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ORIGINAL ARTICLE

Abdominal wall hernia repair: a comparison of Permacol® and Surgisis® grafts in a rat hernia model

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Abstract
Background This study compared two porcine-derived grafts Permacol (Tissue Science Laboratory, Covington, GA, USA) and Surgisis (Cook Surgical, Bloomington, IN, USA) in terms of strength of incorporation (SOI), incorporation of host tissue, and adhesion formation using a rat model.
Methods A prospective randomized study using 48 Sprague–Dawley rats. A standardized 1.5 × 5 cm fascial defect was created and repaired with either Permacol or Surgisis grafts. The rats were then sacrificed at 3, 14, 28, or 60 days. The specimens were examined for SOI, neovascularization, collagen deposition, collagen organization, and adhesion formation.
Results Surgisis had significantly greater SOI than Permacol at 28 (0.115 vs. 0.0754 Mpa) and 60 days (0.131 vs. 0.635 Mpa). Surgisis had significantly more collagen deposition and neovascularization than Permacol at 60 days. The area of adhesions was not significantly different between Surgisis and Permacol.
Conclusion Surgisis is superior to Permacol in terms of SOI and tissue ingrowth at 60 days. Furthermore, Surgisis strengthened over time whereas Permacol decreased in strength.

Keywords Surgisis · Permacol · Abdominal wall reconstruction · Hernia · Mesh · Collagen · Porcine

Introduction

Abdominal wall reconstruction for resection of abdominal wall tumors, repair of ventral hernias, or following trauma can be a complex and challenging task for general surgeons. Multiple techniques have been described in the literature to repair these fascial defects. Primary repair, while certainly the simplest method, is often associated with unacceptably high tension, resulting in hernia recurrence rates between 43 and 63% [1, 2]. The development of prosthetic mesh has significantly decreased the tension and recurrence rates following abdominal wall reconstruction [1, 2]. However, prosthetic mesh is still associated with complications including fistula formation, bowel obstruction, skin erosion, and mesh infection in 1–15% of cases [3–5]. Furthermore, the use of prosthetic mesh in a contaminated field has dismal results with 50–90% of patients requiring eventual mesh removal [6, 7]. Recent studies have challenged the concept that contamination is a contraindication to reconstruction with prosthetic mesh. However, these reports are limited in terms of being small retrospective studies [8, 9]. While this area is controversial

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most surgeons would be hesitant to place a prosthetic mesh in a contaminated field.

The ideal mesh would provide not only strength and flexibility, but would also provide a scaffold for tissue incorporation and resistance to infection. Newer biosynthetic grafts have been developed to satisfy these properties. Currently biosynthetic grafts are available from both human cadaveric (Alloderm) and porcine (Permacol, Surgisis) sources. These grafts are all composed of an acellular collagen scaffold to provide tissue incorporation and neovascularization. Tissue ingrowth and neovascularization are thought to give biosynthetic grafts some inherent resistance to infection. In the literature there are multiple case series to support the use of biosynthetic grafts in contaminated wounds [10–14].

Permacol is a porcine-derived acellular cross-linked dermal matrix, manufactured by Tissue Science Laboratories. Permacol undergoes trypsinization to remove living cells and noncollagenous material, solvent extraction to remove lipids and fat deposits, gamma irradiation, and isocyanate cross linkage [15, 16]. Permacol grafts are available in multiple sizes with a standard thickness of 1 mm for hernia repairs. The sheets are kept moist in sterile saline and can be stored at room temperature.

Surgisis is also a porcine derived graft obtained from the small intestine submucosa, manufactured by Cook Surgical. The graft is acellular and composed of non-cross-linked collagen (Types I, III, and V), glycosaminoglycans, proteoglycans, glycoproteins, and multiple growth factors [17]. Surgisis is also available in multiple sizes and can be stored at room temperature.

Studies have previously demonstrated tissue incorporation and neovascularization of Surgisis in both animal hernia and subcutaneous models [17–20]. Permacol has previously been studied as a soft tissue implant, but has never been studied in an animal model [21, 22]. Furthermore, there are currently no prospective randomized trials to compare commercially available porcine-derived grafts in terms of SOI, tissue ingrowth, neovascularization, and adhesion formation. The purpose of this study was to perform such a comparison of Permacol and Surgisis grafts in a rat hernia model.

Methods

Overview

Research was conducted in compliance with the Animal Welfare Act and followed the guidelines set forth by the Guide for the Care and Use of Laboratory Animals, NRC publications, 1986 edition. All procedures were reviewed and approved by the Institution's Animal Care and Use Committee and were performed in a facility accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care, International. All materials were purchased by the Eisenhower Army Medical Center Department of Clinical Investigations. Forty-eight adult male Sprague–Dawley rats, between ages 14 and 16 weeks, were used in this study. The rats were randomly divided into two groups of 24 rats. Six rats from each group were sacrificed and examined at 3, 14, 28, and 60 days.

Surgical procedure

The rats were anesthetized by intraperitoneal administration of ketamine (65 mg/kg). All surgical procedures were performed under sterile conditions. Under anesthesia each animal's abdomen was shaved and prepped. The right rectus abdominis muscle was exposed through a 5 cm midline skin incision. Adequate skin flaps were raised to expose the underlying abdominal wall fascia. A full-thickness fascial defect of the right rectus abdominis muscle, which was measured to be 1.5 × 5 cm, was then removed (Fig. 1). The fascial defect was then repaired with either Permacol (1.0 mm thickness) or Surgisis Gold (8-ply). The animals were randomly divided into two groups, each consisting of 24 rats. Experimental group I underwent repair of the defect with a Permacol graft. The graft was sutured in an underlay fashion to the fascial defect with interrupted 4–0 silk sutures (Fig. 2). Experimental group II was repaired in an identical fashion with Surgisis Gold. The skin incisions

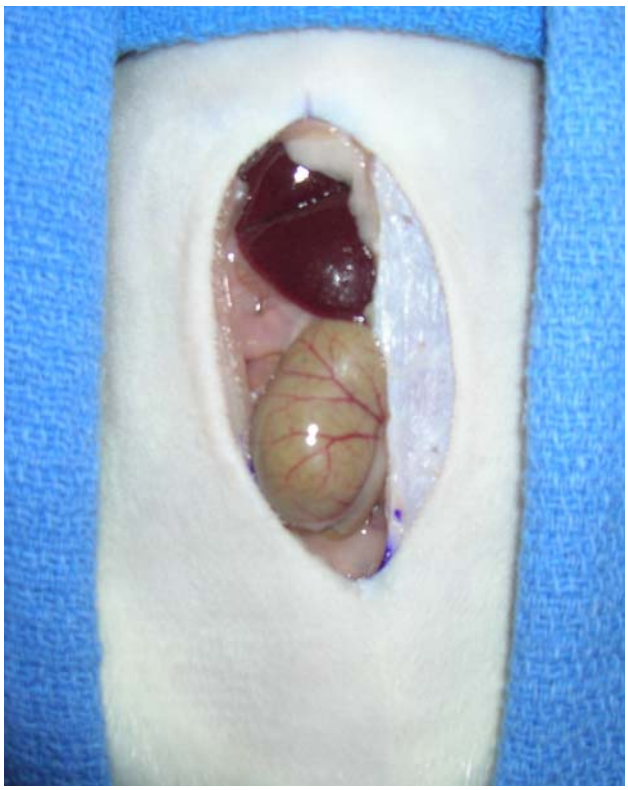

Fig. 1 Standardized 1.5 × 5 cm defect

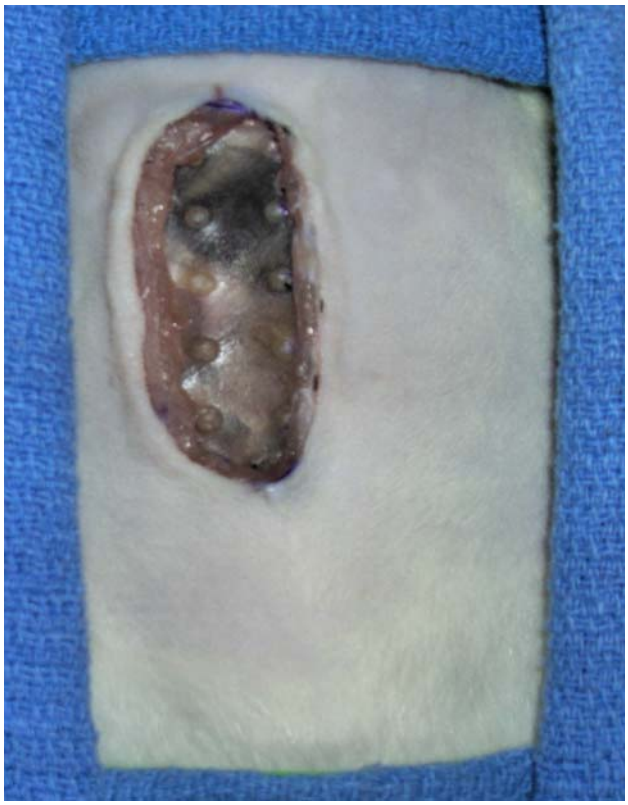

Fig. 2 Underlay repair

were then closed with 4–0 nylon sutures in an interrupted fashion.

The animals were allowed to recover from the surgical procedure. Necropsy and specimen examination of six rats from both experimental groups were conducted at 3, 14, 28, and 60 days. Sacrifice of the rats was performed humanely. The full thickness abdominal wall specimen including the graft and surrounding abdominal wall were excised and evaluated for tensile strength, histological evaluation and adhesion formation.

Tensile strength testing

The breaking strength was tested with an Instron 4502 Tensiometer. After procurement, the specimens were divided into five equal strips. The middle strip of the abdominal wall was placed vertically between two pneumatic clamps of the tensiometer. The force was then applied across the suture line with a one-pound load cell at a constant speed of 10 mm/s, until rupture. The maximal force required for disruption was recorded for each sample.

Histological analysis

Histological samples were taken from both experimental groups at 14 and 60 days. The samples were fixed in 10% formalin after which the specimens were sectioned, mounted, and stained with trichrome blue. A blinded observer determined the collagen organization and amount at 10× magnification under light microscopy. The scale used in our study is a semi quantitative histological analysis, which is analogous to that described by Konstantinovic et al. (Table 1) [17]. Four random sites at the graft abdominal wall interface were examined under 40× magnification. The mean number of blood vessels/hpf of each randomly selected site were then recorded and averaged for each specimen.

Adhesion assessment

At 60 days, any adhesions to the graft were removed by sharp dissection and marked with India ink stain. A digital photograph was taken of the explanted biological implants. A blinded observer calculated the area of the adhesion. The area of adhesion was then divided by the area of the implant at explantation and recorded for each specimen.

Statistical analysis

Two-way analysis of variance was used to compare the tensile strength (in megapascals) of the repaired abdominal wall and calculated as the maximal breaking strength (in newtons) per cross-sectional area (in square millimeters) between the two meshes at different time points. The average amount and organization of collagen deposition at 60 days was tabulated and compared by the Student's *t* test. The average number of blood vessels/hpf was also compared by Student's *t* test between the graft explants at 60 days. A *p* value of less than 0.05 was considered statistically significant for all tests.

Results

All the study rats survived until the completion of the experiment. At the time of sacrifice no hernias had occurred in either group. No wound infections occurred in either group.

Strength of incorporation

The tensile strength (in mega pascals) of the graft abdominal wall interface was calculated as the maximal breaking

Table 1 Histological scoring system for microscopic examination

Collagen	Score			
	0	1	2	3
Organization	Disorganized	Mildly organized	Moderately organized	Well organized
Amount	None	Mild	Moderate	Abundant

strength (in newtons) per cross-sectional area (in square millimeters) (Table 2). The data were analyzed by two-way analysis of variance with a $p < 0.05$ considered significant (Fig. 3). All grafts in the study were noted to disrupt at the graft abdominal wall interface. At baseline (3 days) there was no statistical difference between the SOI of the two grafts (SIS 0.0329 ± 0.00913 MPa vs. Permacol 0.0383 ± 0.00913; $p = 0.67$). At 28 days the Surgisis had significantly greater SOI compared with Permacol (0.115 ± 0.00913 MPa vs. 0.0754 ± 0.00913 MPa; $p = 0.004$). The SOI of Surgisis remained statistically greater than Permacol at 60 days (0.131 ± 0.00913 MPa vs. 0.0587 ± 0.00913 MPa; $p < 0.001$). Overall the SOI of Surgisis increased from day 14 (0.101 ± 0.00913 MPa) to day 60 (0.131 ± 0.00913 MPa), however the increase was not statistically significant ($p = 0.117$). Permacol decreased in strength from day 14 (0.0879 ± 0.00846 MPa) to day 60 (0.0587 ± 0.00913), but this also was not statistically significant. Furthermore, when comparing Permacol at 3 and 60 days there was no statistical difference in SOI (0.0383 ± 0.00913 Mpa vs. 0.0587 ± 0.00913 Mpa; $p = 0.401$).

Collagen amount and organization

Table 3 exhibits the semi-quantitative results of neovascularization, collagen amount, and collagen organization. All the histological examinations were compared utilizing the Student's *t* test with a significant *p* value of less than 0.05. The blood vessel count per high powerfield was statistically higher $p < 0.05$ in the SIS group (20.042 ± 1.531 vessels) compared with the Permacol group (12 ± 1.368 vessels) at 60 days. The collagen amount for the Surgisis (2.5 ± 0.224) group was greater than for the Permacol group (1.167 ± 0.167) $p < 0.05$ at 60 days. Surgisis also displayed a more organized pattern of collagen deposition (2.667 ± 0.211) compared to Permacol (1.667 ± 0.211) $p < 0.05$ (Figs. 4, 5). Additionally, the Permacol graft persisted throughout the study and was noted to have collagen deposition only peripherally encapsulating the graft (Fig. 5).

Table 2 Tensile strength testing

Days	Surgisis		Permacol		*N*
	MPa	SEM	MPa	SEM	
3	0.0329	0.00913	0.0383	0.00913	6
14	0.101	0.00913	0.0879	0.00846	6
28	0.115	0.00913	0.0754	0.00913	6
60	0.131	0.00913	0.0587	0.00913	6

Strength of incorporation at 3, 14, 28, and 60 days in MPa (megapascals)

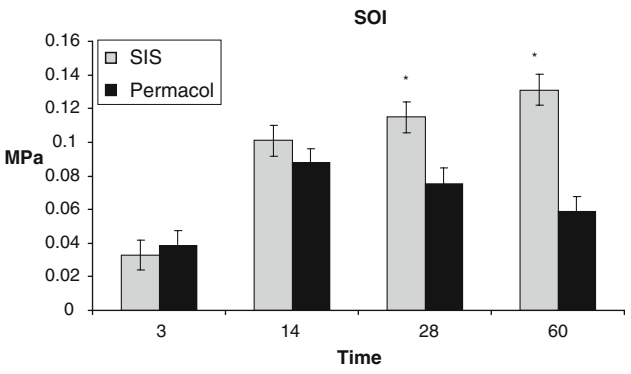

Fig. 3 Strength of Incorporation at 3, 14, 28, 60 days. At 28 days (SIS 0.115 MPa vs. Permacol 0.754 MPa; $p = 0.004$) and 60 days (SIS 0.131 MPa vs. Permacol 0.0587 MPa; $p < 0.001$). *SIS* surgisis; *MPa* megapascals. *Asterisks* indicate statistical significance

Adhesion assessment

There was no statistical difference in the amount of adhesion formation between the treatment groups $p > 0.05$. The average amount of adhesion formation for the SIS group was 25.82% ± 5.881 and that for the Permacol group was 24.530 ± 5.834.

Discussion

Our study compared two commercially available-porcine derived biosynthetic grafts Permacol and Surgisis Gold. The goal of our study was to compare Permacol and Surgisis in terms of SOI, tissue ingrowth, neovascularization, and adhesion formation in a rat model.

The SOI is a well-established measurement of the incorporation of host tissue into a graft [17, 23]. This provides relevant clinical information on the likelihood of hernia recurrence in animal models [24]. In our study the SOI was determined at baseline (3 days) to estimate the strength of the silk sutures in maintaining the interface between the graft and the adjacent abdominal wall. The SOI of the two grafts were then compared at 14, 28, and 60 days. Surgisis showed significantly greater SOI at 28 days. The disparity between the grafts continued to increase by day 60. Overall, the SOI of Surgisis increased over the 60 days, in contrast to that of Permacol, which decreased after day 14 and by day 60 Permacol showed no statistical difference compared to our baseline measurement.

Tissue ingrowth in terms of collagen amount, organization, and neovascularization was also compared between the two grafts. Microscopic evaluation demonstrated significantly more collagen deposition in Surgisis grafts at 60 days. Surgisis also displayed a more organized pattern of collagen deposition compared with Permacol at 60 days. Furthermore, Surgisis showed collagen deposition throughout the graft at 14 days and by day 60 the graft was completely replaced by

Table 3 Histologic scores of microscopic examination of Surgisis versus Permacol

Days	Groups	*N*	Neovascularization	Collagen	
				Amount	Organization
60	Surgisis	6	20.042 ± 1.531*	2.5 ± 0.224*	2.667 ± 0.211*
60	Permacol	6	12 ± 1.368	1.167 ± 0.167	1.667 ± 0.211

Values are mean ± SEM ($n = 6$)
* $p < 0.05$ (Surgisis vs. Permacol)

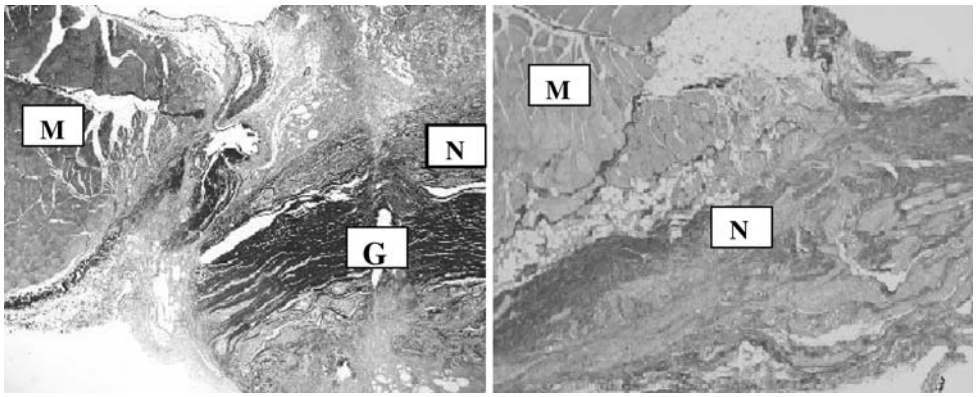

Fig. 4 Surgisis at 14 weeks (*left*) and 28 weeks (*right*). *M* muscle; *G* graft; *N* new collagen deposition

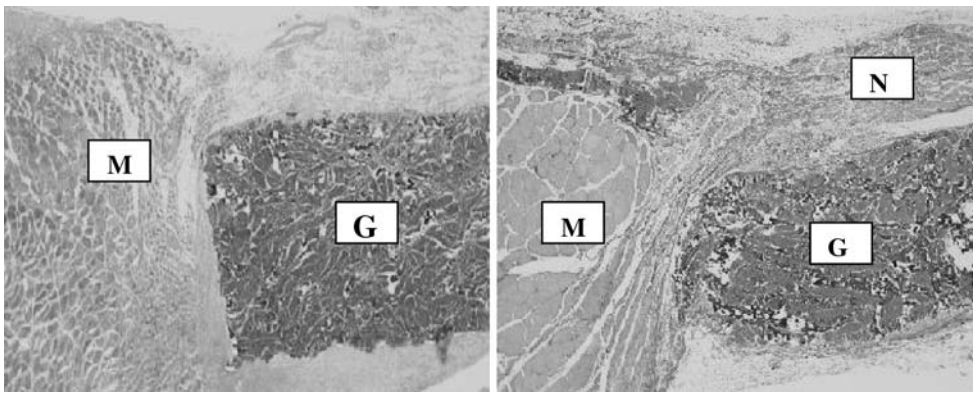

Fig. 5 Permacol at 14 weeks (*left*) and 28 weeks (*right*). *M* muscle; *G* graft; *N* new collagen deposition

new collagen deposition (Fig. 4). Permacol, however, persisted throughout the study and by day 60 was encapsulated by neocollagen (Fig. 4). Surgisis showed significantly more neovascularization. Neovascularization in Surgisis occurred throughout the graft compared with that in Permacol, which occurred only peripherally.

As predicted, both grafts displayed minimal adhesion formation with no statistical difference when compared. Previous animal studies have demonstrated that biosynthetic grafts elicit a minimal inflammatory response resulting in minimal adhesions to the underlying intestine when compared with polypropylene grafts [17, 18].

We believe the superior tissue ingrowth noted on microscopic evaluation directly correlates with the improved SOI of Surgisis. The improved tissue ingrowth and neovascularization of Surgisis is likely multifactorial. The cross-linked architecture of the Permacol graft could account for the observed histological differences. Additionally, Surgisis has previously been shown to contain multiple growth factors (VEGF, VGF2, TGF-β, and CTGF) in addition to the connective tissue scaffold, which also may assist in tissue ingrowth and neovascularization [15].

In conclusion, Surgisis showed a clear advantage over Permacol with regard to SOI, tissue ingrowth and neovascularization. The advantage was evident at 28 days and became more dramatic by 60 days.

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