In October 2017, TELA Bio® convened a panel of 7 expert surgeons to review the current landscape of mesh-based hernia repair. This meeting provided a forum for these surgeons to present the rationale and important factors that guide their hernia repair material selection process. The surgeons also presented their experience and representative cases with OviTex® Reinforced BioScaffolds (RBSs), a new category of hernia repair materials. Collectively, the 7 surgeons have experience with over 200 cases using OviTex RBSs. This article summarizes the themes and discussions of the 2-day conference. The objective of this paper is to present the learnings and conclusions from the conference to a larger audience so that others can benefit from the panel’s expertise and insights.

INTRODUCTION

Ventral hernia repair is one of the most common surgeries in the United States with approximately 350,000 procedures performed annually.1 Safety and long-term outcomes are persistent problems in mesh-based hernia repair that require resolution. In October 2017, a panel of 7 expert surgeons met to review the current landscape of mesh-based hernia repair. This meeting provided a forum for each surgeon to present the rationale and important factors that guide the selection process of a hernia repair technique and material. Understanding the circumstances under which certain types of mesh materials perform best and where they fail is essential to achieving the best possible repair and long-term patient outcomes.

Based on training and experience, most general and plastic surgeons have developed their own algorithms that guide their selection of appropriate repair materials for various types of hernia. However, this decision-making process has become difficult due to lingering concerns about numerous mesh options in the market and reports of continued suboptimal outcomes. The surgeons stated numerous clinical factors that influence their algorithms, including hernia type, size, location, classification of the

SURGEONS’ CONSSENSUS ON THE STATE OF HERNIA REPAIR AND REINFORCEMENT MATERIALS IN 2017

Developments in the Hernia Repair Market:

- “Mesh fatigue”: Over the past several years, a myriad of mesh products have been introduced, yet, for most, there is little that distinguishes them from each other. Performance remains suboptimal, and surgeons cannot keep track of differences and evidence for changes in mesh designs
- Streamlined regulatory pathways allow companies to enter the market quickly without having to generate extensive preclinical or clinical data to establish their clinical and/or safety benefit, leading to many “me-too” products
- Value analysis committees (VACs) play an increasingly powerful role in product selection, substantially increasing the time necessary before the product can be trialed in the operating room, and even longer to get on the hospital shelf. Existing manufacturer contracts also serve as a barrier to new product entry
- Increase in patient litigation, in part as a fallout of the vaginal and pelvic floor mesh lawsuits
- Better-educated patients who ask surgeons more questions and increasingly request specific repair materials (eg, biologics)
operative wound, patient comorbidities, prior surgeries, intended plane of placement, and compatibility with surgical technique. More recently, additional factors are affecting the decision-making process. These include cost, product availability at a given hospital system, patient preferences, and possible litigation. The goal of mesh-based hernia repair has remained the same—life-long biocompatible and infection-resistant reinforcement that results in permanent hernia repair while maintaining quality of life. No single mesh design to date has emerged at the forefront in the treatment of the many variations of hernias.

PERMANENT SYNTHETIC MESHES

Permanent synthetic meshes are the oldest category of hernia repair materials. The most commonly used are composed of polypropylene, polyester, or expanded polytetrafluoroethylene. Differences in parameters such as fiber density, strength, filament type (multifilament vs monofilament), mesh pore size, compliance, and 3-dimensional construction account for the various synthetic mesh products in the market. Some of the appealing aspects of synthetic meshes are strength, permanence, and the low upfront cost. This creates a low barrier to entry for synthetic meshes within hospital purchasing departments when compared to high-priced biologic and resorbable synthetic meshes. However, mesh selection based on low initial cost, without taking into account other important considerations of performance, may be problematic for both short- and long-term success of the hernia repair.

The attractive low upfront cost and high strength of modern synthetics is offset by ongoing concerns of inflammatory reaction and persistent foreign body response. Permanent synthetic meshes elicit a foreign body response, setting in motion a long-term process in which the body encapsulates the mesh. This chronic inflammatory response has resulted in mesh contracture and pain and leaves the mesh permanently susceptible to infection due to the inability of the immune system to penetrate the material. Furthermore, surgeons discussed the chronic, long-term postoperative pain after inguinal and ventral hernioplasty as a serious sequela and point of concern associated with the use of synthetic mesh in hernia repair. While the etiology of chronic postherniorrhaphy pain is multifactorial, the primary factor is likely the chronic inflammatory response arising from the presence of synthetic material within the body.

Recently, long-term data have been published on outcomes after synthetic mesh and nonmesh repairs. After 5 years of follow-up, while the rate of recurrence was lower in the mesh repair group (12.3%) compared with nonmesh repair (17.1%), the cumulative incidence of mesh-related complications was 5.6% compared with 0.8% in non-mesh repair. Long-term complications included bowel obstruction, bowel perforation, bleeding, chronic surgical site infections (SSIs), late intra-abdominal abscess, enterocutaneous fistula, seroma, hematoma, nonhealing wound, and diagnostic surgery due to pain that was not required for patients who did not get mesh. Surgeons agreed that minimizing chronic pain and the amount of foreign body would result in better long-term outcomes.

BIOLOGIC MATERIALS

As surgeons sought to lower the foreign body response, a promising class of biologic materials sourced from cadaveric or animal tissue entered the market for hernia repair in the late 1990s. The goal behind these biologic materials was to address the biomechanical requirements of the repair while providing

### Strengths and Deficiencies With Permanent Synthetic Meshes

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Deficiencies</th>
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<tbody>
<tr>
<td>Initial low cost</td>
<td>Sustained inflammation/foreign body response</td>
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<tr>
<td>Biomechanical strength</td>
<td>Susceptibility to infection</td>
</tr>
<tr>
<td>Durability</td>
<td>Contracture</td>
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<tr>
<td>Handling</td>
<td>Pain</td>
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<tr>
<td>Long-term foreign body</td>
<td>Limited to use in clean (non-infected) cases</td>
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a scaffold upon which endogenous collagen could grow and replace the load-carrying capacity of the mesh. Decellularized extracellular matrix (ECM) material provides a scaffold upon which endogenous cells can infiltrate to allow for revascularization, tissue growth, and remodeling. Effective revascularization may lead to improved wound healing and better clearance of bacteria in the setting of infection. The goal of biologic material is to provide structural support to the wound while simultaneously promoting active endogenous tissue repair. Biologic meshes are engineered to transition their load-carrying capability to the newly repaired native tissue. An ideal biologic would result in low inflammatory response and remodel into tissue that exhibits similar strength and compliance of native fascia.

In many regards, biologics compensate for the deficiencies of synthetic meshes. However, criticisms of biologics revolve around being more expensive, being prone to laxity, and having higher rates of hernia recurrences. The RICH study, a prospective study evaluating Strattice™ Reconstructive Tissue Matrix (RTM) (porcine dermis, LifeCell), reported 19% recurrence rate at 12 months and 28% at 24 months post-surgery. However, it is generally accepted that complexity (as described by Ventral Hernia Working Group [VHWG] grade or Centers for Disease Control and Prevention [CDC] wound class) and the ability to achieve primary fascial closure correlate to higher rates of recurrence. The RICH study patient population skewed to the complex, which may, in part, account for the observed recurrence rates.

Considering several studies with biologic meshes, it may be difficult to reconcile the long-term performance of the biologic mesh with its high cost (eg, the average selling price for Strattice™ RTM is approximately $7,500). It is likely that biologic mesh has been relegated to complex cases due to its high upfront cost, but biologics may potentially offset the significant costs associated with subsequent repairs of failed and infected synthetic meshes, as well as more morbid complications such as obstructions and erosions. Removal of infected or failed synthetic mesh can be difficult and time-consuming, contributing to increased operating room time and length of hospital stay. While associated infection rates are high with biologic mesh due to its preponderance of use in contaminated/infected fields, it is rarely necessary to remove biologic mesh due to infection.

Surgeons agreed that the high cost is more of an issue than the higher recurrence rates associated with biologic meshes. Reoperation of a biologic recurrence is surgically less difficult, with less sacrifice of surrounding healthy tissue when compared to reoperations due to complications or recurrences with synthetic meshes.

In cases of serial hernia repairs with synthetic meshes, planes of tissue are sacrificed and eroded, leaving the surgeons with an increasingly difficult repair and the quality of the patient’s tissue compromised. Biologics are often implanted in these patients, but the best repair is not often possible at this point; it would be preferable to use the biologic material earlier in the treatment paradigm to maximize the chances of an optimal repair.

Biologic meshes follow the bioengineering principle that what goes in safely should come out safely, as well as the surgical principle not to burn bridges when reoperation is possible.

A third category of mesh material is resorbable synthetic mesh, which degrades over time. The foreign-body reaction persists while the mesh is being resorbed but diminishes once the mesh resorbs. Resorbable synthetics are polymer-based, and their biomechanical properties as well as the rate of strength degradation can be engineered into the design. While the idea behind resorbable synthetics is sound, surgeons questioned their performance given the lack of an ECM scaffold to promote healing and remodeling. Resorbable
synthetics commit to leaving behind a scar plane when dissolved. The surgeons questioned what reinforcement and quality of tissue was being left behind once the polymer was bioabsorbed and degraded, given the high inflammatory environment in which this process takes place. The quality of healed tissue left behind following a hernia repair is critical to the long-term success. Positive preclinical work on Phasix™ Mesh (C. R. Bard, Inc.) has since been extended to the clinic in the form of a multicenter, single-arm, prospective study. In this trial, 121 subjects received Phasix Mesh during open hernia repair for primary or recurrent ventral and incisional CDC class I wounds; all subjects had ≤3 prior repairs and all had ≥1 high-risk criteria. The mesh was implanted in either the retrorectus or onlay plane. The mean defect and mesh size was 115.7 cm² and 580.9 cm², respectively. Postoperative physical examinations and quality-of-life assessments were conducted at 1, 3, 6, 12, and 18 months. Of the 121 subjects enrolled, 95 (79%) participated in the 18-month follow-up. At 18 months, there were a total of 11 instances (9%) of hernia recurrence; in addition, there were 11 cases (9%) of SSI and 7 cases (6%) of seroma requiring intervention. While these early results are encouraging, the authors intend to follow the patients for 36 months. It is expected that the Phasix Mesh will have fully resorbed by 18 months so the material should not be providing load sharing between 18 and 36 months. The results of the Phasix study to date appear to be favorable; however, it’s important to note that all patients in the study had CDC class I clean wounds. Therefore, the results cannot be compared to those obtained from the patients included in the RICH study (biologics; wounds were CDC classes II to IV).

A distinct type of resorbable polymer, a polyglycolic/trimethylene carbonate copolymer (Bio-A® Tissue Reinforcement, W. L. Gore & Associates), has been investigated in a multicenter, single-arm, prospective clinical study. The Complex Open Bioabsorbable Reconstruction of the Abdominal Wall (COBRA) study enrolled subjects with incisional hernias of at least 9 cm² undergoing elective, open, single-staged repair classified by the CDC as either clean-contaminated (CDC class II) or contaminated (CDC class III). At the 24-month follow-up, 16 subjects (17%) had experienced recurrence: 13 at the midline and 3 parastomal hernia sites. The recurrence rate was significantly higher for those instances when the mesh was placed in the intraperitoneal position (4/10, 40%) vs the retrorectus position (12/94, 13%). SSIs (19/104, 18%) led to a higher risk of recurrence (P<0.01). Although the authors noted the favorable ~11% reduction in recurrence at 24 months compared to the RICH study, authors note that overall reduction is likely due to technique, as all the patients in the COBRA study had primary fascial closure and 90% had retrorectus placement. It is also important to recognize that the average hernia defect size in the RICH study was larger than the defect size in the COBRA study.

A recent study conducted by the Americas Hernia Society Quality Collaborative evaluated early wound morbidity after open ventral hernia repair with polypropylene and resorbable synthetic meshes in clean (77.1%) and contaminated (22.9%) wounds. The study revealed that resorbable synthetic meshes did not offer advantages in surgical site occurrences (SSOs), length of stay, and unplanned readmission rates compared with permanent polypropylene synthetic meshes at 30 days. Interestingly, rates of SSIs, SSOs requiring procedural interventions, and unplanned reoperation were higher for the resorbable synthetic meshes compared to rates for permanent polypropylene synthetic meshes. Although the limitation of the study is the short-term outcome, it does raise a concern about the replacement of permanent polypropylene meshes by resorbable synthetic meshes.

**Strengths and Deficiencies With Resorbable Mesh**

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Deficiencies</th>
</tr>
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<tbody>
<tr>
<td>No foreign body left behind</td>
<td>Cost (vs permanent synthetics)</td>
</tr>
<tr>
<td>Unknown long-term strength</td>
<td>Heightened inflammatory response during resorption</td>
</tr>
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</table>
REINFORCED BIOSCAFFOLDS

Three categories of hernia repair materials—permanent synthetics, biologics, and resorbable synthetics—have their own strengths and deficiencies. Permanent synthetics offer strength and cost advantages over biologic implants; however, they lack a biologic scaffold (ECM) and induce an inflammatory and foreign body response, which may lead to downstream complications and difficulty for subsequent repairs (as well as other non-related abdominal surgery). Resorbable synthetics provide a shorter duration of the presence of the synthetic material in the body; however, they also lack a biologic scaffold (ECM), and their cost is significantly higher than that of permanent synthetics. Biologics provide the ECM for tissue remodeling, improved biocompatibility, and a lower risk of downstream complications due to minimal long-term foreign body response. However, they exhibit higher rates of recurrence, laxity over time, and higher cost when compared to synthetic meshes. There still exists a need for a natural repair that would address the drawbacks of permanent and resorbable synthetics as well as the laxity and high cost associated with biologics.

Reinforced BioScaffolds (RBSs; OviTex, TELA Bio) are a new category of hernia repair devices, which were introduced to the market in July of 2016. RBSs were purposefully designed for hernia repair and abdominal wall reconstruction in close collaboration with more than 100 surgeons. They are created by embroidering layers of ECM derived from ovine (sheep) rumen with polymer. The surgeons likened the polymer grid in RBSs to rebar in concrete—the grid shares a significant amount of the implant’s tensile load. The biologic material serves as a scaffold to help limit the inflammatory response and provides an ECM scaffold for rapid population, revascularization, and remodeling. The polymer provides additional strength and improves handling characteristics. RBS implants were designed to meet or exceed physiological biomechanical requirements, to be isotropic, to exhibit positive cellular and fluid kinetics, compliance strain within the physiological range, and provide load sharing during tissue healing and remodeling. Furthermore, RBSs are offered at a significant cost reduction to leading biologics and resorbable synthetics. Cost-impact studies with hospitals have demonstrated 14% to 37% savings when using RBSs in place of biologics and/or resorbable synthetics.

OviTex RBSs come in 3 layered configurations: a 4-layer implant (OviTex), a 6-layer implant with one "smooth" side, which can contact viscera (OviTex 1S), and an 8-layer implant with 2 smooth sides (OviTex 2S). Modifying the embroidery pattern results in lower polymer density, creating the smooth side of the implant. Each of these 3 configurations are reinforced with either permanent (polypropylene) or resorbable (polyglycolic acid) polymer, creating a total of 6 distinct product lines.

Extensive preclinical research was conducted for OviTex RBSs prior to product launch in July 2016. The OviTex preclinical study in non-human primates is the largest most extensive study that has been done to date for any hernia mesh product on the market. Genetically, non-human primates are 98% homologous to humans and are a well-validated model. Furthermore, a prospective, multicenter study—the BioScaffold Reconstruction of Abdominal Wall and Ventral Hernia Defects With Open or Laparoscopic Repair (BRAVO) study—is underway to investigate the performance of OviTex in ventral hernia repairs. The study will enroll 100 subjects and will evaluate subjects at 1, 3, 6, 12, and 24 months postoperatively for SSOs such as seroma, wound infection, bulging, and true recurrence.

Strengths and Deficiencies With Reinforced Bioscaffolds

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Deficiencies</th>
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<tbody>
<tr>
<td>Biocompatibility</td>
<td>Long-term durability to be determined</td>
</tr>
<tr>
<td>Strength over time (vs biologics)</td>
<td>Cost (vs permanent synthetics)</td>
</tr>
<tr>
<td>Cost (vs biologics and resorbable synthetics)</td>
<td>Handling (vs biologics)</td>
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CLINICAL EXPERIENCE WITH REINFORCED BIOSCAFFOLDS

The surgeons shared their clinical experience with OviTex RBSs and presented representative cases at the conference. Collectively, the 7 surgeons have experience in over 200 cases using OviTex RBSs. This section will summarize the presented cases, highlighting the VHWG grades and CDC wound classes.

Thirty-two cases were collectively presented by surgeons. The histograms in Figure 1 show the distribution by VHWG grade and CDC wound class. The VHWG distribution was 12.5% grade 1, 21.9% grade 2, 28.1% grade 3, and 37.5% grade 4. The CDC wound class distribution was 34.4% class I (clean), 3.1% class II (clean-contaminated), 25.0% class III (contaminated), and 37.5% class IV (dirty). The cases presented included open, laparoscopic, and robotic surgical approaches.

OVITEX RBS USE PROFILE IN VENTRAL HERNIAS:
HISTOGRAMS OF CASE VHWG GRADES AND CDC WOUND CLASSIFICATIONS

<table>
<thead>
<tr>
<th>VHWG 1</th>
<th>VHWG 2</th>
<th>VHWG 3</th>
<th>VHWG 4</th>
<th>CDC I</th>
<th>CDC II</th>
<th>CDC III</th>
<th>CDC IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>4</td>
<td>7</td>
<td>9</td>
<td>12</td>
<td>11</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>%</td>
<td>12.5%</td>
<td>21.9%</td>
<td>28.1%</td>
<td>37.5%</td>
<td>34.4%</td>
<td>3.1%</td>
<td>25.0%</td>
</tr>
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</table>

In summary, two-thirds (65.6%) of the cases presented were VHWG grades 3 and 4, and 62.5% were CDC classes III and IV, representing a challenging patient population. Early outcomes in these demanding cases have been very promising, and to date, no adverse events were possibly or definitely related to the implant. Surgeons commented that OviTex RBSs handle well compared to biologic implants and are suited for use in open and minimally invasive surgeries. Furthermore, surgeons agreed that the histograms reflected the versatility of the OviTex RBS product portfolio for a wide range of ventral hernias.
Case details: 76-year-old female who had previously undergone laparoscopy for ischemic sigmoid colitis that was converted to an open low anterior resection with a loop ileostomy. The patient presented with an incarcerated parastomal hernia, midline incisional hernia, and pneumoperitoneum (Figure 2). VHWG grade 4, CDC class IV.

Surgical procedure: Left colectomy and small bowel resection of the loop ileostomy was performed, followed by midline and right lower quadrant incisional hernia repair. OviTex 1S Resorbable RBS (18 × 22 cm) was used for the repair. Resorbable reinforcement was chosen to provide a repair that would not leave a permanent polymer in the body long term. OviTex 1S Resorbable RBS was placed in the retrorectus plane along with bilateral transverse abdominis release (TAR). The surgery concluded with an end dissecting colostomy (Figure 3).

Patient follow-up: Patient healed with no wound complications. At 17-month follow-up, repairs of both midline and parastomal hernias remained intact, with no evidence of recurrence. The colostomy also functioned well.
Case 02

Case details: 72-year-old female with a body mass index of 35 who presented 2 years prior with a stercoral ulcer perforation of the sigmoid colon. She had chronic symptoms of pelvic floor dysfunction and constipation and a recent exacerbation of lumbar back pain associated with increased narcotic use. She presented initially for colostomy takedown and repair of an incisional hernia of her long midline incision. She was referred for formal assessment of the pelvic floor and proceeded with a robotic takedown of her colostomy, which was uncomplicated. The patient then returned for abdominal wall reconstruction. VHWG grade 3, CDC class I.

Surgical procedure: Abdominal wall reconstruction was done with an elected panniculectomy (Figure 4). On elevation of her skin flap, a subcutaneous abscess associated with her previous colostomy site was encountered. OviTex 1S Resorbable RBS (18 × 22 cm) was placed in retrorectus space. Perioperative course was uncomplicated. There were no skin/wound breakdowns. Retrorectus drain was removed on postoperative day 4, and 19F Blake flap drains (Ethicon US, LLC) were removed at 3 and 4 weeks.

Patient follow-up: At 4-month follow-up, the patient had no issues, except she was still taking narcotics. At 9-month follow-up, there continued to be no issues, and the patient had discontinued narcotics.

A, B. OviTex 1S resorbable retrorectus placement.
C. Primary closure.

Figure 4
Case 03

Case details: 74-year-old female with a long history of Hirschsprung’s and Crohn’s disease leading to over 20 surgeries arising from her disease, small bowel obstructions, and multiple recurrent incisional hernias. In September 2015, she received a 12-cm bridged Symbotex™ Composite Mesh (Covidien) placement during open hernia repair, and in April 2016 she presented with an incarcerated low midline incisional hernia. This patient presented with a recurrent incarcerated right lower quadrant (RLQ) incisional hernia and left upper quadrant (LUQ) incisional hernia (Figure 5). VHWG grade 1, CDC class II.

Surgical procedure: Both hernias were repaired with OviTex 1S Permanent RBS via a laparoscopic approach using ReliaTack™ (Medtronic), a 10 × 12 cm piece and primary fascial closure for the LUQ hernia, and a 10 × 20 cm piece and primary fascial closure for the RLQ hernia. Permanent reinforcement was chosen because of clean field and desire to maximize the product’s strength retention over time.

Patient follow-up: Patient healed with no wound complications. At 15-month follow-up, both hernia repairs remained intact, with no evidence of recurrence.

A. Trocar placement.

B. Laparoscopic placement of OviTex 1S Permanent RBS to repair LUQ hernia.

C. Laparoscopic placement of OviTex 1S Permanent RBS to repair RLQ hernia.
SUMMARY: SURGEONS’ CONSENSUS STATEMENTS

- There is a growing concern among surgeons that short-term product priorities outweigh lifelong patient benefits.

- Chronic inflammation and foreign body response, need for removal in cases of infection, and long-term complications limit the utility of permanent synthetic meshes. Long-term strength retention, laxity over time, and high cost are the primary factors that limit the utility of biologic meshes.

- Recurrence rates and long-term performance of biologics do not justify their high cost. However, if the cost were more manageable, recurrences arising from use of biologics would be significantly easier to re-operate on in the long run than reoperations of complications arising from failed synthetic meshes.

- OviTex RBSs have been designed to exploit the desirable features of current mesh materials. OviTex RBSs combine the biocompatibility of biologics with the strength retention (durability) of synthetics at a fraction of the cost of leading biologics. Quality clinical data are needed.

- Surgeons agreed that based on their design and construction, OviTex RBSs are appropriate for moderate-to-complex ventral hernia patients (VHWG grades 2-4) and are suitable in both open and minimally invasive surgical approaches.

- While reduction in hernia recurrence is the universally accepted, long-term performance goal of hernia repair, a demonstrable reduction in SSOs can establish the cost-effectiveness of a mesh material while collecting long-term recurrence data.

- There is growing evidence that lifelong safety of implanted mesh is becoming the priority.
**IMPORTANT SAFETY INFORMATION**

OviTex Reinforced BioScaffolds are intended for use as a surgical mesh to reinforce and/or repair soft tissue where weakness exists. Indications for use include the repair of hernias and/or abdominal wall defects that require the use of reinforcing or bridging material to obtain the desired surgical outcome. Do not use OviTex in patients known to be sensitive to materials of ovine (sheep) origin. For additional important safety information, please see the OviTex Reinforced BioScaffold Instructions for Use. The statements made or results achieved by TELA Bio customers described herein were achieved in their specific setting. Due to variations in clinical experience and technique, there is no guarantee that these results are typical. For prescription use only.

A surgeon must use his or her own clinical judgment when deciding which products are appropriate for treatment of a particular patient. Always refer to the package insert, product label, and/or instructions for use before using any TELA Bio product. Products may not be available in all markets because product availability is subject to the regulatory and/or medical practices in individual markets. Please contact your TELA Bio representative if you have questions about TELA Bio products.

**REFERENCES**
