patients underwent surgical treatment in the form of fixation of fragments of the tibia with an expanding intramedullary rod, and autogenous pelvic bone grafting between the tibia and the fibula and around the CPT to create a cross union between tibia and fibula. We used images that were taken before surgery and 1 year after surgery. The optical density of the cortical layer of both shin bones was

determined, for which they were conventionally divided into 7 zones. Five zones P1-P5 were located in the proximal bone fragments (above the nonunion line) and two zones D1-D2 in the distal fragment (below the nonunion line). The scheme of measurement zones is shown in Fig. 1.

The measurements were performed using the X-Rays software package developed at Kharkiv National University of Radio Electronics [6-8].

The experimental data were processed statistically. The mean value (M) and its standard deviation (SD), as well as the minimum and maximum values were calculated. Within one group, comparisons were performed using a

Table IV. Fibula density in patients with CPT before surgery

Area	Index	Optical density, Un.		T_test
		Normal	Abnormal	
P5	M±SD	150±7	153±6	t=-2,219; p=0,157
P4	M±SD	143±4	162±8	t=-2,955; p=0,098
P3	M±SD	138±5	178±3,2	t=-7,419; p=0,018
P2	M±SD	112±6	121±5	t=-1,942; p=0,192
P1	M±SD	115±4	169±6	t=-12,610; p=0,006
D1	M±SD	90±5	153±8	t=-19,089; p=0,003
D2	M±SD	95±6	124±7	t=-10,961; p=0,008

Table V. Fibula density in patients with CPT one year after surgery

Area	Index	Optical density, Un.		T_test
		Abnormal	Normal	
P5	M±SD	161±10	171±11	t=-1,975; p=0,187
P4	M±SD	180±14	205±6	t=-2,789; p=0,108
P3	M±SD	172±9	220±11	t=-14,500; p=0,005
P2	M±SD	120±8	132±8	t=-1,459; p=0,282
P1	M±SD	217±15	228±11	t=-2,692; p=0,115
D1	M±SD	203±4	205±5	t=-1,606; p=0,250
D2	M±SD	144±15	154±9	t=-0,814; p=0,501

Table VI. Comparative analysis of fibula density in patients with CPT before and after surgery

Area	Period	Optical density, Un.			
		Normal	T_test	Abnormal	T_test
P5	before	150±7	t=-5,959	153±6	t=-6,203
	after	151±10	p=0,027	171±11	p=0,025
P4	before	143±4	t=-38,105	162±8	t=-5,730
	after	180±14	p=0,001	205±6	p=0,029
P3	before	138±5	t=-7,653	172±3	t=-10,852
	after	172±9	p=0,017	220±11	p=0,008
P2	before	112±5	t=-5,022	121±5	t=-1,588
	after	120±8	p=0,037	132±8	p=0,253
P1	before	115±4	t=-127,752	169±6	t=-9,344
	after	217±15	p=0,001	228±11	p=0,011
D1	before	90±5	t=-9,006	153±8	t=-29,670
	after	202±4	p=0,012	205±5	p=0,001
D2	before	95±6	t=-54,250	124±7	t=-3,492
	after	144±15	p=0,001	154±9	p=0,073

paired T-test (regenerate / bone of the recipient), comparisons between groups were performed using a T-test for independent samples, calculating the critical value of the test (t) and statistical significance (p). Data analysis was performed in a package for statistical analysis IBM Statistic SPSS 20.0 [9].

RESULTS

As a result of the study, data were obtained on the optical density of the cortical layer of healthy and damaged tibia in patients with CPT before surgery. The results of statistical processing of these data are given in Table I.

Table VII. Comparative analysis of the ratio of the density of the patient abnormal/normal tibia in patients with CPT before and after surgery.

Area	Period	The ratio of bone density Abnormal/Normal	
		M±SD	T_test
P5	before	0,91±0,03	t=-2,467
	after	0,96±0,03	p=0,132
P4	before	0,64±0,04	t=-18,520
	after	0,93±0,04	p=0,003
P3	before	0,50±0,05	t=-9,236
	after	0,90±0,06	p=0,012
P2	before	0,81±0,06	t=-1,876
	after	0,90±0,02	p=0,201
P1	before	0,35±0,04	t=-16,593
	after	0,93±0,03	p=0,004
D1	before	0,38±0,05	t=-29,747
	after	0,91±0,05	p=0,001
D2	before	0,83±0,02	t=-1,488
	after	0,86±0,03	p=0,275

Table VIII. Comparative analysis of the ratio of patient abnormal/normal fibula density in patients with CPT before and after surgery.

Area	Period	The ratio of bone density in abnormal/normal	
		MG_B/Z	T_test
P5	Before	0,98±0,01	t=1,796;
	After	0,89±0,10	p=0,214
P4	Before	0,88±0,06	t=0,080
	After	0,88±0,07	p=0,943
P3	Before	0,80±0,04	t=0,767
	After	0,78±0,02	p=0,523
P2	Before	0,92±0,07	t=0,108
	After	0,91±0,11	p=0,924
P1	Before	0,68±0,03	t=-9,681
	After	0,92±0,02	p=0,01
D1	Before	0,59±0,03	t=-44,923
	After	1,0±0,02	p=0,001
D2	Before	0,77±0,03	t=-2,092
	after	0,94±0,14	p=0,172

The results of the study suggest that in all patients with CPT before treatment there was a statistically significant decrease in the optical density of cortical bone tissue of the damaged tibia compared to the contralateral. A statistically significant difference in density was determined in all studied areas of the tibia.

It is possible to visually compare the values of the optical density of the cortical layer of the tibia in patients with CPT in all control areas using the diagram shown in Fig.2.

The diagram clearly shows that the largest difference in the density of the cortical layer of healthy and damaged tibia is determined in the area of pseudoarthrosis, both in the proximal and distal fragments (areas P1 and D1). As you move away from the zone of pseudoarthrosis, the

difference in the density of the cortical layer decreases, but it does not lose the statistical significance.

The results of determining the optical density of the cortical layer of healthy and damaged tibia in patients with CPT 1 year after surgery are given in Table II.

One year after surgery, the optical density of the cortical layer of the tibia of the healthy and operated limbs is compared. This is evidenced by the indicators of comparative analysis by T-test, which do not determine the statistical significance of the density difference in almost all studied areas. An exception is the distal part of the fragment below the pseudoarthrosis zone (zone D2), where the density difference remains statistically significant at the $p = 0.020$ level, and also the P2 zone,

where the density difference also remains statistically significant ($p = 0.013$). For a clear comparison of the optical density values of the cortical layer of healthy and damaged tibia in patients with CPT 1 year after surgery, the diagram shown in Fig. 3.

The diagram clearly shows the decrease in the difference in the optical density of the cortical layer of healthy and operated tibia patients with CPT a year after surgery in all studied areas.

The next stage was the study of changes in the density of the cortical layer, which occurred separately in the operated and healthy tibia during the year after surgery. The results of comparative analysis by T-test of tibia density in patients with CPT before and after surgery are given in Table III.

As shown by the results of comparative analysis by T-test, during the year after surgery there was an increase in the optical density of the cortical layer of both tibia of the studied patients. The increase in the density of the nonoperated tibia can be attributed to the active growth of patients, as evidenced by the lack of statistical significance of the difference in the density of the cortical layer in the proximal areas P2-P5. In the distal part, changes in density became statistically significant at the level of $p < 0.05$ (zones P1, D1, D2).

As for the operated limb, an increase in the density of the cortical layer obtained statistical significance in all the areas studied, it can be attributed not only to the growth of patients, but also the possibility of active loading of the operated limb.

The results of the study of the optical density of the cortical layer of the fibula in patients with CPT before surgery are given in Table IV.

The results of the study showed that the difference in the optical density of the cortical layer of the fibula of healthy and damaged limbs is less pronounced than on the tibia. So statistically significant ($p < 0.05$) differences are observed mainly in the distal part of a bone, namely in zones D2, D1, P1, and also in the middle of a diaphysis (zone P3). In other studied areas, the difference in cortical layer density does not become statistically significant.

The diagram shown in Fig. 4 allows to get a clear idea of the values of the optical density of the cortical layer of the fibula in patients before surgery.

In the Table V shows data on the values of the optical density of the cortical layer of the fibula in patients with CPT 1 year after surgery.

The results of statistical analysis showed that 1 year after surgery, the optical density of the cortical layer of the fibula of healthy and operated limbs is compared, as evidenced by the absence of statistically significant ($p > 0.05$) differences in this indicator along the entire length of the fibula.

Visually compare the values of the optical density of the cortical layer of healthy and operated fibula in patients with CPT a year after surgery will help the diagram shown in Fig. 5.

To determine the level of significance of differences in the density of the cortical layer of the fibula during treatment,

a comparative analysis of the T-test of these indicators before and after surgery. The results of statistical analysis are given in Table VI.

Comparative statistical analysis showed that the optical density of the cortical layer of the fibula of both extremities tends to increase. On the nonoperated limb, the increase in the optical density of the cortical layer of the fibula becomes statistically significant (at $p < 0.05$) in all studied areas except for zones P2 and D2, where the level of significance is determined at $p = 0.253$ and $p = 0.073$, respectively. On the operated limb in all studied areas, the increase in the optical density of the cortical layer of the fibula is determined to be statistically significant.

The last stage of the study was a comparative analysis of the ratio of the density of the cortical layer of the tibia between the abnormal and normal extremities before and after surgery. This test should show how much the density of the operated limb is close to that of healthy bone. Ideally, this ratio should be equal to 1. The results of the comparative analysis for the tibia are given in Table VII.

The results of the analysis showed that in all the studied areas there is an increase in the ratio of the density of the cortical layer of the tibia of the operated and nonoperated limbs. In almost all studied areas, the changes become statistically significant at the level of $p < 0.05$. Exceptions are the zone P5, P2, D2 where this ratio before the operation was determined at a fairly high level (0.91 ± 0.03), (0.81 ± 0.06) and (0.83 ± 0.02), respectively. In this case, the density in these areas did not have a range for large changes.

A clear idea of the changes in the ratio of the optical density of the cortical layer of the nonoperated tibia and operated tibia during treatment is provided by the diagram shown in Fig. 6.

As you can see in the diagram, the largest changes in the density of the cortical layer of the tibia occurred around the site of pseudoarthrosis, namely in areas P1 and D1.

The results of a comparative analysis of the ratio of the optical density of the cortical layer of the fibula of normal and operated limbs during treatment are given in Table VIII.

As you can see, the ratio of the density of healthy and operated fibula is not growing as noticeably as the tibia, as evidenced by the statistical significance of differences in this indicator before and after surgery, which do not reach $p = 0.05$, in almost all studied areas. Exceptions are zones P1 and D1 where the difference in the ratio of the optical density of the cortical layer of healthy and operated limbs becomes statistically significant $p = 0.01$ and $p = 0.001$, respectively.

The diagram shown in Fig. 7, gives a clear idea of the changes in the ratio of the optical density of the cortical layer of the fibula of healthy and operated limbs during treatment.

DISCUSSIONS

CPT in children is an orphan disease characterized by the formation of a pseudoarthrosis zone, and, as a con-

sequence, leads to the secondary deformation of the tibia and persistent gait disorders, limping [2].

It is known that CPT is accompanied by complex violations of the biological properties of the periosteum, with the growth of pathological tissue - hamartoma and disorders of the bone tissue of the tibia [10].

Surgical treatment of CPT remains a serious challenge for pediatric orthopedists.

One of the unresolved aspects of surgical treatment of CPT is the extent of resection of pathologically altered soft tissues, periosteum and bone in the pseudoarthrosis zone.

Nowadays there is a limited number of studies that examine the nature of changes in the bone tissue of the leg before and after surgery.

Diachkov KA et al. showed the changes in the MRI signal of the periosteum and bone in the pseudoarthrosis zone [11].

Dr Paley proposes a radical periosteal resection in the pseudoarthrosis zone with gentle bone resection [12].

Our research showed that patients with congenital pseudoarthrosis of the tibia have a decrease in the density of the tibia of the affected limb, while the density decreases in the direction of the nonunion zone.

The decrease of the cortical layer density of the tibia of the injured limb is less noticeable, and there are significant changes in the pseudoarthrosis zone.

It is confirmed by the data on the presence of impaired quality of bone tissue in the CPT conditions [3].

There is a statistically significant ($p < 0.01$) increase in the cortical layer density of bones of both operated and healthy limbs a year after the surgical treatment of congenital pseudoarthrosis of the tibia, which can be explained by a positive appearance of an increased exertion on the operated limb.

The cortical layer optical density of the bones of the operated leg is statistically significant ($p > 0.05$) close to the bone density of a healthy limb a year after a surgery.

It can be explained by the several factors coincidence.

Firstly, when achieving consolidation, the patient begins a progressive increase exertion to the limb, and secondly, there is a completely or partly restoration of bone during the growth of the child.

The obtained data confirm the rationality of orgone-preserving surgical treatment aimed at achieving the fusion of pseudoarthrosis in patients with CPT. [13].

CONCLUSIONS

In all patients with CPT before treatment, a statistically significant decrease in the density of cortical bone tissue of the damaged tibia compared with contralateral.

As a result of the carried-out treatment approximation of density of bone tissue of the operated extremity to indicators of an intact contralateral bone is noted.

REFERENCES

- Shannon C.E., Huser A.J., Paley D. Cross-Union Surgery for Congenital Pseudarthrosis of the Tibia. *Children*. 2021;8:547. doi:10.3390/children8070547.
- Hefti F., Bollini G., Dungal P. et al. Congenital Pseudarthrosis of the Tibia: History, Etiology, Classification, and Epidemiologic Data. *J. Pediatric Orthop. Part B*. 2000; 9: 11–15.
- Shah H., Joseph B., Nair B.V.S. et al. What Factors Influence Union and Refracture of Congenital Pseudarthrosis of the Tibia? A Multicenter Long-term Study. *J. Pediatric Orthop.* 2018;38:e332–e337.
- Khmyzov S.O., Katsalap Ye.S., Karpinsky M.Yu., Yaresko O.V. Mathematical modeling of osteosynthesis of the lower leg bones during their congenital pseudarthrosis in the middle third. *Bulletin of problems in biology and medicine*. 2020;4 (158): 239–246.
- Packer D., Robb J., Liu R. et al. Combined pharmacologic and biological treatment of congenital pseudarthrosis of the tibia; 100% union; no re-fractures! *J. Child. Orthop.* 2016;1: 19–20.
- Patent 60345. IPC A61B 5/107 (2006.01) A method for diagnosing osteoporosis / Averyanova LO (UA); Golovenko VM (UA); Sklyar OI (UA); Sharmazanov OP (UA) (Patent owner Kharkiv State Technical University of Radio Electronics (UA); Kharkiv Medical Academy of Postgraduate Education (UA)). Application 2000042287 dated 21.04.2000. Publ. 15.10.2003, bul. № 10
- Tymoshenko O.P., Karpinsky M.Yu., Veretsun A.G. Research of diagnostic possibilities of the X-rays software package. *Medicine*. 2001; (1): 62–64.
- Bondarenko S., Filipenko V., Karpinsky M. et al. Osseointegration of porous titanium and tantalum implants in ovariectomized rabbits: A biomechanical study. *World J Orthop.* 2021; 12(4): 214–222. doi: 10.5312/wjo.v12.i4.214.
- Nasledov A. SPSS 19: professional statistical data analysis. - SPb: Piter. 2011, 400p.
- Paley D. Congenital pseudarthrosis of the tibia: biological and biomechanical considerations to achieve union and prevent refracture. *J Child Orthop.* 2019;13(2):120–133. doi:10.1302/1863-2548.13.180147.
- Galina D., Diachkov K.A., Borzunov D., Kutikov S.A. Complex Radiological findings in Congenital Pseudarthrosis of the Tibia. *J Orthop Disord.* 2018;1(1):5.
- Paley D. Congenital pseudarthrosis of the tibia: combined pharmacologic and surgical treatment using bisphosphonate intravenous infusion and bone morphogenic protein with periosteal and cancellous autogenous bone grafting, tibio-fibular cross union, intramedullary rodding and external fixation. *Zorzi A*. 2012, 106p.
- Shannon C.E., Huser A.J., Paley D. Cross-Union Surgery for Congenital Pseudarthrosis of the Tibia. *Children*. 2021;8:547. doi:10.3390/children8070547.

This study was performed as part of research work of Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine on «Develop a comprehensive approach to the treatment of congenital pseudoarthrosis of the tibia in children» (No state registration 0119 U102343).

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Conflict of interest:

The Authors declare no conflict of interest.

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Received: 19.08.2021

Accepted: 29.06.2022

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis,
D – Writing the article, **E** – Critical review, **F** – Final approval of the article