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SURGICAL CORRECTION OF JOINT DEFORMITIES AND HYALINE CARTILAGE REGENERATION

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Aim. To determine a method of extra-articular osteochondral fragment formation for the improvement of surgical correction results of joint deformities and optimization of regenerative conditions for hyaline cartilage.
Materials and Methods. The method of formation of an articular osteochondral fragment without penetration into the joint cavity was devised experimentally. More than 30 patients with joint deformities underwent the surgery.
Results. During the experiments, we postulated that there may potentially be a complete recovery of joint defects because of hyaline cartilage regeneration. By destructing the osteochondral fragment and reforming it extra-articularally, joint defects were recovered in all patients. The results were evaluated as excellent and good in majority of the patients.
Conclusion. These findings indicate a novel method in which the complete recovery of joint defects due to dysplastic genesis or osteochondral defects as a result of injuries can be obtained. The devised method can be used in future experiments for objectification and regenerative potential of hyaline cartilage (e.g., rate and volume of the reformed joints that regenerate, detection of cartilage elements, and the regeneration process).

Keywords: joint deformities, surgical correction, cartilage.

A series of experimental works has proven the possibility of articular cartilage regeneration. The maximum sizes of regenerated cartilage defects (mostly round in shape) were 3–5 mm. However, even in cases of successful cartilage defect healing, the novel hyaline-like cartilage was revealed to be inferior to normal articular cartilage in terms of longevity and function [1]. Larger osteochondral defects that heal with assistance from fibrous cartilage lack the strength of hyaline cartilage, which subsequently leads to early arthrosis. Some previous literature are optimistic with regard to autologous osteochondral and autologous chondrocyte transplantation into areas of articular surface defects; however, we do not support this optimism because the space between autografts and the surrounding cartilage is usually filled with fibro-cartilaginous tissue that cannot transform into hyaline cartilage [2-4]. Apparently, the complete regeneration of articular cartilage is difficult because in all experiments, the development of newly formed hyaline cartilage was due to undifferentiated endosteal connective tissue cells [5]. To date, no reports in the literature have demonstrated the possibility of articular cartilage self-regeneration. Several papers suggest the involvement of bone marrow mesenchymal stem cells in the process of cartilage differentiation [6-8].

Only experimental work conducted at the Saratov Research Institute of Traumatology and Orthopedics has revealed that “in 50% of cases, the regeneration of articular cartilage originates not only from the subjected bone trabeculae but also from chondroblasts of articular cartilage surface sections on the edges of osteochondral injury” [9]. Data obtained in this experiment introduced the prospect of research on a more important issue, that is, the regeneration of hyaline cartilage.

Objective: To develop a method to promote the extra-articular formation of osteochondral articular fragments, thus improving the results of surgical joint deformity correction and optimize conditions for hyaline cartilage regeneration.

Materials and methods

During the initial stage of this study, we performed 22 experiments on 16 mongrel dogs of different ages and analyzed 32 microsamples prepared from the tibial and femoral bone condyles of human corpses after manipulation to determine a surgical technique for the isolation of osteochondral fragments. The animals were kept under standard vivarium conditions with a feeding regimen and free access to water. The experiments were performed in accordance with the 1985 Geneva Convention "International biomedical research using animals" guideline, USSR Ministry of Health order from 08/12/1987, No 755 "Rules of work with experimental animals," and approval from the Ethics Committee at the Saratov Research Institute of Traumatology and Orthopedics. Experiments to prove the possibility of instantaneous osteochondral articular fragment formation without joint dissection and to develop a method for the surgical correction of periarticular knee joint deformities were performed on animals subjected to intrapleural mononarcosis with a 5% solution of sodium thiopental at a dosage of 0.03 g/kg of weight.

The clinical portion of the study included 30 children and adolescents with periarticular knee joint deformities due to rickets, Erlacher–Blount disease, hematogenous osteomyelitis, or trauma, as well as deformities of an unknown congenital etiology. The ages of the patients ranged from 12 to 17 years. The study included 7 male and 23 female patients.

Surgical correction of periarticular knee joint deformities was performed according to the developed method, which was based on the performance of a series of osteotomies in a particular order [10].

Technique of osteotomy. Bone dissection is usually initiated using chisels or a vibrosaw, starting from the periphery (metadiaphyseal area of the deformed side) to the border of the deformed and non-deformed joint sections while avoiding injury to the cruciate ligament attachment sites. Transperiosteal bone dissection is preferable for preserving the vessels that supply the formative fragment. In young patients, dissection of the metadiaphyseal cartilage area is performed in a strictly central manner to prevent the possible subsequent formation of secondary deformities. Special attention is paid to dissection of the subchondral bone layer. This procedure involves bone excochleation using Volkmann's spoon or a careful operation with a small-diameter ball reamer. The emergence of the osteochondral fragment mobility indicates complete removal of the subchondral bone layer; this can only be confirmed manually. The formed mobile osteochondral fragment, which is connected through soft tissues to the joint and through hyaline cartilage to the adjacent condyle, is moved to the position required for joint deformity correction. This correction is promoted by viscoelasticity of the cartilage, specifically the ability to reverse deformation upon compression and possess sufficient strength to resist breakage upon stretching [11]. Additional components of the deformation (e.g., varus, valgus, recurvation, antecurvation) are eliminated via corrective osteotomy of the metaphyseal area contralateral to the first osteotomy. Furthermore, the second osteotomy is performed after fixing the formed osteochondral fragment in the corrective position using any available method. In this type of surgery, osteosynthesis must be very stable in order to support joint function beginning in the early postoperative period. Joint function is necessary not only for the production of synovial fluid, but the movement of this fluid in the joint cavity as articular cartilage is known to be supplied by this fluid [12, 13].

The mobility of the formed osteochondral fragment should only be validated by palpation; for this purpose, the use of any tool as a lever is unacceptable.

Patients were monitored for 5–9 years. Therapeutic results were assessed using clinical and radiological controls, computed tomography, and ultrasound examination of the joint.

Results

The technique to achieve instantaneous osteochondral articular fragment formation without joint cavity dissection was experimentally practiced on dogs.

Histological samples of cadaver tibial and femoral bone condyles were used to establish that partial destruction of the subchondral bone layer results in articular cartilage fracture upon an attempt to validate mobility in the formed osteochondral articular fragment. The absence of articular cartilage damage was confirmed using contrast arthrography in the upright joint position, as well as visual monitoring of the articular surface during dissection.

The experiment demonstrated the complexity and uniqueness of the articular cartilage configuration, as well as the subchondral bone layer. Along with a certain level of skill, the instruments used (Volkmann's spoon, ball reamers) allowed the destruction of the subchondral bone layer along the osteotomy line, with minimal damage to the cartilage itself and no further effects on the function of the osteochondral fragment. In the experiments, the maximum lengths and depths of single fissures in the cartilage basal parts did not exceed 110 μm, or 1/10 of the articular cartilage thickness.

Among our patients subjected to surgery for joint deformities, special attention should be given to four cases in which articular defects were restored by distraction of the osteochondral fragment using a technique that we presented in an earlier report [14]. In two cases of hip dysplasia, acetabular roof deficits were reconstructed using full autografts without joint dissection. In one case, we liquidated a deficit in one of the femur condyles in a patient with osteomyelitis. A clinical observation is presented below as an example.

Patient M. was 15 years of age and had received a diagnosis of recurvation-valgus deformity of the left knee joint. As the tibial plateau in the dorsoventral direction is 9-mm smaller than the opposite side and was chamfered in the caudal direction by 10° (Figs. 1 and 2), a deformity with a dysplastic genesis could be assumed (Figs. 1 and 2). This was also indicated by the clinical manifestation of a 15° joint hyperextension. Surgery was performed on December 12, 2005 and involved corrective multiplanar tibial osteotomies in the proximal tibia with abarticular formation of the condyle osteochondral articular fragment, transverse osteotomy at the level of the middle third of the fibula, fragment fixation with two wires, and mounting of an external fixator on the lower leg. Because of a metaepiphyseal osteotomy of the tibia in the frontal plane with scooping of the subchondral bone in the cross-sectional plane, a mobile osteochondral fragment was formed from the front half of tibia condyles and was further distracted using a horseshoe-shaped Kirschner wire (Fig. 3) and a screw shaft that was introduced into the fragment through the bottom of the patellar ligament. The recurvation and valgus of the lower leg in this area were simultaneously eliminated by the wedge osteotomy of the posterior tibial metadiaphysis. A wire was used to fix the fragment in the apparatus (Fig. 4). Beginning on the 6^{th} day after surgery, distraction of the front fragment was performed strictly in the ventral direction at a rate of 0.25 mm per day (0.03 mm per 1.5 h) for a total of 51 days. The fragment was lengthened by a total of 12.24 mm. The total estimated area of the accrued articular cartilage was 10.45 cm^2. During the postoperative period, the patient was treated with one capsule of Theraflex, Sagmel, Inc., USA twice daily for 3 weeks) to stimulate cartilage regeneration; after discharge from the hospital, this dosage was changed to one capsule per day for 30 days. Three knee punctures were performed to study the synovial fluid composition. Exercise therapy was

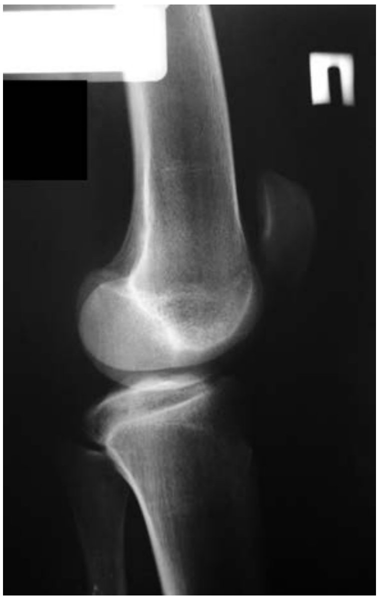

Fig. 1. Radiograph of the right knee, lateral view. The length of the tibial plateau is 60 mm

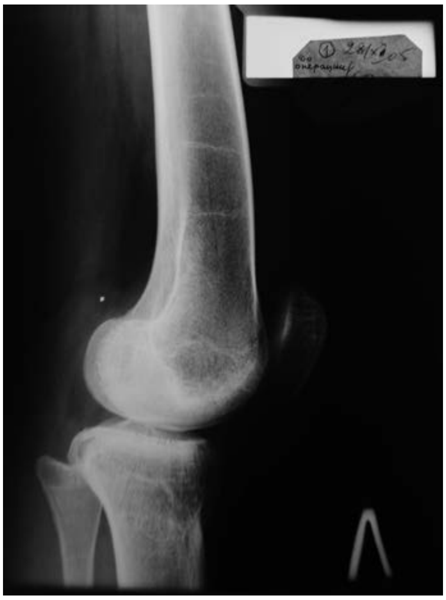

Fig. 2. Preoperative radiograph of the left knee, lateral view. The length of the tibial plateau is 51 mm

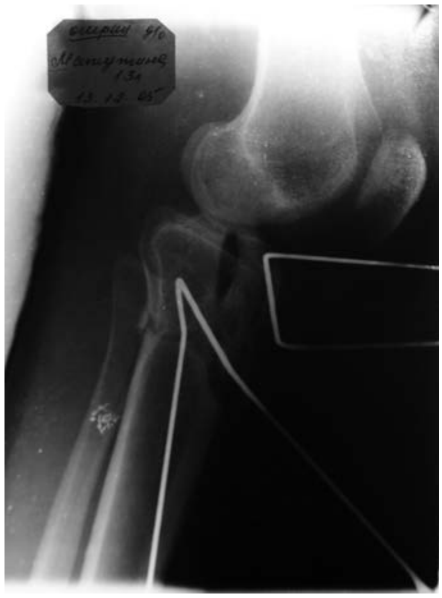

Fig. 3. Postoperatvie radiograph of the left knee after tibial osteotomy and fixation with 2 wires

administered daily and was aimed at left knee joint development, with some limitation of full extension, as well as massage of the muscles in the left hip and right lower leg. Limited load bearing (walking with crutches) on the left leg was permitted 2 months after surgery. The external fixation device was removed after 3.5 months. Full load bearing on the operated limb was permitted 8 months after surgery. The patient did not complain of problems during a postoperative follow up of 5 years and 9 months (Fig. 5). The left lower limb axis was corrected and full joint function was available. A small cosmetic defect approximately 5–6 cm distal to the tibial tuberosity remained (the patient abstained from its elimination). The restored cartilage maintained its size at almost 6 years after corrective surgery. However, this area was found to be osteoporotic because of the recommended partial restriction of full knee joint extension. Postoperative ultrasound and computed tomography studies did not reveal any changes in the area of articular cartilage distraction.

This method, which was developed to surgically correct periarticular knee joint deformities and was clinically tested in 30 patients, yielded excellent and good results in 100% of cases with mild and moderate knee deformities. In contrast, 90.1% of cases with severe and extremely severe deformities did not achieve excellent results, whereas 71.4% achieved good results and 14.3% achieved satisfactory or poor results [10, 15]. It should be noted that these outcomes were determined in a group that contained many patients with deformities of a multiplanar nature.

Therefore, highly efficient compensation of articular defects with a dysplastic genesis is possible only in cases of hyaline cartilage regeneration. These cases can be promoted by a number of conditions:

1) Cartilage should not be damaged during joint osteochondral fragment formation; the generated fragment must be sufficiently large relative to the surrounding soft tissues that provide trophism;

2) Joints must always function during articular defect compensation to produce synovial fluid, which provides nourishment for the cartilage;

3) Osteochondral fragment distraction should occur at a small shot pace (0.03 mm every 1.5 h), and the daily maximum distraction must not exceed 0.25 mm. However, this condition requires experimental verification.

Discussion

The conducted experimental studies demonstrated the requirement for complete destruction of the subchondral bone layer during movable osteochondral fragment formation. This requirement is due to the high mineral density of subchondral bone (0.36–0.40533 g/cm^2, and 0.2–0.25 g/cm^2 in metaphyseal areas), which means that even the presence of a thin layer under the hyaline cartilage maintains the stiffness of the

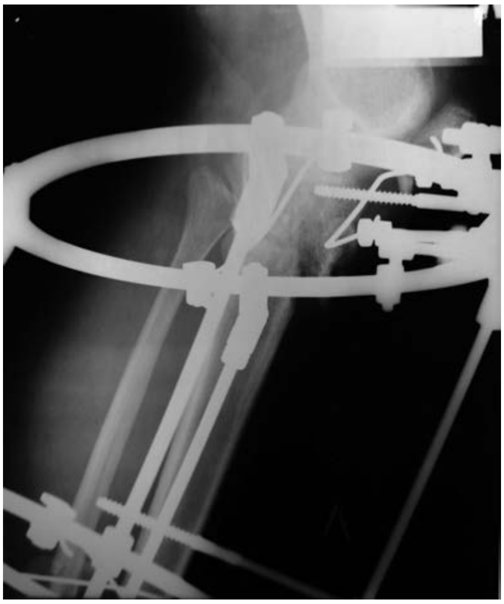

Fig. 4. Postoperatvie radiograph of the left knee after tibial osteotomy with external fixation

Fig. 5. Radiographsof the left knee, anteroposterior and lateral view 5 years 9 months postoperatively. The length of the tibial plateau is 64 mm

cartilage-bone system [16]. A bone fracture results in cartilage fracture. Total removal of a bone, which occurred in 73.7% of cases of the studied microsamples, renders this system elastic and allows the potential determination of the specific movement of osteochondral fragments in different planes; accordingly, the motion of this fragment becomes possible both simultaneously and gradually by distraction.

Successful experiments conducted at the Saratov Research Institute of Traumatology and Orthopedics and a careful study of the literature devoted to articular cartilage regeneration allowed us to make more conclusive statements about the regenerative capabilities [17].

The issues related to joint deformity compensation are known. However, poor surgical treatment results (up to 50% recurrence) do not eliminate the urgency of this orthopedic problem [18]. Periarticular osteotomies do not affect joint deformation, whereas more efficient subchondral osteotomies can be accompanied by intra-articular fractures, hemarthrosis, subchondral bone dystrophy, and degeneration of hyaline cartilage. Inevitably, these conditions will all result in arthritis.

Integrity throughout the articular cartilage thickness is ascertained in children with knee joint deformities during corrective surgery based on our own technique. Consequently, we can draw the conclusion that the cartilage increases its size as a result of self-regeneration, and the intercolumnar spaces between the cartilage cells (extracellular matrix) extend during the initial phase of distraction. We assume that at some point during distraction, mitosis occurs within the columns of chondrocytes that are rigidly connected to the bone as distraction creates maximum stress in these areas. Subsequently, distraction forces are transmitted to the cartilage bridge, which is not connected to the bone. As a result, chondrocyte mitosis within this bridge will be slightly dilatory. During further distraction, the extracellular matrix that surrounds newly formed chondrocytes columns expands, accompanied by a reduction in mitotic activity; these phenomena indicate the completion of cartilage regeneration.

The abovementioned hypothetical hyaline cartilage regeneration processes are based on the fact that the extracellular matrix comprises collagen fibers, which exist in a concentrated solution of proteoglycans, or molecules that exist in a compressed and woven form and strengthen the cartilage matrix [19]. On one hand, distraction loosens the extracellular matrix and reduces proteoglycan molecule compression; on the other hand, distraction directly irritates the chondrocytes. Moreover, active mitosis is initiated in type I chondrocytes (those closest to the articular cartilage surfaces); later, less active mitosis occurs in type II and III cells. Otherwise, cartilage wound healing would occur only in superficial areas of the articular cartilage and would not extend throughout the depth of cartilage injury. However, traumatic articular defects may not fully heal because even if the defect is compensated with an osteochondral fragment, the edge between this fragment and the cartilage injury will still be healed by fibrous cartilage. In such cases, autologous transplantation of chondrocytes into the area of contact between the displaced osteochondral fragment and the edge of the cartilage injury following the near-complete restoration of articular cartilage may yield a more effective result [4,11].

These assumptions, which require experimental confirmation, are not only theoretically but also practically significant as they would allow a more effective regeneration of hyaline cartilage involving restoration with various medical agents (e.g., hyaluronic acid agents, chondroprotectors, synovial fluid protectors) during the distraction stage.

Conclusion. The restoration of articular deformations and, especially, compensation of joint defects are directly related to the issue of hyaline cartilage regeneration. This technology, which was developed to facilitate extra-articular osteochondral articular fragment formation, allows the successful and complete correction of joint deformities (including multiplanar deformities) while excluding the negative features of subchondral osteotomies.

This clinically tested surgical method of articular cartilage regeneration introduces a broad perspective with regard to the treatment of patients in the early stages of arthritis with a dysplastic etiology, as well as patients with traumatic osteochondral defects. Issues related to the optimization of hyaline cartilage regeneration conditions (e.g., speed and pace of distraction, required amount of osteochondral regeneration, medical software) should be addressed in further experimental investigations.

References

1. Frenkel SR, Di Cesare PE. Degradation and repair of articular cartilage. *Front Biosci.* 1999;4:671-685. doi: 10.2741/frenkel.

2. Barber FA, Chow JC. Arthroscopic osteochondral transplantation. *Histologic results Arthroscopy.* 2001;17(8):832-835. doi: 10.1016/s0749-8063(01)90006-4.

3. Perka C, Schultz O, Lindenhayn K, et al. Joint cartilage repair with transplantation of embryonic chondrocytes embedded in collagen-fibrin matrices. *Clin Exp Rheumatol.* 2000;18(1):13-22.

4. Эйсмонт О.Л., Скакун П.Г., Борисов А.В., и др. Современные возможности и перспективы хирургического лечения повреждений и заболеваний суставного хряща // Медицинские новости. – 2008. – № 7. – С. 12-19. [Eysmont OL, Skakun PG, Borisov AV, et al. Sovremennye vozmozhnosti i perspektivy khirurgicheskogo lecheniya povrezhdeniy i zabolevaniy sustavnogo khryashcha. *Meditsinskie novosti*. 2008;7:12-19. (In Russ).]

5. Лаврищева Г.И., Михайлова Л.Н. О репаративной регенерации суставного хряща // Ревматология. – 1985. – № 4. – С. 47–50. [Lavrishcheva GI, Mikhaylova LN. O reparativnoy regeneratsii sustavnogo khryashcha. *Revmatologiya.* 1985;4:47-50. (In Russ).]

6. Маланин Д.А. Пластика полнослойных дефектов гиалинового хряща в коленном суставе: экспериментальные и клинические аспекты репаративного хондрогенеза: автореф. дис. … д-ра мед. наук. – Волгоград, 2002. – 39 с. [Malanin DA. Plastika polnosloynykh defektov gialinovogo khryashcha v kolennom sustave: experimentalnye i klinicheskie aspekty reparativnogo khondrogeneza [dissertation]. Volgograd, 2002. 39 p. (In Russ).]

7. Смирнов С.В., Сычевский М.В., Ваза А.Ю. Матрикс-терапия — новое направление регенеративной медицины. Сборник тезисов IX съезда травматологов-ортопедов России. Т. 3. – Саратов, 2010. – С. 1143. [Smirnov SV, Sychevskiy MV, Vaza AJu. Matrix-terapia – novoe napravlenie regenerativnoy meditsiny. In: Sbornik tezisov IX s'ezda travmatologov-ortopedov Rossii. Saratov, 2010;3:1143. (In Russ).]

8. Passler HH. Microfracture for treatment of cartilage defects. *Zentralbl Chir.* 2000;125(6):500-504.

9. Косицина А.М., Плотнягина В.И., Левошин В.В., и др. Влияние импульсного ультразвука на заживление внутрисуставного перелома коленного сустава в эксперименте // Ортопедия, травматология и протезирование. – 1980. – № 11. – С. 21–24. [Kositsina AM, Plotnyagina VI, Levoshin VV, et al. Vliyanie impulsnogo ultrazvuka na zazhivlenie vnutrisustavnogo pereloma kolennogo sustava v experimente. *Ortoped Travmatol.* 1980;11:21-24. (In Russ).]

10. Патент РФ на изобретение № 2185114/20.07.02. Бюл. № 20. Норкин И.А., Винокуров В.А., Царева Е.Е. Способ хирургической коррекции околосуставных деформаций коленного сустава у детей. [Patent RUS 2185114/20.07.02. Byul. № 20, Norkin IA, Vinokurov VA, Tsareva EE. Sposob khirurgicheskoy korrektsii okolosustavnykh deformatsiy kolennogo sustava u detey. (In Russ).]

11. Буланов Ю.Б. Хрящ // Muscle Nutrition Review. – 2002. – № 8. – С. 35–42. [Bulanov JB. Khryashch. *Muscle Nutrition Review*. 2002;8:35-42. (In Russ).]

12. Павлова В.Н. Синовиальная среда суставов. – М.: Медицина, 1980. – 295 с. [Pavlova VN. *Sinovialnaya sreda sustavov*. Moscow: Meditsina; 1980. 295 p. (In Russ).]

13. Neidel J, Schulze M. Value of synovial analysis for prognosis of matrix synthesis of transplanted chondrocytes. *Der Orthopade.* 2000;29(2):158-63.

14. Патент РФ на изобретение № 2316281/10.02.08. Бюл. № 4. Царева Е.Е., Куркин С.А., Винокуров В.А., Норкин И.А. Способ внесуставной коррекции деформаций коленного сустава. [Patent RUS 2316281/ 10.02.08. Byul. № 4. Tsareva EE, Kurkin SA, Vinokurov VA, Norkin IA. Sposob vnesustavnoy korrektsii deformatsiy kolennogo sustava. (In Russ).]

15. Царева Е.Е. Хирургическое лечение деформаций коленного сустава у детей и подростков: автореф. дис. … канд. мед. наук. – Саратов, 2008. [Tsareva EE. Khirurgicheskoe lechenie deformatsiy kolennogo sustava u detey i podrostkov. [dissertation] Saratov; 2008. (In Russ).]

16. Барабаш Ю.А. Оптимизация и стимуляция процессов остеорепарации при хирургическом лечении переломов длинных костей и их последствий (клинико-экспериментальное исследование): автореф. дис. … д-ра мед. наук. – СПб., 2001. [Barabash JA. Optimizatsiya i stimulyatsiya protsessov osteoreparatsii pri khirurgicheskom lechenii perelomov dlinnykh kostey i ikh posledstviy (kliniko-experimentalnoe issledovanie) [dissertation]. Saint-Petersburg, 2001. (In Russ).]

17. Винокуров В.А., Норкин И.А., Царева Е.Е., Куркин С.А. Репаративная регенерация гиалинового хряща в аспекте хирургического лечения околосуставной деформации конечности. В кн.: Актуальные вопросы детской травматологии и ортопедии. – СПб., 2004. – С. 46–47. [Vinokurov VA, Norkin IA, Tsareva EE, Kurkin SA. Reparativnaya regeneratsiya gialinovogo khryashcha v aspekte khirurgichesko lecheniya okolosustavnoy deformatsii konechnosti. In: *Aktual'nye voprosy detskoj travmatologii i ortopedii*. Saint-Petersburg, 2004. P. 46-47. (In Russ).]

18. Завьялов П.В., Плаксин И.Т. Деформирующий остеохондроз большеберцовой кости у детей (Болезнь Эрлахера — Блаунта). – Ташкент: Медицина УзССР, 1974. – 175 с. [Zavjalov PV, Plaksin IT. *Deformiruyushchiy osteokhondroz bolshebertsovoy kosti u detey (Bolezn Erlakhera-Blaunta)*. Tashkent: Meditsina UzSSR, 1974. 175 p. (In Russ).]

19. Лаврищева Г.И., Оноприенко Г.А. Морфологические и клинические аспекты репаративной регенерации опорных органов и тканей. – М.: Медицина, 1996. – 207 с. [Lavrishcheva GI, Onoprienko GA. *Morfologicheskie i klinicheskie aspekty reparativnoy regeneratsii opornykh organov i tkaney*. Moscow: Meditsina, 1996. 207 p. (In Russ).]

ХИРУРГИЧЕСКАЯ КОРРЕКЦИЯ ДЕФОРМАЦИИ КОЛЕННОГО СУСТАВА И РЕГЕНЕРАЦИЯ ГИАЛИНОВОГО ХРЯЩА

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Цель: разработать способ внесуставного формирования костно-хрящевого суставного фрагмента для улучшения результатов хирургической коррекции деформаций суставов и оптимизации условий регенерации гиалинового хряща.

Материалы и методы. Экспериментально разработан способ формирования костно-хрящевого суставного фрагмента без проникновения в полость сустава. Прооперировано 30 больных с суставными деформациями.

Результаты. В ходе экспериментов появилась идея возможности полноценного восполнения суставных дефектов за счет регенерации гиалинового хряща. Путем дистракции костно-хрящевого фрагмента, сформированного внесуставно, у больных восполнены суставные дефекты. У большинства пациентов результаты лечения оценены как отличные и хорошие.

Заключение. Полученные результаты открывают перспективу полноценного восполнения суставных дефектов диспластического генеза, костно-хрящевых дефектов суставов после травм. Разработанный способ может быть использован в последующих экспериментах для объективизации и уточнения регенераторных возможностей гиалинового хряща (темпа и объема образуемого регенерата; определения элементов хряща, участвующих в процессе его регенерации, и др.).

Ключевые слова: суставные деформации, хирургическая коррекция, хрящ.

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