Fully Absorbable Poly-4-hydroxybutyrate (P4HB) Scaffold Provides Mechanical Support at 12 months Following Vaginal Implantation in an Ovine Model

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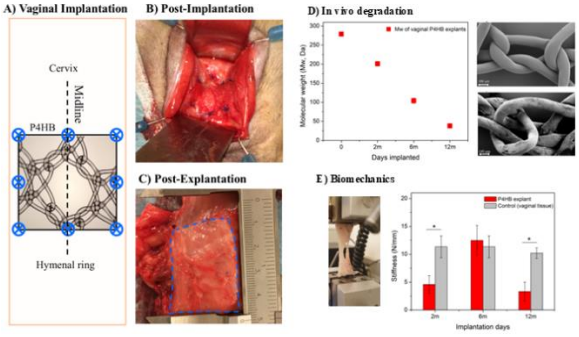
Statement of Purpose: Pelvic organ prolapse (POP) is a common condition resulting from damage to the supportive structures of the pelvic floor, which cause protruding of the visceral organs of the pelvic cavity out of the vagina[1]. The annual incidence of surgery for POP is approximately 4.9 cases per 1000 women, and the overall life-time risk for surgery is 11%[2]. Synthetic permanent meshes are often used during the surgical repair of prolapse to provide mechanical support to the tissues by inducing a foreign body response[3]. However, they have been associated with clinical complications, therefore our current research focuses on a fully absorbable alternative for POP repair to minimize the risk of long-term complications.

Our research group has identified Poly-4-hydroxybutyrate (P4HB) as a candidate material for vaginal POP surgery. P4HB is a fully absorbable polymer with high strength and durability, and unlike other absorbable polyesters, does not create an acidic environment during degradation[4]. Our previous *in vitro* results have shown gradual scaffold degradation over time, enhanced vaginal fibroblast proliferation/collagen deposition[5], and decreased bacterial adhesion[6], as compared to permanent synthetic mesh. Therefore, we aimed to further evaluate the *in vivo* performance of a P4HB scaffold over time following vaginal implantation in an ovine model.

Methods: P4HB scaffolds (35 mm x 35 mm) (n=8 per time point) were surgically implanted within the posterior vaginal wall of sheep. Specimens were explanted at 2-, 6- and 12-months following implantation. Specimens stained with hematoxylin-eosin for polymorphonuclear (PMN) and foreign body giant cell (FBGC) evaluation at the scaffold-tissue interface. The inflammatory response was subsequently evaluated by semi-quantitative scoring (absent=0, mild presence=1, large presence=2, abundance=3, great abundance=4). Furthermore, stiffness of the vaginal explants was determined by uniaxial tensile testing using a 200N load cell. Lastly, P4HB scaffold degradation was evaluated by measuring polymer molecular weight (Mw) via gel permeation chromatography (GPC).



Results: P4HB scaffold resulted in moderate foreign body response indicated by mild FBGC and PMN presence. The stiffness of the vaginal P4HB explants after 6-months was significantly increased to 12.498 ± 2.66 N/mm, as compared to 2 months post-implantation, and exhibited a comparable stiffness with the native vaginal tissue (11.343 ± 1.96 N/mm). At 12 months, the stiffness of the vaginal explants was lower (3.32 N/mm ± 0.95). P4HB scaffold gradually degraded over time, as indicated by an 86% reduction in Mw observed by 12 months (T0: 279 kDa, 2m: 201 kDa, 6m: 104 kDa and 12 m: 39 kDa).

Conclusions: The P4HB scaffold exhibited an acceptable foreign body response and tissue integration in vaginal tissue over time. The scaffold provided acceptable mechanical support without creating excessively stiff tissue and facilitated gradual load transfer to vaginal tissue. The P4HB scaffold may provide an alternative to permanent synthetic mesh for soft tissue support within pelvic floor. Our next goal is to clinically evaluate the performance of P4HB scaffold for the treatment of POP in humans.

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