

Evaluation of polycaprolactone scaffold for guided bone regeneration in maxillary and mandibular defects: A clinical study

ABSTRACT

Objective: This study was carried out to assess bone regeneration following the use of polycaprolactone (PCL) scaffold in maxillary and mandibular osseous defects.

Materials and Methods: This prospective study included ten patients with maxillary or mandibular osseous defects present due to enucleation of periapical cysts or alveolar clefts requiring bone grafting and for lateral ridge augmentation that were treated with PCL scaffold. The patients were assessed clinically for pain, swelling, infection, and graft exposure at 1 week, 3rd, and 5th month postoperatively and were also evaluated radiographically for bone fill using intraoral periapical and/or panoramic radiographs at 4th, 6th, and 9th month postoperatively.

Results: PCL scaffold was used in a total of six alveolar clefts and three cases of periapical cysts and one case of lateral ridge augmentation. Nine out of ten cases demonstrated wound dehiscence and scaffold exposure in the oral cavity. Radiographically, on comparison to the control regions, all these nine cases failed to demonstrate appreciable bone density gain. Only one case of radicular cyst in the mandible was recorded to have satisfactory healing.

Conclusion: Although PCL scaffold has the potential for bone regeneration in osseous defects, the scaffold exhibited marked tendency for dehiscence in intraoral defects that significantly affected bone healing. A long-term study designed with a larger sample size and categorization of the defects is required to assess its efficacy in varied defects. Moreover, comparative evaluation of PCL and autogenous or alloplastic bone grafting material could provide assenting results.

Keywords: Alveolar bone grafting, bone tissue engineering, polycaprolactone scaffold, radicular cyst, ridge augmentation, scaffolds in oral surgery

INTRODUCTION

Reconstruction of bone defects poses a functional and an esthetic challenge to maxillofacial and reconstructive surgeons. It requires extensive surgical intervention involving the use of bone grafting techniques and other procedures in which healing is often unpredictable. Multitudes of bone graft materials have been used in pursuit of gaining maximum quantitative and qualitative bone fill. Most of the traditional reconstructive methods available are rather invasive and associated with certain amount of morbidity. Hence, the impetus for this study was to use a material that obviates donor site morbidity while gaining clinically and radiographically demonstrable bone fill.

Traditionally, the augmentation of bony defects is carried out using autogenous bone, allografts, alloplasts, and xenografts.

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The shortcomings of these conventional bone graft materials have led scientists to work on biomaterials in pursuit of “ideal” bone graft substitute. A scaffold is a three-dimensional construct that provides the necessary support for cells to proliferate and maintain their differentiated function, and its architecture defines the ultimate shape of the new bone or cartilage.^[1] Polycaprolactone (PCL) is one of the earliest polymers synthesized in the early 1930s, that became commercially available following efforts to identify synthetic polymers that could be degraded by microorganisms.^[2,3] This study assesses the ability of PCL biodegradable scaffold to regenerate bone in maxillary and mandibular defects.

MATERIALS AND METHODS

After obtaining clearance from the Institutional Ethics Committee, this study was carried out on patients who visited the Department of Oral and Maxillofacial Surgery in our institution. A written consent was obtained from each patient in the study for undergoing the surgery and for use of documented data for publication and/or presentation purpose.

Material used

The material used was PCL scaffold Scaffold Osteoplug™ (Osteopore International Pvt. Ltd., Singapore).

Study design

This prospective study was carried out on ten patients. Patients requiring bone grafting following enucleation of odontogenic cysts and cleft patients requiring alveolar bone grafting and those requiring ridge augmentation were chosen for the study. Patients with existing comorbidities such as those with immunocompromised diseases, endocrine or metabolic disorders, patients who have undergone radiation therapy, those with preexisting local/systemic infections, and smokers were excluded from the study. All patients were informed about the study, and a written consent was obtained for the same. Routine hematological investigations were carried out. Preoperative intraoral periapical view and/or panoramic radiographs (orthopantomogram) of recipient sites were obtained.

Postoperatively, patients were examined clinically for pain, swelling, infection, and scaffold exposure at 1 week, 3 months, and 5 months after the placement of the scaffold. Intraoral periapical view and/or panoramic radiographs (orthopantomogram) of the recipient sites were assessed at 4th, 6th, and 9th month postoperatively. The radiographs were assessed for bone density using a gray value histogram.^[4]

PCL scaffold (Osteoplug™) was shaped according to the size and shape of the defect. The scaffold was placed in the defect

and if necessary, it was stabilized using resorbable suture. Mucoperiosteal flaps were mobilized to ensure periosteal coverage over the scaffold and tension-free closure was achieved. The closure was done using 4-0 polyglactin 910 (Vicryl™) or 3-0 Silk (Mersilk™).

Radiographic evaluation of bone density

Intraoral periapical radiographic imaging was performed by long cone/extension cone paralleling technique using a Rinn positioning device (Dentsply, USA) and Kodak RVG 6100 CMOS sensor (Eastman Kodak, Rochester, NY, USA) using identical exposure settings. Orthopantomogram was made using Kodak 8000C Digital Panoramic and Cephalometric System (Carestream Health, Inc. NY). A single examiner, who was neither involved in the surgery nor in the preoperative and postoperative examination, demarcated the outline of the lesion and the gray value was recorded [Figure 1]. The gray value (radiopacity) of the adjacent sound bone was used as a control group for comparison. The control regions from radiographs taken at different times were matched, and the mean gray-level values of the regions of interests were calculated and then compared with each other.

Statistical analysis

To test the equality of means for the five groups with respect to gray values of bone density, the Kruskal–Wallis test was carried out at 5% level of significance. To find medians of which group differ significantly, the Mann–Whitney U test is performed. For intergroup comparison between preoperative values, 4th month, 6th month, 9th month postoperative values and control values, Wilcoxon matched pair and signed-rank test was used. In all the above tests, $P < 0.05$ was taken to be statistically significant. The data were analyzed using GraphPad InStat® (GraphPad Software, Inc. La Jolla, CA, USA).

RESULTS

In the present study, the PCL scaffold was used in ten patients with maxillary or mandibular osseous defects. These include six cases of unilateral cleft alveolus patients who required secondary alveolar bone grafting (Case # 1, 3, 4, 6, 9, and 10) [Figure 2]; one case of lateral ridge augmentation in the maxillary anterior region (Case # 2); and three cases of radicular cysts which include two radicular cysts in the maxillary anterior region (Case # 5 and 7) [Figure 3] and one in the mandibular posterior region (Case # 8).

Patients were in the age group of 6–37 years with six males and four females. All patients were assessed clinically and radiologically. Clinically, none of the patients presented with any significant pain, swelling, or infection; however, nine

patients showed scaffold exposure intraorally [Table 1]. The radiographic changes in bone density were evaluated using gray value histogram [Table 2]. All cases except case 8 showed that the gray value of the operated site failed to approach gray value of the control region.

Wound dehiscence was noted as early as 4th week in one case (case 3). Attempts were made to close dehiscence in all cases; however, repetitive exposure of scaffold was seen which necessitated second surgery and removal of scaffold at 9th postoperative month in five cases. Removed scaffolds were also sent for histopathological examination which revealed no evidence of bone formation.

DISCUSSION

PCL scaffold is a synthetic polymer which can be used for guided bone regeneration. The solubility of PCL, its low melting point (59°C–64°C), and exceptional blend compatibility has stimulated extensive research into its potential application in the biomedical field.^[5-7] Some of its biomedical application includes its use as sutures (Monocryl™), wound dressings, contraceptive devices, root canal filling material in dentistry, and most importantly as scaffolds for tissue engineering.^[8-12] The degradation of PCL has been studied extensively with variable outcomes. Lam *et al.*^[13] studied the comparison of the degradation of PCL and PCL-tricalcium phosphate (PCL-TCP). They concluded that the incorporation of calcium phosphate significantly increases the degradation rate. Yeo *et al.*^[14] studied degradation profile of a PCL TCP scaffold and reported that at 24 weeks, the scaffold demonstrated significant degradation (molecular weight

loss of up to 60%), while maintaining mechanical properties which are comparable to human cancellous bone.. This slow degradation is extremely useful for its application in drug delivery or for the release of signaling molecules in tissue engineering; however, it can often be counterproductive

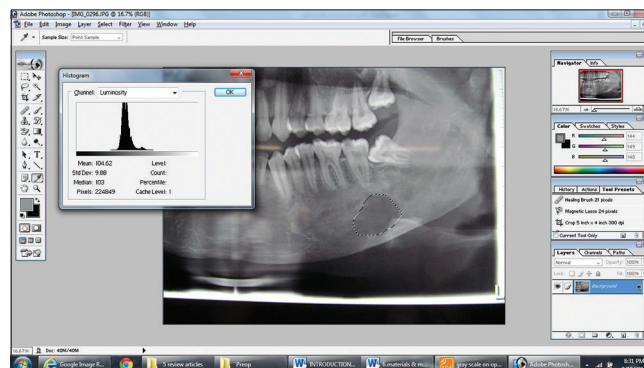


Figure 1: Radiographic evaluation of bone density

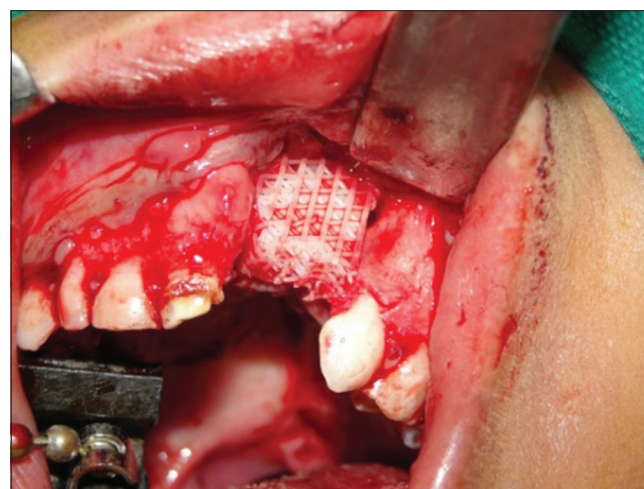


Figure 2: Polycaprolactone scaffold in an alveolar cleft

Table 1: Clinical evaluation at 1st week, 3rd and 5th month postoperatively after the placement of grafts

Parameters	Outcome	7th day postoperatively	3rd month postoperatively	5th month postoperatively after the placement of implant
Pain	No	10	10	10
	Yes	0	0	0
Swelling	No	9	10	10
	Yes	1	0	0
Infection (Pus discharge)	No	10	10	10
	Yes	0	0	0
Scaffold exposure	No	10	3	1
	Yes	0	7	9

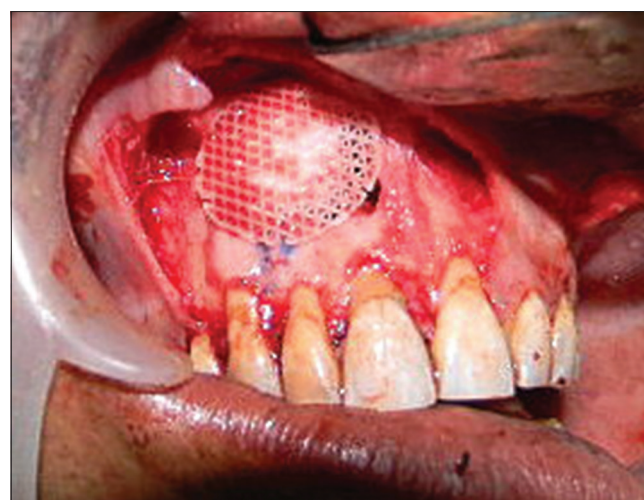


Figure 3: Polycaprolactone scaffold secured over the bony window of cystic cavity

Table 2: Assessment of bone density according to gray value histogram

Cases	Pre-operative (Test site)	4 th month Post-operative	6 th month Post-operative	9 th month Post-operative	Control
1.	62.8	62.8	73.6	64.2	101.23
2.	53.8	53.8	49.62	70.31	97.35
3.	64.0	64.0	75.25	70.21	86.12
4.	55.97	55.97	55.7	74.94	118.53
5.	71.81	71.81	111.26	102.22	135.37
6.	48.62	48.62	75.65	65.28	114.65
7.	64.17	64.17	100.32	84.35	116.37
8.	110.87	110.87	168.89	189.05	173.00
9.	62.31	62.31	92.45	75.54	122.21
10.	45.78	45.78	72.69	75.82	100.96

when it comes to its application in oral surgery, particularly implant dentistry.

Polycaprolactone in secondary alveolar bone grafting

Secondary bone grafting of the residual alveolar cleft in patients with cleft lip and palate has become a well-established procedure. Iliac crest particulate cancellous bone is most commonly used for this purpose. To the best of our knowledge, there is no documented case of alveolar bone grafting in which PCL scaffold is used.

Radiographic analyses of all six cases depict that there is an increase in gray value for the initial 4 months in all cases. Results also showed minimal escalation in gray values from 4th to 6th postoperative month in all except one case (case 4) which showed drop in gray value. All six cases of alveolar bone grafting eventually showed decrease in gray values at 9th month follow-up suggestive of lack of bone density. Moreover, none of the gray values measured at 9th postoperative month matched that of the control group indicating poor bone regeneration in the cleft.

Polycaprolactone scaffold for lateral ridge augmentation in the anterior maxilla

Autologous bone grafts are still considered to be the gold standard for ridge augmentation.^[15] Yeo *et al.* have compared results of lateral ridge augmentation in pigs using autogenous block graft and PCL-TCP scaffold. Clinical, microcomputed tomography and histomorphometric analyses showed that bone volume fraction in the control group (autogenous grafts) was superior to those seen with PCL-TCP scaffold.^[16] Out of ten, five PCL-TCP augmentation sites revealed exposure of scaffold into the oral cavity. Negligible amount of new bone was observed in these sites. Other sites have shown satisfactory bone formation. This animal study concluded that PCL has demonstrated potential application for lateral ridge augmentation.^[16]

In our study, one case of lateral ridge augmentation was done in the maxilla (Case 2). The scaffold was secured using a titanium screw. The postoperative period was uneventful

till 6 weeks following which labial mucosa showed signs of inflammation. Dehiscence was soon noted at 8th week exposing scaffold to the oral environment. Dehiscence was repaired by resuturing the dehisced wound margins using 4-0 polyglactin 910 suture (Vicryl™). However, soon there was reappearance of dehiscence. Bone density analysis done using gray value histogram revealed decrease in gray value for the first 6 months possibly due to repeated episodes of inflammation and wound dehiscence. A marginal increase in gray value was seen at 9th month follow-up after repair of dehiscence. However, the gray value measured at 9th month is far less than the control (adjacent sound bone) value suggestive of inadequate bone formation.

Polycaprolactone scaffold in cystic cavities

PCL was used to fill bony windows formed following enucleation of radicular cyst (Cases 5, 7, and 8). Two cases done in the maxillary anterior region (Cases 5 and 7) have shown scaffold exposure at 8th and 13th postoperative weeks, respectively [Figure 4]. Despite our attempts to repair the dehiscence, there was scaffold exposure seen repeatedly. Scaffolds were eventually removed in both these cases at 9th month follow-up [Figure 5] and wound allowed to heal by secondary intention [Figure 6]. Scaffold placed following enucleation of cyst in the mandibular posterior region showed uneventful healing (Case 8). This is the only case which did not demonstrate any dehiscence and scaffold exposure.

Gray values' data gathered using gray value histogram revealed that there was a steady increase in gray value for 3 months after which two cases (Cases 5 and 7) have shown decrease in gray value indicating decreased bone density. The third case of mandibular radicular cyst (Case 8) has shown remarkable increase in gray value throughout the healing period. Gray values measured at 9th month follow-up marginally exceeded the gray value of the control group indicative of excellent bone formation.



Figure 4: Scaffold exposure at 8th week postoperatively



Figure 5: Scaffold removed at 9th month follow-up



Figure 6: Three weeks after the removal of scaffold

There is a paucity of literature available related to use PCL scaffolds for intraoral defects. Schuckert *et al.*^[17] have shown satisfactory bone fill following the use of PCL scaffold in a case of peri-implantitis bony defect in the anterior mandible.

In contrast to the present study, they have used custom fabricated scaffold along with platelet-rich plasma and recombinant human bone morphogenetic protein 2. Goh *et al.* have investigated the use of PCL scaffold in preserving alveolar ridge following the extraction and reported that there was better maintenance of alveolar ridge height in extraction sockets with PCL scaffolds than control.^[18]

The choice of PCL scaffold in this study was based on these case reports and animal studies which have documented encouraging results in intraoral defects. To the best of our knowledge, this is the largest series documenting the use of this material for intraoral defects. In the present study, however, this venture of using PCL scaffold in various intraoral defects has not given satisfactory results in terms of gain in bone fill. Scaffold when used intraorally has tendency to cut through the delicate oral mucosa leading to its exposure in the oral cavity. This is probably due to its nonmalleable nature and the sharp edges. Once the scaffold is exposed to the oral environment, it gets covered with plaque and debris which prevents osteoblasts from migrating into the scaffold. Thus, the bone regeneration is affected. One case of mandibular radicular cyst has not shown any evidence of dehiscence possibly because this plug-shaped scaffold was better adapted to the cystic defect and did not come in direct contact with mucosa as opposed to other cases. Thus, it is our observation that scaffold is not a “mucosa friendly” material in this noncustomized form, and perhaps, the use of custom fabricated scaffold will give better results intraorally as demonstrated by Schuckert *et al.*^[17] At present, the cost involved in such strategies may seem inordinate, but the research on scaffolds is in its primitive stage. The comparison of its cost-effectiveness with that of other established strategies such as the use of alloplastic grafts may be inappropriate at this stage.

The limitations of this study include smaller sample size, varied bone defects, and lack of control group for comparison. Nevertheless, tissue engineering is in its infancy, and it is important that every success or more importantly the failures be documented so that it can act as a guide for other clinicians and researchers to work on. Authors believe that a larger sample size, longer follow-up, and categorization of the defects is required to assess its efficacy in respective defects. Moreover, the combination of an osteoinductive strategy with an osteoconductive customized scaffold and its comparison with a control group such as that with an autogenous bone will provide more assenting results.

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Conflicts of interest

There are no conflicts of interest.

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