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Research

Evaluation of a Novel Absorbable Mesh in a Porcine Model of Abdominal Wall Repair

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Background: Bioabsorbable meshes have seen increasing clinical use to reinforce soft tissue, and exist on a spectrum of strength loss versus absorption: several retain their strength for months, but remain in situ for years. Others lose strength fully by 6 weeks. An intermediate profile, with some strength for 3 -4 months, but consistent absorption in less than a year, may be an optimal balance of near-term support and long-term safety. In this large animal study, we evaluate such a mesh (DuraSorb, SIA), assessing its utility in a porcine model of abdominal wall repair.

Methods: Two full-thickness defects were created in the abdominal walls of nine Yucatan swine via midline approach and repaired preperitoneally with either DuraSorb or long-lasting control mesh (TIGR, Novus Scientific). At 30 days, 3 months, and 1 year, the implantations were assessed by clinical pathology, post-necropsy histopathology, and burst strength testing.

Results: No device-associated complications were found in vivo, at necropsy, or histologically. DuraSorb was well-integrated and vascularized by 30 days. DuraSorb demonstrated minimal/mild inflammation and fibroplasia, and lower inflammatory scores when compared with TIGR at all time points ($P < 0.05$). Burst strength of the repair sites was higher than adjacent abdominal wall at all time points ($P < 0.05$).

Conclusions: DuraSorb provided durable long-term support, minimal inflammation, and consistent absorption in this porcine model of abdominal wall repair, as compared to a long-term control. Clinical data is needed, but these results suggest that this mesh provides adequate structural support while potentially reducing long-term device reactions. *(Plast Reconstr Surg Glob Open 2021;9:e3529; doi: 10.1097/GOX.0000000000003529; Published online 25 May 2021.)*

INTRODUCTION

Patients undergoing abdominal wall repair often report postoperative chronic pain, with estimated rates reaching 10%–20%.[1] The use of permanent surgical mesh—which may lead to a chronic inflammatory reaction—has been proposed as a mechanism of postoperative chronic pain.[2] Studies[3] on explanted mesh from humans have confirmed that persistent foreign body reactions associated with permanent meshes lead to long-term wound complications, and groups have demonstrated that less material leads to significantly lower rates of postoperative pain and foreign body sensation.[4] Additionally, permanent mesh is associated with high rates of mesh-related erosion and other long-term complications.[5,6] These findings have led to the use of absorbable mesh, which can be biologic or synthetic.

Biologic mesh provides an acellular matrix for native cells to populate, thereafter gradually replacing said matrix with native connective tissue during the course of normal cell turnover and neocollagenesis.[7] Although useful in contaminated settings due to their rapid revascularization and clearance of bacteria,[8,9] they exhibit high variability due to their differing sources and methods

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for decellularization and sterilization that influences their thickness, handling, biocompatibility, foreign body response (FBR), and immunogenic potential.[10,11] These are also more expensive than synthetic meshes, raising questions of healthcare cost-efficiency[12–14] in the general and plastic surgery literature.

Bioabsorbable meshes to reinforce soft tissue have seen increasing clinical use, and exist on a spectrum of strength loss versus absorption: there are longer-term meshes that retain strength for months, but remain in situ for >18 months, and there are shorter-term meshes that fully lose strength in just 6–8 weeks. A medium-term absorbable mesh that maintains some strength for 3–4 months, but consistently absorbs over the course of less than a year may be an optimal balance of near-term wound support and long-term safety. However, no such mesh construct has been available for commercial use, and is fully resorbed thereafter to eschew late-presenting surgical site complications.

In this study, we sought to understand the mechanical properties, resorption profile, and histological characteristics of a novel medium-term dioxanone-based absorbable mesh (DuraSorb, Surgical Innovation Associates, Inc., Chicago, Ill.) and evaluate its efficacy in the reinforcement of excisional abdominal wall defects at 1 month, 3 months, and 1 year in a porcine model when compared with a long-term polyglycolic-acid-trimethylene-carbonate (PGA-PMC)-based absorbable mesh (TIGR Matrix Surgical Mesh, Novus Scientific, Uppsala, Sweden). TIGR was chosen for its comparatively protracted strength retention and persistence in vivo, allowing the current study to answer the question of how that effects biocompatibility, and whether increased duration of foreign material actually increases the longevity or magnitude of repair site strength.

METHODS

Materials

DuraSorb is a fully absorbable, macroporous, monofilament surgical mesh that degrades by bulk hydrolysis, once implanted.[15] DuraSorb maintains some strength for 3–4 months before fully resorbing over approximately 9 months. The control TIGR mesh is a macroporous, multifilament, absorbable surgical mesh that fully resorbs by bulk hydrolysis after approximately 3 years.[16] Figure 1 shows the images of the test and control devices before implantation.

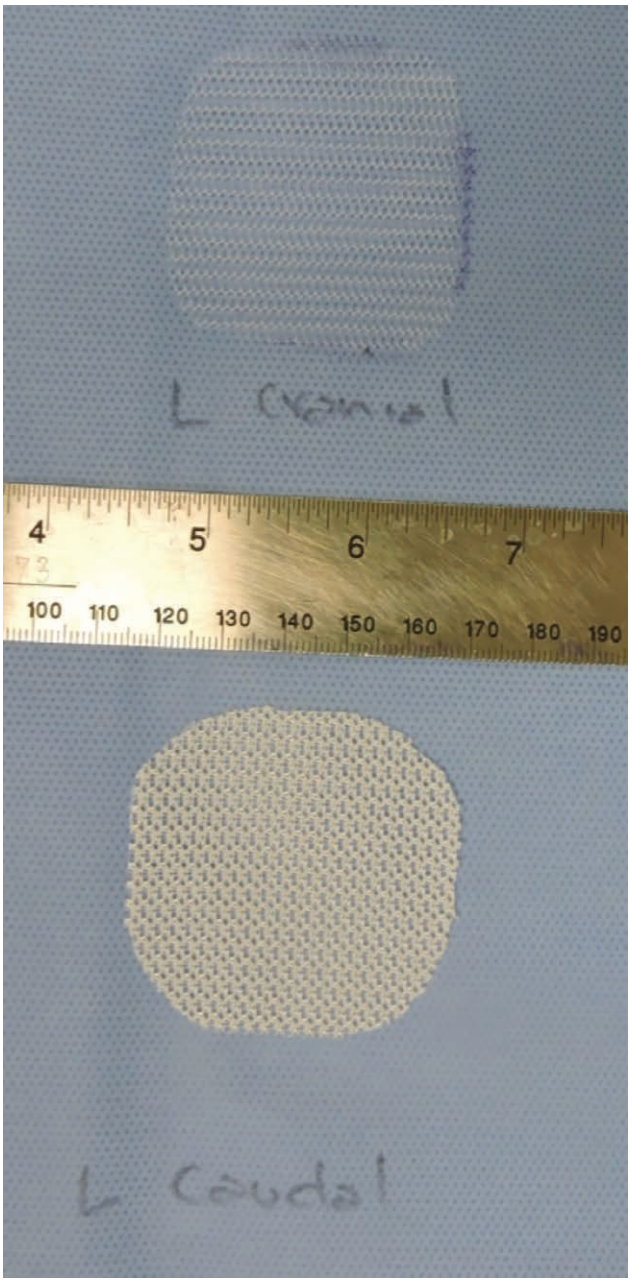

Fig. 1. Devices. Top, Durasorb polydioxanone surgical scaffold. Bottom, TIGR PGA-PMC matrix. Both pieces were trimmed to size.

In Vitro Ball Burst Testing

Specimens were soaked in 1× phosphate buffered saline at 37°C for 0, 2, 4, 8, 12, and 17 weeks. At each interval, the specimens were removed from the bath for mechanical evaluation using a calibrated universal electromechanical testing system (Instron Ball Burst Compression Fixture ASTM D3787). An appropriate load cell (2000 N) was selected such that the applied forces were within the operating range of the load cell. Each sample was clamped in the ball burst fixture and a rounded probe was lowered at a rate of 305 mm/minute until fully forced through the sample. Peak ball burst force data were collected in newtons.

Animal Study

The overall study design is demonstrated in Supplemental Digital Content 1. (**See supplemental figure 1, Supplemental Digital Content 1,** which displays a flowchart depicting the study design. **http://links.lww.com/PRSGO/B623**.)

In this IACUC-approved protocol, female Yucatan miniature swine were prepared for surgery and anesthetized using accepted veterinary care standards. After a 12-hour preoperative fast, animals were sedated with zolazepam (Telazol; Zoetis, Kalamazoo, Mich.; 4–6 mg intramuscularly per kilogram of body weight), intubated endotracheally, and anesthetized with isoflurane (Fluriso, Vetone, MWI,

Boise, Idaho; 1%–5% in oxygen/1–2 L/minute). After surgical disinfection of the abdomen, (1) midline laparotomies were performed through the transversalis fascia, leaving the peritoneum intact, to allow broad visualization of and access to the abdominal wall in the extraperitoneal space. (2) Standardized 2-cm-diameter round defects were excised bilaterally, cranially, and caudally, working from deep to superficial through the abdominal wall, while the skin was left intact. (3) Continuing to work through the midline incision, the defects were bridged with a 5-cm-diameter circular piece of mesh. Defects were randomized to TIGR or DuraSorb. (4) The mesh was placed over the defect in the preperitoneal plane without closing the fascia, to place a more significant strain on the mesh component of the repair. (5) The mesh was fixated circumferentially around the defect using absorbable sutures. (6) The midline laparotomy incision was closed in a standard fashion. Each animal received test control devices, with locations of implant randomized. The implant configuration is shown in Supplemental Digital Content 2. (**See supplemental figure 2, Supplemental Digital Content 2,** which displays device implantations. A, Excisional defect before mesh implantation. B, Durasorb polydioxanone surgical scaffold. C, TIGR PGA-PMC matrix. **http://links.lww.com/PRSGO/B624**.)

Implant site observations were performed daily until incision sites were healed and weekly thereafter. Animals were kept alive for 1 month, 3 months, or 1 year (n = 3 in each group). Before euthanasia, animals were tranquilized with Telazol and anesthetized via isoflurane inhalant. An overdose of potassium chloride solution (IV) was administered in accordance with accepted AVMA guidelines.

A limited necropsy consisting of examination of the implant sites was performed on all animals to determine the presence of seroma, hematoma, fascial dehiscence, herniation, and mesh migration. The skin overlying the implanted regions was removed as superficially as possible. A transverse, full-thickness incision was made to enter the abdomen above the most cranial aspect of the mesh. The abdomen was slowly reflected caudally, and the entire abdominal wall was then explanted en bloc (including the 4 surgical defect repairs/devices with native abdominal wall (NAW) tissue as far lateral as possible) and then placed in saline solution (0.9% NaCl) until mechanical testing.

Macroscopic Analyses

All implants were evaluated for integration into host tissue at all time points (30-day, 90-day, and 365-day) upon killing the animal. Animals were evaluated for serous fluid collections, hematomas, herniations, mesh migrations, and areas of tissue necrosis.

Histology

Unimplanted (T_0) and implant-site tissue samples were trimmed to yield one cross section from the medial-to-lateral aspect, paraffin-embedded, and microtome-sectioned to 5 μm and stained with hematoxylin and eosin (H&E) and Masson's Trichrome (MT) for assessment via light microscopy to characterize local host responses to the implant. Samples were scored for inflammation/inflammatory cell infiltrates (neutrophils, eosinophils, macrophages, lymphocytes, and giant cells), necrosis, neovascularization, and fibrosis, as specified in Table 1. Other evaluated parameters included tissue ingrowth/collagen deposition within implants, vascular ingrowth into implant, fibroplasia, and hemorrhage. All scoring was conducted by a blinded, board-certified veterinary pathologist.

In Vivo Ball Burst Testing

Mechanical evaluations were completed using a calibrated universal electromechanical testing system (Instron ElectroPuls E1000) on the day of explantation. An appropriate load cell (2000 N) was selected such that the applied forces were within the operating range of the load cell. Four control T_0 (nonimplanted) test and control devices were evaluated. Explanted abdominal wall was tested as excised en bloc (without skin or peritoneum). For each repair site tested, an immediately adjacent sample of NAW tissue was also tested for comparison. Peak ball burst force data were collected in newtons. The peak load (ball burst force) was recorded using the computerized data acquisition required to test device failure. After mechanical testing procedures were complete, approximately half of each device was harvested and placed in 10% neutral buffered formalin for histomorphological analysis.

Statistical Analysis

Microsoft Excel software was used to log and analyze all data. *T*-tests, 1-factor ANOVA, and 2-factor ANOVA were

Table 1. Semiquantitative Scale for Assessing Pathologic Cell Infiltrate and Morphologic Changes

Score	Inflammation/Inflammatory Cells (Poly Cells, Lymphocytes, Plasma Cells, Macrophages)
0	Absent
1	Rare, minimal 1–5/per high power field (hpf; 40× obj)
2	Mild, 5–10/hpf
3	Heavy infiltrate, with preservation of local architecture
4	Packed, with effacement of regional architecture
Score	**Necrosis**
0	Absent
1	Minimal, focal, nearly imperceptible
2	Mild, focally extensive, inconspicuous
3	Moderate, multifocal or locally extensive, readily apparent
4	Severe, regionally extensive, overwhelming with effacement of regional architecture
Score	**Neovascularization**
0	Absent
1	Minimal capillary proliferation, focal, 1–3 buds
2	Groups of 4–7 capillaries with supporting fibroblastic structures
3	Broad band of capillaries with supporting structures
4	Extensive band of capillaries with supporting fibroblastic structures
Score	**Fibrosis**
0	Absent
1	Minimal, narrow band, approximately 1–2 cell layers thick
2	Thin, localized band, approximately <10 cell layers thick
3	Moderately thick, contiguous band along length of tissue
4	Extensive, thick zone with effacement of local architecture
Score	**Pertinent Microscopic Observations**
0	No response
1	Minimal/focal/barely detectable
2	Mild/focal or rare multifocal/slightly detectable
3	Moderate/multifocal to confluent/easily detectable
4	Marked/diffuse/very evident

performed on ball burst data as appropriate using an alpha value of 0.05 to report significance. Wilcoxon signed-rank tests were performed on histologic data using an alpha value of 0.05 to report significance. The manual tracing and measurement software used for histomorphometry was the Olympus cellSens Dimension Desktop (version 1.16).

Oversight

There were significant safeguards in place to protect the overall integrity of this study. Namely, this entire work was performed under good laboratory practice regulations to support submission to the US Food and Drug Administration and outside regulatory bodies. The study was designed as a joint effort by the sponsor, consulting surgeons, veterinarians, and regulatory consultants. With the exception of the surgery itself, the study procedures were performed by a third party research laboratory—CBSET, whis is a not-for-profit organization that provides medical device testing and histopathology services, among others. CBSET is accredited by AAALAC International and ensures that all animal testing is in compliance with the USDA and AWA1/AWR2. All analyses were performed, and final reports were generated by CBSET, including biomechanical testing (by their trained laboratory personnel) and histopathology (by a board-certified pathologist) using internationally standardized scales and endpoint definitions (ISO-10993-6:2016).

RESULTS

In Vitro Biomechanical Testing

Five data points were recorded for each time point (n = 5). Figure 2 shows average burst strength of the test device over this time interval. This figure demonstrates strength retention over time in phosphate buffered saline solution at physiologic temperature. The ball burst strength declined as anticipated, with a statistically significant difference between each timepoint during the study (all $P < 0.05$).

In-life Observations

All animals in this study survived until their scheduled euthanasia. One documented postoperative complication was noted, consisting of mild swelling at the DuraSorb-implanted right caudal site through postoperative day 14.

Macroscopic Analyses

All implants (test and control) were fully incorporated into host tissue at all time points (ie, grossly visible tissue infiltration throughout implants) and were still grossly apparent at 30-day and 90-day time points. At 365 days, TIGR Matrix was grossly visible at the relevant repair sites, but DuraSorb was not. No serous fluid collections, hematomas, herniations, mesh migrations, or areas of tissue necrosis were noted at necropsy. (**See figure 3, Supplemental Digital Content 3,** which displays macroscopic pathology at 365 days. At 365 days, TIGR Matrix (A) was grossly visible at the relevant repair sites, whereas DuraSorb (B) was not visible. **http://links.lww.com/PRSGO/B625**.) One animal experienced a 4 × 2-cm focus of osseous metaplasia associated with its midline ventral incision, which was not associated with either device.

Histological Assessment of Inflammation

Example micrographs of control and test devices are shown in (Fig. 3). Inflammatory cell types were heterogeneous and included neutrophils (30-day endpoint only), lymphocytes, macrophages, giant cells, and eosinophils. No foam cells or granulomata were observed during the study. Macrophages were the most prominent cell type

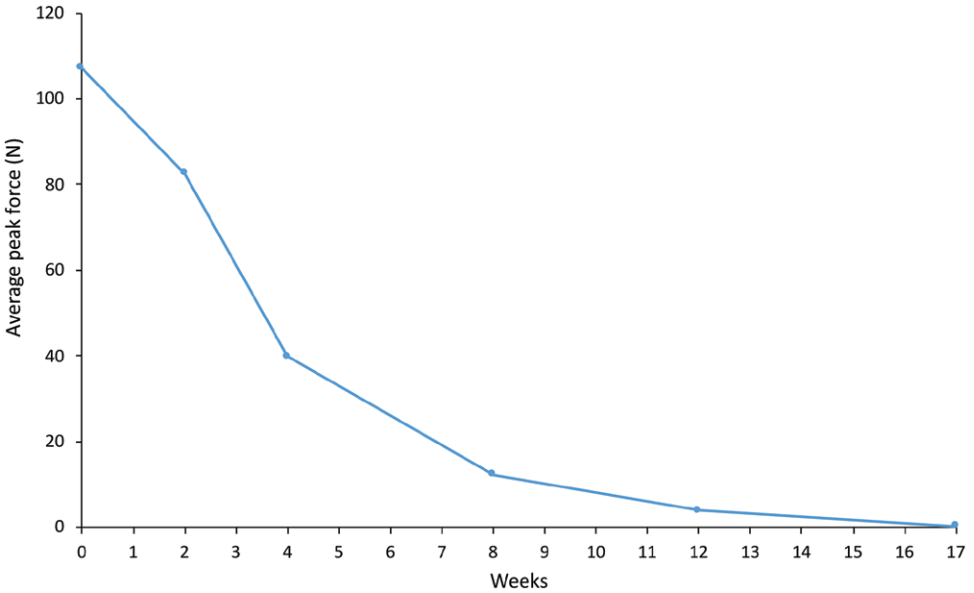

Fig. 2. In vitro strength testing. Durasorb maintains its strength over time in phosphate buffered saline solution at physiological temperature. The ball burst strength declined, with a statistically significant difference between each timepoint.

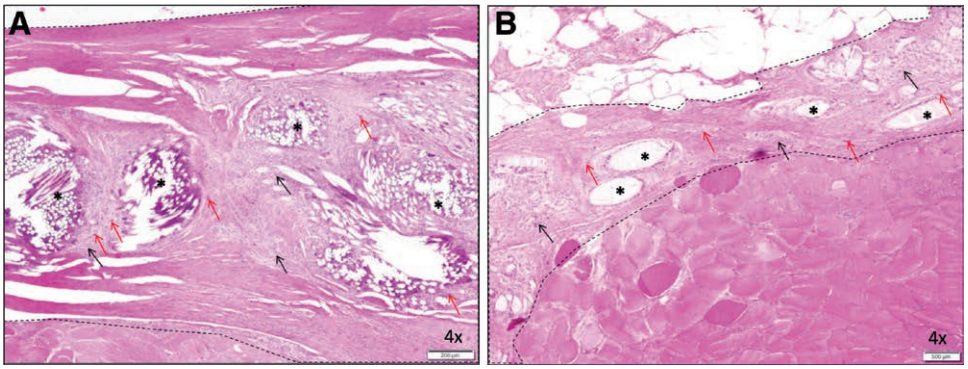

Fig. 3. Microscopic pathology. A. 4x view of H&E-stained segment of implanted TIGR mesh/mesh fibers (asterisks). Mesh fibers are surrounded by fibrovascular tissue (interrupted line). Inflammatory cells (black arrows) and neovascularization (red arrows) are visible. B 4x view of H&E-stained segment of implanted DuraSorb mesh/mesh fibers (asterisks). Mesh fibers are surrounded by fibrovascular tissue. Inflammatory cells (black arrows) and neovascularization (red arrows) are visible.

at days 30 and 90 for both devices, whereas lymphocytes were the most prominent cell type for the test device at day 365. A summary of results can be seen in Table 2. At 30 days, DuraSorb demonstrated a significantly lower overall inflammatory score, driven by lower preponderance of macrophages, and giant cells (both $P < 0.05$). Similar differences were observed at 3 months, though these differences were not significantly different. At 1 year, DuraSorb again exhibited significantly lower overall inflammatory score, driven primarily by the absence of macrophages and giant cells observed in the control device (both $P < 0.05$).

Histomorphological Observations

Pertinent histomorphological scores are summarized in (Table 3). Necrosis and mineralization were not observed during this study. There was no significant difference between test and control device for scores related to neovascularization and vascular integration at days 30 and 90 (both $P > 0.05$). Both devices had mean scores commensurate with mild/conspicuous neovascularization and vascular integration at each time point. At 30 days there was no difference in scores for collagen deposition between the control and test device ($P > 0.05$). The control device showed a significantly higher score for collagen deposition at 90 days ($P < 0.05$). The only hemorrhage observed was in the control device at day 365 (33% of implant sites). DuraSorb was fully absorbed as anticipated at 365 days, precluding comparative assessment of device-associated vascular integration or tissue ingrowth. However, mean fibrotic thickness of the sites at which DuraSorb had been implanted was 0.70 mm (SD = 0.22 mm) despite absence of the device at all sites evaluated. In contrast, the mean fibrotic thickness associated with the control article was 0.63 mm (SD = 0.15 mm), despite persistence of foreign material at all sites evaluated (Fig. 4).

In Vivo Ball Burst Testing

Biomechanical testing was performed in accordance with ASTM D3787 on DuraSorb and TIGR repair sites—as well as on native abdominal tissue—at T_0, day 30, day 90, and day 365. A summary of the data is presented in Figure 5.

The NAW burst strength held relatively stable, as shown by the mean measurements taken on day 30 (87.2 N ± 11.8), day 90 (101.6 N ± 40.4), and day 365 (171.5 N ± 64.4). No significant difference in ball burst strength was demonstrated between NAW and control device at day 30, day 90, and day 365 samples (all $P > 0.05$). The ball burst strength

Table 2. Inflammation and Inflammatory Cell Types Observed

		Day 30		Day 90		Day 365	
Parameter		**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**
Inflammation	DuraSorb	1	1.25	0	1	0	0
	TIGR	1	2.25	1	2	0	0
Neutrophils	DuraSorb	0.5	1	0	0	0	0
	TIGR	1	0.75	0	0	0	0
Eosinophils	DuraSorb	0	0.75	0	0.75	0	0
	TIGR	1	0	0.5	1	0	0
Macrophage/histiocytes	DuraSorb	2	0	2	0	0	0
	TIGR	3	0	2	0	1	0
Lymphocytes	DuraSorb	1	0	0	0	0	0
	TIGR	1	0	1	0.75	0.5	1
Giant cells	DuraSorb	1	0	1	0	0	0
	TIGR	2	0	1.5	1	1	0

Inflammation/Inflammatory Cells Scoring Matrix: 0 = absent, 1 = rare, minimal 1–5/per high power field (hpf; 40× obj); 2 = mild, 5–10/hpf; 3 = heavy infiltrate, with preservation of local architecture; 4 = packed, with effacement of regional architecture.

Table 3. Pertinent Histomorphology Observations

Parameter		Day 30		Day 90		Day 365	
		Median	IQR	Median	IQR	Median	IQR
Neovascularization	DuraSorb	2	0	2	0.75	0	0
	TIGR	2	0	2	1.5	1	0
Fibrosis	DuraSorb	1	0	1.5	1	1	0
	TIGR	1	0.75	2	0	2	1.5
Tissue growth	DuraSorb	4	0	4	0	0	1.5
	TIGR	4	0	4	0	0	1.5
Collagen deposition	DuraSorb	2	0	1.5	1	1	0.75
	TIGR	2	0	1.5	1.75	2	0
Vascular integration	DuraSorb	2	0	2	1	0	1
	TIGR	2	0	2	2	0	1
Fibroplasia (granulation tissue)	DuraSorb	1	0	0	0	0	0
	TIGR	1	0.75	1	0.75	1	0.75
Hemorrhage	DuraSorb	0	0	0	0	0	0
	TIGR	0	0	0	0	0	0

Necrosis Scoring Matrix: 0 = absent; 1 = minimal, focal, nearly imperceptible; 2 = mild, focally extensive, inconspicuous; 3 = moderate, multifocal or locally extensive, readily apparent; 4 = severe, regionally extensive, overwhelming with effacement of regional architecture.
Neovascularization Scoring Matrix: 0 = absent; 1 = minimal capillary proliferation, focal, 1–3 buds; 2 = groups of 4–7 capillaries with supporting fibroblastic structures; 3 = broad band of capillaries with supporting structures; 4 = extensive band of capillaries with supporting fibroblastic structures.
Fibrosis Scoring Matrix: 0 = absent, 1 = minimal, narrow band, ~1–2 cell layers thick; 2 = thin, localized band, < ~10 cell layers thick; 3 = moderately thick, contiguous band along length of tissue; 4 = extensive, thick zone with effacement of local architecture.
Pertinent Microscopic Observations Scoring Matrix: 0 = no response, 1 = minimal/focal/barely detectable; 2 = mild/focal or rare multifocal/slightly detectable; 3 = moderate/multifocal to confluent/slightly detectable, 3 = moderate/multifocal to confluent/easily detectable; 4 = marked/diffuse/very evident.

of the test device significantly increased from day 0 to day 90 ($P < 0.05$). When compared with T_0 samples, the mean mechanical ball burst strength of the test device increased at day 30 (158.4 N ± 54.8) and day 90 (270.7 N ± 69.9). The test device ball burst strength was stable at day 365 (248.3 N ± 86.8) when compared with day 90 measurements. A similar trend in mean mechanical ball burst strength was observed in the control device with 30-day (191.2 N ± 56.7), 90-day (224.1 N ± 72.6), and 365-day (174.8 ± 78.7) time points. However, this trend was not shown to be significant ($P > 0.05$). When test and control devices were compared at day 30, day 90, and day 365, no significant difference in ball burst strength was observed between the test and control device at any time point (all $P > 0.05$).

DISCUSSION

Historically, absorbable meshes have seen infrequent usage, as their strength retention and tissue ingrowth have proved inadequate for most applications.[17–20] In the last 10 years, long-term absorbable meshes made from improved materials have been introduced to facilitate tissue ingrowth and gradual load transfer to surrounding neocollagenous tissue.[21–23] However, these products persist for years and have been associated with late complications that call into question the benefit of their absorbable nature in the first place.[24–26] The DuraSorb mesh presented here is fully synthetic and absorbable, which offers several benefits over alternative biological meshes, which have several known downsides, including higher cost,[10] increased risk of long-term recurrence,[10] potential for disease transmission,[27] and infection.[28] Absorbable meshes, on the other hand, promote postoperative fibroblast activity,[27] reduce late-term fistula development, reduce risk of infection, and have a significantly lower cost.[29] The objective of this study was to understand and compare the mechanical properties, resorption profile, and histological characteristics of a novel medium-term absorbable mesh (DuraSorb), and

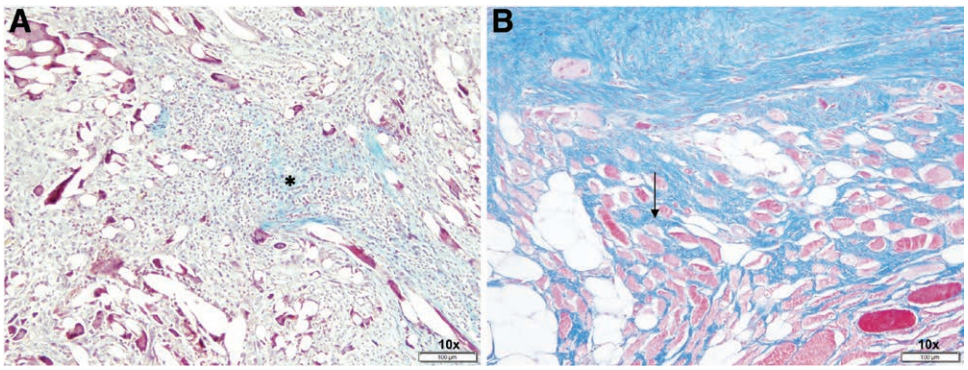

Fig. 4. Histomorphological observations. A, Control TIGR Matrix device at 365 days. Device fibers are surrounded by small amounts of collagen (blue fibers; asterisk). 10× magnification. B, Test Durasorb device at 365 days. Fine collagen fibers (blue fibers; arrow) at the site of device, which has since completely resorbed. 10× magnification.

to evaluate its efficacy in the reinforcement of excisional abdominal wall defects in a porcine model, when compared with a long-term absorbable mesh (TIGR).

This study found a low inflammatory response to the test device at all timepoints, as judged by semi-quantitative scoring. This was true on an absolute basis (score <2 out of 5), and on a relative basis ($P < 0.05$ at both day 30 and day 365) in comparison with the TIGR control. Many factors contribute to the degree of inflammation and FBR to a mesh. Dioxanone-based polymers (such as that used in DuraSorb) have been extensively characterized as implantable materials and are known to elicit a minimal inflammatory and FBR compared with other biomaterials.[30–32] Such dioxanone-based materials have been used widely in surgical sutures, orthopedic pins, and cardiovascular valves, along with numerous other applications.[33] Thus, material selection likely contributed to the test device's biocompatibility. Compared with multifilament meshes such as TIGR (PGA-PMC), monofilament meshes such as DuraSorb have less propensity for bacterial adhesion and subsequent infection and inflammation.[34]

Some degree of FBR is imperative for tissue ingrowth and collagen deposition, adding strength to the healing repair site. Certain elements of mesh design affect these endpoints; for example, macroporous mesh carries well-validated benefits. The ideal diameter has not been defined in the literature, but thresholds such as 800 µm have been delineated, above which bridging granulomata can be avoided, fibroblasts can infiltrate, and neovascularization can occur.[35–37] The test device has a mean pore diameter >1 mm, exceeding this requirement. The histologic analysis in the current study demonstrated a high degree of tissue ingrowth, collagen deposition, vascular integration, and neovascularization, even at the earliest timepoint examined (30 days), which is beneficial for surgery. Early establishment of tissue ingrowth is essential for maintenance of a durable soft tissue repair. This is particularly important in the context of any absorbable mesh, which directly contributes strength only for a limited time, after which there is an indirect contribution from associated collagen deposition and then, ultimately, no contribution at all, as the remnant tissue takes over full load-bearing responsibility. We found that active collagen deposition—a component of ongoing FBR—was unsurprisingly higher in the TIGR sites (given its continued presence at 1 year), while mean fibrotic thickness—the aggregate result of collagen deposition over time—was higher in the DuraSorb sites, despite absence of the device itself at all sites evaluated. We believe total thickness is a better proxy for overall reinforcement than the extent of active collagen deposition.

Classic studies of wound healing indicate that some strength contribution is needed for at least 3 months, until tissue remodeling occurs, and strength reaches a plateau.[38] This is mirrored in postoperative protocols for surgeries, including hernia repair, abdominoplasty, and DIEP flap breast reconstruction, which often restrict activity for 2–3 months.[39] Results from our ball-burst tests show DuraSorb was stronger than the tissue from the NAW at the time of implantation and exceeded the clinical requirement of 16 N/cm, calculated by Deeken et al for a demanding ventral hernia repair.[40] This initial load is transferred from the mesh to the soft tissue as wound healing and tissue ingrowth continue. This is demonstrated by the increasing strength of the repair site during the in vivo portion of the study, which can be seen in (Fig. 6) overlaid with the in vitro results to estimate the relative contributions of tissue versus mesh. Thus, the test device avoids one of the major drawbacks of short-term meshes: absorption before the critical 3-month timepoint when mesh support and neocollagenesis is required. At the same time, it avoids a potential drawback of long-term meshes: foreign material that persists far beyond the crucial period of tissue ingrowth and remodeling. Indeed, one of the most notable findings of the current study is demonstrated in (Fig. 5). The test device repair sites were not significantly weaker at 1 year than those of the control device. The test sites were nominally higher (248.3 ± 86.8 N versus 174.8

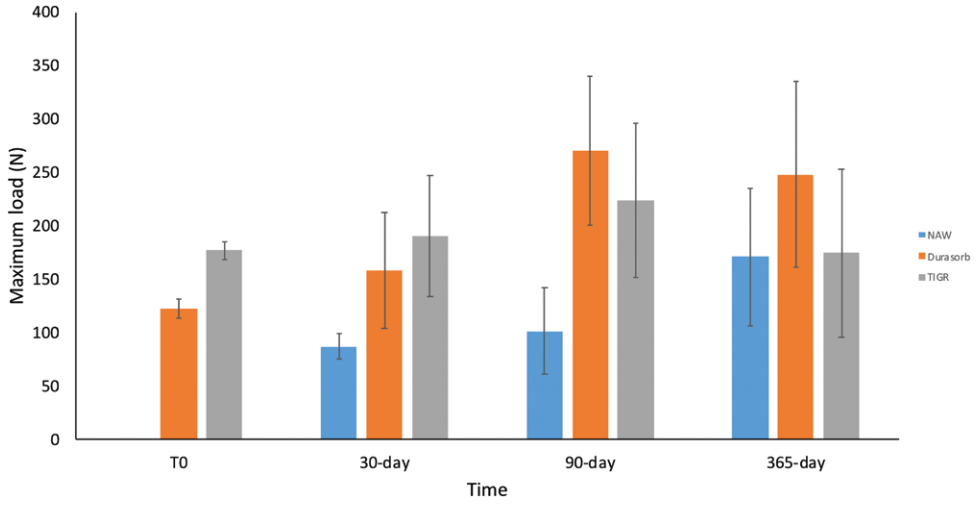

Fig. 5. Strength summary. Biomechanical testing of Durasorb and TIGR repair sites along with native abdominal tissue. There is no significant difference in maximum load bearing between Durasorb and TIGR from 30 days onward.

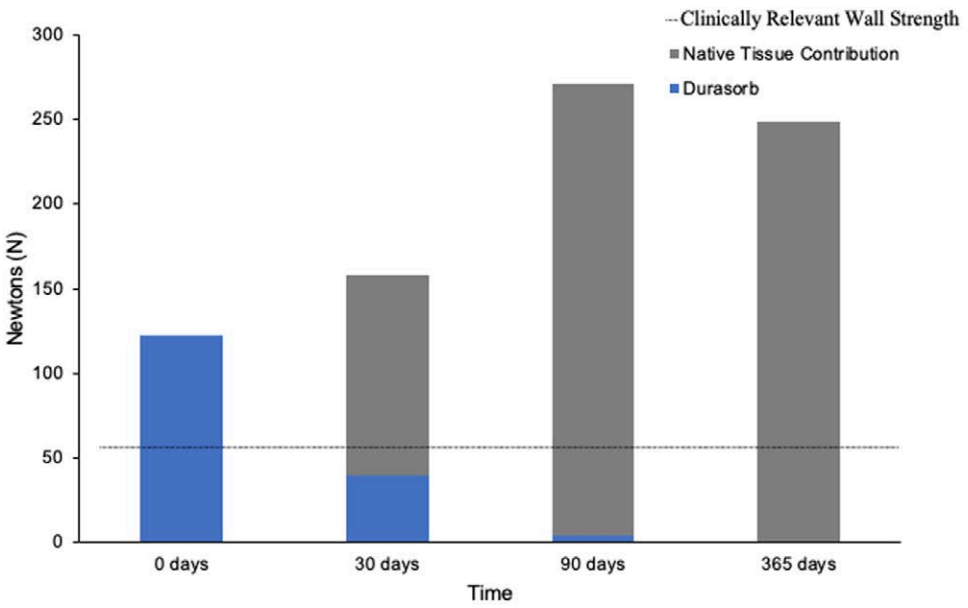

Fig. 6. Durasorb support and strength data over the 1-year study. The reference line represents a geometric transformation of 16 N/cm to an absolute value of 47.88 N, based on the ball burst parameters and aperture diameter; 16 N/cm is a conservative estimate of intra-abdominal stress in an obese man while jumping, modeling the abdominal cavity as a spherical pressure vessel with a radius of 15.8 cm[47] and a pressure of 20 kPa.[48]

± 78.7 N, $P > 0.05$), despite the fact that the test mesh was fully absorbed (as determined by both gross and microscopic analysis of explanted tissue, in which the mesh was not identifiable even employing high-powered fields of up to 200× as dictated by ISO 10993-6:2016), while the control sites still had mechanical strength contributed directly by the long-term control mesh. The native abdominal strength increased over time as the animals used in this study were sexually mature, but not fully grown; we had a moving control to accommodate for the known growth that occurred over the 1-year time period of this study.

These results demonstrate that it is possible that the load-transfer that occurs with appropriate tissue ingrowth may obviate the need for a long-term strength-retaining construct such as a permanent mesh. Indeed, it is well known that a significant portion of the strength in any mesh repair is actually conferred by the FBR and associated collagen deposition.[41] Other materials, including VICRYL, may simply not last long enough for this response to leave a lasting effect; in addition, these are pro-inflammatory, and may thus leave non-viable, friable tissue in their wake.[42,43] In an animal study involving a hamster model, the use of VICRYL mesh was associated with greater inflammation and reduced tissue growth when compared with PROLENE and ULTRAPRO meshes.[17] The authors concluded that the aggressive FBR to VICRYL did not facilitate improved tissue incorporation, as was expected.[17]

PHASIX mesh is derived from monofilament poly-4-hydroxybutyrate (PH4B), which degrades via hydrolysis and an enzymatic digestive process, resulting in full resorption in approximately 18 months. However, there is a lack of clinical data on this material, despite being on the market for several years. The long-term presence of this foreign material may introduce the same feared surgical site complications that might lead to the selection of an absorbable mesh in the first place. In a recent study of Phasix onlay in abdominal wall repair, 5% of patients had an infected mesh, 2.8% required reoperation, and 6% developed a seroma.[44] Similarly, a silk-derived fibroin mesh (SERI, Sofragen, Medford, Mass.) previously demonstrated promising preclinical and early clinical data, only to be plagued with late-presenting infectious and inflammatory complications that led to over 300 FDA-reportable adverse events,[45] academic publications questioning the product's safety,[24] and at least 1 lawsuit.[46] In a previous work, Phasix was evaluated in a porcine model of hernia repair,[22] in which the mesh similarly bolstered the strength of the NAW, and remained elevated despite material resorption over time. Of note, Phasix demonstrated a higher inflammation score at 12 weeks and 1 year when compared with DuraSorb in this study. We believe a medium-term mesh, such as DuraSorb, combines the best of Phasix (maintains strength for 3–4 months to reduce hernia recurrence), and addresses its possibility for long-term complications by resorbing into surrounding tissue over approximately 9 months.

It should be noted that this study was performed in a model where an abdominal wall defect was artificially created, meaning that no previous soft tissue defect existed natively in sample subjects. A patient population being treated for soft tissue weakness or defects may have collagen deficiencies which could have an impact on treatment results for any mesh. Future studies should investigate the use of DuraSorb in patient populations with existing soft tissue defects. Although this study demonstrates that no additional strength or tissue thickness is conferred by using a mesh that lasts for years in comparison with one

that lasts for less than a year, one limitation here is that we implanted the mesh in healthy animals without recurrent defects being repaired. Thus, this data is most relevant to primary mesh placement in patients without known collagen disorders, and recurrent defects represent a key area for future study. Additionally, long-term (3- to 5-year) effects should be studied to understand whether mesh absorption negatively impacts the area of interest. There was 1 minor complication consisting of mild swelling at a DuraSorb implanted site. However, no sequalae were apparent at necropsy or on histopathology.

CONCLUSIONS

This is the first study of a novel bioabsorbable monofilament mesh, DuraSorb. The test mesh and associated tissue ingrowth provided durable, long-term support for an excisional abdominal wound in a porcine model, equivalent to that of a longer-lasting control mesh. DuraSorb also demonstrated lasting collagen deposition, while eliminating the chronic inflammatory response associated with the control mesh. Thus, we demonstrate that soft tissue ingrowth and neocollagenesis can provide significant strength regardless of the persistence of the mesh itself at 1 year. This novel mesh may play a role in hernia repair or other areas of plastic and reconstructive surgery, in cases where the need for permanent strength from the mesh construct itself is in question, or in situations where the risks to the patient of such permanence may outweigh the clinical benefit.

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REFERENCES

1. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaesth*. 2005;95:69–76.
2. Öberg S, Andresen K, Rosenberg J. Absorbable meshes in inguinal hernia surgery: a systematic review and meta-analysis. *Surg Innov*. 2017;24:289–298.
3. Klinge U, Klosterhalfen B, Müller M, et al. Foreign body reaction to meshes used for the repair of abdominal wall hernias. *Eur J Surg*. 1999;165:665–673.
4. Zhong C, Wu B, Yang Z, et al. A meta-analysis comparing lightweight meshes with heavyweight meshes in Lichtenstein inguinal hernia repair. *Surg Innov*. 2013;20:24–31.
5. Balla A, Quaresima S, Smolarek S, et al. Synthetic versus biological mesh-related erosion after laparoscopic ventral mesh rectopexy: a systematic review. *Ann Coloproctol*. 2017;33:46–51.
6. Leber GE, Garb JL, Alexander AI, et al. Long-term complications associated with prosthetic repair of incisional hernias. *Arch Surg*. 1998;133:378–382.
7. Hodde J, Janis A, Ernst D, et al. Effects of sterilization on an extracellular matrix scaffold: part I. Composition and matrix architecture. *J Mater Sci Mater Med*. 2007;18:537–543.
8. Franklin ME Jr, Treviño JM, Portillo G, et al. The use of porcine small intestinal submucosa as a prosthetic material for laparoscopic hernia repair in infected and potentially contaminated fields: long-term follow-up. *Surg Endosc*. 2008;22:1941–1946.
9. Harth KC, Broome AM, Jacobs MR, et al. Bacterial clearance of biologic grafts used in hernia repair: an experimental study. *Surg Endosc*. 2011;25:2224–2229.
10. FitzGerald JF, Kumar AS. Biologic versus synthetic mesh reinforcement: what are the pros and cons? *Clin Colon Rectal Surg*. 2014;27:140–148.
11. Badylak SF, Gilbert TW. Immune response to biologic scaffold materials. *Semin Immunol*. 2008;20:109–116.
12. Kim JYS, Mlodinow AS. What's new in acellular dermal matrix and soft-tissue support for prosthetic breast reconstruction. *Plast Reconstr Surg*. 2017;140:30s–43s.
13. Macadam SA, Lennox PA. Acellular dermal matrices: economic considerations in reconstructive and aesthetic breast surgery. *Clin Plast Surg*. 2012;39:187–216.
14. Bower C, Roth JS. Economics of abdominal wall reconstruction. *Surg Clin North Am*. 2013;93:1241–1253.
15. Lin HL, Chu CC, Grubb D. Hydrolytic degradation and morphologic study of poly-p-dioxanone. *J Biomed Mater Res*. 1993;27:153–166.
16. Dieterich M, Faridi A. Biological matrices and synthetic meshes used in implant-based breast reconstruction – a review of products available in Germany. *Geburtshilfe Frauenheilkd*. 2013;73:1100–1106.
17. Laschke MW, Häufel JM, Scheuer C, et al. Angiogenic and inflammatory host response to surgical meshes of different mesh architecture and polymer composition. *J Biomed Mater Res B Appl Biomater*. 2009;91:497–507.
18. Lamb JP, Vitale T, Kaminski DL. Comparative evaluation of synthetic meshes used for abdominal wall replacement. *Surgery*. 1983;93:643–648.
19. Zieren J, Castenholz E, Baumgart E, et al. Effects of fibrin glue and growth factors released from platelets on abdominal hernia repair with a resorbable PGA mesh: experimental study. *J Surg Res*. 1999;85:267–272.
20. Dayton MT, Buchele BA, Shirazi SS, et al. Use of an absorbable mesh to repair contaminated abdominal-wall defects. *Arch Surg*. 1986;121:954–960.
21. Gross JE, Horan RL, Gaylord M, et al. An evaluation of SERI surgical scaffold for soft-tissue support and repair in an ovine model of two-stage breast reconstruction. *Plast Reconstr Surg*. 2014;134:700e–704e.
22. Deeken CR, Matthews BD. Characterization of the mechanical strength, resorption properties, and histologic characteristics of a fully absorbable material (Poly-4-hydroxybutyrate-PHASIX Mesh) in a porcine model of hernia repair. *ISRN Surg*. 2013;2013:238067.
23. Hjort H, Mathisen T, Alves A, et al. Three-year results from a preclinical implantation study of a long-term resorbable surgical mesh with time-dependent mechanical characteristics. *Hernia*. 2012;16:191–197.
24. Almesberger D, Zingaretti N, Di Loreto C, et al. Seri: a surgical scaffold for breast reconstruction or for bacterial growth? *J Plast Reconstr Aesthet Surg*. 2015;68:870–871.
25. Crowley TP, Collin T. Re: 'Seri: a surgical scaffold for breast reconstruction or for bacterial ingrowth?'. *J Plast Reconstr Aesthet Surg*. 2015;68:1629.
26. Hallberg H, Lewin R, Elander A, et al. TIGR matrix surgical mesh – a two-year follow-up study and complication analysis in 65 immediate breast reconstructions. *J Plast Surg Hand Surg*. 2018;52:253–258.
27. Baylón K, Rodríguez-Camarillo P, Elías-Zúñiga A, et al. Past, present and future of surgical meshes: a review. *Membranes (Basel)*. 2017;7:47.

28. Elango S, Perumalsamy S, Ramachandran K, et al. Mesh materials and hernia repair. *Biomedicine (Taipei)*. 2017;7:16.
29. Ganz OM, Tobalem M, Perneger T, et al. Risks and benefits of using an absorbable mesh in one-stage immediate breast reconstruction: a comparative study. *Plast Reconstr Surg*. 2015;135:498e–507e.
30. Laufer N, Merino M, Trietsch HG, et al. Macroscopic and histologic tissue reaction to polydioxanone, a new, synthetic, monofilament microsuture. *J Reprod Med*. 1984;29:307–310.
31. Sanz LE, Patterson JA, Kamath R, et al. Comparison of Maxon suture with Vicryl, chromic catgut, and PDS sutures in fascial closure in rats. *Obstet Gynecol*. 1988;71(3 pt 1):418–422.
32. Kosan M, Gonulalan U, Ozturk B, et al. Tissue reactions of suture materials (polyglactine 910, chromed catgut and polydioxanone) on rat bladder wall and their role in bladder stone formation. *Urol Res*. 2008;36:43–49.
33. Martins JA, Lach AA, Morris HL, et al. Polydioxanone implants: a systematic review on safety and performance in patients. *J Biomater Appl*. 2020;34:902–916.
34. Klinge U, Park JK, Klosterhalfen B. 'The ideal mesh?'. *Pathobiology*. 2013;80:169–175.
35. Jerabek J, Novotny T, Vesely K, et al. Evaluation of three purely polypropylene meshes of different pore sizes in an onlay position in a New Zealand white rabbit model. *Hernia*. 2014;18:855–864.
36. Zhu LM, Schuster P, Klinge U. Mesh implants: an overview of crucial mesh parameters. *World J Gastrointest Surg*. 2015;7:226–236.
37. Junge K, Binnebösel M, von Trotha KT, et al. Mesh biocompatibility: effects of cellular inflammation and tissue remodelling. *Langenbecks Arch Surg*. 2012;397:255–270.
38. Levenson SM, Geever EF, Crowley LV, et al. The healing of rat skin wounds. *Ann Surg*. 1965;161:293–308.
39. Ruiz-Jasbon F, Norrby J, Ivarsson ML, et al. Inguinal hernia repair using a synthetic long-term resorbable mesh: results from a 3-year prospective safety and performance study. *Hernia*. 2014;18:723–730.
40. Deeken CR, Abdo MS, Frisella MM, et al. Physicomechanical evaluation of polypropylene, polyester, and polytetrafluoroethylene meshes for inguinal hernia repair. *J Am Coll Surg*. 2011;212:68–79.
41. Jordan SW, Fligor JE, Janes LE, et al. Implant porosity and the foreign body response. *Plast Reconstr Surg*. 2018;141:103e–112e.
42. Lock AM, Gao R, Naot D, et al. Induction of immune gene expression and inflammatory mediator release by commonly used surgical suture materials: an experimental in vitro study. *Patient Saf Surg*. 2017;11:16.
43. Cavallaro A, Sciacca V, Cisternino S, et al. Experimental evaluation of tissue reactivity to vascular sutures: dacron, polypropylene. *PTFE*. 1987;21:82–86.
44. Levy AS, Bernstein JL, Premaratne ID, et al. Poly-4-hydroxybutyrate (Phasix) mesh onlay in complex abdominal wall repair. *Surg Endosc*. 2020. [E-pub ahead of print]
45. U. S. Food & Drug Administration. MAUDE – Manufacturer and User Facility Device Experience. 2019. Available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/textResults.cfm. Accessed March 26, 2019.
46. Law Offices of Robert Vaage. The Law Offices of Robert Vaage Settles $1M+ Case Involving Alleged Conspiracy Between Cosmetic Surgeon & Medical Device Company. 2018. Accessed March 7, 2019. Available at https://www.prnewswire.com/news-releases/the-law-offices-of-robert-vaage-settles-1m-case-involving-alleged-conspiracy-between-cosmetic-surgeon–medical-device-company-300628444.html.
47. NHLBI. Classification of Overweight and Obesity by BMI, Waist Circumference, and Associated Disease Risks. 2021. Accessed 02-05-2021. Available at https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmi_dis.htm.
48. Cobb WS, Burns JM, Kercher KW, et al. Normal intraabdominal pressure in healthy adults. *J Surg Res*. 2005;129:231–235.