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ORIGINAL ARTICLE

A Novel Bioresorbable Implant for Repair of Orbital Floor Fractures

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ABSTRACT

Purpose: To describe clinical, radiologic, and safety outcomes of orbital floor fracture repair using a novel bioresorbable polycaprolactone (PCL) mesh implant (Osteomesh^{TM}, Osteopore International, Singapore).

Methods: This is a prospective interventional case series of orbital floor fractures repaired using a novel PCL mesh implant. Clinical evaluation was conducted at presentation and postoperatively at 1, 4, 12, 24 and 48 weeks. Computed tomography (CT) of the orbits was performed 1 year postoperatively.

Results: A total of 20 patients were recruited. Mean follow up was 50.4 ± 31.88 weeks. The majority of the patients were male (60%) and of Chinese ethnicity (75%), and the mean age was 39.35 (range 13–69) years. The most common mechanism of injury was assault. The average fracture size was 21.9 mm (range 12–32 mm) in the anteroposterior meridian and 18.65 mm (range 6–27 mm) in the horizontal meridian. Fifty percent of the patients were classified as having a large orbital defect (horizontal width $\geq$20 mm). The binocular single vision (BSV) score improved from 72.1% preoperatively to 90.8% postoperatively ($P < 0.05$) for 17 patients who had pre and postoperative charts. BSV improvement did not differ significantly between those with large and small orbital fracture sizes. There were features of neobone formation on CT scan performed 1.5 years after implantation.

Conclusion: This bioresorbable implant is a promising material for the repair of both small and large orbital floor fractures, giving good functional and aesthetic outcomes.

Keywords: Biointegrable, bioresorbable, implant, orbital fracture, polycaprolactone

INTRODUCTION

Current strategies for the repair of orbital floor fractures include the use of autografts, allografts, and synthetic grafts. More recently, a few groups have reported success with the use of bioresorbable materials, but their utility has been confined to small fractures.[1] Polylactides possess excellent mechanical properties but these materials undergo continuous hydrolysis, breaking down into smaller by-products that might provoke an immune response.[2] Polydioxanone (PDS) has also been used but has been found to yield a scar that provides inadequate support of the globe upon degradation, resulting in 50% of patients developing enophthalmos or hypophthalmos.[3]

We have developed a polycaprolactone (PCL) mesh which has potential for use in the repair of orbital floor fractures. PCL is a biodegradable polymer that is non-toxic and biocompatible, degrading without producing harmful by-products. In this article, we aim to investigate the performance of the Osteomesh, a macroporous bioresorbable PCL mesh, in the repair of orbital floor defects of various sizes.

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MATERIALS AND METHODS

Fabrication of PCL Mesh

Porous PCL meshes (Osteomesh™, Osteopore International, Singapore) were fabricated using a fused deposition modelling technique in a current Good Manufacturing Practice (cGMP) environment (ISO 13485), and gamma sterilized before use. The meshes consist of filamentous structures 0.3 mm in diameter, forming a porous interconnected architecture with a lay-down pattern of 0/60/120° and porosity of 70%. The implants were fabricated as 20 mm by 20 mm squares, with a thickness of 0.75 mm (Figure 1A and B). We have previously shown that upon implantation, blood is absorbed into the pores of the implant via capillary action, trapping the blood and its cellular contents.[4]

Patient Recruitment, Ethics and Classification

A total of 20 patients with orbital floor fractures that did not involve the orbital rim were recruited. Patients who were younger than 12 years of age or who had had previous orbital or extraocular muscle disease or surgery were excluded. The indications for surgery included diplopia, enophthalmos ≥2 mm, tissue entrapment and poor ocular motility contributed by large fracture size.

Written informed consent was obtained from all patients and the study was conducted in accordance with the tenets of the Declaration of Helsinki as revised in 1989. Institutional Review Board (IRB) approval was obtained.

Surgical Procedure

Patients with orbital floor fractures underwent repair via a transconjunctival approach. A periosteal incision was made along the anterior orbital rim and the periosteum was reflected to expose the orbital floor fracture. Entrapped tissue was freed from all edges and elevated prior to the insertion of the implant. The Osteomesh implant was sized, trimmed (Figure 1C), soaked in warm water to improve malleability (~40 °C) and molded to conform to the orbital shape before insertion over the bony

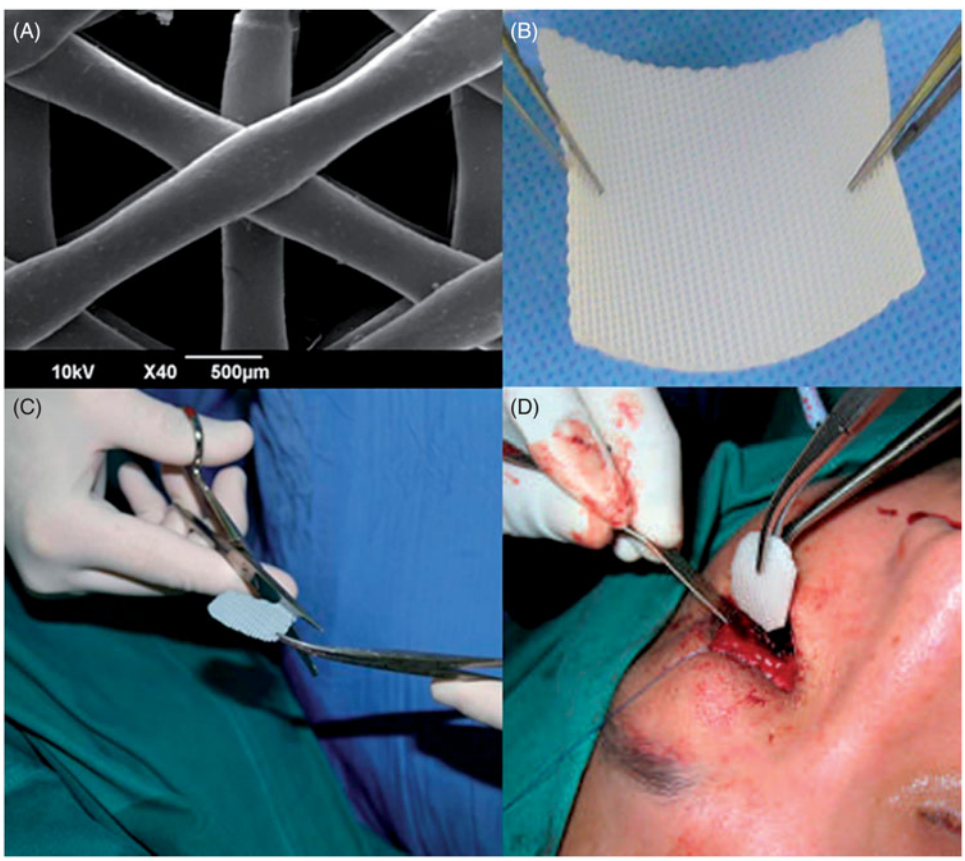


FIGURE 1. Intraoperative photos of the surgical procedure. (A) Scanning electron microscopy of the Osteomesh implant showing high porosity with 0/60/120° lay-down pattern. (B) Demonstration of malleability of implant. (C) The implant is easily cut into shape using surgical scissors. (D) Surgical procedure shows the insertion of the Osteomesh implant into the bony defect in the subperiosteal space with the smooth side positioned to appose the periosteum and the corrugated surface placed against the orbital bony defect.

defect in the subperiosteal space, with the smooth side apposed against the periosteum and the corrugated surface placed against the orbital bony defect (Figure 1D).

Forced duction tests were then conducted to ensure all orbital tissue was freed from the fracture site. No suturing of the implant was required. The periosteum and conjunctiva were closed over the implant. Postoperatively, oral prednisolone and antibiotics were given and a topical ophthalmic antibiotic-steroid preparation was applied according to the surgeon's preference.

Clinical Evaluation

Clinical evaluation was conducted at the first consultation and post-operatively at weeks 1, 4, 12, 24, and 48. Evaluations at each visit included: visual acuity, slit lamp examination, Hertel exophthalmometry, and ocular motility. Enophthalmos was defined as a difference of $\geq$2 mm compared with the contralateral side. Ocular motility was assessed by (a) observation of the Hirschberg reflexes, (b) Hess chart, and (c) assessment of the field of binocular single vision (BSV) using an Aimark perimeter. Restricted ocular motility was defined by $<30^{\circ}$ in any direction of gaze. The BSV score was calculated using the method described by Woodruff et al.[5] In this method, each rhomboid on the BSV chart was allocated a score ranging from 1–4, with the central area being allocated a higher score. The total score for the 55 segments was 124. The score for the area of BSV was then calculated based on the formula below and recorded as a percentage (X%).

$$\text{Score for area of BSV}/124 \times 100\% = \text{X}\%$$

All patients underwent computed tomography (CT) of the orbits prior to surgical intervention with a repeat CT one year after surgery. Non-contrast coronal and axial CT scans of the affected orbit were performed for soft tissue and bone using the Siemens Somatom Definition (Siemens, Erlangenm Germany); voltage 120 kV, MAS 125, measuring seven seconds with 2 or 3 millimetres (mm) slices increment and reconstruction. The fracture size was measured in the antero-posterior (AP) and horizontal directions of the fractured orbit from right to left. The AP axis was measured by counting the number of coronal cuts the fracture traversed and multiplied by section thickness. The horizontal measurement of the fracture was taken by recording the greatest width of the fracture as seen on the coronal view of the CT scan by using the software metric rule. Fractures equal to or greater than 20 mm in the horizontal direction were classified as large orbital defects.

RESULTS

Clinical Features

The patients' demographics, cause of injury and assessments of their orbital fractures are as tabulated in Table 1. The mean age of the 20 patients was 39.35 years old (13–69 years old) with a 3:2 ratio of males to females. The average fracture size was 21.9 mm (range 12–32 mm) in the AP meridian and 18.65 mm (range 6–27 mm) in the horizontal meridian. Of these, 50% (n = 10) of the patients were noted to have a horizontal size of 20 mm or more, and were hence classified as having large orbital defects (Table 1, shaded boxes).

Clinical features of the patients at presentation and last follow up are presented in Table 2. All 20 patients tolerated the surgical procedure well. The mean duration of follow up was 50.4 ± 31.9 weeks. There was an improvement in subjective symptoms of diplopia, infraorbital anaesthesia and enophthalmos. At the last follow up visit, none of the patients had signs of inflammation such as injection and chemosis. Postoperatively, there was reduction in limitation of ocular motility and fewer patients had infraorbital anaesthesia. Of the 6 patients with preoperative enophthalmos, 5 of them had more than 50% reduction in their enophthalmos at the end of follow up. The remaining patient with persistent postoperative enophthalmos had a 50% improvement from 4 mm to 2 mm of enophthalmos. One patient developed lower lid entropion (Patient 16) and one patient (Patient 18) developed a mucoid cyst around the implant requiring surgical drainage. None of the patients had implant migration or extrusion for the duration of follow up.

Binocular Single Vision

The mean BSV improved from 72.1% preoperatively to 90.8% postoperatively ($P < 0.05$) in the 17 patients in whom pre and postoperative BSV data were available, including 9 who had large defects and 8 patients with small defects. Subjects with large and small orbital fractures did not differ significantly in terms of BSV improvement ($P > 0.05$) (Figure 2).

CT Imaging

Preoperative and postoperative CT data sets were obtained for 10 patients (Table 3). The mean interval between pre and postoperative CT scans was 15 months. Postoperative CT scans showed support of the orbital tissue and orbital repositioning of the prolapsed orbital content in all patients. The orbital implant remained properly positioned with no downward displacement of the implant. One patient

TABLE 1. Demographics, fracture size and BSV score of 20 recruited subjects.

Patient	Age	Race	Gender	Cause of Injury	Fracture size		BSV score (%)	
					AP/mm	Horiz/mm	Pre	Post
1	53	Chinese	M	Assault	24	20	41.13	92.74
2	18	Indian	M	Sports accident	27	27	82.26	99.19
3	43	Bangladeshi	M	Industrial accident	18	17	52.42	96.77
4	60	Chinese	F	Fall	21	21	81.45	75.81
5	21	Chinese	M	Assault	21	23	99.19	87.90
6	36	Chinese	M	Assault	18	25	95.16	87.10
7	38	Chinese	F	Road traffic accident	16	14	77.42	80.65
8	31	Indian	M	Assault	21	21	16.94	98.39
9	14	Chinese	M	Assault	15	17	NA	97.58
10	53	Chinese	F	Assault	24	15	18.55	97.58
11	43	Chinese	F	Fall	27	18	99.19	56.45
12	56	Chinese	M	Road traffic accident	32	17	100.00	100.00
13	20	Chinese	M	Assault	15	15	79.03	99.19
14	40	Chinese	M	Fall	24	21	74.19	77.42
15	13	Chinese	F	Sports accident	12	6	91.13	100.00
16	59	Chinese	F	Fall	30	16	NA	100.00
17	48	Chinese	M	Assault	24	21	34.68	97.58
18	69	Chinese	F	Fall	21	20	100.00	100.00
19	38	Malay	F	Assault	18	20	83.06	97.58
20	34	Indian	M	Assault	30	19	NA	NA

Patients classified as having large orbital defects are those with a horizontal measurement of ≥20 mm (shaded boxes).

TABLE 2. Clinical features of patients at presentation and last follow-up.

	At presentation ($n = 20$)		At last follow-up ($n = 20$)	
	Number	Percentage	Number	Percentage
Symptoms				
Diplopia	15	75	5	25
Infraorbital anaesthesia	9	45	8	40
Enophthalmos	7	35	2	10
Signs				
Limitation in ocular motility	16	80	6	30
Elevation	13	65	6	30
Depression	10	50	2	10
Adduction	5	25	1	5
Abduction	4	20	1	5
Infraorbital anaesthesia	10	50	8	40
Enophthalmos	6	30	1	5
Injection	9	45	0	0
Chemosis	4	20	0	0

developed a mucoid cyst around her implant requiring surgical drainage (Patient 18).

Case Study of Large Orbital Defect: New Bone Formation

To demonstrate the efficacy of the osteoconductive PCL mesh in directing new bone formation in a large orbital defect, we present Patient 1 (AP = 24 mm; Horiz = 20 mm) with a large fracture for discussion. In the CT scan taken 16 months post-operatively, there were two parallel lines of hyperdensity along the edge of the implant where it contacted the fracture site (Figure 3B: arrow). The superior line was less radiodense compared to the inferior one. We postulate that the superior line represents neobone undergoing calcification and the inferior line represents the reposited bone fragment. The implant restored orbital volume and provided adequate mechanical support for the orbital contents. The postoperative ocular motility continued to remain full 1 year after the surgery on Hess charting (Figure 3C and D). The patients' preoperative area of diplopia was reduced (Figure 3E and F) and was only noted in the extremes of gaze.

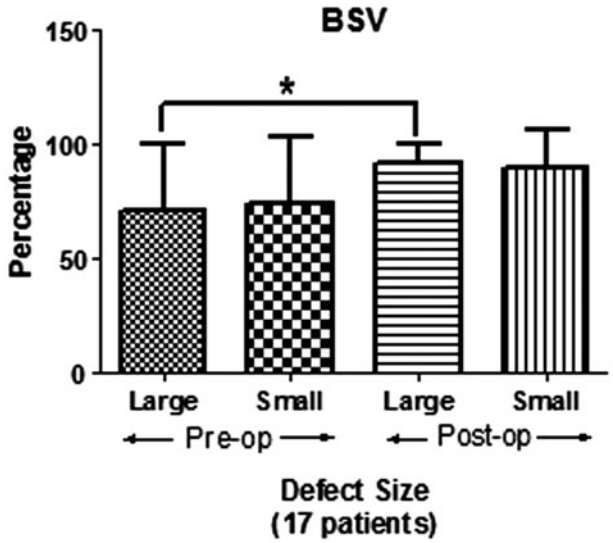


FIGURE 2. Bar chart representation of BSV improvement in the 17 patients who had pre and postoperative BSV charts, including nine patients who had a large defect and eight patients with a small defect. There was a significant improvement in BSV for all the patients with no difference between the groups with a large (marked with asterix) or small fracture.

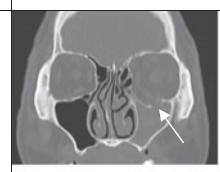
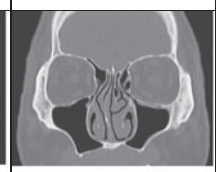
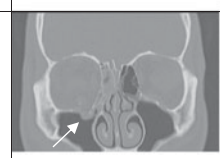
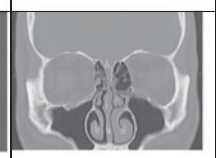
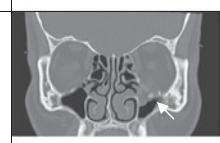
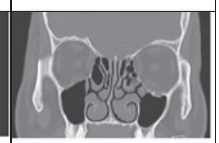
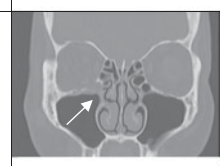
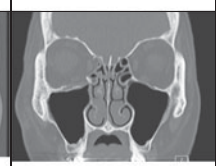
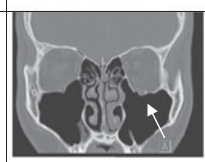
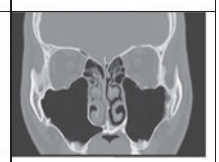
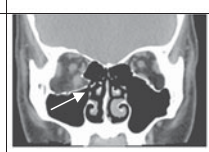
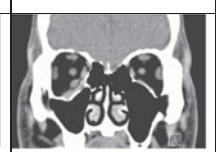
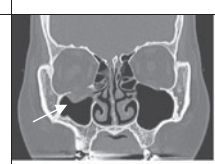
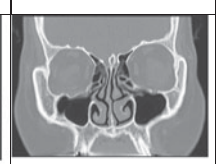
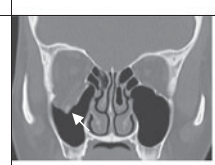
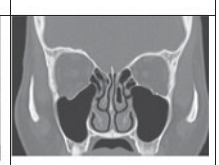
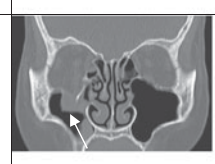
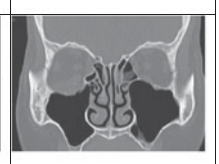
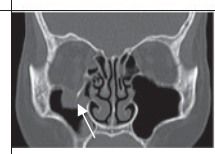
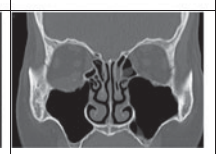
DISCUSSION

Our study reports the use of a novel biodegradable PCL implant for the repair of orbital fractures in humans. This implant has shown good functional and aesthetic outcomes in our study, with demonstrable improvements in ocular motility and binocular single vision.

The introduction of biomimetic implants in the field of bone tissue engineering has influenced the way orbital defects are being reconstructed. Various biomaterials aim to restore bone defects by providing a suitable environment for surrounding osteogenic cells to migrate, colonise the implant and eventually synthesize new bony matrix.[4] Currently, autologous, non-resorbable and resorbable implants are available for orbital floor reconstruction.

Autologous implants are advantageous in that there is no risk of rejection.[6] However, there is significant donor site morbidity, and the rigidity and unpredictable thickness of the donor tissue may not allow it to conform exactly to the recipient site.[7] Non-resorbable orbital implants such as titanium, porous polyethylene or silicone elastomers provide good tensile strength, but remain as permanent foreign bodies with the persistent risk of complications. Titanium mesh possesses good mechanical strength and biologically inert properties, but has poor osteointegration and has been reported to result in orbital adherence syndrome with decreased ocular motility and eyelid retraction that is severe enough to warrant explantation.[8,9] Porous polyethylene

TABLE 3. Preoperative and postoperative CT scans of the 9 patients (white arrows indicate the side of fracture).

Patient	Preoperative	Postoperative
1		
2		
3		
4		
5		
6		
7		
15		
17		
18		

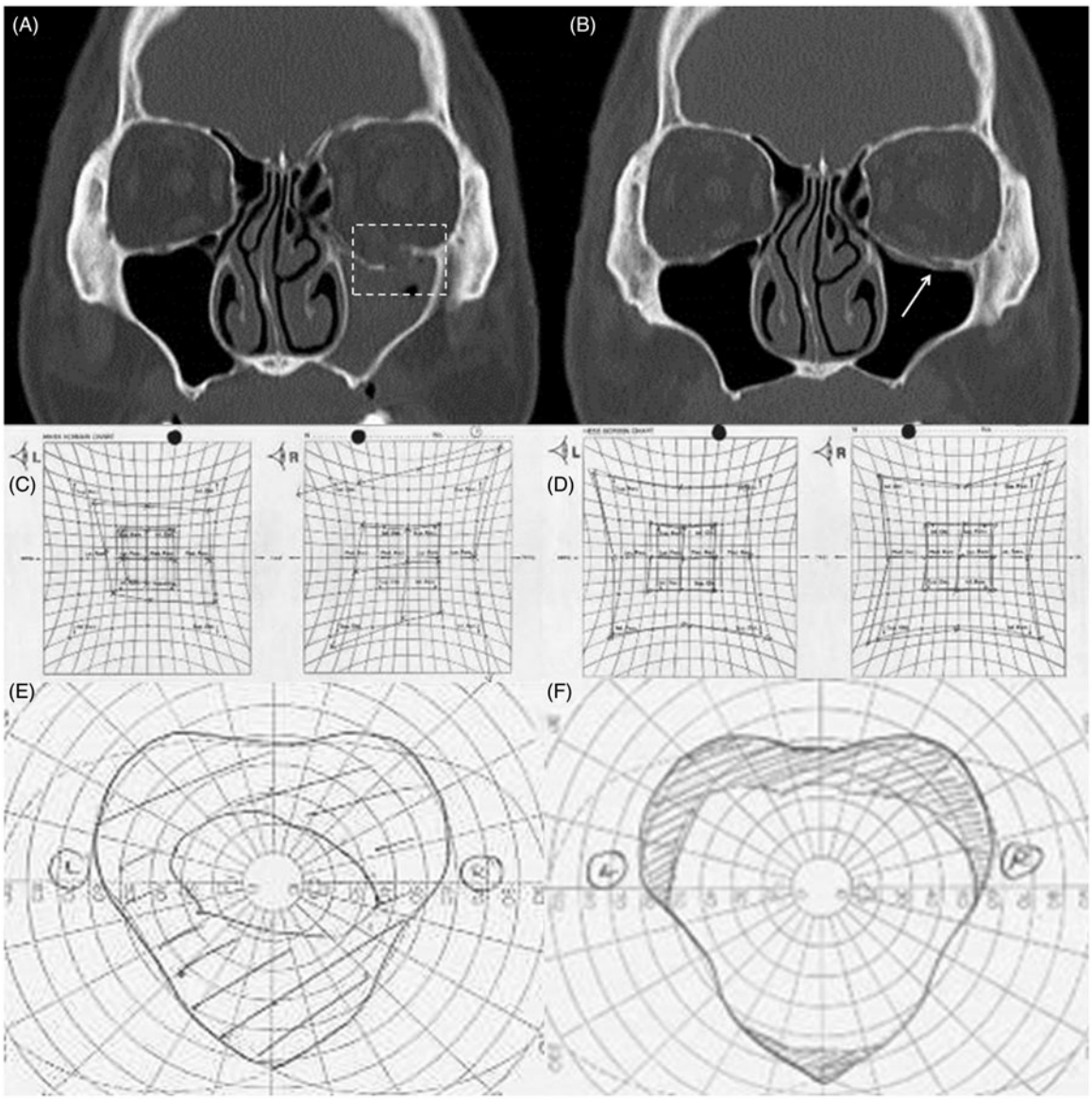


FIGURE 3. Detailed clinical examination of Patient 1 with a large defect on the left side (A). Two parallel lines of radiodensity (white arrow in B) was seen along the floor of the bony orbit where the Osteomesh scaffold was implanted. (C) Preoperative Hess chart demonstrates restriction of eye movement of the left eye with corresponding overaction of the right eye. (D) This normalizes after fracture repair with the Osteomesh implant. The improvement of binocular single vision is also evident after fracture repair as seen by the improvement of BSV (reduction in the shaded area of diplopia from preoperative (E) to postoperative (F)).

(Medpor) has been inserted successfully in the last two decades with minimal complications.[10,11]

It is favoured as an implant because it can be easily manufactured, sized and shaped precisely to fit an orbital defect. It appears to be biocompatible with minimal host tissue reaction and demonstrates stability and mechanical strength. Due to its porous structure, vascular ingrowth creates the potential to transport cellular products that fight infection deep into the implant.[12,13] However, due to its non-resorbable nature, there is a potential lifelong risk of infection and inflammation around the implant.[10] With the silicone implant, implant migration, extrusion and infection have all been reported.[14,15] There have even been reports of implant extrusion up to 17 years after implantation of a silicone sheet for orbital fracture repair.[16]

Resorbable *implants* such as copolymers of poly-L-lactic acid (PLLA), poly-D-lactide (PLDLA), polyglycolic acid (PGA) and polydioxanone (PDS) are currently available for use. Lieger et al.[17] reported stable bridging of soft or hard bone tissue in $\leq$15 mm defects upon degradation of P(L/DL)LA 70/30 implant (PolyMax) within 24 months, without any sagging of the reconstructed area. A study by Han et al.[18] found the polylactide implant to be as safe and efficacious as porous polyethylene implant. Despite the excellent mechanical properties, these materials undergo continuous hydrolysis and subsequently break down into smaller by-products that might

provoke an immune response.[2] In another study, polydioxanone (PDS) was used but the scar was found to provide inadequate support for the globe upon degradation, resulting in 50% of patients developing enophthalmos or hypophthalmos.[3] A study by Dietz et al. found that using a 0.15-mm perforated PDS foil for reconstruction of the orbital floor was functionally and cosmetically comparable to a 0.3-mm titanium mesh.[19] However, it was also suggested that PDS is likely not suitable for defects larger than 20 mm and titanium is still recommended for use in larger defects.[20]

PCL implants have a long degradation time of more than 2 years.[21] This makes them ideal as bone implants as they degrade in tandem with neobone regeneration. PCL is FDA-approved and has been widely used as an implant material in various areas of tissue engineering as well as drug delivery.[22–25] The PCL implant has been shown to provide an osteoconductive environment that is desirable for guiding cellular growth, bone-directed differentiation and tissue formation within the interconnected honeycomb architecture.[26]

Earlier work has demonstrated PCL-based implants to have adequate structural integrity to withstand biomechanical loads over time.[27–32] Schantz et al. presented histological evidence of neobone formation with partial integration into the surrounding host tissue in a critical-sized rabbit calvarial defect using autologous mesenchymal progenitor cells and osteoblasts seeded onto PCL implants.[30] Rai et al.[29] achieved high success rates of bone union 12 weeks post-surgery in a segmental rat femoral defect when platelet-enriched plasma was loaded onto PCL/TCP implants.[29] Clinically, this PCL implant has also been used in more than 1500 patients and shown to have successful outcomes for various oral maxillofacial indications.[4,33]

Our study reports the use of these biodegradable PCL implants for orbital reconstruction in humans. These implants have shown good functional and aesthetic outcomes in our study. This was demonstrated by the improvement and maintenance of BSV and ocular motility for the duration of our study, regardless of the size of the fracture. There are four patients who did not appear to improve after surgery. Patient 4, had dementia and the accuracy of her test results was questionable. Patient 11 had the postoperative BSV charting performed 1 week after surgery when a significant amount of postoperative swelling could have accounted for the worsening binocular diplopia.

However, as he was lost to follow up from the fourth week onwards, we were not able to chart his progress. Patients 5 and 6 did not have much diplopia preoperatively but fracture fixation was indicated due to enophthalmos of more than two millimeters. Diplopia was only slightly increased, mostly in upgaze, and functionally the patients still did well. There were no signs of marked inflammation or infection, migration or displacement of the implant in our series of patients, suggesting good biocompatibility and biointegration of the implant. There was, however, one case of a mucoid cyst developing around the implant. This could have been a retrograde implantation cyst from the nasal mucosa. This is a known complication of fracture fixation with implant insertion via a transconjunctival approach.[34,35]

There was evidence of calcification in one case of a large orbital floor defect at 16 months. CT scan performed at 16 months after surgery for this patient showed patchy areas of linear hyperdensity on the surface of the implant (white arrow in Figure 3). We postulate that this is new bone as it appears to grow linearly along the surface of the implant, with the original bone fragment parallel and inferior to it. The lack of consistent evidence of calcification in the other cases could be due to a technical setting of the X-ray exposure, or the timing at which the CT scan was done (the majority of the cases had CT scans performed at 12–13 months). Our previous experience with imaging new bone formed via tissue engineering approaches has shown that the different stages of bone formation[36] have various threshold ranges of grey values which might not be captured by X ray during the early stages.

Our PCL implant appears to have the desirable qualities of the Medpor implant[37,38] in that it avoids donor site morbidity, is malleable and easy for surgeon handling, is biocompatible with host tissue with minimal soft tissue reaction, is strong enough to support the orbital contents, and possesses porosity that encourages fibrovascular ingrowth. The added advantages of the PCL implant are that it may stimulate neobone formation and is bioresorbable. However, a direct comparison between the two implants cannot be made until a long term, randomized controlled trial is conducted.

The limitations of our study include the noncomparative nature of the study and the small sample size with relatively short follow up. Long term follow up of these patients is necessary to determine the outcome after complete resorption of the implant has occurred, which could be more than 2 years as previously reported.[39] It remains to be seen if the orbital volume remains the same after these changes have taken place.

In conclusion, the use of this novel bioactive PCL implant has presented promising data for the repair of both small and large orbital floor fractures, offering therapeutic opportunities for bony regeneration. This could lead to a shift in reconstructive surgery away from simply repairing bony defects, towards functional and aesthetic regeneration of the damaged

tissue. Further studies are needed to define the long-term tissue remodeling and efficacy profile.

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DECLARATION OF INTEREST

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