Experimental Mandibular Regeneration by Distraction Osteogenesis with Submerged Devices: Preliminary Results of A Canine Model

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The authors describe a new technique for reconstruction of mandibular body defects. The feasibility of distraction osteogenesis with submerged (internal) devices for reconstruction of segmental mandibular defects is investigated in an experiment with five adult dogs. A segmental mandibulectomy was performed on the horizontal ramus. The bony defect was regenerated using distraction osteogenesis (bone transport) at a rate of 1 mm daily. The animals were killed after the consolidation period.

Complete bone regeneration of the surgically created gap was successful in three of five dogs. Two animals failed to create new bone. In these two cases, the screws did not offer proper stability to the bony fragments, and this caused a lack of ossification.

This experimental study demonstrates the possibility to use internal distraction devices to reconstruct segmental mandibular defects in a canine model. Internal devices show enormous advantages in comparison with the external ones. This method with no donor-site morbidity may become a very useful option in human mandibular reconstruction.

Reconstruction of the mandible after ablative surgery is difficult to achieve both from an aesthetic and functional point of view. The use of free vascularized flaps has improved the results in extense defects but unfortunately, the surgical procedure is complex, and morbidity and costs are high.

Distraction osteogenesis is a simple procedure in which new bone is produced without the need for bone grafts. Mandibular distraction osteogenesis

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(MDO) has shown to be effective to treat congenital or acquired mandibular hypoplasias.[1] The process of generating new bone by stretching a bony callus has proven successful as a way of reconstructing segmental mandibular defects. Experimental[2–6] and clinical studies[7–9] have applied mandibular lengthening by gradual distraction in segmental defects. The mandibular gap can be replaced by new bone grown from the remaining mandible. Excellent results have been obtained in experimental studies even under extreme conditions, such as distraction in previously radiated mandibles.[10]

However, we could not find reports about segmental mandibular regeneration by means of submerged distraction devices. Internal MDO has shown to be related to improved stability, optimal patient compliance, and no visible scars when compaired to the extraoral technique.[1]

A new application of the internal distraction technique to reconstruct segmental mandibular defects is described in this report. In a canine model, a 2-cm segmental mandibular body defect was filled with regenerated bone in 20 days, at a rate of 1.00 mm daily using an internal unidirectional distraction device with a transcutaneous activator. The results suggest that this technique can be used in mankind for segmental mandibular reconstruction.

Material and Methods

A total of five non-growing healthy Beagle dogs weighing 10 Kg were used as experimental animals at the Department of Small Animal Surgery, Hospital Clínico Veterinario, Universidad Complutense de Madrid (Spain). Initial photographs and radiographs were taken before the surgical procedure, once the animal was under general anaesthesia.

Surgical Procedure

The surgical procedure was performed under general endotracheal halothane anesthesia, with thiopental induction. The surgical field was prepared by shaving the area and draping under sterile conditions. The dogs received IV cephalosporin (cephazolin) preoperatively and postoperatively.

The animals were operated in a lateral position. The skin was incised over the mandible, extending from the angle to the level of the canine tooth. The mandibular body was exposed completely in a subperiosteal manner. The mental neurovascular bundle was identified and sectioned. A titanium reconstruction plate was molded and applied to the inferior basilar aspect of the mandibular body, from the angle to the canine region.

Three bicortical screws (2.0 mm) were used proximally and distally to fix the plate. A 20 mm-segmental defect was created in the first premolar area (Fig 1) with a micro-oscillating saw and copious irrigation with sterile saline. The rest of the teeth were preserved.

At this time the transport disk was designed. An osteotomy was performed proximally to create the transport disk of approximately 20 mm (the width of the second premolar), avoiding the adjacent molar and premolar roots. The distraction device used in this study (AO Synthes®, Oberdorf, Switzerland) was originally created to lengthen the ascending ramus of the mandible.[1] The body of the distraction device was fixed bicortically with 4 screws, two screws in each side of the osteotomy (1.5 mm in diameter and 10 to 14 mm in length). The anterior two screws fixed the moving part of the distraction device to the transport disk. The posterior two screws were fixed to the posterior and stable part of the mandible, just in the area of the great molar. After fixation of the distraction device the osteotomy was completed with a small osteotome. Activation of the distraction device was tested for several mm (Fig 2) and returned to its original position (Fig 3). This maneuver allowed to control bleeding from the proximal osteotomy. After completing the surgery the soft tissues were sutured in layers, maintaining the periosteum to cover the body of the distraction device, the plate, and the osteotomy line. Only the activator of the device was allowed to project externally in the auricular area (Fig 4).

All the animals received similar care including careful analgesia postoperatively, and a soft diet dur-

Fig 1 Intraoperative view. Segmental resection in the first premolar area.

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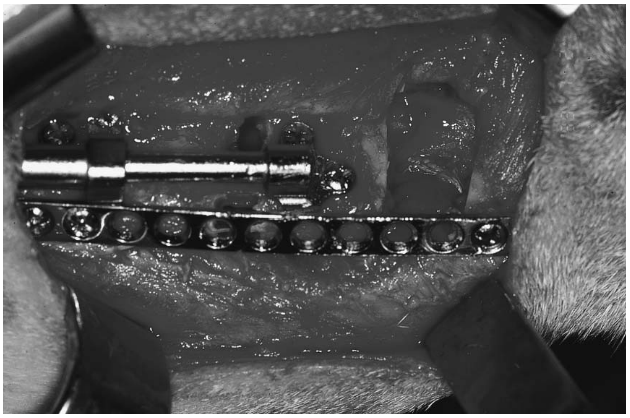

Fig 2 Reconstruction plate and distraction device in place after completion of the osteotomy, creating the transport disk. The distraction device has been activated several mm to test that both bony fragments are completely separated.

Fig 4 Only the activator of the device is allowed to project externally in the auricular area.

ing the entire distraction period. When the distraction was finished, during the consolidation period, they were fed with solid food. Radiographic and photographic records were taken at the end of the surgical procedure. The postoperative periods of the study were:

Neutral fixation: five days (0–4th day)
Gradual distraction: 5th–25th day, with a rate of 1 mm per day
Consolidation period: the device is kept in place for a period of 90 days. The animals were killed after the end of this consolidation period.
Autopsy: macroscopic and microscopic analysis.

Radiographic Examination

Radiographic observation was done until the dogs were killed, and once the mandibles have been dissected. Oblique, lateral, and occlusal radiographs were taken after placement of the distraction appliance. Radiographies were also taken at the completion of disk transport and at two-week intervals until death. Additional radiographic examination was performed whenever it was considered to be necessary.

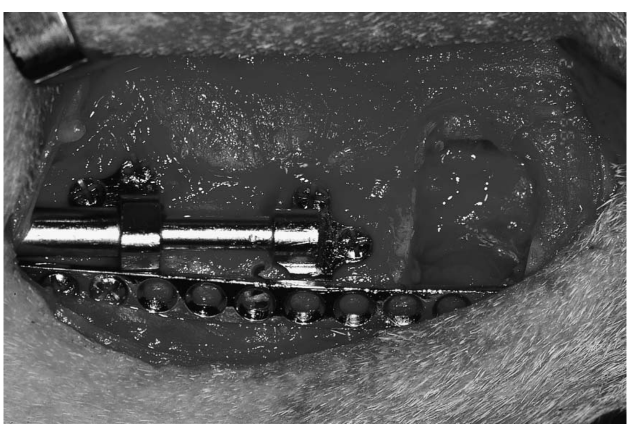

Fig 3 After activation, the distraction device is returned to its original position.

Histopathologic Examination

Thereafter, the specimens were harvested to pathological study, to ascertain if the structure of the lengthened gingiva is normal, and to describe the osteogenesis of the regenerated bone.

After death, the entire mandible and surrounding tissues were removed intact from each animal, with the distraction device and the reconstruction plate still in place. The mandibles were fixed with formaldehyde solution. The regenerated bone was observed macroscopically; then, the distraction device and plate were removed. The mandibles were sectioned through the regenerated bone (coronal sections). The sections were decalcified in 12% hydrochloric acid solution and embedded in paraffin; representative sections were stained with hematoxylin–eosin. Histologic sections were evaluated by two pathologists.

RESULTS

Complete bone regeneration of the surgically created gap was succesful in three of five dogs. All the animals survived the whole length of the study. There were no problems with oral nutrition while the distraction devices were in place. Activation of the distraction devices appeared to cause some temporary discomfort. A wound infection developed in one ani-

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mal. This complication was treated with surgical drainage and parenteral antibiotics.

Two animals failed to create new bone. In these two cases, and during the active distraction period, it was noted that the distraction devices were loose. When the activation was completed, a lack of ossification at the new gap was evident. It was decided not to interrupt the study, and the two animals continued to be examined in the same fashion as the others. These two animals developped an extensive area of plate and distraction device exposure intraorally on the fourteenth and nineteenth day postoperatively. Copious water irrigation locally and antibiotics were used to treat this complication. The intraoral defects never completely healed.

Radiographic Examination

Immediately after surgery, all the devices were shown to be in the right position. At the end of the distraction period, the regenerated bone had radiographically the same density as the surrounding soft tissue. Five to six weeks after initiating distraction, radiopaque material tapered from the surface of the transport disk and proximal mandibular stump to the center of the regenerate. By 6 to 12 weeks the entire gap showed progressive calcification. At death (12 weeks after the end of the distraction period) dense and homogeneous calcification could be seen throughout the regenerate. However, the filled gap was still slightly less dense than preexisting mandible (Fig 5). There was no radiographic evidence of complete bone callus formation between the distal mandibular stump and the transport disk in any case. In one case the axis of the new bone had grown in a lingual direction (Fig 5). In the two failed cases, the gap remained radiolucid during the whole consolidation period.

Fig 5 Radiograph showing the new bone formation after mandibular distraction. Complete calicification can be seen in the entire gap; density of the new bone is, however, lesser than the adjacent mandible. In this case the axis of the new bone had grown in a lingual direction.

Histopathologic Examination

Macroscopic examination

The regenerated segment was similar when compared with the rest of the mandible (Fig 6). The specimens showed an outer thick fibrous layer surrounding the new bone. In one case the axis of the new bone had grown in a lingual direction. In two cases soft tissue was present between the transport segment and proximal mandibular stump. In these two cases, examination revealed loosening of the majority of the screws, and a lack of bone formation along the entire gap.

Microscopic examination

In three of five cases, the histologic examination of the bone confirmed the presence of new bone deposition along the mandibular defect.

The regenerate segment was comparable in diameter with the transport disk. The exact location of the junction between the regenerate and the preexisting bone could not be determined.

The new bone showed an outer cortical layer and an inner trabecular medullary space in all specimens. The regenerated bone, less calcified but more cellular and vascular than the preexisting mandibular bone, consisted of numerous trabeculae aligned in the direction of distraction. No differences be-

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Fig 6 Macroscopic examination. The regenerated segment is similar when compared with the rest of the mandible.

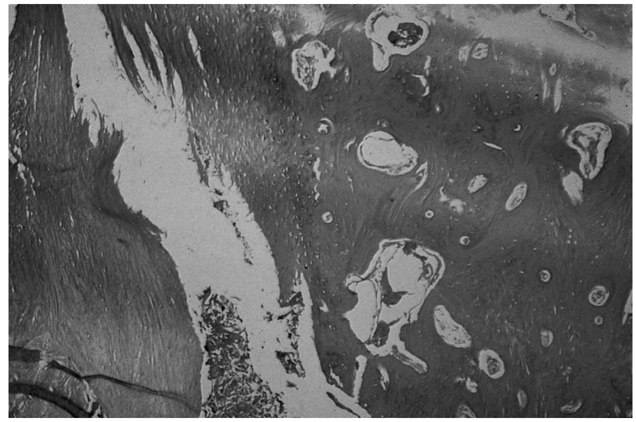

Fig 8 Microscopic examination of one of the two failed cases. Fibrocartilage islands in the distraction gap. New bone deposition in small areas among the chondroid cells. Hematoxilin-eosin, original magnification x375.

tween the lengthened gingiva and the original gingiva were appreciated by microscopic examination. No evidence of reparative bone callus at the junction of the transport disk and the distal mandibular stump was found in any case.

In the other two cases, the segmental defect was not filled with bone (Fig 8). A small amount of bone was deposited on the proximal stump, and in small areas in the gap. A pseudoarthrosis between the transport disk and the remanent mandible was demonstrated. Fibrocartilage tissue was observed in the central region of the distracted gap. Collagen fibers were rectilinear stretched out and oriented to the distraction vector. Newly deposited bone is observed in small areas among the matrix of chondrocytes and oriented in the same direction as the distraction (Fig 8).

Fig 7 During activation of the distraction device; the maneuver is easy to perform.

The inferior alveolar nerve did not regenerate in any of the animals, but was found to terminate just proximal to the transport disk osteotomy site.

Discussion

In recent years, promising results have been obtained in mandibular reconstruction by means of distraction osteogenesis.[2–9] In this experimental study a new application of a mandibular internal distraction device is presented. This device, although initially developed for ascending ramus placement[1], has been used in this study to ascertain if it is useful to reconstruct the mandibular body by means of transport of a bone disk.

By means of this procedure, new bone is created while donor site morbidity is eliminated and the complexity of the procedure is less. Moreover, D.O. offers another advantage in comparison with microvascularized flaps: reaching our goal of an accurate anatomical reconstruction. The regenerate segment is similar in size and structure to the preexisting mandibular bone, which is difficult to achieve with microvascularized osseous flaps.

Complete bone regeneration was successful in three of five dogs (60%). These data support the hypothesis that internal distraction osteogenesis is useful in obtaining new bone within segmental mandibular defects, anatomically and histologically comparable with the adjacent residual bone.

The use of submerged devices shows considerable advantages with respect to the external devices.[1] Internal devices are socially more acceptable than the external distraction devices, and are less prone to

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trauma, infections or unaesthetic scars. Internal distraction devices are very comfortable and allow the patients to perform their normal activities immediately after the operation. Moreover, external devices are shown to be related to poor stability in previous studies.[1,11,12]

When this internal distraction device with transcutaneous activator is applied to reconstruct segmental defects in the mandibular body, the transcutaneous rod exit is hidden in the auricular area (Fig 4). Activation of the device is easy to perform in comparison with the internal distraction devices with transmucosal activator (Fig 7).

The absence of pins through the skin of the face just over the distracted zone can represent another advantage: an experimental study suggests that the existence of previous radiotherapy has no negative effects on the regenerative process.[10] If further studies show that postoperative radiotherapy does not affect the process, internal distraction, with the transcutaneous activator far away of the distraction site, may become the technique of choice. However, further studies are necessary to fully assess the role of this technique in reconstructive post-oncologic head and neck surgery.

The maximal length that can be obtained with this device is 40 mm. To achieve maximal lengthening it is necessary to fix the device with both plates in contact, which is easy to achieve. In those cases with deficiencies more than 40 mm, an additional distraction procedure will be necessary; if the defect is closely matching 40 mm, a bony graft will be sufficient. A similar internal appliance with a maximal distraction length of 80 mm would be useful for the largest segmental defects.

The technique failed in two cases (40%) due to technical problems. In the two dogs in which MD was unsuccessful, a pseudoarthrosis was confirmed during the post-mortem examination. The titanium plate and/or the distraction device did not offer proper stability to the bony fragments in these cases, and this caused a lack of ossification, and a large intraoral exposure. The majority of the screws were loose, and therefore, this resulted in an excessive mobility of plates and distraction devices. Movements probably lead to nonunion of the fibrous type or cartilage formation, and delayed and/or uncomplete bone formation.

Distraction bone healing has been recently studied in the mandible.[13–18] It appears that the mode of osteogenesis after lengthening differs from bone repair by fracture callus. Karp et al. [14] reported a predominantly intramembranous ossification in the dog mandible after distraction. However, several experimental studies have demonstrated the existence of endochondral ossification within the distraction gap in mandibular lengthening.[13,15–18] The presence of the cartilage precursor has been related to instability of the bone fragments.[13,15,16,18] Movements in the distraction gap due to instability of the distraction device, or due to strong biting forces may be a possible explanation.[13] Masticatory canine forces are uncontrolled, and may be much higher than in mankind. Movements in the distraction area perhaps disturb the local vascular regeneration, diminishing oxygen tension and changing the bone formation via cartilaginous tissue.[13]

Rigid fixation promotes primary bone healing without cartilage precursor.[15] It is essential, therefore, to provide a perfect stability to the mandible, even though it may be difficult, and time-consuming. Accurate bending of the reconstruction plate, and the use of bicortical screws to fix both the plate and the distraction device to the bone will secure the mandibular bony fragments in the right position. If stability is provided, uneventful ossification will appear.

The stability provided by the internal devices is excellent when applied for its clinical use in mandibular lengthening.[1] However, adaptability of the device to the irregular outer surface of the canine mandibular body is not perfect, and this may contribute to the instability of the device during the procedure. In one case (Fig 5), the distraction vector was forced towards a lingual direction in an attempt to adapt the distraction device to the convexity of the mandibular body. Modifying the original structure of the device will be necessary to perform bone transport in the canine mandible. Nevertheless, anatomy of the human mandible is more favorable, and adaptability of the device will be probably better. This technique may be appropriate not only for the reconstruction of the mandibular body, but for the ascending mandibular ramus and condyle as well. Clinical application will answer all these still open questions.

Considering the great vascularization of the mandible, the consolidation period utilized in this study seems reasonable. In cases of instability, however, delayed bone formation must be expected, and an increase of the consolidation period may be necessary. Additional experimental studies may improve our knowledge on bone transport in the mandible, resulting in a more precise application of the distraction periods.

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