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# EXPERIMENTAL STUDY OF THE USE OF OSTEO-CELLULAR GRAFTS IN WRIST ARTHRODESIS

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**Abstract.**

**Introduction.** Wrist arthrodesis is a surgery performed in advanced osteoarthritis of the wrist joint of various etiology, posttraumatic consequences or diseases of carpal bones. It is a rescue surgery and is performed with the cost of losing of range of movement, but remove the pain syndrome and increase the strength of the hand.

**Aim of study**. Evaluation of osteo-cellular grafts (OCG) using in wrist arthrodesis in experimental study on laboratory animals.

**Material and Methods.** The study was based on experimental research on 21 New Zealand rabbits, splited in 3 study groups. As methods of implementation of the study included: preparation of allogeneic demineralized bone grafts, bone marrow sampling and isolation of autologous stem cells, obtaining OCG, and performing 3 different techniques of wrist arthrodesis.

**Results.** Imagistic results showed us, that the group were performed arthrodesis using combined graft with stem cells, the ankylosis were achieved faster. Histological examinations indicated more active involvement in the process of osteogenesis in the use of combined stem cell transplantation.

**Conclusion.** Our study showed that compared to the control group, the arthrodesis of the wrist using the allograft have good impact in the process of osteogenesis, but the best results were performed by using allograft combined with stem cells.

**Keywords:** wrist arthrodesis, autologous stem cells, osteo-cellular graft.

**Rezumat. Studiu experimental al utilizării grefelor osteo-celulare în artrodeza radio-carpiană.**

**Introducere.** Artrodeza articulației radio-carpale este o intervenție chirurgicală efectuată în osteoartroza avansată de etiologie diversă, consecințe posttraumatice sau anumite patologii ale oaselor carpiene. Este o intervenție chirurgicală de salvare și se efectuează cu costul pierderii amplitudinii de mișcare, dar în schimb elimină sindromul algic și crește puterea mâinii.

**Scopul studiului.** Evaluarea grefelor osteo-celulare (GOC) utilizată în artrodeza pumnului în studiul experimental pe animale de laborator.

**Material si metode.** Studiul s-a bazat pe cercetări experimentale pe 21 de iepuri Nou Zeelandez, împărțiți în 3 grupuri de studiu. Ca metode de implementare a studiului au inclus: pregătirea grefelor osoase alogene demineralizate, prelevarea de probe din măduvă osoasă și izolarea celulelor stem autologe, obținerea GOC și efectuarea a 3 tehnici diferite de artrodeză radio-carpiană.

**Rezultate.** Rezultatele imagistice ne-au arătat, că în grupul unde s-a efectuat artrodeza folosind grefa combinată cu celule stem, anchiloza osoasă s-a realizat mai rapid. Examenele histologice au indicat o implicare mai activă în procesul de osteogeneză în cazurile cu utilizarea GOC.

**Concluzie.** Studiul ne-a arătat că, în comparație cu grupul de control, utilizarea alografa în artrodeza radio-carpiană are un impact bun în procesul de osteogeneză, dar cele mai bune rezultate au fost realizate prin utilizarea alografei combinate cu celule stem.

**Cuvinte cheie:** artrodeză radio-carpiană, celule stem autologe, grefă osteo-celulară.

## Introduction

The wrist is an extremely complex and versatile structure that bridges the hand to the forearm [1]. Carpal stability can be described as the ability to maintain a normal balance between the joint partners at the physiological demands and physiological movements [2]. Stability of the wrist can be affected at any level, including the radiocarpal joint, midcarpal joint, distal carpal row, and proximal carpal row. Any injury or disease modifying bone geometry, articular inclination, ligament integrity, or muscle function may alterate the carpal motion, leading to carpal instability [3].

The term “carpal instability” was introduced in 1972 by Linscheid et al. The most accepted definition of “carpal instability” means any disturbance of the

static and dynamic balance of forces at the wrist under the conditions of daily living [2]. The degree of carpal instability is determined by the extent of the ligaments and/or osseous lesions [4].

Wrist joint instabilities are injuries associated with sprains, subluxations, dislocations, fractures, nonunion or osteoarticular diseases of carpal bones. If the buttresses are insufficient to maintain the normal joint arrangement, this balance may be disturbed [5]. Most instability patterns are caused by acute or repetitive injuries of the wrist. Hyperextension injuries commonly lead to ligamentary lesions on the radial side [6]. Fractures of radius or scaphoid can be associated [7]. The infrequent hyperpronation injuries can cause instability patterns on the ulnar side. Aside from traumatic causes, carpal instability can arise from other conditions and comorbidities, like avascular osteonecrosis (i.e., Kienbock disease), systemic inflammatory disease (i.e., rheumatoid arthritis), neurological disorders (i.e., syringohydromyelia), and specific congenital malformations (i.e., Madelung's deformity) [4, 8-12].

The instability of the wrist joint leads to the appearance and development of deforming osteoarthritis of the joint which in turn leads to painful and limited range of movements, decreased strength and impaired hand function [13-15]. Respectively, the instability of the fist joint is caused by the development of arthrosis, which in turn is in 95% of post-traumatic origin [16].

Nowadays, wrist instability and its consequences impose big issues in socioeconomic areas, as it affects young people, the important functional disorders of the wrist joint, the decrease in work capacity, the insufficient resolution of the problems of diagnosis and surgical treatment generate needs to be studied as to improve the quality of life of these patients [3, 8, 17].

The treatment of carpal instability is a voluminous challenge due to the variety of this pathology [8, 18, 19]. There are different types of surgery to resolve wrist instability problems. One of the surgical techniques is intercarpal fusion - arthrodesis, it leads to the neighboring bones consolidation in the wrist joint, performing ankylosis. It is a rescue surgery and is performed with the cost of losing of range of movement, but remove the pain syndrome and increase the strength of the hand [15, 19-21].

There is no ideal treatment for end-stage degenerative wrist disorders and subsequent carpal collapse [22]. In this experimental study, we made an evaluation of using osteo-cellular grafts (OCG) in wrist arthrodesis at New Zealand White rabbits.

**Materials and methods.**

To achieve the study aim it was necessary to included tissue engineering work. For the initial stage, it was prepared demineralized allografts (Fig. 1). It was necessary to sacrificed one laboratory animal. Then was collected bone marrow from iliac crest of researched rabbit from group C (Fig. 2).

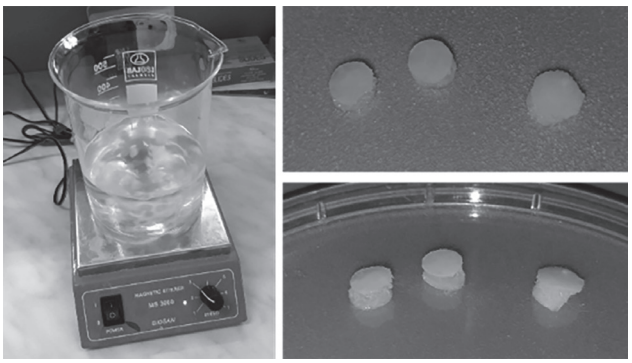

*Figure 1.* Preparation of allogenic demineralized bone grafts.

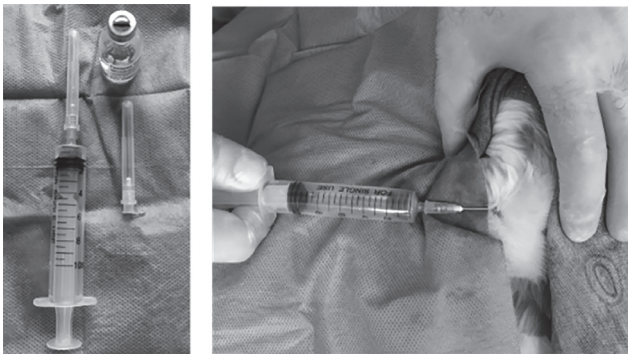

*Figure 2.* Bone marrow collection from the iliac crest.

After was performed isolation of autologous stem cells, enrichment through tissue engineering, counting and trypsinization of the cells (Fig. 3). Viability is 100% 69:8=8.625 cells x 20000 × 11 = 1897500 cells .

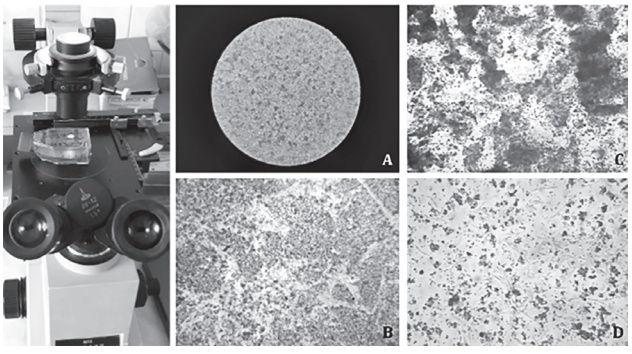


*Figure 3.* A - Isolation of autologous stem cells; B - enrichment; C - Counting and trypsinization; D - Viability of the cells.

Autologous stem cells are soaked in demineralized allograft and was obtained OCG (Fig. 4).

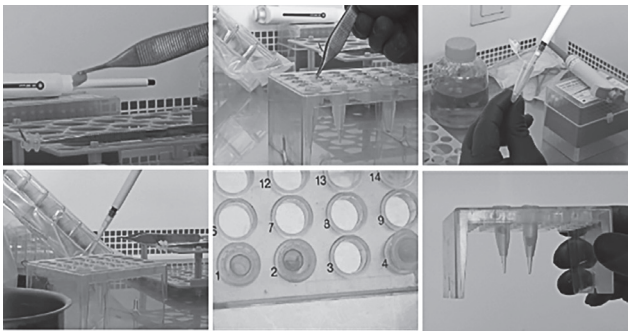

*Figure 4.* Obtaining of osteo-cellular grafts (OCG)

All laboratory work done in collaboration with Tissue Engineering and Cell Cultures Laboratory of *Nicolae Testemitanu* State University of Medicine and Pharmacy.

Experimental study was performed on laboratory animals. Twenty-one adults New Zealand White rabbits (5-6 months old, 3.0-3.5 kg) were used. It was determined that none of the rabbits had trauma in wrist region.

All animals were handled in accordance with the approved protocols by the Research Ethics Committee of *Nicolae Testemitanu* State University of Medicine and Pharmacy, decision No. 02 of 23.10.2017.

All laboratory animals were divided into 3 groups: in control Group A – were performed 7 standard arthrodesis of wrist joint; study Group B – 7 arthrodesis with using allogenic demineralized bone grafts and last study Group C – were performed 7 arthrodesis using the allograft combined with stem cells.

The surgeries were done in aseptic conditions, under general anesthesia (intramuscular injection of ketamine 35mg/kg and xylazine 5 mg/kg). Right wrist of the laboratory animals was preferred for surgeries.

The stages of a surgery were consisted from:

1. Preoperative preparation: antibiotic prophylaxis, anesthesia and trimming.
2. Asepticization and isolation of the operating region.
3. By dorsal approach – wound length 1,5-2 cm, opening wrist joint, modeling the chondral defect between carpal bone.
4. Group A – standard arthrodesis with k-wires.

Group B – arthrodesis with allograft.

Group C - arthrodesis with osteo-cellular grafts (Fig. 5).

5. Wound suturing.

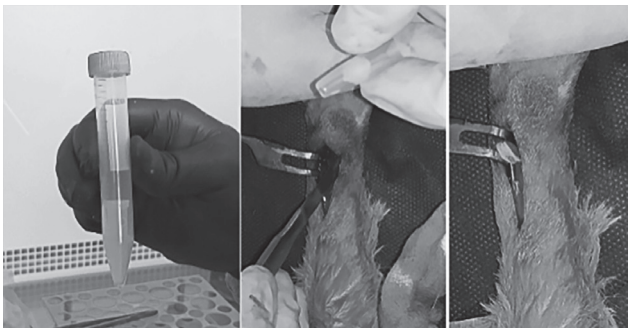

*Figure 5.* Uses allograft combined with stem cells in wrist arthrodesis.

In all 21 cases, an immediate postoperative radiograph was performed (Fig. 6A) and immobilization was applied for 4 weeks.

X-ray control were performed 4 weeks after the surgery in all cases, and in 5 cases from Group C, we found starting callus formation in contrast to Group A and B (Fig. 6B).

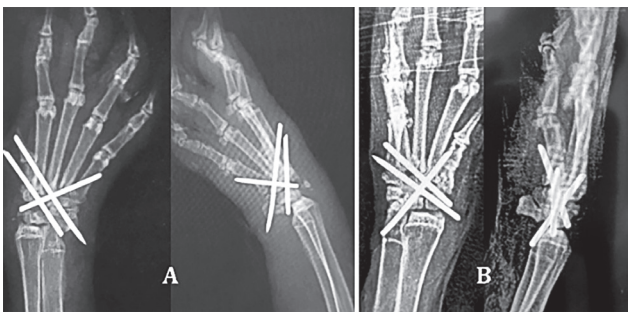


*Figure 6.* X-ray after wrist arthrodesis with OCG at New Zeeland rabbit: A – immediate postoperative x-ray; B – x-ray 4 weeks after the surgery.

The k-wires were removed from the wrist 6 weeks after the surgery. The radiological control was performed 8 weeks (Fig. 7A) then 12 weeks after the arthrodesis (Fig. 7B).

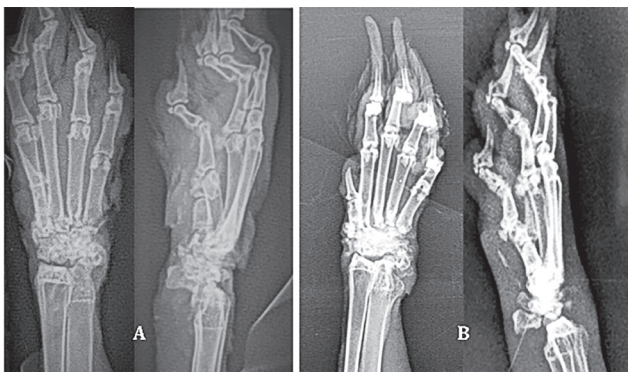


*Figure 7.* X-ray after wrist arthrodesis with OCG at New Zeeland rabbit: A – 8 weeks after the surgery; B – 12 weeks after the surgery.

Computer tomography was done 12 weeks postoperatively in all cases (Fig. 8).

*Figure 8.* Computed tomography after wrist arthrodesis with OCG at New Zeeland rabbit

**Results and Discussion**

Imagistic result showed achieved ankylosis in 3 cases of control Group A, 4 cases of study group B and all 7 cases of study Group C after 3 months from wrist arthrodesis.

The follow-up of all 21 rabbits was performed, each rabbit seemed to be in good health, and they all ate normally. Clinical evaluation was made every day in the first 2 weeks, then at every 3 days. Seven days after the surgery it was noticed local septic complication at one laboratory animal from Group B, respectively it was removed from the experimental study.

By histopathological examination, in all three groups, was observed osteogenic response. In the control Group A, where was performed the standard wrist arthrodesis, on histological samples was noticed the activation of the osteogenesis process (Fig. 9).

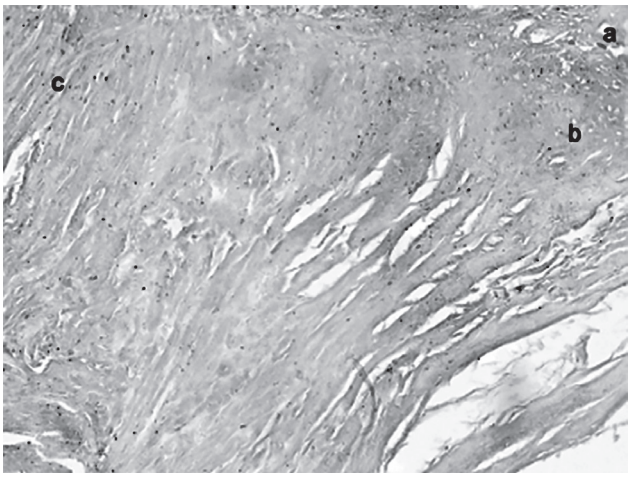


*Figure 9.* Histopathological sample from wrist joint with standard arthrodesis: Bone trabeculae (a), chondrocyte hyperplasia (b), solitary collagen fibers (c). Van Gieson's picrofuchsin x 90.

On histological examination of the study Group B, where was performed the arthrodesis with use of allogenic demineralized grafts, on joint surface we can see a slight osteogenesis process with osteoblast cells and collagen fibers (Fig. 10).

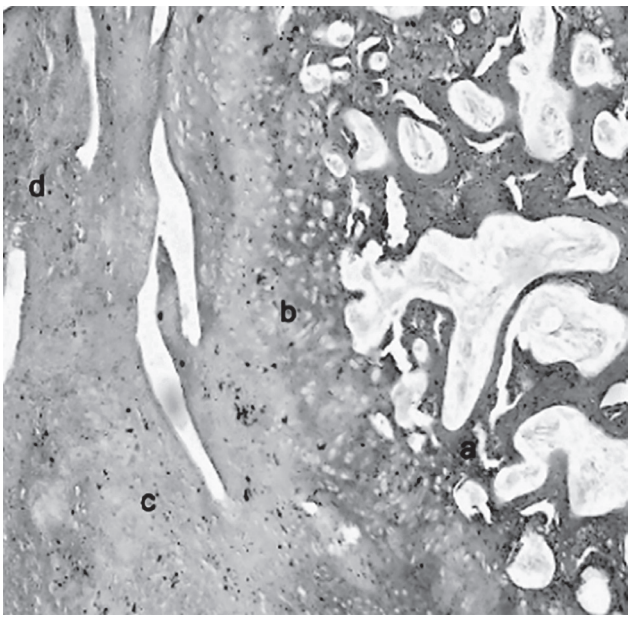


*Figure 10.* Histopathological sample from wrist joint with arthrodesis using allografts: Bone trabeculae with hypertrophy of osteoblast cells (a), hypertrophy of chondroblasts with hyperplasia (b), connective tissue (c), collagen fibers (d). Van Gieson's picrofuchsin x 90.

In the study Group C, where was performed arthrodesis using the allograft combined with stem cells is determined the best process of osteogenesis, with presence of the intense proliferation of fibroblasts (Fig. 11).

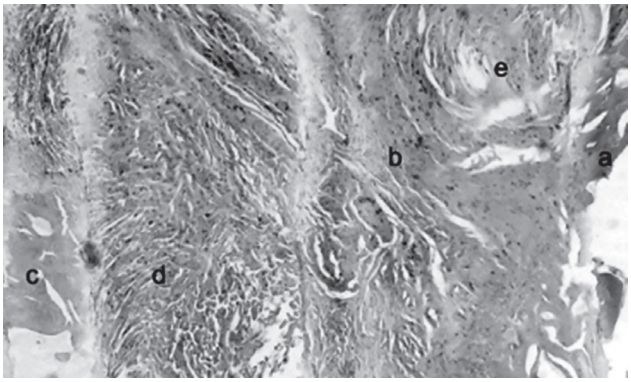


*Figure 11.* Histopathological sample from wrist joint with arthrodesis using osteo-cellular graft: Bone trabeculae with hypertrophy of osteoblast cells (a), diffuse connective tissue (b), acellular spongy bone trabeculae (c), diffuse collagen fibers (d), intense proliferation of fibroblasts (e).

Histopathological examinations indicated, that in the study group where was implemented the combined allograft with stem cells, obtained by tissue engineering, more active involvement in the process of osteogenesis is determined.

**Conclusions.**

Our experimental research developed an innovative method of surgical treatment - arthrodesis using the combined graft with stem cells. It turned out to be a harmless, safe method and effective.

Imagistic results demonstrated, that the group were performed arthrodesis using combined graft with stem cells, the ankylosis were achieved faster.

Histopathological evaluation indicated more active involvement in the process of osteogenesis in the study group uses allograft combined with stem cell.

Our study showed that compared to the control group, the arthrodesis of the wrist using the allograft have a positive impact in the process of osteogenesis, but better results were performed by using OCG.

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