J Mater Sci (2022) 57:20716–20725

Materials for life sciences

Nature-inspired discontinuous calcium coatings on polyglycolic acid for orthopaedic applications

F. H. Y. Lui[1,*], Y. Wang[2], R. J. Mobbs[3], and C. C. Sorrell[1,*]

[1] School of Materials Science and Engineering, UNSW Sydney, E10 Gate 2 Avenue, Kensington, NSW 2052, Australia
[2] Mark Wainwright Analytical Centre, UNSW Sydney, Chemical Sciences Building, High Street, Kensington, NSW 2052, Australia
[3] Australia School of Medicine, Neuro Spine Clinic, Prince of Wales Hospital, Sydney, Sydney, Australia Barker Street, Randwick, NSW 2031, Australia

Received: 5 July 2022
Accepted: 28 October 2022
Published online: 15 November 2022

© The Author(s) 2022

ABSTRACT

Non-union in spinal fusion surgeries (SF) is a key cause of failure. Demineralized bone matrix is used in SFs to facilitate bone growth throughout the segment, and polyglycolic acid (PGA) meshes are used for their containment. A discontinuous calcium mineral coating could transform the function of PGA meshes from passive to active, where dissolved calcium ions could act as a chemoattractant for bone cells or it could form a barrier to prevent hydrolytic degradation of the mesh to better align its degradation profile with the fusion process. Challenges to depositing a mineral coating on PGA include its low glass transition temperature (~ 35 °C) and hydrolytic degradation.

Inspired by calcite rafts in limestone cave pools, calcite grains were deposited on PGA meshes at the air–solution interface of supersaturated Ca(HCO3)2 (33 °C 6 h). X-ray diffraction (XRD) and 3D confocal microscopy were performed to assess phase composition and coating morphology. Durability was qualitatively assessed by mechanical tests. In vitro incubation was performed to elucidate the dynamic interactions between coating dissolution and PGA degradation; pH and calcium concentration of the solution were measured.

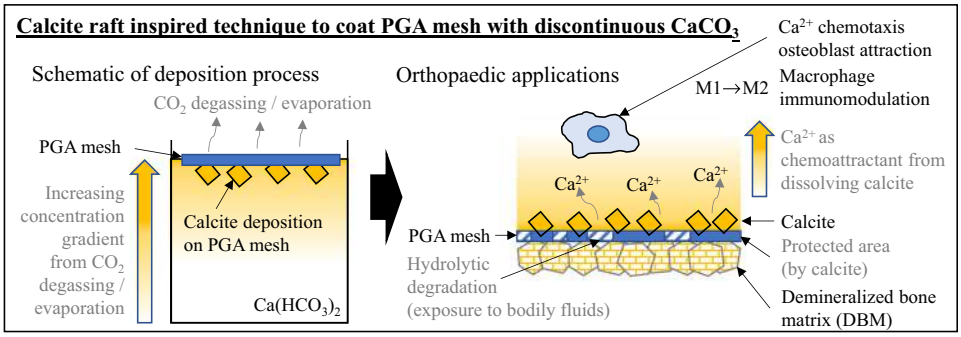
XRD confirmed that coated PGA meshes were comprised of PGA and crystalline calcite. 3D confocal microscopy showed that the coatings were discontinuous and comprised of rhombohedral microcrystals. Retention of the particles following ultrasonic treatment and flexure/tensile testing indicates durability. Notably, the grains were compliant as the mesh was contorted. The interaction effect between the incubation time and pH for the uncoated and coated samples was statistically significant ($p < 0.05$).

Handling Editor: Yaroslava Yingling.

Address correspondence to E-mail: f.lui@unsw.edu.au; c.sorrell@unsw.edu.au

https://doi.org/10.1007/s10853-022-07903-4

GRAPHICAL ABSTRACT



Introduction

Polyglycolic acid (PGA) has wide-ranging applications in the biomaterials field, from surgery to engineering musculoskeletal tissues [1]. Woven PGA meshes are used as containment bags for demineralized bone matrix (DBM) in spinal fusion surgery (SF) because they have appropriate mechanical strength and are bioresorbable [2] (for example, Magnifuse™ Bone Graft [3]). There is potential to transform their role from passive containment to active through the deposition of a discontinuous calcium-based mineral coating. The dissolution of the coating in vivo would release calcium ions that could act as a chemoattractant for bone cells. It could also act as a partial barrier that delays hydrolytic degradation of the mesh to better align its degradation profile with the bone healing process.

Osteoclast-mediated bone resorption is known to increase the concentration of extracellular Ca^{2+} in the microenvironment up to 40 mm [4]. The previous studies have shown extracellular Ca^{2+} concentrations to have a chemo-attractive effect on osteoblasts, mesenchymal stem cells, and monocytes through the calcium-sensing receptor (CaSR) [5] 6, 7]. The leaching of Ca^{2+} from a Ca-containing biomaterial into the microenvironment of the surgical site could simulate bone resorption and so attract osteoblasts and monocytes for the bone healing process.

Incorporation of bone grafts is initiated by osteoclasts rather than osteoblasts; extensive resorption begins from two weeks after surgery and increases until six months, after which the resorption rate gradually decreases to a normal rate at around one year [8]. Stability of new bone formation, indicated by the consistency and thickness of the new bone, has been observed for six months after DBM grafting [9]. Consequently, it is advantageous for a PGA mesh containment bag to retain sufficient structural integrity and strength up to six months. Further, glycolic acid released by the slow degradation of PGA may osteoimmunodulate macrophages to switch from the M1 to M2 phenotype, which is more conducive to bone formation [10]. However, PGA meshes have been reported to degrade significantly over a three-month period in vitro [3].

A discontinuous Ca-based mineral coating on the PGA mesh could both serve as a chemoattractant for bone cells through the diffusion of Ca^{2+} and protect the coated regions of the mesh from hydrolytic degradation to delay its degradation profile. The low onset of the glass transition temperature of PGA (35 °C [1]) represents a key technical challenge in forming a mineral coating on the mesh. Hence, low-temperature wet chemical techniques are a common way to coat PGA with apatite [11], 12, 13]. However, these methods typically require extended exposure (up to 16 days) to simulated bodily fluids (SBF), which could severely compromise the mechanical strength of PGA due to hydrolytic degradation [14].

Inspired by calcite rafts in limestone cave pools [15, 16], calcite grains were deposited on PGA meshes at the air–solution interface of supersaturated $Ca(HCO_3)_2$ at 33 °C for 6 h (Figure 1). The technique is performed with the PGA mesh positioned along

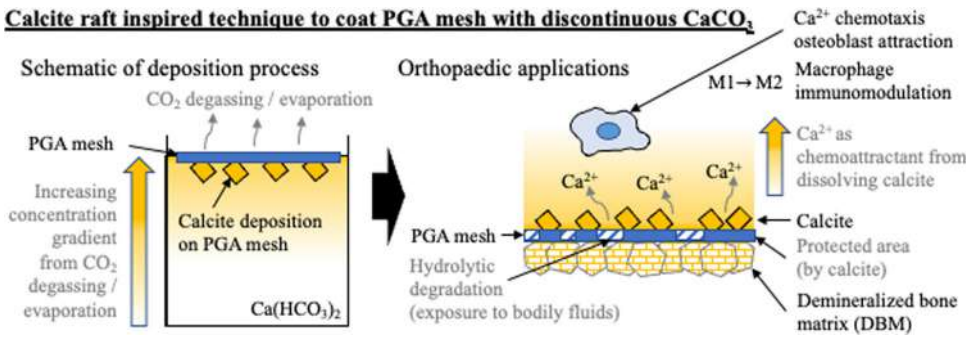


Figure 1 Calcite raft inspired technique to coat PGA mesh with discontinuous $CaCO_3$. Inspired by calcite rafts in limestone cave pools [15, 16], calcite grains were deposited on PGA meshes at the air–solution interface of supersaturated $Ca(HCO_3)_2$. The supersaturation gradient created by CO_2 degassing or evaporation is conducive to heterogeneous mineral deposition on the mesh. The PGA mesh with a discontinuous $CaCO_3$ coating has orthopaedic applications: (1) delay in the degradation profile of PGA mesh to match the bone healing process; (2) Ca^{2+} leaching for a chemo-attractive effect on osteoblasts, MSCs, and monocytes [5], 6, 7]; (3) release of glycolic acid for immunomodulation [10].

the air–solution interface. The supersaturation gradient created by CO_2 degassing or evaporation is conducive to heterogeneous mineral deposition on the mesh. $CaCO_3$ is more soluble than calcium phosphates [17] and so is a desirable candidate as a chemoattractant, owing to the likely more rapid leaching of Ca^{2+}.

X-ray diffraction (XRD) and 3D laser confocal microscopy (3D microscopy) were performed to assess phase composition and coating morphology. Durability was assessed by flexural/shear/tensile mechanical tests. In vitro incubation of the samples was performed for up to three weeks to elucidate the dynamic interactions between coating dissolution and PGA degradation; pH of the solution was measured, and inductively coupled plasma–optical emission spectrometry (ICP-OES) was used to measure calcium concentration.

Materials and methods

Raw materials and coating deposition

$CaCO_3$ Nanoparticles. Precipitated $CaCO_3$ nanoparticles ($CaCO_3$-NPs) (PlasmaChem GmbH; Berlin, Germany) were used as raw materials to prepare $CaCO_3$ nanoparticulate suspensions ($CaCO_3$ suspensions) and supersaturated calcium bicarbonate solutions ($Ca(HCO_3)_2$). The $CaCO_3$-NPs were calcite, with average particle size of $\sim 90 \pm 15$ nm (manufacturer's data).

Preparation of supersaturated calcium bicarbonate solution. A supersaturated solution of $Ca(HCO_3)_2$ was prepared using a custom-designed batch reactor according to a previously described method [18].

PGA Mesh. PGA meshes were provided by Medtronic, Minneapolis, MN. The mesh fabric was cut into 15 mm × 15 mm squares.

PGA Coating Process. The PGA meshes were coated with $CaCO_3$ grains by a nature-inspired interfacial technique [15], 19]. The PGA meshes were positioned along the air–solution interface of a supersaturated $Ca(HCO_3)_2$ solution (5.5 mL) in a glass vial and heated in a drying oven at 33 °C for 6 h. These conditions were selected because 33 °C is below the onset of the glass transition temperature at 35 °C [1] and 6 h is the sufficient time for deposition without excessive risk of hydrolytic decomposition of the mesh. The coated PGA meshes were removed from the glass vial and rinsed with deionized (DI) water; then, they were cleaned ultrasonically in DI water for 5 min in order to remove loosely adhered grains.

Materials characterization

3D microscopy (VK-X200; Keyence Corporation, Japan) was used to image the samples (20 X objective lens) and to determine the morphology/size of the coatings.

XRD (Empyrean II; Malvern PANalytical Ltd., Netherlands) was used to determine the phase composition of the samples. Key scanning parameters were X-ray source (CoKα), converted to CuKα during analysis, accelerating voltage (45 kV), current

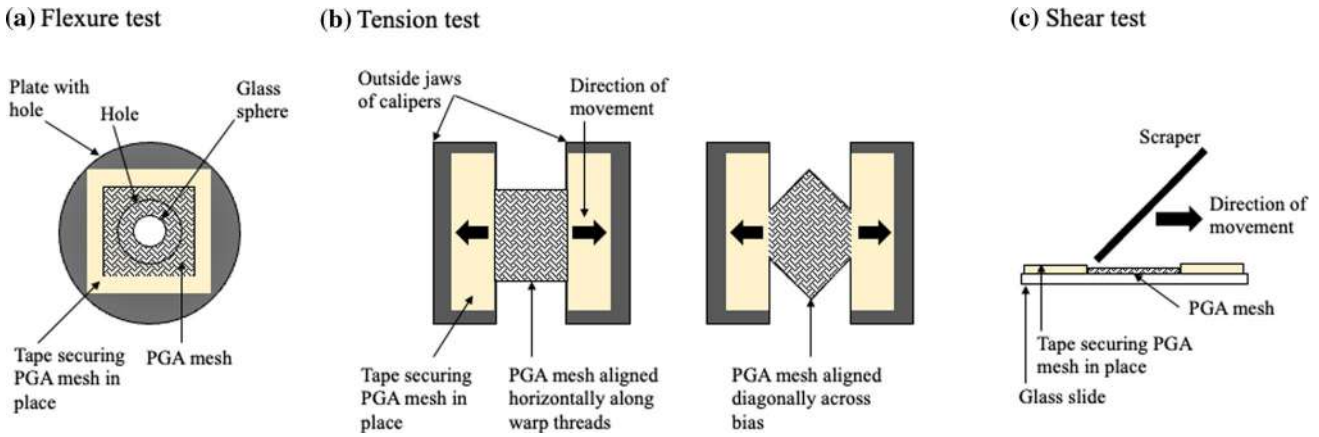


Figure 2 Experimental set-up for mechanical testing to qualitatively assess the durability of the discontinuous coating on PGA meshes. **a** Flexure test: A PGA mesh was secured onto a plate with a hole in the centre. A glass sphere (6.0 mm Ø) was loaded downwards into the PGA mesh for 3 mm at 1 mm/s; **b** tensile test: A PGA mesh was secured (aligned horizontally along warp threads and diagonally across bias) to the outside jaws of callipers with tape and pulled outwards; **c** shear test: A PGA mesh was secured to a glass slide with tape, and a scraper was dragged gently by hand (~ 45° orientation) across the surface unidirectionally.

(40 mA), and scan axis (theta/2-theta). The measurements were in reflection mode. The sample was placed between two layers of Kapton® polyimide thin film (7.5 µm) and fixed to a sample holder.

Mechanical tests (flexure, tensile, shear; $n = 3$) were performed for qualitative determination of the durability of the coatings under stresses typical of the graft preparation and implantation process. A universal testing machine (Instron® Universal Testing Machine; Instron Deutschland GmbH, Germany) was used to perform the flexure tests (3-point bending test); this indicates how the coating may deform when DBM is loaded into the containment bag (Figure 2a). A glass sphere (6.0 mm Ø) was forced downwards into the PGA mesh for 3 mm at 1 mm/s with the coated side facing down. Tensile tests were performed by securing PGA mesh (aligned horizontally along warp threads and diagonally across the bias) to the outside jaws of callipers and pulled outwards; this indicates how the coating may deform when the containment bag is stretched during the DBM loading process (Figure 2b). Shear testing was performed by securing a PGA mesh to a glass slide with tape and gently hand-dragging (~ 45° orientation) a scraper across the surface unidirectionally; this indicates how the coating may deform during the DBM loading and implantation process (Figure 2c).

In vitro incubation

In vitro incubation was conducted in order to assess $CaCO_3$ dissolution over a 3-week period. The method is an adapted version of the 2017 Medtronic White Paper entitled *Degradation and Removal of the Graft Delivery Bag Component of Magnifuse™ Bone Graft* [3]. Samples (uncoated and coated) were placed in 10 mL of PBS (10 mM, pH = 7.6) and incubated at 37 °C. The samples were removed and analysed after 1 week (7 days), 2 weeks (14 days), and 3 weeks (21 days) of incubation ($n = 3$, 18 samples in total). They were rinsed with DI water and dried. The pH of the solvent (5 mL) was analysed using a pH meter (Mettler Toledo Ltd., VIC, Australia). The remaining 5 mL of solvent was analysed by ICP-OES (PerkinElmer Avio, PerkinElmer Inc., Waltham, MA, USA) in order to assess the in vitro diffusion of Ca ions from the coated samples. The error bars denote standard error (SE) values ($n = 3$). Analysis of variance (ANOVA) was used to determine the statistical significance of the results. The preliminary studies showed that gravimetric analysis was not suitable to determine the degree of degradation with the above-mentioned protocol owing to the low weight of the samples and relatively short duration of the study.

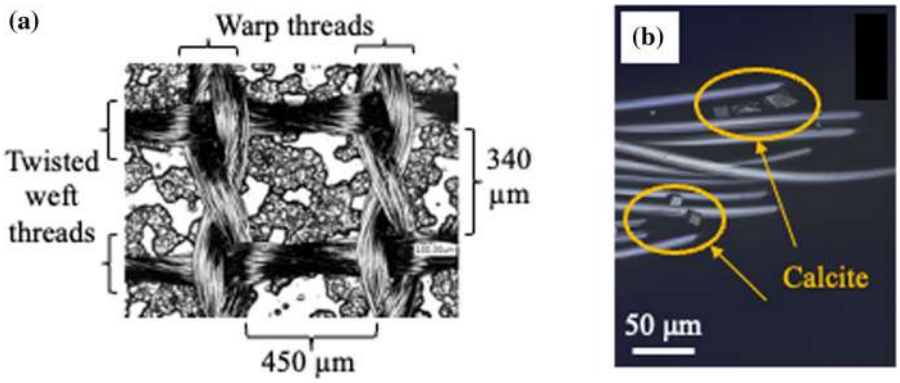


Figure 3 Size and morphology of uncoated/coated PGA mesh. **a** Uncoated PGA mesh; **b** coated PGA mesh.

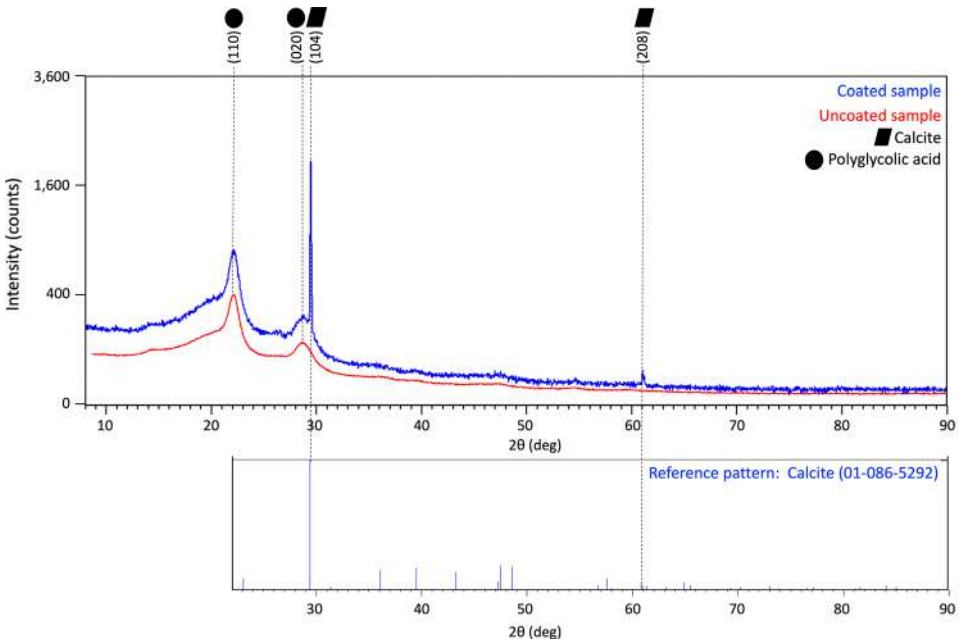


Figure 4 XRD patterns of uncoated and coated PGA meshes. XRD patterns of: uncoated PGA mesh (red) and coated PGA mesh (blue). Reference used for calcite (ICDD 01–086-5292) (shown) and polyglycolic (ICDD 00–067-1537) phase identification.

Results

$CaCO_3$ coating on PGA mesh

3D confocal micrographs in Figure 3a show that the uncoated PGA mesh structure was comprised of woven weft and warp threads. Each thread is comprised of multiple fibres that are ~ 10 µm in diameter. The coating was comprised of rhombohedral calcite crystals with sharp terminations; the grains varied in size and ranged from ~ 10 to 25 µm, as observed in Figure 3b. The coating was discontinuous and observed on and between threads deeper in the textile structure.

The XRD pattern of an uncoated PGA mesh is shown in Figure 4/red. It includes signals from the polyimide thin film that was used to hold the sample in place. This pattern shows that the PGA sample is not fully crystallized and hence partially amorphous.

The XRD pattern of the coated sample of Figure 4/blue shows that after subtraction of the background pattern for the uncoated PGA mesh, the coating consists of well crystallized and highly oriented $CaCO_3$. Comparison with the reference pattern for calcite (ICDD 01–086-5292) reveals that the preferred orientation is in the (104) plane; the only other diffracting peak is the fractional (208) plane.

Durability of coated PGA mesh

PGA meshes used as containment bags for DBM are exposed to a range of mechanical stresses during the DBM insertion and implantation process. The performance of coated PGA meshes under flexure,

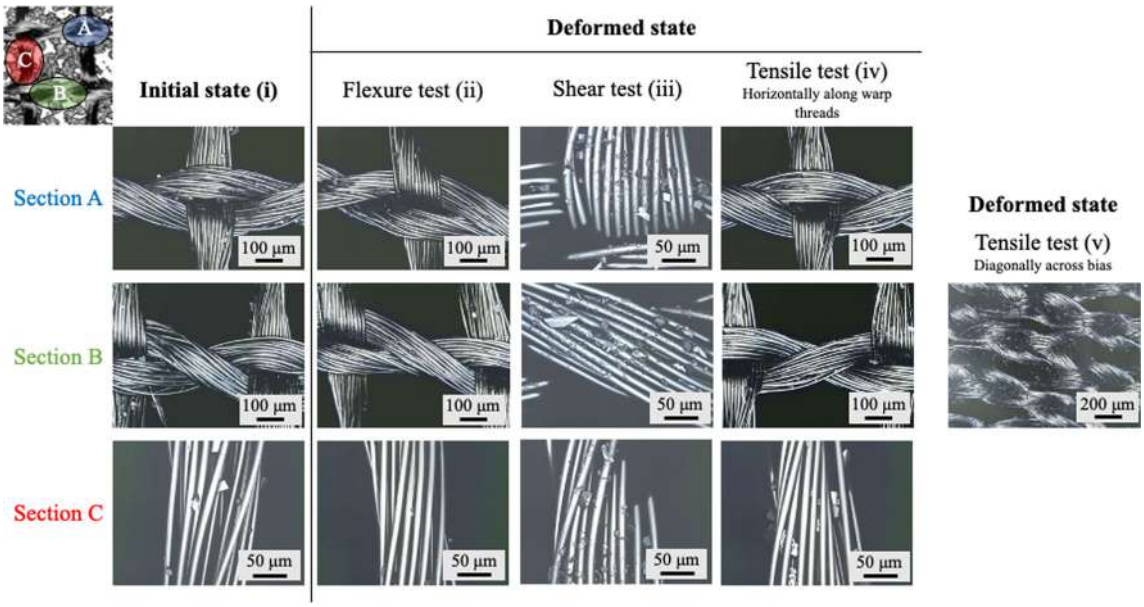


Figure 5 Micrographs of coated PGA meshes before and after mechanical tests. Three consistent areas for flexure, tensile (along warp threads), and shear testing (Sections A, B, and C). Separate area for tensile (across bias) testing.

tensile (across bias and warp), and shear stresses was assessed qualitatively in order to determine the durability (viz. continued attachment) of the discontinuous $CaCO_3$ coating.

Flexure testing

3D confocal micrographs shown in Figure 5 represent different sections of the PGA mesh before and after mechanical testing. The initial state of the coating is shown in Figure 5(1); small individual grains are observed on and between the fibres. Figure 5(2) shows the deformed state of the mesh following flexure testing; the results highlight the compliance of the microstructure, where no obvious changes in shape, number, or distribution of the grains are observed following testing.

Shear testing

3D confocal micrographs of the coated PGA mesh following shear testing are shown in Figure 5(iii). These images indicate that the gentle hand-scraping was sufficient to alter the morphologies of the calcite grains significantly, although not to scratch the PGA fibres. The apparent crushing and fragmentation resulted in more widespread distribution of the grains.

Tensile testing

3D confocal micrographs of the coated PGA mesh following tensile testing along the warp threads are shown in Figure 5(4). Again, the shape, number, and distribution of grains on the fibres before and after testing remained relatively unchanged owing to the microstructural compliance. However, for testing along the bias, as shown in Figure 5(5), the coating distribution density appears to have increased upon deformation.

In vitro incubation

pH

The pH of the solvent (PBS) following incubation of uncoated and coated samples is shown in Figure 6. The pH values of the uncoated and coated samples exhibit the same trends, where they increased from ~ 7.60 to ~ 7.65–7.70 after one week of incubation and decreased gradually to ~ 7.30 by the end of the third week. The coated samples showed higher pH values than uncoated samples in Week 1 and 2; the values converged in Week 3. The interaction effect between the incubation time and pH for the uncoated and coated samples is statistically significant ($p < 0.05$).

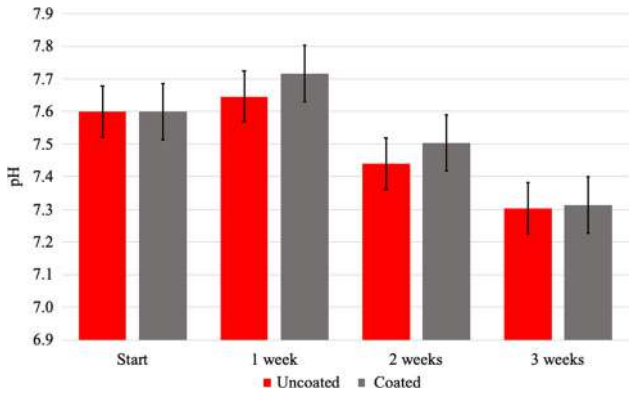


Figure 6 pH of solvent (PBS) following incubation for up to three weeks.

Calcium concentration

The changes in $[Ca^{2+}]$ of the solvent following in vitro incubation of coated samples in PBS are shown in Figure 6. There was no statistical difference in the $[Ca^{2+}]$ between the immersion intervals ($p = 0.65$). This point aside, the average values suggest a minimum at two weeks.

Discussion

A $CaCO_3$ coating was deposited on the PGA mesh by positioning the PGA mesh at the air–solution interface of a supersaturated solution of $Ca(HCO_3)_2$ at the beginning of the deposition process. It is maintained at this interface until the end of the experiment owing to surface tension and the CO_2 gas bubbles that rise to the air–solution interface due to buoyancy [20]. A deposition duration of 6 h was selected as a compromise between (1) extent of nucleation/growth of the grains and (2) hydrolytic degradation of the mesh from exposure to the solution. The crystals that nucleate earlier in the process (primary growth crystals) have more time to grow compared to crystals that nucleate later in the process (subsequent growth crystals) [16]. The solution also has access between the fibres, enabling crystal nucleation in the interstices.

The XRD results suggest that the microcrystal growth mechanism, consisting of nucleation of the (104) plane on the PGA mesh fibres and growth into the supersaturated $Ca(HCO_3)_2$ solution, is an analogue of the growth mechanism at the air–solution interface of limestone cave pools [21] and of an equivalent experimental study [16] in which calcite precipitated over 6 h at the air–solution interface of supersaturated $Ca(HCO_3)_2$ with (104) preferred orientation. It is likely that that the driving force for attachment of the $CaCO_3$ microcrystals to the PGA mesh is opposite surface charges, where $CaCO_3$ exhibits a positive surface charge at pH $\leq$ 11.4 [22] and hydrolysed PGA, which forms upon the degradation of the mesh, is negative [23].

A series of mechanical tests (flexure, tensile, shear; $n = 3$) were performed for qualitative determination of the durability of the coatings under stresses typical of the graft preparation and implantation process.

Fewer grains were observed at high magnification (Section C) following flexure testing; this may be attributed to grain loss and/or inhomogeneous distribution during the deposition process. The discontinuous nature of the coating, which is comprised of individual and small clusters of calcite microcrystals on and between the PGA mesh fibres, enables the coating to remain intact. This represents an advantage over continuous hard mineral coatings, which would likely crack and/or delaminate.

Shear testing showed that the apparent crushing and fragmentation resulted in more widespread distribution of the grains. These effects may be advantageous for the intended application because smaller particles have higher surface areas consistent with higher rates of dissolution, thus resulting in more rapid release of chemoattractants (Ca^{2+}). However, the smaller particles may have reduced ability to delay the degradation of the PGA mesh due to higher rates of dissolution. The retention of larger particles, likely present deeper within the textile structure, would dissolve more slowly to prolong the chemoattractant effect.

The coating distribution density appears to have increased upon deformation following tensile testing. This suggests that the calcite grains entrapped within the woven mesh structure surfaced when the fibres were reoriented. An alternative interpretation is that the calcite fragmented during testing across bias, although this seems unlikely as the same effect is not observed for testing along warp threads.

The unique formation mechanism enabled the supersaturated $Ca(HCO_3)_2$ solution to penetrate the interstices between the fibres, resulting in crystal nucleation and growth of embedded calcite grains throughout the duration of the deposition process. PGA fibres in contact with $Ca(HCO_3)_2$ behave

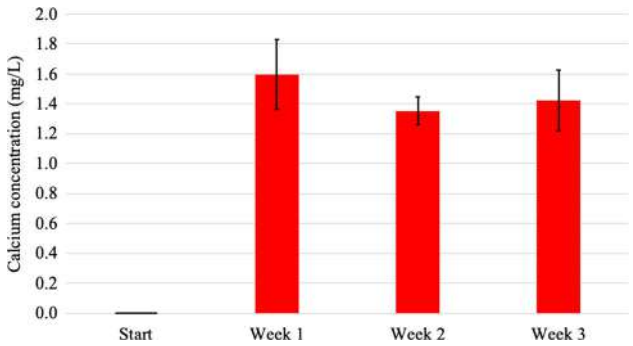


Figure 7 Calcium concentration of solvent (PBS) following incubation for up to 3 weeks.

analogously to cotton fibres in the traditional indigo dye process [24], where cotton fibres are immersed in leuco-indigo, a soluble form of indigo dye. This enables more indigo dye to be precipitated and become entrapped between the cotton threads when lifted from the vat.

In vitro incubation was conducted in order to assess $CaCO_3$ dissolution over a 3-week period.

The in vitro incubation of coated samples caused opposing effects on the pH of the solvent. That is, dissolution of the coating (CaCO3 grains) increases [Ca^{2+}] and [HCO_3^-] in the solvent, which increase the pH [25]. In contrast, glycolic acid, the degradation product of PGA [26], decreases the pH of the solvent.

The PBS solution initially does not contain Ca^{2+} (as measured by ICP-OES; see below). Hence, $CaCO_3$ dissolution would dominate in Week 1; the higher pH of coated samples than uncoated samples is consistent with this interpretation. The decreasing trend in pH observed in Weeks 2 and 3 may be attributed to PGA degradation; the pH of coated samples remains higher than uncoated samples due to the continuing dissolution of $CaCO_3$. The pH values for uncoated and coated samples converged in Week 3. There are a few possible interpretations: (1) the coating had completely dissolved, resulting in no additional Ca^{2+} and HCO_3^- release in the solution; (2) the solution became saturated with respect to calcite; or (3) the opposing effects of PGA degradation and $CaCO_3$ dissolution had a balancing effect on pH.

Further, the data presented in Figure 7, and those of Figure 5, indicate that the calcium concentration fluctuates throughout the incubation period. During week 1, the solubility of $CaCO_3$ is high owing to intrinsic solubility of Ca^{2+}in PBS and there is limited mesh degradation. During week 2, the solubility of $CaCO_3$ decreased as the solvent approaches saturation with respect to calcite under static conditions. During week 3, the solubility of $CaCO_3$ increased as the continued degradation of PGA results in higher levels of glycolic acid. The convergence of the pH values for uncoated and coated samples at this time point reflects equalization of the opposing effects ($CaCO_3$ dissolution and mesh degradation).

Conclusions

A discontinuous $CaCO_3$ coating was deposited on PGA meshes by an original interfacial technique. The PGA meshes were maintained at the air–solution interface of a supersaturated solution of $Ca(HCO_3)_2$ and heat-treated at 33 °C for 6 h. The saturation gradient that formed due to evaporation and CO_2 degassing enabled the heterogeneous nucleation/growth of $CaCO_3$ along the PGA mesh at the air–solution interface. This technique overcomes several challenges presented by the existing techniques to coat PGA with hard minerals: the deposition temperature is below the onset of the glass transition temperature of PGA (35 °C) [1], and the exposure time is relatively short, thereby avoiding hydrolytic degradation [11], 12, 13].

XRD and 3D microscopy showed that the coating was comprised of microcrystals of calcite ranging in size from ~ 10 to 25 μm and that they were deposited on and throughout the textile structure. The mechanical tests (flexure, tensile, and shear) showed that the coating was durable when exposed to stresses typical of the graft preparation and implantation process. Notably, the grains moved with the mesh when contorted and the tension test performed diagonally across the bias confirmed that grains were embedded within the textile structure. This is attributed to the deposition technique, where supersaturated $Ca(HCO_3)_2$ can access the interstices between fibres, enabling crystals to nucleate and grow in these locations. The interaction effect between the incubation time and pH for the uncoated and coated samples was statistically significant ($p < 0.05$).

The in vitro studies also suggested that the variable chemistry and pH were derived from the competing effects of $CaCO_3$ solubility in PBS, which raises the pH, and PGA mesh degradation and glycolic acid production, which lowers the pH. The solution would have become saturated with respect to calcite

and increasingly acidic due to the static incubation conditions. Consequently, the lifetime of the discontinuous coating would likely be shortened by the localized acidic environment formed by the glycolic acid product of mesh degradation in these static conditions.

PGA mesh with a discontinuous $CaCO_3$ coating has orthopaedic applications: (1) delay in the degradation profile of PGA mesh to match the bone healing process [8], 9]; (2) Ca^{2+} leaching for a chemo-attractive effect on osteoblasts, MSCs, and monocytes [5], 6, 7]; (3) slow release of glycolic acid for immunomodulation [10].

Acknowledgements

The authors thank Mr. B. Joe and Dr. G. Yang (School of Materials Science and Engineering, UNSW Sydney) for assistance with characterization techniques, equipment set-up, and training. The authors thank Ms. R. Akter for performing ICP-OES (Mark Wainwright Analytical Centre, UNSW Sydney). The authors acknowledge in-kind materials support from Medtronic, Minneapolis, MN, through the External Research Program as well as funding support from the Australian Commonwealth Government via the Research Training Program.

Funding

Open Access funding enabled and organized by CAUL and its Member Institutions.

Declarations

Conflicts of interest The authors declare no conflicts of interest.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

References

[1] Budak K, Sogut O, Aydemir Sezer U (2020) A review on synthesis and biomedical applications of polyglycolic acid. J Polym Res 27:1–19. https://doi.org/10.1007/s10965-020-02187-1

[2] NaPier Z, Kanim LEA, Thordarson S et al (2016) demineralized bone matrix bone biology and clinical use. Semin Spine Surg 28:196–216. https://doi.org/10.1053/j.semss.2016.08.003

[3] Medtronic MM (2017) White Paper: degradation and removal of the graft delivery bag component of magnifuseTM bone graft. Minneapolis

[4] Silver IA, Murrills RJ, Etherington DJ (1988) Microelectrode studies on the acid microenvironment beneath adherent macrophages and osteoclasts. Exp Cell Res 175:266–276. https://doi.org/10.1016/0014-4827(88)90191-7

[5] Sugimoto T, Kanatani M, Kano J et al (1993) Effects of high calcium concentration on the functions and interactions of osteoblastic cells and monocytes and on the formation of osteoclast-like cells. J Bone Miner Res 8:1445–1452

[6] Yamaguchi T (2008) The calcium-sensing receptor in bone. J Bone Miner Metab 26:301–311. https://doi.org/10.1007/s00774-008-0843-7

[7] Lee MN, Hwang H, Oh S et al (2018) Elevated extracellular calcium ions promote proliferation and migration of mesenchymal stem cells via increasing osteopontin expression. Exp Mol Med 50:1–16. https://doi.org/10.1038/s12276-018-0170-6

[8] Khan SN, Cammisa FP, Sandhu HS, et al (2005) The biology of bone grafting

[9] Kim YK, Kim SG, Lim SC et al (2010) A clinical study on bone formation using a demineralized bone matrix and resorbable membrane. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. https://doi.org/10.1016/j.tripleo.2010.01.012

[10] Zhang J, Xie B, Xi Z et al (2020) A comparable study of polyglycolic acid's degradation on macrophages' activation. Mater Sci Eng C 109:110574. https://doi.org/10.1016/j.msec.2019.110574

[11] Kang SW, Yang HS, Seo SW et al (2008) Apatite-coated poly(lactic-co-glycolic acid) microspheres as an

injectable scaffold for bone tissue engineering. J Biomed Mater Res - Part A 85:747–756

[12] Chen YZ, Mak AFT, Wang M (2005) Accelerated formation of bone-like apatite on biodegradable polymer substrates. Key Eng Mater 284–286:509–512. https://doi.org/10.4028/www.scientific.net/kem.284-286.509

[13] Murphy WL, Kohn DH, Mooney DJ (2000) Growth of continuous bonelike mineral within porous poly(lactide-co-glycolide) scaffolds in vitro. J Biomed Mater Res 50:50–58. https://doi.org/10.1002/(SICI)1097-4636(200004)50:1%3c50::AID-JBM8%3e3.0.CO;2-F

[14] Lanao RPF, Jonker AM, Wolke JGC et al (2013) Physicochemical properties and applications of poly(lactic-co-glycolic acid) for use in bone regeneration. Tissue Eng Part B Rev 19:380–390. https://doi.org/10.1089/ten.teb.2012.0443

[15] Kovacs SE, Reinhardt EG, Werner C et al (2018) Seasonal trends in calcite-raft precipitation from cenotes rainbow, feno and monkey dust, quintana roo, Mexico: Implications for paleoenvironmental studies. Palaeogeogr Palaeoclimatol Palaeoecol 497:157–167. https://doi.org/10.1016/j.palaeo.2018.02.014

[16] Lui FHY, Wang Y, Yao Y et al (2021) Quiescent mineralisation for free-standing mineral microfilms with a hybrid structure. J Colloid Interface Sci 604:327–339

[17] Sawada M, Sridhar K, Kanda Y, Yamanaka S (2021) Pure hydroxyapatite synthesis originating from amorphous calcium carbonate. Sci Rep. https://doi.org/10.1038/s41598-021-91064-y

[18] Lui FH, Mobbs RJ, Wang Y, Koshy P, Lucien FP, Zhou D, Sorrell CC (2021) Dynamic Mineralization: Low-Temperature, Rapid, and Multidirectional Process to Encapsulate Polyether-Ether-Ketone with Carbonate-Rich Hydroxyapatite for Osseointegration. Adv Mater Interfaces 15:2100333

[19] Lui FH, Wang Y, Yao Y, Mobbs RJ, Pogson RE, Koshy P, Lucien FP, Zhou D, Sorrell CC (2021) Quiescent mineralisation for free-standing mineral microfilms with a hybrid structure. J Colloid Interface Sci 604:327–339

[20] Liger-Belair G, Sternenberg F, Brunner S et al (2015) Bubble dynamics in various commercial sparkling bottled waters. J Food Eng 163:60–70. https://doi.org/10.1016/j.jfoodeng.2015.04.016

[21] Taylor MP, Drysdale RN, Carthew KD (2004) The formation and environmental significance of calcite rafts in tropical tufa-depositing rivers of Northern Australia. Sedimentology 51:1089–1101. https://doi.org/10.1111/j.1365-3091.2004.00661.x

[22] Plank J, Bassioni G (2007) Adsorption of Carboxylate Anions on a CaCO3 Surface

[23] Gao J, Niklason L, Langer R (1998) Surface hydrolysis of poly (glycolic acid) meshes increases the seeding density of vascular smooth muscle cells. J Biomed Mater Res: Off J Soc Biomater Jpn Soc Biomater Aust Soc Biomater 42(3):417–424

[24] Nakagawa K, Takeuchi M, Kikuchi M et al (2021) Mechanistic insights into indigo reduction in indigo fermentation: A voltammetric study. Denki Kagaku 89:25–30. https://doi.org/10.5796/ELECTROCHEMISTRY.20-00123

[25] Gutjahr A, Dabringhaus H, Lacmann R (1996) Studies of the growth and dissolution kinetics of the CaCO 3 polymorphs calcite and aragonite I. Growth and dissolution rates in water 1. J Cryst Growth 158:296–309

[26] Chu C-C, Louie M (1985) A chemical means to study the in vitro hydrolytic degradation of Poly(glycolic acid). J Appl Polym Sci 30:3133–3141

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.