Received: 31 August 2017 | Revised: 7 October 2017 | Accepted: 23 October 2017

DOI: 10.1111/cid.12560

ORIGINAL ARTICLE

WILEY

Age-related new bone formation following the use of cancellous bone-block allografts for reconstruction of atrophic alveolar ridges

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Abstract

Background: An age-related decrease in the number of osteogenic progenitor cells may compromise bone augmentation.

Purpose: Histomorphometrical assessment of age-related new bone formation, following atrophic alveolar ridge reconstruction, using cancellous bone-block allografts.

Material and methods: Ninety-three consecutive patients (58 females and 35 males) were referred for implant-supported restoration of 122 severe atrophic alveolar ridges. Alveolar ridge deficiency locations were classified as anterior maxilla ($n = 58$), posterior maxilla ($n = 32$), and posterior mandible ($n = 32$). A bony deficiency of at least 3 mm horizontally and up to 3 mm vertically according to computerized tomography (CT) in the posterior mandible and anterior maxilla, served as inclusion criteria. In the posterior maxilla, a residual alveolar ridge up to 4 mm vertically according to CT served as inclusion criteria. Augmentation was performed by the use of cancellous bone-block allografts. Bone biopsies (9-month posterior maxilla, 4 months anterior maxilla and posterior mandible) of young (≤40 years) versus older (>40 years) patients were histomorphometrically evaluated.

Results: In the posterior maxilla, no statistically significant histomorphometric differences were noted. While at the anterior maxilla and posterior mandible, statistically significant more newly formed bone was found in young versus older individuals, respectively (38.6% vs 19.8%, $P = 0.04$ and 69% vs 31%, $P = .05$).

Conclusion: New bone formation following residual alveolar ridge bone grafting is age-related. Longer bone consolidation and healing time may be recommended for older individuals.

KEYWORDS

alveolar ridge bone allograft, bone formation, histological analysis, reconstruction

1 | INTRODUCTION

Bone grafting is a well-established procedure for reconstruction of bone deficiencies. The etiology may be atrophy—following tooth loss as a result of decay, periodontal defects, and so on, pathology (inflammatory, tumor, cyst, etc) invasion and/or resection, developmental-hypodontia, oligodontia, alveolar clefts, and trauma.[1–9]

Bone augmentation is an age-related decrease in the number of osteogenic progenitor cells, reported in different animal models,[10–12] and human studies,[13–15] is considered one of the main suggested mechanisms. Moreover, the percentage of pluripotent cells within the bone marrow decreases with age.[16,17] The reduced numbers of osteogenic cells at recipient sites combined with low vascularity[18] are additional factors that might be responsible for compromised bone augmentation outcome in elderly individuals.

Autografts can be harvested from extra- or intraoral sites. In both cases, osteogenic cells are located within the periosteum and the marrow compartment.[19,20] The transplanted osteogenic cells contribute to

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the dynamic process of graft consolidation. Hence autografts were considered the gold standard in maxillofacial surgery.[21] However, it can be speculated that the quality of an autograft drastically decreases with age due to the significantly lower number of vital osteogenic cells within the transplanted bone.[22]

A major drawback for using autografts is donor site morbidity. Immediate postoperative pain and edema, infections, hematomas, and neurosensory deficits are reported complications which limit to a great extent the possible use of autogenous bone blocks.[23–25] Recently, the use of block allografts for the treatment of alveolar ridge atrophy emerged, to overcome the donor site morbidity, yielding high survival rates.[26–31]

The present study assesses histomorphometrically the effects of aging on new bone formation following atrophic alveolar ridge reconstruction using cancellous bone-block allografts.

2 | MATERIAL AND METHODS

Augmentation by the use of mineralized cancellous bone-block freeze-dried allografts was a mandatory inclusion criteria. All procedures were fully explained to the patients who signed an informed consent, and the Ethics Committee of the Tel Aviv University approved the study protocol.

In the posterior mandible and anterior maxilla, a bony deficiency of at least 3 mm horizontally and up to 3 mm vertically according to computerized tomography (CT) served as inclusion criteria. The buccal aspect of the alveolar ridge was exposed. The recipient site was perforated to allow communication between the bone-block allograft and the recipient site bone marrow. The grafts were shaped to allow intimate contact between the graft and the recipient site. Stability was achieved by fixation with bone lag-screws. A collagen resorbable membrane was used to cover the block. Soft tissue margins were approximated using resorbable mattress sutures. Provisional restorations were adapted to avoid any pressure to the healing tissues. Access was obtained after 4 months for implant placement. Surgical exposure revealed well integrated bone-block allografts incorporated into the surrounding bone. Biopsies were taken with a trephine during implant osteotomy preparation. Rough surface titanium implants placed at the crestal level were used. Second stage surgery was performed 3 months after implant placement.

In the posterior maxilla, a residual alveolar ridge up to 4 mm vertically according to CT served as inclusion criteria. A window was created in the lateral sinus wall which allowed for elevation of the Schneiderian membrane. A cancellous bone-block allograft was trimmed. The bone-block allograft was inserted in a gentle press-fit fashion up to the palatal wall of the sinus cavity. Stability of the block allograft was initially achieved with the window bony frame. Implant sites were marked using a surgical stent. Rough surface titanium implants were placed. The locking of the block to the alveolar crest by the implants allowed implant stabilization in all directions. Initial primary stability was maintained in all cases. A resorbable collagen membrane, was applied over the lateral window. The flap was closed using resorbable sutures. Biopsies were taken with a trephine, 9 months after implant placement, from the lateral window, between the implants, at second stage surgery. Life expectancy in Israel according to the central bureau of statistics is about 80 years. Hence, age of 40 served to divide between young and older individuals.

In all cases, 4–6 weeks were allowed for soft tissue maturation. The implants were restored with fixed partial ceramo-metal restorations.

2.1 | Histomorphometric evaluation

Specimens were fixed in 10% buffered formalin for 24 hour. The bony cores first underwent rapid decalcification for ~72 hour (EDTA, pH = 6). Afterwards, they were routinely embedded in paraffin and hematoxylin and eosin stained slides were prepared. Using a light microscope (Olympus BH-2, Tokyo, Japan) with a mounted digital camera (Olympus BH-2, Tokyo, Japan) each bony core was photographed. The entire area of the cores was covered-contained in five consecutive, nonoverlapping photomicrographs performed at x200. A 10 x 10 graphical square grid was prepared, where the center of each square was marked by a "+." This grid was superimposed on each photomicrograph in the power point presentation.

Histomorphometric evaluation of the photomicrographs was performed using a modified point-counting methodology. The parameters evaluated in the study were bone, residual cancellous block-allograft and connective tissue. Each time one of these parameters overlapped the "+" mark, it was awarded one point. Whenever a "+" fell outside the tissue, that point was extracted from the total points counted for each photomicrograph (ie, 100 points), allowing only the "effective" points for the final calculations. After all five fields from each photomicrograph were examined; the sum of the points overlying each parameter was calculated and divided by the total "effective" points. This allowed calculation of the mean volume fraction for each of the evaluated parameters. The results are expressed as the mean volume fraction (%) of each evaluated parameter.

2.1.1 | Statistical analysis

Fisher's exact test and one-way analysis of variance were used for statistical analysis.

3 | RESULTS

Ninety-three consecutive patients (58 females and 35 males) aged between 17 and 70 years (mean 44 ± 17 years) were referred for implant-supported restoration of 122 severe atrophic alveolar ridges. A total of 258 rough surface implants were placed. Alveolar ridge deficiency locations were classified as anterior maxilla ($n = 58$), posterior maxilla ($n = 32$ sinuses), and posterior mandible ($n = 32$).

In augmented sinuses, no statistically significant ($P = .293$) histomorphometric differences (29.82% vs 24.43%) regarding newly formed bone were found between young (≤40 years) and older (>40 years) subjects (Figures 1 and 2).

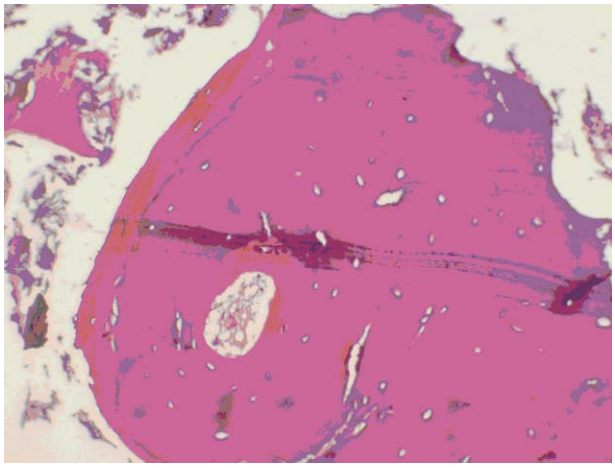

FIGURE 1 Histological view (Hematoxylin and Eosin staining original magnification x200) from an augmented sinus in an old individual (9 months)

In the anterior maxilla, statistically significant histomorphometric differences regarding newly formed bone (38.6% vs 19.8%, $P = .04$) and residual cancellous block-allograft (20.1% vs 38.4%, $P = .05$) were found between young and older patients, respectively. Age did not affect the mean of marrow and connective tissue (41.3% vs 41.8%, $P = .49$) (Figures 3 and 4).

In the posterior mandible statistically significant histomorphometric differences regarding newly formed bone (69% vs 31%, $P = .05$) were found between young and older patients, respectively. Histomorphometric differences regarding residual cancellous block-allograft (17% vs 35%) and of the marrow and connective tissue (14% vs 34%) were not statistically significant (Table 1).

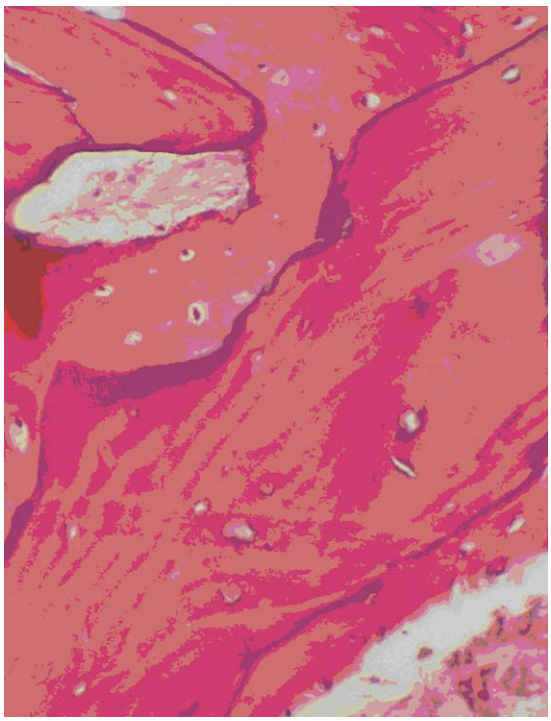

FIGURE 2 Histological view (Hematoxylin and Eosin staining original magnification x200) from an augmented sinus in a young individual (9 months)

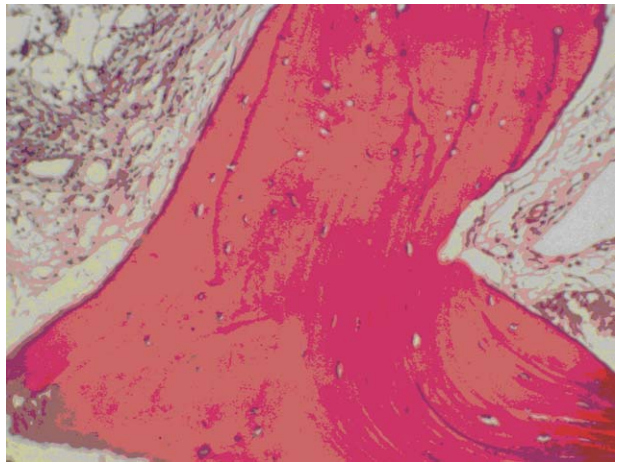

FIGURE 3 Histological view (Hematoxylin and Eosin staining original magnification x200) from an augmented anterior maxilla in an old individual (4 months)

4 | DISCUSSION

Aging may reduce new bone formation in grafted defects.[13–15,21,32] Animal models suggest that 6 versus 26 versus 52 -week-old rats regain normal bone after 4, 10, and 26 weeks respectively, after a fracture.[33] Aging induces a delayed onset of periosteal reaction, cell differentiation, and decreased bone formation.[12] Mouse and rabbit models of calvarial healing showed differences in the regenerative abilities of young and older.[10,11]

Active periosteal tissue in children allows reossification of calvarial defects until approximately 2 years of age.[21,34] Hence, the capacity of the bone to regenerate is compromised with aging, a mechanism that might also apply to the process of graft consolidation at defect sites.

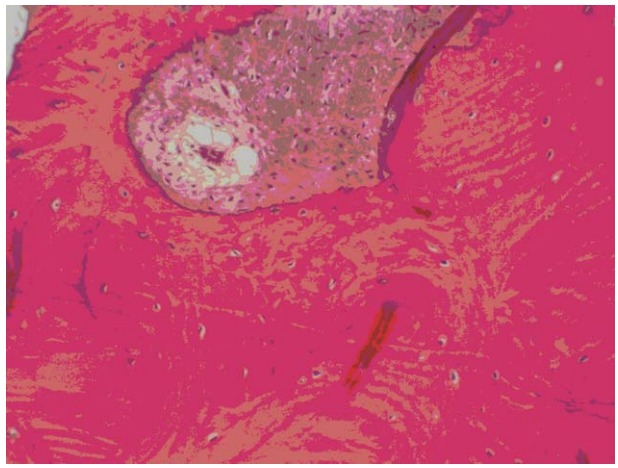

FIGURE 4 Histological view (Hematoxylin and Eosin staining original magnification x200) from an augmented anterior maxilla in a young individual (4 months)

TABLE 1 Histomorphometrical data

	Young group			Older group			
	New bone	Residual particles	Connective tissue	New bone	Residual particles	Connective tissue	*p* Value of new bone formation
Anterior maxilla	38.6%	20.1%	41.3%	19.8%	38.4%	41.8%	0.04
Posterior maxilla	29.82%	14%	56.18%	24.43%	26%	49.57%	0.293
Posterior mandible	69%	17%	14%	31%	35%	34%	0.05

This has been also attributed to the osteogenic potential of the implant bed, following bone grafting. Moreover, the osteogenic potential of autografts, is also reduced in elderly individuals due to a thinner periosteum[20] and a smaller number of mesenchymal cells in the bone marrow.[17]

The model presented in this study used bone-block allografts, devoid of cells, for bone grafting. Hence, new bone formation was based merely on the osteogenic potential of the residual alveolar ridge. In both anterior maxilla and posterior mandible, the amount of new bone formation was twofold (statistically significant) in young compared to older individuals. It can be speculated that the anterior maxilla and posterior mandible in young versus older individuals contained a larger number of cells capable of migrating from the recipient site into the graft. Moreover, besides the number, a stronger mitogenic activity of cells in the young contributed to the differences observed. Furthermore, the larger number of cells contributed to the consolidation process.

No such differences were noted in posterior maxilla biopsies regarding new bone formation in young vs. older individuals, although similar differences in the number of cells and mitogenic potential between young and old individuals do exist in the posterior maxilla. The use of two different procedures requiring two different waiting times enabled the unique evaluation of the comparison between new bone formation at two different time frames as a function of age. The healing time prior to the posterior maxilla biopsy was 9 months, whereas in the anterior maxilla and posterior mandible 4 months. It can be speculated that the longer time (9 vs 4 months) interval for bone consolidation might have compensated for the smaller amount of cells and lower mitogenic potential. It can be recommended that improved results, in terms of new bone formation, may be achieved in older populations following a longer waiting time from the bone grafting procedure (preferably 9 months).

Another mechanism of compromising bone augmentation with age may be surgical complications. Such an evaluation in a model of cancellous allogeneic bone-block graft augmentation demonstrated that age had no statistically significant effect.[35]

Although, bone healing related to patients' age was compared, other parameters, may have affected the evaluated results theoretically. Bone graft exposure for example, could significantly affect results. According to previous reports with a similar bone augmentation procedure, a large incidence of block exposure was found, especially in the posterior mandible (less in the anterior and in the posterior maxilla, in decreasing order). Differences in new bone formation, in the present report followed the same pattern. This may suggest to evaluate blocks exposure in the two age groups and compare histomorphometry of exposed versus nonexposed cases within and between each age group. Statistical analysis, previously reported, demonstrated that age and gender had no statistically significant effect on block exposure.[35]

5 | CONCLUSION

New bone formation following residual alveolar ridge bone grafting is age dependent. Longer bone consolidation and healing time is recommended for older (>40 years) individuals.

CONFLICT OF INTEREST

No conflict of interest.

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How to cite this article: Nissan J, Kolerman R, Chaushu L, Vered M, Naishlos S, Chaushu G. Age-related new bone formation following the use of cancellous bone-block allografts for reconstruction of atrophic alveolar ridges. *Clin Implant Dent Relat Res.* 2017;00:1–5. https://doi.org/10.1111/cid.12560