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Functional Evaluation of a Novel Multi-Axial Alveolar Distractor—Preliminary In Vivo Animal Study

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Abstract: This study evaluates the biomechanical performance of a new multi-axial alveolar distractor using an animal study. The multi-axial alveolar distractor is designed with a ball and socket joint mechanism that can rotate up to 60° toward the buccal/lingual and mesial/distal sides intra-operatively to achieve vector control. The transport segment can be moved through activating the transport screw with 0.25 pitch, allowing 13 mm in distraction height. This distractor was fixed at the right angulus mandibular of experimental rabbits and adjusted 15° toward the mesial side and 25° toward the buccal side as Group TMB (toward mesial-buccal) (n = 3), and 15° toward the mesial side as Group TM (toward mesial) (n = 3). Group TC (control) was the control group. The distractors were activated 1 mm/day for 13 days. Living bone growth was observed at various periods. The total bone growth length at the angulus region and buccal side distraction thickness after distraction were calculated. The variations in bone growth geometric shape at the mandible angulus were also recorded. Fracture testing was performed to understand the variations in the mechanical strength between the distracted and intact bone specimens. The digital radiography results showed that the osteotomy areas at the mandible angulus were healed and the bone growth completed after surgery. The average bone growth length of Group TMB was 17.68 mm. This was greater than that of Group TM at 14.79 mm. The corresponding buccal side distractor thicknesses for Group TMB and TM after distraction were 5.12 ± 0.52 mm and 3.32 ± 0.37 mm, respectively. The tensile strengths of the bone specimens after distraction of Groups TMB, TM and TC were 172.13 N, 119.27 N and 304.24 N, respectively, and the percentage of distraction bone tensile strength to normal bone was 57% and 39% for Groups TMB and TM, respectively. This study concluded that this new multi-axial alveolar bone distractor can drive bones to grow in accordance with the direction/angle of the distraction plan. The bone growth healed gradually and presented insufficient mechanical strength.

Keywords: distractor; multi-axial; bone regeneration; ball and socket joint

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1. Introduction

Alveolar distraction osteogenesis (ADO) is a new bone formation biological process that occurs between bone segment surfaces and involves the gradual, controlled displacement of surgically created bone fragments resulting in concurrent soft tissue and bone volume expansion [1,2]. ADO has become one of the superior predictable treatment options for increasing bone height before implant placement [2–12].

In spite of the literature discussing several different types of distraction devices, the uniaxial distractor can only pull the bone linearly along the transport screw and bidirectional distractor axis with the buccal-lingual adjustable angulation intra-operatively not able to affect anatomical limitations such as the sinus/cavity, thin cortex bone region and alveolar nerve [13]. Distraction can provide free-angle bone growth (tongue/cheek, near/tele centric, occlusal direction, etc.) with precise evaluation of the planned movement and maintain the desired vector direction during the alveolar distraction process. These are the most important issues for ADO application [14,15].

Accurate control of the possibility for multidimensional distraction in different directions is considered desirable for a novel alveolar distractor design [15–18]. A distractor designed with a ball and socket joint and the capability to control 3-dimensional movements during transport osteogenesis has been proposed in previous studies to achieve multi-axial distraction with various angle adjustments for alveolar ridge curve limitations, soft tissue pulls, inappropriate device positioning, or poor device trajectory [18–20]. Serious mechanical functional tests, including four-point bending resistance testing of the base bone plate, pull out testing of the multi-axial alveolar distractor, welding strength testing between the base bone plate and ball and socket joint mechanism and torque strength testing of the ball and socket joint, were approved to ensure the effectiveness and safety of our new multi-axial alveolar distractor [18].

This study used the previously developed multi-axial alveolar distractor that has been alternative safe and effective by mechanical tests to evaluate the feasibility of the distraction function in rabbit mandibles.

2. Materials and Methods

2.1. Multi-Axial Alveolar Distractor Design Concept and Mechanical Tests

The most important design concept in the previously proposed multi-axial alveolar distractor is that it uses a ball and socket joint mechanism wielded to the base bone plate up to 60° toward the buccal/lingual and mesial/distal sides intra-operatively (Figure 1). The ball and socket joint can be relocked by tightening the hex nut after vector adjustment according to the pre-operative plan. The base bone plate and transport plate can be fixed onto the residual bone and the transport segment can be vectored through activating the transport screw with 0.25 pitch and 13 mm distraction height. The alveolar distractor and screw were manufactured with Ti6Al4V alloy by the ISO13485 quality management systems company (HUANG LIANG Biomedical Technology Co., Ltd., Luzhu Dist., Kaohsiung City, Taiwan) (Figure 1 top-left). The mechanical functional tests were performed to evaluate the effectiveness and safety of this new multi-axial alveolar distractor in a previous study [18].

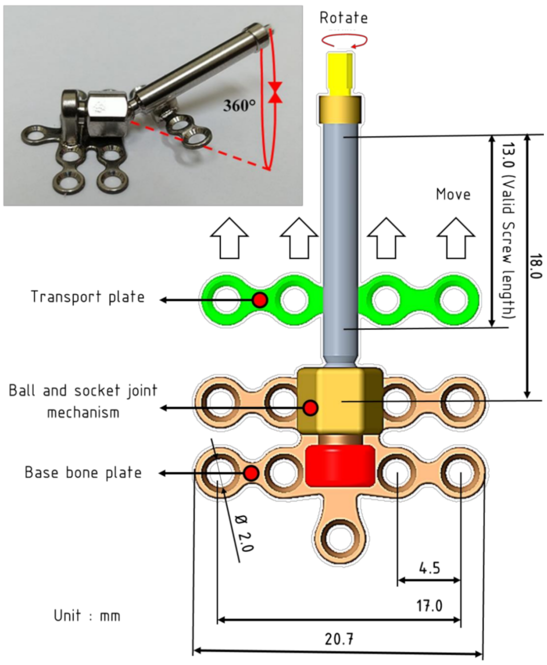

Figure 1. The new developed multi-axial alveolar distractor consists of an extra-osseous system with a ball and socket joint mechanism wielded to a base bone plate, transport plate and activating transport screw. The upper left part shows the physically manufactured distractor made of Ti6Al4V alloy.

2.2. Experimental Design and Surgical Technique

This study was reviewed and approved by the ethics review committee of The Institutional Animal Care and Use Committee (IACUC) of National Yang-Ming University (IACUC No.: 1040609). Eight female skeletally mature New Zealand rabbits weighing 2.79~4.2 kg (mean (SD) 3.55 (0.45) kg) with an average age of 24 weeks' old (error within 3 days) were used to perform this animal study. The tested multi-axial alveolar distractors were designed to fix at the right angulus mandibular of the experimental rabbits. Eight rabbits were divided into three groups of 3, 3 and 2 each. The distractor direction was adjusted 15° toward the mesial side and 25° to the buccal side in Group TMB (n = 3). The corresponding distractor direction was only adjusted 15° toward the mesial side in Group TM (n = 3) (Figure 2). Group TC was the control group with no surgery performed. The multi-axial alveolar distractor was not used for the other 2 rabbits.

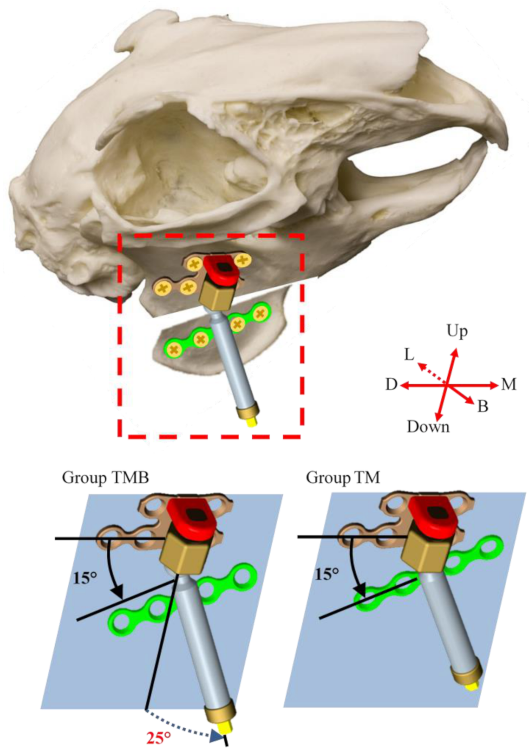

Figure 2. The distractor placement illustration defined that the multi-axial alveolar distractors were designed to fix at the right mandibular of the experimental rabbits. The distractor direction was adjusted 15° toward the mesial side and 25° to the buccal side in Group TMB (n = 3) and 15° toward the mesial side in Group TM (n = 3).

Animal experiments were performed using intramuscular injection (IM) to mix ketamine (Imalgene 1000, Merial Laboratoire de Toulouse, Toulouse, France) 35–44 mg/kg BW and xylazine (Rompun, Bayer Korea Ltd., Ansan-si, Gyeonggi-Do, Korea) 5–10 mg/kg BW for surgical anesthesia. The multi-axial alveolar distractor was adjusted to the corresponding directions for Groups TMB and TM before surgery. The rabbit was placed in the supine position with a skin incision about 2 cm long made at the corresponding right angulus mandibular of the rabbit. The multiaxial alveolar distractor was applied. The periosteum was kept intact and carefully raised to expose the mandibular bone inferior border.

The distractor was fixed to the right angulus of the mandible using 8 titanium screws, 2.0 mm in diameter and 8.0 mm length (4 for base bone plate and 4 for transport plate). After the fixation was completed, the bone between the multi-axial alveolar distractor base bone plate and transport plate was cut using an electric bone cutting saw. Before the distractor was finally placed, the adjustment was checked and the wound closed. The multi-axial alveoli distractor adjustment mechanism was exposed to the skin's exterior.

The rabbits were given a subcutaneous 10 mg/kg xylene sedative injection for pain relief two days after the operation. The rabbits were housed separately and fed a soft food diet for one week and observed every 2 to 3 days. The rabbits were recorded for health, bowel movements, suture loss and wound status (whether mass/redness, secretions). Food and water intake and body weight were monitored and recorded daily [21].

2.3. Distraction Procedure and Animal Cadaver Observation

Figure 3 shows the experimental program diagram after surgery. The distractors were activated 1 mm/day for 13 days (13 mm in total length for distractor's capability) after a 14-day latency period. The consolidation phase lasted 8 weeks (12 weeks after safe); a direct digital radiography (X-ray image) was taken every 2 weeks of the experimental rabbits to observe the growth of living bones in various periods. The shooting angle, distance and relative coordinate position between the camera and the experimental rabbit were maintained for each photographic shoot to ensure that all X-ray images had the same angle. The experimental rabbits were subsequently sacrificed. This study was approved by Affidavit of Approval of Animal Use Protocol, China Medical University, number: 2016-319.

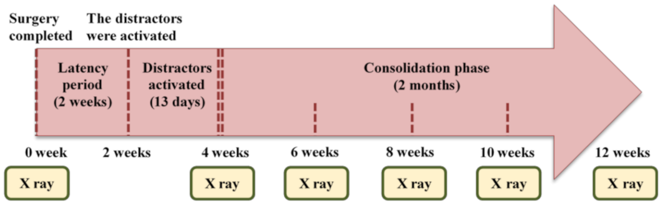

Figure 3. Whole experimental program diagram after surgery.

After the experimental rabbits were sacrificed, the rabbit mandibular included the distractor and surrounding soft tissues were removed manually using a scalpel. The mandible was then removed to observe the differences in bone growth between the left and right sides of the angulus region.

The growth bone shape corresponding to the distractor transport bone plate movement was measured, thereby calculating the traction stroke and bone growth amount of the alveolar bone retractor (Figure 4). The bone growth total length at the angulus region corresponding to the distractor transport bone plate movement before and after distraction was calculated by measuring the bending steel wire attached the growth bone surface. The variations in bone growth geometric shape observed in Groups TMB, TM and TC at the mandible angulus from the back and lateral views were also recorded (Figure 5). Buccal side angulus distraction thickness was quantified after distraction to compare the variations between Group TMB and TB. A statistical *t*-test was used to analyze the differences between groups.

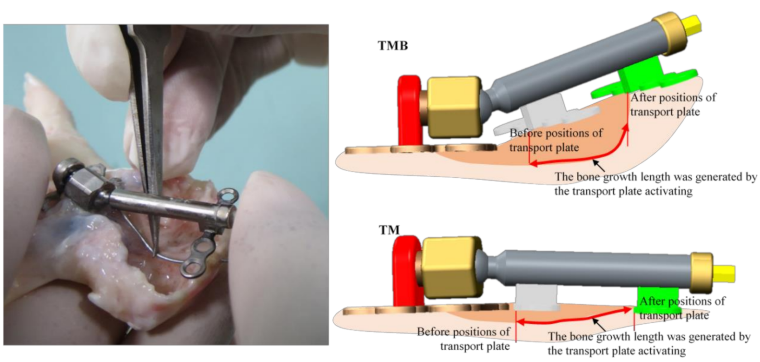

Figure 4. Bone growth total length at the angulus region corresponding to the distractor transport bone plate movement before and after distraction, calculated by measuring the bending steel wire that was attached to the bone growth surface.

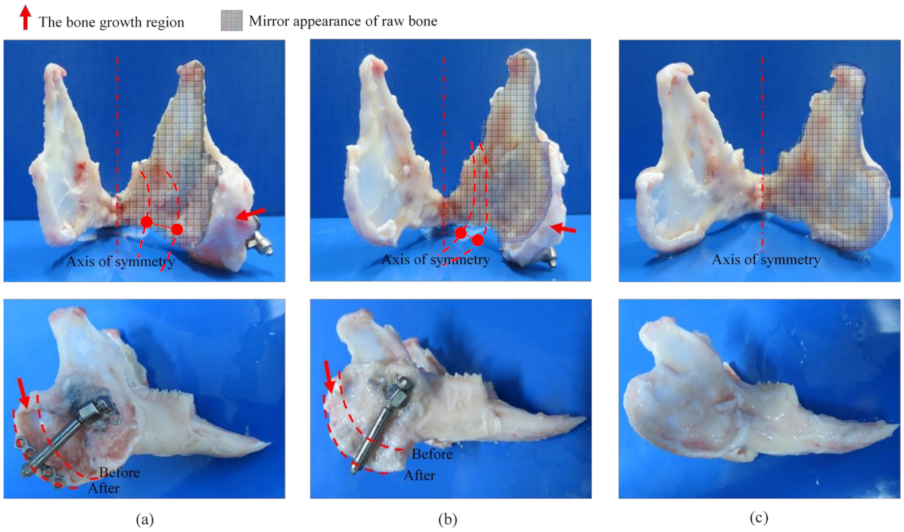

Figure 5. The variations in bone growth geometric shape observed in Groups TMB (**a**), TM (**b**) and TC (**c**) at the mandible angulus from back and lateral views were recorded. Buccal side thickness of the angulus after distraction was also calculated to compare the variations between Groups TMB and TM.

2.4. Distraction Bone Mechanical Testing

The multi-axial alveolar bone distractors in Groups TMB and Group TM were removed from the experimental rabbit mandible. The mandible right angulus was cut along the bone distraction direction to form a symmetrical bone specimen with a width of 20 mm. The specimen was embedded in a 40 mm × 50 mm × 20 mm resin block (Shang Hsin Resins No. 1500, Chin Shun Yi Enterprise Co., LTD., Taiwan) with the upper and lower boundaries at 2 mm and 6 mm of the transport plate distraction positions, respectively (Figure 6). Similar corresponding intact bone areas of Groups TMB and TM (left angulus) and mandibular annulus of Group TC were also cut and embedded as the control specimens.

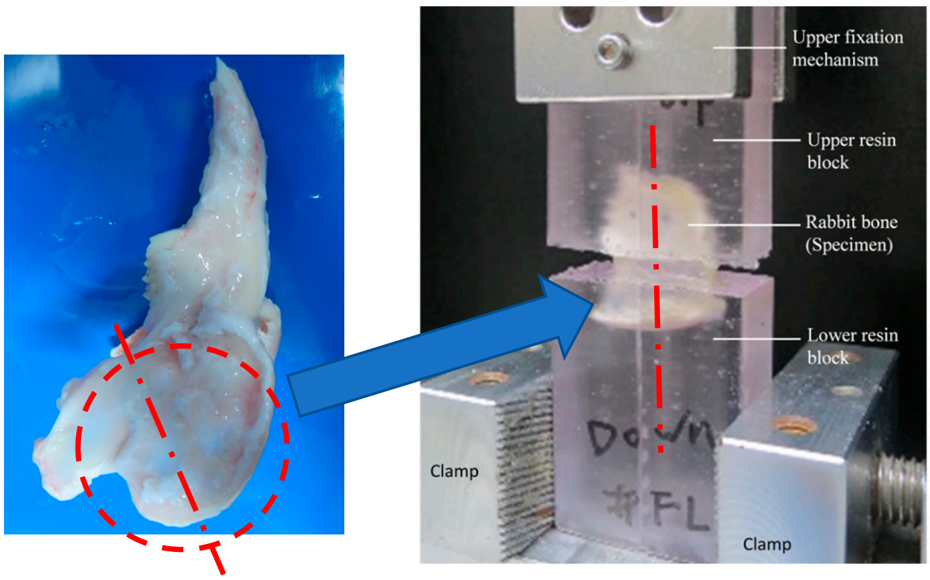

Figure 6. Right: the test specimen (mandibular bone after distraction and intact bone) was clamped and fixed to the materials test system to perform the fracture test. Left: the red circle shows the cutting area and the dotted line is the alignment line with the test machine axis.

Each test specimen was clamped and fixed to the material's test system (HT-2402EC, Hung Ta Instrument Co., LTD., Taiwan) to perform the fracture test. The vertical pull load was adjusted in alignment with the embedded test specimen axial to avoid a bending load during fracture testing. An upward load of 1 mm/min was applied to the specimen until the test specimen fractured (defining the load when it drops to 30% of the maximum load). The maximum load and displacement changes were recorded.

3. Results

The digital radiography results showed that the osteotomy areas at the mandible angulus were healed and the bone growth was completed 4 weeks after surgery for all rabbits using multi-axial alveolar bone distractors (Figure 7). The TC group in Figure 7 shows the X-ray image tracking observation under the condition that this group did not use any multi-axial alveolar bone distractor.

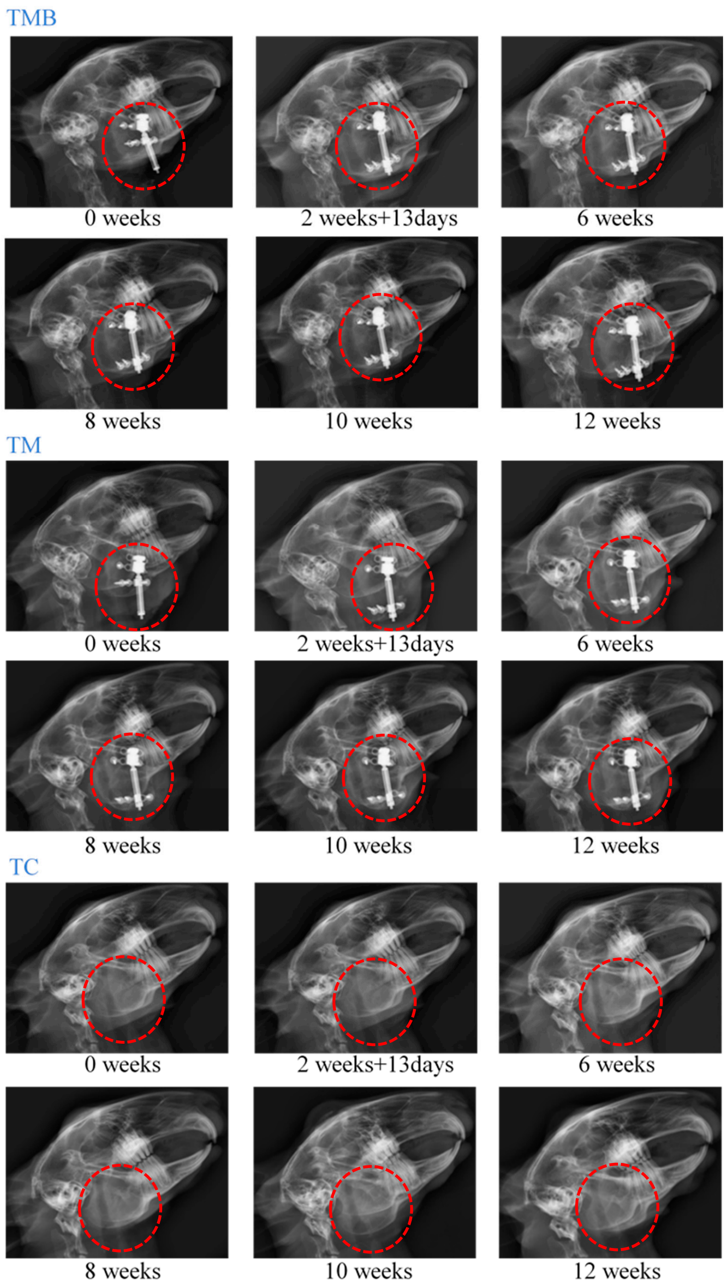

Figure 7. The digital radiography results show that the osteotomy areas at the mandible angulus healed and the bone growth was completed 4 weeks after surgery for all rabbits using multi-axial alveolar bone distractors.

The rabbit cadaver observation results show that the average and standard bone growth length deviation in the corresponding bone positions before and after transport bone plate movement in Groups TMB and TM were 17.68 ± 1.51 mm and 14.79 ± 0.97 mm, respectively. The corresponding buccal side distraction thicknesses for Groups TMB and TM after distraction, were 5.12 ± 0.52 mm and 3.32 ± 0.37 mm, respectively. The mean bone growth length value and buccal side distraction thicknesses for Group TMB were significantly greater ($p < 0.05$) than that of Group TM (Figures 4 and 5).

The fracture test results showed that the bone specimen tensile strengths after distraction for Groups TMB and TM were 172.13 ± 19.04 N ($n = 3$) and 119.27 ± 17.52 N ($n = 3$), respectively. The results showed that the bone strength of Group TMB was higher than that of Group TM. However, the intact bone tensile strength was 304.24 ± 73.90 N ($n = 8$) and presented significant differences between Groups TMB and TM. The distraction bone tensile strength to normal bone percentages were 57% (172 N/304 N) and 39% (119 N/304 N) for Groups TMB and TM, respectively.

4. Discussion

The main alveolar bone distractor principle is to generate new bone by gradually pulling the periosteum from the bone. Several kinds of alveolar bone distractors have been circulating in clinical applications. However, the current alveolar bone distractors only achieve axial direction distraction along the transport screw or biaxial adjustment with buccal-lingual adjustable angulation intra-operatively [13]. These existing distractors do not permit free-angle adjustment in different directions and cannot be applied in conjunction with clinically complex situations and irregular alveolar bone defect shapes. In our previous study a new multi-axial alveolar bone distractor design was presented based on the high degree of freedom mechanism for the ball joint to attain multi-axial distraction directions [18]. However, only static mechanical function tests were performed in the previous in vitro safety and effectiveness experiments. It remains unclear whether this new distractor can be applied to living bone for distraction and whether the ball and socket joint can withstand the bone growth force during distraction without causing the ball joint surface to slip, causing the distraction direction to change. Further studies are required to determine whether the bone growth direction determined with a novel multi-axial distractor can be maintained during distraction. We therefore investigated the feasibility and stability of the novel multi-axial distraction function by conducting in vivo pilot experiments using the rabbit mandible angulus.

The primary objective of this in vivo experiment was to observe whether the bone growth direction determined before surgery with a multi-axial distractor can be maintained during distraction. The choice of suitable animals and their corresponding bone regions for fixing a novel multi-axial distractor was challenging because the distractor ball and socket joint opposing force should be higher than the bone distraction and growth forces during the experimental period. The bone distraction force might exceed the capability of our new multi-axial distractor if it is used on the mandibles of large animals such as pigs and sheep. Therefore, the mandible angulus of the New Zealand rabbit was selected because of its circular shape and thin cortex. These features make it better suited to planning multi-axial distraction, in a predetermined direction, compared with a mandible body with only straight geometric features.

To the best of our knowledge, a ball and socket joint mechanism with the capability of such a high-degree-of-freedom cone trajectory motion was first applied to the alveolar bone distraction by our research team. Whether our novel multi-axial distractor can be further applied to the living body remains the most substantial challenge despite performing rigorous mechanical functional tests. The distractor direction adjusted to 25° at the buccal side was based on two relative pieces of literature [22,23]. The angle of 15° set at the mesial side was smaller than that at the buccal side because of the mandible and muscle interference angulus space limitation. However, bone growth direction and deformation prediction at the angulus region following distraction was challenging, because its thin circular shape is completely different compared with other study animals. Therefore, two rabbits that were not subjected to distraction were retained as a control group to facilitate subsequent morphological comparisons.

The computed tomography (CT) image resolution of the distraction bone was not sufficiently accurate to represent the final distraction bone proximal to the bowl shape with uniform thickness because of the irregular CT scan intervals. Moreover, the large test sample size impeded the use of a micro CT scan. The bone growth measurement, in terms of length or volume, cannot be performed using medical image reconstruction. Therefore, the bone growth total length at the angulus following distraction was directly calculated by measuring the bending steel wire attached to the growing bone surface. A fracture test was conducted on the newly formed bone to compare it with the intact bone.

Comparing the bone growth geometric shape observed in Groups TMB, TM and TC at the mandible angulus showed that the left and right mandibles were symmetrical to the axis of the incisors in Group TC (control group). Both Groups TMB and TM presented bone growth with a tendency toward the buccal outer side at the mandible angulus. The bone outer length thickness in Group TMB was thicker than that of Group TM. The bone growth geometric shape of Group TMB was observed to develop obviously more outward than that of the bowl, while the corresponding bone shape of Group TM was relatively flat. The difference in bone growth morphology may be caused by the fact that Group TMB has more than 15° to the mesial side in distraction than Group TM. This phenomenon can also be explained in the bone growth mechanical strength test. The fracture strength of Group TMB was higher than that of Group TM.

The mechanical fracture test found that the fracture strength at the distraction side was lower than that of the bone on the normal (control) side. The result showed that the distraction bone to normal bone tensile strength percentages were 57% and 39% for Groups TMB and TM, respectively.

Since the bone at the osteotomy region gradually healed during distraction, the bone healing undergoes a fragile period (formation period of the epiphysis) and an intensity increase period (reconstruction period) to return to its original intact strength. However, bone growth affects its healing state due to factors such as age, constitution and healing time. A review study indicated that the consolidation phase duration is a major factor that influences the overall treatment time and primary stability of implants placed in the distracted bone [13]. Although, a histochemical study in rabbits by Piattelli et al. indicated no major morphological differences between the bone appearance at 2 and 6 months, i.e., bone maturation in rabbits, around titanium implants at least 2 months old [24]. However, Saulacic and Turker reported that a period of 12 weeks is sufficient for bone maturation ready for dental implantation figure [25].

Bone augmentation has been verified with clinical, histological and radiographic evidence that bone distraction is a predictable and reliable surgical method. Therefore, the consolidation phase in our study lasted only 8 weeks, suggesting that longer consolidation is required for bones to heal to their original bone strength. The mechanical strength of the newly formed bone can be improved.

As mentioned in our previous article [18], the ball-and-socket joint design dimension is slightly larger than that of the commonly used hinge-type distractors and may interfere with flap closure, further leading to dehiscence. This could be overcome using a flap design with adequate periosteum release and modifying the ball-and-socket mechanical design/manufacturing process in the future.

5. Conclusions

This preliminary in vivo animal study concluded that the novel multi-axial alveolar bone distractor can drive bones to grow in the osteotomy region in accordance with the distraction plan direction/angle. The bone growth heals gradually but presents insufficient mechanical strength. A larger number of future in vivo experiments must be executed to establish the novel distractor use effect.

Author Contributions: All authors have made substantial contributions to conception and design of the study. C.-H.W., K.-C.C., Y.-S.L. and Y.-C.L. have been involved in data collection and data analysis. C.-H.W., K.-C.C. and C.-L.L. were involved in data interpretation, drafting the manuscript and revising it critically and given final approval of the version to be published. All authors have read and agreed to the published version of the manuscript.

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