Bone tissue regeneration in Russia

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In Russia, the work focused on creating contemporary materials for bone regeneration began in the late 1990s. At the time, most developed countries had been using calcium phosphate materials (such as hydroxyapatite and tricalciumphosphate of natural or synthetic origin) and products with a biopolymer collagen of animal origin for approximately 20 years.

Initial products (already in the RF) were registered at the RF Ministry of Health in 1994, followed by rapid development of medical materials of this type.

Today, there are seven companies in the RF producing over 50 various products intended for medical purposes and used for bone tissue regeneration. It was for this particular reason that the year 2011 witnessed the Symposium "Tissue and cell engineering in dentistry and maxillofacial surgery" as part of the 26th All-Russian conference; the event confirmed the emergence of a new direction in the medical industry, namely, the development and manufacture of materials for bone tissue regeneration, consequently, the widespread use of these materials in medicine.

Given the above and the demand in the practical medicine for such products, the authors' group issued methodological recommendations in the hope that it will be used widely by practicing doctors, graduate and undergraduate students.

The POLYSTOM company was the first company in Russia who engaged in the development and production of materials for bone tissue regeneration.

These developments were used as a basis to do research and produce Hydroxyapol (pure HA in powder and granules) and compound collagen-HA; these Medical products were registered after long pre-clinical tests and clinical approbation at the RF Ministry of Health in 1994-95. Later, the clinical use data contributed to developing the KP Series KOLAPOL compounds (KP being an acronym of "bone grafting" in Russian) representing a combination of collagen and HA powder, KOLAPOL KP-2 and KP-3 (containing granules of HA and ß-TCP), PARODONKOL (membranes for guided bone regeneration, representing a combination of a collagen film with a thin layer of HA).

In 2002, POLYSTOM activities resulted in including of Subgroup 93 9180 "Materials for bone tissue regeneration" in the Industry-wide classifier of production (ICP) of RF also containing other subgroups. Sometime later, the corporate author POLYSTOM was awarded the RF State Prize in science and technology.

The development of osteoplastic materials containing signal molecules that can provide an osteoinductive effect of implanted materials became possible due to studies performed by K.S. Desyatnichenko. Studying some types of non-collagen proteins of bone tissue (NPB, the minor fraction of an extracellular bone matrix) he found that approximately 20 of them have a biologic effect of local growth factors (LGF), they produce a dose-dependent effect on proliferative activity of osteoprogenitor cells, hematopoietic progenitor cells and immunocompetent progenitor cells, their differentiation and expression of tissue-specific proteins by differentiated cells. Infusion of several NPBs with LGF properties has greater influence on reparative osteogenesis due to their co-operative effect. Singlet LGFs and their compositions are currently used to potentiate reparative osteogenesis, their osteoinductive properties were revealed. Also, NPB affinity differences were found with different physiological effects related to three basic ingredients of bone tissue: HA, TCP and collagen.

Biological and physicochemical properties of these NPB compounds with various physiological functions make it possible to create various tissue engineering systems, i.e. to construct products and materials with a planned biological effect. POLYSTOM used this principle to develop the INDOST series osteoplastic materials.

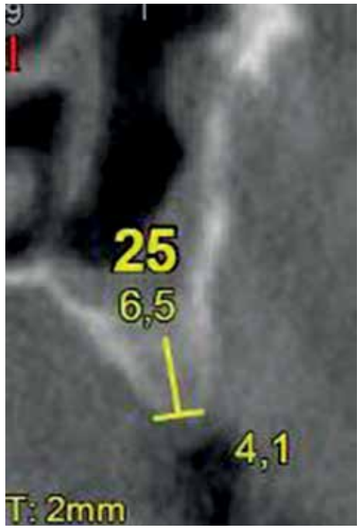
To date NPO POLYSTOM has worked to improve osteoplastic materials focusing on the following objectives:

1. To improve osteoinductive properties to use them during operations on patients with compromised regenerating potential (for cases of osteopathy and osteoporosis of involutive, iatrogenic and alimentary nature).
2. To optimize surrounding tissues' reaction to implantation of an osteoplastic material into a bone defect – to decrease an aseptic inflammation activity and an oxidative stress.
3. To remove osteoplastic materials cytotoxicity to create cell-and-tissue engineering structures – the most promising direction of regenerative medicine.
4. To create gel- and paste-type osteoplastic materials to decrease the surgical aggression level when repairing bone defects.

Below we introduce some practical examples of POLYSTOM materials' use.

1. USING THE INDOST GEL + IN THE SINUS LIFTING SURGERY

Surgery and post-surgical period. Dissect the frontolateral area of the upper jaw alveolar process near the absent tooth. Separate a mucoperiosteal flap. Cut a bone window without injuring the Schneiderian membrane. Place the osteoplastic material INDOST gel into the cavity, then cover the defect with a resorbable PARODONKOL membrane. Placed the flap back and fix it with noose sutures.



a) CT reveals a deficiency of the alveolar process bone of the upper jaw near the absent 25 tooth (h=6.5mm).

b) The focal radiography 2 months after the sinus lifting surgery. The bone tissue is restored partially, predominantly in the lower portion.

c) The focal radiography 6 months after the sinus lifting surgery reveals clear contours of the restored bone tissue. The bone structure is homogeneous.

Fig. 1. A clinical example of the sinus lifting using the INDOST gel +

In the postsurgical period, cold should be applied to the cheek for 15 minutes every hour on the day of the surgery. A week-long anti-inflammatory treatment should be prescribed: flemoxin solutab 500 mg 3 times a day (7 days), claritin 1 time a day (7 days), cetanov – 1 tablet in case of severe pain; local mouth baths using a 0.05% chlorhexidine solution 3 times a day (10 days).

2. JAW BONES DEFECT RESTORATION AFTER A CYSTECTOMY

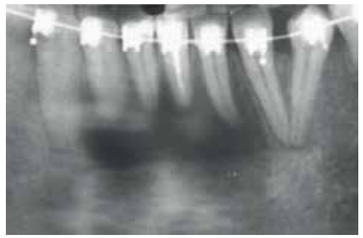
Jaw cysts are the most widespread diseases of jaw bones. The true cyst is a cavity with a wall that consists of a fibrous tissue with epithelium-lined internal surface. There is transparent (sometimes slightly opalescent) liquid inside the cyst cavity. The most common type is a radicular (root) cyst, which forms as a result of chronic inflammation of periodontium and formation of an apical granuloma. Dystrophic changes in the granuloma lead to formation of small internal cavities followed by formation of a single cystic cavity. Radicular cysts account for 80% among all types of jaw cysts. Usually, a cyst diameter is 0.5 to 2cm, but sometimes cysts may be up to 3cm or more in diameter.

Cystectomy is a radical operation involving total removal of a cyst capsule and suturing of the surgical wound. Indications: 1) a cyst as a defect of the odontogenic epithelium development; 2) a small cyst located in a toothed jaw segment, limited to 1 or 2 intact teeth; 3) a large cyst on the lower jaw characterized by absence of teeth in the cyst zone and preservation of sufficient bone thickness (up to 0.5-1cm) near the jaw's base, which saves it from a possible pathological fracture; 4) a large cyst on the upper jaw characterized by absence of teeth in the cyst zone and of a preserved bone wall in the nasal cavity bottom. The bone defect restoration after cystectomy is necessary to preserve functionality of the teeth located in the projection of the cyst or, if the teeth are absent, for prosthetic reasons.

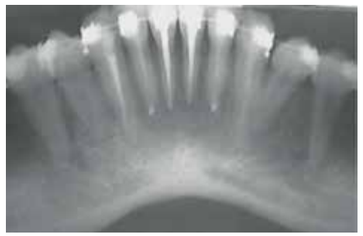
3. TREATMENT OF ODONTOGENIC CYSTS USING KOLAPOL KP-3

Surgery procedure. Under a local (infiltrative and conductive) anesthesia the sulcular/marginal dissection should be made. Separate a full-thickness mucoperiosteal flap, widen the bone defect or perforate the cortical bone, separate and remove the cyst capsule, resect the tooth root apex, if necessary backfill the root canal. Fill the bone defect with KOLAPOL KP-3. Place the flap back and fix it using noose sutures. Prescribe rinsing the mouth with a 0.12% chlorhexidine solution; antibiotic therapy should be prescribed according to indications. In the post-surgical period clinically assess the operated area for hyperemia of the mucosa, edema, the wound discharge amount, body temperature changes, pain syndrome severity. Sutures should be removed 7 to 10 days later.

Where a cyst grows into a maxillary sinus the surgery should be performed as described above. The bone defect connected to the maxillary sinus should be filled with KOLAPOL KP-3 up to the lower edge of the sinus. The material should be left uncovered. In future, it will be replaced by fibrous connective tissue.



a) before the surgery



b) 6 months after the surgery

Fig. 2. A clinical example of the lower jaw defect restoration (after a cystectomy) using KOLAPOL KP-3

We stated only some examples of our products use. The product line of POLYSTOM can be used almost in all fields of dentistry, such as dental surgery, therapeutic dentistry, parodontics and dental implantation. Irrespectively of this all the materials are biocompatible, biodegradable, noncytotoxic and osteoinductive. Collectively the listed properties facilitate their use for bone defects restoration not only in dentistry but also in maxillofacial surgery, ENT surgery, traumatology, and orthopedics. By the year 2017 more than 3 million of operations were conducted using the materials of POLYSTOM. Clinicians depending on their own preferences and encountered challenges may choose any material second to no similar foreign products in its biological properties. All these materials are designed to be used in clinics supported by the widest range of budgets and are affordable for various strata of population.