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THE RESULTS OF USING A BIOACTIVE GLASS-BASED COATING BY DEPOSITION ON THE CONTACT SURFACE OF PLATES IN BONE FRACTURES ASSOCIATED WITH TUMORS

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ABSTRACT — The article reports on the results of surgical treatment in 20 patients with bone tumors using a coating containing bioactive glass on the contact surface of the fixation plate. As a result of metallic osteosynthesis of the bones, infectious complications were observed in 1 (5%) patient and tumor recurrence was observed in 2 (10%) patients. Limb function after metallic osteosynthesis ranged from 72.3% to 97.4% depending on the location of the lesion focus. The quality of life of the operated patients increased to 75–85 points. Thus, the use of plates with bioactive glass-based material deposited on the contact surface of the plate, in metallic osteosynthesis for pathological bone fracture or at the risk of pathological bone fracture achieves more effective integration of metal plate with bone. Consequently, a better functional stability of the bone is achieved at the fracture site. Morphological examination of bone biopsy samples from the implantation site of the plate and the plate itself with the deposited bioactive glass-based coating revealed active regeneration of bone tissue. This resulted in an increase in the density of the restored bone. According to the results of histological and morphometric examination it can be stated that deposition of a material containing bioactive glass on the contact surface of the metal plate promotes reparative osteogenesis at the site of bone damage and its morphogenesis of the lamellar type.

KEYWORDS — metallic osteosynthesis, plate, bioactive glass-based (BG) coating, bone tumor, morphological study.

INTRODUCTION

In the treatment of fractures and diseases of the skeletal system, internal (intramedullary and periosteal) and external (pins and nails) fixators are used to ensure the most reliable osteosynthesis of bone. Complete reposition and stable fixation of bone frag-

ments, optimal rate and rhythm of distraction, sparing attitude to osteogenic tissue, good blood supply to the operated limb, the possibility of functional use of the limb, starting from the first days after surgery, represent conditions for reparative regeneration of bone tissue [1, 2]. A study of the reference literature shows the application of autogenous grafts of bone tissue and various bioactive products of decalcified bone and biocomposite matrices, recombinant human bone morphogenetic proteins and ceramics. All the materials including new cellular technologies are used to stimulate osteogenesis, [3, 4, 5]. Over recent years, there has been an active trend in the development of biomaterials aimed at creating composites that replace damaged tissues including bone tissue [6]. In orthopedics, this was facilitated by the development of the major joint arthroplasty industry and the use of bioceramic implants. [7, 8, 9]. Biomaterials used as implants or as temporary fixators for broken bone (periosteal plates, intramedullary nails) can be represented by biotolerant materials (stainless steel and cobalt-chromium alloys), bioinert (titanium and aluminum oxides), bioactive (calcium phosphate ceramics and silicon-based bioglass) [7]. There are no bioactive metals that would accelerate reparative osteogenesis. In orthopedics, chromium-nickel and chromium-nickel-molybdenum corrosion-resistant steels, alloys of cobalt, tantalum, titanium, pure metals — nickel, silver, titanium are most often used for the manufacture of surgical implants [10].

Typical representatives of bioactive materials include bioglass (the most commonly used composition is 24.5% Na₂O, 24.5% CaO, 45.0% SiO₂, 6% P₂O₅, varying the composition, you can change their bioactivity and resorption) and materials based on hydroxyapatite (HA) — Ca₁₀(PO₄)₆(OH)₂ (dense and porous ceramics) [11, 12]. Hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂) is one of the few bioactive materials that supports bone ingrowth and osseointegration when used in orthopedic implants due to its high biocompatibility.

In the last few years, a special term has appeared in the literature — *biocompatible nanoceramics*, which means nanostructured ceramic material used in medicine to restore (replace) damaged hard tissues [9, 13]. The creation of composite materials based on

biphasic ceramics using various binding components, biologically active substances that would provide osteoinduction of osteoplastic material to form a matrix, on which bone tissue will be formed, is one of the promising areas [14]. The concept of biphasic composite materials in the system “HA – TCF (tricalcium phosphate)” was developed based on the assumption of the possibility of regulating the kinetics of biodegradation by changing the ratio: less (HA) and more (TCF) of soluble phases in one material. Dissolution of the TCF component in body fluid promotes the process of mineralization, and the biological behavior of biphasic ceramics depends on the ratio of HA/TCF [15]. The bioactivity of materials is determined mainly by chemical factors, such as the crystalline phase and molecular structure of the material, as well as physical factors — roughness and porosity of the material surface and the ability to form a chemical bond with the surrounding bone [8, 11]. A number of complex and closely interrelated processes take place on the surface of a bioactive implant. The surface of the material, its biocompatibility is closely related to the adhesion of osteogenic and mesenchymal stem cells on its surface [16, 17]. It is the adhesion as well as the distribution of these cells that will affect their ability to proliferate and differentiate into osteoblasts upon contact with the implant. The latter is crucial in the process of establishing a mechanically strong interface with complete fusion between the implant surface and bone tissue without a layer of fibrous tissue, which is usually formed on the surface of a bioinert metal implant [18, 19, 20, 21]. In this article we report on the use of titanium plates in bone fractures on the background of tumors with a BG-based material, deposited on their contact surface.

Objective:

To show the possibilities of application of periosteal plates with a bioactive glass containing material deposited on the contact surface to improve integration of the plate with bone in pathological bone fractures associated with tumors.

MATERIAL AND METHODS

During the period from 2017 to 2020, in Institute of Traumatology and Orthopedics of NAMS of Ukraine 20 operations on metallic osteosynthesis were performed using periosteal plates with a bioactive glass-based coating deposited on the contact surface of the plate, in pathological fractures or at risk of pathological fractures secondary to tumors of long tubular bones. The average age of patients was 39.2 ± 1.4 years (from 28 to 57 years), among them there were 13 (65%) women and 7 (35%) men.

Metallic osteosynthesis was performed using periosteal plates of different lengths and configurations. Plates (medical steel grade BT6) had the following composition: titanium as the main substance, aluminum content — 3.9/2.8 nm, manganese content — 1.3/1.2 nm, iron content — 0.4/0.1 nm, silicon content — 0.1/0.1 nm, calcium content on the surface of the plate — 0.3 nm, chlorine content — 0.2 nm, sulfur content — 0.1 nm.

Table 1 presents the morphological types of tumors identified during metallic osteosynthesis using plates with a BG-based coating deposited on the contact surface.

Table 1. Morphological types of tumors identified during metallic osteosynthesis using plates with a BG-based coating deposited on the contact surface

Morphological types of tumors	Number of cases	%
Metastatic tumors	14	70
Chondroma	3	15
Giant cell tumor of bone	1	5
Solitary myeloma	1	5
Lymphosarcoma of bone	1	5
Total	20	100

The scope of surgery depended on the location of the tumor: patients underwent intraosseous bone resection with the tumor; bone defect in chondroma and giant cell tumor was filled with allograft or material containing bioactive glass; in metastatic tumor, solitary myeloma and lymphosarcoma bone defect was filled with polymethyl methacrylate, after which metallic osteosynthesis was produced using a BG-based coating deposited on the contact surface.

Table 2 presents location and number of cases of metallic osteosynthesis of bones using a BG-based material deposited on the contact surface of the implant.

The use of plates with a bioactive glass-based coating deposited on the contact surface achieves a better integration of the plates with the bone, as well as the fact that in bone tumors, the plates are usually not removed over time.

The material deposited on the contact surface of the plate was an implant material containing bioactive glass — Syntekist Biocomposite (certificate of state registration No. 3653/2005 dated January 28, 2005), which was synthetically produced in the laboratory of the Institute of Materials Science of the National Academy of Sciences of Ukraine by the team of prof. V.A. Dubok.

Implant material — Syntekist biocomposite is a multiphase inorganic material synthetically produced

Table 2. Location and number of cases of metallic osteosynthesis of bones using a BG-based material deposited on the contact surface of the implant

Location	Number of cases	%
Distal femur	7	35
Humeral diaphysis	4	20
Tibial shaft	3	15
Proximal tibia	2	10
Distal tibia	1	5
Proximal femur	1	5
Radial shaft	1	5
Femoral shaft	1	5
Total	20	100

by chemical precipitation and ceramic technology. Its phase composition includes bioactive glass — 50–65 wt.%, hydroxyapatite — 14–17 wt.%, whitlockite — 14–17 wt.%, wollastonite — 7–9 wt.%. The chemical composition is shown in Table 3 (in terms of oxides).

Table 3. Chemical composition of Syntekist biocomposite

Composition	Na ₂ O	K ₂ O	SiO ₂	CaO	P ₂ O ₅	Ag ₂ O
	15,54	0,173	27,58	35,45	21,27	-
Range of permissible composition	15–17	0,1–0,3	25–28	34–37	20–23	0,01–0,08

It is a bioactive and osteoconductive biomaterial, which is available in the form of powders, granules, blocks and implants of complex shape with different activity, dispersion and adsorption capacity, with a significant range of porosity and mechanical properties. The contact surface of the plate was covered with a BG-based material by means of gas detonation deposition. Abrasive treatment of the contact surface of the plate was performed in the gas detonation deposition unit before depositing the BG-based coating; on the surface a surface relief of a given depth was formed, which was equal to the size of osteon and provided a large contact area and adhesion strength between the bone and the plate. Next, the deposition of a layer of the BG-based material has been carried out, which allows to solve the problem of amorphization of the coating. Due to the presence of bioactive compounds in the coating, evenly distributed throughout its thickness, in the process of resorption of the coating in the body, it caused antibacterial, osteoconductive, antiresorptive and other effects throughout the life of the plate (see Fig. 1).

The functional result of the operated limb was determined according to the MSTs Rating scale (Musculo-Skeletal Tumor Staging /System/). Patients' quality of life was determined in points according to the EORTC QLQ-30 questionnaire. Patient survival was determined using the Kaplan-Meier method.

FINDINGS

Of 20 patients, infectious complications were observed in 1 (5%) patient and tumor recurrence was observed in 2 (10%) patients after metallic osteosynthesis for pathological fractures and the risk of pathological bone fractures. In a patient with an infectious complication, after removal of the plate, radical surgical treatment of the wound was performed with removal of all pathologically changed tissues, inoculation of fluid for culture from the place of installation of a plate, washing the wound with antiseptic solutions and installing an active drainage system with antibiotic irrigation.

In 2 patients with tumor recurrence a bone biopsy was performed after plate removal at the point of contact with the BG-based coating deposited on the plate. A biopsy of the metal plate surface was performed followed by morphological microscopic examination

of the obtained material. These 2 patients subsequently underwent resection of bone articular segment and joint endoprosthesis replacement due to tumor recurrence.

Functional outcome in the limb (according to the MSTs scale) after metallic osteosynthesis of the distal femur was 82.5%; in the humeral diaphysis — 95.4%, of the tibial shaft — 91.6%; in the distal tibia amounted to 86.8%; in the proximal tibia — 93.2%, in the proximal femur — 72.3%; in the radial shaft — 97.4%; in the femoral shaft — 76.4%.

The quality of life of patients according to the EORTC QLQ-30 questionnaire before metallic osteosynthesis was estimated as 20–30 points, after metallic osteosynthesis it was 75–85 points.

The overall three-year survival of the patients was $46.5 \pm 2.9\%$, and the five-year survival was $26.2 \pm 4.1\%$.

Here is an example from our practice: Patient Ya., 40 years old, considers herself ill since October 2020, when pain and swelling appeared in the distal segment of the left lower leg. According to the patient, the pain intensified within a month, so the patient was forced

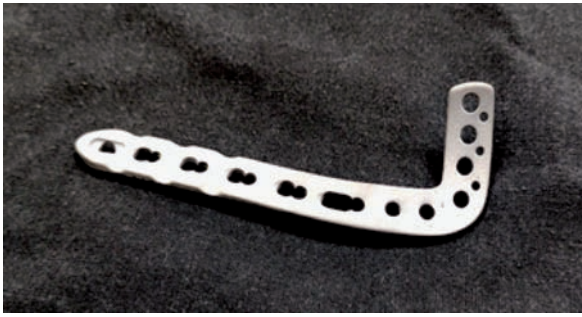


Fig. 1. A metal plate with a BG-based coating deposited on the contact surface

to walk on crutches. A month later, the patient went to the clinic of the State Institution "ITONAMNU", where X-ray examination revealed a tumor of the left distal tibia (see Fig. 2). In November 2020, the patient underwent an open biopsy of the lesion focus in the distal part of the left tibia. Histopathological findings: giant cell tumor of bone. In December 2020, the patient underwent an intraosseous resection of the lesion focus in the distal part of the left tibia with a tumor and a plastic repair of the defected femur using a BG-based material and extramedullary metallic osteosynthesis of the distal tibia using plate with a BG-based coating by deposition on its contact surface (see Fig. 3). No complications were observed in the postoperative period. The function of the left lower leg (according to the MSTs scale) was 86.8%. There was no tumor recurrence on X-ray in 1.5 months.

In 2 patients with tumor recurrence after plate removal (in 2 months after implantation) during the morphological examination of bone tissue from the area of plate removal and the surface of the metal plate coated with BG-based material we found out: in the subject No.1 bone perimeter was characterized by active osteogenesis. Crystalline granules were detected, which probably represent biocomposite residues after plate removal. Almost the entire surface of the plate was surrounded by newly formed bone tissue, mainly woven bone. Although in some areas the morphogenesis of lamellar bone tissue has been observed in newly formed trabeculae (Fig. 4). The relative surrounding of the bone defect (at the site of bone trepanation) by newly formed bone tissue amounted to 82.0 (78.3–91.7)%.

In the subject No.2 during morphological examination at the site of the defect, a damaged hyaline cartilage of the articular surface and the metaphyseal plate with replacement by connective tissue was revealed. In the areas where the granules of the biocomposite got into the lacunae of the cortical bone, active



Fig. 2. Photographs of radiographs (A is a frontal and B is a lateral projection) of the left tibia of patient Ya. with a giant cell tumor of the distal tibia

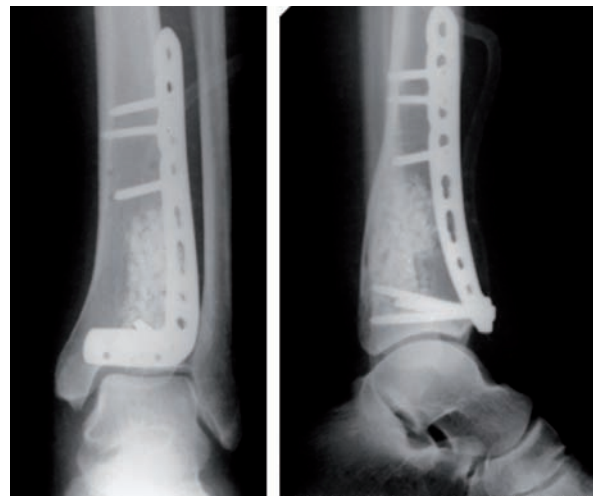


Fig. 3. Photographs of radiographs (A is a frontal and B is a lateral projection) of the left tibia of the patient Ya. after metallic osteosynthesis for a giant cell tumor of the distal tibia using plate with a BG-based coating deposited on its contact surface. The defect of the bone was repaired and filled with the BG containing material

osteogenesis was detected around this material (Fig. 5). The biocomposite was partially surrounded by connective tissue, mostly an osseous one. Morphogenesis corresponded to the formation of lamellar bone tissue. The relative density of the newly formed bone tissue around the granules of the biocomposite reached 89.6 (72.6–97.8)%.

In the subject No.3 an epiphyseal defect was revealed during the morphological examination, and

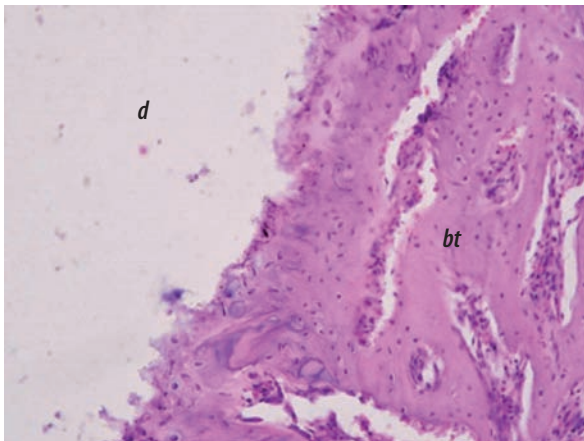


Fig. 4. Active osteogenesis around the metal plate. Note: *d* — defect; *bt* — bone tissue. Hematoxylin-eosin, vol. 20, approx. 10

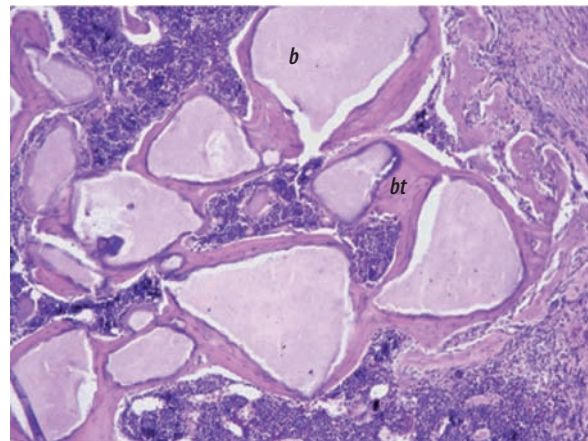


Fig. 6. Active osteogenesis around the biocomposite. Note: *b* — biocomposite; *bt* — bone tissue. Hematoxylin-eosin, vol. 10, approx. 10.

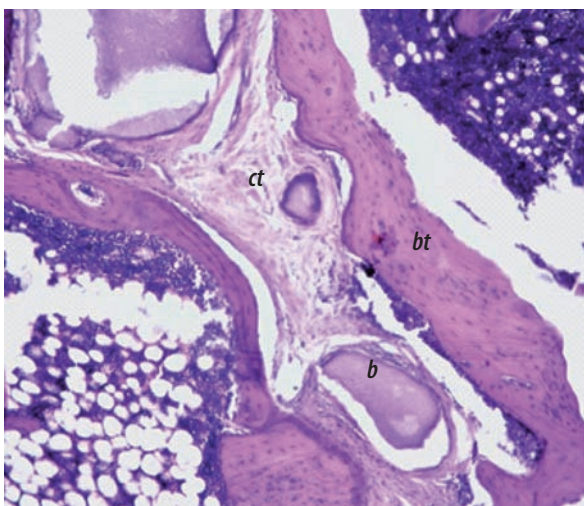


Fig. 5. Active osteogenesis around the biocomposite. Note: *b* — biocomposite; *ct* — connective tissue; *bt* — bone tissue. Hematoxylin-eosin, vol. 10, approx. 10.

ected. The perimeter of the defect was surrounded by newly formed bone tissue, but the boundary between the defect and the bone tissue remained partially filled with connective tissue (Fig. 7).

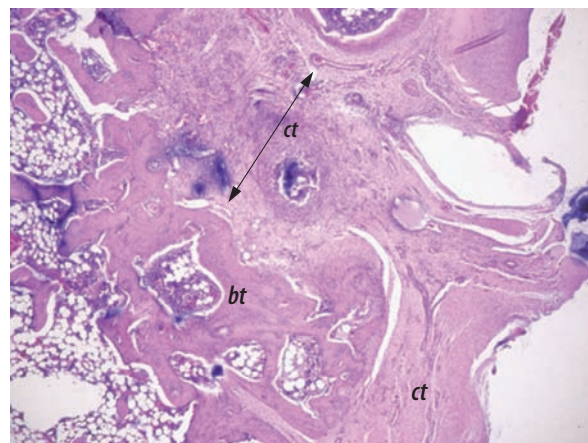


Fig. 7. The bone defect is filled with connective tissue with macrophage infiltration. Note: \longleftrightarrow defect; *bt* — bone tissue; *ct* — connective tissue. Hematoxylin-eosin, a. vol. 4, approx. 10

the centers of active osteogenesis around the granules of the biocomposite were detected in the cavities of the trabecular bone (Fig. 6). Almost the entire surface of the granules (92.5 (83.5–95.6)%) was surrounded by newly formed bone tissue (the lamellar type dominated). Isolation of the biocomposite from the surrounding morphofunctional bone formations (bone marrow, cartilaginous tissue of the articular surface, metaphyseal plate) was observed.

In the subject No.4 during the morphological examination it was detected that the bone defect was filled with connective tissue. Foci of inflammatory infiltration (neutrophils and macrophages) were de-

In the subject No.5, a morphological examination revealed an area of bone defect with biocomposite granules. Osteogenesis around the biocomposite granules was uneven: one part was surrounded by connective tissue, and the other part was totally integrated into regenerated bone tissue (Fig. 8). Newly formed bone tissue in most areas is lamellar.

During morphological examination in the subject No.6 (Fig. 9) the defect was detected at the level of epiphysis, filled with connective tissue, articular and

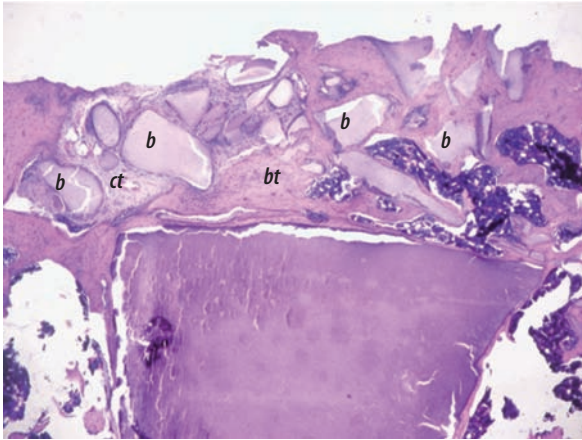


Fig. 8. Heterogeneous osteogenesis around the biocomposite. Note: *b* — biocomposite; *ct* — connective tissue; *bt* — bone tissue. Hematoxylin-eosin, vol. 20, approx. 10

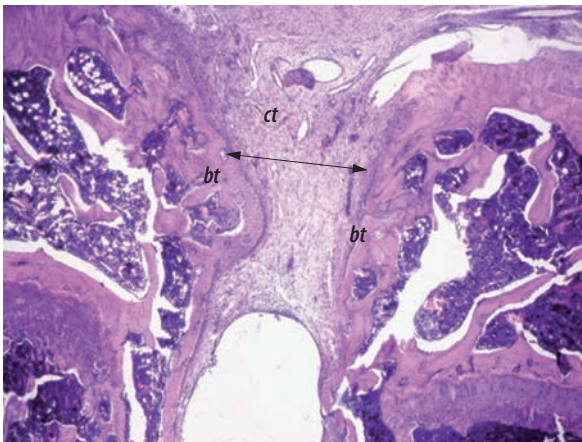


Fig. 9. The defect is filled with connective tissue, active osteogenesis is present. Note: \longleftrightarrow defect; *bt* — bone tissue; *ct* — connective tissue. Hematoxylin-eosin, vol. 4, approx. 10

metaphyseal hyaline cartilage are deformed. The metaphyseal plate is penetrated by a defect surrounded by newly formed bone tissue, which is lamellar to a greater extent. The level of regeneration was 87.2 (86.7–88.1)%.

RESULTS

As a result of metallic osteosynthesis in pathological bone fracture or at risk of pathological bone fracture associated with bone tumors, positive treatment results were obtained: limb function ranged from 72.3% to 97.4% depending on the location of the lesion focus, quality of life of operated patients increased to 75–85 points. Morphological examination of bone biopsy material from the site of implantation

of the plate and from the plate itself with the deposited BG-based material revealed active regeneration of bone tissue leading to an increase in the density of the restored bone. The results of histological and morphometric examination demonstrate that the deposition of the BG-based material onto the contact surface of the metal plate promotes reparative osteogenesis at the site of bone damage and its morphogenesis of the lamellar type.

CONCLUSION

1. As a result of application of periosteal plates with deposition of the BG-based material for pathological bone fractures we observed infectious complications in 1 (5%) patient and tumor recurrence in 2 (10%) patients, out of 20 patients with bone tumors.

2. The results of histological and morphometric examination showed that the deposition of the BG-based material onto the contact surface of the metal plate for metallic osteosynthesis promotes more effective integration of the plate with bone, which leads to a greater functional stability of the bone at the fracture site.

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