Biodegradable Meshes in Abdominal Wall Surgery

Garth Jacobsen and Christopher DuCoin

Introduction

Tension-free hernia repair with reinforcement by synthetic, nonresorbable mesh has led to a drastic reduction in the rate of hernia recurrence. However, these permanent foreign materials have been implicated in causing the development of chronic inflammation and fibrosis, which have been attributed to post-operative issues such as chronic pain and abdominal wall stiffness [1–3]. Most surgeons fear their use in contaminated environments due to the high risk of mesh infection and subsequent required explant [4]. Thus acellular, biological meshes of both human and animal origin have been suggested as the alternative to the synthetics in contaminated fields [5, 6]. However, the high cost of biological meshes, at roughly $25–30 per cm^2, has been shown to result in a median net financial loss of $8370 per hospital admission for large abdominal wall hernias [7]. Recently, the use of reduced-weight polypropylene synthetic mesh in clean-contaminated and contaminated fields was studied and found to have both similar surgical site occurrences and mesh removal rates when compared to biologics [8]. However, no mesh to this point has been FDA approved for the use in contaminated

surgical fields. This leaves us in a state of confusion. The dogma remains that synthetic mesh provides radically lower rates of hernia recurrence and that biologics are supreme when used in dirty surgical fields. There may be more lure to these assumptions than evidence based understanding, and thus these teachings should no longer be taken as definitive rule. So where does this leave us, is there a happy medium between synthetic and biologic? Yes, the benefits of both synthetics and biologics can be found in the synthetic bioabsorbable meshes.

Types of Bioabsorbables

Bioabsorbables are composed of synthetic resorbable monofilament polymers, either in a single or double layer that is gradually degraded over time. Yet, as the mesh is being degraded it is also providing the structural framework for the host tissue to incorporate with, and allows for the remodeling of the abdominal wall with native tissue. The end result is that the abdominal wall strength is provided by the host's own tissue. Thus, as there is no permanent foreign body, the likelihood of infection is drastically reduced. Currently there are four major types of bioabsorbable mesh. These meshes include Ethicon Vicryl Mesh (Ethicon Inc., Somerville, NJ), Phasix Mesh (C. R. Bard, Inc./Davol Inc., Warwick, RI), Tigr Matrix (Novus Scientific, Uppsala, Sweden), and Gore Bio-A (W.L. Gore

G. Jacobsen, M.D. (✉) • C. DuCoin, M.D., M.P.H.
Department of Surgery, University of California,
San Diego, 9500 Gilman Drive, MC 0740 l,
La Jolla, CA 92093-0740, USA
e-mail: gjacobsen@ucsd.edu; cducoin@ucsd.edu

Table 8.1 Inventory of Bioabsorbable meshes

	Collagen deposit	Majority of strength lost	Full resorption (months)	Studies
VICYRL	Low	75% of strength lost in 14 days	2–3	Animal
				Human
PHASIX	Not reported	4–8 months	12–18	Animal
TIGR	Mixed ratio over 36 months	8–9 months	36	Animal
				Human
BIO-A	100% Type 1 at 30 days	3–4 months	6	Animal
				Human

Electron Microscopy of Synthetic Bioabsorbable Mesh
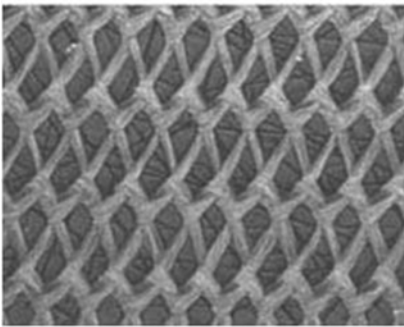
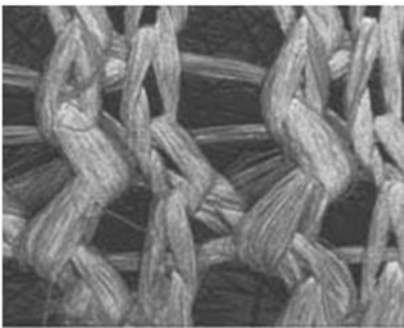

Vicryl™ Mesh
SEM photo, 20x
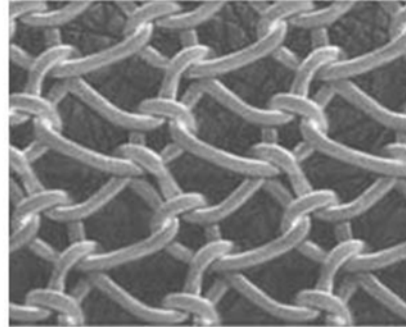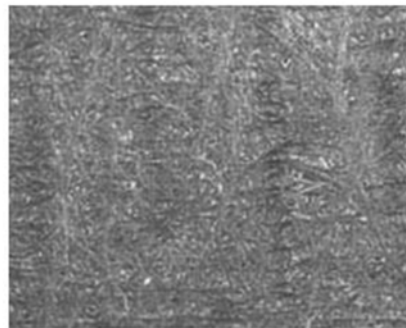
Phasix™ Mesh
SEM photo, 20x

TIGR® Matrix
SEM photo, 20x

Bio-A®Mesh
SEM photo, 20x

Fig. 8.1 Electron microscopy of synthetic bioabsorbable mesh at twenty times magnification. The images delineate the intricate woven matrix styles and size, along with the caliber of porosity. Vicryl mesh is a tightly woven single layer mesh with a symmetrical pattern. Phasix mesh has a greater caliber matrix with more porosity. TIGR Matrix is composed to two polymers that are degraded at different rates, with differed caliber size and vast porosity. Bio-A mesh is also composed of copolymers but possesses a unique non-woven matrix

and Associates, Inc., Flagstaff, AZ) which will be reviewed in greater detail (Table 8.1). Fundamentally these meshes have very different structural patterns as can be seen with electron-microscopy (Fig. 8.1).

Vicryl (polyglactin 910) woven mesh is prepared from a synthetic absorbable co-polymer of glycolide and lactide. This tightly woven mesh is prepared from uncoated, undyed fiber identical in composition to that used in Vicryl synthetic

absorbable suture. This material has been found to be inert, nonantigenic, nonpyrogenic and to elicit only a mild tissue reaction during absorption. Vicryl woven mesh is intended for use as a buttress to provide temporary support during the healing process. However, Vicryl loses 77% of its strength in the first 14 days (0.5 month) in rat models, and it is fully resorbed in approximately 60–90 days (2–3 months). Thus, Vicryl mesh is absorbed the fastest of all the synthetic bioabsorbables. Vicryl degrades in vivo through hydrolysis and is known to decrease the pH in the local tissues [9]. When compared to other biologics, Vicryl was found to have lower collagen deposition and neovascularization, which has been attributed to this decrease in pH [9, 10]. There is also an increase in inflammation at the wound site as Vicryl mesh degrades [9, 10]. Overall, Vicryl mesh is resorbed quickly, losing its mechanical strength too fast, making it less than ideal for hernia repair [11]. A mesh that provides greater structural support of the hernia site for a longer period of time will be required to allow for adequate completion of tissue remodeling [11].

Thus, more recent absorbable scaffold designs have been developed which utilize long lasting polymers that degrade slower. Bard's Phasix Mesh is constructed of monofilament poly-4-hydroxybutyrate (P4HB), a resorbable polymer. P4HB is a naturally derived, fully absorbable polymer produced by *Escherichia coli* K12 bacteria via transgenic fermentation techniques [12]. P4HB degrades in vivo through both hydrolysis and a hydrolytic enzymatic digestive process and is fully resorbed in approximately 365–545 days (12–18 months) [12]. The resulting by-products (carbon dioxide and water) are metabolized quickly via the Krebs Cycle and beta-oxidation, with minimal effect on the local wound environment [12]. Unlike absorbable scaffolds such as Vicryl, whose by-products decrease the local pH, degradation of P4HB is not as acidic, which may reduce the inflammatory response associated with these materials [12]. An animal study evaluated Phasix Mesh and P4HB Plug repair sites over a 52 week period and showed a significantly greater burst strength and relative stiffness with the mesh when compared to the native abdominal wall at all-time intervals [11]. In addition, histological assessment revealed a comparable and mild inflammatory response, and mild to moderate granulation tissue/vascularization associated with the P4HB material regardless of its configuration as a mesh or a plug [11]. Studies thus far have all been completed in animal models and additional human models will hopefully show the same benefits.

Tigr Matrix is knitted from two fibers having different resorption rates. The first fiber makes up approximately 40% of the overall mesh by weight and is a copolymer of polyglycolide, polylactide, and polytrimethylene carbonate. This fiber degrades in vivo through hydrolysis, loses substantial mechanical strength in the first 14 days (0.5 month), and is fully resorbed in approximately 120 days (4 months). The second fiber makes up approximately 60% of the overall mesh by weight and is a copolymer of polylactide and polytrimethylene carbonate. This fiber also degrades in vivo through hydrolysis, but it retains its mechanical strength longer than the first fiber. It begins to demonstrate loss of mechanical strength after approximately 270 days (9 months) and is fully resorbed in approximately 1095 days (36 months). Tigr Matrix has been evaluated in a long-term animal model, and a clinical trial is currently underway. In the animal study, Tigr Matrix was compared to permanent polypropylene mesh in sheep with full thickness abdominal wall defects over the course of 4, 9, 15, 24, and 36 months [13]. The results showed the typical long-term inflammatory response found with the permanent polypropylene mesh. However, Tigr Matrix demonstrated a medium-term inflammatory response similar to that of polypropylene, with the important difference being that inflammation declined after 24 months and was practically absent after 36 months once the mesh had been completely resorbed [13]. Tigr Matrix also exhibited collagen deposition at the repair site that increased over time and eventually resembled native connective tissue [13]. In the study no defect recurrences were noted in either the test or control group. Since Tigr Matrix loses the bulk of its mechanical strength after 6 months, it can be assumed that the restored tissue is evidently

strong enough to carry the abdominal loads found in these sheep models [13]. In the clinical trial, 40 subjects were enrolled and followed for 1 year after placement of Tigr Matrix to repair a primary inguinal hernia [14]. Pain and recurrence were evaluated at 0.5, 1, 3, 6, and 12 months, and pain scores were reduced from an average of 17.4 before surgery to 0.3 after just 6 months post operatively [14]. In conclusion, Tigr Matrix is fully resorbed in 3 years, shows an inflammatory response that reduces over time, and is associated with a reduction in post-operative pain.

Gore Bio-A is a copolymer composed of polyglycolic acid and trimethylene carbonate (PGA-TMC) that degrades in vivo through both hydrolytic and enzymatic mechanisms. Bio-A is fully resorbed within approximately 180 days (6 months). Published studies to date are mainly in animal models with an international multi-center human clinical trial having just been completed. In an animal study, Bio-A showed higher degree of cellular and vascular ingrowth, and collagen deposition than three commonly used biologic meshes in a sterile field [15]. In regard to vascular ingrowth, Bio-A showed a statistically significant increase in blood vessel ingrowth when compared to biologics ($p < 0.0001$) [15]. The vascular ingrowth for Bio-A was greatest between days 7–14, while the biologics had no significant change after 7 days [15]. Samples of Bio-A demonstrated that at 30 days the collagen was 100% Type 1 [15]. This is significantly earlier than the biologics ($p = 0.006$) [15]. Bio-A also exhibited the least inflammatory infiltrate over time [15]. The outcomes thus far have been promising with low rates of recurrence, infection, and pain.

A recently completed international multi-center prospective human study evaluated Bio-A in clean contaminated and contaminated ventral hernia repairs with outcome measures of hernia recurrence, surgical site events (SSE), and quality of life. Of the 104 patients enrolled the mean follow-up time was 16 months. Findings at that time of evaluation showed a hernia recurrence rate of 14% and a SSE rate of 28%, with a surgical site infection rate (SSI) of 18% ($n = 21$). When the group analyzed the risk factors for hernia recurrence they found that body mass index (BMI), previous infected mesh, position of mesh, and post-operative SSI were statistically significant contributors to risk of recurrence. It was also found that the average BMI for no midline recurrence was 27 kg/m^2 while the BMI for recurrence of midline hernia was 34 kg/m^2 (p-value 0.004), and that previous mesh infection had a p-value of 0.031. Position of mesh was also important in that there was a significantly lower recurrence rate when the mesh was placed into the retro-rectus position. When the mesh was placed in an intrapertioneal position the recurrence rate was 30%, yet when placed retro-rectus the recurrence rate dropped to 5% (p-value 0.028). Also, with a post-operative SSI the recurrence rate was 21% while in those without post-operative SSI the recurrence rate was 5% (p-value 0.035). In regard to SSI, 18% had infections post-operatively, but since all Bio-A mesh was placed into contaminated fields in this study, it can be argued that 82% of patients were cured of their previous infection. Of the SSI's, nine were superficial and responded to antibiotic treatment only, while ten were deep requiring drain placement with antibiotics. However, no mesh required explant. When looking at risk factors for SSI, diabetes mellitus ($p = 0.042$), fistula take down ($p = 0.001$), and previous mesh ($p = 0.019$) were found to be significant risk factors. When evaluating for quality of life scores, the data showed an initial drop. However, over time there was a significant improvement. The authors concluded that the hernia recurrence rate was acceptable and improved with retro-rectus placement, that mesh infection could be managed conservatively, and patients benefited from an improved quality of life.

Placement into Infected Surgical Fields

The infected surgical field remains the most challenging area of mesh placement as mesh infection can be a catastrophic and mortal event to the patient. As mentioned above, synthetic bioabsorbable mesh has been used successfully in this setting. The study above showed that Bio-A used
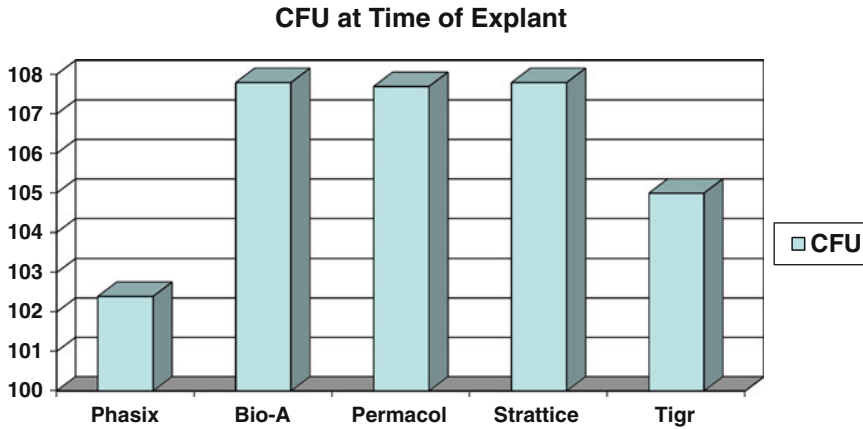
Fig. 8.2 Bacterial clearance

in clean contaminated and contaminated ventral hernia repairs had a post operative surgical site infection rate (SSI) of 18%. The astonishing finding in this study is that no mesh required removal and that all infections, both superficial and deep, could be treated with conservative measures. An animal study found that Bio-A was safe to use in a contaminated surgical field [16]. In a rat model, that used methicillin resistant *Staphylococcus aureus* (MRSA) as contaminate, bacteria were cleared from the Bio-A mesh more effectively than either Vicryl or Tigr Matrix at an inoculum greater than 106 [16]. However, at an inoculum of 104 or less, all three scaffolds performed equally. All three of the scaffolds exhibited reduced tensile strength and increased rate of mesh failure regardless of composition if there was any inoculum present [16]. A similar study recently completed by Dr. Voeller et al. compared Phasix Mesh to various other mesh types. In this study, a rabbit dorsal model using one of the mesh types was inoculated with MRSA 1×10^8 colony forming unites (CFU)/mL. On post operative day number seven the mesh was explanted then examined for number of CFU/mL. All mesh types showed a decrease in CFU/mL, however Phasix and Tigr Mesh showed the greatest reduction (Fig. 8.2). As the data of these two studies can be somewhat confusing, each study showing a different mesh with better bacterial clearance, it is still evident that synthetic bioabsorbable mesh can not only tolerate placement into an infected field, but can also clear the bacteria present.

Another animal study examined the infection rates when the mesh was impregnated with antibiotics, specifically cefazolin [17]. In this study 90 white rats were divided into four groups where Bio-A was placed in an intraperitoneal position. Group 1 consisted of mesh only (control group), in group 2 the mesh was infected at 1 week post operative with 1×10^8 CFU of *S. aureus*, in group 3 antibiotic-impregnated mesh used and then infected at 1 week's time, and in group 4 the antibiotic quantity was double that of group 3 and subsequently infected at 1 weeks time. The groups were then examined at 1 week post infection, or post-op week 2 for bacterial colonization. Evident decrease of bacterial colonization was observed in groups 3 and 4, the ones impregnated with cefazolin, in comparison with the group 2, infected without previous antibiotic impregnation, with statistically significant results ($p < 0.001$). Thus, the authors suggest that impregnation of an absorbable hydrophilic prosthesis, such as Bio-A, with cefazolin will help reduce the rate of mesh infection when placed in a contaminated field.

Which Mesh to Use and When to Use It and Where to Put It

It has been our practice to base the type of mesh selection on a case-by-case basis, as truly every patient is unique in regard to abdominal wall reconstruction. When using synthetic mesh we prefer lightweight macro-porous mesh. We have moved away from the classic biologic mesh as empirically little benefit was found at an extremely elevated cost when compared to the synthetic bioabsorbables. Synthetic bioabsorbable mesh is roughly 1/3–1/10 the cost of a matched piece of biologic mesh. Over the last 5 years when treating complex abdominal wall hernias with the possibility of either a clean-contaminated or contaminated field we have opted to use a bioabsorbable mesh. Our outcomes have been so positive that we no longer stock biologic mesh at our center.

When looking at our data in regard to bioabsorbable mesh for complex abdominal wall hernias we found that over the last 5 years 147 patients have been treated with either Bio-A or Tigr Matrix. These hernia defects have consisted of extremely large areas with the average hernia defect being 130.8 cm^2. Of these 147 patients, 52 of them (35.4%) presented with a recurrent hernia that had undergone previous attempted repair, with a cumulative of 83 previous attempted hernia repairs. A CDC wound classification was found to be Class II or greater in 41 patients (27.9%). The average follow-up duration for this study population was 582 days. There was a total number of 27 (18.3%) wound complications, consisting of seroma ($N=13$), wound infection ($N=7$), retro-rectus hematoma ($N=4$), and flap necrosis ($N=3$). In the study population there were four recurrences (2.7%), and a single explant. Though the average follow-up for this study group is less than 2 years, we feel the wound complication rate and the drastically lower recurrence rate when compared to biologic mesh warrants the use of synthetic bioabsorbables in large complex abdominal wall hernia reconstruction where there is risk of contamination.

In regard to placement of mesh, we use a very straight forward algorithm (Fig. 8.3). Our goal is to always place the mesh in a sublay fashion, in an attempt to reduce wound complications and infections, in the belief that it is a more appropriate physiological placement. For any defect less than 25 cm^2 we will attempt to place our mesh in a retro-rectus position. We have found that for defects larger than 25 cm^2 an alternate fascial release is required. In determining which type of release to use, we use resection of panniculectomy as the determinant. If a panniculectomy is to be performed usually the morbidity of creating skin flaps has already taken place. Thus, we will use a standard component separation with an onlay mesh placement that is sutured to the lateral edge of the released external oblique fascia under moderate tension. If a panniculectomy is not part of the abdominal wall hernia repair, then we will continue with our retro-rectus dissection and extend it to a Transversus abdominis muscle release (TAR), detailed in Chapter 13. In this fashion the midline can be brought back together and the mesh placed behind the transversus abdominis and the rectus muscles, cut to fit and not affixed. Multiple drains are placed to combat seroma formation and allow for good tissue approximation and mesh ingrowth.

Conclusion

Synthetic bioabsorbable meshes provide the initial rigidity found in synthetic mesh while degrading over time, much like a biologic, reducing the risk of infection and need for mesh removal. Our data supports that they have a lower recurrence rate when compared to biologics while maintaining the same complication risk when used in contaminated fields. They do this at a drastically reduced cost. Excluding Vicryl mesh, bioabsorbable meshes have been shown to have collagen deposition that resembles native connective tissue. When compared to synthetics they have a lower inflammatory response which facilitates greater tissue ingrowth. Thus, in large complex abdominal wall hernias where there is a possibility of clean contaminated or contaminated wounds, we have chosen synthetic
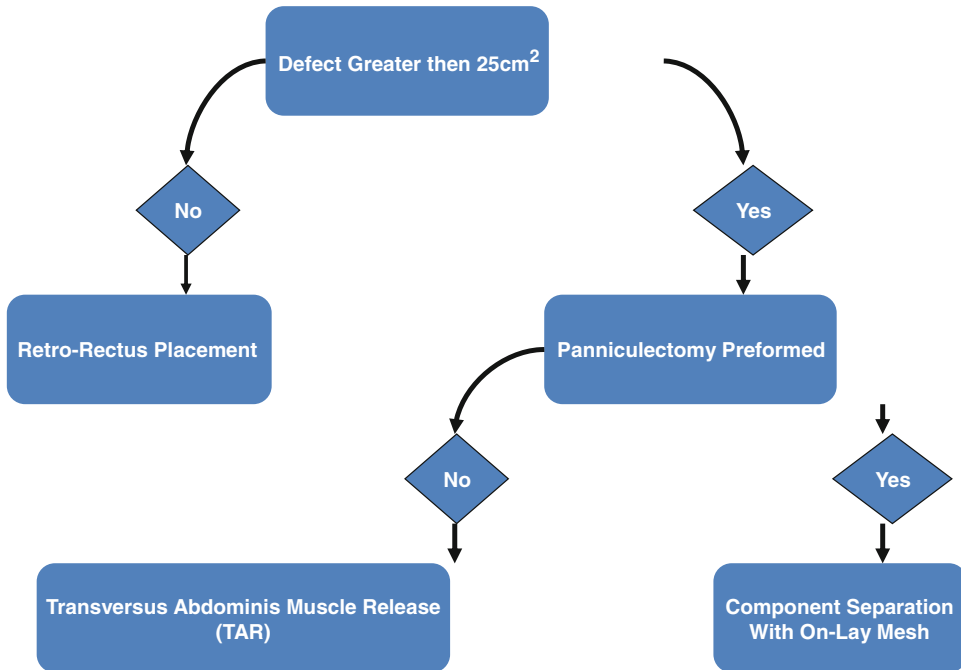
Fig. 8.3 The UCSD algorithm for mesh placement. It is our institutional preference to perform mesh placement in an underlay fashion. We have found that if the defect is less than 25 cm^2 the mesh can be placed into the retro-rectus space without tension. However, if the defect is larger than 25 cm^2 a greater facial release will be required.

We prefer the Transversus Abdominis Muscle Release (TAR). However, if a panniculectomy is performed simultaneously with the hernia repair and the morbidity of the skin flaps has already been created, then we perform the standard components separation with an onlay mesh

bioabsorbable mesh over biologics. Both, a large multi-center international study along with our data supports this decision, that there is a lower hernia recurrence rate with similar wound complications when compared to biologics at a reduced cost.

References

1. Kingsnorth A, LeBlanc K. Hernias: inguinal and incisional. Lancet. 2003;362:1561.
2. Binnebose M, Von Trotha KT, Jansen PL, Conze J, Neumann UP, Junge K. Biocompatibility of prosthetic meshes in abdominal surgery. Semin Immunopathol. 2011;33:235.
3. Peeters E, Barneveld K, Schreinemacher M, Hertogh G, Ozog Y, Bouvy N, Miserez M. 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(2):274–83.
4. Engelsman AF, Van Der Mei HC, Ploeg RJ, et al. The phenomenon of infection with abdominal wall reconstruction. Biomaterials. 2007;28:2314–24.
5. Badylak SF. The extracellular matrix as a biologic scaffold material. Biomaterials. 2007;28:3587.
6. Cavallaro A, Lo Menzo E, Di Vita M, et al. Use of biological meshes for abdominal wall reconstruction in highly contaminated fields. World J Gastroenterol. 2010;16(15):1928–33.
7. Reynolds D, Davenport DL, Korosec RL, Roth JS. Financial implications of ventral hernia repair: a hospital cost analysis. J Gastrointest Surg. 2013;17(1):159–66.
8. Carbonell AM, Criss CN, Cobb WS, Novisky YW, Rosen MJ. Outcomes of synthetic mesh in contaminated ventral hernia repairs. J Am Coll Surg. 2013;217(6):991–8.
9. Rice RD, Ayubi FS, Shaub ZJ, Parker DM, Armstrong PJ, Tsai JW. Comparison of surgisis, AlloDerm, and Vicryl Woven Mesh grafts for abdominal wall defect repair in an animal model. Aesthetic Plast Surg. 2010;34(3):290–6.
10. Laschke MW, Häufel JM, Scheuer C, Menger MD. Angiogenic and inflammatory host response to surgical meshes of different mesh architecture and polymer composition. J Biomed Mater Res B. 2009;91(2):497–507.
11. 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;2013:238–67.

12. Martin DP, Williams SF. Medical applications of poly-4-hydroxybutyrate: a strong flexible absorbable biomaterial. Biochem Eng J. 2003;16(2):97–105.

13. Hjort H, Mathisen T, Alves A, Clermont G, Boutrand JP. Three-year results from a preclinical implantation study of a long-term resorbable surgical mesh with time-dependent mechanical characteristics. Hernia. 2012;16:191.

14. Ruizjasbon F. Norrby six months results of first-in-man trial of a new synthetic long-term resorbable mesh for inguinal hernia repair. Istanbul: European Hernia Society; 2010.

15. Zemlyak AY, Colavita PD, Tsirline VB, Belyansky I, El-Djouzi S, Norton HJ, Lincourt AE, Heniford BT. Absorbable glycolic acid/trimethylene carbonate synthetic mesh demonstrates superior in-growth and collagen deposition. Abdominal Wall Reconstruction Conference, June 13–16, 2012, Washington, DC.

16. Blatnik JA, Krpata DM, Jacobs MR, Novitsky YW, Rosen MJ. Effect of wound contamination on modern absorbable synthetic mesh. Abdominal Wall Reconstruction, June 2011.

17. Suarez JM, Conde SM, Galan VG, Cartes JA, Durantez FD, Ruiz FJ. Antibiotic embedded absorbable prosthesis for prevention of surgical mesh infection: experimental study in rats. Hernia. 2012;19(2):187–94.