T Peltomäki

# Stability, adaptation and growth following distraction osteogenesis in the craniofacial region

### Author's affiliation:

*T. Peltomäki*, Clinic for Orthodontics and Pediatric Dentistry, Center for Dental and Oral Medicine, University of Zurich, Switzerland

### Correspondence to:

*Timo Peltomäki* Clinic for Orthodontics and Pediatric Dentistry Center for Dental and Oral Medicine University of Zurich Plattenstrasse 11 CH-8032 Zurich Switzerland E-mail: timo.peltomaki@zzmk.uzh.ch

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### Structured Abstract

### Author – Peltomäki T

The objective of the study was to provide a comprehensive review of the literature describing research done on the stability, adaptation and growth of craniofacial structures following distraction osteogenesis (DO). The design of the study was a literature review of clinical and experimental studies using electronic search with several keywords. Despite immediate normalization of craniofacial relationships after DO, post-distraction mandibular and midface stability and growth is variable in the long-term based on the initial condition. Unpredictable and/or unstable outcomes after DO can arise mainly from three main sources: 1) true relapse, 2) return to original morphology and 3) defective growth. Despite the biologic and clinical feasibility of DO in the craniofacial region, relapse, compromised adaptation, and defective post-distraction growth can lead to variable clinical outcomes. When important structures for the mandibular forward and downward displacement are rudimentary or missing in syndromic patients, DO can not 'correct' the condition and post-distraction growth will be defective. Non-syndromic patients have a better potential to respond favourably to DO.

Key words: distraction; growth; mandible; maxilla; stability

# Introduction

Distraction osteogenesis (DO) is a unique form of clinical tissue engineering in which the clinician is able to guide formation of new bone by a mechanical means without the application of an external agent. The principles and guidelines for today's distraction protocol are mainly based on the studies and clinical trials of Dr. Ilizarov (1–3). While he worked on long bones, Dr. McCarthy and associates (4) are acknowledged for introducing the technique to reconstruct membranous bones of the craniofacial skeleton.

Biological rationale of DO has been extensively studied and molecular mechanisms revealed (5, 6). Distraction devices have been improved from initial extraoral, unidirectional devices, to intraoral, multidirectional ones to allow not only mandibular and/or midface DO, but also distraction of

single or groups of teeth (7-10). The importance and difficulty in obtaining optimal vectors of distraction for each case has been described (11, 12). Limitations, unexpected events, and complications of the technique have also been reported and demand for long lasting commitment from the patient/family has been emphasized (13-15). It has become clear that DO certainly works, but the initial enthusiasm and expectations towards the technique have gradually settled and indications have become more clearly delineated. Current indications for DO in the craniofacial region include advancement of mandible or maxilla at an early age in children with severe airway obstruction, lengthening a short mandibular ramus at any age, and advancement of mandible/maxilla when large movements are required. From the very beginning of the DO era in the craniofacial region, stability, adaptation and post-distraction growth have received particular attention (4, 16, 17). Concerning the mandible, these issues are linked with the adaptability of the temporomandibular joint (TMJ) to distraction.

Muscles and other soft tissues have been considered the major limiting factors in the reconstructive surgery, preventing lengthening of bones and causing relapse (18). Based on the experimental studies with long bones it has been found that expansion of the soft tissues proceeds parallel to skeletal distraction, called distraction histogenesis (1, 2). Because of the potential for soft tissue adaptation it has been claimed that no relapse following craniofacial DO would occur, and superior results could be achieved compared with conventional osteotomies (16, 19). Studies on experimental mandibular distraction have indeed shown that muscles in line with the distraction vector adapt well with compensatory regeneration and hypertrophy (20, 21). Simultaneous expansion of the overlying soft tissues along with bone elongation might help in achieving a stable result. However, the cases where DO is clinically applied are variable with defects also found in the soft tissues. Therefore, instability and unpredictable outcomes can be anticipated. Three main reasons for unstable outcome can be defined: 1) true relapse, 2) return to original morphology and 3) defective growth. In many cases the reasons for the instability are difficult to differentiate.

The aim of this paper is to review the present knowledge on the stability, adaptation and growth of craniofacial structures following DO.

# Materials and methods

Using keywords 'distraction', 'osteogenesis', 'growth', 'mandible', 'maxilla', 'stability', 'adaptation', an electronic search was performed in the PubMed database through August 2008. Additional hand searches were made to collect the data. Because of lack of publications with high level evidence, such as prospective, randomized clinical trials, all varieties of study designs were accepted, including experimental investigations.

# Results and discussion True relapse

True relapse, that is loss of the gained length, may occur due to resorption of the bone generated by DO during the consolidation phase or afterwards. Because of the dynamic nature of the consolidation, external factors such as masticatory loads and muscle forces at rest can affect the regenerate composed of not yet mineralised bone (22). Six to eight weeks consolidation time has commonly been recommended and applied (23), and mineralization of the regenerate has often been studied by routine radiology. A scintigraphic study shows that mineralization of the new bone has not been completed before 10 weeks in children, and between 10 and 14 weeks in adults (24). Therefore the recommended consolidation time may be too short. The use of ultrasound examination during the consolidation phase may be a viable non-invasive method to assess bone maturation and before removal of distraction devices (25).

Stability of fixation, particularly during the consolidation period, is essential for successful new bone formation in DO (26). Micromovement across a mandibular distraction site has been documented during mastication in the pig (27). If the distraction device has not been well stabilized to the bone, greater movement may occur. Consequently, cartilaginous connective tissue will develop in the distraction gap preventing the preferred direct intramembranous bone formation (26). The mineralization process may then be prolonged and the risk for immediate relapse increases. Therefore, stability of the device has to be secured during the whole distraction treatment, and attempts to enhance the consolidation should be considered, for example, True relapse has been found to have occurred within the length of the distracted mandibular ramus at the one year post-distraction follow-up in hemifacial microsomia (HFM) patients (30–32). This decrease may have taken place in the newly formed bone and/or in the head of the condylar process. Advancement of the maxilla/midface with DO is most commonly done in patients with cleft lip and palate. While there are some studies indicating no post-distraction relapse (33–35), others with follow-up at 6 and 12 months post-distraction report about 20% relapse in the achieved maxillary advancement (36–39). However, differing post-distraction protocols make comparison of the studies difficult.

True relapse, i.e., resorption, may also occur in the mandibular condyle due to increased loading of the cartilage by the distraction force. In a study of 13 nongrowing adult patients with severe class II malocclusion, condylar resorption was found in 20% of the condyles, with risk factors associated with the amount of distraction and pre-existing temporomandibular joint disorder (TMD) and TMJ pain during distraction (40). A close look at the case report titled 'Condylar resorption following distraction osteogenesis' (41) shows that after successful mandibular distraction, the patient was involved in an accident with an injury to his chin. The authors conclude that the major cause for the condylar resorption could have been the accident, but that DO may have made an additional contribution.

Experimental studies indicate that compressive forces resulting from distraction lead to mild changes in the condylar cartilage not only on the distracted side, but in unilateral DO, also on the non-distracted side (42-46). It has been found that in the condyle the faster the distraction rate and the greater the amount of bone created, the more severe the degenerative, arthritic-like changes (45, 47, 48). Nearly total loss of the condylar cartilage has been found in rabbits with reduced vascularity/nutrition of bone and cartilage due to previous irradiation, in comparison with the control condyles which had only minor changes (44, 49). Different rotational forces are placed on the mandibular condyles by transverse distraction in the mandibular symphyseal area and consequently more severe histological changes in the condylar cartilage have been reported (50, 51). These experimental findings were not substantiated by a clinical follow-up study (52). Application of findings from animal experimentation to humans have to be made with great care because in most cases when DO is used clinically, the structure and function of the TMJ is compromised and may therefore respond differently than with experimental animals.

### Return to original morphology

Forces from masticatory muscles and other soft tissues affect the regenerate during and after DO and can significantly modify the outcome. A finite element analysis indicates that soft tissues create resistance towards bone elongation during the active phase of mandibular distraction (53). Conversion to the original morphology without actual shortening of the elongated mandible has been reported in patients with Treacher Collins and Nager syndrome (54-56), and this is likely due to muscular/soft tissue action. The anticipated adaptation of the masticatory muscles due to DO, and particularly that of the pterygomasseteric sling has been recently questioned (57). Based on a CT study, Huisinga-Fisher et al. (30) report that 3 years after mandibular distraction a small volumetric increase was found with only some masticatory muscles on the affected/distracted side, in comparison with the muscles on the normal side. On the other hand, Mackool et al. (58) found significant volumetric increase in the medial pterygoid muscle in a small group of very young patients. It seems that adaptation of muscles and soft tissues in DO is not adequate to secure the new orientation of the mandible, which often has included anterior rotation, known to be an unstable movement in conventional orthognathic surgery (59). A complicating issue is that assumptions regarding muscle hypoplasia and/or function are not reliable if based on skeletal hypoplasia in syndrome patients (60, 61). In line with this suggestion, it has been reported that soft tissue changes that accompany correction of skeletal deformity by DO are unpredictable and vary individually (62). Attempts to plan mandibular DO using computer modelling have had related difficulties, where simulation of soft-tissue resistance to mould the regenerate has been difficult to model, requiring parameters that are difficult to obtain (63-65).

### Post-distraction growth

Initially great hopes were placed on DO being able to correct craniofacial dysmorphologies with growth disorders. In line with the functional matrix hypothesis (66), it was thought that when soft tissue volume is increased by distraction, function would be improved or normalized, and normal craniofacial growth would take place. Recently published long-term follow-up studies show that despite immediate normalization of craniofacial relationships after DO, post-distraction mandibular and midface growth is defective in certain cases.

Distraction osteogenesis is mostly used in patients with craniofacial anomalies, having abnormal growth and function, i.e., a dysfunctional matrix. Therefore knowledge on how an abnormal structure would grow without intervention is important to assist the clinician in planning when and how to correct the abnormality. Fig. 1, modified from Dufresne and Richtsmeier (67) and Carlson (68), shows possible patient population interactions. Because of a syndrome, patients may have not only defective/missing skeletal and soft tissues (malformation, disruption) but also malfunctioning growth mechanism (dysplasia). Therefore, immediate treatment outcome and growth that follows may remain poor and unpredictable. A poor response to treatment by any means (surgery, dentofacial orthopaedics) and defective growth reflects a condition that includes a growth disorder. On the other hand, patients with a dental malocclusion, with a mild skeletal component (deformation) in which growth process is not



*Fig. 1.* Patient population of craniofacial distraction osteogenesis, modified from Dufresne and Richtsmeier (67) and Carlson (68). Because of a syndrome (malformation, disruption, dysplasia), in addition to defective/missing skeletal and soft tissues, patients may also have a malfunctioning growth mechanism. Therefore, treatment outcome and growth following treatment often remains poor and unpredictable. Patients with a dental malocclusion with a mild skeletal component (deformation), in which growth process is not initially affected, respond well to treatment and good treatment outcomes can be achieved.

initially affected, respond best to treatment and good treatment outcomes can be achieved.

Distraction osteogenesis is commonly applied in patients with hemifacial microsomia to lengthen the short mandibular ramus. The extent of TMJ and mandibular dysmorphology largely determines the timing and type of treatment. The mildest forms are characterized by a slightly hypoplastic mandibular condyle and thinner than normal condylar cartilage, with fairly normal endochondral ossification (69). The severe forms of HFM commonly exhibit aplasia or severe hypoplasia of the TMJ structures, and even if the condyle is present, cartilage and endochondral ossification may be completely lacking (69, 70). In the mild cases mandibular growth can be expected to be only slightly deficient, but in the severe ones growth on the affected side is grossly defective and may come to an early standstill. Without treatment, increasing facial asymmetry has indeed been found to correlate with the severity of the mandibular deformity (71). Recent publications concerning post-distraction craniofacial growth should be interpreted in this context. In growing HFM patients facial asymmetry can certainly be significantly improved with DO. Depending on the severity of the condition, growth on the affected side may proceed, but as with no treatment, at a rate less than on the non-affected side. This can lead to recurrence of ramus height and facial asymmetry and an occlusal cant (32, 72-74). Mommaerts and Nagy (75) and Baek and Kim (76) have emphasized the need to differentiate between the different types of HFM, as this can significantly influence success or failure of DO.

Children with Pierre Robin sequence (PRS) should also not be considered as a single entity but should be placed to different diagnostic subgroups in order to understand treatment need and post-treatment success (77, 78). In PRS neonates, mandibular DO is not considered the first choice of treatment, but reserved for children with failures of prone position therapy and tongue-lip adhesion who would otherwise be candidates for tracheostomy to increase airway (79, 80). If the airway obstruction is localized to the tongue base, mandibular advancement by DO can be expected to increase oropharyngeal airway and result in asymptomatic children, with normal breathing, sleep and feeding (80).

Post-distraction maxillary growth in cleft children has been reported to be minor, if any (37–39, 81). To

compensate for mandibular growth in these children, considerable overcorrection has been recommended (82). The postulate of 'the expansion of the soft tissue functional matrix by distraction' (34) to lead to stability, adaptation and normal maxillary displacement also has to be questioned with regard to the midface.

Concerning post-distraction mandibular growth, it can be concluded that if important structures for the mandibular forward and downward displacement are rudimentary or missing, such as the condylar cartilage, pterygoid lateralis muscle, DO cannot eliminate the dysfunctional matrix and post-distraction growth will be case sensitively defective. A study of 50 class II malocclusion patients (mean age 14.7 years) has revealed that not even non-syndromic growing patients remain stable and/or post-distraction mandibular forward displacement proceeded favourably at 1-year follow-up to bilateral DO (83). It was found that the patients with initially high mandibular plane angle  $(>38^{\circ})$  had re-opening of the angle in 57% of the cases in comparison with 8% in low-angle patients in response to DO. Non-syndromic patients belong to the 'Malocclusion-deformation' group of the patient pool (Fig. 1), but yet some of them show unfavourable treatment response. This may be due to the undesirable polymorphism of important genes having a role in the growth and adaptation of soft tissues and the condylar cartilage. In an association study it has been found that healthy individuals with certain polymorphism in the growth hormone receptor gene have significantly shorter mandibular rami than those with another type of polymorphism (84, 85). The short mandibular ramus relates to the high mandibular plane angle. Nonsyndromic patients with unfavourable growth and treatment response to DO may hence belong to a 'Clinical' group of patients described by Carlson (68), as illustrated in the Fig. 2.

### TMJ adaptation

A finite element analysis based on computed tomography and magnetic resonance imaging scans of a patient with mandibular ramus distraction has verified increasing loads in the TMJ along with the increasing bone elongation (86). A schematic presentation of the consequences of TMJ load/compression due to mandibular distraction is depicted in the Fig. 3, modified from Arnett et al. (87, 88). In a non-syndromic patient



*Fig. 2.* Due to an undesirable polymorphism, some non-syndromic patients in the pool of 'Malocclusion-deformation' belong to the 'Clinical' group described by Carlson (68). Therefore, they may have uncertain treatment response and post-distraction growth and adaptation.



*Fig.* 3. A schematic presentation of the sequence of events of TMJ load/compression due to mandibular distraction, modified from Arnett et al. (87, 88). In a non-syndromic patient with adequate adaptive capacity (normal polymorphism), condylar cartilage adapts to the increased load with functional remodelling. Normal mandibular growth takes place and mandibular ramus height remains stable or increases. Condylar cartilage of a patient with diminished adaptive capacity (undesirable polymorphism) does not adapt to the change in the load, but dysfunctional remodelling occurs. Consequently, mandibular growth may be reduced, ramus height remains short or condylar resorption occurs, and mandibular retrusion with class II malocclusion and anterior open bite may progressively develop.

with adequate adaptive capacity (i.e., normal polymorphism), condylar cartilage is able to adapt to the increased load, and functional remodelling occurs. Normal mandibular growth takes place and mandibular ramus height remains stable or increases. On the contrary, condylar cartilage of a patient with diminished adaptive capacity (i.e., undesirable polymorphism) does not adapt to the change in the load and dysfunctional remodelling occurs. Therefore, mandibular growth may be reduced, ramus height remains short, or condylar resorption may occur. Progressive mandibular retrusion can be noted in the long term along with development of a class II malocclusion with a tendency to open bite. Clinical and experimental evidence suggest that in the mandibular DO, pre-existing TMD, TMJ pain during distraction (40), reduced nutrition of bone and cartilage (44, 49), and pre-treatment short mandibular ramus with high mandibular plane angle (83) can be considered as signs of diminished adaptive capacity of the TMJ, with elevated risk for dysfunctional remodelling. High rates of distraction and large amounts of new bone created are additional factors that increase TMJ compression, possibly lowering the nutrition of the bone and cartilage, and reducing the adaptive capacity of the condyle (46-48).

# Conclusions

After two decades of use and extensive research there is no question about the biologic and clinical feasibility of DO in the craniofacial region. Syndromic patients, in whom the technique is often applied, respond unpredictably to the treatment and post-distraction craniofacial growth and adaptation is commonly defective depending on the severity of the dysmorphology. Nonsyndromic patients have a better potential to respond to DO in a favourable way. Individual variation due to undesirable polymorphism of important genes for growth and adaptation may lead occasionally to compromised treatment results. Despite the potential for distraction histogenesis to expand also muscles and soft tissue along with the skeletal expansion, relapse, compromised adaptation, and defective post-distraction growth cannot always be prevented with the DO.

# Clinical relevance

Distraction osteogenesis is a feasible technique to treat various craniofacial conditions. Immediate postdistraction outcomes are usually good, but relapse, compromised adaptation and defective post-distraction growth can lead to variable clinical outcomes in the long term. Particularly syndromic patients, in whom the technique is often applied, respond unpredictably to the treatment, whereas non-syndromic patients have a better potential to respond to DO in a favourable way.

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