Bone Regeneration Under Tension: Advances in Distraction Osteogenesis.

Keywords

Distraction osteogenesis , Craniofacial reconstruction , Mandibular distraction , Midface advancement , Alveolar ridge augmentation , Dental implant rehabilitation , Bone regeneration under tension , Digital surgical planning , Regenerative medicine , Orthognathic surgery

Abstract

Distraction osteogenesis (DO) is a biologically driven reconstructive technique that promotes new bone formation through the application of controlled tensile forces between osteotomized segments. In dental and craniofacial surgery, DO has evolved into a versatile modality for managing mandibular deficiencies, midface hypoplasia, syndromic craniosynostosis, alveolar ridge atrophy, and complex post-traumatic or oncologic defects. Unlike conventional graft-based approaches, DO enables simultaneous skeletal expansion and adaptive soft tissue histogenesis, reducing donor-site morbidity and enhancing volumetric stability.

Recent advances in digital surgical planning, three-dimensional (3D) printing, and internal distraction devices have significantly improved vector control, precision, and patient comfort. Concurrently, biologic augmentation strategies; including growth factors, stem cell therapy, and mechanotransduction modulation; have demonstrated potential in accelerating consolidation and improving regenerate quality. Despite its advantages, DO remains technique-sensitive and may be associated with complications such as regenerate insufficiency, relapse, neurosensory disturbance, and temporomandibular joint dysfunction.

Emerging technologies integrating artificial intelligence, fully implantable automated distractors, and regenerative medicine approaches are expected to further refine treatment outcomes. This review synthesizes contemporary evidence (2018–2025) on dental and craniofacial distraction osteogenesis, highlighting clinical applications, limitations, innovations, and future directions in maxillofacial reconstruction.

Introduction

Distraction osteogenesis (DO) is a biologically based surgical technique that induces new bone formation between vascularized bone segments through the application of gradual tensile forces. In the craniofacial region, this principle has been adapted to correct skeletal deformities, augment deficient alveolar ridges, and manage complex congenital and acquired maxillofacial conditions. Unlike conventional osteotomies that rely on acute repositioning and rigid fixation, DO allows progressive skeletal advancement while simultaneously promoting expansion of surrounding soft tissues, including muscle, skin, mucosa, nerves, and vasculature.[1]

The biological foundation of DO lies in the “tension-stress effect,” whereby controlled

mechanical strain stimulates intramembranous ossification and angiogenesis within the distraction gap. Contemporary molecular studies demonstrate upregulation of osteogenic markers such as bone morphogenetic proteins (BMPs), vascular endothelial growth factor (VEGF), and activation of mechanotransduction pathways including Wnt/β-catenin signaling during the distraction phase.[2,3] These biologic responses are particularly advantageous in the craniofacial skeleton, where vascularity is robust but bone volume may be limited or anatomically constrained.

In dental and maxillofacial surgery, DO has significantly expanded therapeutic options. Mandibular distraction osteogenesis (MDO) is now routinely employed for the management of micrognathia, hemifacial microsomia, and airway compromise in pediatric patients. Gradual mandibular advancement not only corrects skeletal deficiency but also improves glossoptosis and airway patency, often eliminating the need for tracheostomy in severe neonatal cases.[4] Midface distraction has similarly transformed the management of syndromic craniosynostosis, allowing greater skeletal advancement with improved soft tissue adaptation compared with traditional orthognathic approaches.[5]

In implant dentistry, alveolar distraction osteogenesis offers a biologically favorable alternative to vertical ridge augmentation with autogenous block grafts. By gradually transporting a dentoalveolar segment, clinicians can achieve simultaneous bone and soft tissue expansion while minimizing donor-site morbidity. Recent systematic reviews report predictable vertical bone gain and high implant survival rates in distracted segments.[6]

Despite these advantages, craniofacial DO remains technique-sensitive and requires meticulous planning of osteotomy design, distraction vector, rate, and consolidation period to ensure stable outcomes. Advances in digital surgical planning, internal distractor systems, and biologic enhancement strategies continue to refine the predictability and safety of the procedure.[5,7]

Biological Basis of Distraction Osteogenesis

Mechanobiological Framework

Distraction osteogenesis (DO) is a mechanically driven regenerative process in which gradual tensile forces applied across an osteotomy gap stimulate new bone formation. The biological response is classically divided into latency, distraction, and consolidation phases. During latency, inflammatory mediators and progenitor cells accumulate; during distraction, controlled mechanical strain maintains proliferation and alignment of fibrovascular tissue within the gap; and during consolidation, progressive mineralization and remodeling convert woven bone into mature lamellar bone. Successful regenerate formation depends on maintaining a stable mechanical environment that sustains osteogenic signaling throughout these phases.[8]

Mechanotransduction Signaling Pathways

The biological core of DO lies in mechanotransduction — the conversion of tensile mechanical forces into intracellular biochemical signals. DO-focused mechanotransduction literature highlights mechanosensing through integrin–focal adhesion systems, cytoskeletal tension transmission, and mechanosensitive ion channels, with downstream activation of pathways

including Wnt/β-catenin, TGF-β/BMP-Smad, MAPK/ERK, PI3K/Akt, and Hippo signaling. These networks regulate osteogenic transcriptional programs and coordinate angiogenesis–osteogenesis coupling, providing a mechanistic rationale for why distraction rate, rhythm, and stability strongly determine regenerate quality.[9]

Angiogenesis–Osteogenesis Coupling

Vascular adaptation is essential for regenerate formation because oxygen delivery and nutrient supply must keep pace with high metabolic demands during new bone formation. In DO models, promoting vascularization enhances bone regeneration, supporting the concept that angiogenesis is not merely supportive but biologically coupled to osteogenesis. Evidence from DO research shows that interventions capable of stimulating both vascular growth and osteogenic activity can accelerate regenerate development, reinforcing the central role of vascular–skeletal coupling in distraction biology.[10]

Osteoimmune Regulation

The immune microenvironment significantly influences DO outcomes. DO-specific reviews describe dynamic phase-dependent changes in immune cell behavior and cytokine signaling that shape progenitor recruitment, angiogenesis, and osteogenic differentiation. In particular, macrophage-mediated regulation is emphasized as a key controller of tissue repair balance, where excessive or prolonged inflammatory signaling may impair mineralization, while coordinated immunoregulation supports efficient regenerate maturation.[11]

Stem Cell Contribution and Paracrine Signaling

Bone marrow–derived and periosteal mesenchymal stem cells contribute substantially to regenerate formation, and mechanical strain promotes their osteogenic commitment. Recent DO studies also demonstrate that extracellular vesicles, including exosomes, can enhance both angiogenesis and osteogenesis within the distraction environment through pathway-level regulation (for example PI3K/Akt and ERK signaling). This supports the emerging view that DO regeneration is coordinated not only through direct cell differentiation but also through paracrine signaling systems that integrate vascular and osteogenic responses.[12]

Neural and Microenvironmental Influences

Craniofacial DO models indicate that neural integrity contributes to regenerate success. Experimental denervation in mandibular DO has been associated with impaired bone formation, supporting the concept that neurotrophic and neurovascular signals help regulate the regenerative microenvironment during distraction. These findings reinforce that DO is a whole-microenvironment process involving coordinated mechanical signaling, vascular supply, immune regulation, and neural contributions, particularly relevant in craniofacial reconstruction.[13]

Clinical Craniofacial Applications

1. Mandibular Distraction Osteogenesis

Mandibular DO is now a well-established intervention for hemifacial microsomia, micrognathia, and syndromic craniofacial deficiencies. In pediatric patients with airway compromise (e.g., Pierre Robin sequence), early mandibular advancement improves glossoptosis and frequently avoids tracheostomy. Recent multicenter outcomes show significant improvement in airway patency, feeding, and long-term skeletal stability.[1,4]

2. Midface Advancement

Midface distraction (Le Fort III or monobloc advancement) is widely applied in syndromic craniosynostosis such as Crouzon and Apert syndromes. Compared with conventional osteotomy, gradual distraction allows greater advancement with improved soft tissue adaptation and lower relapse rates. Advances in internal distractor systems have reduced infection and scarring while enhancing patient compliance.[1,5]

3. Vertical Alveolar Ridge Augmentation

Alveolar distraction osteogenesis is increasingly used for vertical ridge augmentation before implant placement. It is particularly beneficial in severe alveolar atrophy where conventional grafting would require autogenous donor sites. Recent systematic reviews report predictable vertical bone gain (5–15 mm), high implant survival rates, and reduced donor-site morbidity compared with block grafting.[6,19]

4. Segmental Alveolar Reconstruction

Segmental transport distraction in localized ridge defects preserves vascularity and promotes simultaneous soft tissue expansion. Current literature supports its application in complex implant rehabilitation cases, particularly where soft tissue deficiency coexists.[6]

5. Oncologic and Post-Traumatic Reconstruction

In mandibular continuity defects following tumor resection or severe trauma, distraction-based bone transport offers a biological reconstructive option. It enables gradual regeneration of vascularized bone without reliance on free flaps in selected cases. Recent case series demonstrate acceptable functional and aesthetic outcomes, especially when combined with digital surgical planning and patient-specific devices.[5,14]

Advances Over Conventional Techniques in Distraction Osteogenesis

Distraction osteogenesis (DO) has undergone significant refinement over the past decade, evolving beyond traditional circular external fixation and conventional bone grafting methods. Modern developments have focused on improving mechanical precision, enhancing biological regeneration, reducing complication rates, and optimizing patient outcomes.

A. Development of Internal Lengthening Systems

One of the most important advancements in DO is the transition from external fixators to motorized intramedullary lengthening nails. Magnetically controlled systems enable gradual bone distraction without prolonged external frame application. Compared with classical Ilizarov frames, internal devices are associated with improved patient comfort, reduced pin-site infection rates, and better cosmetic acceptance [20,21.] Hybrid strategies such as lengthening-over-nail (LON) and lengthening-and-then-nailing (LATN) shorten external fixation duration and improve regenerate stability[22].

B. Computer-Assisted and Hexapod Frame Technology

Modern hexapod external fixators permit simultaneous correction of multiplanar deformities using software-guided calculations. This improves alignment precision while minimizing manual adjustment errors[23]. Digital deformity analysis and virtual simulation enhance surgical planning and predictability.

C. Biological Enhancement Strategies

Recent research has explored biologic augmentation to accelerate bone formation. Controlled delivery of osteoinductive molecules such as BMP-2 and VEGF has shown promise in enhancing angiogenesis and mineralization[24]. Mesenchymal stem cell–based therapies and scaffold-supported delivery systems aim to strengthen osteogenic activity and shorten consolidation time[25]. Modulation of mechanotransduction pathways including Wnt/β-catenin, FAK-ERK, and PI3K/Akt signaling has also demonstrated enhanced regenerate quality.[26]

D. Adjunctive Physical Stimulation

Low-intensity pulsed ultrasound (LIPUS) and electrical stimulation have been investigated as non-invasive methods to improve regenerate maturation and mineral deposition.[27]

E. Digital Planning and Personalized Surgical Approaches

Three-dimensional imaging, virtual surgical simulation, and patient-specific device customization improve vector control and osteotomy accuracy compared with conventional manual planning.[28]

F. Comparative Advantages Over Conventional Bone Grafting

Compared with traditional autologous or vascularized grafting techniques, DO stimulates simultaneous regeneration of bone, soft tissue, and neurovascular structures while avoiding donor-site morbidity[29].

Complications and Limitations in Craniofacial Distraction Osteogenesis

Distraction osteogenesis (DO) in the craniofacial skeleton presents unique biomechanical and anatomical challenges compared with long bones. The proximity to dentition, neurovascular bundles, airway structures, and temporomandibular joint (TMJ) increases the complexity of treatment.

1. Device-Related and Surgical Complications

Both internal and external distractors used in mandibular, midface, and alveolar applications may lead to:

- Infection (particularly with transcutaneous activation arms)
- Device loosening or mechanical failure
- Scarring and soft tissue irritation
- Inaccurate distraction vector leading to asymmetry

Internal distractors have reduced visible scarring and infection rates compared with external devices; however, they require secondary removal surgery.[4,5]

2. Regenerate Bone Quality Issues

In craniofacial DO, regenerate formation can be compromised by:

- Inadequate vector planning
- Poor vascularity (especially in scarred or previously operated tissues)
- Rapid distraction rate
- Thin alveolar bone plates

Complications include fibrous union, delayed mineralization, or relapse after consolidation. In alveolar distraction, insufficient buccolingual bone thickness may compromise implant placement.[6]

3. Dental and Occlusal Complications

Because distraction occurs in tooth-bearing segments, complications may involve:

- Dental root injury during osteotomy
- Tooth vitality loss
- Periodontal attachment compromise
- Malocclusion or open bite development
- Uncontrolled tooth tipping during alveolar transport

Orthodontic coordination is often required before and after distraction to achieve stable occlusion.[1,6]

4. Neurosensory Disturbances

Mandibular DO may cause transient or, rarely, persistent inferior alveolar nerve paresthesia. Careful corticotomy design and gradual distraction minimize nerve injury risk.[4]4

5. Temporomandibular Joint (TMJ) Concerns

Excessive or improperly directed mandibular advancement may lead to:

- TMJ pain
- Condylar resorption
- Altered mandibular growth in pediatric patients

Long-term follow-up studies highlight the importance of monitoring joint adaptation during growth.[1]

6. Relapse and Stability

Relapse remains a concern, particularly in midface distraction for syndromic craniosynostosis and vertical alveolar augmentation. Stability depends on adequate consolidation time, rigid fixation, and proper orthodontic-prosthetic rehabilitation.[5]

Emerging Advances in Craniofacial Applications

1. Digital Planning and 3D Surgical Simulation

Virtual surgical planning (VSP) has significantly enhanced precision in craniofacial DO. Three-dimensional imaging combined with computer-guided osteotomies improves vector control and symmetry in mandibular and midface advancement. Patient-specific distractors fabricated via 3D printing are increasingly utilized to improve accuracy and reduce operative time.[7]

2. Internal and Resorbable Distractor Systems

Modern low-profile internal distractors reduce scarring and infection risk. Experimental bioresorbable distractors are under investigation to eliminate secondary hardware removal procedures.[4]

3. Biologic Enhancement of Regenerate Formation

Adjunctive therapies being explored in dental craniofacial DO include:

- Platelet-rich fibrin (PRF) to enhance angiogenesis
- Recombinant bone morphogenetic protein-2 (rhBMP-2)
- Mesenchymal stem cell augmentation
- Low-intensity pulsed ultrasound (LIPUS)

Preclinical and early clinical reports suggest improved mineral density and reduced consolidation time with biologic stimulation.[2,6]

4. Orthodontic–Distraction Integration

Integration of skeletal anchorage systems (miniscrews and miniplates) allows improved control of dentoalveolar segments during distraction. Hybrid orthodontic-distraction protocols are being developed to reduce relapse and improve occlusal stability.[1]

Future Directions in Craniofacial Distraction Osteogenesis

1. Personalized Vector and Rate Optimization

Artificial intelligence–assisted modeling may allow prediction of soft tissue response and optimize distraction rate and direction based on patient-specific anatomy and bone density.[7]

2. Regenerative Medicine Integration

Future approaches may combine DO with scaffold-based tissue engineering, growth factor delivery systems, and gene-modulated stem cells to accelerate consolidation and enhance bone quality in compromised patients (e.g., cleft patients or irradiated tissues).[2]

3. Fully Implantable Automated Systems

Next-generation automated internal distractors aim to provide continuous micro-distraction without patient activation, potentially improving regenerate uniformity and comfort.[4]

4. Combined Orthognathic–Distraction Hybrid Procedures

Hybrid strategies integrating acute orthognathic correction with gradual distraction may allow large skeletal advancements with improved stability and reduced relapse, especially in severe craniofacial deformities.[7]

5. Long-Term Stability and Growth Studies

There remains a need for multicenter longitudinal studies evaluating:[2]

- Skeletal stability after growth completion
- TMJ adaptation
- Implant survival in distracted alveolar bone
- Cost-effectiveness compared with grafting or free flap reconstruction

References

1. Steinbacher DM. Advances in craniofacial distraction osteogenesis. *Clin Plast Surg*. 2019;46(2):241–253.
2. Liu Y, Wu X, Chen J. Biological enhancement strategies in distraction osteogenesis: recent progress and future perspectives. *J Orthop Res*. 2021;39(4):742–754.
3. Sun Y, Xu L, Huang S. Mechanotransduction pathways in distraction osteogenesis: recent insights. *Bone Res*. 2020;8:33.
4. Resnick CM, Padwa BL. Mandibular distraction osteogenesis in pediatric patients: indications and outcomes. *Oral Maxillofac Surg Clin North Am*. 2020;32(2):205–217.
5. Flores RL, Tholpady SS. Midface distraction osteogenesis in syndromic craniosynostosis: contemporary outcomes. *Plast Reconstr Surg*. 2018;141(3):735–747.

6. Al-Harbi F, Al-Harbi M. Vertical alveolar ridge distraction osteogenesis: systematic review. *Int J Oral Maxillofac Implants*. 2019;34(4):e85–e95.

7. Choi JW, Kim N. Virtual surgical planning and 3D printing in craniofacial distraction osteogenesis. *J Craniofac Surg*. 2021;32(4):1345–1352
8. Liu Z, Liu Q, Guo H, Liang J, Zhang Y. Overview of Physical and Pharmacological Therapy in Enhancing Bone Regeneration Formation During Distraction Osteogenesis. Front Cell Dev Biol. 2022 Apr 28;10:837430.
9. Yang J, Jiang L, Wang Z, Li Z, Liu Y. Advances in mechanotransduction signaling pathways in distraction osteogenesis. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi. 2025 Jul 15;39(7):912-918. Chinese.
10. Li S, Wu H, Wang F, Kong L, Yu Y, Zuo R, Zhao H, Xu J, Kang Q. Enhanced Bone Regeneration through Regulation of Mechanoresponsive FAK-ERK1/2 Signaling by ZINC40099027 during Distraction Osteogenesis. Int J Med Sci. 2024 Jan 1;21(1):137-150.
11. Yang S, Wang N, Ma Y, Guo S, Guo S, Sun H. Immunomodulatory effects and mechanisms of distraction osteogenesis. Int J Oral Sci. 2022 Jan 24;14(1):4.
12. Liao F, Liao Z, Zhang T, Jiang W, Zhu P, Zhao Z, Shi H, Zhao D, Zhou N, Huang X. ECFC-derived exosomal THBS1 mediates angiogenesis and osteogenesis in distraction osteogenesis via the PI3K/AKT/ERK pathway. J Orthop Translat. 2022 Sep 23;37:12-22.
13. Tevlin R, Griffin M, Chen K, Januszyk M, Guardino N, Spielman A, Walters S, Gold GE, Chan CKF, Gurtner GC, Wan DC, Longaker MT. Denervation during mandibular distraction osteogenesis results in impaired bone formation. Sci Rep. 2023 Feb 6;13(1):2097.
14. Borzunov DY, Shastov AL. Bone transport in the treatment of long bone defects: current concepts. *World J Orthop*. 2019;10(7):266–276.
15. Urban IA, Monje A, Lozada JL. Vertical ridge augmentation and distraction osteogenesis: current clinical evidence. *J Periodontol*. 2021;92(3):333–343.
16. Laubscher M, Mitchell C, Timms A, Goodier D, Calder P. Outcomes following femoral lengthening with the PRECICE intramedullary limb-lengthening system. Bone Joint J. 2018;100-B(9):1166–72.
17. Fragomen AT, Rozbruch SR. Intramedullary limb lengthening: current concepts. J Am Acad Orthop Surg. 2020;28(18):e803–14.
18. Xu WG, et al. Lengthening over nail versus Ilizarov method: a meta-analysis. J Orthop Surg Res. 2018;13:95.
19. Horn J, Huhnstock S, Steen H. Limb deformity correction using the Taylor Spatial Frame. Strategies Trauma Limb Reconstr. 2019;14(1):1–8.
20. Liu Y, et al. Controlled BMP-2 release enhances bone formation during distraction osteogenesis. J Orthop Res. 2021;39(4):824–33.
21. Huang Y, et al. Functionalized mesenchymal stem cells in bone regeneration. Stem Cell Res Ther. 2023;14:210.
22. Hu K, Olsen BR. Mechanotransduction pathways in bone regeneration. Bone. 2021;151:116–27.
23. Leighton R, et al. Low-intensity pulsed ultrasound in fracture and bone healing: systematic review. Injury. 2020;51(Suppl 2):S57–67.

24. Wang X, et al. 3D printing and digital planning in orthopedic deformity correction. Appl Sci. 2022;12(1):537.
25. Kocaoglu M, et al. Distraction osteogenesis for large bone defects: current perspectives. Orthop Clin North Am. 2022;53(1):65–78.