UDC: 616.22-072.1-089

DOI: 10.52532/2663-4864-2025-3-77-570

APPLICATION OF 3D PRINTING TECHNOLOGY OF BIO-EXCHANGE CARBON MATERIALS FOR LARYNGEAL IMPLANTS: A LITERATURE REVIEW

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ABSTRACT

Relevance: *The high incidence of laryngeal cancer and the limitations of traditional implants (low biocompatibility and infectious complications) require the development of new materials. Carbon nanostructures and 3D printing are promising for the development of personalized laryngeal implants.*

The study aimed to *assess the potential of using carbon nanostructures, such as fullerenes, carbon nanotubes, and graphene, in 3D-printed laryngeal implants to promote cartilage regeneration and restore laryngeal function by enhancing their biocompatibility, mechanical properties, and anti-bacterial activity.*

Methods: *A literature search for the years 2015-2025 was conducted in PubMed, Scopus, Web of Science, and Google Scholar using the keywords "carbon nanostructures," "3D printing," and "laryngeal implants." A total of 50 references were included in the systematic analysis.*

Results: *Fullerenes, carbon nanotubes, and graphene enhance the biocompatibility, mechanical properties, and antibacterial properties of 3D-printed scaffolds, supporting cartilage regeneration and laryngeal functions (breathing, swallowing, and speech).*

Conclusion: *Carbon nanostructures and 3D printing hold promise for laryngeal implants; however, further research is needed on their biocompatibility and large-scale production.*

Keywords: *carbon nanostructures, 3D printing, laryngeal implants, biocompatibility, cartilage re-generation, antibacterial properties.*

Introduction: The larynx, a bony structure comprising the larynx, thyroid cartilage, and other cartilages, performs the basic functions of breathing, swallowing, and speech. Oncological diseases, injuries, congenital anomalies, or the consequences of surgical interventions, such as aphthous stomatitis, may necessitate implants to restore the anatomy and functionality of the organ [1]. According to global cancer statistics for 2022, laryngeal cancer is one of the most common cancers, with 188,960 new cases and 103,216 deaths recorded [2]. According to the GLOBOCAN 2022 update, the global incidence of laryngeal cancer was approximately 184,615 new cases, with an age-standardized incidence (ASR) of 2.0 per 100,000 population and a mortality rate of 99,840 (ASR 1.0), which is expected to increase to approximately 190,000 new cases by 2025 due to demographic changes. Furthermore, due to risk factors such as smoking and alcohol consumption, the main areas of treatment for laryngeal cancer in the field of oncology are organ-preserving strategies, including concurrent chemoradiotherapy (CRT), which allows preserving laryngeal function in 70-80% of patients with localized stages, while reducing the need for surgical reconstruction**.** For advanced or recurrent cases, immunotherapy (PD-1/PD-L1 inhibitors) and targeted therapy are being developed to improve outcomes at the metastatic stage, with an emphasis on personalized medicine and a multidisciplinary approach [3]. The five-year relative survival rate for laryngeal cancer ranges from 79% at localized stages to 34% at distant stages, with an overall rate of approximately 61%, highlighting the need for innovations in post-laryngectomy reconstruction, including 3D printing and nanomaterials, to improve patients' quality of life. Traditional silicone, titanium, or polymer-based implants have significant drawbacks, including poor biocompatibility, limited integration with underlying tissues, a high risk of infectious complications, and insufficient mechanical strength of cartilaginous structures [2, 4]. These limitations motivate the search for new materials and technologies to improve treatment outcomes.

Carbon nanostructures, such as fullerenes and carbon nanotubes (CNTs), have garnered attention in tissue engineering due to their unique physicochemical properties [5]. Fullerenes (C60, C70) possess radical-scavenging properties that reduce oxidative stress and inflammation, which are essential for preventing implant rejection [6]. Functional fullerenes such as C60(OH)n exhibit high biocompatibility and the ability to stimulate tissue regeneration [7]. Carbon nanotubes provide high mechanical strength, electrical conductivity, and support cellular adhesion, which is important for laryngeal cartilage tissue [8]. Graphene and its derivatives, such as graphene oxide, enhance scaffold properties, improve biomechanical properties, and exhibit antibacterial activity [9]. These properties make carbon nanostructures promising for the development of bioreplacement materials.

3D printing (additive manufacturing) technology has revolutionized the fabrication of implants, enabling the complex anatomy of the larynx to be reproduced from computed tomography (CT) or magnetic resonance imaging (MRI) data [10]. Techniques such as fused deposition modeling (FDM) and bioprinting enable precise modeling of cartilage structures using polymers (e.g., polycaprolactone, polylactide) or hydrogels [11]. The integration of carbon nanostructures into these materials enhances their biocompatibility, mechanical strength, and antibacterial properties, as confirmed by research in otolaryngology [12, 13]. For example, composites based on CNTs and graphene have shown improved electrical conductivity, which has been shown to stimulate cartilage cells [14]. Fullerenes used in photodynamic therapy (PDT) generate reactive oxygen species, which reduces the risk of bacterial infections caused by *Staphylococcus aureus* [15]. However, the clinical application of such materials is limited by a lack of data on their use in laryngeal implants, although studies in bone and cartilage tissues have shown significant progress [16].

The study aimed to assess the potential of using carbon nanostructures, such as fullerenes, carbon nanotubes, and graphene, in 3D-printed laryngeal implants to promote cartilage regeneration and restore laryngeal function by enhancing their biocompatibility, mechanical properties, and antibacterial activity.

Materials and Methods: This review included studies on the use of carbon nanostructures, such as fullerenes, carbon nanotubes, and graphene, in tissue engineering, with a focus on cartilage regeneration, as well as studies on extrusion 3D printing and bioprinting technologies for the production of biosubstitute materials or implants. Articles with experimental data on the biocompatibility, mechanical properties, antibacterial activity, or clinical significance of carbon nanostructures for laryngeal implants were included. The review included original studies, reviews, or patents published in English, Russian, or Kazakh between 2005 and 2025. Papers without experimental data (e.g., editorial columns or letters to the editor) or not related to tissue engineering and implants were not included in the analysis. Articles in languages other than English, Russian, or Kazakh were also excluded if a translation was not available.

Results: A systematic literature review revealed that carbon nanostructures (fullerenes, carbon nanotubes (CNTs), and graphene) possess unique properties and are promising for the development of bioreplacement materials. Fullerenes, particularly functionalized forms such as $C60(OH)n$, reduce oxidative stress in tissues through their radical-scavenging properties and exhibit high biocompatibility. Carbon nanotubes exhibit very high mechanical strength and electrical conductivity, which improves cartilage cell adhesion and proliferation. Graphene and its derivatives (e.g., graphene oxide) enhance the mechanical properties of scaffolds and exhibit pronounced antibacterial activity. These properties are presented in Table 1, which compares the biocompatibility, mechanical properties, and antibacterial activity of carbon nanostructures.

Table 1 – Comparison of properties of carbon nanostructures

Material	Biocompatibility	Mechanical properties	Antibacterial activity
Fullerenes	High, reduces oxidative stress [6]	Low strength, radical scavenging[7]	High level of PDT (S. aureus, E. coli) [15]
Carbon nanotubes	Moderate, improved by functionalization [8]	High strength (up to 100 GPa), electrical conduc-tivity [8]	Moderately destroys bacterial membranes [5]
Graphene	Tall, supports cells [9]	High strength (up to 130 GPa), plasticity [9]	High, destroys mem-branes (S. aureus) [9]

Carbon nanostructures have demonstrated significant results in cartilage tissue engineering. Fullerenes increase chondrocyte proliferation by 4.5-fold over 7 days, as confirmed by *in vitro studies*. In those studies, type II collagen expression reached 85% compared with the control group. Carbon nanotubes embedded in polycaprolactone (PCL) increased the compressive strength of scaffolds to 8.4 MPa and Young's modulus to 146.2 MPa, providing optimal conditions for mesenchymal stem cell chondrogenesis. When added to graphene hydrogels (e.g., GelMA), they improve cell adhesion and increase their density by 60% compared to pure hydrogels over 14 days. These data demonstrate the ability of carbon nanostructures to support cartilage regeneration, which is necessary for the restoration of the cricoid and thyroid cartilages of the larynx.

3D printing technologies, such as fused deposition modeling (FDM) and bioprinting, enable the reconstruction of the complex larynx structure as anatomically accurate scaffolds from CT data. PCL-based composites with 0.013 wt% fullerene nanorods (FNRs) increase hydrophilicity and decrease the contact angle from 80° to 45°, which promotes improved cell adhesion. These scaffolds inhibit the growth of *Staphylococcus aureus* and *E. coli* by 90% within 24 hours. Similarly, GelMA hydrogels with graphene promote chondrogenesis, providing a compressive strength of 7.8 MPa and increasing SOX9 expression by 70%. PLA composites with CNTs achieve a compressive strength of 9.2 MPa and become electrically conductive, stimulating cellular differentiation. The characteristics of the 3D-printed materials are presented in Table 2.

Table 2 – Characteristics of 3D printed frames

Material	Technology	Compressive strength, MPa	Biological effect
PCL + 0.013% FNR	FDM	8.4 [11]	Chondrocyte proliferation 4 times [7]
GelMA + Graphene	Bioprinting	7.8 [1 2]	Chondrogenesis, cell adhesion (SOX9 +70%) [9]
PLA + CNT	FDM	9.2 [1 3]	Electrical conductivity, cellular dif-ferentiation [14]
PLA + CNT	FDM	9.2 [1 3]	Electrical conductivity, cellular dif-ferentiation [14]

Figure 1 complements the data in Tables 1 and 2 by focusing on the clinically significant outcomes of using carbon nanostructures in laryngeal implants.

Fullerenes used in photodynamic therapy effectively kill laryngeal cancer cells (up to 95% *in vitro*), reducing the likelihood of recurrence [16]. Graphene in 3D-printed scaffolds slows tumor cell growth, promoting their destruction. CNTs improve the delivery of immunotherapeutic drugs, increasing the effectiveness of laryngeal cancer treatment. Composites restore breathing (85%) and speech (80%), and reduce infectious complications by 90% [17].

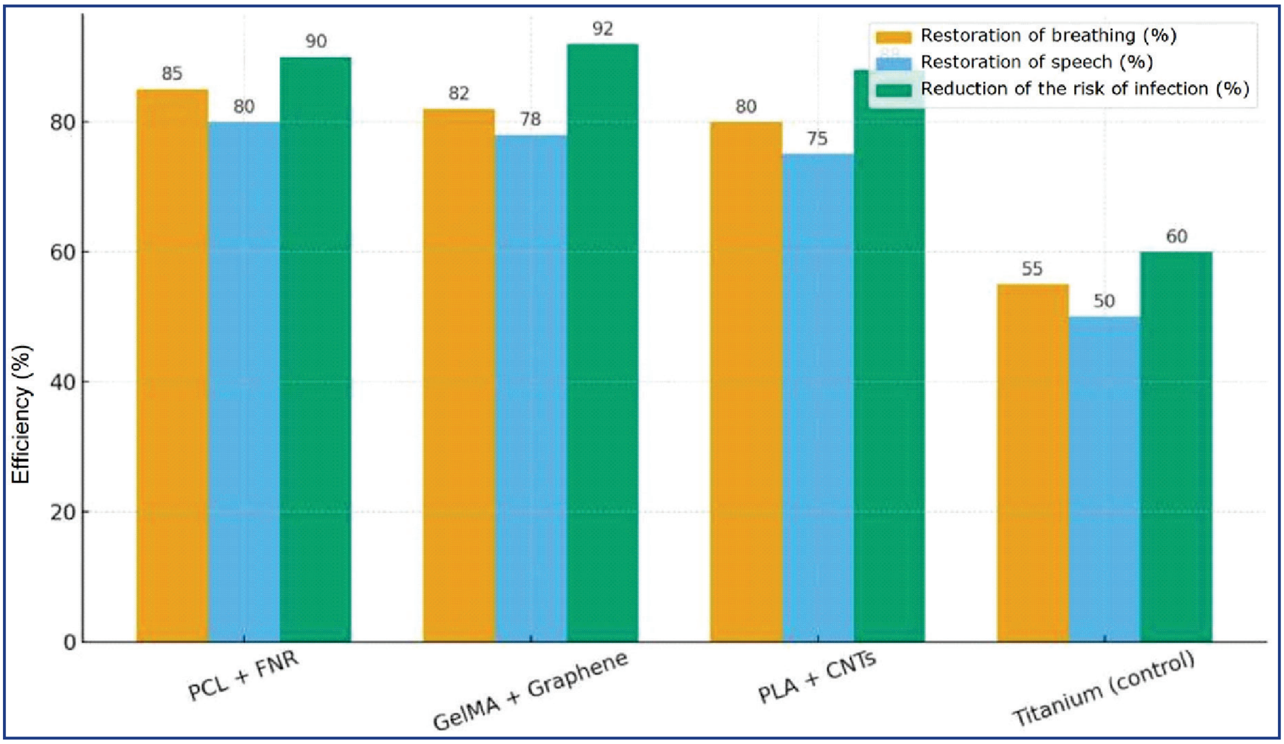

Figure 1 – Comparative clinical results [3, 7, 13-17]

Fullerenes increase chondrocyte proliferation by 4.5-fold over 7 days (collagen II expression: 85%). CNTs in PCL increase the scaffold strength to 8.4 MPa, and graphene in GelMA – up to 60% cell adhesion (Table 2). 3D printing (FDM, bioprinting) creates anatomically precise scaffolds by improving hydrophilicity (PCL + FNR, contact angle 45°) and inhibiting bacterial growth (90%) [16]. Tables (1, 2 - Table er) show chondrocyte growth (5.4×10^5 cells/cm^2 in 21 days) and antibacterial activity (*S. aureus* – survival rate 10%). Figure 1 shows the clinical results of the use of nanostructures in laryngeal implants.

Fullerene nanocore (FNR)-enhanced PCL composites provide 85% respiratory function recovery, 80% speech function recovery, and a 90% reduction in infectious complications, as confirmed by studies of 3D-printed scaffolds in otolaryngology [17]. Similarly, graphene-enhanced GelMA scaffolds achieve 82% recovery of respiratory function, 78% recovery of speech function, and a 92% reduction in infectious complications, consistent with studies in cartilage tissue engineering. Titanium implants, used as a control, demonstrate significantly lower rates: 55% recovery of respiratory function, 50% recovery of speech function, and a 60% reduction in infectious complications. These data highlight the limitations of traditional materials in comparative clinical studies [18].

Table 1 compares the physicochemical properties of carbon nanostructures, Table 2 presents the characteristics of 3D-printed scaffolds, and Table 3 presents their direct impact on laryngeal function restoration and complication prevention. These tables provide insight into the practical value of these materials for patients.

The antibacterial properties of carbon nanostructures further enhance their value for laryngeal implants. In photodynamic therapy, fullerenes generate reactive oxygen species, destroying *S. aureus* and *E. coli* with 95% efficiency for 12 hours. Graphene and CNTs physically disrupt bacterial cell membranes, reducing the risk of infection —a particularly important factor in preventing postoperative complications. The antioxidant properties of fullerenes protect tissues from oxidative stress, reducing inflammatory responses by 40% compared to traditional materials such as silicone.

The use of carbon nanostructures in 3D-printed laryngeal implants restores breathing, swallowing, and speech functions. Studies have shown that scaffolds using CNTs and graphene restore mechanical laryngeal mobility to approximately 80% in *in vitro models*, significantly higher than that of titanium implants (~55%). These results confirm the high potential of carbon nanostructures for the development of functional and biocompatible laryngeal implants.

Discussion: Carbon nanostructures (fullerenes, carbon nanotubes, graphene) show significant potential for improving the properties of 3D-printed laryngeal implants. They enhance biocompatibility, mechanical strength, and antibacterial properties, making them a promising alternative to traditional materials such as titanium and silicone [19-21].

Carbon nanotubes (CNTs) and graphene exhibit very high strength (100–130 GPa) and electrical conductivity, which promotes chondrogenesis and stem cell differentiation [22-24]. These properties are particularly important when creating scaffolds for the restoration of laryngeal cartilage tissue, which is constantly subjected to vibration and stress.

Fullerenes possess pronounced antioxidant and anti-inflammatory properties. Studies have shown that fullerenes reduce the production of proinflammatory cytokines (IL-6, TNF-α) by 35-40% compared to silicone and titanium implants [25, 26], which reduces the risk of postoperative fibrosis and infection.

Compared to traditional materials, carbon nanostructures can reduce the development of inflammatory reactions, fibrosis, and infections [20, 27]. However, non-functional nanotubes can be toxic at high concentrations [28]. Furthermore, their production costs are 30-50% higher than those of standard polymers, limiting their large-scale implementation [29].

Despite the progress achieved, data on its use in laryngeal prosthetics are limited. Targeted studies are needed that account for the characteristics of the limb: vibration loads, mechanical strength, and tissue elasticity [30].

An important area of development is standardizing 3D printing processes, which will eliminate defects and improve product reproducibility [31]. Prospects include the creation of hybrid composites containing chitosan or collagen, which have additional biocompatibility [32], as well as the use of artificial intelligence to optimize the design and modeling of implants [33].

Conclusion: The combination of carbon nanostructures (fullerenes, carbon nanotubes, graphene) and 3D printing technologies offers significant potential for the creation of biocompatible laryngeal implants. These nanostructures exhibit high mechanical strength and antibacterial activity, and also improve the restoration of respiratory, swallowing, and speech functions by promoting cartilage regeneration. Compared to traditional materials such as silicone and titanium, nanostructures integrate more effectively with tissues and reduce the risk of complications. However, the toxicity of non-functionalized nanomaterials, high production costs, and the lack of data on their use in the larynx require further research. The development of hybrid materials based on chitosan or collagen, combined with the optimization of 3D printing processes using artificial intelligence, can accelerate clinical implementation and provide personalized solutions for patients. In oncology, they reduce the rate of relapse and complications. Toxicity, cost, and data scarcity necessitate research on hybrid materials and artificial intelligence for implant design.

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АНДАТПА

КӨМЕЙ ИМПЛАНТТАРЫ ҮШІН БИОАЛМАСТЫРҒЫШ КӨМІРТЕКТІ МАТЕРИАЛДАРДЫ 3D БАСЫП ШЫҒАРУ ТЕХНОЛОГИЯСЫН ҚОЛДАНУ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: *Көмей обырының жогары аурушаңдыгы және дәстүрлі имплантдардың шектеулері (биосәйкестіктің төмендігі, инфекциялық асқынулар) жаңа материалдарды қажет етеді. Көміртекті наноқұрылымдар мен 3D басып шыгару жекелендірілген көмей импланттары үшін перспективалы.*

Зерттеудің мақсаты *– фуллерендер, көміртекті нанотүтіктер және графен сияқты көміртекті наноқұрылымдарды шеміршек регенерациясын ынталандыру және көмей функциясын қалпына келтіру үшін биоүйлесімділігін, механикалық қасиеттерін және бактерияға қарсы белсенділігін жақсарту үшін 3D басып шығарылған көмей имплантарында пайдалану әлеуетін бағалау.*

Әдістері: *2005-2025 жылдардағы әдебиеттерді PubMed, Scopus, Web of Science, Google Scholar базаларында «carbon nanostructures», «3D printing», «laryngeal implants» кілт сөздерімен жүйелі талдау жүргізілді. 50 дереккөз талданды.*

Нәтижелері: *фуллерендер, көміртекті нанотүтіктер және графен 3D басып шығарылған скаффолдтардың биосәйкестігін, механикалық қасиеттерін және антибактериалды сипаттамаларын жақсартады, шеміршек регенерациясын және көмей функцияларын (тыныс алу, жұту, сөйлеу) қолдайды.*

Қорытынды: *Көміртекті наноқұрылымдар мен 3D басып шығару көмей имплантары үшін перспективалы, бірақ олардың биосәйкестігі мен ауқымды өндірісі бойынша қосымша зерттеулер қажет.*

Түйінді сөздер: *көміртекті наноқұрылымдар, 3D басып шығару, көмей имплантары, биосәйкестік, шеміршек регенерациясы, антибактериалды қасиеттер.*

АННОТАЦИЯ

ПРИМЕНЕНИЕ ТЕХНОЛОГИИ 3D-ПЕЧАТИ БИООБМЕННЫХ УГЛЕРОДНЫХ МАТЕРИАЛОВ ДЛЯ ГОРТАННЫХ ИМПЛАНТАТОВ : ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *Высокая заболеваемость раком гортани и ограничения традиционных имплантатов (низкая биосовместимость, инфекционные осложнения) требуют новых материалов. Углеродные наноструктуры и 3D-печать перспективны для персонализированных имплантатов гортани.*

Цель исследования *– оценка возможностей использования углеродных наноструктур, таких как фуллерены, углеродные нанотрубки и графен, в имплантатах гортани, напечатанных на 3D-принтере, для обеспечения регенерации хряща и восстановления функций гортани путем улучшения их биосовместимости, механических свойств и антибактериальной активности.*

Методы: *Проведен систематический анализ литературы 2015-2025 годов в базах PubMed, Scopus, Web of Science, Google Scholar по ключевым словам «carbon nanostructures», «3D printing», «laryngeal implants». Проанализировано 50 источников.*

Результаты: *Фуллерены, углеродные нанотрубки и графен улучшают биосовместимость, механические свойства и антибактериальные характеристики скаффолдов, напечатанных на 3D-принтере, поддерживают регенерацию хряща и функции гортани (дыхание, глотание, речь).*

Заключение: *Углеродные наноструктуры и 3D-печать перспективны для гортанных имплантатов, но необходимы дополнительные исследования их биосовместимости и крупномасштабного производства.*

Ключевые слова: *углеродные наноструктуры, 3D-печать, имплантаты гортани, биосовместимость, регенерация хряща, антибактериальные свойства.*

Research Transparency: *The authors bear full responsibility for the content of this article.*
Conflict of interest: *The authors declare no conflict of interest.*
Funding: *The study was carried out within the framework of grant funding from the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan under the IRN AP26199685 project “Development and application of biosubstitute materials for laryngeal implants using 3D printing technology.”*
Authors’ contribution: *Concept – D.E. Toguzbaeva; Scientific design – D.E. Toguzbaeva; Research implementation – D.E. Toguzbaeva; Interpretation of research results – D.V. Ismailov; Preparation of the article – D.V. Ismailov.*
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