Review Article

https://doi.org/10.36377/ET-0146

Clinical application of collagen in combination with growth factors and cells in regenerative dentistry

Sergei Yu. Voloshin, Khadizhat A. Gadzhieva, Kamila R. Zhalilova, Igor P. Ashurko, Petr S. Timashev, Artem A. Antoshin ✉

Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation

✉ antoshin_a_a@staff.sechenov.ru

Abstract

Type I collagen, being the main structural protein of the extracellular matrix, provides optimal conditions for cell adhesion and proliferation and can also serve as a system for localized delivery of bioactive molecules. However, for a number of clinical conditions, the regenerative capacity of collagen alone remains insufficient, which has stimulated the development of combined systems designed to enhance its regenerative potential. The combination of collagen implants with growth factors and stem cells represents a promising approach in regenerative dentistry. This review summarizes clinical studies focused on the use of collagen matrices combined with mesenchymal stem cells, dental pulp cells, fibroblasts, as well as with growth factors such as PDGF-BB, BMP-2, and FGF-2.

Despite the limited clinical evidence, the integration of collagen with bioactive components already demonstrates consistent advantages over conventional treatment methods. Studies show that these combined constructs accelerate the regeneration of hard and soft tissues, thereby reducing the need for autografts and minimizing surgical trauma.

Keywords: collagen, stem cells, growth factors, guided bone regeneration, guided tissue regeneration

Article info: received – 14.10.2025; revised – 01.12.2025; accepted – 05.12.2025

Conflict of interest: The authors report no conflict of interest.

Acknowledgements: The study was conducted within the framework of the state assignment of the Ministry of Health of the Russian Federation, project No. NZAF-2024-0025.

For citation: Voloshin S.Yu., Gadzhieva K.A., Zhalilova K.R., Ashurko I.P., Timashev P.S., Antoshin A.A. Clinical application of collagen in combination with growth factors and cells in regenerative dentistry. *Endodontics Today.* 2025;23(4):710–716. https://doi.org/10.36377/ET-0146

Клиническое применение коллагена в комбинации с факторами роста и клетками в регенеративной стоматологии

С.Ю. Волошин, Х.А. Гаджиева, К.Р. Жалилова, И.П. Ашурко, П.С. Тимашев, А.А. Антошин ✉

ФГАОУ ВО Первый МГМУ им. И.М. Сеченова Минздрава России (Сеченовский Университет), г. Москва, Российская Федерация

✉ antoshin_a_a@staff.sechenov.ru

Резюме

Коллаген I типа, являясь основным структурным белком внеклеточного матрикса, обеспечивает оптимальные условия для адгезии и пролиферации клеток, а также может служить системой локальной доставки биологически активных молекул. Однако для ряда нозологий регенеративная активность коллагена является недостаточной, что стимулировало поиск комбинированных систем, усиливающих его регенеративный потенциал.

Комбинация коллагеновых имплантатов с факторами роста и стволовыми клетками представляет собой перспективное направление регенеративной стоматологии. Настоящий обзор обобщает результаты клинических исследований, посвящённых применению коллагеновых матриц, заселённых мезенхимальными стволовыми клетками, клетками пульпы, фибробластами, а также дополненных факторами роста PDGF-BB, BMP-2 и FGF-2.

Несмотря на ограниченность клинических данных, совмещение коллагена с биологически активными компонентами уже демонстрирует устойчивые преимущества по сравнению с традиционными методами лечения. Показано, что такие комбинированные конструкции ускоряют восстановление кости и мягких тканей, снижая потребность в применении различных видов аутотрансплантатов и уменьшая травматичность хирургических вмешательств.

Ключевые слова: коллаген, стволовые клетки, факторы роста, направленная костная регенерация, направленная тканевая регенерация

Информация о статье: поступила – 14.10.2025; исправлена – 01.12.2025; принята – 05.12.2025

Конфликт интересов: авторы сообщают об отсутствии конфликта интересов.

Благодарности: Работа выполнена в рамках государственного задания Минздрава России, тема № NZAF-2024-0025.

Для цитирования: Волошин С.Ю., Гаджиева Х.А., Жалилова К.Р., Ашурко И.П., Тимашев П.С., Антошин А.А. Клиническое применение коллагена в комбинации с факторами роста и клетками в регенеративной стоматологии. *Эндодонтия Today.* 2025;23(4):710–716. https://doi.org/10.36377/ET-0146

INTRODUCTION

In contemporary regenerative dentistry and maxillofacial surgery, tissue engineering methods utilizing biocompatible scaffolds, cells, and growth factors are widely applied. Among available biomaterials, collagen matrices, such as sponges and membranes, are of particular relevance, since they perfectly imitate the extracellular matrix. Type I collagen, which is predominant in gingival tissues, the periodontal ligament, and jawbone, provides mechanical support and a biochemical environment that promotes adhesion, migration, and differentiation of oral cavity cells [1–3]. It demonstrates hemostatic properties, low immunogenicity, and stimulates periodontal fibroblast chemotaxis [4; 5]. These characteristics make collagen-based materials a widely used tool in guided bone and tissue regeneration procedures (GBR/GTR) in dentistry. On the other hand, such materials have limitations. Collagen is prone to rapid biodegradation, which leads to the loss of implant volume and restricts its capacity to support guided tissue regeneration over an extended period. As a result, collagen matrices without additional modifications may degrade prematurely before the completion of bone or soft tissue regeneration [6].

To overcome these limitations, one promising approach involves combining collagen with growth factors. Bone morphogenetic protein-2 (BMP-2), bone morphogenetic protein-7 (BMP-7), growth differentiation factor-5 (GDF-5), platelet-derived growth factor-BB (PDGF-BB), and transforming growth factor-β (TGF-β) exhibit strong osteoinductive and angioinductive activity. They regulate the proliferation, differentiation, and migration of bone and soft tissue progenitors. For example, it has been demonstrated that loading a collagen membrane with GDF-5 and PDGF leads to a more pronounced enhancement of bone formation in experimental *in vivo* models [7]. At the same time, recombinant PDGF-BB, which is approved for clinical use in regenerative dentistry, improves both hard and soft tissue healing and stimulates the activity of mesenchymal stem cells (MSCs) [1]. Cell-based therapy is another perspective option: autologous mesenchymal stem cells derived from bone marrow, periodontal tissues, and pulp as well as other cell types can be loaded into a collagen scaffold to directly regenerate the damaged tissue, thus significantly accelerating and improving the quality of regeneration [8; 9].

Collagen-based materials serve as an effective platform for localized delivery of biological agents. They are capable of providing sustained release of adsorbed or integrated growth factors locally, thereby reducing systemic exposure and minimizing adverse effects [10; 11]. Similarly, the three-dimensional architecture of collagen scaffolds is optimal for the attachment and survival of transplanted cells, which maintains their functional activity for osteogenesis and angiogenesis [1; 12; 13].

This review analyzes current clinical applications of collagen matrices combined with living cells and growth factors. In evaluating clinical cases, we emphasize not only the strengths of these therapeutic strategies but also their potential limitations and controversial aspects. We hope that this review will serve as a starting point for dental practitioners, encouraging the integration of contemporary tissue engineering approaches into everyday clinical practice.

CELL-BASED APPROACH

Mesenchymal and Periodontal Cells

Clinical studies demonstrate that the addition of mesenchymal stem cells to collagen matrices enhances periodontal regeneration. In the randomized trial NCT02449005, a biocomplex composed of autologous bone marrow–derived MSCs, platelet lysate, and collagen implant (Parasorb® fleece) was evaluated for the treatment of intrabony periodontal defects in comparison with control groups without cell component. At 12 months, the cell-containing group showed the most pronounced improvement: probing pocket depth decreased from 6.7 ± 1.6 mm to 3.2 ± 1.1 mm, while clinical attachment level improved from 7.3 ± 1.5 mm to 4.6 ± 1.6 mm. Biochemical data showed a >2.5-fold increase in BMP-7 and approximately a 60% reduction in TNF-α at 6–9 months, indicating anti-inflammatory and osteogenic effects of the collagen matrix with cells [14].

Another example is the trial where cultured gingival fibroblasts and associated gingival MSCs (NCT03638154) were applied. A collagen membrane with β-TCP granules (Collagene AT®) seeded with autologous cells produced superior results at 6 months: probing depth decreased from 6.8 ± 1.2 mm to 3.5 ± 0.8 mm, while the attachment gain reached 3.3 ± 0.9 mm compared with 2.1 ± 0.8 mm in the cell-free control [15]. Radiographically, new bone height averaged 3.1 ± 0.7 mm, versus 1.8 ± 0.6 mm in the cell-free group. During the first postoperative weeks, the cell group also demonstrated a 1.8–2.3-fold increase in PDGF-BB concentration in gingival crevicular fluid, indicating enhanced angiogenesis and cell proliferation induced by the cell-loaded collagen scaffold.

It is noteworthy that not all studies have achieved statistically significant superiority for cell-based methods. For example, in a clinical investigation [16] where autologous periodontal ligament cell sheets were applied (30 patients), their combination with a bone substitute

(Bio-Oss®) and a collagen membrane (Bio-Gide®) was safe and biocompatible, but it resulted in only slightly greater bone fill compared with the cell-free control, with no statistical significance. The authors emphasize the need for larger-scale clinical trials to verify the advantages of this approach.

In maxillofacial surgery, collagen-MSC constructs have proven to be a viable alternative to autogenous grafts, offering substantially reduced surgical morbidity. For example, in the randomized controlled trial NCT03563495, a scaffold composed of collagen and hydroxyapatite (Osteovit®) seeded with osteogenically differentiated autologous MSCs was compared with augmentation using iliac crest autografts [17]. After 12 months, the volume of newly formed bone in the test group reached 87% ± 5.2, which was comparable to the autograft group (89% ± 6.1). Additionally, bone density in the MSC group increased from approximately 560 to 820 HU between 6 and 12 months, whereas in the autograft group it remained stable at approximately 780 HU.

In the trial NCT04545307, allogeneic bone marrow MSCs seeded onto an atelocollagen matrix were used for revitalization of necrotic pulp in immature teeth [18]. After 12 months, all treated cases demonstrated formation of tissue resembling healthy pulp, healing of periapical lesions, restoration of tooth sensitivity, and partial root apex closure. These findings indicate that collagen-based matrices combined with stem cells are capable of initiating regeneration of both periodontal structures and the pulp-dentin complex.

Allogeneic somatic cells

Collagen matrices combined with allogeneic epithelial and connective tissue–derived cells represent a promising approach for restoring keratinized mucosa without the need for autograft harvesting. In the study of the living cell construct (LCC, CelTx™) [NCT01134081], which contained allogeneic fibroblasts and keratinocytes on a collagen scaffold, a marked increase in VEGF, IL-8, FGF-2, and PDGF-BB levels was observed as early as day 7 postoperatively, indicating active secretion of regenerative factors. Clinically, the gain in keratinized gingival width was comparable to that achieved with conventional autografts, while patients in the LCC group reported lower pain levels and no complications associated with donor site tissue harvesting [19].

Similar results were reported in study NCT00587834 applying the same LLC construct (Gintuit™). At 6 months, the thickness of the newly formed keratinized mucosa reached at least 2 mm, with color and texture indistinguishable from the surrounding intact tissue. Patients also preferred this method over traditional free gingival grafts, likely due to its significantly lower invasiveness [20].

Dental Pulp Cells

Stem cells derived from dental pulp show promise for regenerating both periodontal and jawbone structures. In the study NCT03386877, microfragments of autologous pulp containing dental pulp stem cells (DPSCs, Condress®) were applied onto a collagen sponge and placed into periodontal defects ⩾6 mm deep [21]. The DPSC-loaded scaffold demonstrated superior clinical and radiographic outcomes at 12 months compared with a cell-free collagen sponge, including greater pocket depth reduction (≈4.9 vs 3.4 mm), higher clinical attachment gain (≈4.5 vs 2.9 mm), and increased radiographic defect fill (≈3.9 vs ≈1.6 mm). In addition, a substantially higher proportion of patients in the DPSC group achieved a residual pocket depth <5 mm (≈70% vs ≈29%).

Similarly, in a clinical trial addressing alveolar cleft defects in children (NCT01932164), a collagen-hydroxyapatite matrix (Bio-Oss Collagen®) seeded with pulp stem cells from deciduous teeth achieved 75.6% ± 4.8 bone defect fill at 6 months, comparable to the autologous bone group (75.4% ± 4.0) and significantly higher than the rhBMP-2 growth factor group (59.6% ± 9.9) [22]. By 12 months, new bone volume reached 80.4% ± 5.3, continuing to increase due to mineralization. Clinically, the stem cell approach was less invasive: no complications were observed, whereas rhBMP-2 caused pronounced swelling in 37.5% of patients, while autografts induced donor site pain in 87.5%.

In regenerative endodontics, combining collagen with pulp cells enabled the restoration of viable pulp–dentin tissue. In study [23], autologous dental pulp stem cells were implanted into the root canal of an immature permanent tooth with pulp necrosis following endodontic treatment, using an atelocollagen-based scaffold. No significant adverse effects were observed over 24 weeks; by 4 weeks, 4 of 5 treated teeth responded positively to sensitivity testing, indicating pulp recovery. By 24 weeks, MRI demonstrated formation of intracanal tissue resembling normal pulp, and CBCT in 3 patients confirmed the development of functional secondary dentin.

GROWTH FACTORS-BASED APPROACH

Among different growth factors, PDGF, TGF-β, BMP-2, BMP-9, GDF-5, and FGF-2 (fibroblast growth factor-2) are of particular interest for clinical use [24–26]. PDGF stimulates the proliferation of progenitor cells, TGF-β regulates osteoblast differentiation, BMPs initiate osteoinduction, and FGF enhances vascularization of the defect. In preclinical models, membranes containing BMP-9 have demonstrated nearly complete closure of bone defects, while PDGF and GDF-5 promoted early angiogenesis and cell migration. Although experimental data strongly support their effectiveness, the number of clinical trials remains limited.

PDGF

In the triple-blind randomized controlled trial NCT04462237 involving 30 patients, the addition of recombinant PDGF-BB to a Fibro-Gide® collagen matrix under a coronally advanced flap for the treatment of gingival recessions improved clinical outcomes [27]. At 6 months, the test group achieved an average root coverage of 88.25% compared with 77.72% in the control group, with a concomitant increase in gingival thickness of 0.43 ± 0.09 mm from baseline. Patients reported faster healing, reduced discomfort, and improved esthe-

tics, and morphometric analysis confirmed increased soft tissue volume and stability of the outcome.

On the other hand, in studies evaluating post-extraction socket healing, the application of PDGF-BB on a collagen sponge showed only a trend toward increased new bone formation (~+2% versus control) without statistically significant differences [28]. However, pooled analysis confirmed a positive trend and the absence of adverse effects, indicating the safety and potential benefit of PDGF for accelerating osteogenesis in post-extraction defects. These findings are consistent with Jayakumar et al. [29], who investigated the effect of recombinant PDGF-BB on healing of premolar extraction sockets. In the test group, GEM 21S (a combination of PDGF-BB and β-TCP) was applied on a collagen sponge (CollaPlug®) and placed into the alveolar socket, while the control used a sponge without growth factors. After 8 weeks, histomorphometric analysis showed more active new bone formation in the PDGF-BB group (21.3% ± 5.2 versus 17.8% ± 3.8), though the difference was not statistically significant ($p = 0.09$).

Nevertheless, GEM21S proved effective in treating gingival recessions with a coronally advanced flap. In a clinical study, patients with gingival recessions were treated using the GEM21S complex covered with a Healiguide® collagen membrane [30]. At 6 months, root coverage in the test group reached 70.24%, compared with only 34.76% in the membrane-only group, along with greater improvements in clinical attachment and keratinized tissue width. Despite the lack of randomization, the study demonstrates enhanced soft tissue regeneration attributable to PDGF.

FGF-2

We did not identify any published results on the combined use of collagen matrices with FGF-2. In the study NCT04361630, the safety and preliminary efficacy of recombinant human FGF-2 (rhFGF-2) for the treatment of periodontal defects were evaluated. Patients underwent surgical preparation of the affected sites followed by application of rhFGF-2 on a collagen sponge placed into the defect area. The primary outcome measure was keratinized gingival width, with secondary assessments planned for probing pocket depth and clinical attachment level. The study was completed in December 2019; however, the results have not yet been published.

Nevertheless, the related study using FGF-2 incorporated into a cellulose-based hydrogel have shown promising outcomes. In a large Japanese trial involving 253 patients, application of 0.3% FGF-2 in hydroxypropylcellulose gel after surgical treatment of intrabony defects demonstrated a significant increase in bone fill compared with placebo (50.6 ± 31.5% vs. 15.1 ± 21.9%), with an average clinical attachment gain of approximately 2 mm [31]. Improvements persisted at 72 weeks, and no serious adverse events, including ankylosis or hyperostosis, were observed.

Results from another multicenter randomized clinical trial (NCT01728844) confirmed a dose-dependent effect of rhFGF-2 combined with β-tricalcium phosphate (β-TCP). At 6 months, linear bone growth was 3.7 mm in the 0.3% FGF-2 hydrogel group versus 3.1 mm in the control, with defect fill percentages of 75% versus 63%, and clinical attachment gains of +3.0–3.6 mm [32]. No adverse events or antibodies to rhFGF-2 were detected.

Collectively, these data confirm the safety and efficacy of local FGF-2 application as a stimulator of angiogenesis and periodontal tissue regeneration. Combining FGF-2 with a collagen carrier may be even more effective, as the collagen scaffold provides prolonged retention of the growth factor within the defect, gradual protein release, and an optimal microenvironment for periodontal cell migration and proliferation [13].

BMP-2

Bone morphogenetic protein-2 delivered via collagen matrices has been extensively studied for enhancing osteogenesis. In a randomized trial by Alonso et al. [33], children with alveolar clefts underwent defect reconstruction using Infuse® Bone Graft containing rhBMP-2 on a resorbable collagen sponge or autologous iliac bone grafting. At 12 months, complete defect closure and tooth eruption were observed; bone fill volume was 74.4% versus 80.2% ($p = 0.176$), and bone height was 65.0% versus 86.6% ($p = 0.001$) in the rhBMP-2 and autograft groups, respectively. Notably, 87.5% of patients in the autograft group reported donor site pain, whereas only transient swelling occurred in 37.5% of patients in the rhBMP-2 group.

Similar findings were reported by Canan et al. [34], where Infuse® Bone Graft was also used for alveolar cleft closure in children. At 6 and 12 months, cone-beam computed tomography revealed comparable new bone volume and bone attachment levels between the rhBMP-2 and autograft groups, with consistent bone bridge formation and tooth eruption and minimal inflammatory response. Collectively, these studies confirm that rhBMP-2 delivered on a collagen matrix promotes osteogenesis equivalent to autologous bone while substantially reducing donor site morbidity.

Collagen sponges with BMP-2 have also demonstrated effectiveness in preserving the alveolar ridge after tooth extraction. In a pilot RCT [35], extraction sockets were filled with a collagen sponge (Spon-Tiss®) containing rhBMP-2, compared with natural healing. At 12 weeks, vertical resorption of the buccal cortical plate was significantly reduced in the BMP-2 group (~1.8 mm less than control). Although alveolar width did not differ between groups, maintenance of buccal height has clinical relevance, reducing the need for subsequent augmentation prior to dental implantation.

In study NCT05719181, dental implant placement with rhBMP-2 on an absorbable collagen sponge was compared with conventional placement [36]. At 24 weeks, stability scores were higher in the rhBMP-2 group, particularly in the mandible (71.7 vs. 69.9), although the difference was not statistically significant.

In NCT01541345, the use of xenogeneic bone material Bio-Oss Granulat® with rhBMP-2 and coverage with a Bio-Gide® membrane was compared with autologous bone graft for ridge reconstruction [37]. At 4 months, alveolar ridge width was 5.35 mm in the rhBMP-2 group

and 5.15 mm in the autograft group, with no significant difference.

Thus, BMP-2 incorporated into collagen carriers can accelerate bone formation, enhance graft density, and improve early implant osseointegration without adverse effects such as ectopic bone growth or immune-mediated inflammation.

CONCLUSION

The combination of collagen matrices with biological agents, cells and growth factors, demonstrates considerable potential in regenerative dentistry and maxillofacial surgery. Clinical studies indicate that such systems enable faster and higher-quality regeneration of periodontal tissues, alveolar ridges, and dental pulp compared with unmodified collagen matrices.

The use of mesenchymal stem cells, dental pulp stem cells, and allogeneic epithelial cells on collagen scaffolds achieves osteo- and angioinductive effects comparable to autologous grafting, while reducing procedural invasiveness and associated risks. However, despite demonstrated safety, many clinical trials are limited by small sample sizes and short follow-up periods (6–12 months), highlighting the need for larger randomized studies with long-term outcome assessments.

We consider that future advances in tissue engineering for dentistry are expected to focus on the development of standardized bioactive systems with controlled molecule release and the ability to tailor cell components to specific defect types and patient needs, potentially leveraging 3D bioprinting technologies.

REFERENCES / СПИСОК ЛИТЕРАТУРЫ

1. Takayama T., Imamura K., Yamano S. Growth factor delivery using a collagen membrane for bone tissue regeneration. *Biomolecules*. 2023;13(5):809. https://doi.org/10.3390/biom13050809
2. Kumada Y., Zhang S. Significant type I and type III collagen production from human periodontal ligament fibroblasts in 3D peptide scaffolds without extra growth factors. *PLoS ONE*. 2010;5(4):e10305. https://doi.org/10.1371/journal.pone.0010305
3. Feng Y., Li H.P. Optimizing collagen-based biomaterials for periodontal regeneration: clinical opportunities and challenges. *Front Bioeng Biotechnol*. 2024;12:1469733. https://doi.org/10.3389/fbioe.2024.1469733
4. Baek S.-H., Yang B.-E., Park S.-Y., On S.-W., Ahn K.-M., Byun S.-H. Efficacy of cross-linked collagen membranes for bone regeneration: In vitro and clinical studies. *Bioengineering*. 2025;12(8):876. https://doi.org/10.3390/bioengineering12080876
5. Woo H.N., Cho Y.J., Tarafder S., Lee C.H. The recent advances in scaffolds for integrated periodontal regeneration. *Bioact Mater*. 2021;6(10):3328–3342. https://doi.org/10.1016/j.bioactmat.2021.03.012
6. McKay W.F., Peckham S.M., Badura J.M. A comprehensive clinical review of recombinant human bone morphogenetic protein-2 (INFUSE Bone Graft). *Int Orthop*. 2007;31(6):729–734. https://doi.org/10.1007/s00264-007-0418-6
7. Yamano S., Haku K., Yamanaka T., Dai J., Takayama T., Shohara R. et al. The effect of a bioactive collagen membrane releasing PDGF or GDF-5 on bone regeneration. *Biomaterials*. 2014;35(8):2446–2453. https://doi.org/10.1016/j.biomaterials.2013.12.006
8. Theodosaki A.M., Tzemi M., Galanis N., Bakopoulou A., Kotsiomiti E., Aggelidou E., Kritis A. Bone regeneration with mesenchymal stem cells in scaffolds: systematic review of human clinical trials. *Stem Cell Rev Rep*. 2024;20(4):938–966. https://doi.org/10.1007/s12015-024-10696-5
9. Chang Y.T., Lai C.C., Lin D.J. Collagen scaffolds laden with human periodontal ligament fibroblasts promote periodontal regeneration in SD rat model. *Polymers*. 2023;15(12):2649. https://doi.org/10.3390/polym15122649
10. Bai Y., Yin G., Huang Z., Liao X., Chen X., Yao Y., Pu X. Localized delivery of growth factors for angiogenesis and bone formation in tissue engineering. *Int Immunopharmacol*. 2013;16(2):214–223. https://doi.org/10.1016/j.intimp.2013.04.001
11. Wang X., Zeng J., Gan D., Ling K., He M., Li J., Lu Y. Recent strategies and advances in hydrogel-based delivery platforms for bone regeneration. *Nanomicro Lett*. 2024;17(1):73. https://doi.org/10.1007/s40820-024-01557-4
12. Tkachev S., Chepelova N., Galechyan G., Ershov B., Golub D., Popova E. et al. Three-dimensional cell culture micro-CT visualization within collagen scaffolds in an aqueous environment. *Cells*. 2024;13(15):1234. https://doi.org/10.3390/cells13151234
13. Edelmayer M., Wehner C., Ulm C., Zechner W., Shafer D., Agis H. Which substances loaded onto collagen scaffolds influence oral tissue regeneration? – An overview of the last 15 years. *Clin Oral Investig*. 2020;24(10):3363–3394. https://doi.org/10.1007/s00784-020-03520-0
14. Apatzidou D.A., Iliopoulos J.M., Konstantinidis A., Verma M., Hardy P., Lappin D.F., Nile C.J. Inflammatory and bone remodelling related biomarkers following periodontal transplantation of the tissue engineered biocomplex. *Clin Oral Investig*. 2024;28(7):361. https://doi.org/10.1007/s00784-024-05754-8
15. Abdal-Wahab M., Abdel Ghaffar K.A., Ezzatt O.M., Hassan A.A.A., El Ansary M.M.S., Gamal A.Y. Regenerative potential of cultured gingival fibroblasts in treatment of periodontal intrabony defects (randomized clinical and biochemical trial). *J Periodontal Res.* 2020;55(3):441–452. https://doi.org/10.1111/jre.12728
16. Chen F.M., Gao L.N., Tian B.M., Zhang X.Y., Zhang Y.J., Dong G.Y., Lu H. et al. Treatment of periodontal intrabony defects using autologous periodontal ligament stem cells: a randomized clinical trial. *Stem Cell Res Ther*. 2016;7(1):33. https://doi.org/10.1186/s13287-016-0288-1 (Erratum in: *Stem Cell Res Ther.* 2018;9(1):260. https://doi.org/10.1186/s13287-018-1000-4)
17. Kadry W., Eldeftar M., Nassar Y., Abou-El-Fetouh A., Hakam M.M. Clinical, volumetric and densitometric evaluation of tissue engineered constructs for secondary alveolar cleft reconstruction: A randomized clinical trial. *J Craniomaxillofac Surg*. 2021;49(12):1141–1150. https://doi.org/10.1016/j.jcms.2021.09.003
18. Gomez-Sosa J.F., Cardier J.E., Wittig O., Díaz-Solano D., Lara E., Duque K., Ramos-González G. Allogeneic bone

marrow mesenchymal stromal cell transplantation induces dentin pulp complex-like formation in immature teeth with pulp necrosis and apical periodontitis. *J Endod*. 2024;50(4):483–492. https://doi.org/10.1016/j.joen.2024.01.002

19. Morelli T., Neiva R., Nevins M.L., McGuire M.K., Scheyer E.T., Oh T.J. et al. Angiogenic biomarkers and healing of living cellular constructs. *J Dent Res*. 2011;90(4):456–462. https://doi.org/10.1177/0022034510389334
20. McGuire M.K., Scheyer E.T., Nevins M.L., Neiva R., Cochran D.L., Mellonig J.T. et al. Living cellular construct for increasing the width of keratinized gingiva: results from a randomized, within-patient, controlled trial. *J Periodontol*. 2011;82(10):1414–1423. https://doi.org/10.1902/jop.2011.100671
21. Ferrarotti F., Romano F., Gamba M.N., Quirico A., Giraudi M., Audagna M., Aimetti M. Human intrabony defect regeneration with micrografts containing dental pulp stem cells: A randomized controlled clinical trial. *J Clin Periodontol*. 2018;45(7):841–850. https://doi.org/10.1111/jcpe.12931
22. Tanikawa D.Y.S., Pinheiro C.C.G., Almeida M.C.A., Oliveira C.R.G.C.M., Coudry R.A., Rocha D.L., Bueno D.F. Deciduous dental pulp stem cells for maxillary alveolar reconstruction in cleft lip and palate patients. *Stem Cells Int*. 2020;2020:6234167. https://doi.org/10.1155/2020/6234167
23. Nakashima M., Iohara K., Murakami M., Nakamura H., Sato Y., Ariji Y., Matsushita K. Pulp regeneration by transplantation of dental pulp stem cells in pulpitis: a pilot clinical study. *Stem Cell Res Ther*. 2017;8(1):61. https://doi.org/10.1186/s13287-017-0506-5
24. Sheikh Z., Qureshi J., Alshahrani A.M., Nassar H., Ikeda Y., Glogauer M., Ganss B. Collagen based barrier membranes for periodontal guided bone regeneration applications. *Odontology*. 2017;105(1):1–12. https://doi.org/10.1007/s10266-016-0267-0
25. Sammarco V.J., Chang L. Modern issues in bone graft substitutes and advances in bone tissue technology. *Foot Ankle Clin*. 2002;7(1):19–41. https://doi.org/10.1016/s1083-7515(01)00003-1
26. Bunyaratavej P., Wang H.L. Collagen membranes: a review. *J Periodontol.* 2001;72(2):215–229. https://doi.org/10.1902/jop.2001.72.2.215
27. Tavelli L., Barootchi S., Rodriguez M.V., Mancini L., Majzoub J., Travan S. et al. Recombinant human platelet-derived growth factor improves root coverage of a collagen matrix for multiple adjacent gingival recessions: A triple-blinded, randomized, placebo-controlled trial. *J Clin Periodontol*. 2022;49(11):1169–1184. https://doi.org/10.1111/jcpe.13706
28. Li F., Yu F., Liao X., Wu C., Wang Y., Li C. et al. Efficacy of recombinant human BMP2 and PDGF-BB in orofacial bone regeneration: A systematic review and meta-analysis. *Sci Rep*. 2019;9(1):8073. https://doi.org/10.1038/s41598-019-44368-z
29. Jayakumar A., Rajababu P., Rohini S., Butchibabu K., Naveen A., Reddy P.K. et al. Multi-centre, randomized clinical trial on the efficacy and safety of recombinant human platelet-derived growth factor with β-tricalcium phosphate in human intra-osseous periodontal defects. *J Clin Periodontol*. 2011;38(2):163–172. https://doi.org/10.1111/j.1600-051X.2010.01639.x
30. Singh P., Suresh D.K. Clinical evaluation of GEM 21S(®) and a collagen membrane with a coronally advanced flap as a root coverage procedure in the treatment of gingival recession defects: A comparative study. *J Indian Soc Periodontol*. 2012;16(4):577–583. https://doi.org/10.4103/0972-124X.106919
31. Kitamura M., Akamatsu M., Machigashira M., Hara Y., Sakagami R., Hirofuji T. et al. FGF-2 stimulates periodontal regeneration: results of a multi-center randomized clinical trial. *J Dent Res*. 2011;90(1):35–40. https://doi.org/10.1177/0022034510384616
32. Cochran D.L., Oh T.J., Mills M.P., Clem D.S., McClain P.K., Schallhorn R.A. et al. A randomized clinical trial evaluating rh-FGF-2/β-TCP in periodontal defects. *J Dent Res*. 2016;95(5):523–530. https://doi.org/10.1177/0022034516632497
33. Alonso N., Tanikawa D.Y., Freitas R.S., Canan L. Jr, Ozawa T.O., Rocha D.L. Evaluation of maxillary alveolar reconstruction using a resorbable collagen sponge with recombinant human bone morphogenetic protein-2 in cleft lip and palate patients. *Tissue Eng Part C Methods*. 2010;16(5):1183–1189. https://doi.org/10.1089/ten.TEC.2009.0824
34. Canan L.W. Jr, da Silva Freitas R., Alonso N., Tanikawa D.Y., Rocha D.L., Coelho J.C. Human bone morphogenetic protein-2 use for maxillary reconstruction in cleft lip and palate patients. *J Craniofac Surg*. 2012;23(6):1627–1633. https://doi.org/10.1097/SCS.0b013e31825c75ba
35. Thammanichanon P., Ouyyamwongs W., Mai-Ngam K., Rittipakorn P. Clinical outcomes of rhBMP-2-loaded collagen sponge for alveolar ridge preservation: A pilot study. *Eur J Dent*. 2025. https://doi.org/10.1055/s-0045-1810610
36. Abbas A.A., Salman S.A., Wahid M.H.A. Recombinant human bone morphogenetic protein-2 as bone additive and its relation with the dental implant dimensions and stability: Split-mouth randomized clinical trial. *Al-Rafidain Journal of Medical Sciences*. 2023;5:263–268. https://doi.org/10.54133/ajms.v5i.294
37. Thoma D.S., Bienz S.P., Payer M., Hüsler J., Schmidlin P.R., Hämmerle C.H.F. et al. Randomized clinical study using xenograft blocks loaded with bone morphogenetic protein-2 or autogenous bone blocks for ridge augmentation – A three-dimensional analysis. *Clin Oral Implants Res*. 2019;30(9):872–881. https://doi.org/10.1111/clr.13492

INFORMATION ABOUT THE AUTHORS

Sergei Yu. Voloshin – Laboratory Assistant, Center for Innovative Collagen Developments, Institute of Regenerative Medicine, Biomedical Science and Technology Park, Sechenov First Moscow State Medical University (Sechenov University), 8c2 Trubetskaya Str., Moscow 119048, Russian Federation; https://orcid.org/0009-0005-1695-2238

Khadizhat A. Gadzhieva – Postgraduate Student, Department of Oral and Maxillofacial Surgery E.V. Borovsky Institute of Dentistry, Sechenov First Moscow State Medical University (Sechenov University), 8c2 Trubetskaya Str., Moscow 119048, Russian Federation; https://orcid.org/0009-0008-4716-4973

Kamila R. Zhalilova – Student, N.V. Sklifosovsky Institute of Clinical Medicine, Sechenov First Moscow State Medical University (Sechenov University), 8c2 Trubetskaya Str., Moscow 119048, Russian Federation; https://orcid.org/0009-0005-5877-1742

Igor P. Ashurko – Dr. Sci. (Med.), Professor, Department of Oral and Maxillofacial Surgery E.V. Borovsky Institute of Dentistry, Sechenov First Moscow State Medical University (Sechenov University), 8c2 Trubetskaya Str., Moscow 119048, Russian Federation; https://orcid.org/0000-0001-9862-2657

Petr S. Timashev – Dr. Sci. (Chem.), Professor, Scientific Director of the Biomedical Science and Technology Park, I.M. Sechenov First Moscow State Medical University (Sechenov University), 8c2 Trubetskaya Str., Moscow 119048, Russian Federation; https://orcid.org/0000-0001-7773-2435

Artem A. Antoshin – Cand. Sci. (Biol.), Head of the Center for Innovative Collagen Developments, Institute of Regenerative Medicine, Biomedical Science and Technology Park, Sechenov First Moscow State Medical University (Sechenov University), 8c2 Trubetskaya Str., Moscow 119048, Russian Federation; https://orcid.org/0000-0003-0575-0321

ИНФОРМАЦИЯ ОБ АВТОРАХ

Волошин Сергей Юрьевич – лаборант Центра инновационных коллагеновых разработок Института регенеративной медицины Научно-технологического парка биомедицины, ФГАОУ ВО Первый МГМУ им. И.М. Сеченова Минздрава России (Сеченовский Университет), 119048, Российская Федерация, г. Москва, Трубецкая ул., д. 8 стр. 2; https://orcid.org/0009-0005-1695-2238

Гаджиева Хадижат Абдулхакимовна – аспирант кафедры хирургической стоматологии Института стоматологии им. Е.В. Боровского, ФГАОУ ВО Первый МГМУ им. И.М. Сеченова Минздрава России (Сеченовский Университет), 119048, Российская Федерация, г. Москва, Трубецкая ул., д. 8 стр. 2; https://orcid.org/0009-0008-4716-4973

Жалилова Камила Рустамовна – студент Института клинической медицины им. Н.В. Склифосовкого, ФГАОУ ВО Первый МГМУ им. И.М. Сеченова Минздрава России (Сеченовский Университет), 119048, Российская Федерация, г. Москва, Трубецкая ул., д. 8 стр. 2; https://orcid.org/0009-0005-5877-1742

Ашурко Игорь Павлович – д.м.н., профессор кафедры хирургической стоматологии Института стоматологии им. Е.В. Боровского, ФГАОУ ВО Первый МГМУ им. И.М. Сеченова Минздрава России (Сеченовский Университет), 119048, Российская Федерация, г. Москва, Трубецкая ул., д. 8 стр. 2; https://orcid.org/0000-0001-9862-2657

Тимашев Петр Сергеевич – д.х.н., профессор, научный руководитель Научно-технологического парка биомедицины, ФГАОУ ВО Первый МГМУ им. И.М. Сеченова Минздрава России (Сеченовский Университет), 119048, Российская Федерация, г. Москва, Трубецкая ул., д. 8 стр. 2; https://orcid.org/0000-0001-7773-2435

Антошин Артем Анатольевич – к.б.н., руководитель Центра инновационных коллагеновых разработок Института регенеративной медицины Научно-технологического парка биомедицины, ФГАОУ ВО Первый МГМУ им. И.М. Сеченова Минздрава России (Сеченовский Университет), 119048, Российская Федерация, г. Москва, Трубецкая ул., д. 8 стр. 2; https://orcid.org/0000-0003-0575-0321

AUTHOR'S CONTRIBUTION

All the authors made equal contributions to the publication preparation in terms of the idea and design of the article; data collection; critical revision of the article in terms of significant intellectual content and final approval of the version of the article for publication.

ВКЛАД АВТОРОВ

Все авторы внесли равноценный вклад в подготовку публикации в части замысла и дизайна исследования; сбора данных; критического пересмотра статьи в части значимого интеллектуального содержания и окончательного одобрения варианта статьи для опубликования.