Surgical Innovation
2019, Vol. 26(3) 302–311

DOI: 10.1177/1553350619833291
journals.sagepub.com/home/sri


Non-Cross-Linked Collagen Mesh Performs Best in a Physiologic, Noncontaminated Rat Model

Ruth Kaufmann, MD[1], An P. Jairam, MD, PhD[1], Irene M. Mulder, MD, PhD[1,2], Zhouqiao Wu, MD, PhD[1,3], Joost Verhelst, MD, PhD[1], Sandra Vennix, MD, PhD[1,2], Louis J. X. Giesen, MD[1], Marian C. Clahsen-van Groningen, MD, PhD[1], Johannes Jeekel, MD, PhD[1], and Johan F. Lange, MD, PhD[1]

Abstract

Background. In laparoscopic incisional hernia repair, direct contact between the prosthesis and abdominal viscera is inevitable and may lead to adhesions. Despite the large variety of mesh prosthesis, little is known about their in vivo behavior. Biological meshes are considered to have many advantages, but due to their price they are rarely used. A rat model was used to assess biological and conventional synthetic meshes on their in vivo characteristics. *Design*. One-hundred twenty male Wistar rats were randomized into five groups of 24 rats. A mesh was implanted intraperitoneally and fixated with nonresorbable sutures. The following five meshes were implanted: Parietene (polypropylene), Permacol (cross-linked porcine acellular dermal matrix), Strattice (non-cross-linked porcine acellular dermal matrix), XCM Biologic (non-cross-linked porcine acellular dermal matrix), and Omyra Mesh (condensed polytetrafluoroethylene). The rats were sacrificed after 30, 90, or 180 days. Incorporation, shrinkage, adhesions, abscess formation, and histology were assessed for all meshes. *Results*. All animals thrived postoperatively. After 180 days, Permacol, Parietene, and Omyra Mesh had a significantly better incorporation than Strattice ($P = .001$, $P = .019$, and $P = .037$ respectively). After 180 days, Strattice had significantly fewer adhesions on the surface of the mesh than Parietene ($P < .001$), Omyra Mesh ($P = .011$), and Permacol ($P = .027$). After 30 days, Permacol had significantly stronger adhesions than Strattice ($P = .030$). However, this difference was not significant anymore after 180 days. After 180 days, there was significantly less shrinkage in Permacol than in Strattice ($P = .001$) and Omyra Mesh ($P = .050$). *Conclusion*. Based on incorporation, adhesions, mesh shrinkage, and histologic parameters, Strattice performed best in this experimental rat model.

Keywords

biological mesh, incisional hernia, intraperitoneal mesh, rat model, synthetic mesh

Introduction

Incisional hernia is a common postoperative complication. Incidences range from 3% to 20% in the general population with an increased incidence of up to 39% in patients suffering from obesity or aortic aneurysms.[1] Correction of incisional hernias is nowadays most often performed with mesh reinforcement.[2] The use of mesh radically lowered the 10-year recurrence rates after incisional hernia repair.[3] Meshes are produced in a large variety of materials, structures, and shapes, and even composites are available.[4] Conventional synthetic meshes are still used most often in general practice and polypropylene mesh is the most popular product.[5]

In laparoscopic incisional hernia repair, direct contact between the mesh prosthesis and the abdominal viscera is

[1]Department of Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands
[2]Department of Surgery, Academic Medical Center, Amsterdam, The Netherlands
[3]Gastrointestinal Cancer Center, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital & Institute, Beijing, China

Corresponding Author:
Ruth Kaufmann, Department of Surgery, Erasmus University Medical Center Rotterdam, Room Ee-173, Wytemaweg 80, Rotterdam, NL-3015 CN, The Netherlands.
Email: ruth.kaufmann@gmail.com

inevitable. This may lead to an inflammatory reaction resulting in abdominal adhesion formation. Despite the large variety of available mesh prosthesis, there is only limited knowledge on their in vivo behavior. Synthetic meshes have been used for many decades now; however, biological meshes have been introduced just recently.[6,7] Biological meshes are matrices made from collagen containing tissues of human, porcine, bovine, or equine origin. Tissues such as intestines, heart valves, or skin are processed to remove any host debris (cells, cell components, and hairs) as well as various antigens present in the tissue.[8,9] After decellularization and degradation of these tissues, a 3D structure of collagen and some protein remnants such as growth factors remains. After completing this step, additional chemical cross-linking can be done with chemicals like hexamethylene diisocyanate, carbodiimide, glutaraldehyde, or photooxidizing agents.[10,11] Additional cross-linking is performed to increase the strength of the mesh, and to slow down the degradation of the mesh after implantation.[8,12] During this phase of degradation, there is incorporation of host fibroblasts into the mesh and collagen replacement occurs. This so-called xenograft remodeling begins within a few hours after implantation and takes several months to years.

Biological meshes are said to have many advantages, but are also very expensive.[6] Consequently, these meshes are only rarely used, which leads to studies with heterogeneous populations, mostly short-term follow-up, and little data on long-term results.[13-15] Both biological and conventional synthetic meshes were investigated in a physiologic, noncontaminated rat model in an intraperitoneal position to assess the in vivo characteristics of these prostheses with long-term follow-up. The aim of this study was to compare commonly used biological and synthetic meshes in an intraperitoneal environment on incorporation, shrinkage, adhesion formation, abscess formation, and histology after 30, 90, and 180 days. The working hypothesis for this study is that biological meshes behave better than synthetic meshes in an intraperitoneal position.

Methods

Animals

One-hundred twenty male Wistar rats were obtained from a licensed breeder of laboratory animals (Harlan Laboratories, Boxmeer, The Netherlands). The rats were bred under specific pathogen-free conditions and kept under standardized laboratory conditions (environmental temperature 20°C to 24°C; relative air humidity 50% to 60%; and 12 hours light/dark cycles). The rats were housed in pairs in individually ventilated cages. All rats were fed ad libitum with standard rat chow and water. The animals weighed upon arrival in the experimental facility 250 to 325 grams each. The rats were acclimatized at least for 7 days prior to the start of the experiment. The experimental protocol was approved by the Ethical Committee on Animal Experimentation of the Erasmus University Medical Center, Rotterdam, The Netherlands.

Experimental Model

At the start of the experiment, all 120 male Wistar rats were randomly divided into five groups of 24 animals each. Prior to operation, the rats were anesthetized with inhalation anesthesia (mixture of isoflurane [Pharmachemie, Haarlem, The Netherlands] and oxygen) and they received a single dose of buprenorphine analgesia (0.05 mg/kg subcutaneously; Reckitt Benckiser Healthcare (UK) Limited, Kingston-upon-Thames, UK). The rats were weighed, their abdomen was shaved, and the skin was disinfected with 70% ethanol. The rats were positioned in supine position. The abdominal cavity was opened by a 3-cm midline incision and a sterile mesh of 2.5 × 3.0 cm was inserted. This mesh was placed intraperitoneally and fixated transmuscularly with six nonabsorbable nylon sutures (5/0 Ethilon; Ethicon, Somerville, NJ). The fascia and skin were closed separately with a running absorbable suture of polyglycolic acid (5/0 Safil; B. Braun, Melsungen, Germany). After mesh implantation, all animals received a single dose of gentamicin (6 mg/kg intramuscularly) and a dose of 5 mL sodium chlorine 0.9% subcutaneously. Postoperatively, the rats were placed under a heating lamp to recover from anesthesia in the immediate postoperative phase.

Physiologic Rat Model

In this rat model, all meshes were placed in a physiologic, noncontaminated intraperitoneal environment to assess their characteristics in the absence of an infection. This model is contrary to a previous study from this research group in which the same meshes were examined in a contaminated intraperitoneal environment to assess their characteristics in the presence of a fulminant infection.[16]

Mesh Material

Five different meshes were implanted: polypropylene (Parietene, Sofradim, Trévoux, France; part of Covidien-Medtronic, New Haven, Connecticut, USA), cross-linked acellular porcine dermal matrix (Permacol; Sofradim), non-cross-linked acellular porcine dermal matrix (Strattice; LifeCell Corporation, Branchburg, New Jersey, USA), another non-cross-linked acellular porcine dermal matrix (XCM Biologic; Kensey Nash Corporation, Exton, Pennsylvania, USA, distributed by DePuy Synthes, Oberdorf, Switzerland), and condensed polytetrafluoroethylene (c-PTFE; Omyra Mesh, B. Braun, Melsungen, Germany). Prior to implantation, all meshes were prepared in a sterile environment to create smaller meshes of 2.5 × 3

cm. All meshes were handled according to the Instructions for Use of their manufacturers.

Postoperative Outcomes

Wellness and Survival of the Animals. Postoperatively, all animals were weighed on a daily base in the first week and thereafter on a weekly basis. Based on the weighing results mean weight loss was calculated by subtracting the rat's weight at the start of the experiment and the maximum amount of weight loss during the first 7 days of the experiment. During weighing, the animals were assessed for signs of discomfort. To objectify these signs of discomfort, the rat's behavior was assessed with a 12-point wellness scoring system.[17] Rats reached the humane endpoint if they suffered from ≥20% weight loss or a wellness score <5 points. All rats that reached the humane endpoint were euthanized. Euthanized or deceased animals underwent a necropsy. The data of euthanized or deceased animals were included for analyses.

Sacrifice. The experimental end points were 30 days, 90 days, and 180 days after mesh placement. During sacrifice, a photograph was taken from the inner abdominal wall and the mesh site. Figure 1 shows a photograph taken at time of sacrifice showing inner abdominal wall and mesh site (non-cross-linked biological mesh). The black box in Figure 1 shows a schematic representation of the tissue sampling for histopathology. The following parameters were assessed: incorporation and shrinkage of the mesh and adhesion formation (coverage and strength).

Incorporation of the mesh. Incorporation of the mesh was assessed with a slide caliper. The number of millimeters of all sides of the remaining mesh were measured. The standard length and width of the implanted mesh were 30 × 25 mm. Thereafter, the number of millimeters of each side of the mesh that showed incorporation were measured. Both measures resulted in a percentage of incorporation. Full incorporation was incorporation of all sides taking any shrinkage of the mesh into account.

Shrinkage of the mesh. Shrinkage of the mesh was assessed by measurement of the surface of mesh that was present during sacrifice. The measurement was performed with a standardized caliper and the mesh surface found during sacrifice was compared with the standardized implant size (7.5 cm^2) and expressed in a percentage of this standardized implant.

Adhesion formation. Adhesion formation was assessed in two ways. First, a qualitative analysis was performed using the Zühlke score.[18] The Zühlke score was used to assess the strength and tenacity of adhesions. The score ranges from 0 (no adhesions) to 4 (very strong adhesions) (Supplementary data, Table S1, available online). Table S1 shows the Zühlke scoring system for adhesions that was used to assess adhesions in this study. Second, the quantity of adhesions was assessed and expressed in a percentage of adhesions on the surface of the mesh. Two independent investigators assessed both parameters. Discrepancies were discussed between the two investigators and resolved together.

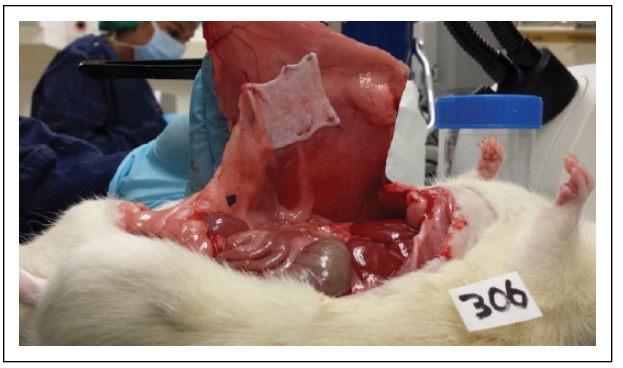

Figure 1. Photograph taken at time of sacrifice showing inner abdominal wall and mesh site (non-cross-linked biological mesh). The black box is a schematic representation of tissue sampling for histopathology.

Abscesses. The presence of mesh abscesses was regarded as an expression of an ongoing intraabdominal infection. The presence of abscesses was assessed with a standardized visual inspection and examination of the abdominal cavity of all rats. If abscesses were present, their size was scored with the Abscess Scoring System[19] (Supplementary data, Table S2). Table S2 shows the abscess scoring system.

Scoring system for the ranking of all meshes. The characteristics that were assessed in this study were incorporation of the mesh, shrinkage of the mesh, adhesion formation, abscess formation, and histologic parameters. To assess the ranking of the meshes, all meshes received a score of 1 (worst performing mesh) to 5 (best performing mesh) for each individual parameter. Adhesions were considered to be the decisive factor, because of the intraabdominal position of the mesh.

Histologic Evaluation

After sacrifice, a full-thickness abdominal wall sample of 1.0 by 0.5 cm was harvested from each rat. This sample was taken from one of the long sides in between the sutures and contained both abdominal wall and mesh (Figure 1). Figure 1 shows a schematic representation of the tissue sampling for histopathology. All samples were fixated in 4% formalin and embedded in paraffin. Samples

Table 1. Overview of the Experimental Groups in This Experiment.

	Parietene	Permacol	Strattice	XCM Biologic	Omyra Mesh
Mesh material	Polypropylene	Cross-linked collagen of porcine dermis	Non-cross-linked collagen of porcine dermis	Non-cross-linked collagen of porcine dermis	Condensed PTFE
Weight (g/m^2)	78	NA	NA	NA	90
Pore size (mm)	1.0-1.6	NA	NA	NA	2.4
Number of animals	24	24	24	24	24
Postoperative deaths	0	0	0	0	0
Number analyzed					
30 days	8	8	8	7	8
90 days	8	8	8	9	8
180 days	8	8	8	8	8

Abbreviations: PTFE, polytetrafluoroethylene; NA, not applicable.

were cut into 4-µm-thick slices and stained with either hematoxylin and eosin (H&E) or Sirius Red (SR) according to standard diagnostic procedure.

The histologic evaluation of all slides was performed in a blind fashion by an experienced pathologist (MC-vG). H&E slides were analyzed by a scoring system described by Peeters et al.[20] (adapted from Jenkins et al.[21]). All cells were assessed under the microscope under 40× magnification and the number of cells per high-power field (40× magnification) was counted. No additional stains were performed. SR slides were assessed with the scoring system described by Deeken and Matthews.[22] The histological analysis of the biological meshes focused on the periprosthetic area. The histological analysis of Parietene and Omyra Mesh focused on both the perifilamentary areas and the pores. Both areas were assessed and a grade was given for the overall number of cells per sample. In the SR slides, the amount of fibrous encapsulation around each mesh was assessed. The histologic scoring systems can be found in Supplementary data, Table S3, Table S4, and Table S5. Table S3 shows the histologic scoring system for inflammatory cell reaction. Table S4 shows the histologic scoring system for mesh-specific parameters. Table S5 shows the histologic scoring system for collagen deposition.

Statistical Analysis

Prior to the start of the experiment, a sample size calculation was performed. The sample size calculation was made regarding an expected decrease in amount of adhesions of 25% to 30%. The expected mortality of the mesh model was 10%. Aiming for a power of 80% and a P value of .05, the necessary number of animals was 24 per group. All meshes were included in the experiment as equal study groups. None of the study groups served as a control group only.

In this experiment, only the data of incorporation of the mesh showed a normal distribution. All other parameters did not show a normal distribution; thus, statistical analyses were performed using nonparametric Kruskal-Wallis tests for independent samples. If the overall statistical test showed significant differences, pairwise tests were done to determine the groups causing the overall statistical significance.

Baseline characteristics like weight loss were summarized in percentages, continuous variables using means and standard errors of the mean, and categorical values were summarized with medians and interquartile ranges. All P values were tested with a 2-tailed test of significance, a P value of $<.05$ was considered statistically significant, and all P values were adjusted for multiple testing using Dunn's posttest. The statistical analyses were performed using SPSS version 21.0.

Results

Animals

All 120 rats survived the operation and thrived afterwards. None of the rats reached the humane endpoint. The maximum postoperative weight loss varied between 0% and 7% among the five groups and was more pronounced in the Parietene group ($P = .001$) and the Permacol group ($P = <.001$). There were no differences observed in weight change or wellness score among the five groups. Table 1 shows an overview of the experimental groups in this experiment. In this table, the distribution of the animals per study group and per study time point can be found.

Incorporation of the Mesh

There was a fluctuating amount of incorporation in all meshes with most often first a decrease in ingrowth at 90

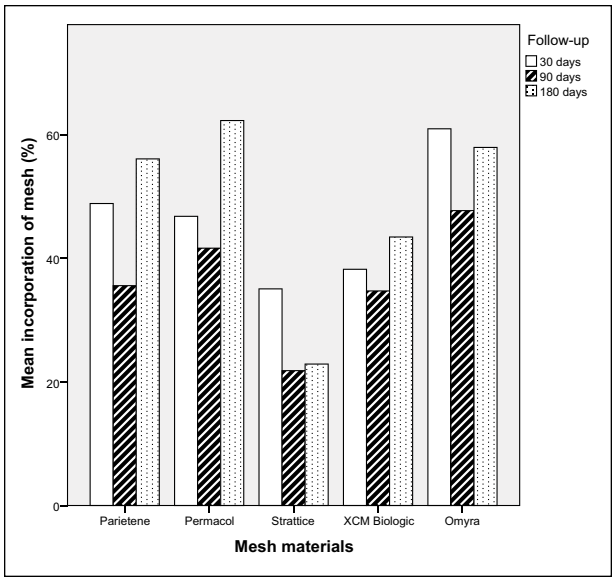

Figure 2. Mean percentage incorporation of each mesh at 30, 90, and 180 days.

days compared with 30 days, followed by an increase after 180 days compared with 90 days. The amount of incorporation strongly varied between the mesh groups. One-hundred and eighty days after implantation, incorporation was most superior in Permacol (62 ± 11%), followed by Omyra Mesh (58 ± 20%), Parietene (56 ± 9%), XCM Biologic (43 ± 12%), and most inferior in Strattice (23 ± 13%). After 180 days, mesh incorporation was significantly lower in Strattice compared with Omyra Mesh ($P = .037$), Parietene ($P = .019$), and Permacol ($P = .001$) (Figure 2 and Table 2). Figure 2 shows the incorporation of the mesh after 30, 90, and 180 days. The mean incorporation is expressed in percentage. Table 2 shows the results of macroscopic mesh-specific parameters after sacrifice.

Shrinkage of the Mesh

All meshes shrunk after implantation; however, the amount of shrinkage varied strongly: 0% to 18% on different time points in different meshes (Figure 3 and Table 2). Figure 3 shows the shrinkage of the mesh after 30, 90, and 180 days. Median shrinkage is expressed in percentage. Table 2 shows the results of macroscopic mesh-specific parameters after sacrifice. After 180 days, shrinkage was most evident in Strattice (18 [15-22] %), followed by Omyra Mesh (13 [8-30] %), XCM Biologic (10 [5-16] %), and Parietene (9 [5-13] %). Shrinkage was least prominent in Permacol (0 [0-4] % at 180 days). After 180 days, there was significantly less shrinkage in Permacol than in Strattice ($P = .001$) and Omyra Mesh ($P = .050$).

Adhesions

One-hundred and eighty days after implantation, the percentage adhesions on the mesh surface was highest in Parietene (85 [70-90] %), followed by Omyra Mesh (75 [60-75] %), Permacol (68 [63-73] %), XCM Biologic (35 [28-35] %), and lowest in Strattice (5 [0-5] %) (Figure 4). Figure 4 shows the adhesions on the mesh after 30, 90, and 180 days. The median value of adhesions is expressed in percentage. Strattice had significantly fewer adhesions on the surface of the mesh than Parietene ($P < .001$), Omyra Mesh ($P = .011$), and Permacol ($P = .027$) after 180 days.

The tenacity of adhesions, expressed in the Zühlke score, was median 3 in Parietene, Strattice, XCM Biologic, and Omyra Mesh, and median 4 in Permacol at all time points. After 30 days, Permacol had significantly stronger adhesions than Strattice ($P = .03$). However, this difference was not significant anymore after 180 days (Table 2). Table 2 shows the results of macroscopic mesh-specific parameters after sacrifice.

Abscesses

There were no abscesses found on either of the meshes or in the intra-abdominal cavity at all time-points.

Histological Evaluation

In one of the rats that had Permacol implanted, there was no mesh left 180 days after implantation. In all other samples, meshes were still present after sacrifice and histologic evaluation was performed. H&E staining of the samples revealed no significant difference in the total count of inflammatory cells between all meshes. There were however significant differences in the number of eosinophils, macrophages, mononuclear cells, and extracellular matrix deposition between the different mesh groups (Supplementary data, Table S6 and Table S7). Table S6 shows the results of histologic evaluation after sacrifice. The results are presented as median (interquartile ranges). Table S7 shows the results of mesh-specific parameters after sacrifice. The results are presented as median (interquartile ranges). All histological findings will be discussed individually. Examples of the histological slides can be found in the Supplementary data, Figures S1 to S6. The H&E slides show samples 180 days after implantation (10× magnification). The samples contain Parietene (Figure S1), Permacol (Figure S2), Strattice (Figure S3), XCM Biologic (Figure S4), and Omyra (Figure S5), respectively. Figure S6 shows an example of a SR staining of Strattice 180 days after implantation (5× magnification).

Table 2. Results of Macroscopic Mesh-Specific Parameters After Sacrifice[a].

	n	Incorporation of Mesh (%)	Shrinkage of Mesh (%)	Adhesions on Mesh (%)	Tenacity of Adhesions
Parietene					
30 days	8	49 ± 13	8 (5-13)	83 (78-90)	3 (3-3)
90 days	8	36 ± 12	7 (5-14)	88 (85-93)	3 (3-3)
180 days	8	56 ± 9	9 (5-13)	85 (70-90)	3 (3-3)
Permacol					
30 days	8	47 ± 18	11 (3-23)	75 (60-85)	4 (3-4)[b]
90 days	8	42 ± 15	7 (3-11)	75 (70-78)	4 (3-4)
180 days	8	62 ± 11	0 (0-4)[c]	68 (63-73)	4 (3-4)
Strattice					
30 days	8	35 ± 14	13 (7-18)	5 (5-10)[d]	3 (3-3)
90 days	8	22 ± 11	15 (6-18)	5 (5-5)[e]	3 (3-3)
180 days	8	23 ± 13[f]	18 (15-22)	5 (0-5)[g]	3 (3-3)
XCM Biologic					
30 days	7	38 ± 6	7 (0-7)	30 (25-55)	3 (3-3)
90 days	9	35 ± 13	12 (8-14)	40 (35-45)	3 (3-3)
180 days	8	43 ± 12	10 (5-16)	35 (28-35)	3 (3-3)
Omyra Mesh					
30 days	8	61 ± 11	16 (13-17)	53 (45-80)	3 (3-3)
90 days	8	48 ± 21	17 (14-31)	63 (45-85)	3 (3-3)
180 days	8	58 ± 20	13 (8-30)	75 (60-75)	3 (3-4)

[a]Incorporation of mesh values are mean ± SD. All other values are median (interquartile range).
[b]Significant difference between Permacol 30 days and Strattice 30 days ($P = .030$).
[c]Significant difference between Permacol 180 days and Omyra Mesh 180 days ($P = .050$), and Strattice 180 days ($P = .001$).
[d]Significant difference between Strattice 30 days and Permacol 30 days ($P = .023$), and Parietene 30 days ($P = <.001$).
[e]Significant difference between Strattice 90 days and Permacol 90 days ($P = .011$), and Parietene 90 days ($P = <.001$).
[f]Significant difference between Strattice 180 days and Omyra Mesh 180 days ($P = .037$), Parietene 180 days ($P = .019$), and Permacol 180 days ($P = .001$).
[g]Significant difference between Strattice 180 days and Permacol 180 days ($P = .027$), Omyra Mesh 180 days ($P = .011$), and Parietene 180 days ($P = <.001$).

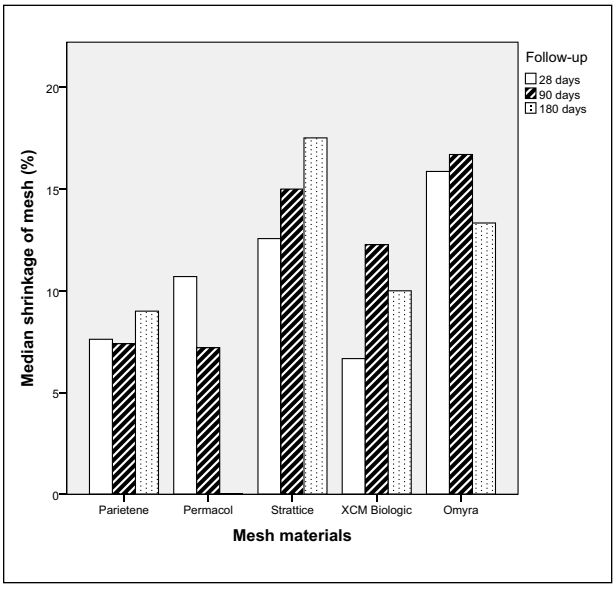

Figure 3. Median shrinkage of each mesh at 30, 90, and 180 days.

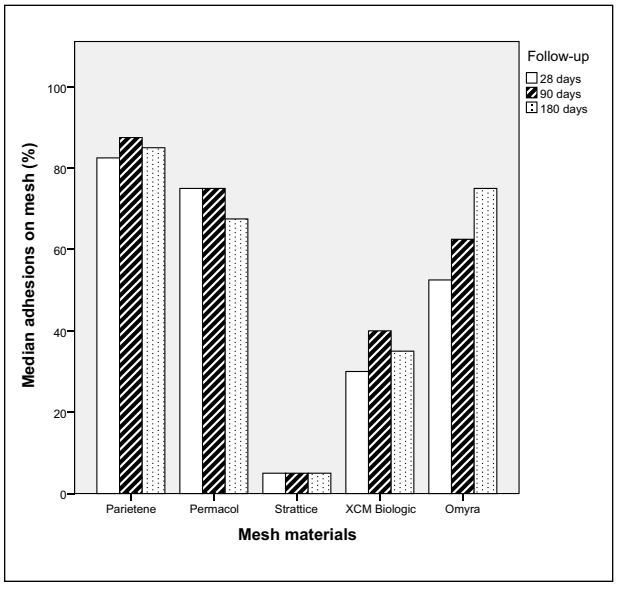

Figure 4. Median percentage of adhesions on each mesh at 30, 90, and 180 days.

Parietene. Parietene mesh had a significantly higher number of eosinophils, neutrophils, and macrophages on various time points when compared with Permacol, Strattice, and XCM Biologic (Supplementary data, Table S6). Table S6 shows the results of histologic evaluation after sacrifice. The results are presented as median (interquartile ranges). After 30 days of follow-up, there was a significantly lower number of mononuclear cells in the Parietene samples compared with XCM Biologic ($P = .019$). Collagen deposition was higher than in the other meshes; however, there was no significant difference when compared with other meshes.

The mesh-specific histological parameters revealed statistically higher scaffold degradation in the non-cross-linked biological meshes XCM Biologic ($P = .049$) and Strattice ($P = .018$) when compared with Parietene 30 days after implantation. Fibrous encapsulation was significantly lower in Parietene than in XCM Biologic after 90 days ($P = .024$). Cellular infiltration and neovascularization were significantly lower in Parietene than in Strattice 90 and 180 days after implantation. Extracellular matrix deposition was low to moderate present in all samples and showed no significant differences with other meshes.

Permacol

Permacol contained only very few eosinophils and neutrophils, significantly less than in Parietene (at all time points). The number of macrophages and mononuclear cells was low to moderate, but there were no significant differences with other meshes. Collagen deposition was moderate, but significantly lower than in Omyra Mesh after 180 days.

The mesh-specific histological parameters revealed that fibrous encapsulation was very low and showed no significant differences with other meshes. Scaffold degradation, neovascularization, and extracellular matrix deposition were significantly lower in Permacol than in Strattice after 90 days. Cellular infiltration was significantly lower than in Strattice after both 90 and 180 days.

Strattice

Strattice mesh contained only very few eosinophils and neutrophils, significantly less than in Parietene (at all time points). After 180 days, only few macrophages were found in Strattice, significantly less than in Parietene ($P = .004$). The number of mononuclear cells and the amount of collagen deposition was quite high, but diminished over time. After 180 days, the amount of collagen deposition was significantly lower than in Omyra Mesh ($P = .003$).

Scaffold degradation was significantly higher in Strattice at all time points. Fibrous encapsulation was low and showed no significant differences with other meshes. Cellular infiltration and neovascularization were significantly higher in Strattice after 90 and 180 days, when compared with Parietene, Omyra Mesh, and Permacol. Extracellular matrix deposition was significantly higher than in Permacol after 180 days ($P = .020$).

XCM Biologic

XCM Biologic contained only very few eosinophils and neutrophils, significantly less than in Parietene after 30 days ($P = .001$). After 90 and 180 days, the number of macrophages was significantly lower in XCM Biologic than in Parietene ($P = .003$ and $P = .010$, respectively). After 30 days of follow-up, there was a significantly higher number of mononuclear cells in the XCM Biologic samples compared with Parietene ($P = .019$). After 90 and 180 days, collagen deposition was significantly lower in XCM Biologic.

After 30 days, scaffold degradation was significantly higher in XCM Biologic than in Omyra Mesh ($P = .049$). After 90 days, fibrous encapsulation was significantly higher in XCM Biologic than in Parietene and Omyra Mesh ($P = .024$ and $P = .024$, respectively). Cellular infiltration, neovascularization, and extracellular matrix deposition were moderate and did not show significant differences when compared with other meshes.

Omyra Mesh

Omyra Mesh contained only few eosinophils and neutrophils, but no significant differences were found with other meshes. After 90 days, significantly more macrophages were found in the Omyra Mesh samples than in the XCM Biologic samples ($P = .003$). Mononuclear cells were present in moderate amount, and there were no significant differences with other meshes. After 90 and 180 days, there was a significantly higher amount of collagen deposition in Omyra Mesh than in XCM Biologic ($P = .070$ and $P = .014$, respectively).

Scaffold degradation was significantly higher in most other meshes at all time points after implantation, when compared with Omyra Mesh. After 90 days, also fibrous encapsulation was significantly lower in Omyra Mesh than in XCM Biologic ($P = .024$). After 90 and 180 days, both cellular infiltration and neovascularization were significantly lower in Omyra Mesh when compared with XCM Biologic. Extracellular matrix deposition was moderate at all time points, and no significant differences were found compared with other meshes.

Discussion

This experimental study in a physiologic, noncontaminated rat model revealed that the use of biological meshes

in an intraabdominal position is feasible. Based on incorporation, adhesions on the surface of the mesh, adhesion strength, mesh shrinkage, and the histologic parameters scaffold degradation, cellular infiltration, neovascularization, and extracellular matrix deposition, Strattice performed best in this experimental rat model with intraperitoneal mesh placement.

Ever since the introduction of mesh-assisted abdominal wall hernia repair, there has been a search for the "ideal mesh."[23,24] The ideal mesh must be tailored to each patient's needs in the current clinical situation.[25] In case of abdominal wall hernia repair in the intraperitoneal plane, one needs a high incorporation of the mesh, little to no shrinkage of the mesh, few to no adhesions on the mesh, and if adhesions are formed, preferably adhesions of a low tenacity.[23-25] None of the examined meshes in this study showed all the requested characteristics within one product.

In this study, the incorporation of the mesh was best in Permacol (62 ± 11%) and worst in Strattice (23 ± 13%) after 180 days. A previous study from this research group with the same mesh materials in a contaminated environment showed similar results for mesh incorporation in Permacol and Strattice.[16] XCM Biologic, however, had a much higher incorporation of the mesh in a contaminated environment than in a physiologic, non-contaminated environment (88 [interquartile range [IQR]: 72-100] % versus 43 ± 12 SD % after 180 days). The other meshes showed a comparable incorporation after 180 days in both the contaminated environment (median [IQR]) and the physiologic, noncontaminated environment (mean ± SD) (Parietene 57 [32-87] % vs 56 ± 9%, Permacol 62 [58-67] % vs 62 ± 11%, Strattice 21 [10-30] % vs 23 ± 13%, and Omyra Mesh 54 [40-66] % vs 58 ± 20%).[16] When reviewing the histological parameters of XCM Biologic in a contaminated environment versus a noncontaminated environment, all the following parameters scored much higher values in the contaminated environment: the total number of inflammatory cells, macrophages and foreign body giant cells, mononuclear cells, and the amount of collagen deposition. It is possible that a more fulminant inflammatory response led to a better incorporation of XCM Biologic in a contaminated environment. All other meshes did not follow this pattern and did not show an increase in total number of inflammatory cells, macrophages and foreign body giant cells, mononuclear cells, and the amount of collagen deposition. As far as currently known, there is no literature on the head-to-head comparison of mesh incorporation between meshes in a contaminated environment versus a noncontaminated situation.

There was a large variety in shrinkage of the mesh in this study: 0% to 18% of shrinkage on various time points. After 180 days, Permacol was shrunken significantly less than Strattice and Omyra Mesh (0% vs 18% and 13%, respectively). In a previous experimental study of Mulier et al., Strattice and Permacol were compared alongside. In that study, the surface area of Permacol remained stable, but Strattice mesh expanded in size 12 months after implantation.[26] This finding might be explained by the growth of the animals; however, it was only found in Strattice, not in Permacol. In this current study, no expansion of Strattice was found; however, this study only had a maximum of 6 months follow-up. Parietene and XCM Biologic showed a moderate amount of shrinkage (9% and 10% after 180 days) in this study. This is contrary to a previous study, in which a very high percentage of shrinkage was found in XCM Biologic (21 [4-36] % at 30 days, 43 [38-66] % at 90 days, and 36 [34-51] % at 180 days).[16] It is unclear why XCM Biologic shrunk excessively in the presence of infection and shrunk less in a physiologic, noncontaminated environment. This finding could again be explained by a more fulminant foreign body response in XCM Biologic in a contaminated environment versus a noncontaminated environment. In the contaminated environment, a higher total number of inflammatory cells, macrophages, foreign body giant cells, mononuclear cells, and the amount of collagen deposition was found. Other meshes that were examined in both a contaminated and a physiologic, noncontaminated environment did not show the same pattern of shrinkage neither did they show the same pattern of foreign body response.

All meshes that were investigated in this study formed strong adhesions. The adhesions formed by Permacol were significantly stronger compared to Strattice after 30 days. The amount of adhesions varied significantly among all groups and varied between 5% and 88% of the surface of the mesh. Strattice had significantly the lowest amount of adhesions, and Parietene had significantly the highest amount of adhesions. The amount of adhesions per mesh are comparable to results from previous studies from this group.[14,27,28] No comparable studies of other research groups were found.

To summarize the findings of this study: when comparing all meshes head-to-head, Permacol and Strattice showed most often desired characteristics for intraperitoneal mesh placement, but also some characteristics that are less eligible for use in the intraabdominal cavity. Permacol had a better mesh incorporation than Strattice, less shrinkage than Strattice, but a much higher adhesion percentage compared with Strattice. After 30 days, significantly higher adhesion tenacity was observed in Permacol compared with Strattice. Strattice, however, had less mesh incorporation than Permacol, higher shrinkage than Permacol, but a much lower adhesion percentage.

Since adhesions can lead to serious complaints and complications in patients, the surgeon's aim should be to place a mesh that leads to the least possible amount of adhesions, when placed intraperitoneally. This mesh could be suitable for laparoscopic mesh placement in an intraperitoneal onlay mesh technique, or for patient with a giant abdominal wall hernia, in which closure of the fascia is not always possible and in which there could be an eminent risk for direct contact between the mesh and the viscera. Further studies are surgically relevant, because this study only assessed feasibility and in vivo characteristics like incorporation, shrinkage, adhesion formation, and histology. In this study, no analyses were performed regarding the biomechanical properties of the meshes. Properties like tensile strength, ball burst strength, and tear resistance resemble clinical parameters that are important for the patients' abdominal wall hernia repair.[29] Future investigations could target the assessment of biomechanical characteristics of the meshes, but moreover postoperative assessment of patients that have undergone abdominal wall hernia repair with a biological mesh. This type of mesh seems feasible for different indications in patients, but a careful selection should be done preoperatively, to select the right indication for the right mesh.

The rat model in this study is suitable to assess the behavior of synthetic and biological meshes experimentally in a physiologic, noncontaminated environment. There are however some limitations to this study. First, only the surface of the mesh could be adjusted; proportionally the mesh implants were much thicker in the rats than that they would be in humans. This may lead to a decreased incorporation of the mesh in the abdominal wall. Second, in this model all meshes were placed intraperitoneally, whereas in the clinical situation one would be cautious to implant Parietene into the abdominal cavity without an anti-adhesive layer. Previous studies showed a more pronounced inflammatory response and adhesion formation after intraperitoneal placement of these meshes compared with extraperitoneal placement.[27,28,30] However, closure of the peritoneum is not always possible in patients with large hernias, and contact between viscera and mesh might still occur. It is therefore important to assess in vivo mesh behavior of synthetic and cross-linked meshes in an intraabdominal environment. The translation of experimental results to the clinical situation should however be done with caution.

Conclusions

Based on incorporation, adhesion surface, adhesion strength, and mesh shrinkage, and the histologic parameters scaffold degradation, cellular infiltration, neovascularization, and extracellular matrix deposition, Strattice performed best in this experiment in a physiologic, noncontaminated rat model with intraperitoneal mesh placement.

Authors' Note

This study was presented at the following meetings: Dutch Surgical Society, fall meeting, Utrecht, The Netherlands (oral presentation), November 28, 2014; World Conference on Abdominal Wall Hernia, Milan, Italy (poster presentation), May 2015; American Hernia Society, Washington, USA (poster presentation), March 2016. Marian C. Clahsen-van Groningen is now affiliated with Department of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands. Johannes Jeekel is now affiliated with Department of Neuroscience, Erasmus University Medical Center, Rotterdam, The Netherlands.

Author Contributions

All authors agreed to be accountable for all aspects of the work.
Study concept and design: J. Jeekel, J.F. Lange.
Acquisition of data: R. Kaufmann, A. P. Jairam, I. M. Mulder, Z. Wu, J. Verhelst, S. Vennix, L. J. X. Giesen, M. C. Clahsen-van Groningen.
Analysis and interpretation: R. Kaufmann, A. P. Jairam, I. M. Mulder, Z. Wu, J. Verhelst, S. Vennix, M. C. Clahsen-van Groningen, J. Jeekel, J.F. Lange.
Study supervision: J. Jeekel, J.F. Lange.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This experiment was funded with grants of DePuy Synthes, Oberdorf, Switzerland, and DSM Medical, Heerlen, The Netherlands. All companies (B. Braun, Melsungen, Germany; DSM Biomedical, Exton, PA, USA, distributed by DePuy Synthes, West Chester, PA, USA; LifeCell, KCI, Branchburg, NJ, USA; DePuy Synthes, Oberdorf, Switzerland; Sofradim, Trévoux, France; part of Covidien-Medtronic, New Haven, CT, USA) provided their meshes free of charge for this experiment. None of the mentioned companies were involved in the design of the study, the operation of the animals, the analysis of the results, or the preparation of the manuscript.

Supplemental Material

Supplemental material for this article is available online.

ORCID iD

Ruth Kaufmann https://orcid.org/0000-0003-1039-0607

References

1. Van Ramshorst GH, Eker HH, Hop WC, Jeekel J, Lange JF. Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study. *Am J Surg*. 2012;204:144-150.
2. Luijendijk RW, Hop WC, van den Tol MP, et al. A comparison of suture repair with mesh repair for incisional hernia. *N Engl J Med*. 2000;343:392-398.
3. Burger JW, Luijendijk RW, Hop WC, Halm JA, Verdaasdonk EG, Jeekel J. Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia. *Ann Surg*. 2004;240:578-585.
4. Cevasco M, Itani KM. Ventral hernia repair with synthetic, composite, and biologic mesh: characteristics, indications, and infection profile. *Surg Infect (Larchmt)*. 2012;13:209-215.
5. Cobb WS, Kercher KW, Heniford BT. Laparoscopic repair of incisional hernias. *Surg Clin North Am*. 2005;85:91-103.
6. Bellows CF, Alder A, Helton WS. Abdominal wall reconstruction using biological tissue grafts: present status and future opportunities. *Expert Rev Med Devices*. 2006;3:657-675.
7. Jacob BP, Ramshaw B. *The SAGES Manual of Hernia Repair*. New York, NY: Springer; 2013.
8. Chand B, Indeck M, Needleman B, et al. A retrospective study evaluating the use of Permacol™ surgical implant in incisional and ventral hernia repair. *Int J Surg*. 2014;12:296-303.
9. Cornwell KG, Landsman A, James KS. Extracellular matrix biomaterials for soft tissue repair. *Clin Podiatr Med Surg*. 2009;26:507-523.
10. Khor E. Methods for the treatment of collagenous tissues for bioprostheses. *Biomaterials*. 1997;18:95-105.
11. Schmidt CE, Baier JM. Acellular vascular tissues: natural biomaterials for tissue repair and tissue engineering. *Biomaterials*. 2000;21:2215-2231.
12. Iacco A, Adeyemo A, Riggs T, Janczyk R. Single institutional experience using biological mesh for abdominal wall reconstruction. *Am J Surg*. 2014;208:480-484.
13. Bryan N, Ahswin H, Smart N, Bayon Y, Wohlert S, Hunt JA. The in vivo evaluation of tissue-based biomaterials in a rat full-thickness abdominal wall defect model. *J Biomed Mater Res B Appl Biomater*. 2014;102:709-720.
14. Ditzel M, Deerenberg EB, Grotenhuis N, et al. Biologic meshes are not superior to synthetic meshes in ventral hernia repair: an experimental study with long-term follow-up evaluation. *Surg Endosc*. 2013;27:3654-3662.
15. Stanwix MG, Nam AJ, Hui-Chou HG, et al. Abdominal ventral hernia repair with current biological prostheses: an experimental large animal model. *Ann Plast Surg*. 2011;66:403-409.
16. Kaufmann R, Jairam AP, Mulder IM, et al. Characteristics of different mesh types for abdominal wall repair in an experimental model of peritonitis. *Br J Surg*. 2017;104:1884-1893.
17. Komen N, van der Wal HC, Ditzel M, Kleinrensink GJ, Jeekel H, Lange JF. Colorectal anastomotic leakage: a new experimental model. *J Surg Res*. 2009;155:7-12.
18. Zühlke HV, Lorenz EM, Straub EM, Savvas V. Pathophysiology and classification of adhesions [in German]. *Langenbecks Arch Chir Suppl II Verh Dtsch Ges Chir*. 1990:1009-1016.
19. Rodgers KE, Schwartz HE, Roda N, Thornton M, Kobak W, diZerega GS. Effect of Oxiplex films (PEO/CMC) on adhesion formation and reformation in rabbit models and on peritoneal infection in a rat model. *Fertil Steril*. 2000;73:831-838.
20. Peeters E, van Barneveld KW, Schreinemacher MH, et al. One-year outcome of biological and synthetic bioabsorbable meshes for augmentation of large abdominal wall defects in a rabbit model. *J Surg Res*. 2013;180:274-283.
21. Jenkins ED, Melman L, Deeken CR, Greco SC, Frisella MM, Matthews BD. Biomechanical and histologic evaluation of fenestrated and nonfenestrated biologic mesh in a porcine model of ventral hernia repair. *J Am Coll Surg*. 2011;212:327-339.
22. Deeken CR, Matthews BD. Ventralight ST and SorbaFix versus Physiomesh and Securestrap in a porcine model. *JSLS*. 2013;17:549-559.
23. Basile F, Biondi A, Donati M. Surgical approach to abdominal wall defects: history and new trends. *Int J Surg*. 2013;11(suppl 1):S20-S23.
24. Shankaran V, Weber DJ, Reed RL 2nd, Luchette FA. A review of available prosthetics for ventral hernia repair. *Ann Surg*. 2011;253:16-26.
25. Eriksen JR, Gögenur I, Rosenberg J. Choice of mesh for laparoscopic ventral hernia repair. *Hernia*. 2007;11:481-492.
26. Mulier KE, Nguyen AH, Delaney JP, Marquez S. Comparison of Permacol™ and Strattice™ for the repair of abdominal wall defects. *Hernia*. 2011;15:315-319.
27. Deerenberg EB, Mulder IM, Grotenhuis N, Ditzel M, Jeekel J, Lange JF. Experimental study on synthetic and biological mesh implantation in a contaminated environment. *Br J Surg*. 2012;99:1734-1741.
28. Mulder IM, Deerenberg EB, Bemelman WA, Jeekel J, Lange JF. Infection susceptibility of crosslinked and non-crosslinked biological meshes in an experimental contaminated environment. *Am J Surg*. 2015;210:159-166.
29. Deeken CR, Eliason BJ, Pichert MD, Grant SA, Frisella MM, Matthews BD. Differentiation of biologic scaffold materials through physicomechanical, thermal, and enzymatic degradation techniques. *Ann Surg*. 2012;255:595-604.
30. Vogels RR, van Barneveld KW, Bosmans JW, et al. Long-term evaluation of adhesion formation and foreign body response to three new meshes. *Surg Endosc*. 2015;29:2251-2259.