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Reconstruction of Canine Mandibular Bone Defects Using a Bone Transport Reconstruction Plate

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Abstract

Objectives—Reconstruction of mandibular segmental bone defects is a challenging task. This study tests a new device used for reconstructing mandibular defects based on the principle of bone transport distraction osteogenesis.

Methods—Thirteen beagle dogs were divided into control and experimental groups. In all animals, a 3 cm defect was created on one side of the mandible. In eight control animals, the defect was stabilized with a reconstruction plate without further reconstruction and the animals were sacrificed two to three months after surgery. The remaining five animals were reconstructed with a bone transport reconstruction plate (BTRP), comprising a reconstruction plate with attached intraoral transport unit, and were sacrificed after one month of consolidation.

Results—Clinical evaluation, cone-beam CT densitometry, three-dimensional histomorphometry, and docking site histology revealed significant new bone formation within the defect in the distracted group.

Conclusion—The physical dimensions and architectural parameters of the new bone were comparable to the contralateral normal bone. Bone union at the docking site remains a problem.

Keywords

Distraction; Osteogenesis; Bone; Transport; Segmental defect; mandible; reconstruction; device; canine; dog

Introduction

Twenty-two thousand new cases of primary oral cancer are diagnosed annually in the United States.¹ Treatment of these patients typically involves surgical excision of hard and soft tissues from the face and oral cavity. Tumor excision may be combined with radiotherapy, which is believed to compromise bone and soft tissue regeneration^{2–5}.

Benign tumors of the mandible may also require segmental bone resection due to high incidence of local recurrence after simple curettage or intra-lesion excision. These benign tumors include ameloblastoma, myxoma, giant cell granuloma and recurrent keratocyst. Furthermore, segmental bone loss may result from blast injuries, high impact trauma, or repeated surgical debridement for treatment of chronic osteomyelitis of the mandible. The resulting tissue deficits represent some of the most complicated problems in reconstructive surgery, not only because of the unique anatomy, but also due to the complexity of tissue function of the oral tissues.^{6, 7} Mandibular reconstruction typically involves bone, gingiva, and teeth. In spite of the wide variety of reconstruction methods, none of them is completely satisfactory^{8–11}.

The general aim of oral reconstruction is to restore both normal physiology and facial esthetics. Ideal functional reconstruction should achieve sufficient alveolar height and thickness, allowing for permanent restoration of dentition, maxillo-mandibular occlusion, mastication (jaw dynamics), deglutition, mandibular continuity, sensibility of the mucosa, lip competence and speech. Esthetic goals include restoring normal appearance of the reconstructed soft-tissues, facial symmetry, restoration of the dental arch, and preservation of the lower facial dimensions. Finally, it is important to avoid and manage complications such as infection and fistula formation and compensate for the decreased vascular supply to irradiated tissues.^{8, 9, 12}

The main method of reconstructing mandibular bone defects has been use of a reconstruction bone plate with or without bone grafting. Definitive bone reconstruction can be primary, at the time of tumor excision, or secondary, following an initial healing period. Although good aesthetic results were reported with reconstruction plate without bone grafting, it deprives the patient of having any restoration of mandibular dentition, even a removable lower denture.^{9, 13}

Non-vascularized bone grafts (NVBG) can be successfully used to reconstruct mandibular defects. However, their use during primary reconstruction is not advised due to high incidence of failure.⁹ On the other hand, secondary grafting may be technically difficult due to extensive fibrosis, loss of anatomical planes and landmarks, and the possibility of vascular injury that can result in serious bleeding or injury to the oral mucosa. Creating mucosal breaks during surgery is hard to avoid and breaks could be associated with a high incidence of resistant postoperative infection. The failure rate of the metal plate with NVBG varied between 16–29%, while the complication rate varied from 45–81%.^{8, 14–17} The failure rate increased sharply to over 60% when the defect span was longer than 6 cm.^{18, 19}

Since the development of vascularized bone grafts (VBG) in the early seventies, these grafts have become the gold standard for primary reconstruction of the mandible, especially when concurrent soft tissue reconstruction or radiotherapy was needed, and in defects larger than 9 cm.^{19, 20} Over the years, many designs for vascularized osseomyocutaneous flaps for mandibular reconstruction have been reported, the most popular of which are the vascularized fibula, scapula and iliac crest. They provided better functional results, with the possibility of carrying tooth restorations for full mouth rehabilitation, and the ability to reconstruct large and composite defects, even during active skeletal growth.^{7, 9, 12, 21}

In spite of their impressive success rates, VBG have high rates of complications, especially medical complications.^{8, 20, 22} These highly demanding techniques, which require specialized surgical teams, add to the longevity and complexity of the primary surgery. Another disadvantage is the donor site morbidity. Leg pain and ankle instability have been reported with the vascularized fibula.²³ Anterior iliac crest grafts have around 23% morbidity,²⁴ including postoperative pain, iliac fractures or instability, persistent hematoma, herniation of abdominal contents, vascular injury, nerve injury, and unsightly contour defects along the iliac crest.^{25–28} Limited shoulder range of motion has been reported with vascularized scapula.²⁹ Most importantly, the characteristics of each flap design limit its use to specific defects, and also limit the prospects for prosthetic rehabilitation.

New treatment options are extensively being explored to reduce the surgical trauma and improve the functional and esthetic results. They include tissue engineering technology and distraction osteogenesis. Bone transport distraction osteogenesis (BTDO) has proven its effectiveness in reconstructing bone defects in the extremities.^{30–32} Sporadic case reports and animal studies presented this technique as a promising alternative to traditional reconstruction methods of the mandible.^{11, 33, 34} The bone quality and physical dimensions of new bone produced by distraction osteogenesis was comparable to those of the original bone before excision.^{10, 11} The surgical trauma was much reduced and no donor site was needed. Most importantly, the new bone was enclosed in a sleeve of healthy, sensible mucosa, and the lingual and buccal sulci could be restored, making it ideal for dental restoration, controlling salivary drooling, and regaining lip and tongue functions.

Therefore, bone transport distraction has great potential for becoming a standard reconstruction option in mandibular bone defects. However, more research is needed, objectively to test the advantages, disadvantages, indications, and limitations of mandibular BTDO. This study tested the radiological and microstructural properties of new bone produced by BTDO, as well as the technical considerations involved in the transport process, in a canine model.

MATERIALS AND METHODS

Animals

Thirteen adult male foxhound dogs were used in the study, with an average weight of 81.5 ± 8.3 pounds. They were randomly divided into two groups: group 1 representing the untreated defect ($N = 8$), and group 2 representing the bone transport group ($N = 5$). In group 1, a segmental bone defect (33 ± 8.4 mm) was created on one side of the mandible and was stabilized by a reconstruction plate with no definitive bone reconstruction. These animals served as surgical controls to confirm the size of the defect as a critical-sized defect. The animals were sacrificed ten weeks after surgery. In group 2, a similar size segmental defect was created (33.8 ± 2.4 mm), followed by bone transport until the transport bone segment docked at the end of the defect. Bone from the equivalent location of the defect on the contralateral side of the mandible served as the control bone for all analyses. Animals were sacrificed after four weeks of consolidation. The housing, care, and experimental protocol were in accordance with guidelines established by the Institutional Animal Care and Use Committee at Texas A&M Health Science Center, Baylor College of Dentistry, Dallas, TX.

Bone transport reconstruction plate (BTRP)

The device is composed of a traditional titanium mandibular reconstruction plate (fig. 1) with a middle segment that functions as a track over which a transport unit can be moved along the plate from one end of the defect to the other. The middle segment of the plate spans the bone defect. The two ends of the plate are stabilized to the bone segments by 3–4 titanium screws (2.7 mm) on either side of the defect. The transport unit is attached to the transport bone segment

(transport disc) via several 1.7 mm titanium miniscrews after the transport disc is separated from the posterior bone segment bordering the defect.

Activation of the transport unit is carried out by clockwise rotation of the activation cable, causing the unit to move forward for one millimeter per complete revolution along the threaded grooves on the surface of the transport track. The surface of the middle segment of the plate facing the gap has an undercut, so that a countersink, or lip, in the transport unit fits into the undercut for added stability during the transport process. The thread of the screw is shaped at its foremost end to cut through any soft tissue growth that may be covering the serrations on the rail. The transport unit is composed of two halves attached at the middle by two connecting 1 mm screws.

Surgical procedure and distraction protocol

Before surgery, the mandibular and maxillary canines on the same side of the surgery were extracted to prevent undue trauma and infection. The anterior teeth and the most posterior molar were preserved to maintain functional occlusion. Prophylactic root canal treatment was done on the same side canine tooth. The root of the canine is long and curved and has the risk of being injured during surgery. Food, not water, was withheld from each dog for 24 hours prior to surgery due to the propensity for bloat and regurgitation. Before surgery, each dog was injected with Atropine 2 mg/100lbs SQ. This was given 15 minutes prior to pre-anesthetic of Diazepam 0.5 mg/kg IM.

Once the animal was sedated, Isoflurane was administered via a mask held over the dog's muzzle. The Isoflurane was administered at 4% in 100% O₂ with a flow rate of 3 to 4 liters per minute. Next, endotracheal intubation was carried out with a size 10 tube, and animals were maintained on Isoflurane at 1–2% in 100% O₂ at a flow rate of 0.5–2 liters per minute, depending on the tidal volume. At this time, dogs were given Penicillin G Procaine with Penicillin G Benzathine at a dose of 300,000 iu./25 lbs. SQ. This dose was repeated every 3 days for 2 weeks.

Under aseptic conditions, one side of the mandible was explored through a 20 cm submandibular incision extending backwards and upwards along the posterior border of the vertical ramus. Bone was exposed by sub-periosteal dissection, except over the bone segment to be removed where dissection was supra-periosteal. The boundaries of that bone segment (~30 mm length) and the potential transport segment (transport disc ~15 mm in length, mesial to the removed segment) were marked. The plate component of the device was then secured to the mandible with four bicortical screws to maintain mandibular proportions before osteotomy and removal of the bone segment.

The plate was then removed and two bicortical osteotomies were carried out to free and remove the 30 mm bone segment using a reciprocating mini-saw (Stryker Craniomaxillofacial, Portage, MI). The inferior alveolar neurovascular bundle was ligated proximally before removal with the bone segment to minimize bleeding. The plate was then replaced using the previously drilled screw holes as guides. After securing the plate, another bicortical osteotomy was done to separate the transport disc from the posterior border of the defect. The burrs and saw blades were cooled while in contact with the bone using continuous irrigation with sterile saline. In addition to preserving the inferior alveolar vessels proximal to the transport disc, dissection of the lingual mucosa was kept to a minimum to maintain the vitality of the bone disc.

Next, the activation cable was introduced through a 20 mm skin incision behind the mandibular ramus into the field. The transport unit was then assembled around the activation screw using the two assembly screws and secured to the transport disc with at least four 1.7 mm titanium miniscrews. The wound was then closed in three layers with 3–0 vicryl sutures.

After surgery, the dogs were continuously monitored until they were awake. Buprenorphine was given at 0.005 mg/kg SQ every 12 hours for pain. Dogs were allowed to eat soft foods the next morning. Food and water consumption was monitored to make sure the animals were eating and drinking properly.

After a 4–5 day latency period, activation of the BTRP device was started. Distraction proceeded at a rate of 0.5 mm/12 hours and continued until the transport segment reached the docking site. The progress of the distraction and consolidation was assessed through biweekly X-rays. Animals were sacrificed using Beuthanasia-D (1 cc IC while under anesthesia) in accordance with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. The mandible was dissected to test device stability, orientation and functionality.

Clinical evaluation

Progress of device activation, stability of bone segments, tissue coverage, signs of infection, eating habits, and change in orientation of transport disc were followed up clinically and radiographically throughout the experiment. Complications were recorded and managed accordingly.

Physical dimensions of the consolidated regenerate

After necropsy, the mandible was excised and sectioned into right and left sides. Both the defect and the corresponding area on the opposite side were radiographed at the same distance and parameters. Height and thickness of the regenerate and contralateral side control bone were measured by direct tracing of the radiographs at three points on each side (fig. 2A and 2B). The average bone height and thickness were calculated and compared between the regenerate and control.

Radiographic density comparison

Both the regenerate and control bone were scanned using a high-resolution CT machine (I-CAT, Imaging Sciences International, Hatfield, PA). Samples were scanned at a voxel size of 0.4 mm. Radiographic attenuation of the regenerate, measured in Hounsfield Units (HU) was compared to those of the outer, inner, and inferior cortices of the control side.

Three-dimensional histomorphometry with micro CT

Bone blocks obtained from the inferior border of both the regenerate and the control sides were scanned using Skyscan 1174 compact micro CT scanner (Skyscan, Kontich, Belgium) at a pixel size of 25 μ m. Three-dimensional reconstruction was performed with NRecon software, and three-dimensional histomorphometry was done on the reconstructed scans using CTAn software (Skyscan, Kontich, Belgium). Two independent, semi-blinded observers conducted the three-dimensional histomorphometry, each observer identifying ten volumes of interest (VOI). Measurements were compared between observers to ensure consistency. Differences between control and regenerate bone were checked in each data set and then in the combined data set. Percent bone volume (BV/TV), bone mineral density (BMD), and degree of anisotropy (DA), trabecular thickness (Tb.Th), trabecular number (Tb.N), trabecular pattern factor (Tb.Pf), and trabecular separation (Tb.Sp) were calculated in all samples. Histomorphometry nomenclature was based on the American Society of Bone and Mineral Research standards.³⁵

Histologic evaluation of the docking site

The docking site was sectioned as one block and embedded in methylmethacrylate. After embedding, the block was sectioned at 75 μ m, ground, polished and stained with Stevenel's

blue for qualitative histological examination. Signs of bone union at the docking site were evaluated. Statistical analysis

Statistical comparisons between the regenerate and control sides were conducted using a non-parametric paired sample Wilcoxon test. All calculations were carried out using SPSS version 15.0 for Windows (SPSS Inc. Chicago, Illinois).

RESULTS

Clinical Evaluation

Four animals had to be excluded from the study and were replaced. In two control animals, severe postoperative infection occurred and was resistant to antibiotics. The infection caused massive dehiscence of the extraoral incision, leading to feeding difficulty. Local cleaning, debridement, and resuturing failed to correct the problem and the animals had to be euthanized. In a third control animal, severe thrombocytopenia was discovered preoperatively and the animal was excluded. In one animal in the experimental group, the animal died intraoperatively due to cardiac arrest.

The surgical procedure went smoothly in the remaining thirteen animals. Blood loss during surgery was kept to a minimum by adequate hemostasis, ligation of the inferior alveolar neurovascular bundle before removal of the bone segment, and preservation of the bundle proximally during osteotomy to separate the transport disc. Device assembly and application was simple and successful in all animals, regardless of the variations in mandibular surface outline. Animals tolerated the postoperative period well.

At the time of sacrifice, control animals showed no signs of bone healing across the defect, confirming the defect was a critical sized defect. The reconstruction plate maintained adequate stability of the bone segments in these animals. Due to complete absence of bone in these defects, no further analyses were conducted on these specimens. In four of the five experimental animals, device activation went smoothly at the planned rate and rhythm. In the 5th animal, premature consolidation required a re-fracture of the transport segment of bone after which device activation continued smoothly. Experimental animals showed good bone formation within the defect, compared to the original bone outline. Radiographic quality of the regenerate markedly improved after the consolidation period (fig. 2C and 2D). Manual testing of the mandible showed adequate stability of the mandible in four animals, except for some movement at the docking site. One animal showed significant lack of stability throughout the regenerate, and radiographic analysis of the mandible showed fracture of the regenerate (fig. 3A).

The docking site mostly showed clinical and radiographic signs of nonunion. Soft tissue interposition, hourglass appearance of bone ends, and lack of physical stability were consistent findings. Radiographically, the recipient bone segment consistently produced a cone of new bone into the defect during the activation process. As the transport segment approached the docking site, it was arrested by the tip of that bone cone, preventing surface-to-surface bone apposition between the transport disc and the recipient bone segment (fig. 3B).

Observed postoperative complications during bone transport included:

1. Wound dehiscence: In most animals, there was some degree of intraoral exposure of the transport segment during the activation period. Repeated cleaning, antibiotics, and re-suturing minimized this problem.
2. Inadequate stability of the transport disc leading to tilting: In two animals, fixation of the transport unit to the transport bone disc was not rigid enough to withstand tissue resistance forces during activation. This resulted in backward tilting of the gingival

end of the bone disc (fig. 3C). In both cases, only four miniscrews were used for stabilization, some of which were not tight enough at insertion. Tilting, however, did not seem to affect bone regeneration within the defect, although it posed a problem at the docking site, where the two bones met at a point rather than a flat surface.

3. Premature consolidation: In one animal, activation of the device was arrested after one week due to premature consolidation. The regenerate had to be explored under general anesthesia for a re-fracture. Subsequent activation went smoothly and no effect on bone regeneration was noted.
4. Regenerate fracture: In one animal, the bone regenerate fractured at two places during consolidation (fig. 3A). The fracture was discovered in a routine radiograph and the animal did not exhibit feeding problems or signs of pain.
5. Mechanical malfunction: In two animals, the two halves of the transport unit of the device were forced apart. This problem was caused by lack of retention of the two screws holding the two halves together. The device was explored under general anesthesia to fix the problem and subsequent activation proceeded uneventfully. The design of the holding screws has been improved to increase retention.

Physical dimensions of the consolidated regenerate

There was no statistically significant difference between the contralateral control side bone and regenerate in average height or thickness (fig. 4A and 4B). Overall, $83.7 \pm 13.7\%$ of the original defect span was bridged with new bone. The remaining defect after reconstruction occurred between the transport disc and the recipient bone segment (at the docking site). The new bone attained $87.5 \pm 23.05\%$ of thickness and $96.2 \pm 21.4\%$ of height relative to the control side.

Radiographic density comparison

Measuring radiographic attenuation using cone-beam CT scan, there were no statistical differences between the upper and lower parts of the regenerate. Likewise, no statistical difference was detectable between the regenerate and the outer or inner cortices of the contralateral control side bone. However, the lower border of the control bone had higher values than all other zones both in the control and regenerate bone ($p = 0.042$) (fig. 5).

Three-dimensional histomorphometry with micro CT

There were no statistically significant differences between the distraction regenerate and contralateral control bone in BMD, DA, Tb.Th, Tb.N, or Tb.Pf (table 1). However, BV/TV was significantly lower ($P = 0.005$) and Tb.Sp was significantly higher ($P = 0.043$) in the regenerate than the contralateral control bone.

Histologic evaluation of the docking site

Histological examination of the docking site revealed lack of bony union between the transport disc and the opposing bone segment. A cleft consistently separated the two segments, with an intervening soft tissue barrier (fig. 6). Some histological sections showed trabecular continuity between the two bone segments, but this finding was not consistent.

DISCUSSION

For the last forty years, patient survival after surgery for removal of malignant tumors of the oral tissues has been 50% to 60%, with most deaths occurring within two years of the primary surgery.^{19, 36} With this perspective, it appears reasonable to delay reconstruction until the first two years have elapsed, or to depend wholly on the reconstruction plate without grafting.⁸

³⁷ However, extensive scarring and tissue collapse during this period decreases the prospect of a successful reconstruction outcome in secondary reconstruction.¹⁹ On the other hand, the lack of bone in the defect raises concerns about metal fatigue of the fixation plate and deprives the patient of any possible dental prosthetic rehabilitation. Overall, the tendency towards primary definitive reconstruction of bone is currently predominant,¹⁹ with a strong trend towards exploring less traumatic methods that produce better functional and esthetic results.

Currently, the gold standard in primary reconstruction is VBG.¹⁹ It is considered the primary option when the bone defect is longer than 9 cm, when simultaneous soft tissue reconstruction is required, and when radiotherapy is planned after surgery.¹⁸ With an impressive greater than 95% success rate, even with pre or postoperative radiotherapy, VBG have gained wide popularity.^{18, 22, 38} There are numerous potential graft sources, and designs can be fashioned to restore the three-dimensional configuration of the mandible. In addition, it is possible to transfer vascularized skin and/or muscles with the bone for concomitant soft tissue reconstruction. Dental implants have been immediately placed into the graft with great success.³⁸

However, the impressive success of VBG has to be evaluated in light of their side effects and limitations. Surgical complications within the donor and recipient sites are quite frequent.^{19, 23} More importantly, medical complications are also high, including increased post-operative mortality.^{8, 22} It can be argued that these grafts are usually used during more extensive tumor surgeries than NVBG, which may account for their higher incidence of medical complications. However, it cannot be disputed that VBG result in increased operating time, longer hospital stays, and greater blood loss during surgery. It has been reported that VBG patients spend an average of 3 more hours in surgery, 12 more days in the hospital, and lose 500 cc more blood during surgery, than patients who receive NVBG.¹⁹

On the other hand, NVBG have lower medical complication rates than VBG. They are frequently used in secondary mandibular reconstruction where there is sufficient soft tissue coverage. Their success rate in secondary reconstruction is around 72%, but drops sharply if the defect size is larger than 6 cm.¹⁸ Their use is not recommended when the defect is larger than 9 cm in length due to very high failure rates.^{18–20} Donor site morbidity is also high.³⁹ Furthermore, NVBG are not recommended in primary reconstruction due to the high incidence of resistant infection.^{18, 19}

Success of distraction osteogenesis techniques in long bone reconstruction has lead many surgeons to start testing them in craniofacial reconstruction. Several experimental studies have investigated the production of new bone during distraction osteogenesis.^{40–44} Reconstruction of mandibular bone defects using bone transport techniques (BTDO) have also been investigated, in both animal models^{10, 11, 45–48} and human patients.^{33, 49–51} This method has shown great potential for treating difficult cases, for which other reconstruction attempts have failed.^{52, 53}

The appeal of BTDO comes from its unique property of producing bone regenerate comparable to the native bone in both physical dimensions and mechanical properties, with a much less invasive surgical procedure than bone grafting.^{10, 11, 54} Surrounding soft tissues simultaneously grow to accommodate the changing osseous dimensions. However, clinical use of BTDO in mandibular defect reconstruction has so far been limited to sporadic case reports.^{33, 34, 55}

In this study, a new device was used to test the efficacy of BTDO in immediate reconstruction of a segmental mandibular bone defect. The surgical procedure and device placement was straightforward and did not significantly add to the surgery time or the amount of blood loss of the excision procedure. Placement of the transport unit onto the bone transport segment took

15–20 minutes after creation of the surgical wound and placement of the reconstruction plate. Stability of the bone segment was maintained throughout the experimental period and bone transport proceeded smoothly until docking, although transport segments in 2 of 5 animals did show some rearward tipping. This was due to the use of 4 screws per transport segment, and it is suggested that more than 4 screws be used to stabilize the transport segment. A very stable transport segment was noted in the remaining animals with placement of more screws.

Another complication of the procedure was dehiscence of the soft tissue at the transport segment. To simulate the surgical reality of removing a full thickness bone segment during tumor resection, the periosteum overlying the defect area was removed with the bone in all animals. This made it difficult to ensure continuous coverage of the transport segment with periosteum as transport progressed. The soft tissue coverage was also weakened by removal of the periosteum and tended to sag downwards, exerting more pressure on the sutures and exposing the upper portion of the transport segment. Debridement of the exposed portion of the bone helped with resuturing. This problem was further minimized by extraction of the opposing upper teeth to prevent friction against the intraoral sutures, and by the use of Polysorb sutures instead of Vicryl sutures. Tooth extraction was appropriate given the natural cross-bite in the dog model. However, it is not expected to be necessary in human procedures, since human occlusion should not result in frictional forces against the opposing gums.

Radiographic assessment showed that the dimensions and quality of the new bone were comparable to the original bone, even though the regenerate was examined only four weeks after the end of the distraction period. The regenerate had an average vertical height of 96% of the control contralateral side bone, an impressive advantage over the 26% reported for vascularized fibula grafts.¹⁹ The insufficient bone height provided by vascularized fibula graft typically limits the prosthetic options for the patient to an implant-supported removable appliance.¹⁹ With the regenerate height produced by BTDO, almost all options are open, including a traditional removable denture, or fixed appliances. Furthermore, regenerate thickness was 87.5% of the control, allowing substantial liberty in choosing implant size and orientation.

Bone density and trabecular parameters of the regenerate were comparable to the contralateral control bone. There was no difference in anisotropy between the two sides. However, the fractional bone volume of the regenerate was less while the trabecular separation was more than that of the control bone. These parameters are the most important architectural determinants of mechanical strength in bone.⁵⁶ While reported findings suggest that mechanical loading can be increased at this relatively early time point, it is apparent that insertion of endosseous implants should be deferred until the bone volume and trabecular separation are normalized. More research is underway to identify the ideal time point for implant placement.

The device used in this study depends on a modified reconstruction plate as a transport track, along which the transport bone disc travels towards the docking site. One problem that was experienced was the failure of the screws holding the two halves of the transport unit together. These screws were redesigned to increase their retention and prevent separation of the two halves of the unit. This transport mechanism of the transport unit traveling along the reconstruction plate provided stability of the bone segments and control of the transport disc, which followed the outline of the original mandibular bone before excision. More importantly, because the transport disc is carried along the plate itself, the transport distance is not limited by a track on a separate or super-mounted device, as in previous designs (ref). This would allow carrying multiple transport discs, and the reconstruction of the curved anterior portion of the mandible, a task that was not possible for some other internal devices. The device application is simple and does not add significant operating time or blood loss to the excision surgery.

The human version of the device has an intraoral activating rod instead of the extraoral cable of the canine version. Therefore, the device, or the plate component alone, can be applied at the primary surgery and retained for as long as necessary until reconstruction time is decided. Then, the activation component can be inserted and the transport disc osteotomized through a minor surgical procedure and the transport process can be started. This provides the flexibility of staging the reconstruction of such anterior defects, without the need to remove or replace the device.

One of the major limitations of BTDO is the typical lack of healing at the docking site, which requires secondary surgical freshening of bone edges with impaction of autogenous cancellous bone grafts to augment healing.^{33, 57} Even though the amount of bone graft material required would be much smaller than the size of the original defect, it would be ideal to eliminate the need for bone grafting and save the patient a secondary surgical site and procedure. This goal can be achieved with bone inducing factors, such as bone morphogenetic proteins (BMP).

The use of BMP in mandibular reconstruction has already been attempted with promising results.^{58–60} However, these materials are expensive, especially when substantial doses are needed in large defects. Furthermore, the unconfined nature of mandibular defects, especially those resulting from tumor excision, raise serious concerns about how well the drug will be kept from escaping into surrounding tissues and the oral cavity. At the docking site, however, the bone edges are close together and the amount of BMP required should be very small. If successful, such a unique combination of surgical and bone engineering technologies would constitute an ideal treatment option for mandibular defects of various sizes. Further studies are underway to explore methods of healing augmentation at the docking site and the procedure for reconstructing curved anterior mandibular defects.

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REFERENCES

1. American Cancer Society. Cancer facts and figures 2006. American Cancer Society, Inc; Atlanta: 2006.
2. Marx RE, Johnson RP. Studies in the radiobiology of osteoradionecrosis and their clinical significance. *Oral Surg Oral Med Oral Pathol* 1987;64:379–390. [PubMed: 3477756]
3. Dudziak ME, Saadeh PB, Mehrara BJ, et al. The effects of ionizing radiation on osteoblast-like cells in vitro. *Plast Reconstr Surg* 2000;106:1049–1061. [PubMed: 11039376]
4. Nussenbaum B, Rutherford RB, Teknos TN, et al. Ex vivo gene therapy for skeletal regeneration in cranial defects compromised by postoperative radiotherapy. *Hum Gene Ther* 2003;14:1107–1115. [PubMed: 12885349]
5. Granstrom G. Placement of dental implants in irradiated bone: the case for using hyperbaric oxygen. *J Oral Maxillofac Surg* 2006;64:812–818. [PubMed: 16631490]
6. Marx RE. Mandibular reconstruction. *J Oral Maxillofac Surg* 1993;51:466–479. [PubMed: 8478754]
7. Olvera-Caballero C. Mandibular reconstruction in children. *Microsurgery* 2000;20:158–161. [PubMed: 10980513]
8. Komisar A. The functional result of mandibular reconstruction. *Laryngoscope* 1990;100:364–374. [PubMed: 2181219]
9. Kuriloff DB, Sullivan MJ. Mandibular reconstruction using vascularized bone grafts. *Otolaryngol Clin North Am* 1991;24:1391–1418. [PubMed: 1792077]
10. Jonsson B, Siemssen SJ. Arced segmental mandibular regeneration by distraction osteogenesis. *Plast Reconstr Surg* 1998;101:1925–1930. [PubMed: 9623838]

11. Ayoub AF, Richardson W, Koppel D, et al. Segmental mandibular reconstruction by microincremental automatic distraction osteogenesis: an animal study. *Br J Oral Maxillofac Surg* 2001;39:356–364. [PubMed: 11601816]
12. Takushima A, Harii K, Asato H, et al. Mandibular reconstruction using microvascular free flaps: a statistical analysis of 178 cases. *Plast Reconstr Surg* 2001;108:1555–1563. [PubMed: 11711927]
13. Shockley WW, Weissler MC, Pillsbury HC. Immediate mandibular replacement using reconstruction plates. *Arch Otolaryngol Head Neck Surg* 1991;117:745–759. [PubMed: 1863439]
14. Branemark PI, Lindstrom J, Hallen O, et al. Reconstruction of the defective mandible. *Scand J Plast Reconstr Surg* 1975;9:116–128. [PubMed: 1103278]
15. Chow JM, Hill JH. Primary mandibular reconstruction using the AO reconstruction plate. *Laryngoscope* 1986;96:768–773. [PubMed: 3724329]
16. Komisar A, Shapiro BM, Danziger E, et al. The use of osteosynthesis in immediate and delayed mandibular reconstruction. *Laryngoscope* 1985;95:1363–1366. [PubMed: 3903402]
17. Komisar A, Warman S, Danziger E. A critical analysis of immediate and delayed mandibular reconstruction using A-O plates. *Arch Otolaryngol Head Neck Surg* 1989;115:830–833. [PubMed: 2660852]
18. Foster RD, Anthony JP, Sharma A, et al. Vascularized bone flaps versus nonvascularized bone grafts for mandibular reconstruction: an outcome analysis of primary bony union and endosseous implant success. *Head Neck* 1999;21:66–71. [PubMed: 9890353]
19. Pogrel MA, Podlesh S, Anthony JP, et al. A comparison of vascularized and nonvascularized bone grafts for reconstruction of mandibular continuity defects. *J Oral Maxillofac Surg* 1997;55:1200–1206. [PubMed: 9371107]
20. August M, Tompach P, Chang Y, et al. Factors influencing the long-term outcome of mandibular reconstruction. *J Oral Maxillofac Surg* 2000;58:731–737. discussion 738. [PubMed: 10883687]
21. Wei FC, Santamaria E, Chang YM, et al. Mandibular reconstruction with fibular osteoseptocutaneous free flap and simultaneous placement of osseointegrated dental implants. *J Craniofac Surg* 1997;8:512–521. [PubMed: 9477839]
22. Haughey BH, Wilson E, Kluwe L, et al. Free flap reconstruction of the head and neck: analysis of 241 cases. *Otolaryngol Head Neck Surg* 2001;125:10–17. [PubMed: 11458207]
23. Holzle F, Kesting MR, Holzle G, et al. Clinical outcome and patient satisfaction after mandibular reconstruction with free fibula flaps. *Int J Oral Maxillofac Surg* 2007;36:802–806. [PubMed: 17614257]
24. Ahlmann E, Patzakis M, Roidis N, et al. Comparison of anterior and posterior iliac crest bone grafts in terms of harvest-site morbidity and functional outcomes. *J Bone Joint Surg Am* 2002;84-A:716–720. [PubMed: 12004011]
25. Boone DW. Complications of iliac crest graft and bone grafting alternatives in foot and ankle surgery. *Foot Ankle Clin* 2003;8:1–14. [PubMed: 12760571]
26. Nocini PF, Bedogni A, Valsecchi S, et al. Fractures of the iliac crest following anterior and posterior bone graft harvesting. Review of the literature and case presentation. *Minerva Stomatol* 2003;52:441–452. [PubMed: 14765029]
27. Velchuru VR, Satish SG, Petri GJ, et al. Hernia through an iliac crest bone graft site: report of a case and review of the literature. *Bull Hosp Jt Dis* 2006;63:166–168. [PubMed: 16878841]
28. Zijdeveld SA, ten Bruggenkate CM, van Den Bergh JP, et al. Fractures of the iliac crest after split-thickness bone grafting for preprosthetic surgery: report of 3 cases and review of the literature. *J Oral Maxillofac Surg* 2004;62:781–786. [PubMed: 15218554]
29. Hartman EH, Spauwen PH, Jansen JA. Donor-site complications in vascularized bone flap surgery. *J Invest Surg* 2002;15:185–197. [PubMed: 12217183]
30. DeCoster TA, Gehlert RJ, Mikola EA, et al. Management of posttraumatic segmental bone defects. *J Am Acad Orthop Surg* 2004;12:28–38. [PubMed: 14753795]
31. Saleh M, Yang L, Sims M. Limb reconstruction after high energy trauma. *Br Med Bull* 1999;55:870–884. [PubMed: 10746336]
32. Hill RA, Tucker SK. Leg lengthening and bone transport in children. *Br J Hosp Med* 1997;57:399–404. [PubMed: 9274665]

33. Herford AS. Use of a plate-guided distraction device for transport distraction osteogenesis of the mandible. *J Oral Maxillofac Surg* 2004;62:412–420. [PubMed: 15085505]
34. Elsalanty ME, Taher TN, Zakhary IE, et al. Reconstruction of large mandibular bone and soft-tissue defect using bone transport distraction osteogenesis. *J Craniofac Surg* 2007;18:1397–1402. [PubMed: 17993888]
35. Parfitt AM, Drezner MK, Glorieux FH, et al. Bone histomorphometry: standardization of nomenclature, symbols, and units. Report of the ASBMR Histomorphometry Nomenclature Committee. *J Bone Miner Res* 1987;2:595–610. [PubMed: 3455637]
36. Ries, L.; Melbert, D.; Krapcho, M., et al. SEER Cancer Statistics Review, 1975–2005. National Cancer Institute; Bethesda, MD: 2007.
37. Head C, Alam D, Sercarz JA, et al. Microvascular flap reconstruction of the mandible: a comparison of bone grafts and bridging plates for restoration of mandibular continuity. *Otolaryngol Head Neck Surg* 2003;129:48–54. [PubMed: 12869916]
38. Keller EE, Tolman DE, Eckert SE. Endosseous implants and autogenous bone graft reconstruction of mandibular discontinuity. *J Oral Maxillofac Impl* 1998;13:767–780.
39. Young CW, Pogrel MA, Schmidt BL. Quality of life in patients undergoing segmental mandibular resection and staged reconstruction with nonvascularized bone grafts. *J Oral Maxillofac Surg* 2007;65:706–712. [PubMed: 17368367]
40. Aronson J, Shen X. Experimental healing of distraction osteogenesis comparing metaphyseal with diaphyseal sites. *Clin Orthop* 1994;301:25–30. [PubMed: 8156684]
41. Cope JB, Samchukov ML. Mineralization dynamics of regenerate bone during mandibular osteodistraction. *Int J Oral Maxillofac Surg* 2001;30:234–242. [PubMed: 11420907]
42. De Bastiani G, Aldegheri R, Renzi-Brivio L, et al. Limb lengthening by distraction of the epiphyseal plate. A comparison of two techniques in rabbit. *J Bone Joint Surg Br* 1986;68-B:545–549. [PubMed: 3733828]
43. 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. *Clin Orthop* 1989;238:249–281. [PubMed: 2910611]
44. Li G, Simpson AH, Kenwright J, et al. Assessment of cell proliferation in regenerating bone during distraction osteogenesis at different distraction rates. *J Orthop Res* 1997;15:765–772. [PubMed: 9420608]
45. Costantino PD, Shybut G, Friedman CD, et al. Segmental mandibular regeneration by distraction osteogenesis. An experimental study. *Arch Otolaryngol Head Neck Surg* 1990;116:535–545. [PubMed: 2328111]
46. Zhou HZ, Hu M, Hu KJ, et al. Transport distraction osteogenesis using nitinol spring: an exploration in canine mandible. *J Craniofac Surg* 2006;17:943–949. [PubMed: 17003624]
47. Gosain AK, Kalantarian B, Song LS, et al. Comparison of canine mandibular bone regeneration by distraction osteogenesis versus acute resection and rigid external fixation. *Plast Reconstr Surg* 2004;114:1490–1499. discussion 1500–1501. [PubMed: 15509937]
48. Annino DJ, Goguen LA, Karmody CS. Distraction osteogenesis for reconstruction of mandibular symphyseal defects. *Arch Otolaryngol Head Neck Surg* 1994;120:911–916. [PubMed: 8074817]
49. Hibi H, Ueda M. New internal transport distraction device for reconstructing segmental defects of the mandible. *Br J Oral Maxillofac Surg* 2006;44:382–385. [PubMed: 16236405]
50. Rubio-Bueno P, Naval L, Rodriguez-Campo F, et al. Internal distraction osteogenesis with a unidirectional device for reconstruction of mandibular segmental defects. *J Oral Maxillofac Surg* 2005;63:598–608. [PubMed: 15883932]
51. Kuriakose MA, Shnyder Y, DeLacure MD. Reconstruction of segmental mandibular defects by distraction osteogenesis for mandibular reconstruction. *Head Neck* 2003;25:816–824. [PubMed: 12966505]
52. Gonzalez-Garcia R, Naval-Gias L, Rubio-Bueno P, et al. Double-step transport osteogenesis in the reconstruction of mandibular segmental defects: a new surgical technique. *Plast Reconstr Surg* 2006;118:1608–1612. [PubMed: 17102734]
53. Sawaki Y, Hagino H, Yamamoto H, et al. Trifocal distraction osteogenesis for segmental mandibular defect: a technical innovation. *J Craniomaxillofac Surg* 1997;25:310–315. [PubMed: 9504307]

54. Mackool RJ, Grayson BH, McCarthy JG. Volumetric assessment of the distracted human mandible. *J Craniofac Surg* 2004;15:745–750. discussion 751. [PubMed: 15346011]
55. Sacco AG, Chepeha DB. Current status of transport-disc-distraction osteogenesis for mandibular reconstruction. *Lancet Oncol* 2007;8:323–330. [PubMed: 17395106]
56. Odgaard A. Three-dimensional methods for quantification of cancellous bone architecture. *Bone* 1997;20:315–328. [PubMed: 9108351]
57. Costantino PD, Friedman CD. Distraction osteogenesis. Applications for mandibular regrowth. *Otolaryngol Clin North Am* 1991;24:1433–1443. [PubMed: 1792079]
58. Boyne PJ, Salina S, Nakamura A, et al. Bone regeneration using rhBMP-2 induction in hemimandibulectomy type defects of elderly sub-human primates. *Cell Tissue Bank* 2006;7:1–10. [PubMed: 16511659]
59. Toriumi DM, Kotler HS, Luxenberg DP, et al. Mandibular reconstruction with a recombinant bone-inducing factor. Functional, histologic, and biomechanical evaluation. *Arch Otolaryngol Head Neck Surg* 1991;117:1101–1112. [PubMed: 1910694]
60. Toriumi DM, OGrady K, Horlbeck DM, et al. Mandibular reconstruction using bone morphogenetic protein 2: long-term follow-up in a canine model. *Laryngoscope* 1999;109:1481–1489. [PubMed: 10499059]

Figure 1.

Bone transport reconstruction plate (BTRP). The titanium reconstruction plate has a middle segment designed as a transport track (A). The two halves of the transport unit (B and C) house an activation screw (D), which is turned with an activation cable (E). Clockwise turning of the activation screw causes the transport unit to move 1 mm along the transport track.

Figure 2. Radiographs of mandible showing bone transport regenerate. This white lines show where regenerate height (A) and regenerate thickness (B) were measured. Increasing radio-opacity, indicative of increasing regenerate density and mineralization is noticeable (arrows) between the end of transport (C) and after one month of consolidation (D).

Figure 3.

Radiographs revealing bone transport complications. Fracture of the distraction regenerate (arrows) (A). Formation of a cone of new bone from the recipient edge of the defect (*) that arrested the transport process and limited the contact between edges of the transport segment and the docking site, causing docking site non-union (B). Backward tilting of the transport disc (white lines and arrow) due to destabilization of the mini-screws (C).

Figure 4. Comparison of bone height and thickness between the regenerate and corresponding area on the contralateral control bone. No significant difference was detectable between experimental and contralateral control bone.

Figure 5.

Comparison of attenuation coefficient, in Hounsfield Units (HU), between the regenerate and different areas in the contralateral control bone, measured by high resolution cone-beam CT scan. Density of the distraction regenerate (Reg) was comparable to the inner (Con_IC) and outer (Con_OC) cortices of control bone. The lower border of the control side of the mandible (Con_LB) was consistently of higher density than other zones. CI, Confidence Interval.

Figure 6.

Micrographs of undecalcified sections through the docking site (1.6x). (A) Representative section of bone union observed between the transport disc (TD) and the recipient bone segment (RS). (B) Section showing the more typical finding of the lack of bone union between transport disc and recipient bone, with fibrous tissue interposition (arrow). Distraction regenerate (DR) is shown in A parallel to the distraction vector.

TABLE 1Micro CT three-dimensional histomorphometry of control bone versus distraction regenerate (mean $\pm$ SD)

Parameter	Control	Regenerate	Unit
BV/TV	95.62 $\pm$ 5.23	75.43 14.46 [*]	%
BMD	0.57 $\pm$ 0.08	0.61 $\pm$ 0.08	g/cm ³
DA	0.61 $\pm$ 0.30	0.55 $\pm$ 0.20	N/A
Tb.Pf	-14.14 $\pm$ 12.48	-7.43 $\pm$ 8.73	mm ⁻¹
Tb.Th	0.36 $\pm$ 0.19	0.29 $\pm$ 0.04	mm
Tb.N	3.38 $\pm$ 1.41	3.04 $\pm$ 0.38	mm ⁻¹
Tb.Sp	0.05 $\pm$ 0.01	0.11 $\pm$ 0.02 ^{**}	mm

(^{*}) Significant difference at $p < 0.005$

(^{**}) Significant difference at $P < 0.043$