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HUMAN RANDOMIZED CONTROLLED TRIAL

The effect of bone particle size on the histomorphometric and clinical outcomes following lateral ridge augmentation procedures: A randomized double-blinded controlled trial

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Abstract

Background: The aim of this randomized clinical trial was to clinically and histologically compare the amount and quality of bone gained after lateral ridge augmentation (LRA) procedures performed using small-particle (SP)-size (250–1000 μm) versus large-particle (LP)-size (1000–2000 μm) size corticocancellous bone allografts at 6 months following surgical intervention.

Methods: Twenty-two patients, each presenting with ridge width <5 mm were enrolled. Patients were randomly allocated to SP- and LP-size graft. The gain in ridge width at the level of the crest and 4 mm apical to the crest was assessed via a standardized procedure before grafting and at time of implant placement, using a surgical caliper and a novel digital technique using cone-beam computed tomography (CBCT). Six months following the procedure, trephine bone cores were taken from 19 augmented sites of 17 patients (14/19 sites were in the posterior mandible) who completed the study for clinical, histologic, and histomorphometric analysis.

Results: Seventeen patients (19 sites) completed the study. An LP-size graft resulted in greater ridge width gain at the level of the crest (LP 5.1 ± 1.7; SP 3.7 ± 1.3 mm; $p = 0.0642$) and 4 mm apical to the crest (LP 5.9 ± 2.2; SP 5.1 ± 1.8 mm; $p = 0.4480$) compared with the SP. No statistical significance for the bone density at the time of implant placement ($p = 1.00$) was found. Vital bone formation was more extensive in the SP compared with the LP (41.0 ± 10.1% vs. 31.4 ± 14.8%, respectively; $p = 0.05$).

Hussein S. Basma and Muhammad H. A. Saleh contributed equally to this manuscript.

Conclusion: The results of the present study show a trend of higher ridge gain using LP during the bone augmentation procedure. Future research with bigger sample size should confirm the results of the present research.

KEYWORDS
allografts, bone regeneration, cone-beam computed tomography, dental implants

1 | INTRODUCTION

Interventions for lateral ridge augmentation (LRA) are very predictable. The reported survival rates of implants after LRA procedures is 87%–95% for the simultaneous approach and 99%–100% for the staged approach.[1] A systematic review assessing the effectiveness of LRA in the anterior maxilla even showed higher percentages of survival for either simultaneous or staged approaches, with 100% and 96.8%, respectively.[2] The reported average ridge width gain following LRA is 3.90 mm in the staged approach and 4.28 mm in the simultaneous approach.[3]

Guided bone regeneration (GBR) procedures are derived from the guided tissue regeneration (GTR) concept, involving usage of a barrier membrane for cell exclusion and, more importantly, to create and maintain space to allow bone formation.[4] GBR procedures were found to be equally successful using either resorbable or nonresorbable membranes.[5–7] Autogenous bone grafts with their osteogenic, osteoinductive, and osteoconductive characteristics are still considered as the gold standard in bone regeneration procedures.[8,9] However, donor site morbidity,[10] limited intraoral quantities,[11] and unpredictable resorption are drawbacks related to autografts that have intensified the search for suitable alternatives.[12,13] Bone substitute materials such as allografts and xenografts have commonly been used as an adjunct or a replacement for autografts with successful clinical and histologic outcomes in bone augmentation.[14–16] Due to their favorable turnover, excellent biocompatibility, and successful attainment of space maintenance properties, allografts have become increasingly popular.

Successful clinical and histological outcomes were demonstrated when mineralized freeze-dried bone allograft (FDBA) was used in bone augmentation procedures both in particulate[15,17] and block shapes.[18] A study found that even FDBA particles farthest away from the host–graft interface were embedded in new bone.[19] A higher percentage of new vital bone may be desired at time of implant placement and is thought to be beneficial for implant osseointegration. It has been suggested to use large-particle (LP) alloplast as grafting material for staged ridge split procedures in the posterior mandible.[20] A study comparing the amount of newly formed bone after sinus floor augmentation with two different particle sizes of demineralized bovine bone mineral (DBBM) using clinical, microcomputed tomographic, and histological techniques found that both particle sizes acted similarly.[21]

Likewise, there is not much data regarding the percentage of newly formed bone using either graft particle sizes. Moreover, to the best of the authors' knowledge, no study ever investigated the effect of the graft particle size on either the clinical, or the histomorphometric outcomes of LRA. Hence, this human randomized clinical trial aimed to clinically, radiographically, and histologically compare the quantity and quality of bone gained following LRA procedures using small-particle (SP)-sized (0.25–1.0 mm) versus LP-sized (1.0–2.0 mm) mineralized corticocancellous bone allografts.

2 | MATERIALS AND METHODS

2.1 | Ethical approval and registration

This study was conducted in accordance with the Helsinki Declaration for the ethical principles for medical research involving human subjects, as revised in 2013. The study was approved by the institutional review board (IRB) of the University of Alabama in Birmingham (UAB) (protocol # F161123001). This randomized controlled clinical trial reports on patients presenting to the Graduate Periodontology Clinic at UAB and requiring LRA for the purpose of implant placement. This randomized controlled trial complies with the CONSORT (Consolidated Standards of Reporting Trials) guidelines[22] (see Table S1 in the online version of the *Journal of Periodontology*).

2.2 | Inclusion requirements

Patients were required to be at least 18 years old and willing to comply with the preoperative and postoperative study visits. Patients had to exhibit an insufficient alveolar ridge width (<5 mm) for endosseous implant placement as

determined by cone-beam computed tomography (CBCT) to be included in the study. Exclusion criteria included heavy smoking (≥10 cigarettes/day), uncontrolled systemic disease, history of poor compliance, active periodontal disease, pregnancy, patients taking oral or systemic antiresorptive medications, and any other diseases that may interfere with bone healing.

2.3 | Enrollment, randomization, and calibration

Since there were no other LRA studies evaluating the influence of particle size, a sinus augmentation study was considered for the power calculation to determine the sample size. Assuming that similar results will be observed as reported by Testori et al.,[21] specifically that vital bone formation with LP and SP will be 26.8% ± 9.6% and 18.8% ± 4.7%, respectively, at least 17 augmentation surgeries in each group of 17 patients (a total of 34 sites in 34 patients) will reach 0.80 statistical power to reject the null hypothesis of equal means with a significance level (alpha) of 0.05 using a two-sided two-sample unequal-variance *t* test. Given that one patient may receive multiple augmentation surgeries, the power can be higher. Power calculation was conducted using PASS 14(NCSS, LLC, Utah). Following enrollment and signing informed consent, patients were randomized into either "Group 1: SP bone allograft (0.25–1.0 mm)" or "Group 2: LP bone allograft (1.0–2.0 mm)" with a 1:1 ratio. The predetermined randomization list (provided by the statistician) was generated utilizing a permuted block randomization strategy with computer-generated random numbers. Surgical guides were prepared by the prosthodontist based on ideal wax-ups and used to standardize the locations of pre- and postoperative measurements on the edentulous ridges. The primary investigator (RVA) conducted all clinical and radiographic exams to determine eligibility according to the aforementioned inclusion criteria, performed all clinical measurements, and was blinded with regards to the randomization. Another examiner (HB) performed the radiographic evaluations and was also blinded to the randomization process. Examiner calibration was performed in two calibration sessions held prior to the beginning of the study on a sample of 10 anonymized CBCT. The second session took place 2 weeks after the first one, and the intraclass correlation coefficient (ICC) was used to assess intraexaminer reliability.[23]

2.4 | Surgical procedures

A loading dose of prophylactic antibiotics was dispensed at the time of surgery (amoxicillin 2 g, 30 min to 1 h prior to surgery). If the patient was allergic to penicillin, clindamycin 600 mg was administered. Patients were given a 0.12% chlorhexidine solution for 1 min to rinse with to disinfect the surgical site to minimize the potential contamination from extraoral sources.[*] Local anesthesia with 4% articaine chlorhydrate and epinephrine 1:100000 was applied. A crestal incision was made with a vertical releasing incision at least one tooth away both mesial and distal to the grafted area. Buccal and lingual full-thickness flaps were reflected to allow adequate access to the surgical site. A superficial periosteal releasing incision was placed on the buccal flap to allow for adequate flap extension and achieve complete coverage of the graft materials and barrier membrane.

To standardize the ridge width measurements, the surgical stent planned to be used for implant placement was used to mark the area at which measurements were to be made at the ridge crest and at 4 mm apical to the crest with standardized surgical calipers. Decortication of the defect site was achieved using a high-speed hand piece with a #2 round bur perforating the cortical plate every 4 mm throughout the area. At that point, it was revealed to the clinician which type of bone allograft would be used (SP or LP) (see Figure S1 in the online version of the *Journal of Periodontology*). To ensure maximum augmentation, the bone graft was extended in all cases slightly over the original bony envelope (Figure 1).

To account for variation in age, race, sex, and related healing potential of different grafts, the graft material was obtained from the same manufacturer lot from the same donor.[†] The same criteria were applied with the absorbable non–cross-linked collagen barrier membrane utilized.[‡] The membrane was fixated with at least four surgical tacks for barrier stabilization. The flap was then mobilized to permit tension-free primary closure. Primary closure was obtained in all cases using a combination of horizontal mattress and continuous interlocking 5-0 vicryl sutures.

Patients returned for follow-up and sutures removal after 2 weeks. Healing status was evaluated, and postoperative instructions on resuming oral hygiene measures were given to the patients.

2.5 | Outcomes

The primary outcome in this study was to evaluate the percentage of new bone formed using either particle sizes.

[*] Peridex Mouthwash (3M ESPE, St. Paul, Minnesota).
[†] Maxxeus Dental, mineralized corticocancellous bone allograft (Community Tissue Services, Kettering, Ohio).
[‡] Memlok Pliable (BioHorizons, Birmingham, Alabama).

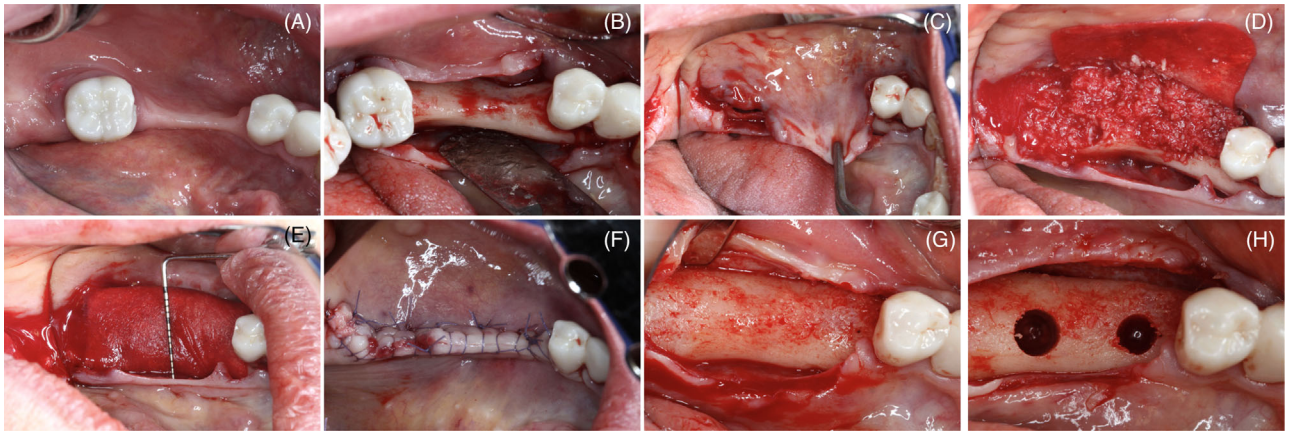

FIGURE 1 (**A**) Presurgical situation showing ridge deficiency and need for lateral ridge augmentation to enable implant placement. (**B**) Full mucoperiosteal flap reflection revealing ridge deficiency. (**C**) Verification of adequate flap release following periosteal flap release. (**D**) Bone graft placement (small particles) in grafted site with cross-linked membrane fixation on buccal side. Membrane was fixed by tacks from both buccal and lingual sides. (**E**) Membrane was folded to completely cover the graft. The volume of bone graft added can be appreciated. (**F**) Tension-free primary closure was achieved in all cases. (**G**) Approximately 6 months post ridge augmentation, full mucoperiosteal flap reflection was performed. The volume of bone gained is evident. (**H**) Core biopsies were taken from both sites of future implant placement, followed by osteotomy for implant placement as per the manufacturer guidelines

The secondary outcome was to compare clinically and radiographically the dimensional changes in the augmented ridges.

2.5.1 | Radiographic measurements

Approximately 6 months post ridge augmentation, a second CBCT scan was taken to evaluate the ridge width changes. The baseline CBCT was superimposed on the new CBCT, and digital implants were placed according to the guides to act as reference points for the radiographic measurements mirroring the clinical ridge width measurements. Buccolingual dimensions at the level of the crest and 4 mm apical to the crest were measured radiographically using an implant planning software with a digital reference.[§] Any ridge height alterations were also evaluated (see Figure S2 in the online version of the *Journal of Periodontology*).

2.5.2 | Clinical measurements

The surgical approach for implant placement was similar to the grafting procedures. After exposure of the augmented bone ridge, the implant sites were located using the same previously used surgical guide, and ridge width was measured at the crest and 4 mm apical to the crest.

2.5.3 | Histomorphometric measurements

Bone biopsy cores were taken from the augmented ridge at the planned implant site using a 2-mm internal diameter trephine. The specimens were then placed in a formalin solution. Following fixation with 10% neutral buffered formalin for 48 h, the bone biopsy specimens were dehydrated, embedded in methyl methacrylate, ground-sectioned at the center of the biopsy in its long axis into 50–70 micron-thick sections,[**] and polished with 4000 grit sandpaper and Novus polish to create a smooth surface. All sections were stained with Goldner's trichrome bone stain and imaged for quantification of bone formation. Histomorphometry was done using a dedicated image analysis software[††] through measuring the total surface of vital bone, residual graft particles, organic matrix, and artifact/air components. Corresponding percentages were calculated for each of these tissues and compared between SP and LP grafts for ridge augmentation separately. These experiments were conducted at the UAB histomorphometry and Molecular Analysis Core and all measurements made by an experienced lab technician blinded to the study protocol.

Implants were placed using the fabricated guide according to manufacturer protocol. Bone density was estimated by the surgeon at time of biopsy according to the classification by Lekholm and Zarb.[24] All biopsy cores (SP and LP

[§] CoDiagnostiX Guided Surgery Software by DENTAL WINGS Inc. (Montréal, Canada).

[**] Exakt Technologies Inc. (Oklahoma City, Oklahoma).

[††] Bioquant Image Analysis Software (R&M Biometrics, Nashville, Tennessee).

groups) were divided into three zones: zone 1 corresponds to the coronal third, zone 2 to the middle third, and zone 3 to the apical third of the biopsy core.

2.6 | Statistical analysis

Patients' demographics and baseline measures were summarized as mean ± SD or frequency (proportion) for each group and compared using a two-sample *t* test or Fisher's exact test where appropriate. Both the primary outcome (new bone formation) and the secondary outcomes (dimensional changes of the augmented sites by clinical and the radiographic methods) were summarized as mean ± SD in each group, and the group comparison was conducted using a generalized estimating equation (GEE) approach. The GEE method was used to handle the dependent observations caused by the facts that some patients had more than one site with surgical procedure in practice. Analysis of demographics was conducted at the patient level, while the analysis of outcomes was conducted at the site level. The correlation between the clinical and radiographic changes in width at the crest was evaluated with Pearson correlation analysis. Statistical analysis was done to calculate the percentage of new bone, residual graft, and connective tissue after measuring the surface area in comparison to the total biopsy surface area. All analyses were conducted using SAS 9.4 (Cary, North Carolina) at a significance level of 0.05.

3 | RESULTS

Due to some uncontrolled reasons, only 22 patients participated in the present study, among which two patients had two qualifying sites. Therefore, a total of 24 qualifying sites were included in this study, with each site comprising a single treatment area. Of the 22 subjects initially enrolled, a total of 17 patients completed the study. The five patients who were disqualified or withdrew from the study were arbitrarily from the SP group. Two patients were no longer able to return for the core biopsy and implant placement due to developing significant medical problems unrelated to their participation in the study. The other three patients were disqualified due to delivering removable prosthetic appliances over the grafted areas, which resulted in failure of the ridge augmentation procedure.

Among those 17 patients who completed the study, one received surgical procedures on two sites, one with SP and the other with LP, one received surgical procedures on two sites, both with LP, and 15 received surgical procedure on one site. As a result, 7 sites from 7 patients in the SP group and 12 sites from 11 patients (1 also in the SP group) in the LP group were included in the analysis.

The participants who completed the study were 7 males and 10 females aged between 46 and 78 years, of whom 15 were Caucasians and 2 African Americans. Consequently, a total of 17 patients and 19 sites were included in the data analyses. The group distribution was as follows: 7 sites in the SP group and 12 sites in the LP group. Patient and site distribution of the included sample are shown in Table 1.

3.1 | Ridge width at crest

Clinically, both treatment groups resulted in significant bone gain after 6 months of healing. GBR in the LP group achieved an average of 5.1 ± 1.7 mm versus an average of 3.7 ± 1.3 mm for the SP group. A clinically greater ridge width gain at the level of the crest (mean of 1.4 mm) was demonstrated with the use of the LP compared to the SP allograft and approached statistical significance ($p = 0.057$). Radiographic results were in accordance with the clinical measurements, including mean gains of 5.1 ± 2.0 mm in the LP and 3.8 ± 1.3 mm in the SP groups, with no statistically significant difference ($p = 0.214$) (Figure 2). Pearson correlation between clinical and radiographic width gain at the crest showed a very high correlation between the two measurements ($r = 0.86$, $p < 0.0001$) (Figure 2).

3.2 | Ridge width 4 mm apical to crest

Clinically, the postgrafting clinical measurements could not be obtained due to significant gain in width at this level of the ridge, prohibiting the use of the surgical calipers. Radiographically, the bone gain at 4 mm apical to the crest was comparable between the two groups (5.9 ± 2.2 mm for the LP and 5.1 ± 1.8 mm in the SP group), with no statistically significant difference ($p = 0.32$).

Correlations between radiographic and clinical measurements could not be evaluated at 4 mm apical to the crest.

3.3 | Vertical ridge changes at crest

The use of SP allografts was associated with a loss of vertical height at the level of the mid-crest (mean of −0.4 ± 0.5 mm), whereas LP allografts resulted in a mean vertical gain (0.3 ± 1.0 mm). However, these results lacked statistical significance ($p = 0.32$) (see Figure S3 in the online version of the *Journal of Periodontology*). Clinical and radiographic changes are reported in Table 2.

TABLE 1 Patient demographics and site variables

Variable	Small (n = 7 patients)	Large (n = 11 patients)	*p*
Age	67.9 ± 5.7	66.1 ± 8.6	0.6442[a]
Race			1.0000[b]
African American	1	1	
Caucasian	6	10	
Sex			0.6371[b]
Female	5	6	
Male	2	5	
Site	Small (n = 7 sites)	Large (n = 12 sites)	1.0000[b]
Anterior mandible	0	1	
Anterior maxilla	1	2	
Posterior mandible	5	9	
Posterior maxilla	1	0	

Note: Values are presented as mean ± SD or frequency (%).
[a]*t* test.
[b]Fisher's exact test.

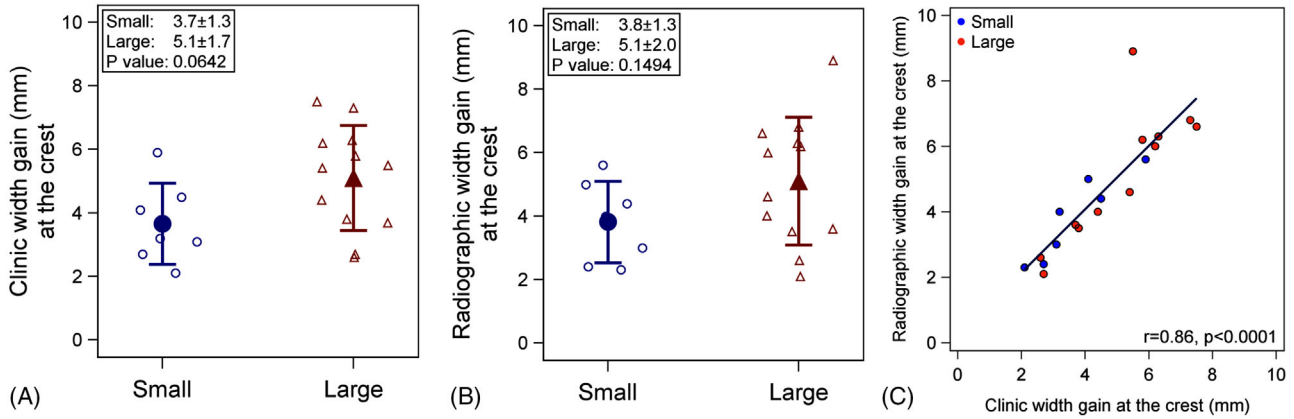

FIGURE 2 (**A**) Scatter plots showing mean ridge clinical gain (mm) in width at crest for both groups. (**B**) Scatter plots showing mean ridge radiographic gain (mm) in width at crest for both groups. (**C**) Pearson correlation between clinical and radiographic width gain at crest (mm) for both groups

TABLE 2 Clinical and radiographic outcomes in test and control groups

Outcome	Small (n = 7)	Large (n = 12)	*p*
Clinic width gain at crest (mm)	3.7 ± 1.3	5.1 ± 1.7	0.0571[a]
Radiographic width gain at crest (mm)	3.8 ± 1.3	5.1 ± 2.0	0.2142[a]
Radiographic width gain at 4 mm from crest (mm)	5.1 ± 1.8	5.9 ± 2.2	0.3178[a]
Vertical change at crest (mm)	−0.4 ± 0.5	0.3 ± 1.0	0.3176[a]
Bone density			1.0000[b]
D1	4 (57.1%)	7 (58.3%)	
D2	3 (42.9%)	4 (33.3%)	
D3	0	1 (8.3%)	

Note: Values are presented as mean ± SD or frequency (%).
[a]Generalized estimating equation (GEE) *F* test.
[b]Fisher's exact test.

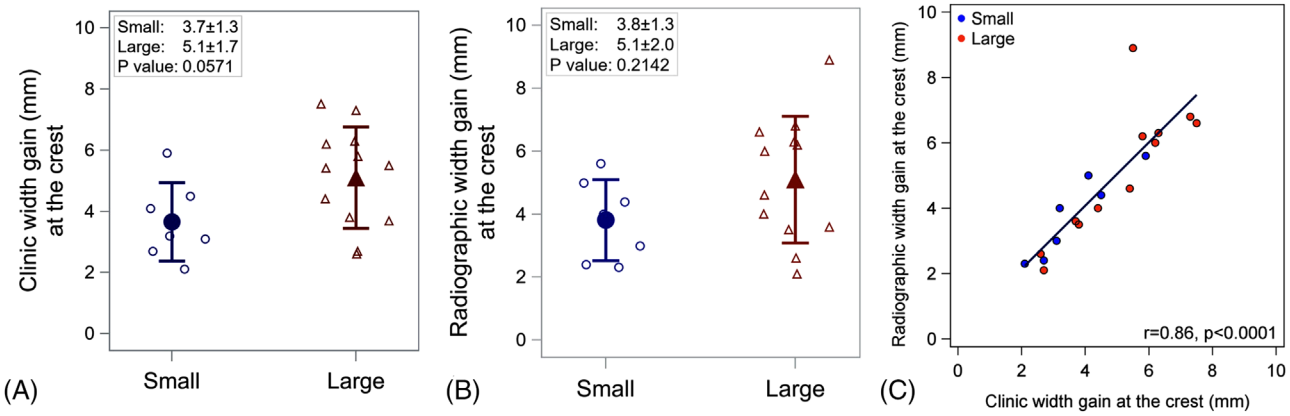

FIGURE 3 All biopsy cores (small- and large-particle groups) were divided into three zones: Zone 1 corresponds to coronal third, zone 2 to middle third, and zone 3 to apical third of the biopsy core

3.4 | Bone density

Four out of seven (57.1%) sites in the SP group had a D1 density, and the remaining three sites (42.9%) had a D2 density. In the LP group, seven out of twelve sites (58.3%) had D1 bone density, four sites (33.3%) revealed D2 density, and only one site (8.3%) had a D3 bone density. No statistical significance was found correlating the particle size to the bone density at the time of implant placement ($p = 1.00$) when using the Fisher's exact test (see Figure S4 in the online version of the *Journal of Periodontology*).

3.5 | Histology and histomorphometric analysis

All biopsies revealed newly formed bone, residual allograft particles, and dense, organized connective tissue encircling the graft particles. Three biopsies had insufficient length to divide into three zones due to nonintact biopsy cores (Figure 3). Allograft particles were identified by the separation lines and the absence of osteocytes in lacunae. The new bone in contact with the residual particles appeared viable with osteocytes in lacunae. Osteoblasts were present in conjunction with newly formed bone surrounding the graft particles. No acute or chronic inflammatory infiltrate was noticed in any of the biopsies.

Statistical analysis showed no significant difference in the percentage of new bone, residual graft particles, and soft tissue between the SP and LP groups or among the three zones between these groups. The only exception was the significant difference found in the percentage of the soft tissue area in zone 1 between the SP group (29.2% ± 7.1%) and the LP group (42.3% ± 15.2%) ($p = 0.05$).

Figure 4 shows the calculated percentage of new bone, residual graft particles, and soft tissue in each zone and overall percentage. For the SP group, the mean new bone formed was 41.0% ± 10.1%, mean residual graft was 33.6% ± 7.3%, and mean soft tissue was 25.5% ± 10.5%. Zone 3 revealed the highest percentage of new bone in this group (49.8% ± 5.32%), while zone 1 exhibited the least (37.2 ± 11.1.%). In the LP group, the mean new bone formed was 31.4 ± 14.8%, mean residual graft was 38.3 ± 19.7%, and mean soft tissue was 30.3 ± 13.8%. Zone 3 showed the highest percentage of new bone formed in this group (47.3 ± 13.6%), while zone 1 was the least (32.6 ± 15.1%) (Figure 5). Hence, the amount of overall new bone formed was higher in the SP group. The amounts of residual graft and connective tissue were higher in the LP group. Zones 1 and 2 showed higher percentages of new bone in the SP group; however, zone 3 of LP contained the larger percentage. Nonetheless, the two-sample *t* test revealed no statistically significant difference for all these measurements.

4 | DISCUSSION

The results of the current study showed that the combination of particulated corticocancellous bone allografts with a stabilized absorbable non–cross-linked collagen membrane can be used safely and effectively for LRA of deficient ridges. There was a trend that LP-size graft resulted in greater ridge width gain at and 4 mm apical to the crest compared with SP-size graft, but this did not reach the level of statistical significance. Vital bone formation was more in SP compared with LP, but without statistical significance.

To our knowledge, this is the first human study that investigates the influence of bone graft particle size on clinical and histologic LRA procedures. Overall, the effect of particle size on the clinical and histological outcomes of GBR has been scarcely studied. In the present study, the SP versus LP group had 41% versus 31.4% new bone

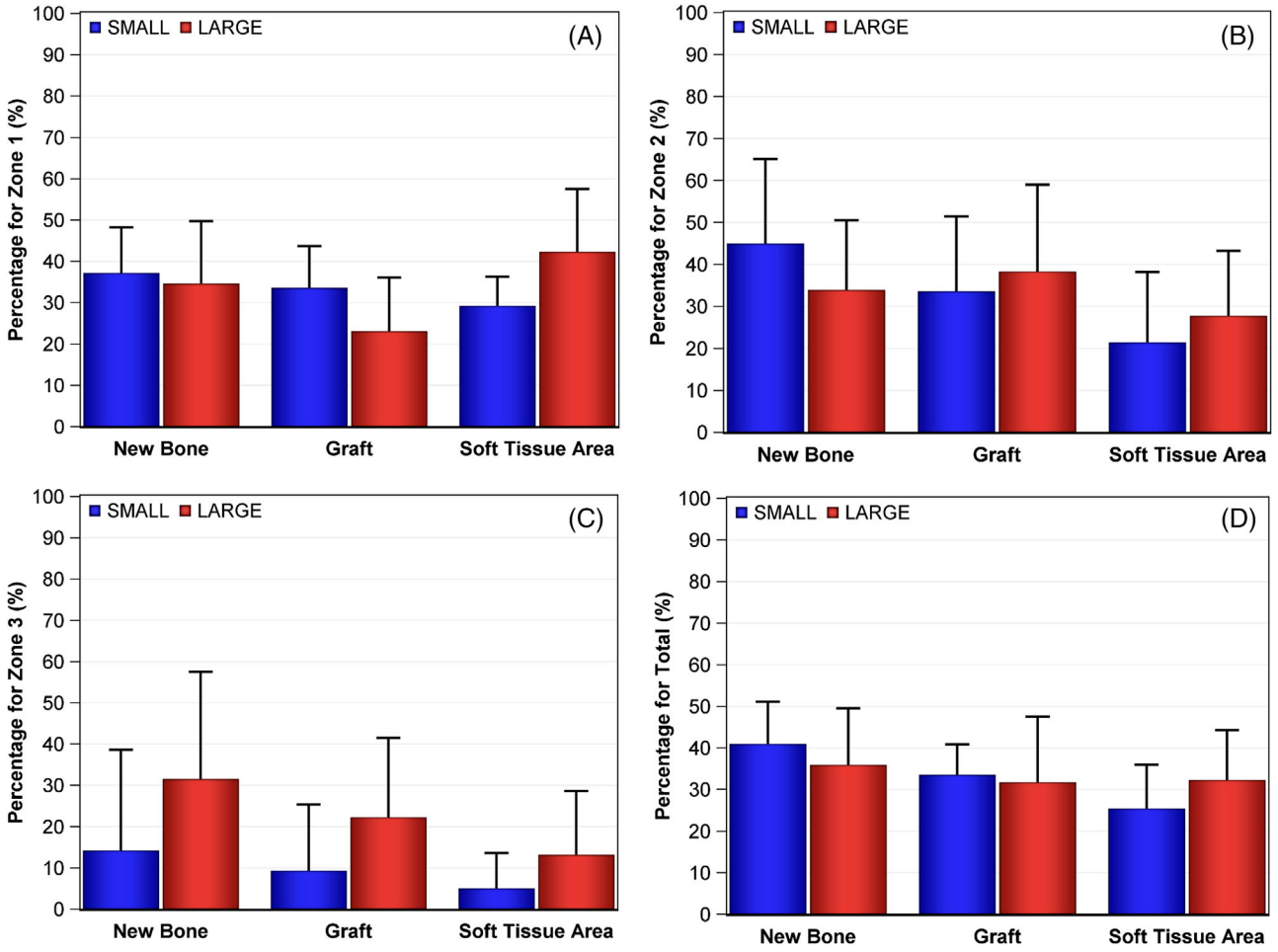

FIGURE 4 Calculated percentage of new bone, residual graft particles, and soft tissue in zones 1 (**A**), 2 (**B**), 3 (**C**), and overall percentage of all zones (**D**)

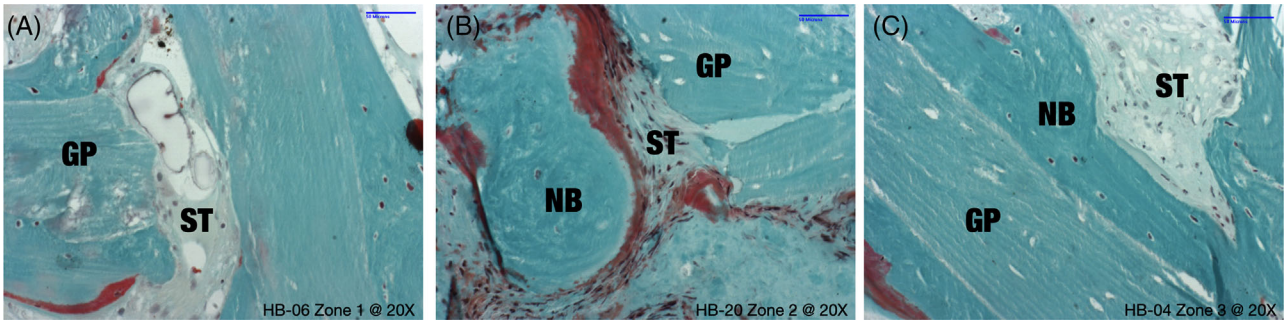

FIGURE 5 Higher magnification (20×) of histologic sections showing new bone, residual graft particles, and soft tissue in zones 1 (**A**), 2 (**B**), and 3 (**C**). GP, graft particle; NB, new bone; ST, soft tissue

formation, 33.6% versus 38.3% residual graft, and 25.5% versus 30.3% soft tissue.

The estimated bone density at augmented sites was found to be high in accordance with the results of an animal study investigating the effect of particle size.[25] In a rhesus monkey study, there was significantly more new bone formation associated with SP FDBA (100–300 μm) when mixed with autogenous marrow than with LP (1000–2000 μm).[26] Also, there was a marked resorption of SP in the new bone formed. It was concluded that SP FDBA enhance osteogenesis when mixed with autogenous marrow by increasing the number of pores.[26] Accordingly,

an increase in the surface area along with an increase in the osteoclastic activity may lead to a better osteogenic induction.[26] Therefore, it is conceivable that the particle size might play a role in the osteogenic activity. Unfortunately, the small number of samples in the current study does not allow for drawing any definitive conclusions in that regard.

Though previous LRA studies with histological analysis did not put emphasis on particle size effect, their results were quite close to the present study. For example, the histomorphometric analysis of ridge augmentation using FDBA plus a titanium re-enforced expanded polytetrafluoroethylene (e-PTFE) barrier demonstrated 47.6% new bone with 52.4% graft particles.[15] Another study that compared the histologic outcomes of demineralized freeze-dried bone allograft (DFDBA) versus FDBA following ridge and sinus augmentations has reported mean percentages of new bone of 41.7% and 41.9%, respectively, with no statistical difference.[27]

In a human randomized controlled trial,[21] the authors compared vital bone formation and residual graft volume in bilateral sinus augmentations performed with either 1.0–2.0-mm- or 0.25–1-mm-particle-size anorganic bovine bone matrix. Vital bone formation was 26.7% for LP compared to 18.7% for SP. Residual xenograft was 20% versus 21.6% for LP and SP, respectively. Similar findings were not shown in an earlier sinus augmentation study, which found no statistically significant difference in the percentage of new vital bone formation.[28] The difference in results between the current and previous studies may be related to differences in study design, graft material, or the nature of regenerated area. A more containing defect like the maxillary sinus should be assumed to regenerate more predictably regardless of used bone graft compared to LRA.[29]

Clinically, topographical differences were detected between the sites augmented with SP versus LP grafts at time of implant placement. Sites augmented with LP grafts resulted in more uneven and rougher ridges that required minor osteoplasty prior to placing implants. Implant placement was possible in all sites without additional augmentation. In all sites, grafts showed good incorporation with the newly formed ridge as histologically evidenced by a dense network of newly formed bone connecting residual graft particles.

In this trial, there was a mean clinical lateral bone gain of 3.8 and 5.1 mm for the SP group versus 5.1 and 5.9 mm for the LP group at the level of the crest and at 4 mm apically, respectively. This gain was around 1.4 mm more in the LP group, but with no statistical significance ($p = 0.06$). In a systematic review and meta-analysis by Sanz-Sánchez et al.,[3] an average of 3.9 mm bone width gain was reported after LRA. That number was based on a weighted mean of various procedures including block grafts, GBR (with absorbable or nonresorbable membranes), or ridge splitting done in either a simultaneous or staged fashion. Though, the study which reported the greatest increase in ridge width (5.7 mm) utilized a mixture of autogenous and anorganic bovine bone mineral covered with a fixated collagen membrane for 8–9 months.[30] Interestingly, from the 40 clinical trials included in that systematic review, only two studies utilized allografts.[3]

LRA studies rarely report on possible ridge height changes. Although there was no statistically significant difference between the SP and LP groups, the SP group resulted in a mean vertical loss of the ridge of −0.4 mm, while the LP group resulted in a mean vertical gain of 0.3 mm. These vertical changes ranged between −1.7 and 1.8 mm. Though our results may not be significant due to sample size, care should be taken in anterior cases where loosing 2 mm of ridge height might cause esthetic challenges.

The current study used a novel radiographic methodology for the measurement of ridge dimensional changes in buccolingual width and height following LRA. The strong correlation ($r = 0.86$, $p < 0.0001$) demonstrated between clinical and radiographic width measurements validates the employed radiographic methodology. This allowed for precise calculations and a simultaneous evaluation of ridge dimensional changes with minimal to no errors in the reproducibility of the location of measurements. This endorses the future use of this methodology in similar study designs.

Limitations of this study include the small sample size, which was compounded by the failure of five patients to complete the study; inability to assess clinical width gain at 4 mm from the crest due to excessive bone gain and surgical caliper accessibility limitations at several sites; lack of reporting on postaugmentation ridge width and subsequent width loss until reentry; lack of data on implant survival; and failure to capture patient-centered outcomes.

5 | CONCLUSION

The results of the present study suggest using bigger bone particles during bone augmentation procedures. Indeed, there was a trend for greater ridge width gain when LP were used in comparison to SP with near statistical significance. There was also a slight gain in ridge height with the LP, whereas a slight loss of ridge height was observed with the SP with no statistical differences. Histologically, there was a trend for more new bone with SP, but the small sample size did not allow for statistical significance. Future research with larger sample size should confirm the results of the present research.

AUTHOR CONTRIBUTIONS

Hussein S. Basma and Ramzi V. Abou-Arraj contributed to the conception and design of the work. Hussein S. Basma, Peng Li, and Ramzi V. Abou-Arraj collected and analyzed the data. Muhammad H. A. Saleh, Hussein S. Basma, Andrea Ravidà, and Ramzi V. Abou-Arraj contributed to the preparation of the manuscript. Hom-Lay Wang and Nico C. Geurs made critical changes and gave their final approval to the manuscript. All authors gave their final approval and agreed to be accountable for all aspects of the work.

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CONFLICT OF INTEREST

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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REFERENCES

1. Donos N, Mardas N, Chadha V. Clinical outcomes of implants following lateral bone augmentation: systematic assessment of available options (barrier membranes, bone grafts, split osteotomy). *J Clin Periodontol* 2008;35:173-202.
2. Kuchler U, von Arx T. Horizontal ridge augmentation in conjunction with or prior to implant placement in the anterior maxilla: a systematic review. *Int J Oral Maxillofac Implants* 2014;29(Suppl):14-24.
3. Sanz-Sanchez I, Ortiz-Vigon A, Sanz-Martin I, Figuero E, Sanz M. Effectiveness of lateral bone augmentation on the alveolar crest dimension: a systematic review and meta-analysis. *J Dent Res* 2015;94:128S-142S.
4. Urban IA, Monje A, Lozada J, Wang HL. Principles for vertical ridge augmentation in the atrophic posterior mandible: a technical review. *Int J Periodontics Restorative Dent* 2017;37:639-645.
5. McAllister BS, Haghighat K. Bone augmentation techniques. *J Periodontol* 2007;78:377-396.
6. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? *Int J Oral Maxillofac Implants* 2007;22(Suppl):49-70.
7. Urban IA, Monje A, Lozada JL, Wang HL. Long-term evaluation of Peri-implant bone level after reconstruction of severely atrophic edentulous maxilla via vertical and horizontal guided bone regeneration in combination with sinus augmentation: a case series with 1 to 15 years of loading. *Clin Implant Dent Relat Res* 2017;19:46-55.
8. Nystrom E, Nilson H, Gunne J, Lundgren S. A 9–14-year follow-up of onlay bone grafting in the atrophic maxilla. *Int J Oral Maxillofac Surg* 2009;38:111-116.
9. Rocchietta I, Simion M, Hoffmann M, Trisciuoglio D, Benigni M, Dahlin C. Vertical bone augmentation with an autogenous block or particles in combination with guided bone regeneration: a clinical and histological preliminary study in humans. *Clin Implant Dent Relat Res* 2016;18:19-29.
10. Nkenke E, Radespiel-Troger M, Wiltfang J, Schultze-Mosgau S, Winkler G, Neukam FW. Morbidity of harvesting of retromolar bone grafts: a prospective study. *Clin Oral Implants Res* 2002;13:514-521.
11. Zeltner M, Fluckiger LB, Hammerle CH, Husler J, Benic GI. Volumetric analysis of chin and mandibular retromolar region as donor sites for cortico-cancellous bone blocks. *Clin Oral Implants Res* 2016;27:999-1004.
12. Buser D, Bragger U, Lang NP, Nyman S. Regeneration and enlargement of jaw bone using guided tissue regeneration. *Clin Oral Implants Res* 1990;1:22-32.
13. Hjorting-Hansen E. Bone grafting to the jaws with special reference to reconstructive preprosthetic surgery. A historical review. *Mund Kiefer Gesichtschir* 2002;6:6-14.
14. Jensen SS, Terheyden H. Bone augmentation procedures in localized defects in the alveolar ridge: clinical results with different bone grafts and bone-substitute materials. *Int J Oral Maxillofac Implants* 2009;24(Suppl):218-236.
15. Feuille F, Knapp CI, Brunsvold MA, Mellonig JT. Clinical and histologic evaluation of bone-replacement grafts in the treatment of localized alveolar ridge defects. Part 1: mineralized freeze-dried bone allograft. *Int J Periodontics Restorative Dent* 2003;23:29-35.
16. Langer B, Langer L, Sullivan RM. Vertical ridge augmentation procedure using guided bone regeneration, demineralized freeze-dried bone allograft, and miniscrews: 4- to 13-year observations on loaded implants. *Int J Periodontics Restorative Dent* 2010;30:227-235.
17. Froum SJ, Wallace SS, Elian N, Cho SC, Tarnow DP. Comparison of mineralized cancellous bone allograft (Puros) and anorganic

bovine bone matrix (Bio-Oss) for sinus augmentation: histomorphometry at 26 to 32 weeks after grafting. *Int J Periodontics Restorative Dent* 2006;26:543-551.
18. Nissan J, Ghelfan O, Mardinger O, Calderon S, Chaushu G. Efficacy of cancellous block allograft augmentation prior to implant placement in the posterior atrophic mandible. *Clin Implant Dent Relat Res* 2011;13:279-285.
19. Piattelli A, Scarano A, Corigliano M, Piattelli M. Comparison of bone regeneration with the use of mineralized and demineralized freeze-dried bone allografts: a histological and histochemical study in man. *Biomaterials* 1996;17:1127-1131.
20. Kheur MG, Kheur S, Lakha T, Jambhekar S, Le B, Jain V. Does graft particle type and size affect ridge dimensional changes after alveolar ridge split procedure? *J Oral Maxillofac Surg* 2018;76:761-769.
21. Testori T, Wallace SS, Trisi P, Capelli M, Zuffetti F, Del Fabbro M. Effect of xenograft (ABBM) particle size on vital bone formation following maxillary sinus augmentation: a multicenter, randomized, controlled, clinical histomorphometric trial. *Int J Periodontics Restorative Dent* 2013;33:467-475.
22. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *J Clin Epidemiol* 2010;63:e1-37.
23. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull* 1979;86:420-428.
24. Lekholm U ZG. Patient selection and preparation. In: *Tissue Integrated Prostheses: Osseointegration in Clinical Dentistry*. Quintessence, 1985:199–209.
25. Zhou X, Zhang Z, Li S, Bai Y, Xu H. Osteoconduction of different sizes of anorganic bone particles in a model of guided bone regeneration. *Br J Oral Maxillofac Surg* 2011;49:37-41.
26. Shapoff CA, Bowers GM, Levy B, Mellonig JT, Yukna RA. The effect of particle size on the osteogenic activity of composite grafts of allogeneic freeze-dried bone and autogenous marrow. *J Periodontol* 1980;51:625-630.
27. Cammack GV, 2nd, Nevins M, Clem DS, 3rd, Hatch JP, Mellonig JT. Histologic evaluation of mineralized and demineralized freeze-dried bone allograft for ridge and sinus augmentations. *Int J Periodontics Restorative Dent* 2005;25:231-237.
28. Chackartchi T, Iezzi G, Goldstein M, et al. Sinus floor augmentation using large (1-2 mm) or small (0.25-1 mm) bovine bone mineral particles: a prospective, intra-individual controlled clinical, micro-computerized tomography and histomorphometric study. *Clin Oral Implants Res* 2011;22:473-480.
29. Schenk RK, Buser D, Hardwick WR, Dahlin C. Healing pattern of bone regeneration in membrane-protected defects: a histologic study in the canine mandible. *Int J Oral Maxillofac Implants* 1994;9:13-29.
30. Urban IA, Nagursky H, Lozada JL. Horizontal ridge augmentation with a resorbable membrane and particulated autogenous bone with or without anorganic bovine bone-derived mineral: a prospective case series in 22 patients. *Int J Oral Maxillofac Implants* 2011;26:404-414.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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