Evaluation of the Efficacy of Porous Titanium Granules in the Treatment of Periodontal Intrabony Defects: A Preliminary Report

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ABSTRACT

Background and objectives: Applications of porous titanium granule (PTG) in periodontal (furcation defects) and non-periodontal treatments have shown promising results. However, its role in periodontal intrabony defects still remains unexplored. Thus, we aim to assess the feasibility of PTG in obtaining reconstruction in intrabony defects and compare the outcome with that of open flap debridement (OFD).

Method: Ten patients (three females and seven males) with a mean age of 34.7 years who constituted twenty (20) bilateral intrabony defects were recruited. Each patient contributed to two defects which were randomly treated by OFD alone (control group) or by OFD followed by grafting with PTG (test group). All the clinical and radiological parameters were recorded at baseline, three, six and nine months and statistically analyzed.

Results: The results of this study demonstrated that in clinical parameters there is no significant differences in the improvement from baseline to nine months. However, regarding the radiographic defect fill, there was significant gain from baseline to nine months only in the PTG sites.

Conclusion: Within the limits of our study, the results of this trial indicate that reconstructive periodontal surgery with PTG offers minimal radiographic defect resolution with no significant improvements in clinical endpoints compared to open flap debridement.

Key words: Guided tissue regeneration, bone grafting, chronic periodontitis

Introduction

Periodontal disease is characterized by the presence of gingival inflammation, loss of connective tissue attachment, periodontal pocket formation and alveolar bone loss around the affected teeth (Listgarten *et al*., 1986). It results in osseous defects of various morphologic forms and the site-specific periodontal breakdown produces three types of defects: suprabony (or horizontal) defects, infrabony (or vertical) defects, and inter-radicular (or furcation) defects (Lindhe *et al*., 2008).

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The goal of periodontal therapy is to arrest the disease process, prevent disease recurrence, and regenerate the lost periodontal supporting tissues, a process which occurs as a result of the ability of cementoblasts, periodontal ligament cells and osteoblasts to regenerate multiple tissues including cementum, periodontal ligament, and bone (Froum *et al*., 2001; Hanna *et al*., 2004; Kwan *et al*., 1998).

Periodontal regeneration can be achieved by a variety of non-surgical and surgical procedures. Surgical modalities of periodontal regeneration include osseous grafts, guided tissue reconstruction, or a combination of both. Bone replacement grafts remain among the most widely used therapeutic strategies for the correction of periodontal osseous defects (Reynolds *et al*., 2003). A wide range of graft materials have been applied and evaluated

clinically, including autografts, allografts, xenografts, and synthetic/semi-synthetic materials (alloplasts) (Garett *et al.*, 1996). Autogenous and allogenic bone grafting have associated complications related to the supply of donor bone for harvesting and transmission of diseases (Mah *et al.*, 2004, Misch *et al.*, 2003). Alloplastic materials thus provide a good bone graft substitute, eliminating the need for second surgical site and the risk of disease transmission (Mah *et al.*, 2004).

One such highly biocompatible alloplastic graft material is the Porous Titanium Granules (PTG) that represents a new alternative in augmenting osseous defects. It is made of pure titanium, has about 80% porosity and a large surface area of 700 to1000 μm in diameter. The total titanium surface of the ultraporous granule is ≈2 cm^2, which offers a substantial area for blood–titanium contact (Wohlfahrt *et al.*, 2012).The titanium granules are non-resorbable, display a high initial mechanical stability; and due to their porous structure, offer the guide rails of bone reconstruction with complete particle inclusion and good long-term results at high mechanical loads (Alffram *et al.*, 2007). The osteogenic properties of titanium have been studied in experimental studies and it has been shown that it stimulates activation of the complement system (being thrombogenic), surface binding of platelets, and platelet activation as reflected by increased levels of platelet-derived growth factor, and hence activate and hasten the wound healing cascade, and promoting bone growth (Fernandes RK *et al.*, 2017, Gupta S *et al.*, 2012, Hong *et al.*, 2005, Gorbet B *et al.*, 2004, Philips SJ *et al.*, 2001, Hong *et al.*, 1999). Its earliest application was seen in orthopedics and was used for stabilization of tibia fractures and fixation of femoral stem (Thor *et al.*, 2013). There is emerging scientific evidence on the osteoconductive potential of this material regarding its use in the maxillofacial area in management of peri-implant osseous defects (Wang 2019, Verket 2018, Guler 2016, Andersen 2017, Wohlfahrt *et al.*, 2010, Wohlfahrt *et al.*, 2012), sinus augmentation (Dursun 2016, Lambert *et al.*, 2013, Bystedt *et al.*, 2009, Verket *et al.*, 2013) and in post-extraction socket preservation (Bashara *et al.*, 2012, Verket *et al.*, 2014,Tavakoli*et al.*,2012).

Recently, a study evaluated the efficacy of PTG in mandibular degree II furcation defects and their results showed no significant improvements in clinical attachment level (CAL) or recession, but they found that the material was safe to be used in close proximity to root surfaces (Wohlfahrt *et al*, 2012). Nevertheless, it is unknown whether PTG has a potential role in the reconstruction of periodontal intrabony defects, as there are no studies done till date exploring it and thus remains to be elucidated. Therefore, the aim of the present study was to investigate the efficacy of PTG in the treatment of periodontal intrabony defects and to compare with open flap debridement by analyzing the clinical and radiographic parameters.

Materials & Method

Patient and site selection

The present pilot study was designed as a 9 month, double blind, prospective clinical trial with a split-mouth design (to avoid the effect of natural variation in different individuals). Twelve systemically healthy, non-smoking subjects, who were age and sex matched (6 males and 6 females; age range: 25 to 55 years; mean age:34.7 years), undergoing periodontal therapy, Department of Periodontology, Krishnadevaraya College of Dental Sciences and Hospital, Bangalore, from April 2013 to December 2013. The recruits were selected for the study after thorough medical history and evaluation.

The inclusion criteria were presence of paired contralateral interproximal intrabony defects greater than 3 mm deep (distance from alveolar crest to base of the defect on the RVG) along with interproximal probing depth >6mm following initial therapy in vital posterior teeth. Further, teeth with gingival recession, endodontic involvement, Miller's grade II mobility and teeth demonstrating fractures were excluded.

All eligible subjects, who volunteered, were informed of the nature, potential risks and benefits of their participation in the study and a written signed informed consent was obtained from them. The ethical clearance for the study was obtained from the ethical committee of Krishnadevaraya College of Dental Sciences and Hospital, affiliated to the Rajiv Gandhi University of Health Sciences.

The study was double blind. The investigator and the patient did not know to which group they were assigned. Randomization was done by investigator (MLVP) with the flip of a coin to allocate the sites into either test or control sites. The test sites received open flap debridement (OFD) followed by grafting with PTG and the control sites received OFD alone. The total sites treated in the present study were 20, out of which 10 are control and 10 are test sites consisting of three wall defects(n= 6), two wall defects(n=3) and one wall defect(n=1) each in either groups. The intrabony defects selected were either one, two, wide three wall or combination bony defects with average defect angle of 30 degrees. The randomization and study design is illustrated in Figure 1.

Presurgical Therapy

All the patients underwent an initial phase of periodontal therapy that included oral hygiene instructions, scaling, root planning under anaesthesia and occlusal adjustments if trauma from occlusion was present. The patients were re-examined 2-4 weeks after the initial phase and a re-evaluated to confirm the suitability of the sites for the study.

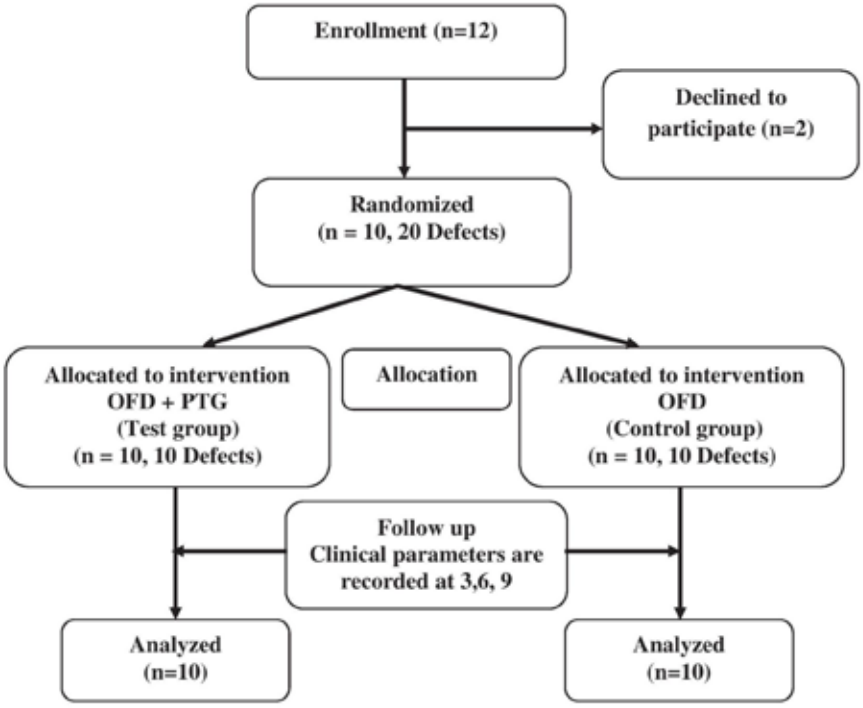

Figure 1 – ***Flow chart of Randomization and study design***

Clinical measurements

Calibration method

20 sites were examined twice for achieving intra-examiner calibration, 24 h separately before starting the study. Measurements similar to 1 mm at baseline and 24 h were included for calibration at the level of 95%.

At baseline, three month, six month and nine month visits, by a well experienced and calibrated investigator (BVK) blinded to the surgical protocol recorded all the clinical outcome variables using a University of North Carolina periodontal probe (UNC-15, Hu-Friedy, Chicago, IL, USA) and a customized acrylic stent, which was prepared on the study model of the patients.

Vertical grooves were made on the stent to guide the angulation and position of probe in the same plane every time it was inserted for recording the measurements andthe valueswere rounded to the nearest 0.5mm. The clinical parameters recorded at the different time intervals included Probing pocket depth (PPD): from the base of the pocket to the level of the gingival margin, Relative attachment level (RAL): from the base of the pocket to the lower border of the acrylic stent, Position of marginal gingiva: from the level of the gingival margin to the lower border of the acrylic stent [Gingival Recession (REC)], Plaque index (PI) (Silness *et al.*, 1964) and Bleeding on probing (BOP) (Mombelli *et al.*, 1987). The changes are illustrated in (Figure 2, 3, 4, 5, 6 and 7).

Radiographic analysis

The radiographic analysis of bone defect morphology was done by the same examiner who recorded the clinical measurements (BVK), using localised Cone Beam Computed Tomography [(CBCT), Kodak 9000] with the CS-3D imaging software with the following technical parameters: slice thickness of 0.2 mm; exposure of 90 kV, 10 mA with a scan timeof 0.018 second/slice. Further, an inbuilt algorithm was used to reduce the noise in image and scatter correction. The image slice with maximum defect depth was used to measure the presurgical and the 9 month follow-up hard tissue parameters that consisted of intrabony defect depth. Using the software, points were marked on the cemento-enamel junction (CEJ), base of the defect (BD) and the alveolar crest (AC). These points were joined to record the distance between the CEJ and the BD, of the defect associated tooth (X-ray CEJ–BD); and the distance between the CEJ and the inter-dental bone crest of the adjacent tooth (X-ray CEJ–BC). The radiographic intrabony component (X-ray INFRA) was calculated as shown in Figure 8 from (CEJ–BD)-(CEJ–BC).

Surgical procedures

All surgical procedures were performed by one trained operator (SV) who was allocated with test or control sites before surgery with concealed and opaque envelops. At the start of the procedures the patient was instructed to rinse with 0.2% chlorhexidine gluconate solution (Chlorhex Mouth Wash®, Dr Reddy lab,Hyderabad, Telangana,India) and the extra oral surfaces were swabbed with 5% povidone iodine solution. The operative site was anesthetized with 2% Lignocaine with 1:200000 adrenaline (Lignox® 2%, Kiltch Drugs India Ltd, Mumbai, India) using block and infiltration

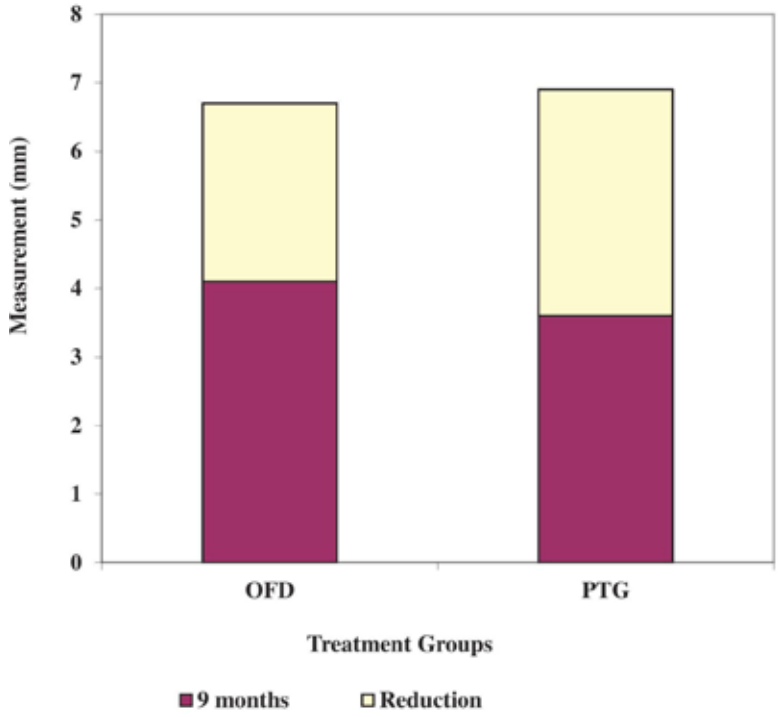

Figure 2- ***Mean Pocket Probing Depth Reduction at 9 months***

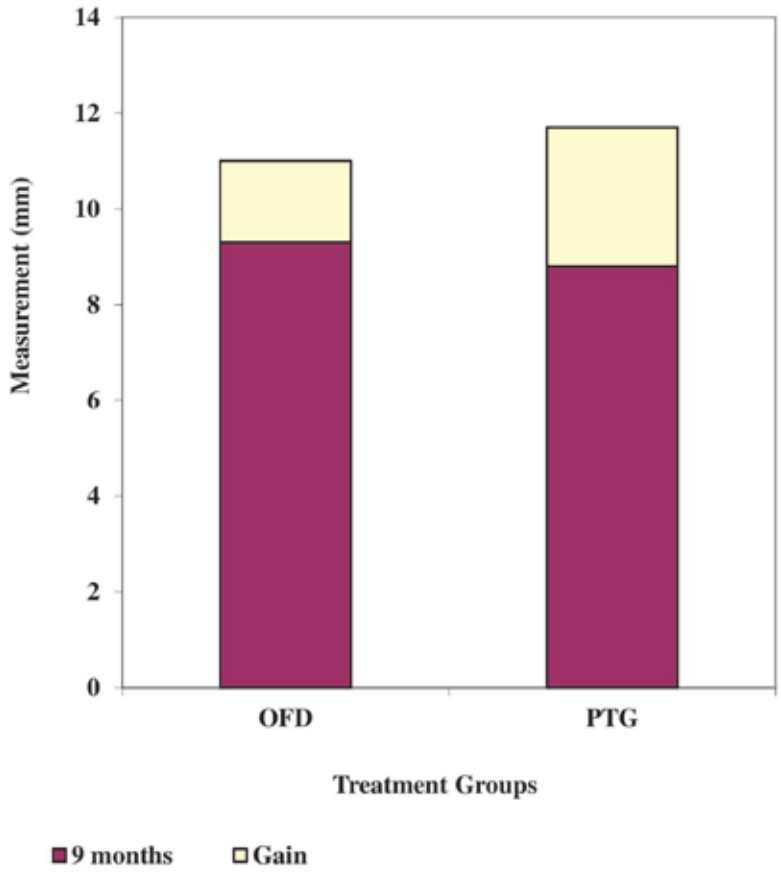

Figure 3 – ***Mean Relative Attachment Level Gain at 9 months***

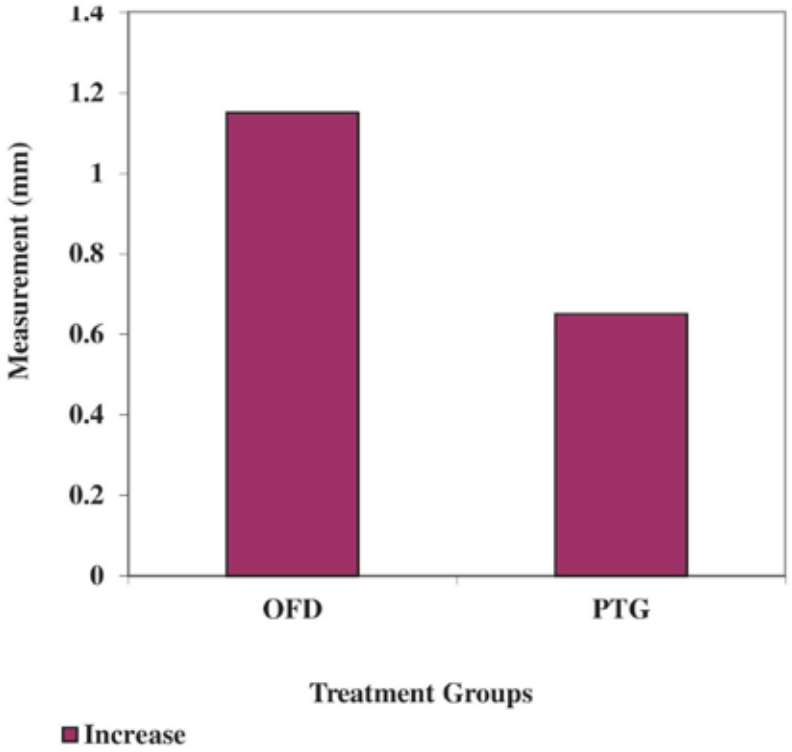

Figure 4 – ***Mean Recession Coverage increase at 9 months***

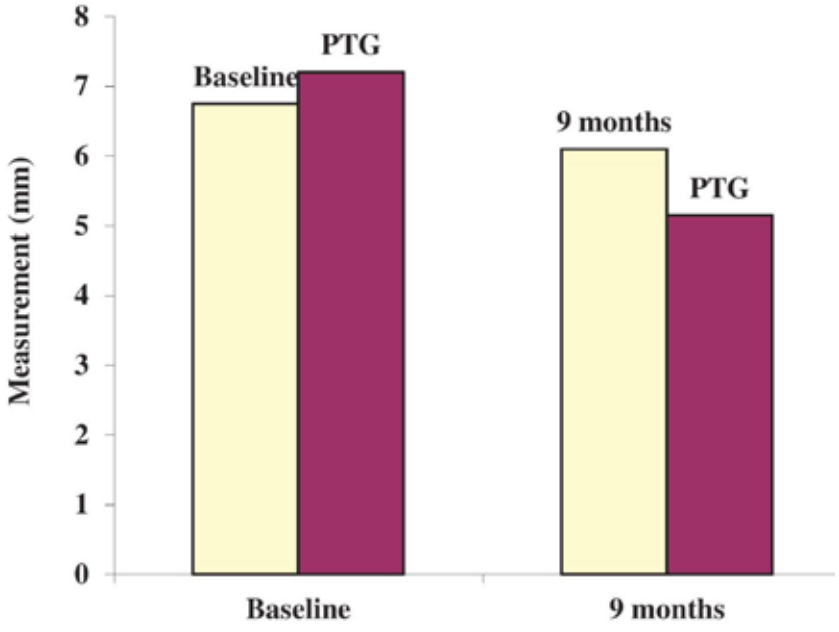

Figure 5 – ***Distance from Cemento-enamel Junction - Base of the defect***

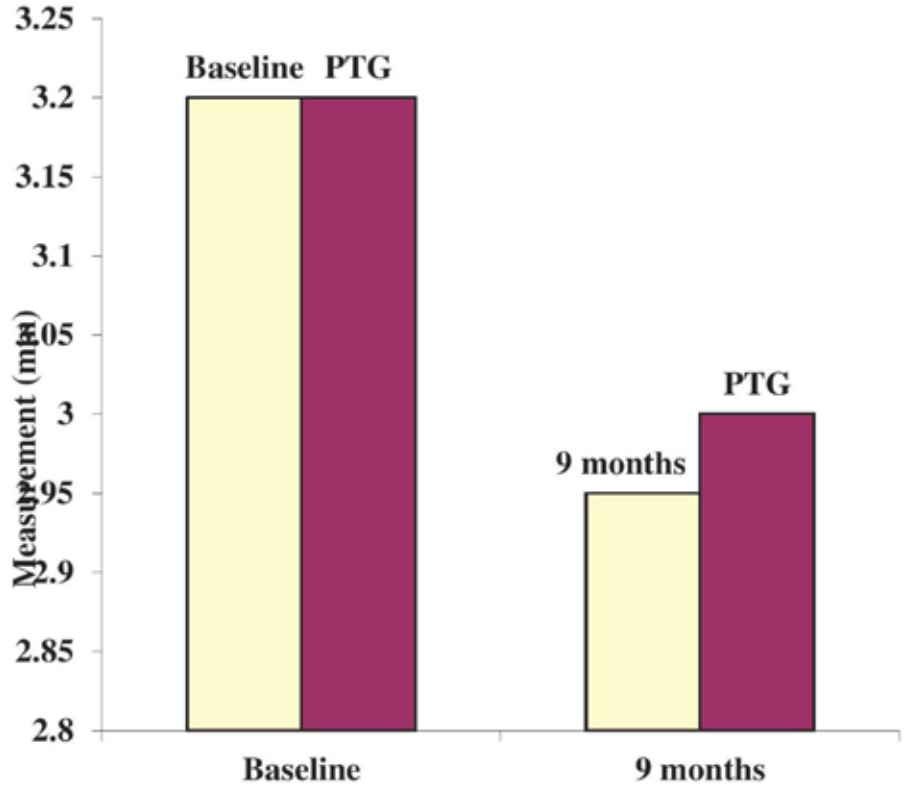

Figure 6- ***Distance from Cemento-enamel Junction – Alveolar Crest***

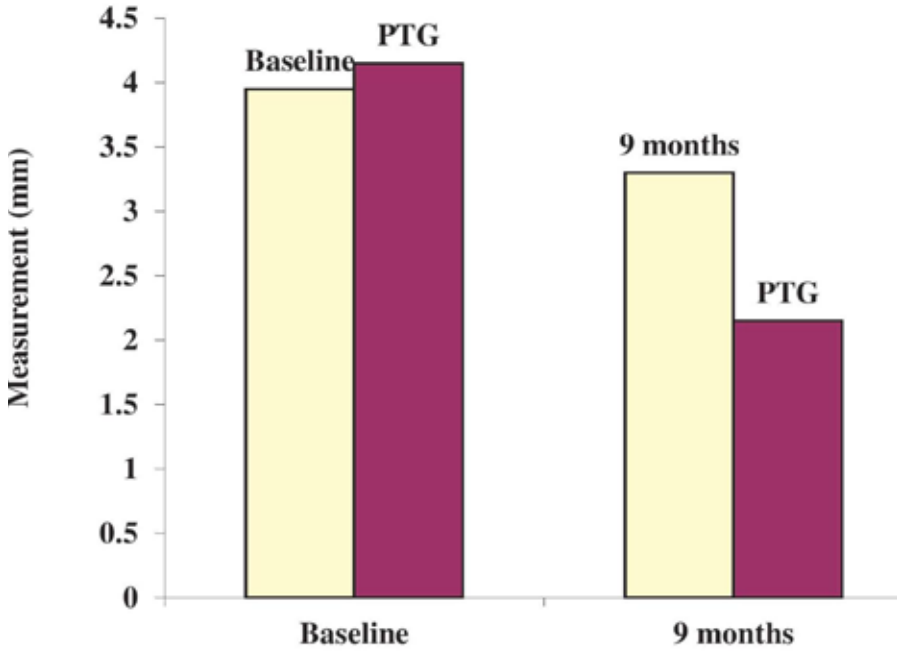

Figure 7- ***Distance from Alveolar Crest – Base of the Defect***

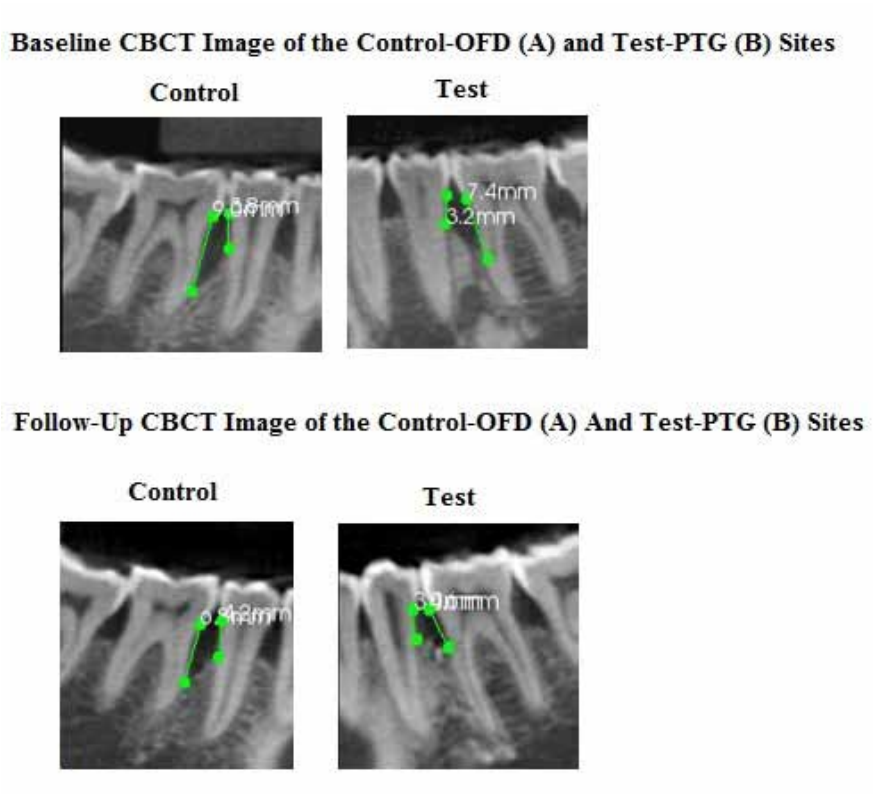

Figure 8- ***Radiographic evaluation of Periodontal Defect***

techniques. Intracrevicular incisions were made; full thickness mucoperiosteal flaps were raised buccally and lingually/palatally. The inter-dental intrasulcular incisions were placed one teeth on either side of the defect, extending one tooth on either side. The defect was thoroughly debrided, and the root surfaces were planed with curettes and ultrasonic instruments. At the test sites, following this, presuturing was done. Presuturing is the loose placement of sutures, left untied, prior to the filling of the defect reduces the possibility of displacing the graft material during the suturing process. It also simplifies the last steps of the procedure, in that once defect fill has been completed, the already placed sutures need only to be tied to complete the surgical procedure.

PTG graft material (Natix®, Tigran Technologies AB, Malmo, Sweden) which has about 80% porosity and a large surface area of 700 to1000 μm in diameter and the total titanium surface of the ultraporous granule is ≈2 cm^2. It was mixed with saline and packed into the defect gently. When they are mixed with the patient's blood or with a saline solution, the granules attach to each other due to the capillary force. The defect was not overfilled. An immediate post-operative RVG radiograph was taken to assess the defect fill by the graft. Flaps (in relation to both test and control sites) were then repositioned at the pre-surgical level to achieve primary closure and were approximated with interrupted suture technique with black braided silk (Mersilk® 3-0, 3/8, reverse cutting needle (Johnson and Johnson, Jhamnagar, Baddi, India). The surgical sites were covered with periodontal dressing (coe-pak). Post-operative instructions were given. Antibiotics every 8 hours for 1 week (Augmentin®, 625mg, GSK India, Nashik) and analgesics b.i.d for 3 days (Divon Plus® - Diclofenac (50 mg) + Paracetamol (325 mg), Micro Labs ltd, Mamning, Sikkim, India) were prescribed, as was chlorhexidine digluconate rinse (0.12%) twice daily for 3 weeks.

Post-operative care

Periodontal dressing and sutures were removed 2 weeks postoperatively and the surgical sites were gently cleansed with 0.12% chlorhexidine digluconate. Gentle brushing with a soft toothbrush was recommended thereafter. Patients were examined weekly for 1 month after surgery and then at 3, 6 and 9 months. At all the recall visits, oral hygiene maintenance was reinforced and mechanical plaque control was carried out whenever necessary.

Post-Surgical Measurements

Clinical soft tissue measurements were recorded at 3, 6 and 9 months after the surgery with previously used acrylic stents. Hard tissue evaluation was repeated with a CBCT scan 9 months following the surgery.

Statistical analyses

Data was analyzed using SPSS (Statistical Package for Social Science, Ver.10.0.5) package. To test the normality of the data the tests of normality, Kolmogorov-Smirnov and Shapiro-Wilk test were applied. The 'p' value for

the Shapiro-Wilk Test was below 0.05 and hence, the data significantly deviated from a normal distribution. Student's't' test, One-Way ANOVA test and Tukey Test were used for assessing PPD, RAL, and REC. Mann Whitney U test, Kruskal-Wallis test and Wilcoxon Sign Rank Test were used to assess PI, BOP and Radiographic hard tissue changes.

Results

Among the twelve patients initially enrolled in the study, ten patients completed the study. All the 20 treated sites showed no adverse effects in wound healing except for spillage of PTG granules. The hard tissue parameters in terms of the intrabony component of the defect [alveolar crest to base of defect (AC-BD)] showed statistically significant reduction in the test group, while the reduction in the control group was insignificant. Control sites presented with a median AC-BD of 6.75 (5.9 – 11.8) and the corresponding value for the Test group was 7.20 (6.2 – 9.6). This distance of CEJ-BD between the two groups at baseline was statistically not significant. However, the median corresponding values at 9 months were 6.10 (4.6 – 10.7) and 5.15 (3.6 – 7.3) for the Control and Test groups respectively, and this difference between the two groups showed minimal significance.

As far as the clinical soft tissue parameters were concerned, all the treated sites showed reduction in PPD, improvement in RAL, and an increase in gingival recession, PI and BOP illustrated in Table 1-3 and Figure 3. However, the differences in the values between the two treated groups were not statistically significant. In three of the cases at the time of post-operative recall visit for suture removal it was noticed that in one-two wall defect there were spillage of graft.

Discussion

The reconstruction of osseous defects caused by inflammatory periodontal disease continues to provide an ongoing challenge in periodontal therapy (Zamet *et al.*, 1997). Efforts have been undertaken for finding an ideal graft material that would aid in achieving the regenerative objective of periodontal therapy (Stahl *et al.*, 1982).

The non-resorbable, osteoconductive bone substitute, Porous Titanium Granules (PTG; Natix, Tigran Technologies AB, Malmo, Sweden) was proposed and used in the stabilization of hip prostheses and surgical treatment of peri-implant osseous defects, where it yielded favorable results suggesting its safety in regenerative procedures (Alffram *et al.*, 2007, Wohlfahrt *et al.*, 2010 , Wohlfahrt *et al.*, 2012).

This novel graft PTG, comprises of a titanium surface which being highly thrombogenic, stimulates the activation of the complement system, helps in platelet agglutination and activation leading to bio-availability of platelet-derived growth factor. These granules are irregular in shape, with interconnected porosity of about 80%, which enhances surface area-to-volume ratio, cell viability and proliferation rate. Further, this structure imitates properties of human bone and bovine bone like Geistlich Bio-Oss, thereby creating a scaffold for bone generation that stimulates osteoblast colonization and osseointegration (Sabetrasekh *et al.*,2011).

In addition, these granules are non-resorbable which helps in keeping their volume during the entire healing period, ensuring mechanical stability and a desired aesthetic result. Lastly, the granules are radiopaque, making them clearly visible on radiographs and they do not set (i.e., no risk of heat injury to the bone) and can therefore be handled without time pressure during surgery (Rompen *et al.*, 1999).

Till date, no clinical trials are available testing the efficacy of PTG in the treatment of human vertical periodontal osseous defects. Therefore, a double blind, prospective, clinical trial which is a first of its kind, was conducted to determine the efficacy of PTG vs OFD in periodontal intrabony defects.

For the study, 20 sites in Ten patients having Stage III, Grade A periodontitis (2017 World Workshop), were selected. The study was of a split-mouth design to avoid the effect of natural variation in different individuals. The defects selected were either one, two, wide three wall or combination bony defects.

The results of our study showed that PTG is biocompatible as the post-surgical healing was uneventful, as evidenced by the absence of clinical inflammation, infection, and swelling during the healing phase, suggesting its safety next to the root surface. When the intergroup comparison was done between the PTG and OFD treated sites, the results indicated that there was little improvement in clinical parameters in the PTG sites when compared to the OFD sites and it was neither statistically significant. However, regarding the radiographic bone fill, there was a minimal significant improvement, in the PTG sites compared to OFD sites. These findings are similar to studies reported in the past with other graft materials, by many authors (Zamet *et al.*, 1997, Brown *et al.*, 1998, Krejci *et al.*, 1987,Rabalais *et al.*, 1981, Yukna*et al.*, 1998, Yukna*et al.*, 1985, Meffert*et al.*, 1985, Shirakata *et al.*, 2008, Yukna *et al.*, 1990). Further, a recent pilot study that evaluated the use of PTG in furcation defects also showed non-significant reduction of attachment levels after a 1 year follow-up period; however, the PPD reduction and radiographic bone gain were statistically significant (Wohlfahrt*et al.*, 2012). It would be noteworthy that the previous studies that used PTG as a graft material were in defect types that were secluded from the oral environment, without the presence of periodontal pathogens and in non-stress bearing areas (Alffram*et al.*, 2007, Wohlfahrt *et al.*, 2010, Lambert *et al.*, 2013 and Verk *et al.,* 2013).

Table 1. Inter and Intragroup comparison of PPD, RAL and REC at different recall intervals for PTG and OFD sites.

Variable		Difference between OFD and PTG							(3 months - 6 months)		(3 months - 9 months)		(6 months - 9 months)	
		Baseline (mm)	'P' value	3 months (mm)	'P' value	6 months (mm)	'P' value	9 months (mm)	'P' value	Mean Difference± SD	'P' value	Mean Difference± SD	'P' value	Mean Difference± SD	'P' value
PPD	*Control (OFG)*	0.20	0.759	0.30	0.596	0.45	0.348	0.50	0.269	0.90 ± 0.56	0.42	1.35 ± 0.55	0.114	0.45 ± 0.50	0.867
	Test (PTG)									1.65 ± 0.46	0.007*	2.15 ± 0.45	<0.001*	0.5 ± 0.40	0.718
RAL	*Control*	0.70	0.256	0.90	0.109	0.15	0.762	0.50	0.343	0.75 ± 0.50	0.489	1.0 ± 0.51	0.243	0.25 ± 0.46	0.964
	Test									1.5 ± 0.51	0.043*	2.4 ± 0.53	0.001*	0.90 ± 0.53	0.363
REC	*Control*	0.35	0.403	0.15	0.739	0.35	0.397	0.15	0.694	-0.40 ± 0.38	0.756	-0.60 ± 0.38	0.457	-0.20 ± 0.42	0.960
	Test									-0.60 ± 0.46	0.473	-0.30 ± 0.44	0.885	0.30 ± 0.36	0.885

From the outcome of our study, it could be interpreted that PTG sites when compared to the OFD sites, did not show promising results as against the initial claims and expectations. The radiographic bone gain did not reflect on the improvements in the clinical parameters, which could be attributed to several reasons. First, there were incidences of minor to substantial graft exfoliation, specifically in few sites with wider non-contained defects; as it was evident in the follow-up radiograph, which could have lowered the mean defect fill. Second, there were no complete fill of the graft at the apical portion of the defect, probably due to larger graft particle size. Third, defect characteristics were not standardized which is an important deciding factor in the success or failure of the graft material, as maximum contact between the bone and graft material must be achieved (Tsitoura *et al.*, 2004, Reddy *et al.*, 1999, Reynolds *et al.*, 1996, Cortellini *et al.*,2005). Due to its radiopacity, meaningful assessments and outcomes were significantly limited. Fourth, the relatively smaller sample size could have affected the statistical significance of the results; had the sample size been larger, the difference could have been significant. Fifth, residual PTG and bonelike radiopaque tissue that were indistinguishable from native bone would have been considered as the new bone. Sixth, in the evaluation of the radiographic bone fill, the coronal extent of the radio-opaque mass was considered and taken as the reference point (whereas this point may not necessarily coincide with the point of recording the clinical parameters) could have possibly led to the discrepancy in the clinical and radiographic values.

However, while interpreting the results of our study, caution has to be exercised, owing to certain limitations that could have affected the outcome. First, non-standardization of the defect characteristics could have interfered with the regenerative ability of the treatment strategy, and the results obtained may not be a true interpretation of the efficacy of PTG. Second, the clinical parameters of PPD and RAL were measured only at the buccal interproximal sites of the defect area in question and the changes obtained at that particular site could not be correlated with the radiographic parameters.

Thus, to further improve the assessment of the regenerative ability of PTG, future studies should be performed with a larger sample size, with age and gender matched subjects, and a standardized defect morphology. In cases where reconstruction is attempted in non-contained defects, use of a membrane would prevent graft exfoliation, thereby improving the treatment outcome. Finally, studies with histologic evaluation of the PTG treated sites would provide a better clue to the regenerative ability of this novel graft material.

Table 2 - Comparison of Median values of Clinical and Radiographic parameters at different recall visits for PTG and OFD sites.

Parameter Type	Variable		Median in mm (min – max)				'P' value within group	'P' value between groups			
			Baseline	3 months	6 months	9 months		Baseline	3 months	6 months	9 months
Radiographic Parameter	**CEJ - BD**	*Control (OFD)*	6.75 (5.9 – 11.8)	NA	NA	6.10 (4.6 – 10.7)	0.150	0.343	NA	NA	0.034*
		Test (PTG)	7.20 (6.2 – 9.6)	NA	NA	5.15 (3.6 – 7.3)	0.001*				
	CEJ - AC	*Control (OFD)*	3.20 (2.2 – 7.6)	NA	NA	2.95 (2.4 – 7.3)	0.197	0.849	NA	NA	0.704
		Test (PTG)	3.20 (2.4 – 5.5)	NA	NA	3.0 (2.2 – 4.8)	0.595				
	AC - BD	*Control (OFD)*	3.95 (1.8 – 5.2)	NA	NA	3.3 (2.0 – 4.0)	0.306	0.495	NA	NA	0.006*
		Test (PTG)	4.15 (2.5 – 5.5)	NA	NA	2.15 (0.4 – 3.5)	0.001*				
Clinical parameter	**PI**	*Control (OFD)*	0.50 (0.0 - 1.0)	2.0 (1.0 - 2.0)	1. 0 (1.0 - 2.0)	1. 0 (1.0 - 2.0)	< 0.001*	0.661	0.065	0.967	0.333
		Test (PTG)	0.0 (0.0 - 1.0)	1. 0 (1.0 - 2.0)	1.25 (0.0 - 2.0)	1.50 (0.0 - 2.0)	0.004*				
	BOP	*Control (OFD)*	1.0 (0.0 – 1.0)	2.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)	0.001*	0.383	0.028*	0.468	0.615
		Test (PTG)	0.0 (0.0 – 1.0)	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)	1.0 (1.0 – 2.0)	0.001*				

CEJ-BD= Distance from CEJ to Base of Defect, CEJ-AC= Distance from CEJ to Alveolar crest, AC – BD= Distance from Alveolar crest to Base of Defect, PI=Plaque Index, BOP= Bleeding on Probing, *=Statistically Significant

Table 3: Intragroup comparison of PPD, RAL and REC at different recall intervals for PTG and OFD sites.

Variable		Baseline	3 months	6 months	9 months	(Base line – 3 months)		(Base line – 6 months)		(Base line – 9 months)	
		(mm)	(mm)	(mm)	(mm)	Mean Difference ±SD	'P' value	Mean Difference ±SD	'P' value	Mean Difference ±SD	'P' value
PPD	*Control (OFD)*	6.70 ±1.6	5.45 ± 1.3	4.55 ± 1.2	4.10 ± 1.1	1.25 ± 0.65	0.16	2.15 ± 0.62	0.004*	2.60 ± 0.60	< 0.001*
	Test (PTG)	6.90 ± 1.3	5.75 ± 1.1	4.10 ± 0.9	3.60 ± 0.8	1.15 ± 0.54	0.09	2.8 ± 0.5	<0.001*	3.30 ± 0.49	< 0.001*
RAL	*Control*	11.0 ± 1.3	10.30 ± 1.3	9.55 ± 1.0	9.30 ± 1.1	0.7 ± 0.58	0.55	1.45 ± 0.53	0.04*	1.70 ± 0.54	0.013*
	Test	11.70 ± 1.3	11.20 ± 1.1	9.70 ± 1.2	8.80 ± 1.2	0.5 ± 0.55	0.79	2.00 ± 0.56	0.004*	2.90 ± 0.57	<0.001*
REC	*Control*	4.40 ± 0.97	4.95 ± 0.7	5.35 ± 0.9	5.55 ± 0.9	- 0.55 ± 0.39	0.53	- 0.95 ± 0.42	0.75	-1.15 ± 0.42	0.035*
	Test	4.75 ± 0.8	5.10 ± 1.2	5.70 ± 0.9	5.40 ± 0.7	- 0.35 ± 0.46	0.83	- 0.95 ± 0.38	0.11	-0.65 ± 0.35	0.403

SD= Standard Deviation, *= Statistically Significant

Conclusion

Within the limits of our study, the results of this trial indicate that reconstructive periodontal surgery with PTG offers minimal radiographic defect resolution with no significant improvements in clinical endpoints compared to OFD.

References

Alffram PA, Bruce L, Bjursten LM, Urban RM and Andersson GB. Implantation of the femoral stem into a bed of titanium granules using vibration: A pilot study of a new method for prosthetic fixation in 5 patients followed for up to 15 years. *Upsala Journal of Medical Sciences* 2007; **112**:183-189.

Andersen H, Aass MA and Wohlfahrt CJ. Porus titanium granules in the treatment of peri-implant osseous defects – a 7 year follow up study. *International Journal of Implant Dentistry* 2017; **3**:50.

Armitage GC. Periodontal diseases: Diagnosis. *American Academy of Periodontology* 1996; **1**:37-215.

Brown GD, Mealey BL, Nummikoski PV, Bifano SL and Waldrop TC. Hydroxyapatite cement implant for regeneration of periodontal osseous defects in humans. *Journal of Periodontology* 1998; **69**:146-157.

Bystedt H and Rasmusson L. Porous titanium granules used as osteoconductive material for sinus floor augmentation: a clinical pilot study. *Clinical Implant Denistry and Related Resarch* 2009; **11**:101-105.

Bashara H, Wohlfahrt JC, Polyzois I, Lyngstadaas SP, Renvert S, Claffey N, *et al.* The effect of permanent grafting materials on the preservation of the buccal bone plate after tooth extraction: an experimental study in the dog. *Clinical Oral Implants Resarch* 2012; **23**:911-917.

Cortellini P and Tonetti MS. Clinical performance of regenerative strategy for intrabony defect: Scientific evidence and clinical experience. *Journal of Periodontology* 2005; **76**:341-350.

Dursun KC, Dursun E, Eratalay K, Orhan K, Tatar I, Baris E *et al.* Effect of Porus titanium granules on bone regeneration and primary stability in maxillary sinus: A human clinical, histomorphometric and microcomputed tomography analyses. *The Journal of Carniofacial Surgery* 2016; **27**:391-397.

Fernandes RK, Zhang Y, Magri PMA, Renno MCA and van den Beucken PJJJ. Biomaterial property effects on platelets and macrophages: An *in vitro* study. *ACS Biomaterials Science & Engineering* 2017; **3**:3318-3327.

Furhmann RAW, Bucker A and Diedrich PR. Furcation involvement: comparison of dental radiographs and HR-CT slices in human specimens. *Journal of Periodontal Resarch* 1997; **32**:409-418.

Froum SJ, Weinberg MA, Rosenberg E and Tarnow D. A comparative study utilizing open flap debridement with and without enamel matrix derivative in the treatment of periodontal intrabony defects: a 12-month re-entry study. *Journal of Periodontology* 2001; **72**:25-34.

Garrett S. Periodontal regeneration around natural teeth. *American Academy of Periodontology* 1996; **1**:621-666.

Gorbet BM, Sefton VM. Biomaterial-associated thrombosis: roles of coagulation factors, complement, platelets and leukocytes. *Biomaterials* 2004; **25**: 5681-5703.

Guler B, Uraz A, Yalm M and Bozkaya S. The comparison of Porus Titanium Granule and Xenograft in the surgical treatment of peri-implantitis: A prospective clinical study. *Clinical Implant Dentistry and Related Research* 2016; **0**:1-12.

Gupta S, Reviakine I. Platelet activation profiles on TiO2: Effect of Ca2+ binding to the surface. *Biointerphases* 2012; **7**:28.

Hanna R, Trejo PM and Weltman RL. Treatment of intrabony defects with bovine-derived xenograft alone and in combination with platelet-rich plasma: a randomized clinical trial. *Journal of Periodontology* 2004; **75**:1668-1677.

Hong J, Azens A, Ekdahl KN, Granqvist CG and Nilsson B. Material-specific thrombin generation following contact between metal surfaces and whole blood. *Biomaterials* 2005; **26**:1397-1403.

Hong J, Andersson J, Ekdahl KN, Elgue G, Axen N, Larsson R, *et al.* Titanium is a highly thrombogenic biomaterial: possible implications for osteogenesis. *Thrombosis Haemostasis* 1999; **82**:58-64.

Jeffcoat M. Radiographic Methods for the Detection of Progressive Alveolar Bone Loss. *Journal of Periodontology* 1992; **63**:367-372.

Kwan SK, Lekovic V, Camargo PM, Klokkevold PR, Kenney EB, Nedic M, *et al.* The use of autogenous periosteal grafts as barriers for the treatment of intrabony defects in humans. *Journal of Periodontology* 1998; **69**:1203-1209.

Lambert F, Lecloux G, Léonard A, Sourice S, Layrolle P, Rompen E, *et al.* Bone regeneration using porous titanium particles versus bovine hydroxyapatite: a sinus lift study in rabbits. *Clinic Implant Dentistry and Related Resarch* 2013; **15**:412-426.

Listgarten M. Pathogenesis of periodontitis. *Journal of Clinical Periodontology* 1986; **13**:418-430.

Mah J, Hung J, Wang J andSalih E. The efficacy of various alloplastic bone grafts on the healing of rat calvarial defects. *European Jounal of Orthodontics* 2004; **26**:475-482.

Misch CE and Dietsh F. Bone-grafting materials in implant dentistry. *Implant Dentistry* 1993; 2:158-167.

Mombelli A, van Oosten MA, Schurch E Jr and Land NP. The microbiota associated with successful or failing osseointegrated titanium implants. *Oral Microbiology and Immunology* 1987; **2**:145-151.

Masters LB, Mellonig JT, Brunsvold MA andNummikoski PV.A clinical evaluation of demineralized freeze-dried bone allograft in combination with tetracycline in the treatment of periodontal osseous defects. *Journal of Periodontology* 1996; **67**:770-781.

N.Ahmed, T Mahmud, S.Shafik andR.Dibany.Titanium granules and nanocrystalline hydroxyapatite in healing of mandibular defects in dogs. *Australian Dental Journal* 2015; **40**:126-132

Philips SJ. Thrombogenic influence of biomaterials in patients with omni series heart valve: pyrolytic carbon versus titanium. *ASAIO Journal* 2001; **47**:429-431.

Rabalais ML Jr, Yukna RA and Mayer ET. Evaluation of durapatite ceramic as an alloplastic implant in periodontal osseous defects. I. Initial six-month results. *Journal of Periodontology* 1981; **52**:680-689.

Rompen EH, Biewer R, Vanheusden A, Zahedi S and-Nusgens B. The influence of cortical perforations and of space filling with peripheral blood on the kinetics of guided bone generation. A comparative histometric study in the rat. *Clinical Oral Implants Research* 1999; **10**:85–94.

Reddy MS and Jeffcoat MK. Methods of assessing periodontal regeneration. *Periodontology 2000* 1999; **19**:87-103.

Reynolds MA and Bowers GM. Periodontal regeneration following surgical treatment. *Current Opinion in Periodontology* 1996; **3**:126-139.

Reynolds MA, Aichelmann-Reidy ME, Branch-Mays GL and Gunsolley JC. The efficacy of bone replacement grafts in the treatment of periodontal osseous defects. A systematic review. *American Academy of Periodontology* 2003; **8**:227-265.

Stahl SS, Froum SJ and Kushner L. Periodontal healing following open debridement flap procedures. II. Histologic observations. *Journal of Periodontology* 1982; **53**:15-21.

Shirakata Y, Setoguchi T, Machigashira M, Matsuyama T, Furuichi Y, Hasegawa K, *et al.* Comparison of injectable calcium phosphate bone cement grafting and open flap debridement in periodontal intrabony defects: a randomized clinical trial. *Journal of Periodontology* 2008; **79**:25-32.

Sabetrasekh R, Tiainen H, Lyngstadaas SP, Reseland J and Haugen H.A novel ultra-porous titanium dioxide ceramic with excellent biocompatibility. *Journal of Biomaterials Applications* 2011; **25**:559-580.

Silness J and Loe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. *Acta Odontologica Scandinavica* 1964; **22**:121-135.

Thor A. Porous Titanium Granules and Blood for Bone Regeneration around Dental Implants: Report of Four Cases and Review of the Literature. *Case Report in Dentistry* 2013; **2013**:410515.

Tavakoli M, Moghareabed A, Farsam T, Abbas FM, Badrian H, Khalighinejad N, *et al.* Evaluation of dental socket healing after using of porous titanium granules: Histologic and histomorphometric assessment in dogs. *Dental Resarch Journal* 2012; **9**:600-606.

Tsitoura E, Tucker R, Suvan J, Laurell L, Cortellini P, Tonetti M, *et al.* Baseline radiographic defect angle of the intrabony defect as a prognostic indicator in regenerative periodontal surgery with enamel matrix derivative. *Journal of Clinical Periodontology* 2004; **31**:643–647.

Vandenberghe B, Jacobs R and Yang J. Detection of periodontal bone loss using digital intraoral and cone beam computed tomography images: an *in vitro* assessment of bony and/or infrabony defects. *Dentomaxillofacial Radiology* 2008; **37**:252-260.

Verket A, Lyngstadaas SP, Rønold HJ and Wohlfahrt JC. Osseointegration of dental implants in extraction sockets preserved with porous titanium granules - an experimental study. *Clinical Oral Implants Resarch* 2014; **25**:100-108.

Verket A, Lyngstadaas SP, Rasmusson L, Haanæs HR, Wallström M, Wall G, *et al.* Maxillary sinus augmentation with porous titanium granules: a microcomputed tomography and histologic evaluation of human biopsy specimens. *International Journal of Oral and Maxillofacial Implants* 2013; **28**:721-728.

Verket A, SP Lyngstadaas, H Tiainen, HJ Ronold, JC Wohlfahrt. Impact of particulate deproteinized bovine bone mineral and porus titanium granules on early stability and osseointegration of dental implants in narrow marginal circumferential bone defects. *International Journal of Maxillofacial Surgery* 2018; 47:1086-1094.

Wang H, Su K, Su L, Liang P, Ji P and Wang C. Comparison of 3D printed porous tantalum and titanium scaffolds on osteointegration and osteogenesis. *Material Science & Engineering C* 2019; **104**:109908.

Wohlfahrt JC, Lyngstadaas SP, Heijl L and Aass AM. Porous titanium granules in the treatment of mandibular Class II furcation defects: a consecutive case series. *Journal of Periodontology* 2012; **83**:61-69.

Wohlfahrt JC, Monjo M, Rønold HJ, Aass AM, Ellingsen JE, Lyngstadaas SP, *et al.* Porous titanium granules promote bone healing and growth in rabbit tibia peri-implant osseous defects. *Clinical Oral Implants Resarch* 2010; **21**:165-173.

Wohlfahrt JC, Lyngstadaas SP, Rønold HJ, Saxegaard E, Ellingsen JE, Karlsson S, *et al.* Porous titanium granules in the surgical treatment of peri-implant osseous defects: a randomized clinical trial. *International Journal of Oral and Maxillofacial Implants* 2012; **27**:401-410.

Young SJ, Chaibi MS, Graves DT, Majzoub Z, Boustany F, Cochran D, *et al.* Quantitative Analysis of Periodontal Defects in a Skull Model by Subtraction Radiography Using a Digital Imaging Device. *Journal of Periodontology* 1996; **67**:763-769.

Yukna RA, Callan DP, Krauser JT, Evans GH, Aichelmann-Reidy ME, Moore K, *et al.* Multi-center clinical evaluation of combination anorganic bovine-derived hydroxyapatite matrix (ABM)/cell binding peptide (P-15) as a bone replacement graft material in human periodontal osseous defects. 6-month results. *Journal of Periodontology* 1998; **69**:655-663.

Yukna RA, Harrison BG, Caudill RF, Evans GH, Mayer ET, Miller S, *et al.* Evaluation of durapatite ceramic as an alloplastic implant in periodontal osseous defects.II. Twelve month reentry results. *Journal of Periodontology* 1985; **56**:540-547.

Zamet JS, Darbar UR, Griffiths GS, Bulman JS, Brägger U, Bürgin W, *et al.* Particulate bioglass as a grafting material in the treatment of periodontal intrabony defects. *Journal of Clinical Periodontology* 1997; **24**:410-418.