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From framework to fusion: engineering bone grafts for the spine's future

Abstract

Tissue-engineered bone grafts represent a transformative advancement in orthopedic and spinal repair, offering biologically active alternatives to traditional autografts and allografts. This paper explores the global market landscape, clinical applications, and ongoing research in this rapidly evolving field. Key market drivers include an aging population, rising surgical volumes, and technological innovations in biomaterials and regenerative medicine. Clinically available products such as INFUSE®, Trinity ELITE®, Vitoss®, and FiberGraft® demonstrate current capabilities, while emerging solutions in clinical trials aim to enhance osteogenesis, integration, and mechanical performance. Together, these developments signal a paradigm shift toward personalized, multifunctional grafts that promise to improve patient outcomes in complex musculoskeletal conditions.

Keywords: tissue engineering, bone grafts, orthopedic repair, spinal fusion, biomaterials, biocompatibility, scaffold design, osteo-conductivity, regenerative medicine, degenerative bone disease, load-bearing defects, hydroxyapatite, polycaprolactone, clinical translation, bone regeneration

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Abbreviations: 3D, three-dimensional; ACS, absorbable collagen sponge; ABM, anorganic bovine-derived matrix; AMIC, autologous matrix-induced chondrogenesis; ASD, adult spinal deformity; β-TCP, beta-tricalcium phosphate; DBM, demineralized bone matrix; DDD, degenerative disc disease; EB-OC, Epibone osteochondral graft; FDA, Food and Drug Administration; KOOS, knee injury and osteoarthritis outcome score; MSCs, mesenchymal stem cells; MRI, magnetic resonance imaging; N-TEC, nasal chondrocyte-based tissue-engineered cartilage; PCL, polycaprolactone; PEG, polyethylene glycol; PFA, patellofemoral arthroplasty; PFOA, patellofemoral osteoarthritis; PLGA, poly(lactic-co-glycolic acid); PROMs, patient-reported outcome measures; rhBMP-2, recombinant human bone morphogenetic protein-2; SEM, scanning electron microscopy; USD, United States Dollar

Introduction

Tissue-engineered bone grafts are an emerging class of biomaterials designed to overcome the limitations of traditional autografts and allografts, offering improved safety, scalability, and regenerative potential.[6,7] With a growing global demand fueled by an aging population, increasing rates of degenerative bone diseases, and a shift toward minimally invasive procedures, the market for advanced bone graft substitutes is rapidly expanding.[1–6]

Physiological role and clinical need

Healthy bone and spinal tissues play vital roles in structural support, calcium regulation, and mechanical load distribution, and their integrity is essential for maintaining mobility and protecting neural elements.[22–24] However, conditions such as osteoporosis and degenerative disc disease can compromise bone quality, reduce healing capacity, and cause instability or chronic pain, necessitating surgical intervention and effective grafting strategies.[27–29]

Current and emerging graft technologies

Several products, such as INFUSE®,[10] Vitoss®,[12] Trinity ELITE®,[13] and FiberGraft®,[14] are currently used in clinical practice, offering diverse solutions through the use of bioactive scaffolds, stem cells, and osteo-inductive factors. Ongoing clinical trials are evaluating next-generation grafts like EB-OC,[16] ZetaFuse™,[17] and ABM/P-15 (i-FACTOR™),[18] which combine cellular, structural, and biochemical cues to enhance integration and regeneration.

Market size and trends

Global market size and trends

The global bone grafts and substitutes market size was USD 3.20 billion in 2024 and is expected to grow from USD 3.38 billion in 2025 to USD 5.68 billion by 2034, at a CAGR of 5.94% from 2025 to 2034 (Figure 1).[1] Technological advancements in the development of advanced orthopedic grafts and alternatives, as well as increasing investments by leading companies to meet the growing global demand for advanced grafts, are further fueling the growth of the industry (Figure 2).[2] Orthopedic and spinal repair applications represent key growth areas, such that the number of posterior spinal fusions is projected to increase by 82% to 102% by 2060, with patients over 75 and women most likely to benefit from increased fusion rates.[3] The market comprises several product categories, including autografts, allografts, and synthetic grafts, with a domination of allografts in use during 2023.[3] Tissue-engineered products also form an emerging segment. Advances in biomaterials and regenerative medicine are expected to boost the adoption of tissue-engineered solutions, enabling this segment to capture a larger market share in the coming years.[4]

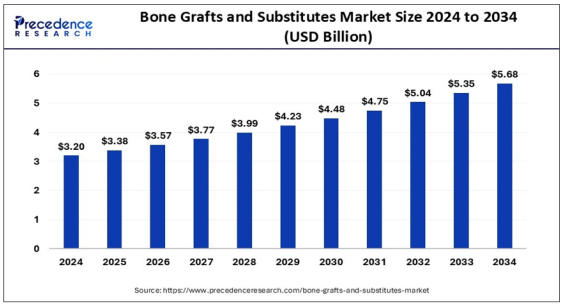

Figure 1 Projected market size of bone grafts and substitutes from 2024 to 2034 (in USD Billion).[1]

The image shows the projected global market size of bone grafts and substitutes from 2024 to 2034, illustrating expected growth in USD billions.

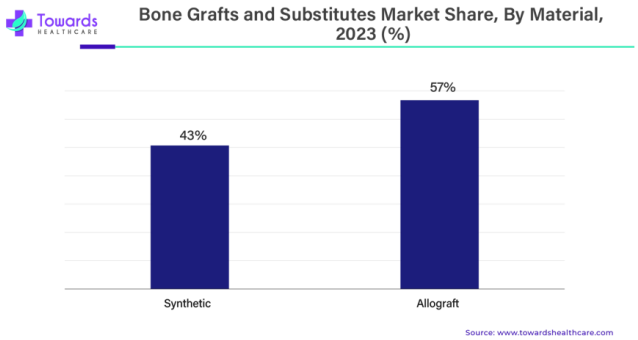

Figure 2 Bone grafts and substitutes market share by material in 2023.[2]

The image shows the distribution of market share by bone graft material types in 2023, providing a visual comparison among autografts, allografts, and synthetic alternatives.

Growth drivers

The aging global population is a key driver of market growth, as older adults face a higher prevalence of orthopedic conditions such as osteoporosis and degenerative disc diseases.[6] Concurrently, the rising number of spinal fusion surgeries, which often require bone grafts for structural support and healing, is further propelling demand.[4] Technological advancements are addressing these needs: innovations in 3D printing, stem cell technology, and biomaterial engineering have enhanced the efficacy and biocompatibility of graft substitutes (Figure 3).[5] Additionally, the growing preference for minimally invasive procedures is bolstering the adoption of synthetic and tissue-engineered grafts.[4] Traditional grafting methods, by contrast, face significant limitations; autografts risk donor site morbidity, while allografts pose potential disease transmission, and these drawbacks are accelerating the shift toward safer, lab-grown alternatives.[7]

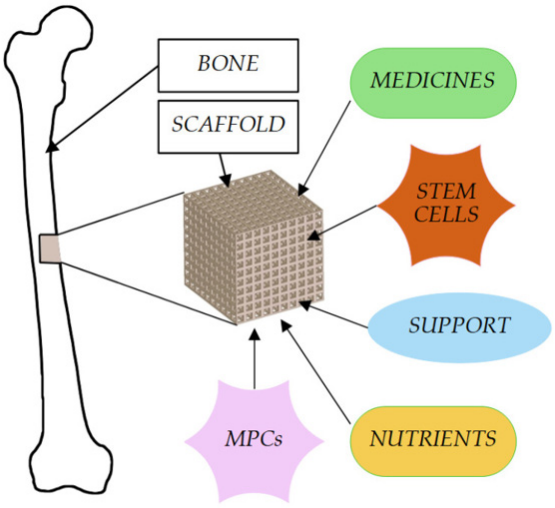

Figure 3 Usage of microporous scaffolds for supporting bone formation.[5]

The image shows microporous scaffolds used to support bone formation, highlighting structural features that promote osteogenesis.

Key market segments

In terms of application, spinal fusion devices have the largest market share owing to the high prevalence of spinal disorders and the frequent need to reinforce structures during surgical procedures.[8] Spinal fusion devices accounted for 59% of the spinal implants and devices market in 2023, driven by the rising prevalence of spinal disorders such as degenerative disc disease, scoliosis, and spondylolisthesis (Figure 4).[8] Other major segments include trauma repair and joint reconstruction, which also contribute significantly to the market demand.[9] The global bone grafts and substitutes market is projected to reach $4.4 billion by 2033, growing at a CAGR of 4.4% from 2024 to 2033, with trauma and joint reconstruction applications being significant contributors.[9] From an end-user perspective, hospitals continue to be the major venue for bone grafting procedures due to their surgical capacity and patient volume.[10]

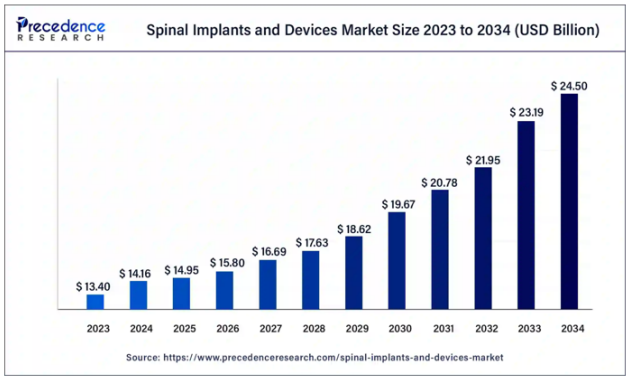

Figure 4 Projected market size of spinal implants and devices from 2023 to 2034 (in USD).[8]

The image shows projected market size of spinal implants and devices from 2023 to 2034, emphasizing growth trends in spinal repair technologies.

Geographic trends

North America leads the global bone grafts and substitutes market, accounting for 47.62% of the total market share in 2024, driven by advanced healthcare infrastructure, high expenditure on orthopedic procedures, and early adoption of innovative technologies (Figure 5).[1] However, the Asia-Pacific region is projected to grow at the fastest rate during the forecast period, with a compound annual growth rate (CAGR) of 8.2% from 2025 to 2030.[3] This growth is largely due to rising healthcare investments, growing awareness of regenerative therapies, and a rapidly aging population, particularly in countries like China and Japan (Figure 6, 7).[1]

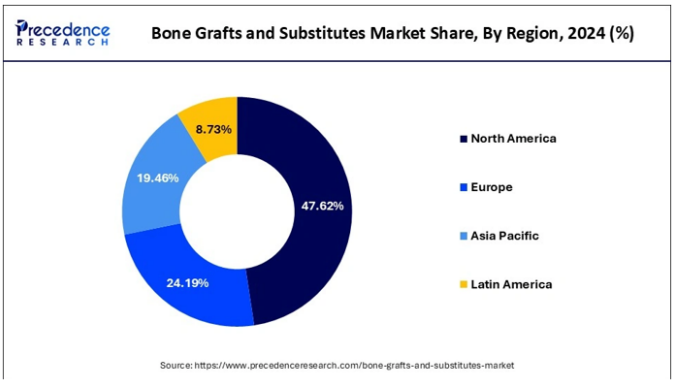

Figure 5 Bone grafts and substitutes market share by region in 2024.[1]

The image shows the regional distribution of the bone grafts and substitutes market share in 2024, with North America leading globally.

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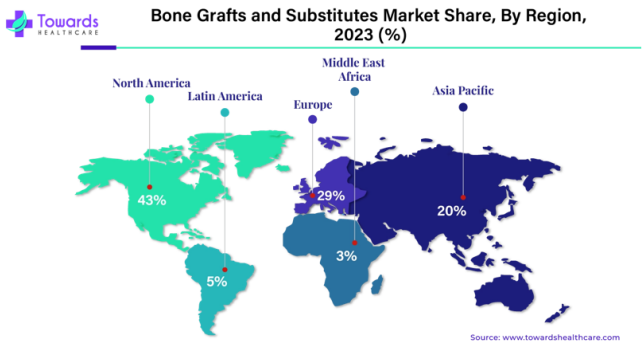

Figure 6 Regional market share of bone grafts and substitutes in 2023.[2]

The image shows the market share of bone grafts and substitutes by region in 2023, providing comparative data across major geographic areas.

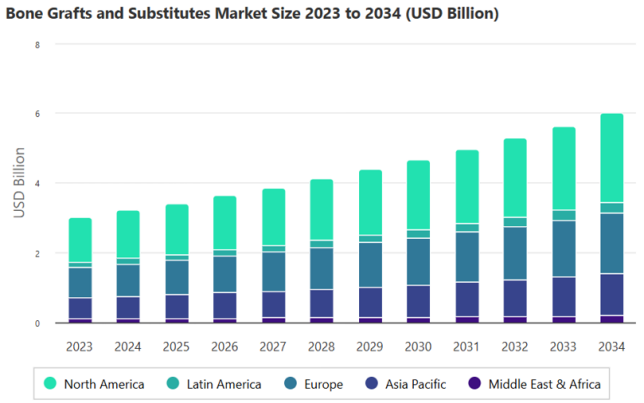

Figure 7 Bone grafts and substitutes market size by region from 2023 to 2034 (USD Billion).[2]

The image shows the projected market size of bone grafts and substitutes by region from 2023 to 2034, showing regional growth trajectories.

Healthy and diseased tissue

Healthy tissue

Healthy bone tissue is a mineralized connective tissue essential for mechanical support, calcium storage, and blood cell production.[19] It comprises two structural types: cortical bone, which is dense and load-bearing, and trabecular bone, which is porous and supports metabolic activities, such as marrow function.[20] The matrix is primarily composed of type I collagen and hydroxyapatite, allowing it to resist both tension and compression.[21] Bone remodeling depends on the coordinated activity of osteoblasts (build bone), osteoclasts (resorb bone), and osteocytes (sense mechanical signals) (Figure 8).[22] These cells maintain structural integrity and repair micro-damage in response to stress (Figure 9).[23] Additionally, bone is highly vascularized, which is critical for nutrient exchange and tissue regeneration after injury or surgical procedures (Figure 10).[24]

Healthy spinal tissue, particularly the intervertebral discs and vertebrae, plays a complementary role by protecting the spinal cord and distributing mechanical loads during movement.[25] Intervertebral discs consist of a tough outer annulus fibrosus and a gel-like inner nucleus pulposus, which function as shock absorbers between vertebrae.[26] These tissues have limited vascularization, making them especially susceptible to degeneration and poor healing capacity after injury.[26]

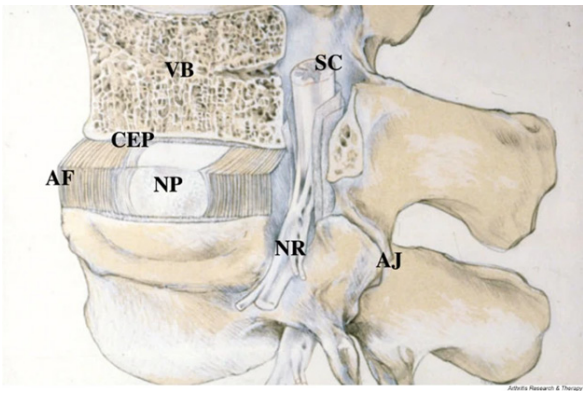

Figure 8 A schematic view of a spinal segment and the intervertebral disc.[22]

The image shows a schematic of a spinal segment, detailing the vertebrae and intervertebral disc structure relevant to load distribution and spinal motion.

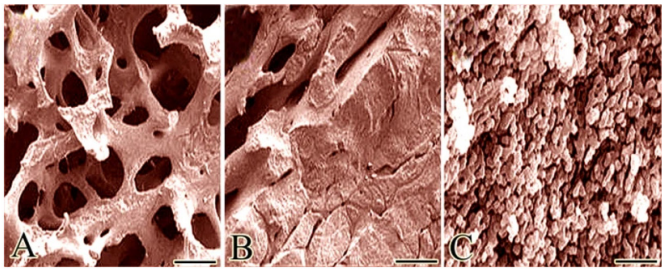

Figure 9 SEM ultramicrographs of the microstructure of natural bone grafts.[23]

The image shows SEM (scanning electron microscopy) ultramicrographs depicting the porous microstructure of natural bone graft materials.

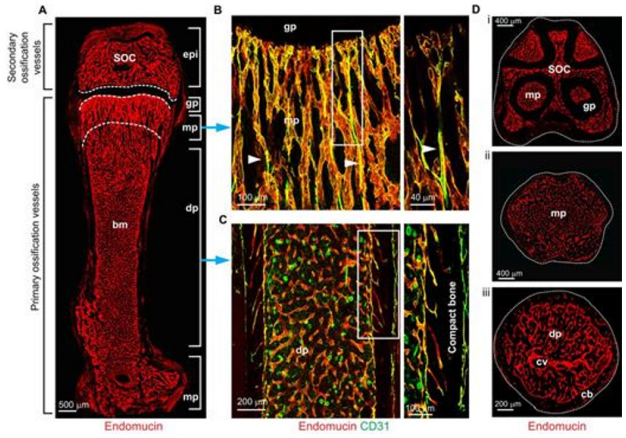

Figure 10 Architecture of the long bone vasculature.[24]

The image shows the vascular architecture within long bones, illustrating blood vessel distribution critical to bone regeneration.

Maintaining the health of both bone and spinal tissues is vital for mobility, stability, and neural protection.[25] For this reason, tissue-engineered bone grafts for spinal repair must address not only structural restoration but also integration with surrounding vertebrae and disc tissues.[27] Engineered grafts must support osteo-conduction, osteogenesis, and osteointegration, while also accommodating spinal biomechanics and load-bearing requirements.[28]

Disease tissue

Degenerative bone disorders disrupt the balance between bone formation and resorption, leading to weakened structural integrity

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and increased fracture risk.[23] One common condition is osteoporosis, characterized by decreased bone mass and microarchitectural deterioration, which compromises mechanical strength and load-bearing capacity.[29] This disease often results from hormonal imbalances, aging, or long-term corticosteroid use, affecting both cortical and trabecular bone.[30]

At the cellular level, osteoporotic bone exhibits reduced osteoblast activity and increased osteoclast-mediated resorption, tipping the remodeling balance toward net bone loss.[31] In addition, osteocytes in diseased bone have impaired mechanosensing function, further hindering bone maintenance and adaptation to mechanical stimuli.[23] As a result, microdamage accumulates over time, and repair mechanisms are inadequate to restore integrity.[32]

Pathological changes also affect spinal tissues, particularly in degenerative disc disease (DDD), where the intervertebral discs lose hydration and elasticity with age.[33] The nucleus pulposus becomes fibrotic, and the annulus fibrosus develops fissures, diminishing shock absorption and increasing susceptibility to herniation.[26] Because intervertebral discs are avascular, their limited nutrient supply further impedes regeneration and accelerates degeneration (Figure 11).[26]

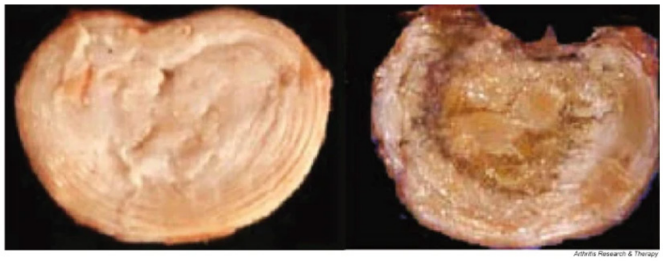

Figure 11 The normal (left) and degenerate (right) lumbar intervertebral disc.[25]

The image shows a comparison between a healthy and a degenerated lumbar intervertebral disc, highlighting structural deterioration associated with disease.

Degeneration of adjacent vertebrae often co-occurs with disc pathology, resulting in vertebral compression fractures and spinal instability.[34] These changes can lead to chronic back pain, nerve impingement, and reduced mobility, significantly impairing quality of life.[35] In severe cases, surgical intervention becomes necessary to restore alignment and mechanical function.[36]

Tissue-engineered bone grafts for disease treatment must be tailored to address these pathological deficiencies, including poor osteogenic potential, compromised vascularization, and altered biomechanical environments.[28] These grafts must not only replace lost tissue but also promote integration and regeneration in diseased environments where native healing is impaired.[28]

Existing products

Several tissue-engineered bone grafts are currently approved for clinical use in orthopedic and spinal repair.[3] These products differ in composition, biological activity, and clinical indications, each offering unique strengths and limitations.[1]

INFUSE® Bone Graft (Medtronic)

One of the most widely recognized products in the bone graft market is INFUSE® Bone Graft by Medtronic (Figure 12).[10] It consists of recombinant human bone morphogenetic protein-2 (rhBMP-2) delivered on an absorbable collagen sponge (ACS), designed to promote robust and predictable bone formation at the implant site.[10] INFUSE® is FDA-approved for specific procedures, including certain types of spinal fusion, tibial shaft fractures, and oral/maxillofacial bone regeneration.[10] A key advantage of INFUSE® is that it eliminates the need for autologous bone harvesting, thereby reducing donor site morbidity and surgical time.[10] The product is backed by extensive clinical data and has been shown to provide consistent outcomes in indicated uses.[10] However, its use is highly regulated, and complications have been reported in off-label applications, highlighting the importance of adhering strictly to approved indications.[10]

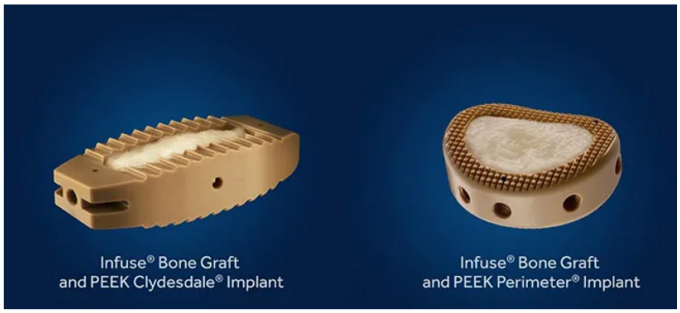

Figure 12 INFUSE® Bone Graft used with PEEK Clydesdale® and PEEK Perimeter® implants.[11]

The image shows the use of INFUSE® Bone Graft with PEEK Clydesdale® and PEEK Perimeter® spinal implants, demonstrating integration in surgical applications.

Vitoss® Bioactive Foam Scaffold (Stryker)

Vitoss®, developed by Stryker, is a bioactive synthetic bone graft substitute composed of beta-tricalcium phosphate (β-TCP) infused with bioactive glass (Figure 13).[12] Its ultra-porous, interconnected structure closely resembles the architecture of human cancellous bone, enhancing osteoconduction and facilitating cellular infiltration and vascularization.[12] This design supports bone regeneration by providing an ideal scaffold for bone cell attachment, proliferation, and matrix deposition.[12] Vitoss® is indicated for use in non-load-bearing skeletal defects, particularly in the extremities and pelvis, where biological remodeling is prioritized over structural load support.[12] While it is fully resorbable and promotes bone bonding, it lacks sufficient mechanical strength for applications requiring long-term load-bearing support.[12]

Figure 13 Vitoss® Scaffold by Stryker is a synthetic cancellous bone void filler made from β-tricalcium phosphate (β-TCP).[12]

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The image shows the Vitoss® synthetic bone scaffold made from β-tricalcium phosphate, designed for cancellous bone void filling.

Trinity ELITE® (Orthofix)

Trinity ELITE® is a cryopreserved cellular allograft that contains viable adult stem cells, osteoinductive demineralized bone matrix (DBM), and an osteoconductive cancellous bone scaffold (Figure 14).[13] It is designed for use in spinal fusion and other orthopedic procedures where bone regeneration is needed. The presence of mesenchymal stem cells (MSCs) and osteoprogenitor cells supports the body's natural healing processes by contributing to new bone formation through cellular differentiation.[13] Trinity ELITE® is processed to retain cell viability while minimizing immunogenic risk and is available in various forms to accommodate surgical preferences.[13] Despite its regenerative potential, clinical outcomes may vary due to donor variability, and as with all allografts, there is a minimal risk of immune response.[13]

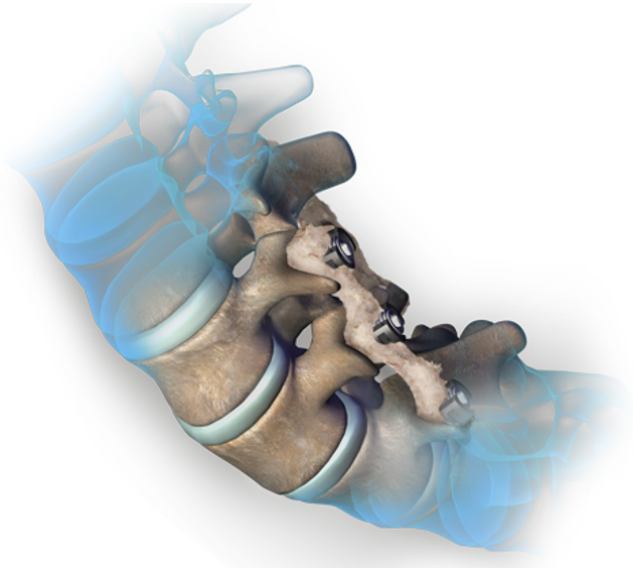

Figure 14 Trinity ELITE® by Orthofix is a cryopreserved allograft containing viable cells.[13]

The image shows the Trinity ELITE® cryopreserved allograft, which contains viable cells, demineralized matrix, and cancellous scaffold components.

FiberGraft® Bone Graft Substitute (DePuy Synthes – Johnson & Johnson MedTech)

FiberGraft®, part of the FiberGraft® Family by DePuy Synthes, is a synthetic bone graft substitute composed of bioactive glass fibers embedded within a porous scaffold matrix (Figure 15).[14] It is engineered to combine both structural integrity and bioactivity, providing a balance between mechanical support and biological remodeling.[14] The product's unique fiber-based architecture enhances handling characteristics while mimicking the extracellular matrix, facilitating cellular attachment and bone tissue infiltration.[14] FiberGraft® promotes osteoconduction and has been shown to facilitate consistent new bone formation across a variety of clinical indications.[14] It is available in multiple formats, including moldable putty, strips, and granules, allowing surgeons to choose the most appropriate form based on the surgical site and defect geometry.[14] While it offers enhanced versatility and ease of use, its application is still limited to non-load-bearing scenarios where biological remodeling is prioritized over mechanical strength.[14]

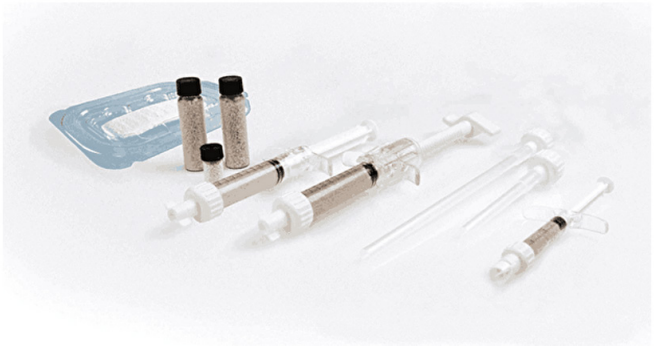

Figure 15 FiberGraft® by DePuy Synthes is a family of bone graft substitutes that utilize bioactive glass fibers to enhance osteo-conductivity and handling properties.[14]

The image shows the FiberGraft® bone graft substitute composed of bioactive glass fibers within a porous matrix to support osteoconduction.

Pre-clinical products and products in clinical trials

N-TEC (Nasal Chondrocyte-Based Tissue-Engineered Cartilage)

One promising product in clinical development is N-TEC (Nasal Chondrocyte-Based Tissue-Engineered Cartilage), an autologous cartilage implant currently being evaluated in the Phase II ENCANTO trial—a randomized, controlled, multicenter study for patellofemoral osteoarthritis (PFOA).[15] The graft is engineered by expanding a patient's nasal chondrocytes within a collagen type I/III scaffold, creating a personalized, biologically integrated solution.[15] The trial compares N-TEC against two established approaches: Autologous Matrix-Induced Chondrogenesis (AMIC) for early-stage PFOA and patellofemoral arthroplasty (PFA) for late-stage disease.[15] Primary endpoints include clinical efficacy, measured by the KOOS (Knee injury and Osteoarthritis Outcome Score), and regenerative potential, assessed via radiographic and MRI-based structural outcomes.[15] With 150 patients enrolled across 11 centers, ENCANTO represents one of the largest clinical trials to date investigating tissue-engineered cartilage for PFOA.[15] If successful, N-TEC could redefine treatment paradigms, offering a cell-based regenerative alternative to conventional joint-preserving or joint-replacing surgeries.[15]

EB-OC (Epibone Osteochondral Graft)

A first-in-human Phase I/IIb clinical trial (NCT06895889) is evaluating EB-OC, a novel living tissue-engineered osteochondral graft developed by Epibone, Inc., for full-thickness chondral and osteochondral knee defects.[16] The EB-OC graft combines an allogeneic mesenchymal stem cell-derived hyaline-like cartilage layer with a biocompatible bone scaffold, designed to regenerate both cartilage and subchondral bone in a single procedure.[16] This prospective, randomized, open-label study compares EB-OC to abrasion chondroplasty in 36 patients, with a 24-month follow-up and a 12-month crossover option for control subjects.[16] Primary endpoints include safety (adverse event rates) and graft performance, while secondary assessments incorporate patient-reported outcomes (KOOS, IKDC), MRI-based evaluations (AMADEUS, MOCART), and clinical integration metrics.[16] As one of the first trials investigating a living osteochondral construct, EB-OC represents a significant advancement in ortho-biologic repair, potentially offering a transformative alternative to current palliative approaches.[16]

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ZetaFuse™ Bone Graft

The ZetaFuse™ Bone Graft, Zetagen Therapeutics' novel osteogenic biomaterial now transitioning from preclinical to clinical evaluation, is currently under investigation in a first-in-human Phase I feasibility trial (NCT05971329) for cervical spinal fusion following discectomy in degenerative disc disease.[17] Designed for implantation within PEEK interbody cages, this graft leverages its osteoconductive properties and potential osteoinductive capacity to facilitate biological fusion of cervical vertebrae.$_{17}$ The pilot study will enroll 10 patients to primarily assess radiographic fusion outcomes, while secondary endpoints evaluate patient-reported quality of life (SF-12v2) and graft performance metrics.[17] As an initial clinical investigation, the trial focuses on establishing safety parameters, surgical handling characteristics, and preliminary efficacy data—critical milestones in developing this next-generation bone graft alternative for spinal applications, with the potential to address current limitations in fusion technologies.[17]

ABM/P-15 (i-FACTOR™) Bone Graft

A pivotal Phase III clinical trial (NCT05038527) is currently investigating the efficacy of ABM/P-15 bone graft (i-FACTOR™) in adult spinal deformity (ASD) corrective surgery.[18] This prospective, randomized controlled study compares the composite graft, comprising anorganic bovine-derived hydroxyapatite (ABM) coupled with a synthetic P-15 peptide—against standard grafting materials (autologous bone and allogenic femoral head grafts).[18] The ABM/P-15 matrix demonstrates a tri-modal mechanism of action: osteoconductive scaffolding, osteoinductive stimulation, and targeted cell signaling through α2β1 integrin binding to enhance osteogenesis.[18] The multicenter trial will enroll 240 patients, representing one of the largest investigations of peptide-enhanced bone grafts in long-segment spinal fusions, with primary endpoints including fusion rates (assessed via CT), revision surgery incidence, and patient-reported outcome measures (PROMs) over 24 months.[18] Should the trial demonstrate non-inferiority to conventional grafts, ABM/P-15 could establish itself as a clinically effective and potentially cost-saving alternative for complex spinal reconstruction, addressing current limitations of autograft supply and allograft variability.[18]

Conclusion and future considerations

Tissue-engineered bone grafts are transforming orthopedic and spinal repair. These grafts provide biologically active alternatives to traditional autografts and allografts.[6,7] Unlike conventional options, they offer better safety and scalability.[6,7] Demand for advanced bone substitutes is rising, the global market is projected to grow from USD 3.38 billion in 2025 to USD 5.68 billion by 2034, driven by increasing surgical demand and innovations in regenerative technologies.[1,3]

Healthy bone and spinal tissues are essential for mobility, structural support, and load-bearing function.[20] Cortical bone provides mechanical strength, while trabecular bone supports metabolic processes like hematopoiesis.[19–21] Bone matrix components, including type I collagen and hydroxyapatite, allow it to resist both tensile and compressive forces.[21] These tissues are maintained by osteoblasts, osteoclasts, and osteocytes, and their high vascularity supports regeneration after injury.[22–24] In the spine, vertebrae and intervertebral discs protect the spinal cord and enable flexibility.[26] The limited vascularity of intervertebral discs, however, makes them especially prone to degeneration and poor healing.[25–27]

Degenerative conditions such as osteoporosis and degenerative disc disease compromise bone quality and increase fracture risk.[19] These diseases disrupt cellular remodeling balance, diminish mechanical strength, and impair healing responses.[23,28,29] Osteoporotic bone exhibits elevated resorption, impaired mechanosensing, and an accumulation of microdamage.[23,30,31] Degeneration of spinal tissues leads to disc dehydration, vertebral instability, chronic pain, and may necessitate surgical repair.[27,32–35]

Tissue-engineered grafts are well-suited to meet these clinical needs. Some products, like INFUSE®, Trinity ELITE®, and FiberGraft®, are already in use.[10,13,14] These demonstrate the success of biomaterial and cell-based innovations EB-OC. Meanwhile, new candidates in clinical trials promise even greater customization and regenerative potential.[16–18] EB-OC aims to repair osteochondral defects with a dual-layered cell-based graft;[16] ZetaFuse™ targets spinal fusion with osteoinductive potential;[17] and i-FACTOR™ employs peptide-enhanced scaffolds to improve spinal deformity outcomes.[18]

The continued advancement of bone graft technologies hinges on three pivotal factors: sustained clinical research to validate long-term safety and efficacy, optimization of regulatory pathways to accelerate translation of promising technologies, and breakthroughs in material science to address current limitations in mechanical performance and biological integration.[4,5] These steps will expand patient access and improve outcomes. The field is evolving rapidly. Soon, tissue-engineered grafts may become standard in ortho-biologic treatment Appendix.

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Conflicts of interest

Authors declare that there is no conflict of interest.

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