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Characterization of poly-4-hydroxybutyrate mesh for hernia repair applications

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ABSTRACT

Background: Phasix mesh is a fully resorbable implant for soft tissue reconstruction made from knitted poly-4-hydroxybutyrate monofilament fibers. The objectives of this study were to characterize the *in vitro* and *in vivo* mechanical and resorption properties of Phasix mesh over time, and to assess the functional performance in a porcine model of abdominal hernia repair.
Materials and methods: We evaluated accelerated *in vitro* degradation of Phasix mesh in 3 mol/L HCl through 120 h incubation. We also evaluated functional performance after repair of a surgically created abdominal hernia defect in a porcine model through 72 wk. Mechanical and molecular weight (MW) properties were fully characterized in both studies over time.
Results: Phasix mesh demonstrated a significant reduction in mechanical strength and MW over 120 h in the accelerated degradation *in vitro* test. *In vivo*, the Phasix mesh repair demonstrated 80%, 65%, 58%, 37%, and 18% greater strength, compared with native abdominal wall at 8, 16, 32, and 48 wk post-implantation, respectively, and comparable repair strength at 72 wk post-implantation despite a significant reduction in mesh MW over time.
Conclusions: Both *in vitro* and *in vivo* data suggest that Phasix mesh provides a durable scaffold for mechanical reinforcement of soft tissue. Furthermore, a Phasix mesh surgical defect repair in a large animal model demonstrated successful transfer of load bearing from the mesh to the repaired abdominal wall, thereby successfully returning the mechanical properties of repaired host tissue to its native state over an extended time period.

1. Introduction

The development of a resorbable mesh that can provide an abdominal closure with adequate long-term mechanical stability remains an attractive goal, provided that recurrence rates and chronic complications can be minimized. However, until now, the use of fully resorbable synthetic surgical meshes in hernia repair has resulted in a high frequency of incisional hernias because of the short-term strength retention of those materials [1]. For this reason, fully resorbable meshes have traditionally been used for temporary, short-term wound support rather than for long-term use in hernia

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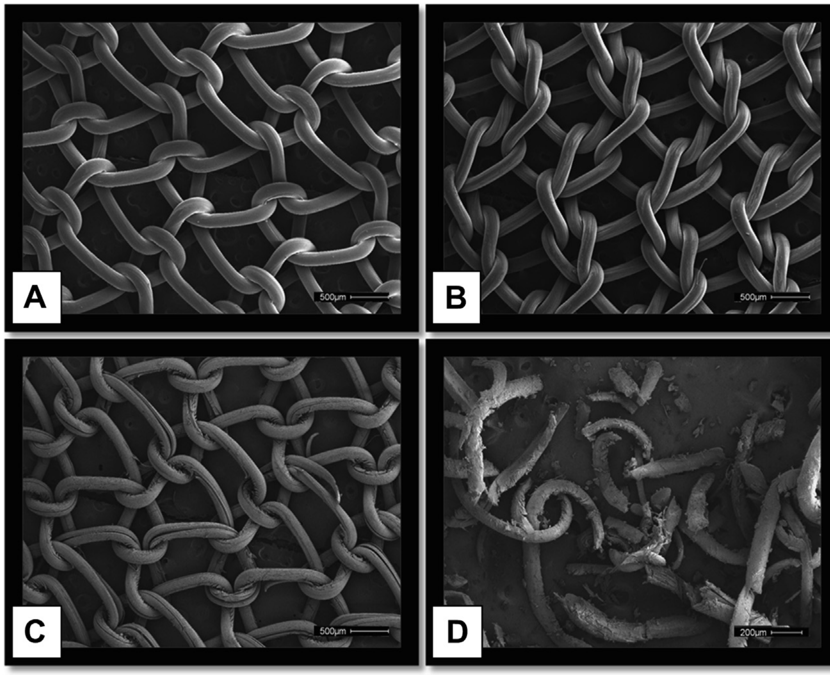

Fig. 1 – Scanning electron microscopy photomicrographs of Phasix mesh before (A) and after incubation in 3 mol/L HCl (simulating polymer degradation) for 32 (B), 72 (C), and 96 (D) h. Note the higher magnification of (D) (scale bar = 200 *versus* 500 μm for [A–C]), which better illustrates the near-complete loss of the fiber integrity.

repair, and permanent meshes remain the standard for hernia repair.

As an alternative to permanent mesh, our goal was to develop a long-term, resorbable hernia repair mesh that could provide the necessary support at the repair site during the initial wound healing period while allowing tissue ingrowth and progressive transfer of mechanical load from the mesh to the host tissue over time. We hypothesized that this gradual load transfer would promote tissue remodeling such that the repaired tissue could eventually provide long-term function similar to that of native tissue. Once the repaired tissue is capable of supporting the load and the mesh is no longer needed, a resorbable mesh can degrade to leave behind healthy host tissue. Preferably, at the time of implant, the resorbable mesh should also offer comparable properties to traditional hernia mesh materials, such as polypropylene, and similar wound healing with compliance at the repair site that would ultimately mature to that of the native abdominal wall (NAW) as the mesh becomes integrated and resorbed over time.

Phasix mesh (C.R. Bard, Inc [Davol], Warwick, RI) is a biosynthetic resorbable monofilament mesh, derived from poly-4-hydroxybutyrate (P4HB), specifically designed for hernia repair. Poly-4-hydroxybutyrate is a fully resorbable polymer produced by the microorganism *Escherichia coli* K12 via transgenic fermentation techniques [2]. Phasix mesh is made of knitted monofilaments of this naturally derived polymer (Fig. 1A). The mesh provides immediate short-term support similar to traditional nonresorbable meshes, but provides an absorbable scaffold that enables the abdominal wall to remodel to host tissue over time. Poly-4-hydroxybutyrate is a high-strength polyester [2] that degrades in a predictable and steady manner to a natural metabolite (4-hydroxybutyrate [4HB]) that is normally present in human tissues [3]. The metabolite has an *in vivo* half-life of approximately 30 min [4,5] and is eliminated via the Krebs cycle as carbon dioxide and water [2,6]. The Phasix mesh has a knitted mesh pattern similar to traditional Bard polypropylene mesh (C.R. Bard, Inc); before implantation, the mechanical properties also resemble those of Bard mesh (Table 1).

The purposes of this study were to evaluate the performance of the Phasix mesh as a buttress to reinforce the primary repair of an approximate 2.5-cm (or 1-in) circular abdominal wall defect in a porcine model, and to correlate the *in vivo* behavior of the Phasix mesh with its *in vitro* degradation profile. The primary end points of the *in vivo* study were to determine the strength

Table 1 – Comparison of properties of Phasix mesh and Bard mesh.

Mechanical/physical properties	Phasix mesh	Bard mesh
Material	Poly-4-hydroxybutyrate	Polypropylene
Pore size (in^2)	0.0004	0.0009
Thickness (in)	0.02	0.03
Area density (g/m^2)	182	105
Ball burst strength (lb force with 3/8-in ball)	54.11	68.0
Suture pull out strength (kgf)	5.6	8.0

The Phasix mesh used in all studies was a warp knit mesh design made from high-strength P4HB monofilament fiber. The material was sterilized using ethylene oxide. The initial mechanical and physical properties of Phasix mesh are compared with nonresorbable monofilament polypropylene Bard mesh.