

N.V. Dedukh¹, V.B. Makarov², A.D. Pavlov³

¹State Institution "D.F. Chebotarev Institute of Gerontology of the NAMS of Ukraine", Kyiv, Ukraine

²SI "Specialized Multidisciplinary Hospital 1 of the Ministry of Health of Ukraine", Dnipro, Ukraine

³Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine

Polylactide-based biomaterial and its use as bone implants (analytical literature review)

For cite: Bol', sustavy, pozvonočnik. 2019;9(1):28-35. doi: 10.22141/2224-1507.9.1.2019.163056

Abstract. In many areas of medicine, implants from various synthetic and natural biomaterials are widely used. One of the materials that are most often used to create implants is polylactide (PLA), a feature of which is biodegradation in implantation sites, osseointegration, the ability to induce bone formation and high biocompatibility with the body. Aim of the review is to analyze and summarize data on the rearrangement in the bone of biodegradable biomaterials based on polylactide and to identify trends in the development of the problem. The review of the literature presents a general description of PLA and identifies historical milestones in the development of the problem and the use of biodegradable polymers in bone surgery. The data on the factors affecting the biodegradation of this biomaterial in the bones are presented and the peculiarities of its osseointegration are determined depending on composition. The data on the use of PLA and copolymers in bone surgery and regenerative medicine are given. An important direction for future researches will be the development of composite biomaterials based on PLA with the desired qualities of osseointegration and controlled biodegradation. New trends in the use of implants based on composite materials made from PLA in bone surgery and creation of implants using 3D printing are presented.

Keywords: polylactide; PLA; composite materials; implants; biodegradation; bone surgery

Introduction

Implants made of various synthetic and natural biomaterials are widely used in numerous fields of medicine. Their list is ever increasing due to the new ones being developed annually, and their properties being optimized for specific uses [17, 21, 25, 43, 46].

The biomaterials are divided into two groups depending on their properties: bioinert and biodegrading in the implantation areas. Bioinert materials are popular in orthopedics and traumatology [27]; however, it is the biodegrading ones that look most promising due to their complete degradation obliterating the necessity of an additional removal operation and a stable fixation for a certain period of time in case of bone implantation [33, 70, 69].

Developing biodegrading materials for the fixing tools and bone cavity fillers is a complicated task which requires a collaboration of expert material developers and researchers in the fields of biology and medicine.

Studies of human body reacting to various artificial materials become prominent at the time when a range of implants for bone surgery and regenerative medicine expands.

Human tissues are prone to react to the insertion of a foreign body [16, 38]. In this regard, every new biomaterial or biomaterial-based composite is severely tested to prove its biocompatibility and explore features of its remodeling at the implantation sites.

Among the biodegradation-marked materials used in bone surgery, there are polyglycolides (PGA), polylactides (PLA, or polylactic acid), polyglycolides and polylactides (PLGA, co-polymers in various combinations), polydioxanones, propylenes, polysulfones, and polycarbonates. In the implant-producing industry, the prominence is given to the polylactides (PLAs) and polyglycolides (PGAs) thanks to their biodegradation in the implantation areas, osteointegration, bone tissue induction, and a high biocompatibility [36, 46],

© «Біль. Суглоби. Хребет» / «Боль. Суставы. Позвоночник» / «Pain. Joints. Spine» («Bol', sustavy, pozvonočnik»), 2019

© Видавець Заславський О.Ю. / Издатель Заславский А.Ю. / Publisher Zaslavsky O.Yu., 2019

Для кореспонденцій: Дедух Нінель Василівна, доктор медичних наук, професор, ДУ «Інститут геронтології імені Д.Ф. Чеботарєва НАМН України», вул. Вишгородська, 67, м. Київ, 04114, Україна; e-mail: redact@i.ua

For correspondence: Ninel Dedukh, MD, PhD, Professor, State Institution "D.F. Chebotarev Institute of Gerontology of the NAMS of Ukraine", Vysgorodskaya st., 67, Kyiv, 04114, Ukraine; e-mail: redact@i.ua

44]. Moreover, advance of 3-D printers in the medical field makes them ideal candidates for the printed implants.

Purpose of the review: to analyze and generalize the existing data on bioresorptive polylactide-based biomaterial bone remodeling and explore the development prospects.

The date search was performed using Google, Google Scholar, PubMed, Academic Resources Index, Russian Science Citation Index (РИНЦ). The following keywords were administered as tags: polylactide, polylactic acid, composites, biodegradation, clinical use, experimental studies.

General information on PLA

Polylactide is a semi-crystalline polymer synthesized during polymerization or polycondensation. Its molecular weight range is from 180000 to 530000, melting point being set approximately at 174°C and glass transition – at 57°C. At the implantation sites, PLA is degraded by hydrolysis. Depending on its configuration, PLA may act as two different stereoisomers, poly-L-lactide (PLLA) and poly-D-lactide (PLDA), of divergent properties: PLLA's slow degradation takes 2 to 5 years while PLDA's mechanical strength is being lost much faster [23]. For this reason, a lot of orthopedic implants are made of PLLA [6].

Historical aspect

The first animal-based experimental study of PLLA was published in 1966, proving the biomaterials biocompatibility, absence of toxicity and slow degradation at the implantation sites [30]. When the PLLA plates and screws were used to fix the canine lower mandible, there was no side effect revealed in the tissues [29]. In 1971, the clinical study of humans with lower mandible fractures evidenced the prospects of this biomaterial being used in clinical practice [10]. However, the wide-ranging application was still pending as the first PLLA implants tested from 1990 to 1996 triggered inflammation and swelling at the implantation sites in 47 % of patients [6]. Moreover, certain aspects of PLLA implants, namely their fast destabilization and breakage, lack of stiffness and strength compared to the metal counterparts, impeded further use [15].

Most bio-resorptive composites lack osteointegrative properties. Several studies [47, 4, 21] show that PLA has a high tensile strength (3,5-3,8 hPa) and compressive strength (48-110 mPa); however, being fragile, it lacks stiffness. As a result, its application is restricted.

Progress of material engineering paving the way for implants being made of PLA stereoisomers, removal of the material's deficiencies, and development of sterilization methods resulted in a gradual change of the scientific attitude towards implants [25]. The next stage heralded creation of PLA copolymers, PLA-based composites, and improvement

of production technologies and manifested itself in an optimized biodegradation and implant mechanical properties.

Factors affecting implant biodegradation

Biodegradation is a process of polymer being reduced to water and CO₂ under the influence of biologic environment [21]. In case of a complete biodegradation, PLA turns into gaseous products filling the implantation sites with bone tissue.

Mechanical properties, biological mechanisms and biodegradation vary as far as PLA-based composites are concerned, requiring further exploration and optimal surgery application. Biodegrading materials should be biocompatible without any inflammatory or immune response; and the degradation products should not be toxic.

Implant's biodegrading rate depends on their localization at the skeletal sites. If those sites aren't vascularized enough, there is a risk of adverse reaction due to acid debris accumulating and affecting the tissues. Moreover, implants at the increased load sites get degraded a lot quicker than the ones at the reduced load sites [39]. Other sources of influence include the bone quality (trabecular, cortical), thickness of soft tissue layer over the implant, bloodstream, osteosynthetic type (intra- or supra-osseous), and individual features [2, 8]. Total degradation period is a combination of various factors, namely the material quality (hydrophilic or hydrophobic), its structure – crystallinity, original molecular weight, polymer component ratio, implant size and design, production and sterilization technology [8, 9, 40, 50]. Recent studies are targeted at reducing implant's reaction to a foreign body, polymer crystallinity and pH-control under biodegradation.

PLA implant degradation starts with biological substances penetrating the implant crevices and breaking the polymer chains into a multitude of fragments. This process reduces viscosity and impacts mechanical density. Cracks and crevices of the hydrophobic surface may incite an inflammatory reaction, while a biodegradation results in a reduced adhesion and cell proliferation [21]. However, the frequency of side effects at the PLA implantation sites (if the implant is a state-of-the-art technology) is quite low: only 0 to 1 % [6]. Actual weight loss is provoked by the lactic acid dissolution, release of the degraded products through osteoclast and macrophage-assisted phagocytosis and, as a result of Krebs cycle, final reduction to the dual metabolic products: carbon dioxide and water secreted with air and urine [55, 57]. Thus, a polylactide biodegradation ends with metabolic derivatives devoid of toxicity, which makes the material totally applicable in medicine [51].

Polylactide-based composites

PLA is used in bone surgery at the skeletal sites that are not expected to withstand heavy load. In order to

improve PLA strength, its osteointegration and guided degradation, various PLA-based composites are created; among them first and foremost, PLLA-PLDA, PLA-phosphates, PLA-hydroxylapatite, PLA-tricalcium phosphate, PLA-chitosan etc. [5, 13, 47, 52, 65]. Improvement of mechanical qualities was achieved by creating a polymer with a ratio of PLLA: PLDA isomers 85 to 15. Plates made of that polymer were used to fixate fractures [20].

In order to create stiff supra-osseous plates and improve mechanical qualities, researchers suggest a PLA-based composite with tricalcium phosphate [58]. Bioactive supplements, such as ceramics made of calcium phosphate, may improve its biological properties and osteointegration, while under biodegradation calcium phosphate ceramics promote bone regeneration. PLA, combined with hydroxylapatite, increases strength of osteosynthetic plates (OSTEO-TRANS MX®) [41].

Plates and intra-osseous implants made of PLLA, hydroxylapatite and tricalcium phosphate with a ratio of 70:10:20 provide better osteointegrative properties and improve the biomaterial's strength [42]. There is also a PLA-based composite with carbon fibers and hydroxylapatite [41].

When the deteriorated bone state (osteoporosis, osteopenia) was taken into account, a PLA-based composite with apatite and strontium was offered [33].

PLA's osteointegrative and reparative properties increase with spongy structures where the pores have optimal sizes (about 100–200 μm) promoting bone tissue penetration and functional remodeling [35].

Biodegrading implants shaped as perforated plates («Synthes» (Switzerland), «PolyMax») contain L- and DL-lactides in a synthesized ratio of 70:30 %; their resorption taking 12–24 months [35]. These features make the implants perfect, according to their creators.

PLA and PLA-based composites are recently viewed as the most promising biopolymers for the bone surgery [13]. PLA is well researched and proved to be a safe biomaterial for the clinical practice, meet the demands, and draw maximum attention of the scientific community [59]. However, the search for beneficial PLA-based composites goes on.

Innovations in the field of PLA and PLA-based composite production

Major segmental bone defects caused by trauma, infection, tumors seem to be a topical issue for traumatologists. Due to patients' individual and complex defects, material and implants should meet their individual demands, and thus even the most convoluted implant molds easily recreated.

In 1986, Charles Hull used 3D printing for the first time, and since then this technology is on the rise [54]. 3D printing is a novel approach to the production of implants with various sizes and properties for the tissues and organs. 3D printing in the field of medicine

will enable a customized implant to replace a bone defect of a specific form and volume at the traumatized skeletal site. However, the method raises a lot of questions as to the printing materials, opportunities for the newly created biocomposites to be offered depending on their biocompatibility, implantation sites in terms of their load and blood supply.

3D printed biodegradable bone implants have a range of advantages, among them, a relatively non-invasive treatment, no need of a repeat operation to remove the implant, creating a customized implant version for every patient. In 3D printing, only the most innovative biomaterials, i.e. ceramics, various polymers (mostly PLAs and PGAs, as well as their composites) are used [19], thus opening new vistas for bone surgery [37] and enabling surgeons to perform the previously impossible operations. 3D printed PLA implants guarantee mechanical stability, possess a high biocompatibility and osteoconductivity [9].

Studies on PLA endotoxin pollution of 3D printed implants reveal a low margin level the FDA prescribed [49].

These data expand PLA use, especially among the 3D printed bone implants. These implants could also be used as scaffolds in the regenerative medicine, in particular for bone defects.

However, it should be mentioned that PLAs by various producers could affect the printing conditions and quality, as well as they get remodeled in the bone tissue differently, and thus require additional clinical and experimental studies [44].

Experimental studies of PLAs and PLA-composites

Experimental studies among the cell cultures and animals augment the range of biomaterial testing, including biocompatibility, osteointegration, strength and degradation rates [18].

PLA in regenerative medicine. This biomaterial demonstrates its great promise for the tissue engineering, in particular scaffolds of various shapes and volumes for cell cultivation and further implantation into organs and tissues [1, 64]. The cell culture studies prove PLA's biocompatibility, absence of immune response, and cell integration.

In vitro study of cell cultures was performed to compare cell adhesion and proliferation depending on various cell-cultivating scaffolds [64]. Titanium disks and polystyrol scaffolds were tested because of their wide use in bone surgery. Cellular viability was found to be higher on the PLA scaffold ($95,3 \pm 2,1 \%$) as compared with polystyrol ($91,7 \pm 2,7 \%$). Cellular proliferation, by contrast, was more significant on polystyrol disks. However, when PLA and titanium disks were compared, PLA disks were proved to promote greater proliferation. During the scanning electron microscopic analysis, it was found that all the disks were covered with a homogeneous cellular layer; nonetheless, PLA and titanium disks had a higher density of cells.

Comparative analysis of cell cultures was also performed on solid and spongy PLA disks, covered and filled with collagen [49]. Biosamples were 3D printed. Their microscopic analysis showed that various cell types (preosteoblasts, osteoblasts, fibroblasts and endothelial cells) grow and spread on PLA printed disks, proliferating as the biomaterial is compatible and possesses significant adhesive properties.

Recent studies also focus on surface modification of implants, i.e. emergence of spongy structure. Spongy PLA covered with collagen promotes adhesion and growth of endothelial cells, inducing angiogenesis at the implanted sites. 3D printed PLA scaffolds used with gelatinous hydrogels were shown to stimulate osteogenic differentiation of human fat tissue-derived stem cells if cultivated. Thus, they could be used in regenerative medicine to produce bone cavity fillers and support bone regeneration [62].

Experimental studies on animals. Ingeo™ Biopolymer 403, polylactide, a product of L- and D-type lactide polymerization (ratio from 24:1 to 32:1) was tested on rats. Screw-shaped implants were created by means of «Ultimaker3» 3D-printer (build-up fusing method, each layer 0,1-0,2 mm wide). Biopolymer-made screws were implanted into metadiaphysis and diaphysis-located defects of femoral bone [14, 34]. The material was proved biocompatible, with significant osteointegrative properties; it does not provoke inflammation of adjacent soft tissues and bone marrow, as well as destructive bone changes at the implantation sites. At the study's end (after 270 days), polylactide implants retained their shape, no biomaterial got degraded, which signals a prospect of long-term use.

When an experimental study on animals involved a fracture fixation, L-lactide, D-L-lactide, polyglycolide and trimethylene carbonate plates possess the following properties: biocompatibility, absence of bone lysis under the plate and lack of negative impact on regeneration [3]. Other studies showed angiogenic and osteogenic features of PLA-based composites [24, 67]. Performed experimental studies expand extant vision of PLA and PLA-composite interaction with bone tissue.

Polylactide implants in clinical practice

Screws and fixating joint-pins, plates, anchors and cages are often made of biosoluble degrading PLA and PLA-composites [46, 25, 43, 21], afterwards eliminated with no residual toxic effect on the organs and systems [63, 53, 55 21, 25]. PLA-made implants are applied in case of knee, ankle and ulnar fractures, in spondylodesis, as well as at the foot, wrist, pelvis, cheekbone, lower mandible sites, making polylactides a fitting option for orthopedics, traumatology and oral surgery [21, 25, 40, 63, 66].

Fracture fixation with biodegrading materials was found to be as effective as fixation with traditional metals. Nevertheless, they have certain advantages: no

need of removal, controlled biodegradation etc. Formerly viewed as a perfect option for the unloaded skeletal sites [40], PLA-based composites were promoted into the field of bone surgery.

Despite the fact that orthopedic surgery has been using degrading polymers for 30 years, respective spinal implants are a recent development. However, there are a limited number of studies documenting PLA or PLA-based composite use in spinal surgery. Having summarized the review data of degradable implants in human and animal spinal surgery [59, 60], we found indications that in animals implants are effectively resorbed, spondylodesis is formed and cages degraded in the intervertebral spaces. As for humans, biodegrading cages were found to be effective, safe and spondylodesis-promoting. Cages of PLLA:PLDA with a 70:30 ratio (Hydrosorb, produced by Medtronic Sofamor Danek, Memphis, TN.) provided some proven positive results. At the first stage of clinical trials in 2002, 60 patients undergoing transforaminal lumbar interbody fusion (TLIF) with Hydrosorb vertical cylindrical biodegrading cages [30, 32] did not reveal any complications after 4,7 months. Having studied those patients who received recombinant morphogenetic rhBMP2-protein cages after 12-18 months, researchers found the interbody space height to remain stable, spondylodesis to occur in 87 % of patients according to X-ray and in 97 % according to CT results [28]. There were no instances of infection or cage-induced complications recorded.

Another study of TLIF with similar cages revealed spondylodesis in 96,8 % (30 out of 31 patients) after 18,4 months on average [10]. However, there was no indication of cage biodegradation.

Along with positive results of biodegradable cage-induced spondylodesis, there is a comparative study of PLLA: PLDA cages with a ratio of 70:30 and carbon fiber cages [56] which showed an increased non-union frequency (18,2%) and post-surgery cage migration (18,2%) after TLIF.

Overall, cage technology studies require prolonged observations of the respective control groups.

Our analysis of theoretical sources has thus confirmed the prospects of further studies of PLA properties and modifications in view of experimental and clinical applications. Polymer properties even if coming from the uniform substance depend on the industrial process (namely, processing temperature, production and sterilization method etc.). It provides an opportunity to develop materials and implants based on their intended properties as products made of the same input but using different technologies would have different properties, such as strength and biodegradation rates. Data comparison as well as conclusions as to the biomaterial properties should not be based solely on the experimental results of same input material if we do not know anything about processing methods and other details. An important research track is to develop and study composite biomaterials which would give

rise to implants with intended properties of controlled biodegradation and osteointegration. A significant progress is brought by 3D printer of implants. This is a new field of implantology enabling new approach to implant creation and clinical use.

Conflicts of interests. Authors declare the absence of any conflicts of interests that might be construed to influence the results or interpretation of their manuscript.

References

1. Alsaheb R A., Aladdin A, Othman N Z, et al. Recent applications of polylactic acid in pharmaceutical and medical industries. *J Chem Pharm Res.* 2015;7(12):51-63. doi: 10.1023/B:ABME.0000007802.59936.fc.
2. Ambrose CG, Clanton TO. Bioabsorbable implants: review of clinical experience in orthopedic surgery. *Ann Biomed Eng.* 2004 Jan;32(1):171-7.
3. Atali O, Gocmen G, AktopS, Ak E, Basa S, Cetinel S. Bone healing after biodegradable mini-plate fixation. *Acta Cir Bras.* 2016 Jun;31(6):364-70. doi: 10.1590/S0102-865020160060000001.
4. Balakrishnana H, Hassana A, Wahita MU, Yusufa AA, Razakb SBA. Novel toughened polylactic acid nanocomposite: Mechanical, thermal and morphological properties. *Mater Des.* 2010;31(7):3289-3298. doi: 10.1016/j.matdes.2010.02.008.
5. Bleach NC, Nazhat SN, Tanner KE, Kellomäki M, Törmälä P. Effect of filler content on mechanical and dynamic mechanical properties of particulate biphasic calcium phosphate-polylactide composites. *Biomaterials.* 2002 Apr;23(7):1579-85. doi: 10.1016/S0142-9612(01)00283-6.
6. Bohner M. Resorbable biomaterials as bone graft substitutes. *Materials Today.* 2010;13(1-2):24-30. doi: 10.1016/S1369-7021(10)70014-6.
7. Böstman OM, Pihlajamäki HK. Adverse tissue reactions to bioabsorbable fixation devices. *Clin Orthop Relat Res.* 2000 Feb;(371):216-27.
8. Böstman OM, Pihlajamäki HK. Clinical biocompatibility of biodegradable orthopaedic implants for internal fixation: a review. *Biomaterials.* 2000 Dec;21(24):2615-21. doi: 10.1016/S0142-9612(00)00129-0.
9. Chou YC, Lee D, Chang TM, et al. Development of a three-dimensional (3D) printed biodegradable cage to convert morselized corticocancellous bone chips into a structured cortical bone graft. *Int J Mol Sci.* 2016 Apr 20;17(4). pii: E595. doi: 10.3390/ijms17040595.
10. Coe JD. Instrumented transforaminal lumbar interbody fusion with bioabsorbable polymer implants and iliac crest autograft. *Neurosurg Focus.* 2004 Mar 15;16(3):E11. doi: 10.3171/foc.2004.16.3.12.
11. Cutright DE, Hunsuck EE, Beasley JD. Fracture reduction using a biodegradable material, polylactic acid. *J Oral Surg.* 1971 Jun;29(6):393-7.
12. Danoux CB, Barbieri D, Yuan H, de Bruijn JD, van Blitterswijk CA, Habibovic P. In vitro and in vivo bioactivity assessment of a polylactic acid/hydroxyapatite composite for bone regeneration. *Biomatter.* 2014;4:e27664. doi: 10.4161/biom.27664.
13. Davachi SM, Kaffashi B. Polylactic Acid in Medicine. *Polymer-Plastics Technology and Engineering.* 2015;54(9):944-967. doi: 10.1080/03602559.2014.979507.
14. Dedukh NV, Nikolchenko OA, Makarov VB. Restructuring of bone around polylactide acid implanted into defect of diaphysis. *Bulletin of Biology and Medicine.* 2018;(142):275-279. doi: 10.29254/2077-4214-2018-1-142-275-279. (in Ukrainian).
15. Dhillon M S, Lokesh A V. Bioabsorbable implants in orthopaedics. *Indian J Orthop.* 2006;40(4):205-209.
16. Dolzhikov AA, Kolpakov AY, Yarosh AL, Molchanova AS, Dolzhikova IN. Giant foreign body cells and tissue reactions on the surface of implants. *Kursk scientific and practical bulletin Man and his health.* 2017;(3):86-94. doi: 10.21626/vestnik/2017-3/15. (in Russian).
17. Fernandez de Grado G, Keller L, Idoux-Gillet Y, et al. One substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management. *J Tissue Eng.* 2018 Jun 4;9:2041731418776819. doi: 10.1177/2041731418776819.
18. Freire AR, Rossi AC, Queiroz TP, et al. Histometric analysis of bone repair in bone-implant interface using a polylactic/polyglycolic acid copolymer associated with implants in rabbit tibia. *J Oral Implantol.* 2012 Sep;38 Spec No:449-57. doi: 10.1563/AAID-JOI-D-10-00102.
19. Habibovic P1, Gbureck U, Doillon CJ, Bassett DC, van Blitterswijk CA, Barralet JE. Osteoconduction and osteoinduction of low-temperature 3D printed bioceramic implants. *Biomaterials.* 2008 Mar;29(7):944-53. doi: 10.1016/j.biomaterials.2007.10.023.
20. Haers PE, Suuronen R, Lindqvist C, Sailer H. Biodegradable polylactide plates and screws in orthognathic surgery: Technical note. *J Craniomaxillofac Surg.* 1998 Apr;26(2):87-91. doi: 10.1016/S1010-5182(98)80045-0.
21. Hamad K, Kaseem M, Yang HW, Deri F, Ko YG. Properties and medical applications of polylactic acid: A review. *eXPRESS Polymer Letters.* 2015;9(5):435-455. doi: 10.3144/expresspolymlett.2015.42.
22. Jones N. Science in three dimensions: the print revolution. *Nature.* 2012 Jul 4;487(7405):22-3. doi: 10.1038/487022a.

23. Joukainen A, Pihlajamaki H, Makela EA, et al. Strength retention of self-reinforced drawn poly-L/DL-lactide 70/30 (SR-PLA70) rods and fixation properties of distal femoral osteotomies with these rods: An experimental study on rats. *J Biomater Sci Polym Ed.* 2000;11(12):1411-28. doi: 10.1163/156856200744318.
24. Kao CT, Lin CC, Chen YW, Yeh CH, Fang HY, Shie MY. Poly(dopamine) coating of 3D printed poly(lactic acid) scaffolds for bone tissue engineering. *Mater Sci Eng C.* 2015;56:165-173. doi: 10.1016/j.msec.2015.06.028.
25. Hamad K, Kaseem M, Yang HW, Deri F, Ko YG. Properties and medical applications of polylactic acid: A review. *eXPRESS Polymer Letters.* 2015;9(5):435-455. doi: 10.3144/expresspolymlett.2015.42.
26. Kontakis GM, Pagkalos JE, Tosounidis TI, Melissas J, Katonis P. Bioabsorbable materials in orthopaedics. *Acta Orthop Belg.* 2007 Apr;73(2):159-69.
27. Korzh NA, Malyshkina SV, Dedukh NV, Timchenko IB. Biomaterials in Orthopedics and Traumatology - the role of AA Korzh in the development of problem. In: Goridova LD, editor. *Nasledie [The Heritage].* Ukraine: Kharkov; 2014. 35-49 pp. (in Russian).
28. Kuklo TR, Rosner MK, Polly DW Jr. Computerized tomography evaluation of a resorbable implant after transforaminal lumbar interbody fusion. *Neurosurg Focus.* 2004;16(3):E10. doi: 10.3171/foc.2004.16.3.11.
29. Kulkarni RK, Moore EG, Hegyeli AF, Leonard F. Biodegradable poly(lactic acid) polymers. *J Biomed Mater Res.* 1971 May;5(3):169-81. doi: 10.1002/jbm.820050305.
30. Kulkarni RK, Pani KC, Neuman C, Leonard F. Polyactic acid for surgical implants. *Arch Surg.* 1966 Nov;93(5):839-43.
31. Lowe TG, Coe JD. Bioresorbable polymer implants in the unilateral transforaminal lumbar interbody fusion procedure. *Orthopedics.* 2002 Oct;25(10 Suppl):s1179-83; discussion s1183.
32. Lowe TG, Tahernia AD. Unilateral transforaminal posterior lumbar interbody fusion. *Clin Orthop Relat Res.* 2002 Jan;(394):64-72. doi: 10.1097/00003086-200201000-00008.
33. Luo X, Barbieri D, Duan R, Yuan H, Bruijn JD. Strontium-containing apatite/polylactide composites enhance bone formation in osteopenic rabbits. *Acta Biomater.* 2015 Oct;26:331-7. doi: 10.1016/j.actbio.2015.07.044.
34. Makarov VB, Dedukh NV, Nikolchenko OA. Osteoreparation around the polylactide, implanted into the metadiaphys defect of the femur (experimental study). *Orthopedics, traumatology and prosthetics.* 2018;(611):102-107. doi: 10.15674/0030-598720182102-107. (in Ukrainian).
35. Makeev VF, Cherpak MO. Application of polymer osteoplastic materials in dentistry. *Ukrainian Dental Almanac* 2013;(1):116-119. (In Russian).
36. Malyshkina SV, Dedukh NV. Medical-biological studies of artificial biomaterials for orthopaedics and traumatology. *Orthopedics, traumatology and prosthetics.* 2010;(2):93-100. doi: 10.15674/0030-59872010293-100. (in Ukrainian).
37. Mamuladze TZ, Bazlov VA, Pavlov VV, Sadovoy MA. Use of modern synthetic materials at replacement of bone defects with method of individual planimetric plasticity. *International Journal of Applied and Basic Research.* 2016;(11-3):451-455. (In Russian).
38. Mayborodin IV, Toder MS, Shevela AI, et al. The morphological results of metallic implant introduction with various character of the surface in rabbit bone tissue. *Fundamental research.* 2014;(7-1):114-118. (In Russian).
39. Mezentsev VO. Differentiated application of varieties of calcium-phosphate ceramics for plastic cavity bone defects. *Diss cand sci.* 2007. 20 p. (In Ukraine).
40. Middleton JC, Tipton AJ. Synthetic biodegradable polymers as orthopedic devices. *Biomaterials,* 2000;21(23):2335-2346. doi: 10.1016/S0142-9612(00)00101-0.
41. Morawska-Chochół A, Jaworska J, et al. Degradation of poly(lactide-co-glycolide) and its composites with carbon fibres and hydroxyapatite in rabbit femoral bone. *Polym Deg Stab.* 2011;96(4):719-726. doi: 10.1016/j.polymdegradstab.2011.01.005.
42. Pavlov OD, Pastuk VV, Dedukh NV. Reaction of connective tissue on composite poly (l-lactic) acid, hydroxyapatite and tricalcium phosphate. *Bulletin of Biology and Medicine.* 2017;3(4):185-189. doi: 10.29254/2077-4214-2017-4-3-141-185-189. (In Ukraine).
43. Pawara RP, Tekalea SU, Shisodiaa SU, Totrea JT, Dombb AJ. Biomedical Applications of Poly(Lactic Acid). Recent Patents on Regenerative Medicine. 2014;4(1):40-51. doi: 10.2174/2210296504666140402235024
44. Pérez M, Medina-Sánchez G, García-Collado A, Gupta M, Carou D. Surface Quality Enhancement of Fused Deposition Modeling (FDM) Printed Samples Based on the Selection of Critical Printing Parameters. *Materials (Basel).* 2018 Aug 8;11(8). pii: E1382. doi: 10.3390/ma11081382.
45. Pina S, Ferreira JMF. Bioresorbable Plates and Screws for Clinical Applications: A Review. *Journal*

- of Healthcare Engineering. 2012;3(2):243-260. doi: 10.1260/2040-2295.3.2.243.
46. Radchenko VA, Dedukh NV, Malyshkina S, Bengus LM. Bioresorbable polymers in orthopedics and traumatology. Orthopedics, traumatology and prosthetics. 2006;(3):116-124. (In Russian).
47. Rasal RM, Janorkar AV, Hirt DE. Poly(lactic acid) modifications. *Prog Polym Sci.* 2010;35(3):338-356 doi: 10.1016/j.progpolymsci.2009.12.003.
48. Rezwan K, Chen QZ, Blaker JJ, Boccaccini AR. Biodegradable and bioactive porous polymer/inorganic composite scaffolds for bone tissue engineering. *Biomaterials.* 2006 Jun;27(18):3413-31. doi: 10.1016/j.biomaterials.2006.01.039.
49. Ritz U, Gerke R, Götz H, Stein S, Rommens PM. A New Bone Substitute Developed from 3D-Prints of Polylactide (PLA) Loaded with Collagen I: An In Vitro Study. *Int J Mol Sci.* 2017 Nov 29;18(12). pii: E2569. doi: 10.3390/ijms18122569.
50. Rokkanen PU, Віцтман О, Hirvensalo E, et al. Bioabsorbable fixation in orthopaedic surgery and traumatology. *Biomaterials.* 2000 Dec;21(24):2607-13.
51. Santoro M, Shah SR, Walker JL, Mikos AG. Poly(lactic acid) nanofibrous scaffolds for tissue engineering. *Adv Drug Deliv Rev.* 2016 Dec 15;107:206-212. doi: 10.1016/j.addr.2016.04.019.
52. Scaffaro R, Lopresti F, Botta L, Maio A. Mechanical behavior of polylactic acid/polycaprolactone porous layered functional composites. *Composites Part B: Eng.* 2016;98(1):70-77. doi: 10.1016/j.compositesb.2016.05.023.
53. Schaschke C, Audic, JL. Editorial: biodegradable materials. *Int J Mol Sci.* 2014 Nov 21;15(11):21468-75. doi: 10.3390/ijms151121468.
54. Science and society. Experts warn against bans on 3D printing. *Science.* 2013 Oct 25;342(6157):439.
55. Sheikh Z, Najeeb S, Khurshid Z, Verma V, Rashid H, Glogauer M. Biodegradable Materials for Bone Repair and Tissue Engineering Applications. *Materials (Basel).* 2015 Aug 31;8(9):5744-5794. doi: 10.3390/ma8095273.
56. Smith AJ, Arginteanu M, Moore F, Steinberger A, Camins M. Increased incidence of cage migration and nonunion in instrumented transforaminal lumbar interbody fusion with bioabsorbable cages. *J Neurosurg Spine.* 2010 Sep;13(3):388-93. doi: 10.3171/2010.3.SPINE09587.
57. Steffi C, Shi Z, Kong CH, Wang W. Modulation of Osteoclast Interactions with Orthopaedic Biomaterials. *J Funct Biomater.* 2018 Feb 26;9(1). pii: E18. doi: 10.3390/jfb9010018.
58. Szaraniec B. Durability of Biodegradable Internal Fixation Plates Materials Science. 2013;730-732:15-19. doi: 10.4028/www.scientific.net/MSF.730-732.15.
59. Torres-Hernández YG, Ortega-Díaz GM, Téllez-Jurado L, et al. Biological Compatibility of a Polylactic Acid Composite Reinforced with Natural Chitosan Obtained from Shrimp Waste. *Materials (Basel).* 2018 Aug 18;11(8). pii: E1465. doi: 10.3390/ma11081465.
60. Vaccaro A, Madigan L. Spinal applications of bioabsorbable implants. *J Neurosurg.* 2002 Nov;97(4 Suppl):407-12. doi: 10.3171/spi.2002.97.4.0407.
61. Vaccaro A, Singh K, Haid R, et al. The use of bioabsorbable implants in the spine. *Spine J.* 2003 May-Jun;3(3):227-37.
62. Vatchha SP, Kohli A, Tripathi SK, Nanda SN, Pradhan P, Shiraz SM. Biodegradable Implants in Orthopaedics. *Annals of International Medical and Dental Research.* 2015;1(1):3-8.
63. Wuisman, PI, Smit TH. Bioresorbable polymers: Heading for a new generation of spinal cages. *Eur Spine J.* 2006 Feb;15(2):133-48. doi: 10.1007/s00586-005-1003-6.
64. Wurm MC, Möst T, Bergauer B, et al. In vitro evaluation of Polylactic acid (PLA) manufactured by fused deposition modeling. *J Biol Eng.* 2017 Sep 12;11:29. doi: 10.1186/s13036-017-0073-4.
65. Xiao L, Wang B, Yang G, Gauthier M. Poly(Lactic Acid)-Based Biomaterials: Synthesis, Modification and Applications. In: Ghista DN, editor. *Biomedical Science, Engineering and Technology.* Intech Open; 2012. 247-282 pp. doi: 10.5772/23927.
66. Xu H, Han D, Dong JS, et al. Rapid prototyped PGA/PLA scaffolds in the reconstruction of mandibular condyle bone defects. *Int J Med Robot.* 2010 Mar;6(1):66-72. doi: 10.1002/rcs.290.
67. Yeh CH, Chen YW, Shie MY, Fang HY. Poly(Dopamine)-Assisted Immobilization of Xu Duan on 3D Printed Poly(Lactic Acid) Scaffolds to Up-Regulate Osteogenic and Angiogenic Markers of Bone Marrow Stem Cells. *Materials (Basel).* 2015 Jul 14;8(7):4299-4315. doi: 10.3390/ma8074299.
68. Yin X, Jiang L, Yang J, Cao L, Dong J. Application of biodegradable 3D-printed cage for cervical diseases via anterior cervical discectomy and fusion (ACDF): An in vitro biomechanical study. *Biotechnol Lett.* 2017 Sep;39(9):1433-1439. doi: 10.1007/s10529-017-2367-5.
69. Zeng RC, Cui LY, Jiang K, Liu R, Zhao BD, Zheng YF. In vitro corrosion and cytocompatibility of a micro-arc oxidation coating and poly(L-lactic acid) composite coating on Mg-1Li-1Ca alloy for orthopedic implants.

ACS Appl Mater Interfaces. 2016 Apr 20;8(15):10014-28. doi: 10.1021/acsami.6b00527.

70. Zhao MD, Björninen M, Cao L, et al. Polypyrrole coating on poly-(lactide/glycolide)- β -tricalcium

phosphate screws enhances new bone formation in rabbits. Biomed Mater. 2015 Nov 27;10(6):065016. doi: 10.1088/1748-6041/10/6/065016.

Received 15.01.2019 ■

Дедух Н.В.¹, Макаров В.Б.², Павлов А.Д.³

¹ДУ «Інститут геронтології імені Д.Ф. Чеботарєва НАМН України», м. Київ, Україна

²ДЗ «Спеціалізована багатопрофільна лікарня № 1 МОЗ України», м. Дніпро, Україна

³Харківська медична академія післядипломної освіти, м. Харків, Україна

Біоматеріал на основі полілактиду та його використання як кісткових імплантатів (аналітичний огляд літератури)

Резюме. У багатьох галузях медицини широке застосування отримали імплантати з різних синтетичних та природних біоматеріалів. Серед матеріалів, що частіше використовують для створення імплантатів, полілактид (PLA), особливістю якого є біодеградація в ділянках імплантациї, остеоінтеграція, здатність індукувати процеси утворення кісткової тканини та висока біосумісність з організмом. **Мета огляду:** проаналізувати та узагальнити дані щодо перебудови в кістці біорезорбувальних біоматеріалів на основі полілактиду та визначити тенденції розвитку проблеми. В огляді літератури подано загальну характеристику та визначено історичні віхи розвитку проблеми та використання деградуючих полімерів у кістковій хірургії. Надані дані щодо факторів, що впливають на

біодеградацію в кістках цього біоматеріалу, та визначено особливості його остеоінтеграції залежно від складу. Наведено дані щодо використання PLA та співполімерів у кістковій хірургії та регенераторній медицині. Важливим напрямком майбутніх досліджень буде розробка композитних біоматеріалів на основі PLA з бажаними якостями остеоінтеграції та керованою біодеградацією. Подано нові тенденції розвитку напрямку використання в кістковій хірургії імплантатів на основі композитних матеріалів, виготовлених на основі PLA, та новітні способи створення імплантатів та композитів із використанням 3D-принтера.

Ключові слова: полілактид; PLA; композитні матеріали; імплантати; біодеградація; кісткова хірургія

Дедух Н.В.¹, Макаров В.Б.², Павлов А.Д.³

¹ГУ «Институт геронтологии имени Д.Ф. Чеботарева НАМН Украины», г. Киев, Украина

²ГУ «Специализированная многопрофильная больница № 1 МЗ Украины», г. Днепр, Украина

³Харьковская медицинская академия последипломного образования, г. Харьков, Украина

Биоматериал на основе полилактида и его использование в качестве костных имплантатов (аналитический обзор литературы)

Резюме. Во многих областях медицины широкое применение получили имплантаты из различных синтетических и природных биоматериалов. Среди материалов, которые наиболее часто используют для создания имплантатов, полилактид (PLA), особенностью которого являются биодеградация в участках имплантации, остеоинтеграция, способность индуцировать процессы образования костной ткани и высокая биосовместимость с организмом. **Цель обзора:** проанализировать и обобщить данные о перестройке в кости биорезорбувальных биоматериалов на основе полилактида и определить тенденции развития проблемы. В обзоре литературы представлена общая характеристика и определены исторические вехи развития проблемы и использования деградирующих полимеров в костной хирургии. Представлены данные от-

носительно факторов, влияющих на биодеградацию в костях этого биоматериала, и определены особенности его остеоинтеграции в зависимости от состава. Приведены данные по использованию PLA и сополимеров в костной хирургии и регенераторной медицине. Важным направлением будущих исследований будет разработка композитных биоматериалов на основе PLA с желаемыми качествами остеоинтеграции и управляемой биодеградацией. Представлены новые тенденции развития направления использования в костной хирургии имплантатов на основе композитных материалов, изготовленных из PLA, и новые способы создания имплантатов с использованием 3D-принтера.

Ключевые слова: полилактид; PLA; композитные материалы; имплантаты; биодеградация; костная хирургия