



DISTRACTION OSTEOGENESIS

DİSTRAKSİYON OSTEOGENEZİ

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Abstract

Distraction osteogenesis is a treatment method developed and introduced to the world by the Russian orthopedist Gavriil Ilizarov. Approximately 40 years after its inception, this method began to be applied in the maxillofacial region, and today it is used not only for the treatment of syndromic conditions but also for the treatment of tissue deficiencies.

The purpose of this review is to provide readers with an overview of the general concepts of distraction osteogenesis, its role in dental and orthodontic practice, its complications, and how to avoid them.

This article begins with a history of distraction osteogenesis and covers topics such as its current use, application protocols, complications, and management. Databases such as PubMed, Google Scholar, and Scopus were consulted.

The use of distraction osteogenesis in the maxillofacial region has increased over time. With proper use of the distractor and careful planning of the force vector, complex defects in the maxillofacial region can be treated.

Keywords: *Distraction osteogenesis, maxillofacial distraction, complications arising from distraction osteogenesis, cellular biology of distraction osteogenesis.*

Özet

Distraksiyon osteogenezis Rus ortopedist Gavriil İlizarov tarafından ortaya dünyaya tanıtılmış tedavi yöntemidir. Bu yöntem ortaya çıkışından yaklaşık 40 yıl sonra maksilofasiyel bölgede uygulanmaya başlanmış ve günümüzde sendromik durumların tedavisinin yanı sıra doku yetersizliklerinin tedavisinde de kullanılmaktadır.

Bu yayında distraksiyon osteogenezisin tarihçesinden başlanarak günümüzde kullanımı ve uygulama protokolleri, komplikasyonlar ve yönetimi gibi konulara yer verilmiştir. Pubmed, Google Scholar, Scopus gibi veri tabanlarından faydalanılmıştır.

Distraksiyon osteogenezis zaman içinde maksilofasiyal bölgede uygulaması artmıştır. Doğru distraktör kullanımı ve kuvvet vektörünün doğru planlanması ile maksilofasiyal bölgedeki ileri defektler tedavi edilebilir.

Anahtar Kelimeler: *Distraction Osteogenezis, maksilofasiyal distraksiyon, distraksiyon osteogeneziste meydana gelen komplikasyonlar, distraksiyon osteogenezisin hücresel biyolojisi.*



OVERVIEW / GENEL BAKIŞ

Distraction osteogenesis (DO) is a biological process involving the formation of new bone between bone segments that are gradually separated by traction. This process begins when a distraction force is applied to the healing callus connecting the separated bone fragments and continues as long as the tissue is stretched. More importantly, the distraction force applied to the bone also creates tension in the surrounding soft tissues, initiating a series of adaptive changes known as distraction histogenesis (1).

The principles of mechanical manipulation of bone fragments have been applied in medicine since ancient times. Hippocrates described the application of traction forces to broken bones more than 2,000 years ago. He used an external apparatus consisting of two Egyptian leather rings connected by four slightly bent rods made of cornel wood. The first appearance of continuous traction for bone fractures is based on the work of Guy de Chauliac in the fourteenth century. He applied traction using a pulley system consisting of weights attached to the leg with a cord (2).

Kazanjian used the "Over the Face" device activated with elastic bands in 1937. Later, in 1942, he used the Stader mandibular external fixator (3). However, in the 1950s, Ilizarov established the scientific basis for this concept and demonstrated that it was possible to lengthen long bones using this procedure without the use of graft material (4).

Distraction osteogenesis was significantly advanced by the Russian surgeon Gavriil Ilizarov (5,6,7,8,9). Ilizarov invented a new apparatus in 1951. The apparatus consisted of two metal rings connected by three or four toothed rods. Each bone segment was fixed to the rings with two thin tension wires placed at right angles to the bone. This fixation technique has advantages over other methods, such as providing stable but not rigid fixation to allow axial micro-movement of bone segments, physiological function with weight-bearing of the extremity, and complete control over the manipulation of bone segments regardless of their size, shape, or anatomical position. He later developed a low-energy, percutaneous subperiosteal osteotomy technique called corticotomy. Based on his clinical experience, Ilizarov discovered two biological principles of distraction osteogenesis, known as the "Ilizarov effects": the tension-stress effect on tissue formation and growth, and the effect of blood flow and loading on the shape of bones and joints (1).

The mechanism of distraction osteogenesis, reported to occur through tension stress, has attracted considerable interest in both research and clinical settings since the 1950s (10,11). It has been reported that both appropriate mechanical stimuli and sufficient angiogenesis are necessary for



successful bone formation during distraction osteogenesis (12,13). However, excessively rapid distraction can cause localized ischemia, thereby inhibiting bone formation (14,15).

Distraction osteogenesis was first applied to the long bones of the extremities and was clinically successfully applied in cranio-maxillofacial treatment by McCarthy in 1992 (16). Distraction osteogenesis has been a widely used approach in the treatment of cranio-maxillofacial deformities to date (17). Cranio-maxillofacial distraction osteogenesis serves to treat different types of cranio-maxillofacial dysplasia and bone defects and deformities. Crouzon syndrome (18), craniosynostosis (19), vertical bone height deficiencies (20,21), unilateral craniofacial microsomia (22) and similar cranio-maxillofacial dysplasias, bone defects, and their complications. Distraction osteogenesis can significantly reduce surgical trauma, complications, and recurrence rates compared to traditional surgery and can delay the age at which patients can be treated orthodontically (23,24).

In its simplest form, distraction osteogenesis refers to the formation of new bone in a stretched fracture callus (25). When a fracture occurs, the bone ends are usually aligned and stabilized to form a single, uninterrupted length of bone. Once the callus has formed, if the two bone ends are slowly separated using a screw-driven device, new bone can fill the stretched callus tissue. The success of new bone formation is influenced by the speed and rhythm of the separating forces. Distraction osteogenesis consists of 4 stages (26).

Osteotomy

Each bone segment subjected to osteotomy must contain a sufficient number of viable osteocytes to initiate and sustain distraction osteogenesis (27). In the well-vascularized craniofacial region, the periosteum provides sufficient osteoblastic activity, so complete osteotomy is preferred over corticotomy today (26).

Latent Period

The histological sequence during the latent period of distraction osteogenesis is similar to that of fracture healing, and soft callus formation occurs during this stage. It is recommended that the initial latent period be between 5 and 10 days (26).

Immediately after osteotomy, a hematoma forms in the osteotomy site, and inflammatory responses occur with the accumulation and infiltration of various immune cells (28). Pro-inflammatory cytokines such as interleukin-1 (IL-1) and interleukin-6 (IL-6) are released in large amounts for debridement of the osteotomy site. This mechanism may provide a suitable environment for angiogenesis and osteogenesis and may promote the initial migration, proliferation, and differentiation of mesenchymal stem cells (29,30,28). The immunomodulation process during the latent phase of distraction osteogenesis is similar to the inflammatory reaction process in bone fracture healing. However, there are distinct differences between them (31). In the initial phase of fracture healing,



higher expression of IL-1, IL-6, and tumor necrosis factor- α (TNF- α) promotes the accumulation of inflammatory cells and extracellular matrix secretion, resulting in an anti-inflammatory response (32,33). After 2-3 days, IL-1, IL-6, and TNF- α expression rapidly decreases to nearly undetectable levels in the subsequent endochondral phase. In contrast, following osteotomy, only IL-1 and IL-6 expression increases during the latent phase of distraction osteogenesis. Meanwhile, TNF- α expression does not increase significantly (30). Following the inflammatory response and regeneration processes, a soft callus containing inflammatory cells, fibroblasts, osteogenic progenitor cells, collagen, fibrin matrix, and spreading capillaries forms at the osteotomy site (34). Distraction osteogenesis requires an appropriate latent period because the formation of these soft calluses is a critical step for subsequent successful bone regeneration (35).

Distraction Period

This phase typically lasts 1-2 weeks and alters the normal development of the traction regeneration process. Tissue formation parallel to the distraction vector, increased and prolonged angiogenesis, and increased proliferation of spindle-shaped fibroblast-like cells exhibiting phenotypic variation create a dynamic microenvironment (36). The tension-stress law proposed by Ilizarov recommends a daily distraction of 1 mm as the optimal value for bone regeneration during distraction osteogenesis. Daily distraction aligns collagen fibers into parallel bundles, directing growing vessels and perivascular cells into longitudinal compartments (36). Intermittent distraction causes microtrauma in the distraction zone due to relatively large movement and higher distraction forces. Vessels rupture and microhematomas form. The healing process is interrupted and must restart after each activation of the distractor, causing a delay in healing (37,38). An increasing distraction rate (2 mm/day) results in nonunion, fibrous union, or weakening of the bone structure. Increased distraction speed is associated not only with poor bone formation but also with severe soft tissue contractures and nerve problems (39). Decreased distraction speed (0.5 mm/day) leads to early consolidation (7,8). Ilizarov recommended a distraction rhythm of 0.5 mm twice a day or 0.25 mm four times a day. Excessive expansion pressure can cause ischemia, leading to soft tissue tearing, nerve, muscle, and periodontal problems (3).

Immune cells, primarily macrophages, play an important role during the distraction period. Numerous studies have shown that an appropriate early inflammatory response during fracture healing facilitates resistance to infection and the recruitment of pluripotent stem cells. Furthermore, an excessive inflammatory response impedes bone regeneration, revascularization, and extracellular matrix mineralization (40,41,42). Successful bone regeneration requires a shift from an inflammatory microenvironment to an anti-inflammatory microenvironment, which causes phenotypic changes in various immune cells, including macrophages, T cells, and B cells, as well as changes in the expression of chemokines and cytokines (43).



The pro-inflammatory cytokine IL-6 plays an important role in the inflammatory response during the latent period. Interestingly, when mechanical stress is applied, elliptical cells, osteoblasts, and chondrocytes in the fibrous region of the rat tibial distraction osteogenesis model can still secrete IL-6 until the end of the distraction period, potentially forming a second peak (30). Recent studies have revealed that stress stimulation is an independent cause of increased IL-6 release (44). Furthermore, the pro-inflammatory effects of IL-6 are important (45). It can increase the accumulation of mononuclear immune cells in the distraction space, and its adverse effect is counteracted by the immunosuppressive effect of mesenchymal stem cell secretions (46). Therefore, the immunosuppressive response is important in distraction osteogenesis (35).

TGF- β 1 is another important factor in distraction osteogenesis (DO). Various studies have shown that TGF- β 1 expression increases significantly during the distraction period in vitro and in vivo (47). Furthermore, it is widely found in the distraction interval, particularly in the active proliferation zone, and cells express TGF- β receptor type 2 at the same site (47,48). Moreover, TGF- β 1 is secreted primarily by osteoblasts, mesenchymal stem cells, and connective tissues surrounding the distraction gap throughout the distraction period (49). Thus, tension stimulation increases high TGF- β 1 expression in the distraction space, particularly in cells associated with osteogenesis (35).

Consolidation Period

Consolidation is a period following the end of distraction during which the fragments stabilize in their final positions. To achieve this, the distractor is no longer activated and is subsequently used as a rigid fixation device. This period lasts between 8 and 12 weeks. During this time, callus mineralization occurs in the osseous gap (3).

TGF- β 1 decreases during the consolidation phase but remains at a certain level (49). Furthermore, it is mainly localized in osteoblasts and is involved in the process of bone mineralization and remodeling (50).

Wnt signaling pathway activity remains at a certain level during the early consolidation period but decreases during the middle and late consolidation periods (51). The role of Wnt in supporting bone mineralization during the bone healing process is clear (52). Xuemei Wang and colleagues administered LiCL, an activator of the Wnt pathway, drop by drop using an injection in a rat model of tibial distraction osteogenesis. The results showed that the Wnt signaling pathway could increase plasma osteocalcin levels and the average mineral density and hardness of new bone during the consolidation period. Therefore, the Wnt signaling pathway plays a role in promoting the mineralization of new bone during the consolidation period (53).

Applications of Distraction Osteogenesis



Distraction osteogenesis is a highly successful bone regeneration technique widely used in the treatment of bone loss due to congenital/acquired causes in both the long and tubular bones of the axial skeleton and the flat bones of the craniofacial skeleton (54). Distraction osteogenesis can be used to restore bone length in many conditions, including congenital bone defects, particularly congenital limb deficiencies, or acquired causes such as growth plate injuries that lead to growth arrest and subsequent limb length discrepancy (55,56). DO is also widely used for the reconstruction of large segmental skeletal defects using a special technique called bone transport. Approximately 150,000 segmental skeletal defects occur each year in the United States as a result of trauma (57).

Distraction Osteogenesis Procedures in The Maxillofacial Region

The application of distraction osteogenesis is not limited solely to the field of orthopedics. Mandibular distraction was first performed in a canine model in 1973 (58). However, it was first reported in humans in 1992 (16). Today, both extraoral and intraoral devices can be used, depending on the condition being treated (59). Commonly treated conditions include craniofacial deficiencies, syndromic craniosynostosis, Pierre Robin sequence, post-traumatic deformities, and sleep-related breathing disorders (60).

Distraction Osteogenesis of the Mandible

Mandibular hypoplasia is a common dentofacial deformity and can affect the entire mandible or certain parts of it—such as the body, ramus, condylar, genial, and dentoalveolar segments—in all three planes. Orthognathic procedures such as bilateral sagittal split ramus osteotomy (BSSRO) and genioplasty are widely performed worldwide to address high aesthetic demands and resolve functional problems. However, there are virtually no orthognathic surgical procedures available to correct deficiencies in the ramus and condyle of the posterior mandible. Cases of transverse mandibular insufficiency and atrophic alveolar ridges are also among the most challenging problems to address surgically (61).

The BSSO procedure, used to treat mandibular corpus deficiency, can correct deficiencies of up to 10 mm. However, for deficiencies exceeding this limit, distraction osteogenesis offers more permanent solutions. Presurgical orthodontic treatment is carried out to eliminate dental compensation so that actual deficiency can be estimated (61).

As distraction applied to the mandibular ramus will result in a change in the patient's occlusion, it is recommended that distraction be applied to the maxilla as well. In this way, the occlusal cantus can also be corrected (61).



In addition to the mandibular body and ramus, distraction can also be applied to the symphysis. In this technique, known as rapid mandibular expansion, an osteotomy is performed at the symphysis along the midline of the teeth, after which force is applied using a tooth- or tissue-supported distractor (62).

Distraction Osteogenesis of the Midface

Midface distraction can be performed at the Le Fort I, II, or III levels, or at the monoblock level. It is important to evaluate cranial volume, periorbital aesthetics and function, and occlusal requirements separately (63).

The distraction vector applied to the midface should be exactly midway between the upper incisor and the nasion. If the force vector is above this area, the maxillary complex rotates clockwise (64).

In monoblock distraction, in addition to the structures distracted in Lefort 3, the frontal region is also advanced, and force is applied using internal distractors (65).

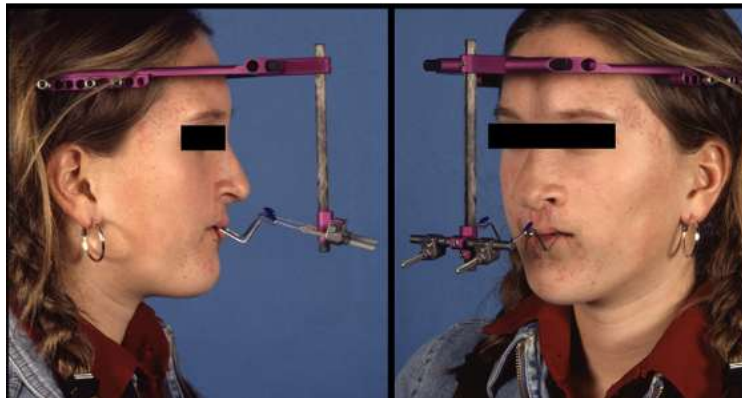
The latent period for distraction following Leforte osteotomies ranges from 3 to 5 days. The daily distraction rate is between 1 and 1.5 mm. In distraction performed following monoblock osteotomies, the rate should not exceed 1 mm. Additionally, for patients under 3 years of age, the latent period may be kept as short as 24 hours to prevent early consolidation. The daily distraction amount is 1–2 mm (66).

Distractors Used in Distraction Osteogenesis

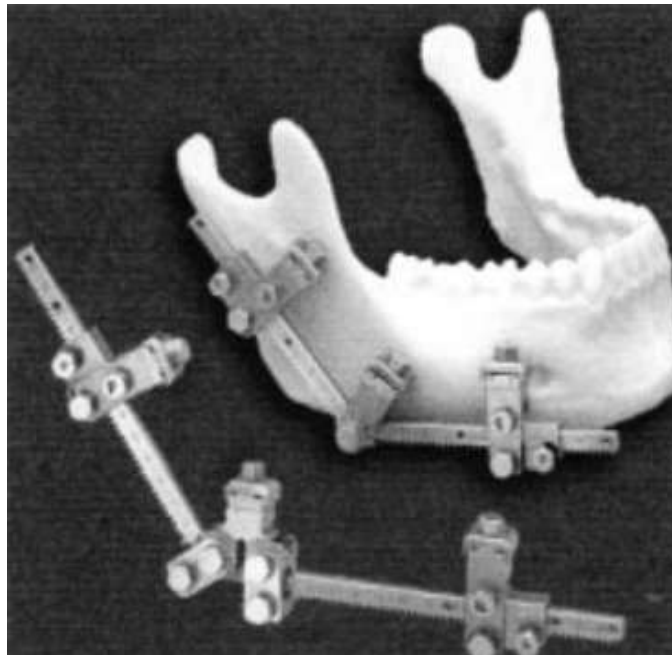
Distractors are classified into three categories based on the region where they are applied (mandible, maxillofacial region, or dentoalveolar region), the direction of the force they apply (unidirectional or multidirectional), and the site of application (internal or external) (67). (Figure 1.)

Factors such as the patient's age, the amount of distraction, and bone plasticity are evaluated when selecting an appropriate distractor. External distractors allow for a more limited amount of distraction compared to internal distractors (68). Due to the high degree of cranial plasticity in patients under three years of age, they cannot retain the fixation screws of external distractors. Internal distractors are more suitable for these patients (69). On the other hand, the need for an additional surgical procedure to remove internal distractors is a disadvantage (70). Because fractures may occur in the bone during activation of internal distractors in patients with a weak zygomatic-maxillary junction, external distractors are recommended for patients with zygomatic hypoplasia (71).

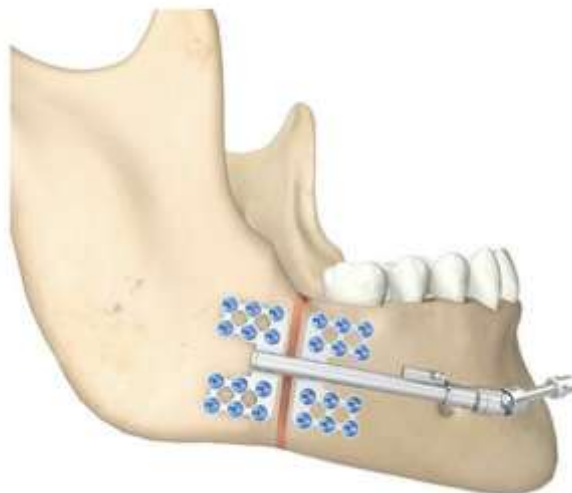
A



B



C



D

Figure 1. The images above show maxillary and mandibular distractors. a. Rigid External Distractor II (RED) (72), b. The ACE-Normed multi-directional distractor developed by Bitter and Klein (73) , c. The Zurich Pediatric Ramus Distractor by KLS-Martin (74), d. An internal distractor used for maxillary midface distraction (75).

Complications Arising During Distraction Osteogenesis

A complication is an unexpected deviation from the treatment plan that, if not properly corrected, will lead to a worsening of the current condition, the development of a new condition, or a recurrence of the initial pathological process (76).

The complications that occur can be summarized as those arising during the intraoperative phase, the distraction phase, and the consolidation phase.

Intraoperative Complications

Damage to Teeth:

The presence of impacted tooth buds in the osteotomy line or, alternatively, in the area where the device is fixed carries a high risk of unintentional iatrogenic injury. Freitas and colleagues evaluated injuries to molar teeth and buds in patients with an average age of 8.1 years who presented with various facial anomalies and underwent surgery due to mandibular DO. They found various outcomes related to dental injury, such as perforation or distal displacement of the tooth bud, damage causing root resorption, and dentigerous cyst formation (77). Preoperative radiographs should be carefully examined to avoid damaging the teeth. If there is a dental germ in the area where the distractor will be placed, the osteotomy should be performed as far as possible (78).

Neurosensory Dysfunction:

Temporary paresthesia in the marginal mandibular nerve has been reported with the surgical approach for device placement. Causes of inferior alveolar nerve injury include (a) direct injury during



osteotomy and distraction device application or device fixation, and (b) indirect injury such as progressive edema or focal nerve compression by device fixation elements. Wijbenga and colleagues reported an incidence of neurosensory dysfunction in 57 patients ($n = 91$) after mandibular DO; this dysfunction either resolved completely or decreased to a mild sensory function change. Subsequent symptoms include paresthesia, sensory and motor function loss, sometimes short-term soft tissue edema, sensory hyperesthesia, and motor dysfunction in the affected nerve (79).

Incomplete Osteotomy:

An incomplete osteotomy may ultimately lead to failure in achieving the desired amount/type of correction and to failure of the distractor. Common developing symptoms include severe pain in the osteotomy site, problems with device activation, and, as a result, damage to the device frame or loosening of the screws in the fixed plates (80). To avoid this complication, the distractor must be activated during surgery, and it must be observed that the bones are moving apart (78).

Bone Fracture:

Due to improper osteotomy, there is a high probability of unwanted fractures occurring in one or both cortices. Excessive force applied during completion of the osteotomy may cause an unwanted fracture in the segment. This fracture may increase the complexity of the surgery and the need for further reduction and fixation. To avoid this complication, it is important to verify that the osteotomy has been completed, to use the osteotome correctly, and to apply optimal force during bone separation (78).

Complications Occurring During the Distraction Phase

Malfunctions Occurring in the Distraction Device:

The term device malfunction covers two broad situations: breakage/damage and loosening/dislodgement of the device. The literature reports a cumulative incidence of 7.5% ($n = 1166$) for these two situations (60). Device breakage has been linked to early consolidation, incorrect activation, external trauma to the device, and unmanaged/neglected occlusal malocclusions (81). This complication is usually resolved with a second surgical procedure. The osteotomy lines are checked, and the device's position is corrected (78).

Pain in the Regeneration Zone:

Pain and functional problems are common findings associated with DO (82). Norholt and colleagues noted that many patients encountered problems activating the device, mostly due to the high speed and rhythm of DO, but all patients complete the procedure (83). To address pain occurring in the distraction area, the following approaches can be taken: selecting an appropriate distractor and



activation arm, prescribing analgesics suitable for the patient, and adjusting the activation increment—for example, using 0.25 mm × 4 instead of 0.5 mm × 2 (78).

Early Consolidation:

Normally, distraction regeneration mineralizes from the outer edges toward the center (84). However, during distraction, a radiolucent fibrous intermediate zone is always present at the center of regeneration. The disappearance of the intermediate zone during distraction indicates early consolidation of the regenerate. Causes of early consolidation include insufficient distraction rate and compressive forces on one side of the regeneration leading to early contact between the osteotomized segments. In this case, the operator will notice that turning the distractor becomes progressively difficult. To avoid this complication, the correct distraction rate must be applied; if union occurs, reoperation should be performed to perform an osteotomy (78).

Distraction Device-Related Interferences:

Most complications reported to be related to TMJ are associated with decreased mobility during the distraction process. In a retrospective study by Norholt and colleagues on patients undergoing mandibular DO, trismus was observed in 9.9% of patients (n = 131) due to the activated distraction device extending under the zygomatic arch (83). Furthermore, in maxillary DO, trismus may occur due to the interaction of the distraction arm with the coronoid process. Depending on the anatomy and distraction vector, procedures that are unproblematic during placement may present issues during removal (e.g., in cases of vertical extension of the ramus, the proximal plate may remain below the zygomatic arch). To avoid this complication, the correct distractor must be selected before surgery, and the force vectors must be planned correctly (78).

Excessive Strain on Soft Tissues:

Excessive strain on soft tissues can occur due to (a) inappropriate distraction forces and (b) natural compression caused by the distraction device's anchorage elements. Damage to various soft tissues such as blood vessels, peripheral nerves, skeletal muscles, and adjacent joints can vary with the amount of tension applied. If ischemia occurs, distraction should be stopped and the tension on the tissues should be reduced; when necessary, an evaluation should be performed via angiography. It should be kept in mind that complications such as cartilage necrosis and muscle atrophy may result from excessive tension, and follow-up visits should be scheduled more frequently (78).

Complications Occurring During the Consolidation Phase

Infection:



Infection is one of the concerning complications that may arise at various stages of distraction. They can routinely present as minor superficial skin infections, sinus tract/fistula/abscess formation, or serious infections that ultimately progress to osteomyelitis (78). Infection may also occur as minor infections due to insufficient stability of the device and fixation plate screws during fixation, failure of oral hygiene measures, the presence of the distractor in the activation area during consolidation (which acts as a potential source of infection), the type of distraction device used, and the quality of the distracted bone. Proper hygiene procedures, along with monitoring screw stability during appointments, to prevent infections that may occur during the consolidation phase (78).

Hypertrophic Scar:

Linear cutaneous scars develop during the distraction period when extraoral appliances are used. These scars are more common in appliances that create a long fistula tract. To avoid this complication, the screws can be placed at an angle or in less visible areas. Hypertrophic scar formation can also be prevented by compressing the skin tissue in the area where the distractor screws will be placed (78).

Incomplete Ossification:

In older patients, those who smoke, those with poor oral hygiene, and those who have undergone radiotherapy to the jaw region, insufficient regenerative ossification may be an expected sequela. With a higher distraction rate, bone may form weakly and appear radiographically porous, thin, or hourglass-shaped. In this case, if the distraction device is removed before the newly formed bone is fully mineralized, the tension of the surrounding muscles and soft tissues overcomes the internal forces of the incompletely ossified region, leading to bending of the newly formed bone or loss of the distracted bone volume (58). To avoid this complication, the device should not be removed until cortical margins are visible on X-rays. In some cases, it may need to be secured with fixation plates (78).

Fracture in the Distraction Site:

This can occur due to an insufficient consolidation period, overly aggressive functional rehabilitation during the remodeling period, inadequate immobilization after device removal when indicated, and excessive force applied to the bone segments (78).

Relapse:

As mentioned, relapse is most commonly associated with maxillofacial distraction osteogenesis. Causes of relapse include increased distraction speed and rhythm, greater reflection of the periosteal flap, and placement of the osteotomy incision proximal to the pterygomasseteric region in cases of mandibular body distraction (78). Van Strijen and colleagues concluded that patients with



a high mandibular plane angle are at increased risk for recurrence (85). To avoid this complication, the distraction rate should be reduced and periosteal stripping should be minimized (78).

Temporomandibular Joint Problems:

In particular, TMJ sequelae following mandibular distraction have been noted in elderly and syndromic patients with pre-existing condylar pathologies, including degenerative arthrosis of the joint surfaces, increased trabecular bone formation, irregularities of the articular cartilage, and reduction of the temporomandibular joint space (85). Schlund and colleagues evaluated three patients with TMJ ankylosis in their retrospective studies and concluded that this possibility is higher in patients with congenitally deformed TMJ. They also suggested the use of costochondral grafts as an alternative in these cases (86)

SUMMARY / SONUÇ

Distraction osteogenesis may represent the most significant advancement in the field of craniofacial surgery in recent years. As experience increases, better data on the various applications of this technology is being obtained.

Distraction osteogenesis is widely used and has a high potential for complications, so it is important to learn more about it. However, all these complications can be minimized or prevented in most cases with proper preoperative planning, comprehensive surgical principles, and postoperative management. Considering all these factors, distraction osteogenesis can be considered a gold standard treatment with widespread applications.

REFERENCES / REFERANSLAR

1. Cherkashin AM. Distraction Osteogenesis: Origins and Evolution. Distraction Osteogenesis and Tissue Engineering. 1998;1-35
2. Peltier LF. A brief history of traction. The Journal of Bone and Joint Surgery. 1968;50(8): 1603–1617.
3. Shankar Natsu S, Ali I, Alam S, Yada Giri K, Agarwal A, Ajit Kulkarni V. The biology of distraction osteogenesis for correction of mandibular and craniomaxillofacial defects: A review. Dental Research Journal. 2014;11(1):16-26.
4. Guerrero CA, Bell WK, Contasti GL, Rodríguez AM. Intraoral mandibular distraction osteogenesis. Seminars in Orthodontics. 1999;5(1):35-40. [https://doi.org/10.1016/S1073-8746\(99\)80040-1](https://doi.org/10.1016/S1073-8746(99)80040-1)



5. Ilizarov GA, Soïbel'man LM. Clinical and experimental data on bloodless lengthening of lower extremities. Eksperimental'naia Khirurgiia i Anesteziologiya. 1969;14(4):27-32.
6. Ilizarov GA. The principles of the Ilizarov method. Bulletin of the Hospital for Joint Diseases Orthopaedic Institute. 1988; 48(1): 1-11.
7. Ilizarov GA. The tension-stress effect on the genesis and growth of tissues. Part I. The influence of stability of fixation and soft-tissue preservation. Clinical Orthopaedics and Related Research. 1989a; 238:249-281.
8. Ilizarov GA. (1989b). The tension-stress effect on the genesis and growth of tissues: Part II. The influence of the rate and frequency of distraction. Clinical Orthopaedics and Related Research. 1989b; 239: 263-285.
9. Ilizarov GA. Some possibilities with our method for treating damage to and disorders of locomotor apparatus. The Journal of Craniofacial Surgery. 1995;6(5): 352-354. <https://doi.org/10.1097/00001665-199509000-00002>
10. Gubin A, Borzunov D, Malkova T. Ilizarov Method for Bone Lengthening and Defect Management Review of Contemporary Literature. Bulletin of the Hospital for Joint Disease. 2013; 74(2): 145-154.
11. Codivilla A. (1994). On the means of lengthening, in the lower limbs, the muscles and tissues which are shortened through deformity. 1904. Clinical Orthopaedics and Related Research. 1994;301: 4-9.
12. Li Y, Chen SK, Li L, Qin L, Wang XL, Lai YX. Bone defect animal models for testing efficacy of bone substitute biomaterials. Journal of Orthopaedic Translation. 2015; 3(3): 95-104. <https://doi.org/10.1016/j.jot.2015.05.002>
13. Dimitriou R, Jones E, McGonagle D, Giannoudis PV. Bone regeneration: current concepts and future directions. BMC Medicine. 2011; 9: 66. <https://doi.org/10.1186/1741-7015-9-66>
14. Moore DC, Leblanc CW, Müller R, Crisco JJ, Ehrlich MG. Physiologic weight-bearing increases new vessel formation during distraction osteogenesis: a micro-tomographic imaging study. Journal of Orthopaedic Research : Official Publication of the Orthopaedic Research Society. 2003; 21(3): 489-496. [https://doi.org/10.1016/S0736-0266\(02\)00234-6](https://doi.org/10.1016/S0736-0266(02)00234-6)
15. Aronson J. Current Concepts Review - Limb-Lengthening, Skeletal Reconstruction, and Bone Transport with the Ilizarov Method*. The Journal of Bone & Joint Surgery. 1997; 79(8): 1243-1258. <https://doi.org/10.2106/00004623-199708000-00019>
16. McCarthy JG, Schreiber J, Karp N, Thorne CH, Grayson BH. Lengthening the Human Mandible by Gradual Distraction. Plastic and Reconstructive Surgery. 1992; 89(1): 1-8. <https://doi.org/10.1097/00006534-199289010-00001>
17. Liu Z, Yang J, Zhou C, Liu Y, Luo E. A bibliometric analysis of research on craniomaxillofacial distraction osteogenesis from 2000 to 2021. Frontiers in Surgery. 2022;9. <https://doi.org/10.3389/fsurg.2022.932164>
18. Tong H, Liu L, Tang X, Song T, Yin N, Zhang Z, Zhao Z. Midface Distraction Osteogenesis Using a Modified External Device With Elastic Distraction for Crouzon Syndrome. Journal of Craniofacial Surgery. 2017;28(6):1573-1577. <https://doi.org/10.1097/SCS.0000000000003377>
19. Akizuki T, Komuro Y, Ohmori K. Distraction osteogenesis for craniosynostosis. Neurosurgical Focus. 2000; 9(3): 1-7. <https://doi.org/10.3171/foc.2000.9.3.2>
20. Urban IA, Montero E, Monje A, Sanz-Sánchez I. Effectiveness of vertical ridge augmentation interventions: A systematic review and meta-analysis. Journal of Clinical Periodontology. 2019; 46(S21): 319-339. <https://doi.org/10.1111/jcpe.13061>



21. Toledano-Serrabona J, Sánchez-Garcés MÁ, Sánchez-Torres A, Gay-Escoda C. Alveolar distraction osteogenesis for dental implant treatments of the vertical bone atrophy: A systematic review. *Medicina Oral, Patología Oral y Cirugía Bucal*. 2019; 24(1): e70–e75. <https://doi.org/10.4317/medoral.22750>
22. Suh J, Choi TH, Baek SH, Kim JC, Kim S. Mandibular Distraction in Unilateral Craniofacial Microsomia. *Plastic and Reconstructive Surgery*. 2013;132(5): 1244–1252. <https://doi.org/10.1097/PRS.0b013e3182a48cf9>
23. Gosain AK. Distraction Osteogenesis of the Craniofacial Skeleton. *Plastic and Reconstructive Surgery*. 2001;107(1): 278–280. <https://doi.org/10.1097/00006534-200101000-00050>
24. Saman M, Abramowitz JM, Buchbinder D. Mandibular osteotomies and distraction osteogenesis: evolution and current advances. *JAMA Facial Plastic Surgery*. 2013;15(3):167–173. <https://doi.org/10.1001/jamafacial.2013.44>
25. Annino DJ, Goguen LA, Karmody CS. Distraction osteogenesis for reconstruction of mandibular symphyseal defects. *Archives of Otolaryngology--Head & Neck Surgery*. 1994;120(9): 911–916. <https://doi.org/10.1001/archotol.1994.01880330005002>
26. Maheshwari S, Verma S, Tariq Mohd, Prabhat K, Kumar S. Biomechanics and orthodontic treatment protocol in maxillofacial distraction osteogenesis. *National Journal of Maxillofacial Surgery*. 2011;2(2): 120. <https://doi.org/10.4103/0975-5950.94464>
27. Aronson J. The Biology of Distraction Osteogenesis. In Chapman MW (Ed.), *Operative Orthopedics*. 1993;2: 873–887.
28. Alman BA, Kelley SP, Nam D. Heal thyself: using endogenous regeneration to repair bone. *Tissue Engineering. Part B, Reviews*. 2011;17(6):431–436. <https://doi.org/10.1089/ten.TEB.2011.0189>
29. Ai-Aql ZS, Alagl AS, Graves DT, Gerstenfeld LC, Einhorn TA. Molecular mechanisms controlling bone formation during fracture healing and distraction osteogenesis. *Journal of Dental Research*. 2008;87(2):107–118. <https://doi.org/10.1177/154405910808700215>
30. Cho TJ, Kim JA, Chung CY, Yoo WJ, Gerstenfeld LC, Einhorn TA, Choi IH. Expression and role of interleukin-6 in distraction osteogenesis. *Calcified Tissue International*. 2007; 80(3): 192–200. <https://doi.org/10.1007/s00223-006-0240-y>
31. Runyan CM, Gabrick KS. Biology of Bone Formation, Fracture Healing, and Distraction Osteogenesis. *The Journal of Craniofacial Surgery*. 2017;28(5):1380–1389. <https://doi.org/10.1097/SCS.00000000000003625>
32. Marsell R, Einhorn TA. The biology of fracture healing. *Injury*. 2011; 42(6): 551–555. <https://doi.org/10.1016/j.injury.2011.03.031>
33. Kon T, Cho TJ., Aizawa T, Yamazaki M, Nooh N, Graves D, Gerstenfeld LC, Einhorn T A. Expression of osteoprotegerin, receptor activator of NF-kappaB ligand (osteoprotegerin ligand) and related proinflammatory cytokines during fracture healing. *Journal of Bone and Mineral Research: The Official Journal of the American Society for Bone and Mineral Research*, 2001;16(6): 1004–1014. <https://doi.org/10.1359/jbmr.2001.16.6.1004>
34. Alshahrani I. Biomolecular phases in transverse palatal distraction: A review. *Saudi Journal of Biological Sciences*, 2018;25(7): 1322–1325. <https://doi.org/10.1016/j.sjbs.2018.05.009>
35. Yang S, Wang N, Ma Y, Guo S, Guo S, Sun H. Immunomodulatory effects and mechanisms of distraction osteogenesis. In *International Journal of Oral Science*. 2022;14 (4). <https://doi.org/10.1038/s41368-021-00156-y>



36. Cano J, Campo J, Moreno LA, Bascones A. Osteogenic alveolar distraction: a review of the literature. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 2006; 101(1): 11–28. <https://doi.org/10.1016/j.tripleo.2005.04.015>
37. Kessler P, Neukam FW, Wiltfang J. Effects of distraction forces and frequency of distraction on bony regeneration. *The British Journal of Oral & Maxillofacial Surgery*. 2005; 43(5): 392–398. <https://doi.org/10.1016/j.bjoms.2004.10.015>
38. Kessler PA, Merten HA, Neukam FW, Wiltfang J. The effects of magnitude and frequency of distraction forces on tissue regeneration in distraction osteogenesis of the mandible. *Plastic and Reconstructive Surgery*. 2002; 109(1): 171–180. <https://doi.org/10.1097/00006534-200201000-00027>
39. Nogueira MP, Paley D, Bhavre A, Herbert A, Nocente C, Herzenberg JE. Nerve lesions associated with limb-lengthening. *The Journal of Bone and Joint Surgery. American Volume*. 2003;85(8): 1502–1510. <https://doi.org/10.2106/00004623-200308000-00011>
40. Schmidt-Bleek K, Schell H, Schulz N, Hoff P, Perka C, Buttgereit F, Volk HD, Lienau J, Duda GN. Inflammatory phase of bone healing initiates the regenerative healing cascade. *Cell and Tissue Research*. 2012;347(3): 567–573. <https://doi.org/10.1007/s00441-011-1205-7>
41. Gerstenfeld LC, Cho TJ, Kon T, Aizawa T, Tsay A, Fitch J, Barnes GL, Graves DT, Einhorn TA. Impaired fracture healing in the absence of TNF- α signaling: the role of TNF- α in endochondral cartilage resorption. *Journal of Bone and Mineral Research : The Official Journal of the American Society for Bone and Mineral Research*. 2003; 18(9): 1584–1592. <https://doi.org/10.1359/jbmr.2003.18.9.1584>
42. Liu H, Li D, Zhang Y, Li M. Inflammation, mesenchymal stem cells and bone regeneration. *Histochemistry and Cell Biology*. 2018; 149(4): 393–404. <https://doi.org/10.1007/s00418-018-1643-3>
43. Tsukasaki M, Takayanagi H. Osteoimmunology: evolving concepts in bone-immune interactions in health and disease. *Nature Reviews. Immunology*, 2019;19(10):626–642. <https://doi.org/10.1038/s41577-019-0178-8>
44. Chen J, Hua J, Song W. Screen Key Genes Associated with Distraction-Induced Osteogenesis of Stem Cells Using Bioinformatics Methods. *International Journal of Molecular Sciences*. 2021; 22(12). <https://doi.org/10.3390/ijms22126505>
45. Hunter CA, Jones SA. IL-6 as a keystone cytokine in health and disease. *Nature Immunology*. 2015; 16(5): 448–457. <https://doi.org/10.1038/ni.3153>
46. Ando Y, Matsubara K, Ishikawa J, Fujio M, Shohara R, Hibi H, Ueda M, Yamamoto A. Stem cell-conditioned medium accelerates distraction osteogenesis through multiple regenerative mechanisms. *Bone*. 2014; 61: 82–90. <https://doi.org/10.1016/j.bone.2013.12.029>
47. Cillo JE, Gassner R, Koepsel RR, Buckley MJ. Growth factor and cytokine gene expression in mechanically strained human osteoblast-like cells: implications for distraction osteogenesis. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*. 2000;90(2): 147–154. <https://doi.org/10.1067/moe.2000.107531>
48. Lammens J, Liu Z, Aerssens J, Dequeker J, Fabry G. Distraction bone healing versus osteotomy healing: a comparative biochemical analysis. *Journal of Bone and Mineral Research : The Official Journal of the American Society for Bone and Mineral Research*, 1998;13(2): 279–286. <https://doi.org/10.1359/jbmr.1998.13.2.279>



49. Mehrara BJ, Rowe NM, Steinbrech DS, Dudziak ME, Saadeh PB, McCarthy JG, Gittes GK, Longaker MT. Rat mandibular distraction osteogenesis: II. Molecular analysis of transforming growth factor beta-1 and osteocalcin gene expression. *Plastic and Reconstructive Surgery*. 1999; 103(2): 536-547. <https://doi.org/10.1097/00006534-199902000-00026>
50. Xie MK, Hu CB, Zhou B, Wu GP. Effect of gene transfection timing on TGF- β 1 expression in rabbit mandibular distraction gap. *Genetics and Molecular Research : GMR*. 2017;16(2). <https://doi.org/10.4238/gmr16029330>
51. Kasaai B, Moffatt P, Al-Salmi L, Lauzier D, Lessard L, Hamdy RC. Spatial and temporal localization of WNT signaling proteins in a mouse model of distraction osteogenesis. *The Journal of Histochemistry and Cytochemistry: Official Journal of the Histochemistry Society*. 2012; 60(3): 219-228. <https://doi.org/10.1369/0022155411432010>
52. Schupbach D, Comeau-Gauthier M, Harvey E, Merle G. Wnt modulation in bone healing. *Bone*. 2020; 138: 115491. <https://doi.org/10.1016/j.bone.2020.115491>
53. Wang X, Zhu S, Jiang X, Li Y, Song D, Hu J. Systemic administration of lithium improves distracted bone regeneration in rats. *Calcified Tissue International*. 2015;96(6): 534-540. <https://doi.org/10.1007/s00223-015-0004-7>
54. Hamdy RC, Rendon JS, Tabrizian M. Distraction osteogenesis and its challenges in bone regeneration. *Bone regeneration*. 2012; 8: 177-204.
55. Birch JG, Samchukov ML. Use of the Ilizarov method to correct lower limb deformities in children and adolescents. *The Journal of the American Academy of Orthopaedic Surgeons*. 2004;12(3): 144-154. <https://doi.org/10.5435/00124635-200405000-00002>
56. Murray J, Fitch R. Distraction Histiogenesis: Principles and Indications. *The Journal of the American Academy of Orthopaedic Surgeons*, 1996;4(6): 317-327. <https://doi.org/10.5435/00124635-199611000-00004>
57. Cierny G, Zorn KE. Segmental tibial defects. Comparing conventional and Ilizarov methodologies. *Clinical Orthopaedics and Related Research*. 1994;301: 118-123.
58. Snyder CC, Levine GA, Swanson HM, Browne EZ. Mandibular lengthening by gradual distraction. Preliminary report. *Plastic and Reconstructive Surgery*. 1973; 51(5): 506-508. <https://doi.org/10.1097/00006534-197305000-00003>
59. Goldwasser BR, Papadaki ME, Kaban LB, Troulis MJ. Automated continuous mandibular distraction osteogenesis: review of the literature. *Journal of Oral and Maxillofacial Surgery : Official Journal of the American Association of Oral and Maxillofacial Surgeons*, 2012;70(2): 407-416. <https://doi.org/10.1016/j.joms.2011.01.042>
60. Mofid MM, Manson PN, Robertson BC, Tufaro AP, Elias JJ, Vander Kolk CA. Craniofacial Distraction Osteogenesis: A Review of 3278 Cases. *Plastic and Reconstructive Surgery*. 2001; 108(5): 1103-1114. <https://doi.org/10.1097/00006534-200110000-00001>
61. Sahoo NK, Issar Y, Thakral A. Mandibular Distraction Osteogenesis. *The Journal of Craniofacial Surgery*. 2019; 30(8): e743-e746. <https://doi.org/10.1097/SCS.00000000000005753>
62. Chung YW, Tae KC. Dental stability and radiographic healing patterns after mandibular symphysis widening with distraction osteogenesis. *The European Journal of Orthodontics*. 2007; 29(3): 256-262.



63. Witherow H, Dunaway D, Evans R, Nischal KK, Shipster C, Pereira V, Hearst D, White M, Jones BM, Hayward R. Functional outcomes in monobloc advancement by distraction using the rigid external distractor device. *Plastic and Reconstructive Surgery*. 2008; 121(4): 1311–1322. <https://doi.org/10.1097/01.prs.0000305538.75347.52>
64. Shetye PR, Giannoutsos E, Grayson BH, McCarthy JG. Le Fort III distraction: part I. controlling position and vectors of the midface segment. *Plast Reconstr Surg*. 2009;124:871-878.
65. Arnaud E, Di Rocco F. Faciocraniosynostosis: monobloc frontofacial osteotomy replacing the two-stage strategy? *Childs Nerv Syst*. 2012;28(9):1557-64. doi: 10.1007/s00381-012-1853-2. Epub 2012 Aug 8
66. Konofaos P, Wallace RD. Distraction Osteogenesis in Craniofacial Surgery: Past, Present, and Future. *J Craniofac Surg*. 2021;32(Suppl 3):1221-1228. doi: 10.1097/SCS.00000000000007333. PMID: 33710057
67. Andrade N, Gandhewar T, Kalra R. Development and evolution of distraction devices: Use of indigenous appliances for Distraction Osteogenesis-An overview. *Annals of Maxillofacial Surgery*. 2011; 1(1): 58
68. Shetye PR, Boutro S, Grayson BH, McCarthy JG. Midterm Follow-Up of Midface Distraction for Syndromic Craniosynostosis: A Clinical and Cephalometric Study. *Plastic and Reconstructive Surgery*. 2007; 120(6): 1621–1632. <https://doi.org/10.1097/01.prs.0000267422.37907.6f>
69. Fearon JA. Halo Distraction of the Le Fort III in Syndromic Craniosynostosis: A Long-Term Assessment. *Plastic and Reconstructive Surgery*. 2005; 115(6): 1524–1536. <https://doi.org/10.1097/01.PRS.0000160271.08827.15>
70. Cohen SR, Holmes RE. (2001). Internal Le Fort III Distraction with Biodegradable Devices. *Journal of Craniofacial Surgery*. 2001;12(3):264–272. <https://doi.org/10.1097/00001665-200105000-00013>
71. Al-Namnam NMN, Hariri F, Rahman ZAA. Distraction osteogenesis in the surgical management of syndromic craniosynostosis: a comprehensive review of published papers. In *British Journal of Oral and Maxillofacial Surgery*. 2018; 56(5):353–366. <https://doi.org/10.1016/j.bjoms.2018.03.002>
72. Nout E, Wolvius EB, van Adrichem LNA, Ongkosuwito EM. Complications in maxillary distraction using the RED II device: a retrospective analysis of 21 patients. *International journal of oral and maxillofacial surgery*. 2006;35(10): 897-902.
73. Cope JB, Samchukov ML, Cherkashin AM. Mandibular distraction osteogenesis: A historic perspective and future directions. *American Journal of Orthodontics and Dentofacial Orthopedics*. 1999; 115(4): 448–460.
74. <https://www.klsmartin.com/en/products/implants-cmf/distractors-and-fixators/>
75. <https://www.resimpex.com.uy/admin/basic/web/contenidos/cajas/1484340795.pdf>
76. Cherkashin AM, Samchukov ML. Potential mistakes and complications. *Craniofacial Distraction Osteogenesis*. 2001; 583-594.
77. Da Silva Freitas R, Tolazzi ARD, Alonso N, Cruz GAO, Busato L. Evaluation of Molar Teeth and Buds in Patients Submitted to Mandible Distraction: Long-Term Results. *Plastic and Reconstructive Surgery*. 2008; 121(4): 1335–1342. <https://doi.org/10.1097/01.prs.0000304444.43168.6a>
78. Kende PP, Sarda AS, Desai H, Landge J, Nimma V, Varte V. Complications of distraction osteogenesis: Narrative review. In *Oral Surgery*. 2021;14(4):412–422. <https://doi.org/10.1111/ors.12613>
79. Wijbenga JG, Verlinden CRA, Jansma J, Becking AG, Stegenga B. Long-lasting neurosensory disturbance following advancement of the retrognathic mandible: distraction osteogenesis versus bilateral sagittal split



osteotomy. International Journal of Oral and Maxillofacial Surgery. 2009; 38(7): 719–725. <https://doi.org/10.1016/j.ijom.2009.03.714>

80. Troulis MJ, Kaban LB. Complications of mandibular distraction osteogenesis. Oral and Maxillofacial Surgery Clinics of North America. 2003; 15(2): 251–264. [https://doi.org/10.1016/S1042-3699\(02\)00101-2](https://doi.org/10.1016/S1042-3699(02)00101-2)

81. Uckan S, Veziroglu F, Arman A. Unexpected breakage of mandibular midline distraction device: case report. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2006; 102(6): e21–e25. <https://doi.org/10.1016/j.tripleo.2006.05.025>

82. Hurmerinta K, Peltomäki T, Hukki J. Unexpected events during mandibular distraction osteogenesis. Scandinavian Journal of Plastic and Reconstructive Surgery and Hand Surgery. 2004; 38(4): 209–214. <https://doi.org/10.1080/02844310410025312>

83. Nørholt SE, Jensen J, Schou S, Pedersen TK. Complications after mandibular distraction osteogenesis: a retrospective study of 131 patients. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2011; 111(4): 420–427. <https://doi.org/10.1016/j.tripleo.2010.05.050>

84. Ahn JG, Figueroa AA, Braun S, Polley JW. Biomechanical considerations in distraction of the osteotomized dentomaxillary complex. American Journal of Orthodontics and Dentofacial Orthopedics. 1999; 116(3): 264–270. [https://doi.org/10.1016/S0889-5406\(99\)70236-2](https://doi.org/10.1016/S0889-5406(99)70236-2)

85. van Strijen PJ, Breuning KH, Becking AG, Tuinzing DB. Stability after distraction osteogenesis to lengthen the mandible: results in 50 patients. Journal of Oral and Maxillofacial Surgery. 2004; 62(3): 304–307. <https://doi.org/10.1016/j.joms.2003.02.003>

86. Schlund M, Touzet-Roumazielle S, Nicot R, Ferri J. Temporomandibular Joint Ankylosis Following Mandibular Distraction Osteogenesis: A Dreadful Complication. Journal of Craniofacial Surgery. 2020; 31(1): 222–225. <https://doi.org/10.1097/SCS.0000000000005911>