Dear colleagues,

We present to your attention a special issue of the journal *Genij Ortopedii*. The articles selected for this issue unite the authors from various countries and institutions with a very important topic. They are devoted to various aspects of the development of bioactive implants and to biological process control in orthopedics. This direction is now being actively developed by scientists and researchers from all over the world. Russia does not lag behind, and even surpasses them in some developments. Universities, institutes, medical and research centers are joining their efforts to build a domestic market for high-tech medical products.

The issue contains articles written by authors from Russia, Serbia, France, Switzerland, the USA, Hungary, and India. Several studies were prepared in collaboration with colleagues from the Ilizarov Center.

The articles present both theoretical and experimental developments, as well as original research on the practical application of innovative technologies and literature reviews on the topic. It is noteworthy that out of 13 articles in the issue, seven studies are devoted to the study of bioresorbable materials and implants that are in demand in contemporary medicine. Thus, Pierre Lascombes, Pierre Journeau and Dmitry Popkov present their own experience of using resorbable implants in pediatric orthopaedics and traumatology. Seven children with long bone fractures were treated using resorbable screws (ActivaScrew™). In the immediate postoperative period, no cases of excessive swelling, hyperemia or other pathological reaction from the soft tissues were detected. In all cases, pain disappeared by the seventh postoperative day. Restoration of weight-bearing ability, the possibility of full weight bearing on the operated limb, and normal physical activity was noted within a standard term for such injuries. The colleagues conclude that the main indications for the use of resorbable implants in children remain fractures and osteotomies that need to be fixed with screws, while the development of the production of plates and elastic screws from resorbable materials will expand the indications for their use.

Authors from Hungary (Gergő Jozsa, Tamas Kassai, Marcell Varga) share their results of using resorbable elastic intramedullary nails for fractures of the forearm bones in 4 patients. Bone union without secondary displacement along with anatomical and functional recovery was observed 5-7 months after surgery in each case. It is claimed that the resorbable osteosynthesis material provides reliable stability and similar results as when using metal nails. The obvious advantage of resorbable implants is that there is no need to remove them. Irritation of soft tissues by the protruding end of the nail is also excluded, since according to the technology it is cut off at the level of the bone. Thus, surgical treatment of forearm fractures using resorbable implants is a reasonable alternative to metal intramedullary nails.

The results of tibial lengthening using an intramedullary degradable implant are presented by authors from Kurgan (Popkov AV, Gorbach ES, Mamedov UF, Stepanov RV). For the first time in clinical practice, a case of surgical lengthening of the tibia with the Ilizarov apparatus and an intramedullary degradable implant made of polycaprolactone (PCL) saturated with hydroxyapatite was used in a 10-year-old patient to stimulate reparative regeneration of the tibia. The process of lengthening the tibia was accompanied by a pronounced formation of a bone "coupling" around the implant, which was directly connected to the endosteum of the tibia. It is concluded that the implant used is not inferior in characteristics to titanium wires coated with hydroxyapatite in terms of osteoinduction and does not require a repeated surgical intervention for removal.

The use of bioactive biodegradable implants made of polycaprolactone for the treatment of osteochondral defects was the topic of the study by Popkov AV, Gorbach ES, Gorbach EN , Kononovich NA , Kireeva EA , Popkov DA. Specialists from the Ilizarov Center conducted a comparative study on 76 Wistar rats, divided into 2 groups, in which an osteochondral defect of the medial femoral condyle was modeled. In the experimental group, the defect was treated with a biodegradable bioactive membrane made of polycaprolactone with hydroxyapatite. In the control group, the simulated defect was not managed. Results were assessed over a one-year period using clinical, anatomical, histological, biomechanical and statistical methods. The range of motion in the knee joint in the animals of the experimental group at all stages of the experiment was significantly better than in the control group. The implant ensured the integrity and congruence of the articular surface. On the 180th day, at the site of the defect filled with the implant, a newly formed area of the articular surface of an organotypic structure was observed with the subchondral bone being replenished with bone tissue, and the articular surface with cartilaginous tissue. The authors conclude that a bioresorbable polycaprolactone implant impregnated with hydroxyapatite particles is effective for healing osteochondral defects.

Experimental work on the production of bioresorbable implants and the study of their properties is presented in three studies.

Scientists from Tomsk Polytechnic University and their co-authors from Kurgan propose a method for applying hydroxyapatite to the surface of three-dimensional scaffolds made of ε-polycaprolactone by processing in a "good/bad" solvent mixture. The proposed processing method ensures uniform coverage of the external and internal surfaces of polycaprolactone scaffolds manufactured by 3D printing with a layer of hydroxyapatite particles, while maintaining their porous structure. The presence of a bioactive layer on the surface of bioresorbable polymer scaffolds can expand their use in clinical practice for surgical treatment of bone defects.

Stogov MV and co-authors (Kurgan, Tomsk) presented the results of studying the rate of degradation of a material with a polylactide (PLLA)/hydroxyapatite (HA) composition depending on the crystallinity of the polymer

structure. The study showed that the crystallinity of PLLA influenced the kinetics of HA release from the samples of the studied materials. As crystallinity increases, the rate of HA hydrolysis increases. This observation can be explained by the fact that the polymer in the crystalline phase underwent hydrolysis faster than in the amorphous state. The authors show that changing the HA content and the PLLA crystallinity enables to control the biological characteristics of PLLA/HA composite materials.

An *in vitro* study of the bactericidal activity of implants made of biodegradable material (polycaprolactone) impregnated with hydroxyapatite and an antibiotic is the topic of the study by Popkov DA et al. (Tomsk, Moscow). The authors demonstrated that porous implants made from PCL and impregnated with an antibiotic have significant antimicrobial activity against the most common gram-negative and gram-positive bacteria that cause purulent complications in surgical practice. Nanostructured hydroxyapatite on the surface of the implant does not decrease bactericidal activity. The proposed implants will help stimulate bone regeneration and simultaneously provide an antimicrobial effect.

The experience of using customized implants is of great interest. Thus, Korytkin AA et al. (Tsivyan Novosibirsk Research Institute of Traumatology and Orthopedics, Novosibirsk) in *in vitro* experiments and clinical studies investigated the biological fixation of customized implants in managing post-traumatic deformities of the acetabulum. The results of the experiment to study the penetration of living fibroblasts into the porous structure of implants with different pore sizes showed that metal structures with a pore size of 400-499 microns can be distinguished from all others, since at a given pore size the penetration of living fibroblasts into the structure of the implant surface is the greatest. Management of bone tissue defects in the acetabulum area using customized implants with a mesh porous structure surface (400-499 microns) showed signs of biological fixation in the bone tissue surrounding the customized implant in the study group after 12 months.

Issues of new treatment methods are discussed in four publications. Leonchuk SS and his co-author from India present a literature review and clinical case of a new surgical approach to the treatment of aneurysmal bone cyst (ABC) of the medial cuneiform bone. A 47-year-old woman with a 10-month history of pain and swelling in her right foot underwent en-bloc resection (complete removal of the medial cuneiform bone remnant), the defect was filled with a fibula graft from the right leg, and an allograft ("Bio-Ost"®) was placed along with the autograft. The postoperative period was uneventful with complete healing of the bone defect without relapse after 12 months of follow-up. The AOFAS score increased significantly from 34 points preoperatively to 92 points at a 1-year follow-up. Based on their work, the authors conclude that the use of a combination of Ilizarov external fixation and bone grafting provided favorable conditions for foot bone defect healing in this ABC case without complications, maintaining the patient's mobility and early axial load.

The use of combined osteosynthesis in the treatment of diaphyseal fractures of the tibia is discussed in the article by Popkov AV et al. (Kurgan), which assessed the effectiveness of a combination of transosseous osteosynthesis with intramedullary reinforcement with elastic titanium nails coated with hydroxyapatite (HA-coated nails) in the treatment of fractures of long bones. It has been shown that the advantages of the combined method contribute to reducing the time of external fixation, reducing the number of wires and half-pins in the external fixation apparatus, stimulating the formation of callus and preventing secondary displacement of bone fragments.

A mini-review of current concepts of mechanical methods of distraction regenerate stimulation is presented by Cherkashin A (Texas Scottish Rite Hospital for Children). It is proposed to define axial dynamization as the ability to provide axial load on the bone regenerate with minimal displacement or bending forces. Axial dynamization can be carried out through direct stimulation of the regenerate by axial cyclic loads and the exclusion of bending and displacement forces. The author concludes that axial dynamization, together with other non-invasive methods of mechanical stimulation of the distraction regenerate, should become a mandatory element in limb lengthening.

Popkov AV and Popkov DA aimed to identify new directions in the study, production and clinical use of bioactive implants for indications similar to autografts. The authors conclude that the main current trends in orthopedic bioengineering are 3D-printed implants that provide deterministic cell migration, proliferation and differentiation and maintain sufficient mechanical strength of their structure for the required time. The combination of biodegradable implants with impregnation with bone morphogenetic protein stimulates the regeneration of the reconstructed bone. Programmed and controlled resorption of implants along with filling the tissue with new bone is the main vector in the development of bone tissue engineering.

We are confident that this thematic issue will be interesting and useful to specialists and will acquaint the expert community not only with the current state of the field, but also outline promising projects for future cooperation.

Have a nice and useful reading!

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