ORIGINAL ARTICLE

Evaluation of the consolidation period during osteodistraction using computed tomography

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The use of distraction osteogenesis offers an alternative approach to the correction of craniofacial deformities. However, little is known with respect to the appropriate length of the consolidation period for the newly formed bone. The objective of this study was to evaluate, by quantitative computed tomography, the regenerate bone produced during osteodistraction of the dog mandible at three different consolidation times. Twelve skeletally mature male beagle dogs were equally separated into three experimental groups. Each dog underwent 10 mm of bilateral distraction osteogenesis to lengthen the mandible. After the distraction period, the bone was allowed to consolidate for 4, 6, or 8 weeks, at which time the animals were sacrificed and the mandibles harvested for computed tomographic imaging. The results demonstrate a significantly lower mean bone density of the regenerate in the 4 week group when compared with either the 6 or 8 week groups ($P < .01$). There was no significant difference, however, in mean bone density between the 6 and 8 week groups. (Am J Orthod Dentofacial Orthop 1999;116:254-63)

Treating deformities of the craniofacial complex with grafting techniques is limited in its ability to change bone form and augment bone volume. Osteodistraction offers an alternative approach for correcting maxillomandibular discrepancies by generating new bone native to the area without the need for secondary donor sites. Specifically, distraction osteogenesis is the de novo formation of bone between two vascular corticotomy surfaces undergoing gradual distraction.[1-3]

Interest in using distraction for the maxillofacial region has progressed rapidly since its clinical introduction by Guerrero.[4] Several factors may account for this. For example, operating time may be minimized, and more patients may be treated in an outpatient setting, thereby minimizing costs to the patient and clinician.[5] In addition, bone plates and screws, as components of the distraction device, are temporary and are usually removed after the procedure. Because the bone segments and soft tissues are gradually stretched with this technique, osteodistraction may allow larger skeletal movements while minimizing the potential relapse seen with acute orthopedic corrections.[2] Finally, osteodistraction provides the possibility of true bone sculpting, ie, changing the shape and form of the bone to maximize the three-dimensional structural, functional, and esthetic needs of the patient.

Systematic studies performed by Ilizarov[6,7] provided the basic guidelines and requirements needed for obtaining predictable results during osteodistraction of *long bones.* Similar studies have not been performed on craniofacial bones, however. The variables that Ilizarov found particularly critical are: (1) a low energy corticotomy with maximum preservation of osteogenic tissues, (2) an adequate duration of the latency period (the time allowed for callus formation between corticotomy and distraction), (3) an optimum rate and rhythm of distraction, (4) stability of bone segments during osteodistraction, and (5) a sufficient consolidation period for mineralization of the newly formed bone (the period from the end of distraction to the removal of the distraction device). Although these parameters were established in limb lengthening, there is no reason to believe that they do not play an equally important role in distraction of craniofacial bones.

The craniofacial bones, unlike the long bones, are membranous in nature and are subject to different biomechanical conditions. For example, the long bones are generally loaded along their anatomic axis, whereas the mandible is loaded perpendicular to its anatomic axis. In support of this concept, Goldstein et al[8] suggest that

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bone formation patterns during distraction osteogenesis depend strongly on tissue morphology, external loading conditions distraction device design parameters, and device material properties. These factors may play an important role in determining the appropriate length of the consolidation period, which is the period that allows for the completion of mineralization and subsequent remodeling of the regenerate bone before unrestrained functional loading. The orthopedic literature has demonstrated that a prolonged consolidation period may lead to weakening of the regenerate as a result of disuse atrophy,[9] whereas a prematurely short consolidation period may lead to fibrous nonunion, late buckling, bending, or fracture of the regenerate.[10] Based on these differences, a simple empirical estimation or translation of the specific duration of the consolidation period based on limb lengthening may prove inadequate.

Because the consolidation period is primarily dependent on the length of the regenerate tissue, an index was developed based on experience with limb lengthening to express the duration of consolidation needed per centimeter of distraction gap. The distraction-consolidation index (DCI) represents the approximate number of days of consolidation (fixation) needed per centimeter of distraction gap.[11] For limb lengthening, approximately 2 days of consolidation is needed per 1 mm of distraction in order to allow complete mineralization of the regenerate tissue.[12] Unfortunately, even in long bones, the DCI varies in response to several variables.[11] These include the specific bone being distracted, the rate and rhythm of distraction, the age and health of the patient, and the site of corticotomy. For example, Fischgrund et al[11] found that the DCI is not constant, even if these variables are controlled for, until the distraction gap is over 8 cm. Because different factors can affect the DCI, it is important to have a method by which healing of the distraction gap can be monitored to determine the appropriate end of the consolidation period.

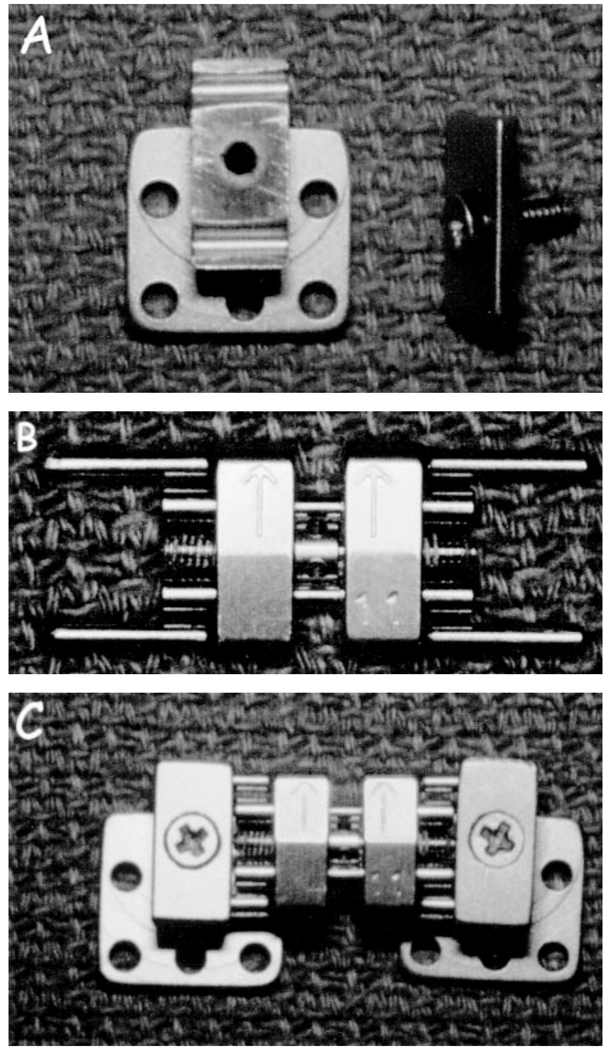

Fig 1. Prototype of intraoral bone-borne distraction device. **A**, Disassembled bone plate with locking top plate; **B**, RPE screw; **C**, assembled device with RPE connected to anterior and posterior bone plates.

Currently, plain film radiographs and clinical evaluation are the standard methods for determining the appropriate time for distraction device removal, however, there are problems with these methods as well. For example, Panjaba et al[13,14] and Fischgrund et al[11] found that the correlation between plain film radiographic density and biomechanical properties of newly formed bone is poor. In addition, Tjernstrom et al[15] showed that axial CT scans demonstrated great variations in regenerate bone appearance even though similar distraction protocols were used and the plain radiographic images were comparable. Finally, plain film imaging in the craniofacial region is more difficult than in the long bones because of the frequent superimposition of adjacent bony structures. Clinical evaluation of the regenerate bone is also limited. Currently, clinical testing includes removal of the distraction device in order to manually stress the bone and check for bone segment mobility.[11] This may be difficult or impossible to perform on some craniofacial bones, however. Because of these problems, other techniques for the evaluation of bony consolidation after osteodistraction in the craniofacial region should be explored and evaluated.

Although distraction of craniofacial bones has been successfully performed on sheep,[16-18] rabbits,[19-21] dogs,[2,22-30] nonhuman primates,[31,32] and human beings,[4,33-35] only two studies[36,37] have attempted to

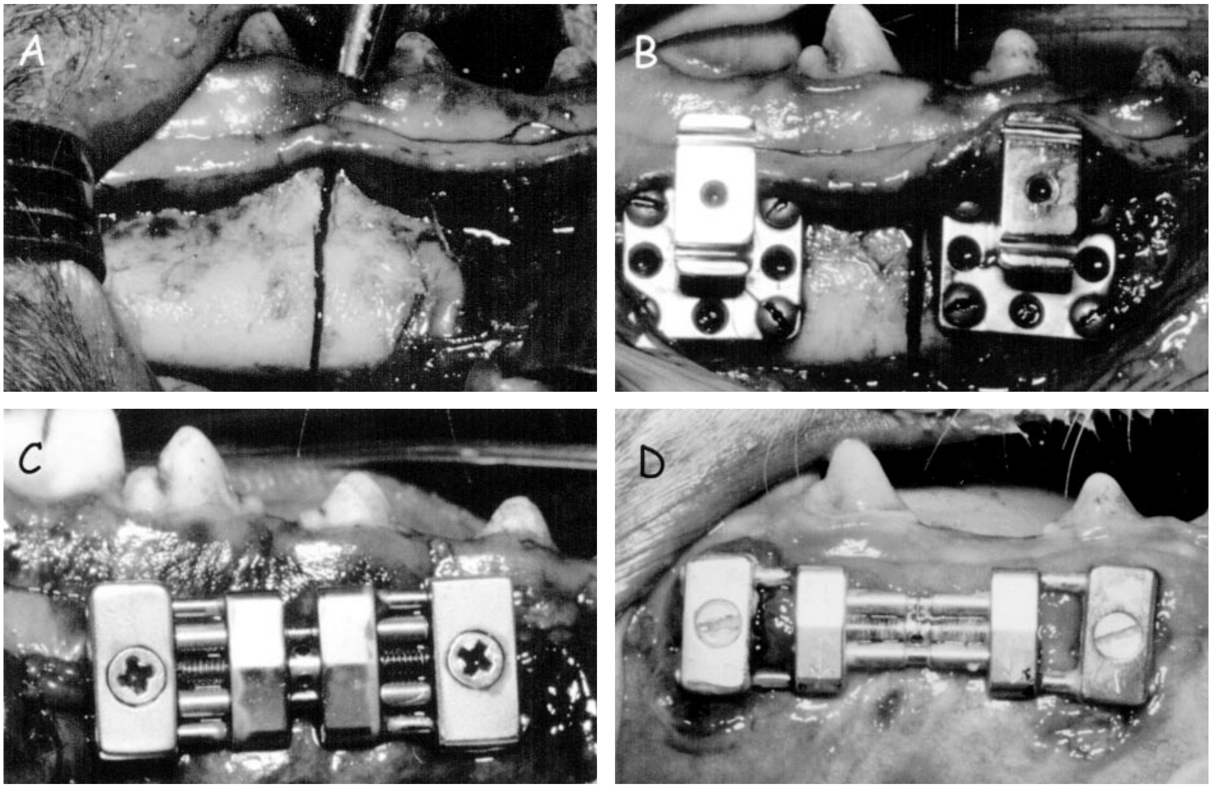

Fig 2. Surgical procedure. **A**, Placement of partial corticotomy; **B**, completion of corticotomy; **C**, final position of distraction device; **D**, position of mandible after 10 mm of distraction.

quantify Ilizarov's critical parameters for the bones of the craniofacial complex. These studies, however, focus on either the latency period[37] or the distraction rate,[36] and no study to date has systematically determined the appropriate length of the consolidation period of the newly formed regenerate bone. Therefore, the purpose of this study was to evaluate, by quantitative computed tomography (QCT), the regenerate produced during distraction of the dog mandible at three different consolidation times.

MATERIAL AND METHODS

Animal Model

Twelve skeletally mature conditioned male beagle dogs weighing 10 to 15 kg were used in this study. The dogs were equally divided into three groups based on consolidation time (group 1, 2, and 3 = 4, 6, and 8 weeks consolidation, respectively). Each group consisted of 4 dogs; all dogs underwent 10 mm of bilateral mandibular midbody lengthening via intraoral distraction osteogenesis. The housing, care, and experimental protocol were in accordance with guidelines set forth by the TAMUS-Baylor College of Dentistry Institutional Animal Care and Use Committee.

Distraction Device

The intraoral bone-borne distraction device (Fig 1) was made of stainless steel and consisted of a 13 mm rapid palatal expander (RPE, Model 620-13 Leone SpA, Firenze, Italy) connected to anterior and posterior bone plates. Each plate had seven predrilled holes for bone attachment by positional screws. The device was designed to allow plate fixation and RPE removal before completion of the corticotomy, thereby maximizing visualization of the corticotomy site and maintaining bone segment position intraoperatively.

Surgical Technique

The animals were sedated with xylazine (0.4 mg/kg/im) and ketamine hydrochloride (4 mg/kg/im). General anesthesia was maintained with endotracheal inhalation with a 2% concentration of isoflurane in oxygen. A bolus dose of penicillin G procaine (75,000 units/kg/iv) was administered postoperatively for antibiotic coverage.

Before mandibular incisions, the right and left maxillary third incisors were extracted to prevent occlusal interferences during distraction. All procedures were performed using sterile techniques. The operative

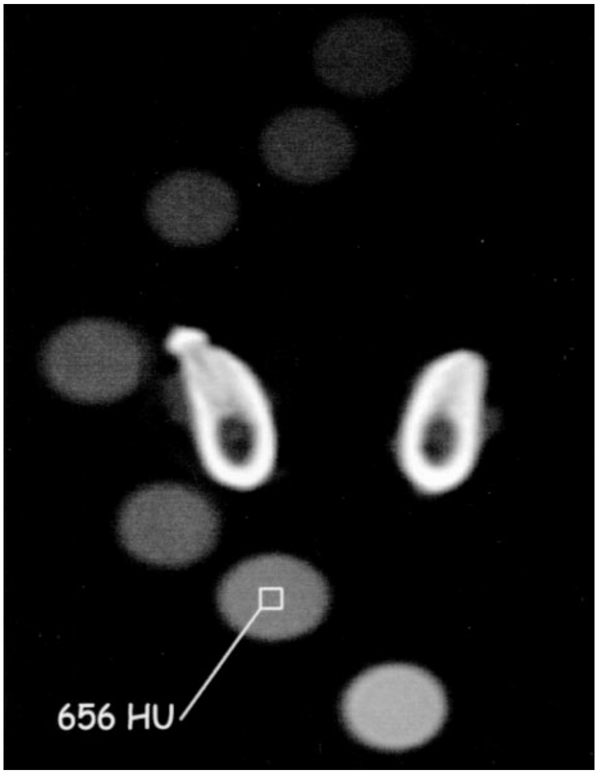

Fig 3. Calibration phantom. Microtubes of K_2HP0_4 scanned with the mandible during CT.

region was infiltrated with 2% lidocaine hydrochloride with 1:100,000 epinephrine for hemostasis. In order to expose the buccal side of the mandible, intraoral curvilinear incisions were made in the vestibule with the most superior aspect of the incision 8 to 10 mm below the alveolar crest of the second and third premolars, along the buccal aspect of the alveolus. The lingual side was exposed with a circumpapilla incision lingual to the third and fourth premolars. The soft tissue and periosteum was reflected and mandibular buccolinguoinferior border partial corticotomy cuts were made between the third and fourth premolars (Fig 2). All bone cuts were made with a standard surgical reciprocating thin saw blade and a 701-fissure bur under irrigation with sterile saline solution. To assure proper approximation of the segments, the preassembled distraction device was attached to the bone by positional screws immediately after the partial corticotomies of the mandible. After device placement, the RPE was removed, and bone division was completed manually with a mallet and a small osteotome, until segment movement was observed. The surgical incisions were then closed with a standard single layer closure with 3.0 and 4.0 polyglactin 910 sutures, followed by RPE replacement.

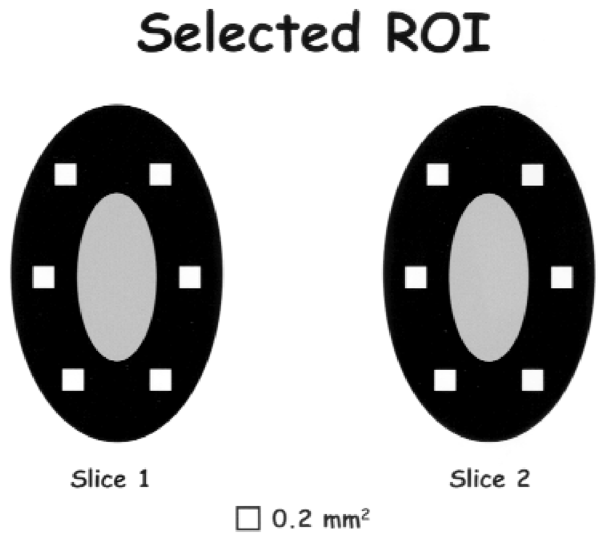

Fig 4. Regions of interest: six ROIs were selected from each frontal CT slice.

Distraction Protocol

After surgery, the dogs were carefully monitored and maintained on a soft diet. Analgesia was achieved for the first 24 hours with butorphanol tartrate (0.4 mg/kg/im). In addition, oral saline irrigation was performed twice daily for 4 days postoperatively. The bone segments were maintained in a neutral position for 7 days (latency period). On the eighth postoperative day, activation of the appliance began at a rate of 0.5 mm twice per day for 10 days to achieve a total distraction of 10 mm, followed by either a 4, 6, or 8 week consolidation period. No analgesics or sedatives were required during the distraction phase, as the dogs showed no signs of discomfort during or after device activation. The dogs were monitored daily during distraction and weekly during the consolidation period. Observations consisted of weighing the animals, examining their oral soft tissues, and checking total device expansion and fixation stability. After consolidation, the animals were sacrificed using sodium pentobarbital (100 mg/kg/iv).

Clinical Regenerate Analysis

At necropsy, the mandible was resected en bloc, and the devices were evaluated for stability of fixation. The RPE was removed, and each bone plate and screw was inspected individually. Resorption around and under the plates was assessed, followed by screw removal. Each hemimandible was then examined clinically, and the distraction regenerate across the bone segments was graded as either having formed a union or nonunion. Union was defined as no detectable mobility between

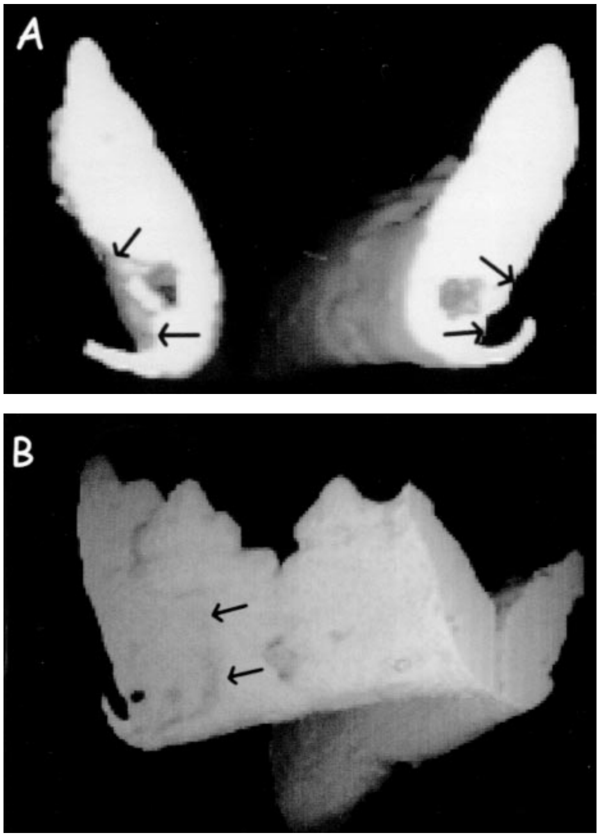

Fig 5. Bone resorption was a common finding under the posterior bone plate when devices were oriented parallel to the mandible. **A**, Frontal view; **B**, lateral view.

the proximal and distal segments. Nonunion was defined as any perceptible mobility noted between the segments. Although this method of evaluation is subjective, it is currently one of the standard methods for clinicians to use when evaluating healing after osteodistraction.[11] After clinical regenerate evaluation, the mandibles were imaged by computed tomography (CT).

Computed Tomographic Imaging Analysis

A Picker 1200SX CT scanner (Picker International, Inc, Cleveland, Ohio) was used to obtain frontal images of the dog mandibles, which were placed in the CT scanner so that the scan planes were parallel to the corticotomy cuts and perpendicular to the long axis of the mandible. The images were scanned at 95 kVp and 110 mA in 2.0 mm thick slices and taken in 1.0 mm contiguous increments along the mandible. All dogs had preoperative CTs taken as an initial baseline. Six different calibration phantoms (Fig 3) of known K_2HP0_4 concentrations were scanned with each mandible. The phantoms were then used to convert the bone mineral density (BMD) of the mandible in Hounsfield units (HU) to a bone mineral equivalent (BME) of K_2HP0_4. A region of interest (ROI) was obtained for each tube of phantom solution and a corresponding CT number recorded. This number was then correlated to each tube's specific K_2HP0_4 concentration by a least-squares regression analysis.[38] This method of calibration has been previously established for quantitative assessment of bone mineral content in vertebrae and healing bones.[38-40]

Six specific ROIs (Fig 4) were analyzed for each of the 11 CT slices within the regenerate and for 5 slices within the host bones segments on either side of the osteotomy sites. The mean BME was determined for each of the 6 regions of interest.[38] These 6 densities were averaged, and 1 mean value determined for each CT slice. Five CT slices from the proximal segment, 5 from the distal segment, and 11 slices from within the regenerate were analyzed for each hemimandible. The data were averaged for the corresponding slice in each group, and the mean BME for each slice was plotted. All three experimental groups were first compared with the use of Kruskal-Wallace nonparametric tests to determine if differences existed among the groups. The groups were then compared with Dunn's sum tests to determine where the differences were. The mean values of the left hemimandibles of one group were compared to the left hemimandibles of the other groups. The right hemimandibles were compared in the same manner. The preoperative and postoperative mean BMEs for the areas adjacent to the regenerate were calculated and compared with Wilcoxon signed ranks tests.

In order to compare the union and nonunion hemimandibles, the BME values of CT slices 4, 5, 6, and 7 (center of regenerate) were averaged and the mean value calculated. The mean BME densities of the union and nonunion mandibles were then compared, using a two-tailed Student's t test for paired samples and unequal variance. For all statistical analyses, a level of $P < .05$ was established as a significant difference between groups.

RESULTS

Clinical Evaluation

On removal of the bone plates at necropsy, localized areas of pressure resorption were seen under some of the plates. The CT scans confirmed that some plates had caused almost total resorption of the underlying buccal cortical bone (Fig 5). Bimanual manipulation of the regenerate tissue between the bone segments revealed that four of eight hemimandibles in the 4 week group were in nonunion. On the other hand, only one of the 6 week and two of the 8 week hemimandibles resulted in nonunion. Although these results suggest a

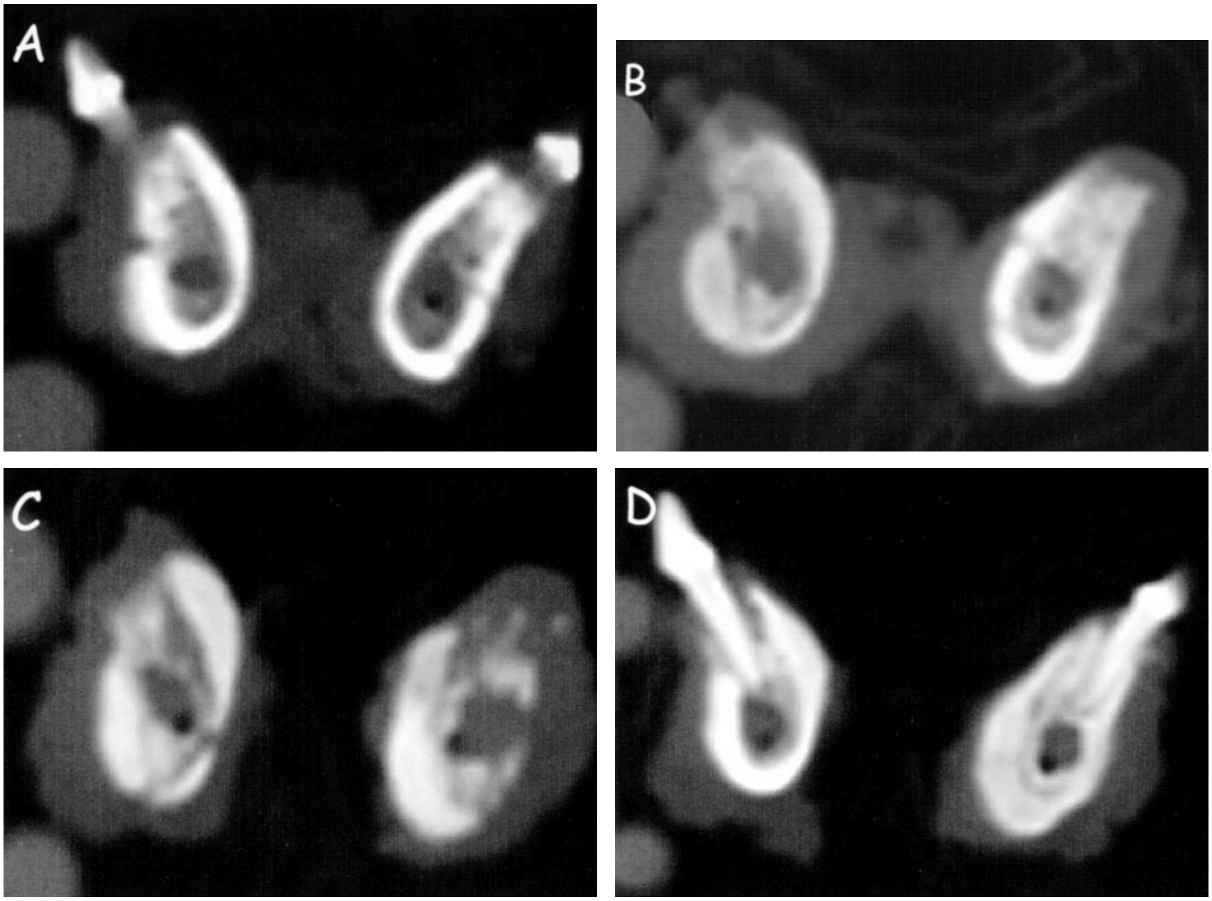

Fig 6. Mandibular CT at necropsy. **A**, Distal segment (host bone); **B**, anterior of regenerate; **C**, center of regenerate; **D**, proximal segment (host bone).

difference between the healing at 4 weeks and that at 6 or 8 weeks, statistical significance was not established. When comparing nonunion hemimandibles (mean, BME = 312 mg/ml) to union hemimandibles (mean, BME = 785 mg/ml), the nonunion group had a significantly lower ($P < .05$) BME than did the union group (Table I).

Bone Density

In general, the density of the regenerate was greater at the periphery of the newly formed bone than in the center (Figs 6 and 7). During consolidation, the regenerate density progressively increased up to and after the fourth week, then leveled off during the sixth and eighth weeks. However, the regenerate never achieved the density level seen in the preoperative bone scans. When comparing the baseline and necropsy CT scans, the postdistraction mean bone mineral density for the host bone adjacent to the regenerate was significantly less ($P < .05$) than the presurgical value for the same area (Fig 8).

Because the results in this experiment for both the left and right hemimandibles were similar, only the results of the left side are presented. When comparing the mean BME densities of the regenerate areas for each hemimandible, a significant difference ($P < .01$) was seen between the three groups. The results demonstrated a statistically significant increase ($P < .01$) in regenerate bone density after 6 or 8 weeks when compared to 4 weeks of consolidation. No significant difference was seen, however, between the 6 and 8 week groups (Fig 7).

DISCUSSION

From a clinical viewpoint, it is important to determine when the regenerate bone is strong enough to remove the distraction device and allow unrestrained functional loading of the distracted complex. Although the appropriate duration of the consolidation period can be approximated during limb lengthening by the distraction-consolidation index, the same index may not be valid in cranial bone distraction. For example,

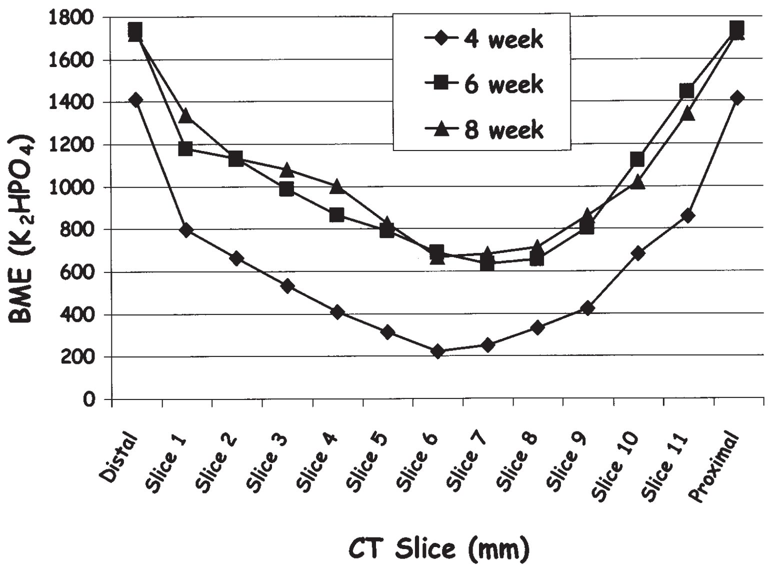

Fig 7. Comparison of individual regenerate slice BMEs for each group. Note: Lower BME of middle slices corresponds to less mineralized fibrous interzone.

Table I. Comparison of consolidation, BME, and bony union status.

		Right side		*Left side*	
Dog number	*Consolidation period (weeks)*	*Union vs nonunion*	*BME [K_2HPO_4]*	*Union vs nonunion*	*BME [K_2HPO_4]*
3	4	Union	578	Union	389
4	4	Union	455	Nonunion	205
5	4	Nonunion	174	Nonunion	324
14	4	Nonunion	288	Union	284
6	6	Union	998	Union	1047
7	6	Union	1058	Union	971
8	6	Union	542	Nonunion	308
15	6	Union	577	Union	651
9	8	Union	607	Union	1167
10	8	Union	819	Union	586
11	8	Union	637	Nonunion	578
16	8	Nonunion	678	Union	849

assume the femur is lengthened or distracted 50 mm over a 50 day period (1 mm/day). Even though it is not evident radiographically until about the 14th day after initiating distraction, mineralization of this newly formed tissue actually begins by the end of first week after initiating tensional forces. The mineralization process begins from the ends of both host bone segments and progresses toward the center of the distraction gap. When distraction is complete and the tension force is stopped at day 50, significant mineralization of the regenerate tissue has already occurred, leaving only a 5 to 10 mm length of regenerate (of 50 mm total) in the center of the gap unmineralized. Because the distraction-consolidation index suggests a consolidation period of 2 days of consolidation for each 1 mm of distraction, 100 days (2 days × 50 mm) remain for this 5 to 10 mm segment to mineralize before device removal. On the other hand, mandibular osteodistraction may average 5 mm. Based on the orthopedic distraction-consolidation index, the consolidation period would only last 10 days (2 days × 5 mm). When comparing the two regenerates, the 5 to 10 mm of unmineralized regenerate in the femur has 100 days to mineralize before device removal, but the 5 mm of unmineralized regenerate in the mandible only has 10 days to mineralize before device removal. This is clearly not enough

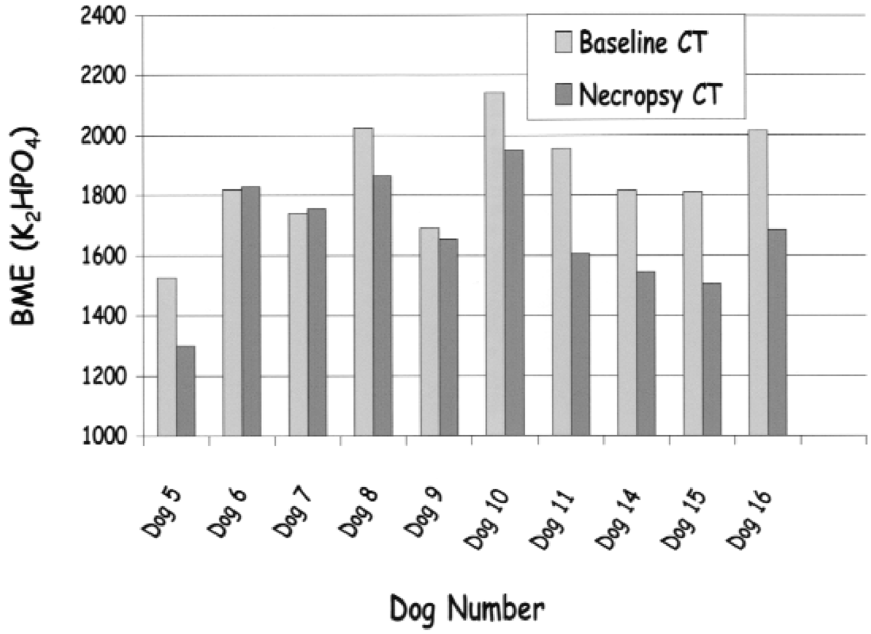

Fig 8. Comparison of baseline and necropsy host bone BMEs for each dog.

time for mineralization of the 5 mm mandibular regenerate. It follows that this index is not valid for distraction of short distances (eg, craniofacial bones), and other techniques must be developed in order to more appropriately determine the time at which the distraction device can be removed. Therefore, the goal of this study was to investigate the influence of the consolidation period during distraction osteogenesis on the subsequent mineralization of the newly formed alveolar and basal bone.

In the present study, some of the bone plates used to attach the distraction device to the mandible were found to cause pressure resorption of the underlying bone. CT imaging confirmed that some plates had caused almost total resorption of the underlying buccal cortical plate. This indicates that a significant amount of pressure is applied to the underlying bone during the distraction and consolidation periods. In this respect, our group has previously demonstrated that device orientation is one of the most important parameters affecting the successful application of osteodistraction.[22,41-43] Specifically, devices oriented parallel to the mandibular body create lateral displacement tendencies at the bone-appliance interface during distraction. These laterally directed forces have been shown to manifest clinically as bending or binding of the device, bone resorption under fixation plates, and loosening of fixation screws. When the bilateral devices were oriented parallel to each other and to the common sagittal axis of distraction, the lateral displacement tendencies did not occur. Interestingly, this resorptive phenomenon corresponded to the dogs in which the devices were oriented parallel to the mandibular body. Consequently, much less resorption was seen in dogs with devices oriented parallel to the axis of distraction.[22] Therefore, future appliance design and placement must consider the biomechanics of device orientation. Another concern is the potential detrimental effects when significant resorption occurs to the depth of the teeth or inferior alveolar nerve. In this regard, Makarov et al[44] demonstrated that resorption of underlying bone had an inhibitory effect on neurosensory function.

Clinically, the regenerate achieved bony union in 13 of 16 hemimandibles in the 6 and 8 week consolidation groups. The 4 week group, however, had only 4 of 8 hemimandibles that achieved union. Although not statistically significant, these data suggest a difference in healing between the 4 week group and the 6 and 8 week groups. When comparing the nonunion and union groups, the CT data indicate that the mean density in the center of the regenerate was significantly lower in the nonunion than the union hemimandibles, which is consistent with the clinical findings. These findings demonstrate a broad variability in healing. Even though a 4 week consolidation period might be sufficient for one dog, 8 weeks may not be long enough for others. Considering this variability, it is possible that some of the nonunion samples might have gone on to achieve union if given more time.

The results presented herein demonstrate a greater density of the regenerate bone closer to the periphery of the distraction gap than that of the regenerate near the center of the distraction gap (Figs 6 and 7). This mineralization pattern is similar to that seen in membranous and endochondral bone[1,19,45] and corresponds to the zonal regenerate pattern seen histologically[45,46] and radiographically.[22] Regenerate bone density progressively increased up to and after the fourth week, then leveled off during the sixth and eighth weeks. However, the regenerate never achieved the density level seen in the preoperative bone scans. Similar results have been reported by other investigators.[19,45,47] For example, Aronson et al[45] found that the regenerate did not reach preoperative density levels until the 17th week after distraction.

Interestingly, the mean bone density at the ends of the host bone segments proximal and distal to the regenerate was significantly lower after distraction. Similar findings have been cited in the orthopedic literature,[48] however, the exact cause remains speculative. Several explanations may account for this host bone osteopenia. For example, necrosis of the osteotomy margins is a common finding after osteotomies. In addition, the host bone may act as a reservoir of minerals to mineralize the newly forming bone during distraction. Finally, a radiographic projection error could have occurred, if the corticotomies were performed in a plane not parallel to the CT scan, inadvertent inclusion of some regenerate tissue could have caused a decreased density reading.

Although no significant differences were seen between the regenerates of the 6 and 8 week groups, a significant difference was seen between these groups and the 4 week group. This suggests that the 2 week period between 4 and 6 weeks of consolidation may play an important role in the mineralization process. Based on the current data, it appears that a 6 week consolidation period is the minimum time that the regenerate should be allowed to mineralize before device removal. It is important to note, however, that these dogs were sacrificed before removal of the distraction device. *Therefore, it is difficult to speculate what might have happened if the devices were removed and the dogs were allowed to function for an additional time period before sacrifice.* In turn, these results should be interpreted with caution. As a rule, it is probably safer to extend the consolidation period by several weeks (up to 10 or 12 weeks) than to assume that a 6 or 8 week consolidation period is broadly applicable to our clinical patient population. Other factors must also be considered when determining the consolidation period clinically. For example, the age and health of the patient, the type of osteotomy, the blood supply available to the bone segments, and the size and shape of the bone to be distracted all affect the regenerate tissue.

The total length of distraction also plays an important role in determining the consolidation period. For example, derivations of DCIs from data presented in craniofacial clinical reports suggest smaller DCIs (23 days/1 cm,[34] and 24.8 days/1 cm[49]) than would be derived from the present study (42 days/1 cm). However, the total regenerate length in the clinical reports is between 20 to 40 mm. Therefore, more regenerate was mineralized during distraction and consequently less regenerate needed to be mineralized during consolidation. The dog regenerates, on the other hand, were only 10 mm long and, hence, were less mineralized at the initiation of consolidation necessitating a longer consolidation period. In any case, because the DCI is not reliable until distraction gaps of greater than 80 mm are reached, it would be advantageous to develop alternative methods of approximating the consolidation period.

CONCLUSION

In conclusion, the results demonstrate that hemimandibles with nonunion had significantly lower BMEs than did the hemimandibles with union. This parallels the clinical findings. In addition, a significant difference in mean bone density was found between the 4 week group when compared with either the 6 or 8 week groups. This suggests that 6 weeks is the minimum time that the regenerate should be allowed to mineralize before device removal. Other factors must be considered, however, when determining the consolidation time in a clinical setting. These include, but are not limited to, age and health of the patient, the type of osteotomy, the local blood supply, the size and shape of the bone, the length of the regenerate, and fixation stability.

Computed tomography provides a means whereby increases in both bone density and bone volume can be quantified. However, as a result of higher costs, increased radiation exposure, and scatter caused by metal devices, CT evaluation is not routinely used for regenerate bone evaluation. Clinical and plain film radiographic evaluation remains the most commonly used tools in determining when to remove distraction devices. Therefore, other methods of estimating the appropriate length of consolidation need to be developed. In this respect, our group is currently evaluating the use of subtraction radiography in quantifying regenerate mineralization and estimating the consolidation period clinically. Nonetheless, QCT provides a tremendous benefit for evaluating the mineralization process and is one of the best diagnostic tools for experimentally quantifying the critical parameters for distraction osteogenesis.

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