VAGINAL MESH
WHAT IS THE FUTURE?
Ryan R. Stratford, MD, MBA
FPMRS
CONFLICTS OF INTEREST

American Urogynecologic Society – Board of Directors
OBJECTIVES

• Discuss the cause for the development of transvaginal graft materials and the differences in their biomechanical properties

• Discuss current scientific understanding of the biologic and mechanical impact of polypropylene mesh on vaginal supportive tissues

• Review current scientific data on using polypropylene mesh in and around the vagina

• Review current FDA statement on transvaginal mesh and discuss differences between statement and media perceptions
PREVALENCE OF POP

• 1 in 3 women have a Pelvic Floor Disorder (PFD)

• 11% lifetime risk of undergoing a single operation for pelvic organ prolapse (1 in 9 women)

• 29% will require a repeat operation

WHY MESH?
POOR LONG-TERM OUTCOMES

- Traditional native tissue repair had poor long-term outcomes
  - Apical or Level I support not taken into account
  - Lack of understanding of anatomical support of vagina
  - Compartment most difficult to treat – ANTERIOR (bladder)
Matt Barber at the Cleveland Clinic recalculated outcomes of Weber et al with new outcome criteria:
- No prolapse beyond the hymen
- The absence of prolapse symptoms (visual analog scale <2)
- The absence of retreatment

88% of women met definition of success at 1 year.

One patient underwent surgery for recurrence 29 months after surgery.

No differences among the 3 groups were noted for any outcomes.
IDEAL PROSTHESIS

• Biocompatible
• Inert
• Lack of allergic or inflammatory response
• Sterile
• Noncarcinogenic
• Resistant to stress and shrinkage
• Affordable
• Easy to handle

Scalon 1953
WHAT IS BEST?

Synthetic or Biologic
<table>
<thead>
<tr>
<th>Type</th>
<th>Component</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xenograft</td>
<td>Procine small intestine&lt;br&gt;Bovine pericardium&lt;br&gt;Others</td>
<td>SIS Cook&lt;br&gt;Pelvicol (Bard)</td>
</tr>
<tr>
<td>Allograft</td>
<td>Dura mater&lt;br&gt;Fascia lata</td>
<td></td>
</tr>
<tr>
<td>Autologous</td>
<td>Rectus sheath&lt;br&gt;Tensor fascia lata&lt;br&gt;Vaginal epithelium</td>
<td></td>
</tr>
</tbody>
</table>
SIS after 7 Days: The Porcine graft is already being invaded by host cells. A mild inflammatory reaction is occurring and matrix deposition by the cells has begun. The Porcine graft remains largely intact at this time point.
BIOLOGIC GRAFTS

• Host response variability
  • Encapsulation
  • Inflammation
  • Degradation

• Variability is higher in vaginal implants than in abdominal implants

DONOR OR VECTOR DISEASE

• Cadaveric:
  HIV = 1 in 1.67 million
  - Simonds 1994

• Animal:
  Bovine Spongiform Encephalopathy = 1 in 2 million
  Prion Disease?
BIOLOGIC GRAFTS OUTCOMES

• Sacrocolpopexy
  • Higher pull-out rate and higher recurrent prolapse rate as compared to polypropylene mesh

• Anterior compartment
  • No studies showing superiority of biologic over synthetic
  • Benefit of biologics over colporrhaphy is not clear
    • In RCTs: Biologic success rate 38-93% and native tissue success rate 42-85%

• Posterior compartment
  • 2 RCTs show no difference and one shows increased failures in biologics

SIS Multilayer Hernia Graft - Strength After Implant

Burst Force (lbs)

Days Implanted

Bars are standard deviation; only upper limits shown to enhance readability

SYNTHETIC VS. BIOLOGIC

• Although erosion rates may not be different, mesh erosions are more likely to result in re-operation (3% vs. 0.3%)
• Mesh issues more likely to be delayed than with biologics (267 days vs. 10 days)
• Mesh in the anterior compartment more likely to erode than in apical or posterior compartments (6% vs. 2% and 2% respectively)
• Reoperation for erosion dependent on materials

Nguyen JN, Obstet Gynecol 2012
SYNTHETIC MESH
MESH PROPERTIES

- Pore size
- Filament
  - Mono versus Multifilament (braided)
- Architecture
  - Woven versus knitted versus geometric
- Tensile strength
  - Easily deformed or resistant to deformation
- Stiffness
  - Soft and compliant or rigid and tough
- Absorption
  - Absorbable versus nonabsorbable
- Density (gm/m²)

ALL of these properties have an impact on Host response
## CLASSIFICATION

<table>
<thead>
<tr>
<th>Type</th>
<th>Component</th>
<th>Trade Name</th>
<th>Fibre Type</th>
<th>Pore Size</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>Polypropylene</td>
<td>Prolene/marlex</td>
<td>Mono</td>
<td>Macro (&gt;75 mic)</td>
</tr>
<tr>
<td></td>
<td>Polyglactin 910</td>
<td>Vicryl/Vypro I/II</td>
<td>Multi</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Expanded PTFE</td>
<td>Gore-Tex</td>
<td>Multi</td>
<td>Micro (&lt;10 mic)</td>
</tr>
<tr>
<td>III</td>
<td>Polyethylene</td>
<td>Mersilene, Teflon, SurgiPro</td>
<td>Multi</td>
<td>Macro with</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>micro braided</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>components</td>
</tr>
<tr>
<td>IV</td>
<td>Polypropylene Sheet</td>
<td>Cellgard, Silastic</td>
<td>Mono</td>
<td>Submicronic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>pore size</td>
</tr>
</tbody>
</table>

*Amid 1997*
THE EFFECTS OF PORE SIZE

- Macrophages can penetrate the pores
  - Cannot enter if <10 microns
  - Macrophages can be helpful and/or destructive *
- Less surface area contact with the native tissue
  - Affects type of macrophages recruited to the site *
- Less evidence of microinfection leading to erosion
- Greater type III collagen deposition and greater attachment strength
- Greater capillary penetration

*Moalli et al. University of Pittsburgh
Macrophages

MACROPHAGE 16-20 UM

LEUCOCYTE 9-15 UM

BACTERIA < 1UM
MACROPOROUS

• Less Erosion
  • Allows rapid cellular and connective tissue in-growth

• Less Infection
  • Allows macrophage penetration to reduce risk of infection and prevent harboring of bacteria

• How?
  • Less surface area contact with native tissue affects type of macrophages recruited to the site
    • Macrophage Type 1 – causes cellular damage (inflammatory reaction)
    • Macrophage Type II – prevents bacterial colonization and promotes long-term remodeling rather than destruction
Polypropylene after 7 Days: The fibers of the polypropylene mesh are easily distinguished from the surrounding tissue. There is an acute inflammatory response occurring on the surface of the graft and also in the immediate area surrounding the implant. Collagen deposition is minor.
Polypropylene after 2 Years: The fibers of the polypropylene mesh are still easily distinguished from the surrounding tissue. Deep seeded inflammation continues to be seen along the surface of the graft, though it is much more focal than the inflammation seen immediately after implantation. Collagen has been deposited around the fibers and blood vessels can be seen.
MESH BEHAVIOR

- **Stress Shielding** (Moali et al. University of Pittsburgh)
  - From biomechanics of orthopedics
  - Long-term erosion rates increase due to atrophy of smooth muscle
Stiffness and Stress Shielding

Moalli et al, IUJPFD Jul 2009
MESH BEHAVIOR

• If too soft and elastic then less effective for Level I support
  • Increased pore size = decreased tensile strength
• Level I Support
  • Key to success – particularly for anterior compartment where at least 80% of defect is due to breakdown of level I support
  • USL – most rigid as compared to round and broad ligaments and as compared to paravaginal support tissues
MESH BEHAVIOR

• More elasticity may be key for Level II support

• Fibromuscular tissue surrounding vagina is elastic
  • Collagen 4% elongation before failure
  • Elastin 70% elongation before failure
  • Smooth muscle (decreased content in POP tissue)

• If more elasticity achieved with macroporous and different geometry that creates less surface area then better outcomes for level II support

Boreham et al. AJOG 2002;187:56-63
CLINICAL OBSERVATIONS

• Mesh Shrinkage
  • 75% in 3D plugs
  • 20% in 2d prostheses

• Effects of Mesh Weight
  • Heavier (g/m2) mesh associated with:
    • Greater and more prolonged inflammation
    • Greater scar plating
    • Less elasticity once incorporated
    • Increased evidence of cell turnover (ongoing inflammation and remodel) at 1 year

Amid PK, Hernia, 1997
POLYPROPYLENE MESH
CLINICAL APPLICATION

• SUI

• Prolapse
  • Transvaginal without kit
  • Transvaginal with kit
  • Transabdominal (open or laparoscopic) sacrocolpopexy

• Class action law suit covers all of the above
MESH FOR SUI
EFFECTIVENESS OF MID-URETHRAL SLINGS

• 17-year outcomes (original Ulmsten cohort)
  • 87% subjective cure rate
  • >90% objectively continent

Nilsson et al. IUJ 2013 Aug;24:1265-9
EROSION RATES FOR SUBURETHRAL SLINGS

- Goretex: 6 - 12%
- Mersilene: 4 - 6%
- Polypropylene: 0 - 3%
- TVT: 1.4%
TYPES OF EROSIONS WITH POLYPROPYLENE MID-URETHRAL SLING

• Anterior vaginal sulci
  • Most “erosions” occur in the anterior sulci and may not represent true erosions

• Midline vaginal incision erosions
  • Anecdotal data 3 erosions over last 8 years (>1,000 mid-urethral polypropylene slings) reported with two secondary to connective tissue disorder

• Urethral erosions
  • Concern for long-term occurrence – case reports in single digits

• Bladder erosions
MESH FOR PROLAPSE
SACROCOLPOPEXY
EROSION WITH SACROCOLPOPEXY

- Visco et al. Duke University
  - Mesh erosion: 5.5% (n=273)
  - Median time to mesh erosion: 15.6 months
  - Median time to suture erosion: 9.0 months

- Review of literature
  - Mesh erosion 3.4%
  - Success rates 78-100% (using polypropylene mesh)

Nygaard et al. Obstet Gynecol 2004 Oct
TRANSVAGINAL MESH FOR PROLAPSE
TRANSVAGINAL MESH
NO KIT
# RCT – MESH FOR ANTERIOR COMPARTMENT

<table>
<thead>
<tr>
<th>Study</th>
<th>Mesh</th>
<th>N</th>
<th>F/U mo</th>
<th>Primary Outcome</th>
<th>Mesh Cure</th>
<th>Ant Rep Cure</th>
<th>P</th>
<th>Comps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sivaslioglu 2007</td>
<td>Mesh</td>
<td>90</td>
<td>12</td>
<td>Anatomic (stg &gt;2)</td>
<td>91%</td>
<td>72%</td>
<td>&lt;.05</td>
<td>6.9% erosion</td>
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<tr>
<td>Nguyen 2008</td>
<td>Perigee</td>
<td>75</td>
<td>12</td>
<td>Anatomic</td>
<td>87% ant</td>
<td>55%</td>
<td>&lt;.05</td>
<td>5.0% exposure</td>
</tr>
<tr>
<td>Carey 2009</td>
<td>Mesh</td>
<td>139</td>
<td>12</td>
<td>Anatomic</td>
<td>81% ant</td>
<td>66%</td>
<td>NS</td>
<td>5.6% exposure</td>
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<tr>
<td>Nieminen 2010</td>
<td>Mesh</td>
<td>202</td>
<td>36</td>
<td>Anatomic</td>
<td>87% ant</td>
<td>59%</td>
<td>&lt;.001</td>
<td>19.0% exposure</td>
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<tr>
<td>Iglesia 2010</td>
<td>Prolift</td>
<td>65</td>
<td>9.7</td>
<td>Anatomic</td>
<td>41% all</td>
<td>30%</td>
<td>NS</td>
<td>15.6% exposure</td>
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<tr>
<td>Withagen 2011</td>
<td>Prolift</td>
<td>194</td>
<td>12</td>
<td>Anatomic</td>
<td>91% all</td>
<td>55%</td>
<td>&lt;.001</td>
<td>16.9% exposure</td>
</tr>
<tr>
<td>Altman 2011</td>
<td>Prolift</td>
<td>389</td>
<td>12</td>
<td>Composite (above 0, no bulge sym)</td>
<td>82% ant</td>
<td>48%</td>
<td>.008</td>
<td>3.2% exposure</td>
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</tbody>
</table>
Mesh-related complications after mid-urethral slings and mesh sacral colpopexies with monofilament polypropylene are rare. An up to 26% mesh erosion rate and up to 38% dyspareunia rate with vaginally introduced mesh for pelvic-organ prolapse repair has been reported.

Bressler et al.
HOW TO MANAGE EROSIONS

• Average time to discovery of mesh erosion is 14 months but newer data suggest >5 year initial occurrence

• If small area of erosion, then usually well managed with vaginal estrogen and mesh excision

• If larger area of erosion and/or pelvic pain, then usually requires surgical excision
“On Oct. 20, 2008, the FDA issued a Public Health Notification ... on serious complications associated with surgical mesh placed through the vagina (transvaginal placement) to treat POP and SUI.”

In July statement, “… the FDA identified surgical mesh for transvaginal repair of POP as an area of ... serious concern.”
FDA STATEMENT
JULY 2011

• “... systematic review of the published scientific literature from 1996 – 2011 ... showed that transvaginal POP repair with mesh does not improve symptomatic results or quality of life over traditional non-mesh repair.”

• “The FDA continues to evaluate the literature for SUI surgeries using surgical mesh and will report about that usage at a later date.”
• “Mesh placed abdominally [sacrocolpopexy] for POP repair appears to result in lower rates of mesh complications compared to transvaginal POP surgery with mesh.”

• “There is no evidence that transvaginal repair to support ... the back wall of the vagina (posterior repair) with mesh provides any added benefit.”

• “… mesh augmentation may provide an anatomic benefit [but] ... may not result in better symptomatic results.”
MEDICAL-LEGAL RESPONSE

• Nationwide campaign maligning all vaginally placed polypropylene mesh in an effort to recruit for Class-action lawsuit in federal courts

• Skyrocketing daily inquiries from patients who fear any type of mesh for the treatment of PFD’s including SUI and POP
ACOG RECOMMENDATIONS

• “strongly support continued audit and review of outcomes, as well as the development of a registry for surveillance for all current and future vaginal mesh implants.”
INDUSTRY IMPACT

• FDA required that 522 studies be performed for each transvaginal mesh product.

• FDA approached AUGS to develop a registry where data could be housed for 522 studies.

• Currently four companies involved in the PFD Registry created by AUGS
PFD REGISTRY

• Launch to begin in late Q1 of 2014
• Initial purpose is to track outcomes for the treatment of POP
• Three levels of PFD Registry
  • I – PFD Registry Core
  • II – PFD Registry Expanded
  • III – PFD Registry Industry-Sponsored
• Initial launch of PFD Registry Industry-Sponsored with Core and Expanded to follow 1-2 months later
HOW CAN YOU PARTICIPATE?

• Sites will be easy to set up at low cost
• Depending on participation level should not be burdensome to enter data after each case
• Training and materials provided by PFD Registry
• May become approved for quality measures required by ACA that affect reimbursement beginning 2015 based on 2013 and 2014
• Likely to expand into data collection for all PFD’s such as SUI and FI
“SURGICAL MESH SHOULD NOT BE USED TO REPLACE GOOD SURGICAL TECHNIQUE”

- Bob Shull
“The majority of cases of prolapse of the vagina can be successfully operated via the vagina. The cure is not infrequently difficult and a great deal of surgical ingenuity is needed.”
OVERVIEW

- Review: “Repair of vaginal vault prolapse and pelvic floor relaxation using polypropylene mesh.”
- Mourtzinos A. and Raz S. (UCLA)
- Summary: The best approach to vaginal vault prolapse remains unknown. The use of graft materials in pelvic floor reconstruction should have limited use in a carefully selected patient population.
OVERVIEW

• Huebner et al. (University of Michigan)

Methods: A Pubmed-search ("anterior vaginal wall" or "cystocele"), ("posterior vaginal wall" or "rectocele") and ("vaginal vault" or "pelvic prolapse") and ("mesh" or "erosion" or "graft" or "synthetic") from 1995 to 2005.

Results: “There are few prospective randomized trials that prove the benefit of implanting grafts in vaginal pelvic floor surgery. Many articles are retrospective case series with small sample sizes or incomplete outcome variables. Serious complications such as erosions are often not mentioned. Inconsistent or unclear criteria for anatomic cure make it difficult to compare outcomes. Quality of life issues such as dyspareunia, urinary or bowel symptoms are often ignored.”

Conclusion: “Due to a lack of well-designed prospective randomized trials, recommendations for using graft materials in vaginal reconstructive surgery cannot be made. At this time, grafts should have limited use in a carefully selected patient population.”
KEY PAPERS

• Only two RCTs prior to mesh kits being developed that compared traditional colporrhaphy to mesh placement
  • Sand et al. (Northwestern University)
  • Weber et al. (The Cleveland Clinic)

• Both studies used absorbable Polyglactin mesh
Consider hypothetical:

"To show a particular mesh or graft material improves the cure rates of rectocele repair without increasing complications. Level II-2 evidence shows that rectocele repair, done with traditional plication methods or with site-specific rectovaginal fascia defect repair, has cure rates of 80-90%. A randomized intervention trial designed to show an improvement with the placement of a prosthetic material from this baseline to 90-95% would require 300-400 subjects in each arm. . . How can we know whether adding this prosthesis is really beneficial?"

However, to assess the same issue in the anterior compartment, assuming a 30% stage II failure rate for traditional anterior colporrhaphy and an improvement of 15%, only 110 patients in each arm would be needed.
Sand et al.

- Cystocele to hymenal ring or beyond
  - Randomized to A&P repair with or without polyglactin 910 mesh reinforcement
  - Postop evaluation at 2, 6, 12, and 52 weeks

- 161 women (some lost to follow up)
  - 80 received mesh
  - 80 did not

- Recurrent cystocele beyond mid-vaginal plane (stage II)
  - 43% without mesh
  - 25% with mesh
Weber et al.

- Cystocele stage II or greater
- 114 women
- Randomized to one of three techniques
  - Standard colporrhaphy
  - Standard colporrhaphy plus polyglactin 910 mesh
  - Ultralateral colporrhaphy
- At 23 months those with optimal outcome (questionnaire)
  - Standard colporrhaphy: 30%
  - Standard plus mesh: 42%
  - Ultralateral colporrhaphy: 46%
POSTERIOR COMPARTMENT REPAIRS
“Rectocele repair: a randomized trial of three surgical techniques including graft augmentation.”

Paraiso et al. (The Cleveland Clinic)

• 106 women with stage II or greater posterior vaginal wall prolapse were randomly assigned to either posterior colporrhaphy (n = 37), site-specific rectocele repair (n = 37), or site-specific rectocele repair augmented with a porcine small intestinal submucosa graft (n=32).

• Conclusion: Posterior colporrhaphy and site-specific rectocele repair result in similar anatomic and functional outcomes. The addition of a porcine-derived graft does not improve anatomic outcomes.
## Posterior Compartment Surgery with Synthetic Mesh

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>n</th>
<th>MESH</th>
<th>COMPLICATIONS</th>
<th>RESULTS</th>
<th>F/UP (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watson et al 1996</td>
<td>9</td>
<td>Polypropylene</td>
<td>11% wound</td>
<td>not stated</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Transperineal</td>
<td>infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sand et al 2001</td>
<td>65 with</td>
<td>Polyglactin</td>
<td>0% erosion</td>
<td>8% with mesh</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>67 without</td>
<td></td>
<td></td>
<td>10% without</td>
<td></td>
</tr>
<tr>
<td>Goh &amp; Dwyer 2001</td>
<td>43</td>
<td>Polypropylene</td>
<td>6% erosion</td>
<td>0%</td>
<td>12</td>
</tr>
</tbody>
</table>
Erosion rate with increasing mesh experience

- Overall p = 0.11
- Linear trend P = 0.03

Peter Dryer et al.
The American Urogynecologic Society strongly opposes any restrictions by state or local medical organizations, healthcare systems, or insurance companies which ban currently available surgical options performed by qualified and credentialed surgeons on appropriately informed patients with pelvic floor disorders.
AUGS POSITION STATEMENT

• Our justification for this position statement is described below.
  • Complete restriction on the use of surgical mesh was not the stated intent of the FDA safety communication.
  • The decision on surgical alternatives should be made by the patient and her surgeon.
  • A ban on surgical mesh would prohibit the surgical studies mandated by the FDA and recommended by the NIH, ACOG, and AUGS.
  • In some circumstances transvaginal mesh for pelvic organ prolapse may be the most appropriate surgical option.
  • Any restriction of mesh slings for the treatment of stress urinary incontinence is clearly not supported by any professional organization or the FDA.
  • Any restriction of mesh placed abdominally for the treatment of prolapse is clearly not supported by any professional organization or the FDA.
  • Instead of a ban on mesh we recommend the implementation of credentialing guidelines so that mesh procedures are performed by qualified surgeons.
AUGS POSITION STATEMENT

• Adopt the published AUGS credentialing guideline for transvaginal mesh and the guideline for sacrocolpopexy at local hospitals.

• Establish a broad group of trained pelvic floor reconstructive experts to review cases and complications of both mesh and non-mesh prolapse repair.

• Ensure that there are appropriate resources and patient management systems in place to identify and manage mesh and non-mesh related complications.

• Track both surgeons and specific products being implanted as these may each influence efficacy and complications. As with any complex surgical procedure, surgeon performance should be assessed and addressed on an individualized rather than collective basis.

• Mandate a thorough, standardized informed consent process for mesh placement. AUGS provides surgeons with an Informed Consent Toolkit as a means to help standardize the quality of the mesh-related consent process. This is available publically on the web at http://www.augs.org/p/cm/ld/fid=174.
SURGICAL TREATMENTS FOR PELVIC ORGAN PROLAPSE

**Anterior Compartment**
- Anterior colporrhaphy

**Apex or Upper Compartment**
- Uterosacral ligament suspension
- Sacrospinous ligament suspension
- Iliococcygeus ligament suspension
- Sacrocolpopexy

**Posterior Compartment**
- Posterior colporrhaphy
- Levator plication
- Colpopereineorrhaphy