Poly-4-hydroxybutyrate (P4HB) Fully Absorbable Scaffolds for Soft Tissue Support in 3D Applications

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Introduction: Plastic and reconstructive surgeons often use cadaveric or animal-derived acellular matrices to support soft tissue in breast applications. However, variability in the species, source, structure, integrity, and processing of donor cadaveric and animal tissue can lead to variable mechanical and tissue integration performance over time.

Poly-4-hydroxybutyrate (P4HB) is a fully absorbable biologically-derived polymer that has been successfully utilized in General, Plastic and Orthopedic Surgery applications when configured as a monofilament knitted scaffold. The performance features of such scaffolds can be well controlled, and the ability to thermally mold P4HB knitted constructs into various shapes makes them well suited for use to support soft tissue in challenging 3-dimensional anatomies. The objectives of this study were to evaluate the mechanical, histological, morphologic and molecular weight properties of a fully absorbable, 3D-shaped P4HB scaffold over time following implantation in a rabbit dorsal model and to highlight some clinical outcomes[1,2] for this device.

Methods: TephaFLEX® P4HB™ biopolymer (Tepha, Inc., Lexington, MA) is biosynthesized through a proprietary fermentation process. Melt extruded P4HB fibers were knitted into macroporous, monofilament scaffolds. The scaffolds were subsequently thermally molded into 3D shapes to form the GalaFLEX® 3DR scaffold (Galatea Surgical, Lexington, MA), see Figure 1. Twelve New Zealand White (NZW) rabbits were implanted with 3D shaped GalaFLEX 3DR and flat GalaFLEX scaffolds for 4, 8, 12 and 40 weeks (n=4 rabbits/group 4, 8 wks, 2 rabbits/group 12 and 40 wks). Each rabbit underwent bilateral dorsal subcutaneous implantation of two (4x4cm) of each scaffold (n=4) and smaller (1x1 cm) samples of each scaffold for histology. Upon explantation, fibrotic tissue was digested with collagenase to allow for testing of the polymeric scaffold only. The scaffolds were mechanically evaluated to determine the residual strength retention over time. Gel permeation chromatography (GPC) was used to evaluate the molecular weight (Mw) of the collagenase-digested P4HB (4x4cm) scaffolds. Lastly, explanted specimens (1x1 cm) were paraffin embedded, sectioned, stained (H&E and Trichrome) and histologically evaluated to determine the resulting host inflammatory and fibrotic response, neovascularization and maturation of remodeled tissue.

Results: The mechanical ball burst strength (3/8" probe) of explanted scaffolds was evaluated after collagenase digestion to remove incorporated tissue. The scaffolds retained approx. 25-35% of their initial bursting strength at 40 weeks post-implantation, with no statistical difference demonstrated between GalaFLEX 3DR and the flat GalaFLEX scaffolds at any time point, see Figure 2. GPC analysis showed a decrease in the polymer Mw of 72-73% at 40 weeks post-implantation, also with no statistical difference between scaffold types. Histologically GalaFLEX 3DR was graded as a non-irritant, as compared to the GalaFLEX scaffold at all time points.

Figure 1. Images of GalaFLEX® 3DR, 3D-shaped P4HB monofilament scaffolds.

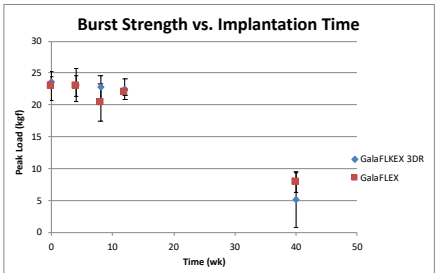

Figure 2. Ball burst strength (3/8" probe) of 3D-shaped GalaFLEX 3DR scaffold over time after implantation, as compared to the control flat GalaFLEX scaffold.

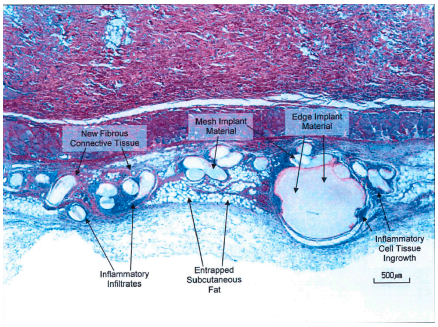

Figure 3. Histological photomicrograph of GalaFLEX 3DR scaffold at 40 weeks post-implantation, indicative of new fibrous connective tissue and neovascularization. H&E stain, 20X magnification.

Conclusions: P4HB scaffolds facilitate rapid cellular infiltration, neovascularization, tissue integration and remodeling with mechanical support of soft tissue over time. 3D-shaped P4HB scaffolds represent a unique fully absorbable biologically-derived alternative to cadaveric- or animal-derived scaffolds for soft tissue repair and support.

References:

1) Adams Jr, W.P., et al. 2018. The use of poly-4-hydroxybutyrate (P4HB) scaffold in the ptotic breast: a multicenter clinical study. *Aesthetic Surgery Journal*, *38*(5), pp.502-518.

2) Van Natta, B., Kortesis, B.G. and Bharti, G., 2020. Use of Soft Tissue Support in Augmentation Mastopexy. In *Augmentation Mastopexy* (pp. 281-290). Springer, Cham.