# Mandibular Midline Distraction Osteogenesis

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**Abstract**

In orthodontics, bone structure, its density and dimensions play an essential role by explaining limitations in magnitude, size and extent of tooth movement. Severe anterior crowding is one of the most frequently encountered dental malocclusions. Its therapy is mostly limited by lack of basal and alveolar bone and it often involves tooth extractions. Mandibular midline distraction osteogenesis is a method of natural bone generation and also a treatment option to achieve space regaining in a much-reduced lower jaw with distinctive frontal place deficit and severe anterior crowding, without sacrificing permanent teeth. McCarthy and Guerrero were of the first researchers reporting on this method applied on human lower jaws and they increased clinical interest in this approach. Although this method has been clinically used ever since, many questions concerning effects on bone regeneration speed, bone quality, tooth movement into regenerated area, periodontal health and long-time stability of treatment outcomes have not been sufficiently investigated. This overview should present the current clinical and biological state of knowledge about bone gain and tooth movement through regenerate bone. Furthermore it should encourage interest in further research on this topic.

*Key Words: Orthodontics, Anterior Crowding, Mandibular Midline Distraction, Osteogenesis, Tooth Movement, Bone Gain*

## Background

Anterior crowding appears very frequently in orthodontic patients [1]. Depending on its severity it can be treated conventionally; however extractions of permanent teeth often cannot be avoided in order to prevent reduced long term results.

On account that the mandibular symphysis fuses around the age of one and cannot be opened with orthodontic devices - at least not in the conventional manner [2] an expansion of the lower dental arch is limited. Mandibular distraction osteogenesis is an alternative to extractions in the case of transverse mandibular deficiency and severe anterior crowding by gaining bone in the alveolar process in order to move teeth through it osteodistraction is a method of tissue engineering that exploits the body's innate capacity to respond to applied controlled gradual mechanical tension forces across a bone gap of two osteotomised bone segments by generating new bone parallel to the direction of traction between them [2-6]. This process of growing new bone by mechanically stretching preexisting vascularized bone tissue [7] comes originally from orthopedics and was described for the first time in 1905 by the Italian Codivilla, who extended a shortened femur [8]. Nevertheless, due to the high complications rate [9] as well as the low acceptance observed for this procedure in professional circles [6], this method initially fell into oblivion [2]. It was the Russian surgeon Illizarov who rediscovered this technique in the 1950s through comprehensive laboratory and clinical studies on long bones and brought it to wider attention [8,10]. This technique was further described in 1973 by Synders who reported the lengthening of a mandible using a canine model [11], but it was not until the early 1990s that this technology was transferred to the human craniofacial region by McCharthy, Perrott and Guerrero [12-14]. In their study they reported the successful lengthening [15] and widening of the human mandible [14]. This method, well known as "Illizarov technic" or "tension stress effect", uses the inert endogenous ability of bone tissue to react on itself by growth adaption (osteogenesis) as well as new tissue formation utilizing its surrounding soft tissue (histogenesis), including nerves and vessels [16].

Nowadays, more than 20 years after its first successful clinical application, interest in this technology is still very high due to the fact that detailed mechanisms of endogenous bone generation are not completely enlightened yet [17,18]. Detailed histological analysis of the ossification process after distraction osteogenesis is available deriving mainly from animal-experimental studies [19] as well as from human biopsy material [18,20]. However, there is still a lack of knowledge regarding the exact biomechanical pathways initiating and maintaining bone formation as well as the conversion of the mechanical stimulus into a cellular answer influencing distraction protocols [19,21].

## Clinical Aspects

Clinically, distraction osteogenesis consists of the fixation of the distractor, pre- or intra-operative, depending on the selected distraction device, the surgical intervention, a latency period, a consolidation period and finally of the remodeling process including orthodontic arch alignment.

Apart from the many specific variations there are typically three distraction devices to discern, depending on the type of fixation and the location of the force vectors. The bone-borne distraction device is located at the basal buccal bone of the mandible corpus and fixated through screws intra-operatively while arms with the active part are passing through the mucosa. A more proportional distraction without dental side effects like tipping has also been reported [22]. The tooth-borne distraction device, usually placed lingually, consists of an activation screw which is attached to orthodontic bands on the premolar and molar teeth. It is less expensive in

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manufacturing, easy to apply and allows an improved optical control of the distraction progression by the orthodontist [23,24] (*Figures 1-4*). A V-shaped opening of the distraction gap with less basal space gain and dental side effects has also been reported [23]. There is no need for a second surgery increasing patients' acceptance [2]. The hybrid device is located at the buccal bony mandibular corpus as well as the dentition. Arms pass through the soft tissue and the screw is located at a comparable place, alike to the bone-borne distractor. A second surgery is afterwards needed to remove it.

***Figure 1.*** *Cast of a patient with severe anterior mandibular crowding, difficult to manage without extractions.*

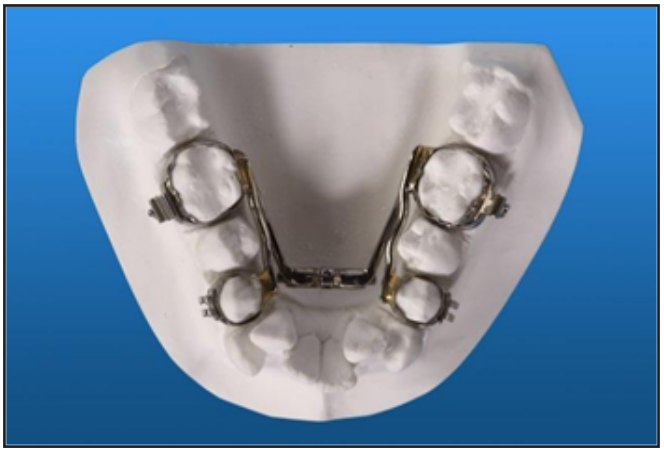

***Figure 2.*** *Cast with a tooth-borne distraction device with 4 fixation points at the Molars and Premolars. The screw is located at the lingual part of the mandible.*

***Figure 3.*** *Situation after distraction and arch alignment with fixed orthodontic appliances.*

Usually the osteotomy to separate the mandible into two bone segments starts at the bottom of the chin, at the symphysis, with a vertical section up to two-thirds of mandibular height where incisor roots starts, using oscillating saws and burs [2,18] (*Figure 5*). Since the osteotomy is carried out in the tooth bearing area of the mandible, interdental separation is completed manually with osteotomes, chisels or a spatula in order not to hurt the incisors' roots [2,9,18]. A test activation of the distraction device ensures that mandibular halves are mobile [18] (*Figure 6*). In order for interdental osteotomy to be performed, adequate bone should exist between the roots for them not to be injured and to allow undisturbed bone regeneration after distraction, as intact alveolar bone at both sides of the osteotomy line, without tooth exposure is deemed necessary for bone induction to be achieved [25]. In

***Figure 4.*** *Cast after successful treatment of anterior crowding by mandibular distraction osteogenesis. A bonded retainer should maintain treatment stability.*

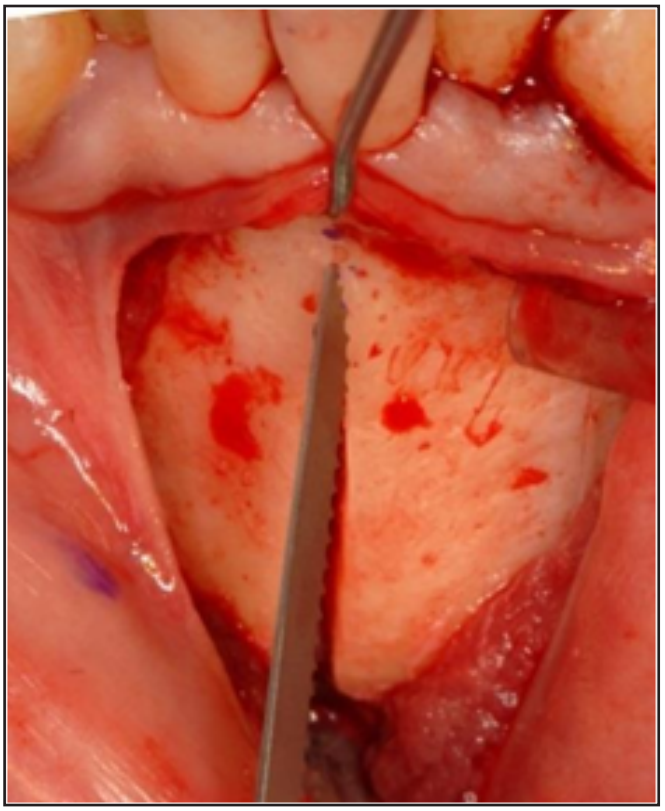

***Figure 5.*** *Surgical intervention of mandibular distraction osteotomy. Vertical incision, starting at the bottom of the chin up to one-third of the mandible corpus, not to hurt the incisor roots.*

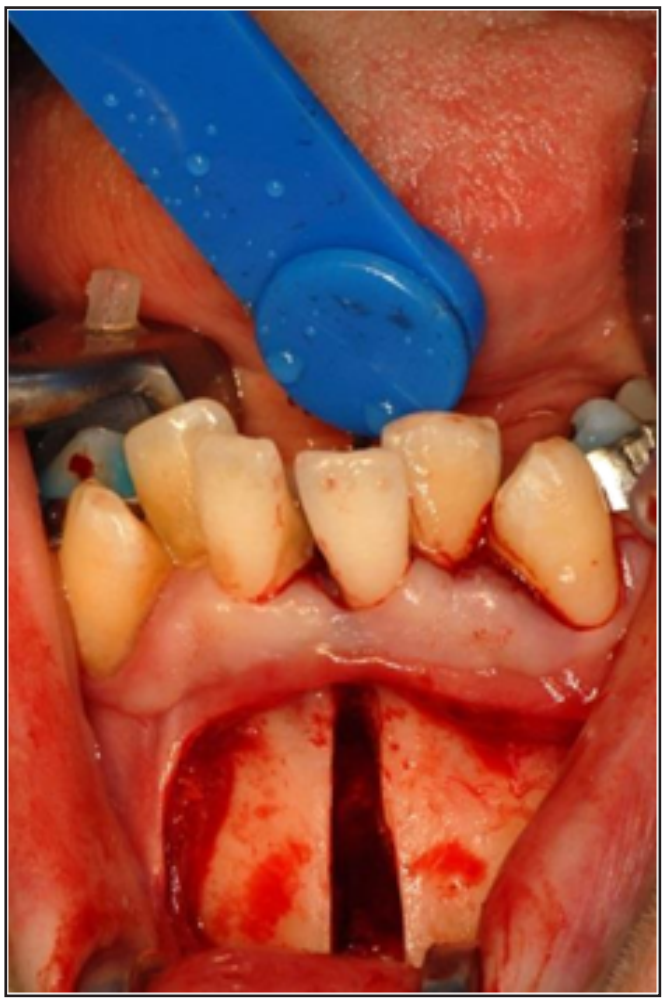

***Figure 6.*** *Intraoperative test-activation of the distraction device, ensuring that osteotomy was successful. Note the asymmetric gap opening presumably due to increased soft tissue resistance.*

cases of severe anterior crowding and limited space between the roots an orthodontic space opening prior to surgery is recommended.

The Latency period represents the time between surgery and device activation, which is required for blood clot stabilization and reparative callus formation between the osteotomised bone segments. An extremely shortened latency time is supposed to affect stability and new bone formation negatively whereas an overly long latency time to assist in the risk of premature bone union [2]. In the literature periods between four to six days [26] or five up to seven days have frequently been reported [2,4,6,9,18,19,27,28]. Research in humans revealed early re-ossification in some cases with a latency of one week, stating that this period, till the device activation, might have been rather long [2]. Additionally in several animal experimental models however, an equivalent clinical elongation and stability with a latency of either zero, four or seven days was achieved, thereby confirming that a latency period is not necessary for successful healing and adequate bone formation [3,29,30].

The term "Distraction period" is used to describe the amount of time needed for a traction force to be applied to the bone segments, in order to create the desired amount of space between them, thereby inducing new bone formation. An overly low distraction rate could compromise the procedure, leading to a premature closure of the distraction gap [4]. Higher and faster rates of activation leads to a higher bone quantity with a nevertheless immature new formed bone matrix [3,9]. The distraction protocol currently applied in the craniofacial region derives from clinical and experimental studies in long bones in orthopedics [16,31,32] and animal-experimental studies in the lower jaw [4,11]. In several animal-experimental studies, the greatest clinical, histological and biochemical stability as well as a higher bone mineralization quality was achieved with a 1 mm rather than 2, 3 or 4 mm distraction per day [3,9,29]. Hence, a slower activation of 1 mm/d with a slight and continuous force application should be preferred [9]. The most frequently reported and currently applied distraction rate in the human craniofacial region is 1 mm per day [16] split into 0.5 mm twice daily [18,26].

The consolidation period begins as soon as sufficient space is generated, the activation of the distraction device is stopped and the application of traction forces is discontinued, thereby allowing the newly generated tissue to mineralize until the distraction device is removed [33]. In the literature there are no clear recommendations for that time point [9]. Different consolidation periods have been reported: they could be equal to twice the duration of the distraction [3,26] five weeks [9], eight weeks [6] or three months [18]. Based on other reports, the distractor should not be removed until radiographic evidence of mineralization is present [6,15] otherwise, the risk of instability and re-fracture is too high [19]. Dual energy-x-ray absorptiometry is useful as a reliable predictor to determine the quality of healing and the most appropriate time for the distraction device to be removed [9].

## Bone Regeneration after Distraction Osteogenesis

The unique aspect of distraction is that both bone (osteogenesis) as well as soft tissue (histogenesis) increase is achieved [16]. The osteogenesis process is well described and essentially similar in all distraction models including long bones and mandibular distraction [34]. However, according to variations in the distraction protocol there is a distinction in the timing of the new bone formation, quality of healing and maturing process.

To induce bone it is necessary to have intact alveolar bone at both osteotomy sides without tooth exposure [25]. The presence and preservation of an intact periosteum could also play an essential role in bone regeneration [3]. Due to the fact that the primary inductive factor for cell transformation, collagen synthesis and bone formation is the application and the vector of tensile forces produced by gradual mechanical distraction, bone regeneration and its direction strongly depend on them [17]. During the latency period regeneration resembles normal bone and fracture healing [17].

After osteotomy a blood clot is formed between both bone segments and begins to organize during the following days. At this point of time, the capacity for bone specific protein synthesis is low, e.g. osteocalcin, whereas the synthesis of connective tissue, e.g. type-I-collagen, starts very early during clot resorption [27].

In the first days of distraction a radiolucent zone is seen in the distraction area consisting of a collagenous matrix with heterogonous cell populations, including endothelial cells and large polymorphic fibroblast like cells with signs of active cell metabolism [17].

Capillary formation starts: fibroblast like cells, mainly located in the central part of the gap, are producing preliminary bone matrix, type-I-collagen, and are functionally active until distraction proceeds [17,27]. Cells are scattered randomly and collagen bundles are thin and unorganized. The organic matrix consists predominantly of heteropolymer type-I-collagen, one of the most important extracellular components, which is constantly produced in quantitatively significant amounts in the matrix [17,27,35], thereby indicating an intramembranous pathway of ossification [9,27]. Three days after distraction has started, the center of the gap is composed approximately 29% of type-I-collagen [27]. An enhanced protein synthesis, especially type-I-collagen, as well as an increase in cell density can be recognized in the gap five days after the distraction has been initiated [27]. After the first week, the distraction area soon starts to organize into different zones. Capillaries are located near the osteotomised bone ends whereas in the center of the distraction gap a relatively avascular fibrous interzone is created mainly composed of type-I-collagen-producing fibroblasts [17]. This forms the scaffold for the osteoblasts and capillaries emerging in the matrix prior to mineralization [27]. At this stage collagen bundles are organized according to the tensile force, indicating that bone regeneration can be stimulated by gradual distraction [36]. The distraction gap is mostly radiolucent until new bone formation starts [5]. Collagen content increases gradually up to 59% [27] and approximately 2% mineral deposition is present in the distraction gap [35]. Early bone formation is initiated with thin osteoids and bone trabeculae formed according to the organized collagen frame [17], starting at the host bone margins towards the center of distraction, radiographically visible as three zonal structure two weeks after the start of distraction [37]. Kallio et al. [27] suggested that mineralization already begins within the first week of distraction. Cope et al. [19] claim that new bone formation starts prior to the 10th day of distraction and initial areas of mineralization are already seen at the beginning of the consolidation period. At the end of the distraction period the generated gap is filled with 70-93% fibrovascular tissue. This fibrous interzone undergoes mineralization starting at the host bone margins towards the center of the distraction [19] where bone lamellae are formed parallel to the direction of the distraction [27] interspersed with vascular channels [19]. The mineral apposition rate contains 2μm/d [19]. Bony trabeculae (2-5%) are orientated parallel to the direction of the distraction and no cartilage tissue is present [19]. Radiographically no bone formation is evident at the end of distraction period [37]. Three weeks after the distraction has begun, mineralization and osteogenesis proceed centripetally from the osteotomised bone ends towards the center of the gap [17] with a progressive increase in trabecular bone and a concomitant decrease in fibrous tissue [19]. The mineral apposition rate is slightly more than 2μm/d [19]. Increased radiodensity is obvious reflecting the three-zonal composition of the gap presenting an irregular band of radiolucency known as fibrous interzone [5,37]. Somewhere around the third or fourth week islands of cartilage tissue were reported to have been present in some studies [4,9,17,19,31,38]. The cartilage content was only about 2-3% [19]. There are several explanations for their occurrence. Some authors connect the appearance of cartilage with probably additional enchondral bone formation [3,4,9,11,19,36,39]. Due to the fact that there is no type-II-collagen produced, this theory is rejected by other authors [17,34]. Another assumption is the formation of a third type of bone called “transchondroid”, where chondrocytes are directly transformed into bone [19,40]. One theory is that a microvascular disruption due to segment mobility is caused by micro-movements leading to an altered osteogenesis [38,41] or by minimal tensile forces in this region [19], resulting from diminished oxygen tension because of reduced vascular supply [4]. Cope et al. [19] found a close and specific location of these cartilage islands near the nerves assuming that a potential release of neuropeptides from the nerve took place, inducing cartilage formation. In the central part of the gap the callus is still fibrous four weeks after distraction, with collagen bundles oriented according to the direction of distraction [4]. Bone formation and mineralization proceed with bone lamellae oriented along the predetermined network of collagen bundles growing from the margins of the osteotomy toward the center of the wound [4,17,19]. There are large numbers of osteoblasts, lining the newly formed bone tissue, depositing osteoid and in the new formed bone numerous osteocystes are observed [4]. Mineral apposition rate gradually increases from the end of distraction up to the fourth week of consolidation and remains relatively constant until sometime before the eighth week, when it decreases slightly as remodeling increases [19]. Apart from the fibrous tissue, a progression of regenerate maturation with a varying degree of interzone obliteration, bony trabeculae orientated linearly from the host bone margins to the center of the gap as well as woven bone, can be identified six weeks after the distraction [19,20]. Osteoid deposition in the fibrous central part of the callus is initiated and no osteoclast activity can be found [4]. At this time new bone is homogenously radiopaque and indistinguishable from the host bone [5]. Eight weeks after distraction fibrous tissue has decreased to 13% [19]. There is a progressive increase in linearly orientated bony trabecular towards the interzone [19]. Ossification has advanced with the central area having the least amount of bone formation [4]. A dense network of woven bone and lamellar structures without transforming into calcified tissue as well as some trabecular transforming into compact bone can be identified [20]. A uniform level of radiodensity fills the entire distraction gap [37], but no complete mineralization of the regenerate can be found at this time interval [4]. Ten weeks after the distraction there is a further bone formation progression with almost complete obliteration of the interzone; if there is no cartilage tissue present, it is difficult to determine its approximate location [19]. Mineral apposition rate is less than 2.34 ± 0.31μm [19]. A good bone content of 35.4% there of 30% in ordered structure and some osteoclast activity indicating woven bone remodeling are present twelve weeks after distraction. Sixteen weeks after distraction a solid union of new bone has formed across the distraction gap [17]

which corresponds to the host bone and supports a successful bony consolidation [37] until within the twentieth week the gap is mostly closed [17]. Progressive maturation of bone regenerate has been evaluated in several studies [19,33]. In the end, remodeling supersedes bone formation [19]. Since remodeling continues up to one year after the distraction takes place [19], until the regenerated bone is almost identical and undistinguishable from the original bone [17,34,42], it is assumed that six month after the distraction the newly formed bone does not have the bone resistance and strength of the native bone [43]. It is claimed that even after one year an average of only 77% of the ultimate strength of the native mandibular bone is achieved [43].

## Tooth Movement During the Consolidation Period

A primary research interest is the movement of teeth through regenerated bone. Typically distraction osteogenesis in the tooth-bearing area of the mandible is performed to solve severe anterior dental crowding, so the resulting gap should be used therapeutically for the anterior tooth movement through the newly generated bone (*Figures 7* and *8*). Clinically, orthodontic tooth movement into regenerated alveolar bone after mandibular distraction osteogenesis is possible and no longer disputed [5,7,37,44]. However, the point of time to start tooth movement into the newly formed bone is still a topic of discussion. A reliable protocol for such a procedure has not yet been established.

Questions still remain regarding the optimum timing to start tooth movement and also related to whether we have to wait until the distracted new bone is matured before moving a tooth through it. Some authors claim it is best to have an early start of tooth movement, parallel to the distraction or in the early stage of the consolidation period, directly after the distraction has stopped [18,45,46]. Theoretically the earliest time to start tooth movement into regenerated bone is during the first few days of distraction, when bone formation has not started yet [7] or in the first few weeks after the distraction when bone tissue is still fibrous and immature and bone resistance is less than that of the native alveolar bone [42,47]. In orthodontics, diminished resistance into the immature fibrous new bone created by distraction osteogenesis could signify faster and easier orthodontic tooth movement [7]. Orthodontic tooth movement into bone tissue of high density may on the other hand promote root resorptions [48].

Different researchers have pointed out that an early tooth movement into less organized immature bone is indeed faster, presumably due to its reduced resistance [49]. Rates of about 1.1 mm–1.2 mm per week have been described [7,49]. Another theory is that at the time of the distraction as well as immediately afterwards, specific signal cascades for bone differentiation are already activated and under their influence could tooth movement be accelerated. At the same time tooth movement into the regenerate may accelerate the bony rebuilding [44]. Furthermore, Liou et al. [44] have demonstrated a creation of compact, thicker and more mature bone along the path of orthodontic tooth movement through the distraction regenerate. The teeth had been moved only half

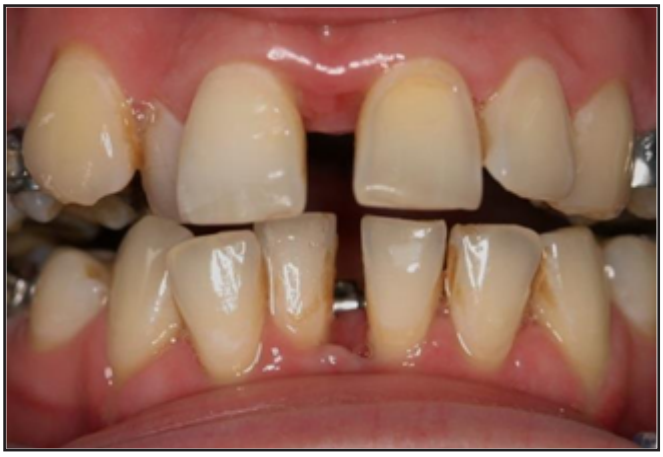

***Figure 7.*** *Clinical situation after surgically assisted rapid palatal expansion and mandibular midline distraction. The developed gap in the tooth bearing area has to be managed orthodontically.*

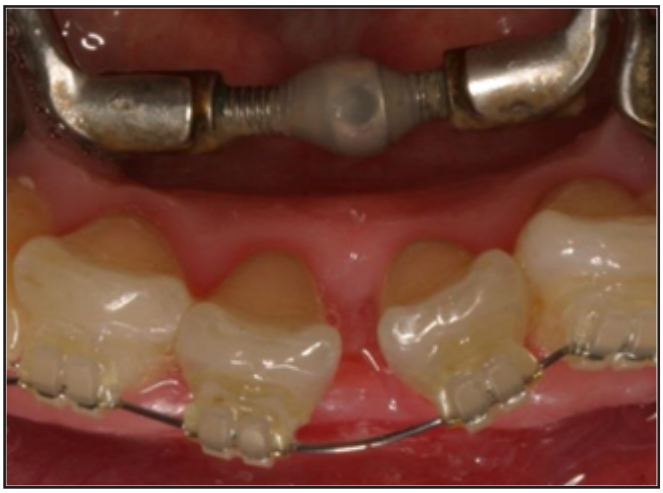

***Figure 8.*** *Orthodontic closure of the distraction gap. Initiation of tooth movement with a fixed appliance bonded in the late consolidation period after distraction. The distraction device is still in situ.*

the way into the distraction gap and the bone they examined was gathered distally to the tooth corresponding rather to the original bone already formed before the distraction had taken place [44]. Hence, it is not surprising, that histologically no differences in bone quality between mature and immature bone could be found. Therefore and also according to the research outcomes of Nakamoto et al. [49] it is much more likely that an early tooth movement into the newly distracted area has no potential effects on bone maturation.

The role of the growth factors BMP-2, BMP-4, IGF as well as TFG-ß/activin within distraction osteogenesis has already been examined [50-52]. During and after the distraction process, these growth factors, which have a high turn-over rate and are positive regulators of bone formation [21], are released from distracted tissue [49,51-53]. These growth factors initiate a signal cascade which activates cell maturation and proliferation of fibroblasts and osteoblasts. The cascade takes place as soon as the distraction period is initiated. With the end of the distraction period comes a down-regulation of these molecules. Astonishingly, during distraction osteogenesis, more of them are present than during normal fracture healing [52]. In the late consolidation period these factors can hardly be encountered [52].

Other sources recommend not to start tooth movement until radiographic evidence of bone formation and mineralization is present [54]. Histological analysis has confirmed an increased radiodensity of the distraction regenerate concomitant with bone maturation and mineralization. It is therefore suggested that radiographic examination of distraction regenerates can be used as a guide before initiating tooth movement [5]. Force application too early in the regenerative process could lead to uncontrolled tipping, periodontal defects, alveolar bone loss and severe root resorptions, even to tooth loss [5,7].

Directly after distraction the new formed tissue still does not possess enough stability and there is lack of supporting bone tissue around the tooth, especially if the interdental bone was very thin before the osteotomy. Initiating early dental tooth movement could result in resorption of the original bone lamella up to the point of its entire dismantling and loss, resulting in uncontrolled tipping into the immature bone. After osteotomy takes place, a remaining alveolar bone thickness of 0.5–1 mm adjacent to the neighbouring teeth is essential as native alveolar bone disappears completely, if tooth movement takes place simultaneously with the distraction [7]. With progressive distraction some authors also reported a tipping of teeth limiting the distraction gap even without applying any active orthodontic forces [25]. To avoid such a tipping, placing a pontic on the arch wire between the front teeth was recommended after the end of the activation until the end of the consolidation period [55]. However, tooth movement in the early stages of the consolidation period is uncontrolled; tipping is often associated with crestal bone loss and severe external root resorptions extending deeply into the dentin [5,37,49]. Severe root resorptions could be explained by the high force magnitudes of 150 g and 10 0g used in the currently mentioned studies as well as the greater bone remodeling activity of the immature bone [5,49].

After a consolidation period of six to 12 weeks less pronounced root resorptions, and an almost bodily tooth movement with low rates of 0.5 mm per week, that corresponds roughly to physiological tooth movement, could be detected [5,49]. Heavy forces and early orthodontic tooth movement are not recommended when teeth are moved through regenerated bone created by distraction osteogenesis in order to avoid tipping and severe root resorptions [49]. Another assumption related to severe root resorptions is that the high expression of growth factors after the distraction and during the consolidation period convert the distraction regenerate in an active stage of remodeling inducing both bone as well as root resorptions [5]. This assumption is very doubtful, because in other investigations a decrease of these growth factors during the consolidation period could be ascertained [52].

Furthermore it is supposed that early tooth movement activates osteoclasts which are normally not found in the newly generating bone tissue, otherwise negatively influencing bone maturing [5]. Sharaby et al. [5] reported in their research a high osteoclastic activity in the area of the pressure side of the tooth movement, which is normally not present during consolidation [4]. There are currently no investigations available having examined the degree of growth factors expression in connection with tooth movement through the regenerated bone.

## Conclusion

The optimal timing for initiation of tooth movement into newly formed bone still remains unclear. Taking into account histological investigations of bone healing after distraction osteogenesis takes place, as well as the above mentioned studies; a bone regeneration enabling teeth to move into the regenerate cannot be achieved before eight weeks of consolidation.

Perhaps the additional application of growth factors could promote cell activity and positively influence the quality and speed of bone maturation after osteodistraction. However, up to now no investigations dealing with the application of growth factors in connection with mandibular distraction osteogenesis are available and the above mentioned assumption is of purely speculative character.

Better knowledge regarding the exact mechanisms of bone formation pathways and molecules involved in these regulatory processes, may facilitate the stimulation of autogenously bone build-up. Thus, further research is necessary to develop an optimized treatment protocol for mandibular distraction osteogenesis as well as for safe and controlled tooth movement into newly formed bone in the future.

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