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CLINICAL AND RADIOGRAPHIC OUTCOMES OF IMMEDIATE IMPLANT PLACEMENT WITH OR WITHOUT NANOCRYSTALLINE BONE GRAFTING MATERIAL IN THE FACIAL GAP DISTANCE: A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Objectives: The aim of this study was to evaluate the clinical and radiographic outcomes of the simultaneous use of nanocrystalline bone grafting material placed in the facial gap distance around immediate dental implants placed in the anterior maxilla and its effect for minimizing the crestal bone loss.

Material and methods: Adult patients were eligible for the study if they needed one immediate implant placement (IIP) replacing a tooth to be extracted within the maxillary anterior region. The patients included in the study were divided into two groups; patients in the first group received IIP without grafting material in the gap distance while patients in the second group received IIP simultaneously with nanocrystalline bone in the facial gap distance. Clinical and radiographic assessments were performed before IIP (baseline) and scheduled 4 and 12 months after implant placement. Clinical assessment included bleeding Index (BI) and probing depth (PD). Facial bone height measurements were performed using cone beam computed tomography (CBCT) to measure the crestal bone loss.

Results: The means of BI and PD values at the 12 months follow up indicated healthy peri-implant soft tissues for both groups, however higher means of BI and PD were shown in IIP without grafting material when compared to IIP with nanocrystalline bone in the facial gap distance. There was no statistically significant difference in CBL between both groups (p=0.924).

Conclusions: The short-term follow-up of 12 months of IIP in the maxillary anterior area revealed successful clinical outcomes as assessed by objective parameters. IIP with or without simultaneous nanocrystalline bone grafting material placed in the facial gap distance around the implants did not prevent crestal bone loss as assessed by CBCT.

Keywords: extraction socket, remodeling, grafting, nanocrystalline, biomaterials, immediate implants, crestal bone loss.

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INTRODUCTION

Immediate implant placed into fresh extraction socket is considered a predictable, safe, successful and acceptable procedure (Barone *et al*., 2006). However, immediate implant is considered aesthetically risky, as the healing of the alveolar bone may lead to unpredictable changes of the contour and the architecture of the gingival tissue around the implant. It has been proven that bone remodeling always takes place, even when an immediate implant is placed, as this phenomenon is associated with the resorption of the bundle bone, present only around the natural teeth. Therefore as bundle bone is a tooth-dependent tissue it will gradually disappear after tooth extraction. Since there is more bundle bone in the crest of the buccal than the lingual wall, hard tissue loss will be more pronounced in the buccal than the lingual wall (Araújo *et al*., 2005) (Araújo *et al*., 2006). Many protocols have been suggested to control or minimize the effects of bone healing process as flapless approach, the use of immediate implant supported provisional restoration or grafting of the alveolar space between the implant and the facial bony wall with different biomaterials (Blanco *et al*., 2008) (Chen, Darby and Reynolds, 2007) (Atieh *et al*., 2009). Over the past few years, the buccal wall thickness has gained significance, mainly as a result of its importance for the immediate implant placement (IIP) (Huynh-Ba *et al*., 2010). Although it is difficult measuring the thin buccal plate of bone around a metallic dental implant using cone beam computed tomography (CBCT), it is the only noninvasive approach to investigate the relationship between covering soft tissue and bone height and thickness around dental implant (Le and Borzabadi-Farahani, 2012). CBCT scans have been widely used in the dental field due to accuracy and the ability to view a detailed three-dimensional image (3D) of the regions of interest (González-Martín *et al*., 2016).

It was demonstrated that the vertical bone loss and the gingival recession related to IIP can be reduced if ≥ 2mm of labial bone thickness is maintained in the anterior region. In the same study, vertical bone loss and gingival recession showed a significant positive correlation, while bone width showed a significant negative correlation to gingival recession. The measurement of alveolar bone thickness and vertical bone loss in that study achieved through CBCT (Miyamoto and Obama, 2011). Another study using CBCT, the authors concluded that there was a low prevalence of buccal wall thicknesses ≥2 mm and that there was a moderately positive correlation between the buccal bone thickness and soft tissue (Younes *et al*., 2016)

The ideal grafting material to induce osseointegration should have osseoinductive and osseoconductive properties (Mavrogenis *et al*., 2009). The maturation and mineralization of the newly formed bone in the extraction socket can be accelerated or improved by graft materials (Mezzomo *et al*., 2011).

The use of xenograft for the reduction in dimensional alterations of a post-extraction site was already described in various animal studies (Araújo and Lindhe, 2005) (Araújo *et al*., 2005) (Araújo, Linder and Lindhe, 2011): in the latter, the authors showed that the use of Bio-Oss® Collagen graft to fill the buccal gap in a post-extraction implant reduced the buccal vertical resorption from 1.3 ± 0.7 mm to 0.1 ± 0.5 mm.

Alloplast bone graft are widely used as bone substitutes for bone defect and accelerates the bone formation that filling the defect. Hydroxyapatite (HA) is one of the alloplast bone graft material which is characterized by its biocompatibility and bioactivity properties. One of the new generations of (HA) is nanohydroxyapetite, which is characterized by a porous structure. This nano / microstructure has particularly high porosity which showed balance between absorption of the nanohydroxyapetite

particles and the rate of regenerative bone formation.

The present study was conducted to evaluate the clinical potential of nanocrystalline bone grafting material in the facial gap distance around immediate dental implants in the anterior maxilla and its significance in reducing crestal bone loss using CBCT.

Hypothesis: there is no clinical difference between immediate implant placement with simultaneous nanocrystalline grafting material in the facial gap distance and immediate implant placement without grafting material in the gap distance**.**

AIM OF THE STUDY

This research studied the clinical significance of using nanocrystalline bone grafting material in the facial gap distance around immediate dental implants in the anterior maxilla and its significance in reducing crestal bone loss.

MATERIALS AND METHODS

The present study was conducted on 14 patients; with age ranged from 21 to 50 years old and randomized into two equal groups (group1 and group 2). Each patient received one immediate implant in the anterior maxilla. The study protocol was approved by the ethical committee for clinical studies of Faculty of Dentistry, Ain Shams University. Patients were selected according to the inclusion and exclusion criteria from the outpatient clinic of the Faculty of Dentistry, Ain Shams University.

Inclusion criteria:

- Patients presented with the need for inevitable extraction of a single tooth in the maxillary anterior region (due to root fracture, root resorption, non-restorable remaining root or failed endodontic treatment).
- Good oral hygiene and good compliance with the plaque- control instructions.
- Natural teeth adjacent to the tooth to be extracted were required to have complete occlusal surfaces and were free from infections.
- The presence of intact buccal bone after tooth extraction as proved by exploring the labial plate of the socket using periodontal probe.
- At least 3mm of bone beyond the root apex was required to guarantee implant primary stability.
- Patients' ability to follow the study protocol and willingness to sign an informed consent form.

Exclusion criteria:

- Inadequate soft tissue because of gingival attachment loss resulting in gingival recession, gingival asymmetry or mucogingival
- The presence of a fenestration ≤ 4 mm apical to the facial alveolar bone crest.
- Acute infection at the tooth site.
- Any systemic diseases or medications that could affect the osseointegration of the dental implants or compromise healing potential.
- Moderate and heavy smokers (>10 cigarettes per day).

An informed consent form was signed by all the patients participating in this study. All patients received standardized diagnosis and treatment planning procedures. This study was a randomized, double-blinded clinical trial with an equal allocation rate. Patients who met the eligibility criteria were randomly allocated using computer assisted randomization by Microsoft excel through numbered sealed envelopes into two groups. Both the patient and the evaluator who assessed the clinical parameters and CBCT were blinded to the group assignment.

Group 1 (Gp 1)

Each patient received one implant that was placed immediately following tooth extraction without flap elevation and without grafting material in the gap distance.

Group 2 (Gp 2)

Each patient received one implant that was placed immediately following tooth extraction, simultaneously with nanocrystalline grafting material in the facial gap distance.

Surgical Procedures:

Atraumatic extraction was performed. No mucoperiostal flap was elevated. Subsequently, a periodontal probe* was used to verify the integrity of bony walls of the socket and the presence of dehiscence or fenestration defects (Chen and Buser, 2009). To be included, all of the four bony walls of the socket were intact. If a dehiscence defect of the facial bone was ≤ 2mm, the subject was included in the study (Degidi *et al*., 2013). Transmucosal sounding of the facial plate of bone was performed to detect the presence of any concavities apical to the socket (Chen and Buser, 2009). If a Fenestration of the facial bone was present ≥ 4mm apical to the alveolar crest and the facial marginal bone was intact, the subject was included (Degidi *et al*., 2013). If the extraction socket met inclusion criteria, an implant** was placed after optimal osteotomy preparation through sequential drilling with copious irrigation according to the manufacturer instructions till the desired dimensions were achieved depending on the selected implant (Buser, Martin and Belser, 2004). The nanocrystalline bone grafting material*** was placed in the facial gap distance around the implant for group 2 patients.

For each patient of both groups; proper healing abutment was screwed to the implant at the end of the surgical procedure; approximation of the papillae was done by figure of eight suture. Postoperative medications were prescribed and instructions were explained for all patients.

Prosthetic procedures:

After complete soft tissue healing, 2 – 3 weeks later, a temporary prosthesis was fabricated for each patient of both groups using auto polymerizing acrylic resin. Four months after implant placement, the final abutment was screwed and conventional loading was applied using permanent porcelain fused to metal crown.

Baseline and Follow-up evaluations:

Clinical examination

Clinical examination was conducted by the same examiner to assess bleeding index score (BI) (Mombelli *et al*., 1987) and probing depth (PD) at baseline (before extraction), 4 months and 12 months post-surgical intervals.

Radiographic examination

Cone beam computed tomography (CBCT) using i-CAT™ **** was taken at the baseline, 4 months and at 12 months post-surgery in order to measure changes in height of the buccal plate of bone and calculate the vertical crestal bone loss (CBL). Standardization during imaging was achieved through adjusting the patient positioning lights as follow: The field of view (FOV) (16 cm x 6 cm). Voxel size= 0.2 mm^3 and scan time= 26.9 seconds. To compare the vertical bone loss, fusion was done between baseline and 12 months post-surgery scans. Superimposition was done using Ondemand semi-automatic wizard, by selecting common points in both CBCT scans and then manual fine tuning was done to maintain the accuracy. The radiographic readings were performed by the same examiner

Statistical analysis

The mean and standard deviation values were calculated for each group in each test. Data were

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**** iCAT Next Generation Cone Beam 3D System by Imaging Sciences International LLC, Hatfield, PA, USA

explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests, PD and CBL data showed parametric (normal) distribution, while BI data showed non-parametric (not-normal) distribution

For parametric data; Repeated measure ANOVA was used to compare between more than two groups in related samples. Paired sample t-test was used to compare between two groups in related samples. Independent sample t-test was used to compare between two groups in non-related samples.

Two-way ANOVA test was used to test the interactions between different variables.

For non-parametric data; Friedman was used to compare between more than two groups in related samples. Wilcoxon test was used to compare between two groups in related samples. Mann Whitney test was used to compare between two groups in non-related samples.

The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM® SPSS® Statistics Version 20 for Windows.

RESULTS

Clinical outcomes:

Bleeding index scores (BI):

No statistically significant difference was found between (Baseline), (4 months) and (12 months) follow up intervals in either (Group 1) or (Group 2) where (*p*=0.056) and (p=0.104) respectively

There was no statistically significant difference between both groups at baseline (p=0.329), but there was a statistically significant difference between (Group 1) and (Group 2) at 4 months and 12 months follow up intervals where (p=0.008) and (p=0.001) respectively. Mean and standard deviation (SD) for BI for different tested groups are presented in **(Table 1)**

Probing depth (PD):

No statistically significant difference was found between (Baseline), (4 months) and (12 months) follow up intervals in either (Group 1) or (Group 2) where (p=0.149) and (p=0.164) respectively

There was no statistically significant difference between both groups at baseline and after 12 months where (p=0.102) and (p=0.162) respectively, while at 4 months follow up interval, there was a statistically significant difference between (Group 1) and (Group 2) (p=0.011). Mean and standard deviation (SD) for PD for different tested groups are presented in **(Table 2)**

- **Two-way ANOVA:**

Data in table (3) shows the results of Two-way ANOVA analysis for the interaction of different variables. The results showed that groups had no statistically significant effect at P-value 0.067. Time had no statistically significant effect at P-value 0.313. The interaction between the two variables had a statistically significant effect at P-value 0.012.

TABLE (1): The mean, standard deviation (SD) values of BI of different groups.

Variables	BI						
	Baseline		4m		12m		p-value
	Mean	SD	Mean	SD	Mean	SD	
Group 1	0.690	0.150	0.929	0.302	0.929	0.131	**0.056ns**
Group 2	0.571	0.278	0.500	0.144	0.321	0.189	**0.104ns**
p-value	**0.329ns**		**0.008***		**0.001***		

; significant (p<0.05) ns; non-significant (p>0.05)

TABLE (2): The mean, standard deviation (SD) values of PD of different groups.

Variables	PD						
	Baseline		4m		12m		p-value
	Mean	SD	Mean	SD	Mean	SD	
Group 1	2.570	0.460	3.711	0.872	3.233	1.084	**0.149ns**
Group 2	3.071	0.590	2.679	0.278	2.607	0.244	**0.164ns**
p-value	**0.102ns**		**0.011***		**0.162ns**		

; significant (p<0.05)** **ns; non-significant (p>0.05)

TABLE (3) Results of Two-way ANOVA for the effect of different variables on PD.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	7.037	5	1.407	3.207	.017
Intercept	372.619	1	372.619	849.192	.000
Groups	1.562	1	1.562	3.560	.067
Time	1.053	2	.526	1.200	.313
Groups * Time	4.422	2	2.211	5.039	.012
Error	15.797	36	.439		
Total	395.453	42			
Corrected Total	22.833	41			

df: degrees of freedom = (n-1), * Significant at P ≤ 0.05

TABLE (4): The mean, standard deviation (SD) values of CBL of different groups.

Variables	CBL						
	0-4m		4m-12m		0-12m		p-value
	Mean	SD	Mean	SD	Mean	SD	
Group 1	-0.904	0.613	-0.334	0.466	-1.239	0.790	**0.031***
Group 2	-0.914	0.204	-0.329	0.192	-1.269	0.194	**<0.001***
p-value	**0.968ns**		**0.977ns**		**0.924ns**		

; significant (p<0.05)** **ns; non-significant (p>0.05)

Radiographic outcomes: Crestal bone loss (CBL):

A statistically significant difference was found in (Group 1) between (0-4m), (4m-12m) and (0-12m) (p=0.031), where a statistically significant difference was found between (4-12m) and (0-12m) (p=0.008), but no statistically significant difference was found between (0-4m) and each of (4-12m) and (0-12m) where (p=0.091) and (p=0.106) respectively.

A statistically significant difference was also found in (Group 2) between (0-4m), (4m-12m) and (0-12m) (p<0.001), where a statistically significant difference was found between (0-4m) and each of (4m-12m) and (0-12m) where (p=0.004) and (p=0.001). Also a statistically significant difference was found between (4m-12m) and (0-12m) where (p<0.001).

There was no statistically significant difference between both groups at (0-4m), (4m-12m) and (0-12m) where (p=0.968), (p=0.977) and (p=0.924) respectively. Mean and standard deviation (SD) for CBL for different tested groups are presented in **(Table 4)** and **(Figure 1)**

TABLE (5) Results of Two-way ANOVA for the effect of different variables on CBL.

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.
Corrected Model	6.083	5	1.217	5.475	.001
Intercept	29.033	1	29.033	130.645	.000
Groups	.001	1	.001	.006	.938
Time	6.080	2	3.040	13.679	.000
Groups * Time	.002	2	.001	.005	.995
Error	8.000	36	.222		
Total	43.117	42			
Corrected Total	14.084	41			

df: degrees of freedom = (n-1), * Significant at P ≤ 0.05

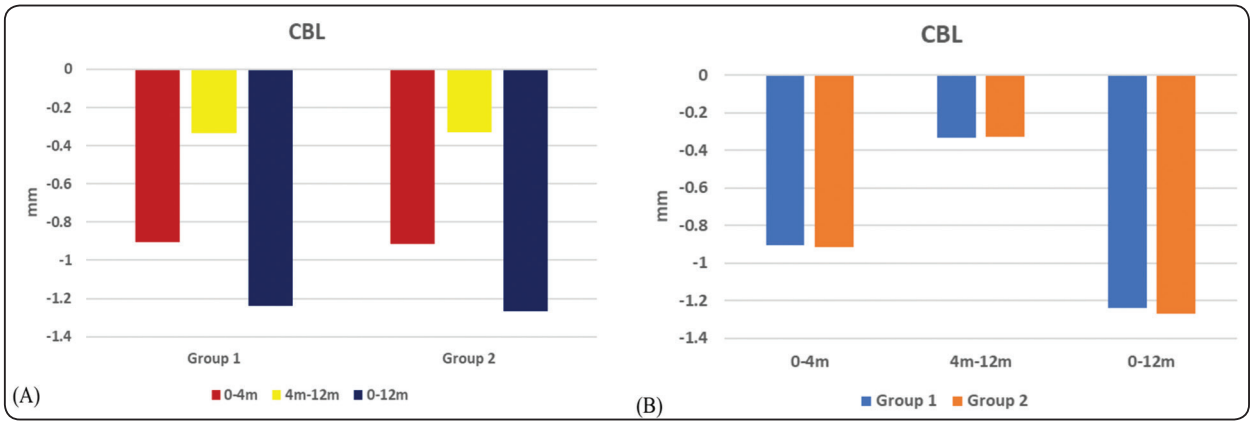

Fig. (1): Bar chart representing CBL for different groups

➢ **Two-way ANOVA:**

Data in table (5) shows the results of Two-way ANOVA analysis for the interaction of different variables. The results showed that groups had no statistically significant effect at P-value 0.938. Time had a statistically significant effect at P-value <0.001. The interaction between the two variables had no statistically significant effect at P-value 0.995.

DISCUSSION

In immediate implant placement (IIP), the horizontal peri-implant gap appeared to affect the healing of bone around the implant. It was shown that when the horizontal width of a peri-implant defect was less than 2 mm, the defect had the capacity to spontaneously heal and produce new bone when immediate implant placement was performed. But when the peri-implant gap width was more than 2mm, bone graft material with or without membrane should be used to seal this defect for proper esthetic outcome (Paolantonio *et al*., 2001).

It was postulated that nanocrystalline bone grafting material embedded in a silica gel matrix has osteoconductive and showed biodegradation in a manner comparable to natural bone remodeling processes. Graft resorption and appear in conjunction with bone apposition around the graft granules (Götz *et al*., 2008). IIP with hydroxyapatite nano-crystals bone graft material showed high significant increase in values of bone density and implant stability more than IIP without any graft material after 6 months postoperative.(Ghanem, Hashem and Mostafa, 2016)

NanoBone® is an approved granular material consisting of nanocrystalline HA embedded in a silica gel matrix which offers advantages of nanostructural biomaterials (Webster and Ahn, 2006). Gerber et al attributed that Nanobone® is able to stimulate the differentiation of bone cells into osteoblasts and osteoclasts, because alkaline phosphatase , osteocalcin, osteopontin and BMP-2 were located in newly formed bone (Gerber *et al*., 2006).

The use of collagen membrane and Nanobone can significantly reduce the horizontal resorption of the alveolar ridge and preserve keratinized tissue more effectively than blood clot alone and natural healing of single-rooted extraction sockets (Salahi , Etemadifar and Moosaali, 2015)

A histomorphometric analysis in an experimental study showed that nanocrystalline bone grafting material with platelet rich fibrin (PRF) significantly preserve the dimensions of extracted bony socket after atraumatic simple extraction (Ghanem et al 2016)

According to the previous studies, the role of nanocrystalline hydroxyapatite as alloplast material in establishment of high success osseointegration of immediate implants and minimizing crestal bone loss needs to be investigated.

The aim of the present study was to evaluate the clinical and radiographic outcomes of the simultaneous use of nanocrystalline bone grafting material placed in the facial gap distance around immediate dental implants placed in the anterior maxilla and its effect for minimizing the crestal bone loss.

The findings from this study showed that implants placed in fresh extraction sites can provide a safe and successful treatment procedure.

This study showed 100 % survival rate of immediate implants. This result is in accordance with Kan et al. who showed a survival rate of 100% for 35 implants that were placed and immediately restored after tooth extraction (Kan et al., 2011).

The means of BI and PD values at the 12 months follow up indicated healthy peri-implant soft tissues. The reduction in the inflammatory reaction could be attributed to the strong patient's motivation

for oral hygiene measures. The results of the current study agreed with the findings of other investigators who reported that plaque accumulation can induce a negative mucosal response (Kan *et al*., 2018) .

The results of the present study are consistent with the findings of other investigators, who reported that marginal tissue around titanium fixtures, in most examined patients had no gingivitis throughout the study (Buser, Weber and Lang, 1990).

Clinical probing is considered as an important and reliable diagnostic parameter in the continuous monitoring of both periodontal and peri-implant tissues (Atassi, 2002).The results of the present study demonstrated that there was no statistically significant difference in BI and PD throughout the study periods within each group. However, there was a statistically significant difference in mean of BI between both groups at 4 months and 12 months follow up intervals where in the latter, the mean BI related to implants placed immediately following teeth extraction without nanocrystalline bone was significantly more than that related to implants placed immediately following teeth extraction with simultaneous nanocrystalline bone placed in the facial gap distance around the implants. There was also a statistically significant difference in mean of PD between both groups at 4 months follow up interval where the mean PD related to implants placed immediately following teeth extraction without grafting material was significantly more than that related to implants placed immediately following teeth extraction with simultaneous grafting material placed in the facial gap distance around the implants, but no statistically significant difference was found in mean of PD between both groups after 12 months.

Many authors showed that the insertion of implants immediately after the extraction is a valuable technique in terms of success and esthetic outcomes (Paolantonio *et al*., 2001) (Cornelini *et al*., 2006) (J. *et al*., 2011)**.** In 2010, Sanz et al. showed that in implants inserted in post-extractive sites without graft, a mean vertical crest reduction of 1 ± 2 mm occurred in the buccal side (Sanz *et al*., 2010).

The thickness of the buccal bone wall can determine the degree to which vertical resorption is produced. Sites with thin facial bone underwent significantly more vertical resorption than sites with thicker facial bone (Chung *et al*., 2011). Mean bone level change around immediate implants is affected by the gap distance between the socket wall and the implant, it was reported that if the jumping distance is over 2mm, grafting is recommended. Smaller distances could heal spontaneously (Chen, Wilson and Hämmerle, 2004) (Esposito *et al*., 2009) .

Concerning the mean crestal bone loss (CBL), both groups of the present study showed CBL during the whole study follow up (0-12months) which was statistically significant for both groups but there was no statistically significant difference between both groups (p=0.924).

These findings were in agreement with findings reported in a recent systematic review in which it was concluded that marginal bone loss occurred most often during the first year after implant placement and with a magnitude of about 0.8–1.0 mm (Lang *et al*., 2012)**,** while these findings were in contrary to another study in which clinical evaluation of immediate implants using either freeze-dried bone allograft or modified hydroxyapatite revealed significant decrease in bone height through one year follow up (Viswambaran *et al*., 2014)**.**

Many studies reported that lack of flap elevation does not prevent bone resorption but the major benefit of this treatment is the preservation of the existing papillae (Migliorati *et al*., 2015)**.** CBL can be minimized through proper case selection, intact socket wall after atraumatic extraction, adequate bone for achieving primary stability, flapless technique, placement of a slowly resorbing grafting material in the gap between the implant and the

buccal socket wall and correct three-dimensional implant positioning. The present radiographic study seems to confirm that, even in the presence of dimensional alterations of the alveolar ridge, it is possible to minimize the effect of these alterations on the buccal side of the implant.

Limitations of the present study: Short-term follow-up and Small sample size of each group

CONCLUSIONS

Within the limitations of this study, it was concluded that:

- Immediate implant placement in the maxillary anterior area revealed successful clinical outcomes as assessed by objective parameters through short-term follow-up of 12 months
- Immediate implant placement with simultaneous nanocrystalline bone grafting material placed in the facial gap distance around the implants did not prevent crestal bone loss during the first year after implant placement as assessed by cone beam computed tomography analysis.

Recommendations

- Future randomized controlled trials should include a longer follow-up and a larger sample size, to assess if immediate implant placement with simultaneous nanocrystalline bone grafting material offers long-term benefits for patients with thin facial bone biotype
- Comparison of long term stability of soft tissue around immediate implant placement with or without simultaneous nanocrystalline bone grafting material.

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