Socket Preservation Using Xenograft Does Not Impair Implant Primary Stability in Sheep: Clinical, Histological, and Histomorphometric Study

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Implant primary stability, which depends mainly on the amount and quality of bone, is important for implant survival. Socket preservation aims to reduce bone volumetric changes after tooth extraction. This animal study aims to examine whether preserving a ridge by using xenograft impairs the primary stability of the implant. Eighteen artificial bone defects were prepared in 4 sheep (5- and 8-mm length). Defects were randomly grafted with xenografts: Bio-Oss (BO), Bio-Active bone (BB), or left for natural healing (control). After 8 weeks, bone biopsy was harvested and dental implants installed. During installation, peak insertion torque (IT) was measured by hand ratchet, and primary stability by the Osstell method. Histomorphometric analysis showed a higher percentage of new bone formation in the naturally healed defects compared to sites with xenograft (control: 68.66 $\pm$ 4.5%, BB: 48.75 $\pm$ 4.34%, BO: 50.33 $\pm$ 4.0%). Connective tissue portion was higher in the BO and BB groups compared to control (44.25 $\pm$ 2.98%, 41 $\pm$ 6%, and 31.33 $\pm$ 4.5%, $P < .05$, respectively). Residual grafting material was similar in BO and BB (7 $\pm$ 2.44%, 8.66 $\pm$ 2.1%, respectively). Mean IT and implant stability quotient (ISQ) values were not statistically different among the groups. A positive correlation was found between IT and ISQ ($r = 0.65$, $P = 0$). In conclusion, previously grafted defects with xenograft did not influence primary stability and implant insertion torque in delayed implant placement. These results may be attributed to a relatively high bone fill of the defect (~50%) 2 months after grafting.

Key Words: primary stability, xenograft, socket preservation, extraction

INTRODUCTION

The use of dental implants for the rehabilitation of missing teeth is an accepted and promising treatment option.[1,2] However, implants can be problematic when the amount and volume of the alveolar bone are poor. The areas that present the most common anatomical limitations are the posterior regions of both maxilla and mandible. The dimensional changes of the alveolar ridge usually occur due to active periodontal disease, trauma, or tooth extraction. The removal of teeth is accompanied by a partial loss of the ridge dimensions on all levels and a change in the ridge topography.

According to the literature, the loss in ridge dimensions can reach 3.87 mm in width and 1.67 mm the height.[3] These results were confirmed in a meta-analysis that showed a higher horizontal loss of 3.79 mm compared to a vertical loss of 1.24 mm, 6 months post-extraction.[4]

Techniques for ridge preservation have been successfully tested in clinical trials using bone substitutes from different sources.[5–7] A previous meta-analysis found that socket preservation may reduce vertical and horizontal bone loss up to 50%, compared to spontaneous healing.[5]

Xenogeneic bone has served as a bone substitute for many years in surgical procedures. The material is harvested from a live source (usually cattle), and is a good matrix for new bone formation. A xenograft is one of the factors that may contribute to preserving ridge dimensions, particularly on midbuccal and midlingual height.[7] In addition to the osteoconductivity of xenografts, it may enhance soft tissue healing and can become an integral part of the woven bone.[8–10]

Xenograft scaffold modification and cover with poly (L-lactide-co-ε-Caprolactone) (PLCL) and polysaccharides determine xenograft properties that enable better cells adhesion, greater percentiles of new bone formation, and better regenerative capacity—providing better outcomes in preserving bone after tooth extraction.[11] It was found that PLCL-coated xenografts had higher vitality and proliferation of mesenchymal stem compared to non-coated xenograft.[12]

One of the criteria for installing implants is the initial stability obtained during procedure.[13] Stability depends on several factors. Among them is the type of bone. A positive association was found between higher mineral density and primary stability of implants.[14] Previous studies examined

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https://doi.org/10.1563/aaid-joi-D-19-00237

differences between implant installations at sites that underwent natural healing, and sites where ridge preservation was carried out using a bone from a xenograft source.[15,16] However, to date, the initial stability obtained after the augmentation of bone defects by PLCL-coated xenografts has not yet been examined.

There are several methods to examine implant stability. The most widely used in the dental field is resonance frequency analysis (RFA), due to its high reliability in determining implant stability;[17,18] bone quality is an important factor when determining RFA readings.[17] Another measure for implant stability is insertion torque (IT).[19] The correlation between those 2 parameters is debatable. Although some point to a positive and statistically significant correlation,[20] others are unsure.[21] Nonetheless, both parameters are valid and in use.

Sheep are a large animal model with jaw bone structure that resembles the human jaw bone. The use of sheep allows creating bone defects with similar bone anatomy and dimensions that mimic extraction sockets in the human jaw. The model also allows taking a large biopsy to examine the results, as was done previously.[22–24]

This animal study aims to examine and compare bone quantity and primary implant stability 2 months after the augmentation of artificial bone defects using 2 types of xenogeneic materials.

We expect the implant's primary stability in the grafted area will result in comparable results with the natural bone healing sites.

Materials and Methods

The study protocol was approved by the Committee for the Supervision of Animal Experiments at the Faculty of Medicine, Technion, IIT (approval No: IL-121-08-2017). The study followed the guidelines of CONSORT 2010. A total of 4 adult sheep (females 2 to 3 years old) with an average weight of 85 kg were used in this study.

Surgical procedure

After the acclimation of the sheep, 2 operations 2 months apart were done on each sheep. Operations were performed under aseptic conditions. Both procedures were performed under general anesthesia using xylazine hydrochloride (0.05 mg/kg, intramuscular), intravenous ketamine (10 mg/kg), intravenous propofol (3–6 mg/kg) and induction of 0.5%–3% isoflurane. To eliminate intraoperative pain, fentanyl (0.05 mg/kg/hr) and local anesthesia (2% lidocaine with 1:100 000 epinephrine) were injected locally at the surgical sites.

Artificial bone defect preparation and grafting

The first procedure included a midcrestal incision on the edentulous ridge distal to the most lateral incisor. The total length of the incision was 25 mm. After flap elevation (Figure 1a), 2 to 3 adjacent artificial defects were created by osteotomy preparation with a final drill diameter of Ø5 mm and 8 mm in depth (Figure 1b) to mimic natural tooth socket. The distance from the middle of the osteotomy to the lateral incisor was measured and documented.

Eighteen bone defects were made and divided randomly to 3 treatment groups (6 in each group) (Figure 1c):

1. Experimental group: Bioactive bone graft (Bioactive Bone; IBI SA via Cantonaie 67. CH-6805 Mezzovico-Vira, Switzerland) was placed in the defect (BB).
2. Positive control: Bio-Oss (Geistlich Pharma, Wolhusen, Switzerland) was placed in the defect (BO).
3. Negative control: No bone grafting; the defect was left to heal naturally (Control).

The flaps were repositioned and sutured with primary closure using resorbable sutures (Vicryl 4-0).

Animals were examined daily for 7 days postoperatively, to monitor food consumption, body weight, and overall health status. A standard postsurgical infection and pain control was used consisting of post-operative analgesics (tolfine, 2 mg/kg, once a day; and tramadol, 2 mg/kg, once daily) for 3 days, and antibiotics (cefalexin) for 1 week. All the sheep were housed and given water and a soft diet.

Implant placement

Two months after the first operation a second operation was done. A midcrestal incision was performed on the edentulous ridge distal to the incisors. After flap elevation, the area of the artificial bone defects was identified (based on the distance from the distal incisor that was taken during the first operation) and bone core biopsies were taken using trephine (Ø1.7 mm) (Figure 2a). Next, dental implants (NEO, Alpha Bio Ltd, Petah-Tikva, Israel), 8 mm length × 3.2Ø mm. were installed in all sites (Figure 2b).

During installation, the peak insertion torque (IT) was measured using calibrated hand ratchet, and primary stability was measured using the Osstell system (Osstell, Göteborg, Sweden) (Figure 2c).

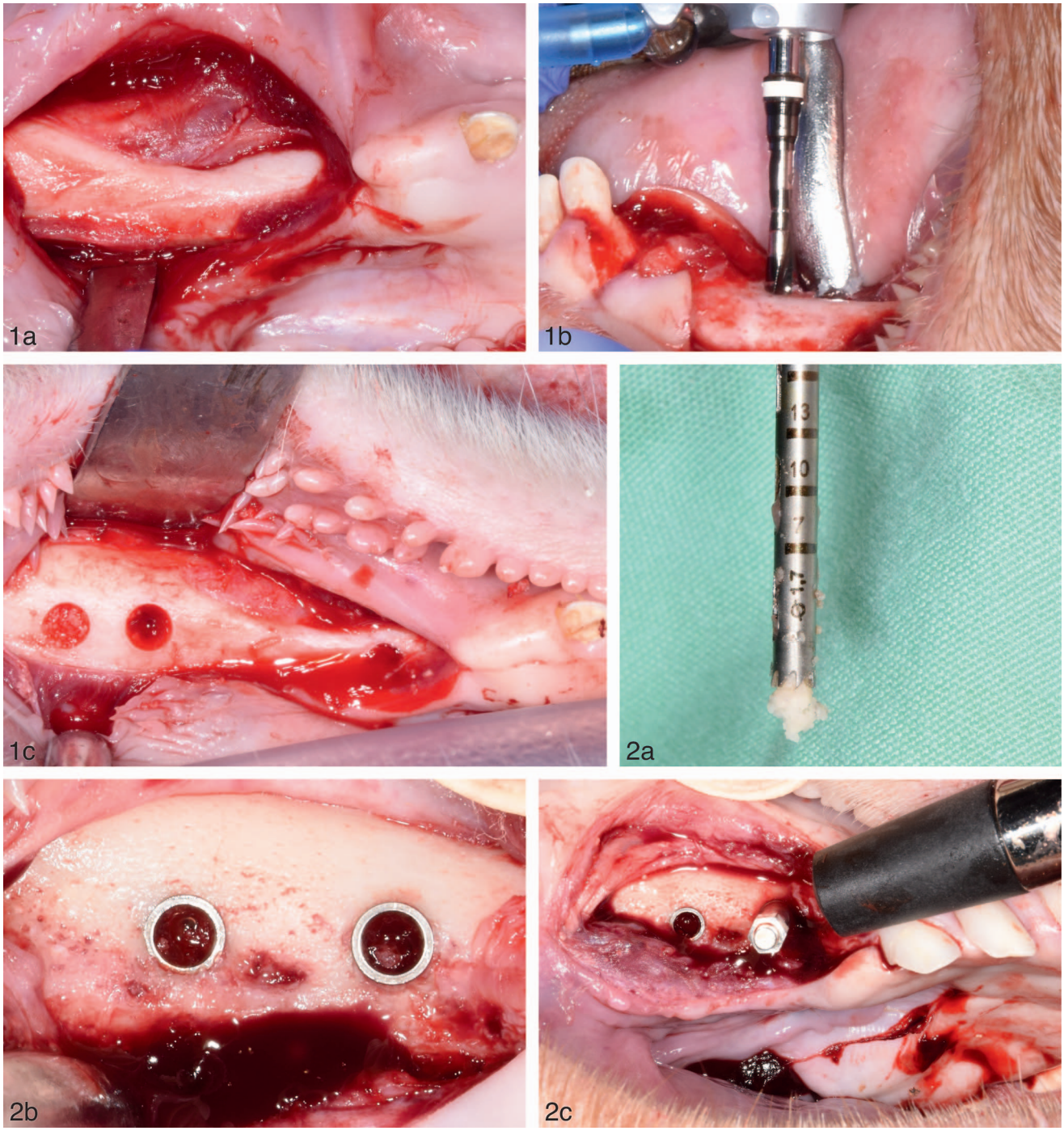
At the end of the surgery, the sheep were sacrificed using pentobarbitone (CTS Chemical Industries Ltd. Kiryat Malachi, Israel) at 200 mg/1.5 kg body weight.

Histological preparation

All specimens were fixed in 4% paraformaldehyde for 2 days, decalcified in 10% ethylenediaminetetraacetic acid for 4 weeks, and cut into 2 halves in the midline. The water within the samples was removed by dehydration, then samples were washed in ethanol baths (in increasing concentrations) to remove residual water. This was followed by a hydrophobic clearing agent (Xylol) to remove the alcohol content. After the samples were dehydrated, cleared, and infiltrated with paraffin wax, they underwent external embedding. For light microscopy, the samples were sectioned using a steel knife mounted in a microtome (Leica RM 2135, Jung RM 2065; Leica Microsystems, Wetzlar, Germany) to a thickness of 8 μm, and the sections mounted on glass microscope slides using paraffin section mounting bath (Electron Microscopy Sciences, Hatfield, England). For the determination of bone morphology, the mounted sections were stained with hematoxylin and eosin.

Histomorphometric analysis

Histomorphometric evaluation of the augmented bone defect region was performed from each specimen, under a light



Figures 1 and 2. Figure 1. First surgical intervention. (a) After incision and reflection of the flaps, alveolar ridge before defect preparation. (b) Creating the defect using a drill diameter of Ø5 mm and 8 mm in depth (c) 4 wall defects, where distal is grafted and mesial left for spontaneous healing. **Figure 2.** Second surgical intervention after 8 weeks. (a) Bone core biopsies were taken using trephine (Ø1.7 mm). (b) After implant placement. (c) Stability measurement using the Osstell system.

microscope (Zeiss Axioskop; Carl Zeiss, Jena, Germany). Images were analyzed using software (ImageJ, National Institutes of Health, Bethesda, Md). The following values were measured: (1) total bone area, (2) connective tissue, and (3) residual bone graft. The measurements were expressed as percentages of the total sample area.

Statistical analysis

The study design and methodology were reviewed by an independent statistician. A power calculation was initially performed to determine sample size. A comparison between the groups' one-way analysis of variance was used. A *P* value of

TABLE 1

Histomorphometric analysis of the defect content (% total sample area, mean ± SD), Bio-Active bone (BB), Bio-Oss (BO)

Group	% Bone	% Connective Tissue	% Residual Graft
BB	48.75 ± 4.34%*†	44.25 ± 2.98%*†	7 ± 2.44%*
BO	50.33 ± 4.0%*‡	41 ± 6%*‡	8.66 ± 2.1%*
Control (natural healing)	68.66 ± 4.5%†‡	31.33 ± 4.5%†‡	-

*BB-BO, $P > .05$.
†BB-C, $P < .05$.
‡BO-C, $P < .05$.

<.05 was selected to determine statistical significance. Percentile of new bone, residual grafting material, and connective tissue were summarized using means and standard deviations. The IT and ISQ values were summarized using means and standard deviations. Finally, the correlation between IT and ISQ was analyzed using the Pearson correlation coefficient test, using a 5% significance level ($P < .05$).

RESULTS

No surgical or postsurgical complications were reported.

Histomorphometric analysis

The amount of bone that filled the bone defect was: 48.75 ± 4.34%, 50.33 ± 4.0%, and 68.66 ± 4.5% in the BB, BO, and Control groups, respectively. New bone was significantly higher in the Control vs BB ($P < .05$) and BO ($P < .05$) groups. No statistical difference was found between BO and BB ($P > .05$).

The percentages of connective tissue that filled the bone defects were: 44.25 ± 2.98%, 41 ± 6%, and 31.33 ± 4.5% in the BB group, BO group, and Control group, respectively. Connective tissue was significantly lower in the Control group compared with the BO and BB groups ($P < .05$, $P < .05$). No statistical difference was found between BB and BO.

The amount of residual graft material was similar between the BB and BO groups: 7 ± 2.44%, 8.66 ± 2.1%, respectively (Table 1).

Primary stability analysis

The mean IT and ISQ values were not statistically different among the 3 groups (Table 2). A positive correlation was found between IT and ISQ for all the implants included in the study ($r = 0.65$, $P = 0$; Figure 3).

TABLE 2

Insertion torque (N/cm) and implant stability quotient (ISQ) values (mean ± SD) of implants divided by grafting materials. Bio-Active bone (BB), Bio-Oss (BO)

Group	Insertion Torque	ISQ
BB	37.5 ± 10.7*†	62.3 ± 12.6*†
BO	40.8 ± 16.9*‡	64.3 ± 15.6*‡
Control (natural healing)	36.6 ± 13.7†‡	60.8 ± 10.6†‡

*BB-BO, $P > .05$.
†BB-C, $P > .5$.
‡BO-C, $P > .05$.

A diagram presents the correlation between the insertions torque (IT) and implant stability quotient (ISQ) (Figure 3). The 2 variables showed a strong, positive, significant correlation (correlation coefficient, $r = 0.65$).

Histology

Inserted bone substitutes were surrounded by newly formed bone, and direct contacts were observed between the bone substitute and the new bone in both groups that demonstrated osteoconductive properties of the tested materials (BB and BO). Collagen fibers in the new vital bone were arrayed in a parallel organized manner. The trabecular spaces were filled with loose connective tissue with thin vessels (Figure 4a through 4c).

DISCUSSION

In the present study, we compared the insertion torque and primary stability of implants that were placed into naturally healed bone defects, to insertion in sites grafted with 2 commercialized xenografts. According to the results, insertion torque and primary stability were similar between the grafted and naturally healed sites, and no differences were found between the tested xenografts. Similar results were found in previous studies conducted in other models, comparing stability of delayed implant in grafted vs spontaneous healing sites.[15,16] However, previous studies found that grafting xenograft in the socket may impede bone maturation in the socket and may delay natural healing.[25,26] Our histological findings were similar to those reports and demonstrated more bone tissue and less connective tissue in the natural healing

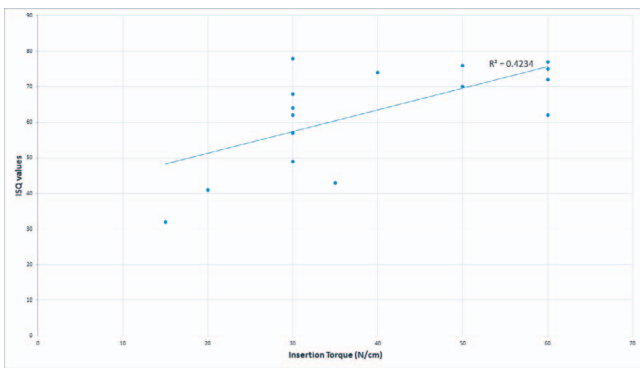


FIGURE 3. Correlation between insertion torque (N/cm) and implant stability quotient values. Pearson correlation coefficient test.

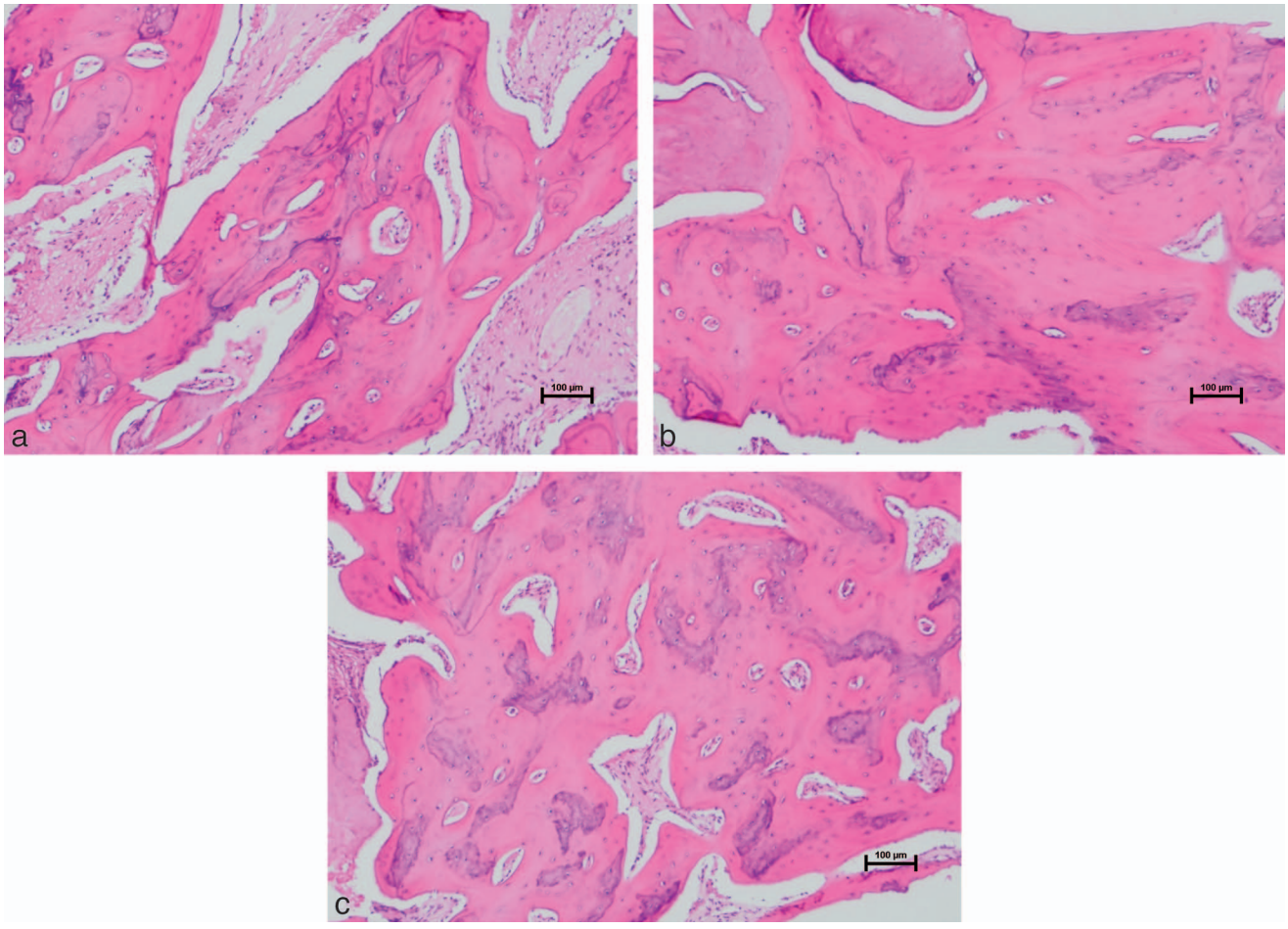


Figure 4. Histologic figure of each group (hematoxylin & eosin staining). (a) Bio-Active bone. (b) Bio-Oss. (c) Control Group. Bone substitutes particles were surrounded by newly formed bone.

group, compared to the 2 other groups with grafted xenograft. It seems that the delayed maturation may not influence the initial implant stability after it reaches a critical mass of alveolar bone tissue.

Immediate grafting and augmentation of the extraction socket using bone substitute has been proposed with a good rate of reduction in dimensional changes after tooth extraction.[6,27] However, good implant stability is an essential factor for implant success.[28,29] Primary stability has been described as the absence of mobility in the alveolar bone immediately after implant installation, which is achieved through mechanical fixation between the implant surface and the surrounding bone.[14] According to the literature, ISQ has a nonlinear correlation to micromobility, and therefore the micromobility may decrease by more than 50% from 60 to 70 on the ISQ scale.[30,31] In our study, most of the implants demonstrated an ISQ above 60 that may enable early loading, according to recent publications.[32,33]

Several surgical techniques and implant designs were performed to enhance the primary stability of the implants.[34,35] One of the most important factors for achieving good primary stability is implant body design. The implant body design should be more specific for immediate loading because the bone does not have time to grow between the threads. Therefore, the number of threads, and their geometry and depth, are very important for the first period of immediate loading.[36]

According to the implant design and the surgical protocol we used, there were no differences among the groups regarding the primary stability of the implants.

The edentulous area in sheep mandible has similar anatomical characteristics to the human jaw. Since socket preservation in a sheep model is not well documented, the duration of healing time followed previous reports.[23,37]

Grafting of PLCL-coated xenograft and non-coated xenograft into bone defects that imitate extraction sockets enables us to achieve uniform bone defects. Two months after the surgery, these artificial bone defects were filled with new bone, connective tissue, and residual graft. The ratio among the elements was similar between the 2 xenograft groups and reached almost 50%. Interestingly, in a previous study, we found a higher bone fill of rat extraction socket using PLCL-coated xenograft compared with non-coated xenograft.[12] This difference can be explained by the different animal models and the size of the artificial bone defect compared to an extraction socket in rats.

There are several methods to examine implant stability. RFA and insertion toque are the most frequently used methods for

analyzing primary stability of the implant.[17–19] Previous studies found a positive correlation between these 2 methods[20,38] while some works did not show this result.[21,39] We found a positive correlation between the ISQ and the insertion torque.

This study has limitations. To be able to accurately compare between the 2 commercialized xenografts we chose to create standardize defect with the same dimensions. This mimics extraction socket healing in some aspects, but misses some aspects and processes, such as the alveolar bone resorption that occurs after tooth extraction. Another limitation can be attributed to the implant system that was used. A tapered implant with dual V-shaped and micro threads that can improve primary stability and enhanced mechanical retention.[40,41] Future studies should include larger sample size, fresh extractions sockets, and different implant systems to strengthen current findings.

The study demonstrated high primary stability of implant installed in artificial standardized bone defects that were grafted with xenograft. No differences were found compared to natural healing. These results may be attributed to a relatively high bone fill of the defect (~50%) 2 months after grafting.

The aforementioned research proposal has been reviewed by the Animal Care and Use Committee of the Technion, Israel Institute of Technology, and found to confirm with the regulations of this Institution for work with laboratory animals (Technion animal experimentation protocol No: IL-121-08-2017).

Conclusion

In conclusion, according to this animal study, previously grafted defects with xenograft may not have influenced primary stability and implant insertion torque in delayed implant placement. These results may be attributed to a relatively high bone fill of the defect (~50%) 2 months after grafting. The results and conclusions of this manuscript were reviewed and approved by an independent statistician.

Abbreviations

BB: Bio-Active bone
BO: Bio-Oss
ISQ: implant stability quotient
IT: insertion torque
PLCL: poly (L-lactide-co-ε-Caprolactone)
RFA: resonance frequency analysis

Acknowledgments

All authors declare that they meet all criteria required for authorship. The authors would like to acknowledge the valuable contribution of Dr Machtei from the Faculty of Medicine, Technion—Israeli Institute of Technology, for the study design and statistical analysis of this manuscript. The study was supported by an educational grant from Alpha-Bio Tec Ltd.

Note

The authors declare that they do not have a conflict of interest regarding the present study. The funders had no role in the study design, data collection, and analysis; decision to publish; or preparation of the manuscript.

References

1. Gokcen-Rohlig B, Yaltirik M, Ozer S, Tuncer, ED, Evlioglu G. Survival and success of ITI implants and prostheses: retrospective study of cases with 5-year follow-up. *Eur J Dent*. 2009;3:42–49.

2. Lambert FE, Weber HP, Susarla SM, Belser UC, Gallucci GO. Descriptive analysis of implant and prosthodontic survival rates with fixed implant-supported rehabilitations in the edentulous maxilla. *J Periodontol*. 2009;80:1220–1230.

3. Van der Weijden F, Dell'Acqua F, Slot DE. Alveolar bone dimensional changes of post-extraction sockets in humans: a systematic review. *J Clin Periodontol*. 2009;36:1048–1058.

4. Tan WL, Wong TL, Wong MC, Lang NP. A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans. *Clin Oral Implants Res*. 2012;23:1–21.

5. MacBeth N, Trullenque-Eriksson A, Donos N, Mardas N. Hard and soft tissue changes following alveolar ridge preservation: a systematic review. *Clin Oral Implants Res*. 2017;28:982–1004.

6. Mayer Y, Zigdon-Giladi H, Machtei EE. Ridge preservation using composite alloplastic materials: a randomized control clinical and histological study in humans. *Clin Implant Dent Relat Res*. 2016;18:1163–1170.

7. Avila-Ortiz G, Elangovan S, Kramer KW, Blanchette D, Dawson DV. Effect of alveolar ridge preservation after tooth extraction: a systematic review and meta-analysis. *J Dent Res*. 2014;93:950–958.

8. Scheyer ET, Heard R, Janakievski J., et al. A randomized, controlled, multicentre clinical trial of post-extraction alveolar ridge preservation. *J Clin Periodontol*. 2016;43:1188–1199.

9. Araújo MG, Liljenberg B, Lindhe J, Dynamics of Bio-Oss Collagen incorporation in fresh extraction wounds: an experimental study in the dog. *Clin Oral Implants Res*. 2010;21:55–64.

10. Lindhe J, Cecchinato D, Donati M, Tomasi C, Liljenberg B. Ridge preservation with the use of deproteinized bovine bone mineral. *Clin Oral Implants Res*. 2014;25:786–790.

11. Pertici G, Carinci F, Carusi G, et al. Composite polymer-coated mineral scaffolds for bone regeneration: from material characterization to human studies. *J Biol Regul Homeost Agents*. 2015;29:136–148.

12. Mayer Y, Ginesin O, Khutaba A, Machtei EE, Zigdon Giladi H. Biocompatibility and osteoconductivity of PLCL coated and noncoated xenografts: an in vitro and preclinical trial. *Clin Implant Dent Relat Res*. 2018;20:294–299.

13. Lioubavina-Hack N, Lang NP, Karring T. Significance of primary stability for osseointegration of dental implants. *Clin Oral Implants Res*. 2006;17:244–250.

14. Marquezan M, Osório A, Sant'Anna E, Souza MM, Maia L. Does bone mineral density influence the primary stability of dental implants? A systematic review. *Clin Oral Implants Res*. 2012;23:767–774.

15. Pang C, Ding Y, Hu K, Zhou H, Qin R, Hou R. Influence of preservation of the alveolar ridge on delayed implants after extraction of teeth with different defects in the buccal bone. *Br J Oral Maxillofac Surg*. 2016;54:176–180.

16. Cardaropoli D, Tamagnone L, Roffredo A, Gaveglio L. Evaluation of dental implants placed in preserved and nonpreserved postextraction ridges: a 12-month postloading study. *Int J Periodont Restorat Dent*. 2015;35:677–685.

17. Becker W, Hujoel P, Becker BE. Resonance frequency analysis: comparing two clinical instruments. *Clin Implant Dent Relat Res*. 2018;20:308–312.

18. Manzano-Moreno FJ, Herrera-Briones FJ, Linares-Recatala M, Ocaña-Peinado FM, Reyes-Botella C, Vallecillo-Capilla MF. Bacterial contamination levels of autogenous bone particles collected by 3 different techniques for harvesting intraoral bone grafts. *J Oral Maxillofac Surg*. 2015;73:424–429.

19. Kotsakis GA, Salama M, Chrepa V, Hinrichs JE, Gaillard P. A randomized, blinded, controlled clinical study of particulate anorganic

bovine bone mineral and calcium phosphosilicate putty bone substitutes for socket preservation. *Int J Oral Maxillofac Implants*. 2014;29:141–151.

20. Sarfaraz H, Johri S, Sucheta P, Rao S. Study to assess the relationship between insertion torque value and implant stability quotient and its influence on timing of functional implant loading. *J Indian Prosthodont Soc*. 2018;18:139–146.

21. Bayarchimeg D, Namgoong H, Kim BK, et al. Evaluation of the correlation between insertion torque and primary stability of dental implants using a block bone test. *J Periodontal Implant Sci*. 2013;43:30–36.

22. Gallego L, Pérez-Basterrechea M, García-Consuegra L., et al. Repair of segmental mandibular bone defects in sheep using bone marrow stromal cells and autologous serum scaffold: a pilot study. *J Clin Periodontol*. 2015;42: 1143–1151.

23. Russmueller G, Moser D, Spassova E, et al. Tricalcium phosphate-based biocomposites for mandibular bone regeneration–A histological study in sheep. *J Craniomaxillofac Surg*. 2015;43:696–704.

24. Li D, Li M, Liu P, Zhang Y, Lu J, Li J. Tissue-engineered bone constructed in a bioreactor for repairing critical-sized bone defects in sheep. *Int Orthop*. 2014;38:2399–2406.

25. Araújo M, Linder E, Lindhe J. Effect of a xenograft on early bone formation in extraction sockets: an experimental study in dog. *Clin Oral Implants Res*. 2009;20:1–6.

26. Su Y, Tang J, Min S, et al. Alveolar ridge dimensional changes following ridge preservation procedure with novel devices: part 3 - histological analysis in non-human primate model. *Clin Oral Implants Res*. 2017;28:e252–e261.

27. Araújo MG, da Silva JCC, de Mendonça AF, Lindhe J. Ridge alterations following grafting of fresh extraction sockets in man. A randomized clinical trial. *Clin Oral Implants Res*. 2015;26:407–412.

28. Johns RB, Jemt T, Heath MR, et al. A multicenter study of overdentures supported by Brånemark implants. *Int J Oral Maxillofac Implants*. 1992;7:513–522.

29. Jeong MA, Kim SG, Kim YK, et al. A multicenter prospective study in type IV bone of a single type of implant. *Implant Dent*. 2012;21:330–334.

30. Pagliani L, Sennerby L, Petersson A, Verrocchi D, Volpe S, Andersson P. The relationship between resonance frequency analysis (RFA) and lateral displacement of dental implants: an in vitro study. *J Oral Rehabil*. 2013;40: 221–227.

31. Trisi P, Carlesi T, Colagiovanni M, Perfetti G. Implant stability quotient (ISQ) vs direct in vitro measurement of primary stability (micro-motion): effect of bone density and insertion torque. *J Osteol Biomaterials*. 2010;1.

32. Kokovic V, Jung R, Feloutzis A, Todorovic VS, Jurisic M, Hämmerle CH. Immediate vs. early loading of SLA implants in the posterior mandible: 5-year results of randomized controlled clinical trial. *Clin Oral Implants Res*. 2014;25:e114–e119.

33. Bornstein MM, Hart CN, Halbritter SA, Morton D, Buser D. Early loading of nonsubmerged titanium implants with a chemically modified sand-blasted and acid-etched surface: 6-month results of a prospective case series study in the posterior mandible focusing on peri-implant crestal bone changes and implant stability quotient (ISQ) values. *Clin Implant Dent Relat Res*. 2009;11:338–347.

34. de Oliveira Silva TS, Mendes Alencar SM, da Silva Valente V, de Moura CDVS. Effect of internal hexagonal index on removal torque and tensile removal force of different Morse taper connection abutments. *J Prosthet Dent*. 2017;117:621–627.

35. González-Serrano J, Molinero-Mourelle P, Pardal-Peláez B, Sáez-Alcaide LM, Ortega R, López-Quiles J. Influence of short implants geometry on primary stability. *Med Oral Patol Oral Cir Bucal*. 2018;23:e602–e607.

36. Dos Santos MV, Elias CN, Cavalcanti Lima JH. The effects of superficial roughness and design on the primary stability of dental implants. *Clin Implant Dent Relat Res*. 2011;13:215–223.

37. Liu J, Schmidlin PR, Philipp A, Hild N, Tawse-Smith A, Duncan W. Novel bone substitute material in alveolar bone healing following tooth extraction: an experimental study in sheep. *Clin Oral Implants Res*. 2016;27: 762–770.

38. Malchiodi L, Balzani L, Cucchi A, Ghensi P, Nocini PF. Primary and secondary stability of implants in postextraction and healed sites: a randomized controlled clinical trial. *Int J Oral Maxillofac Implants*. 2016;31: 1435–1443.

39. Levin BP. The correlation between immediate implant insertion torque and implant stability quotient. *Int J Periodontics Restorat Dent*. 2016; 36:833–840.

40. Lin YS, Chang YZ, Yu JH, Lin CL. Do dual-thread orthodontic mini-implants improve bone/tissue mechanical retention? *Implant Dent*. 2014;23: 653–658.

41. Falco A, Berardini M, Trisi P. Correlation between implant geometry, implant surface, insertion torque, and primary stability: in vitro biomechanical analysis. *Int J Oral Maxillofac Implants*/ 2018;33:824–830.