W4: Current Role of Biological Grafts in the era of Mesh Controversy
Workshop Chair: Elise De, United States
12 September 2017 07:30 - 08:30

Start	End	Topic	Speakers
07:30	07:40	Mesh complications, FDA warning and cause for concern	Elise De
07:40	07:45	Biochemical evidence in tissue repair	Elise De
07:45	08:00	What does research say about biological materials	Dirk De Ridder
08:00	08:15	Clinical evidence in use of biological materials	Rahmi Onur
08:15	08:30	Discussion	All

Speaker Powerpoint Slides
Please note that where authorised by the speaker all PowerPoint slides presented at the workshop will be made available after the meeting via the ICS website www.ics.org/2017/programme Please do not film or photograph the slides during the workshop as this is distracting for the speakers.

Aims of Workshop
The aim of this workshop is to familiarize the audience regarding various biological materials including synthetic meshes which are in use in female pelvic floor reconstruction. What are the complications observed and status of FDA warning.

Learning Objectives
1. To be able to learn about potential mesh complications
2. To learn different types and nature of biological grafts available
3. To learn the efficacy of these grafts and their outcomes.

Learning Outcomes
After the course the students will be able to exercise caution and counsel the patients better in the use of synthetic mesh for pelvic floor reconstruction. This will help them avoid potential morbid complications and avoid any future litigation.

Target Audience
Urologists, Urogynecologists, Nurses, Residents

Advanced/Basic
Advanced

Conditions for Learning
This is not a hands on course but will be interactive and open to at least 50 delegates.

Suggested Learning before Workshop Attendance
The delegates should read about FDA warning issued for the use of meshes in both prolapse and incontinence surgery

Suggested Reading
1. Nitti, V. Complications of midurethral slings and their management. Can Urol J. 2012; Oct6 (5 Suppl 2): S120-122
2. Deng DY1, Rutman M, Raz S, Rodriguez LV.Presentation and management of major complications of midurethral slings: Are complications under-reported? Neurourol Urodyn. 2007;26(1):46-52
3. Daneshgari F1, Kong W, Swartz M. Complications of mid urethral slings: important outcomes for future clinical trials. J Urol. 2008 Nov;180(5):1890-7. doi: 10.1016/j.juro.2008.07.029. Epub 2008 Sep 17
4. Dwyer PL. Evolution of biological and synthetic grafts in reconstructive pelvic surgery.Int Urogynecol J Pelvic Floor Dysfunct. 2006 Jun;17 Suppl 1:S10-5. Review
5. Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Marjoribanks J. Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse. Cochrane Database Syst Rev. 2016 Feb 9;2:CD012079. doi: 10.1002/14651858.CD012079
6. Vandervord PJ, Broadrickk M, Krishnamurthy B, Singla AK. A Comparative Study Evaluating the In Vivo Incorporation of Biological Sling Materials. UROLOGY 75 (5):1228-32, 2010
7. Rahmi Onur, Ajay Singla, Kathleen Kobashi. Comparison of Solvent-Dehydrated Allograft Dermis and Autograft Rectus Fascia for Pubovaginal Sling: Questionnaire Based Analysis. Int Urol Nephrol 40(1):45-9, 2008
8. Leiter V, White SK, Walters A. Adverse Event Reports Associated with Vaginal Mesh:
An Interrupted Time Series Analysis. Women's Health Issues 27-3 (2017) 279–285.

9. Easleya DC, Abramowitcha SD, Moalli PA. Female pelvic floor biomechanics: bridging the gap. Curr Opin Urol 2017, 27:262–267
10. Theofanides MC, Onyeji I, Matulay J, Sui W, James M, Chung DE. Safety of Mesh Use in Vaginal Cystocele Repair: Analysis of National Patient Characteristics and Complications. Journal or Urology Vol 198 p 1-6 Sept 2017.
11. Ghoniem G, Hammett J Female pelvic medicine and reconstructive surgery practice patte
rns: IUGA member survey. Int Urogynecol J (2015) 26:1489–1494.

Mesh complications, FDA warning and cause for concern
Biochemical evidence in tissue repair

Elise De, MD
Department of Urology, Massachusetts General Hospital, Harvard Medical School, Boston Massachusetts.

Vaginal mesh has been in use since the 1970s for prolapse and 1990s for stress incontinence. The FDA first cleared its use in 1996 for SUI (and 2002 for prolapse) on a 510(k) mechanism for medical devices. This mechanism allows for clearance based on 'substantial equivalence' to previously marketed devices, and does not require premarket safety and efficacy studies. In this case the previously cleared mesh was developed for hernia repair. In 2008 and 2011, the FDA issued public communications about vaginal mesh through its website. These communications represent only a fraction of the true complication rate, as reporting is not mandatory. The second communication reported that the FDA received more than 1,000 adverse event reports between 2005 and 2008 and 2,874 between 2008 and 2010. Since these reports, the use of vaginal mesh has decreased not only in the US but worldwide.

Backtracking the R and D in response to continually emerging complications and hesitancy to use mesh, elegant work on biomechanics for the pelvic floor has been done. Mechanics contribute to the onset of prolapse as well as the failure of surgical interventions. The loading conditions of the pelvis, the tissues, as well as the repair (native tissue, biologics, and mesh) as well as the healing properties of all components are paramount for outcome.

Clinical evidence in the use of biological materials in female pelvic floor reconstruction

Rahmi Onur, MD.
Department of Urology, Marmara University, Faculty of Medicine, Istanbul-Turkey.

Transvaginal mesh use for prolapse repair became questionable after Food and Drug Administration (FDA) warnings in 2008 and 2011. Recently, there has been a surge in use of biological grafts for pelvic floor reconstruction. Considering apical prolapse repair, current literature continue to support the use of polypropylene mesh. Similarly, National Institute of Health and Clinical Excellence (NICE) recommends polypropylene mesh use in abdominal sacrocolpopexy (ASC) surgery as a safe and efficacious method of vaginal vault prolapse repair. Although biological grafts have similar or slightly less efficacy, synthetics are still preferred since they have a high success rate maintained by a cheaper material, polypropylene mesh without having increased complication rates in long-term for apical compartment repair. Porcine dermis, cadaveric fascia lata, and porcine intestinal submucosa have higher anatomical failure rates compared with polypropylene mesh when used for ASC. The ASC surgery using mesh is accepted as gold standard but may be associated with short term morbidity and potential foreign body problems.
Considering posterior compartment repairs, both synthetic or biological grafts did not show significant difference compared to posterior colporrhaphy alone. There's limited data evaluating the role of mesh or biological graft augmentation for posterior compartment prolapse repair. In many studies, posterior wall repairs with augmentation did not reveal better results than native tissue repair and lack long-term data.

The 2012 Cochrane meta-analysis concluded that objective success rate is higher in patients receiving anterior colporraphy reinforced with grafts compared to anterior colporraphy alone. However, concerns with synthetic graft use still persist such as, mesh extrusion, bleeding, dyspareunia and pain. Although, biological grafts showed improved anatomical outcomes compared to native tissue repairs, conflicting outcomes were reported which may be related to considerable variation in graft material and surgical technique. Proposed benefits include less risk of erosion for biological grafts, decreased operating time with kits, decreased operating time if autologous tissue not harvested. Disadvantages of biologicals in anterior compartment include host versus graft response, durability and risk of infectious transmission.

Continuing experience with transvaginal mesh surgeries for incontinence treatment supports use of polypropylene mesh and biological graft use. After FDA warnings, there became a tendency to use less synthetic mesh sling for the treatment of SUI at some tertiary care centers however, the difference was not significant. Nevertheless it was shown that there's an increase in the utilization of autologous fascia pubovaginal slings (AFPVS). Cadaveric grafts or

xenograft have also successfully been used in anti-incontinence procedures, however cost-efficiency is the main issue that limit their common use. Biological grafts can be suggested in patients with failed prior surgery, to patients not willing to receive synthetic material or in case of re-inforcement of pelvic floor. Treatment of patients with a failed prior surgical procedure for stress urinary incontinence represent a challenging clinical practice. The selection of surgical technique to achieve continence may vary and ranges from endoscopic bulking agents to re-do midurethral synthetic sling procedures, autologous fascial slings, adjustable devices using meshes or balloons and repeat colposuspension procedures. However, among these alternatives only use of a biological graft, autologous fascia pubovaginal AFPVS has shown long term durability and success rates after failed mesh surgery for SUI.

W4: Current Role of Biological Grafts in the era of Mesh Controversy

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07:30 - 07:40 Elise De:
- **Mesh complications, FDA warning and cause for concern**

07:40 - 07:45 Elise De:
- **Biochemical evidence in tissue repair Elise De**

07:45 - 08:00 Dirk De Ridder:
- **What does research say about biological materials**

08:00 - 08:15 Rahmi Onur:
- **Clinical evidence in use of biological materials**

08:15 - 08:30 All Audience: Discussion

Elise De, M.D.

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Affiliations to disclose†:

None

† All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- [ ] Self-funded
- [x] Institution (non-industry) funded
- [ ] Sponsored by:

Dirk De Ridder

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Affiliations to disclose†:

Astellas: speaker, consultant, unrestricted research grant

Medtronic: unrestricted research grant

Coloplast: clinical study

† All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

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Rahmi Onur, MD

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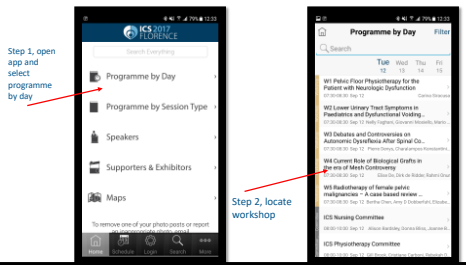
NEW FOR 2017

Please complete the in-app evaluation in the workshop before leaving.



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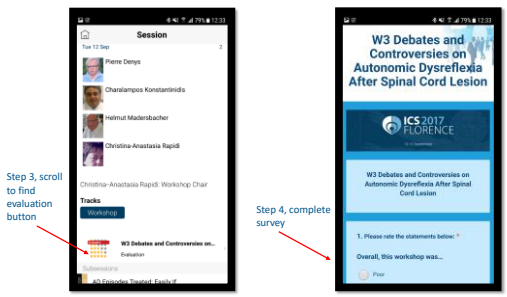


Announcements

- A shortened version of the handout has been provided on entrance to the hall
- A full handout for all workshops is available via the ICS website.
- Please silence all mobile phones
- Please refrain from taking video and pictures of the speakers and their slides. PDF versions of the slides (where approved) will be made available after the meeting via the ICS website.

7:30-7:45

1) Mesh complications, FDA warning and cause for concern
2) Biochemical evidence in tissue repair

Elise De, MD

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

MASSACHUSETTS GENERAL HOSPITAL

Question 1

In the past 10 years, for anterior wall prolapse, what percent of the time have you incorporated a synthetic mesh in the repair?

A.0%
B.25%
C.50%
D.75%
E.95%

Vaginal Mesh

Vaginal mesh:

- In use since the 1970s for prolapse
- In use since the 1990s for stress incontinence.

In the US, FDA first cleared its use on a 510(k):

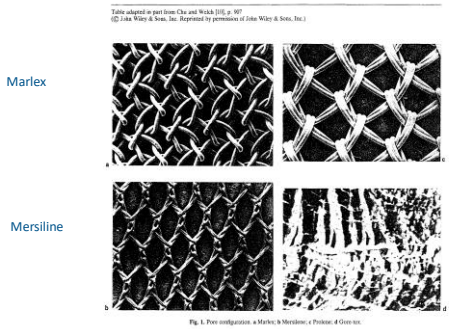
- 1996 for SUI
- 2002 for prolapse
- 'Substantial equivalence'
- Did not require premarket studies.
- Approved based on mesh for hernia repair.

2008 and 2011, U.S.:

•FDA issued public communications about vaginal mesh through its website.

•Since these reports, the use of vaginal mesh has decreased not only in the US but worldwide.

Pore Size



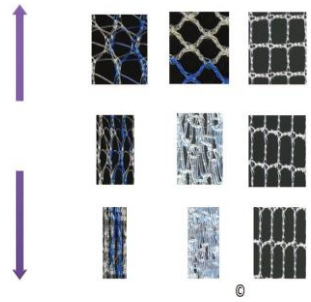
Currently Available Mesh

Publications and internal industry emails document:

- Shrinkage approx 30%
- Degradation
- Altered geometry
- Folding
- Bacterial colonization
- Inflammation
- Rigidity

Tensile Loading impacts Pores

Gynemesh Ultrapro Restorelle



Exploring the basic science of prolapse meshes

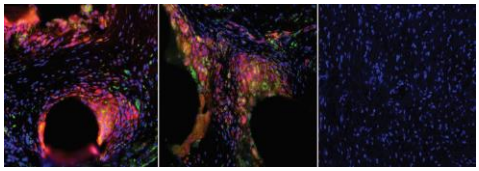
Rui Lianga, Katrina Knight b, Steve Abramowitchb, and Pamela A. Moalli

Volume 28 _ Number 5 _ October 2016

Degradation over time

Pro-inflammatory macrophages: CD68

a) AMS Perigee Mesh b) Gynemesh TVT Secure c) Control Vaginal Tissue



Nolfi AL, Brown BN, Liang R, et al.
Host response to synthetic mesh in women with mesh complications. Am J Obstet Gynecol 2016;215:206.e1-8.

After 2011

FDA required post-market surveillance studies:

- "522 studies"
- To evaluate success and complications of such devices
- Included manufacturers of xenografts (animal-derived)
- Did not require manufactures of allografts (human cadaveric tissue) to run these studies.

Rosenblatt and Von Bargen. Use of biologic grafts in pelvic organ prolapse surgery. Contemporary OB/GYN June 2017.

European Consensus 2017

Risk factors for mesh materials, consider:

1. Overall **surface area** of the material used (which is greater for POP than for SUI)

2. Mesh **design** (eg, physical characteristics of the mesh, size of the pore as a predisposing factor to infection—in particular with a **pore size of <75 microns**)

3. **Material** (biocompatibility, long-term stability, flexibility, elasticity, etc.)

4. No discussion of biologic grafts!

Consensus Statement of the European Urology Association and the European Urogynaecological Association on the Use of Implanted Materials for Treating Pelvic Organ Prolapse and Stress Urinary Incontinence EUROPEAN UROLOGY 7 2 (2 01 7) 4 2 4 – 4 3 1

Types of grafts

1. Allografts (eg, cadaveric fascia and dura mater)
2. Xenografts (eg, porcine and bovine)
3. Autografts (eg, fascia lata and rectus fascia)
4. Synthetic meshes (nonabsorbable, eg, PP mesh as well as absorbable)

Grafts differ in:

- Origin (autograft, allograft, xenograft)
- Source (eg, dermis, fascia, pericardium, small
- intestinal submucosa)
- Life stage (fetal, adult)
- Proprietary processing (washes, enzymes, chemicals, lyophilization)
- Cross-linking (eg, gluteraldehyde)
- Sterilization (eg, ethylene oxide, gamma irradiation).

Currently Available in the U.S.

TABLE Overview of clinically available biological grafts for pelvic floor reconstruction

Trade Name	Source	Cross-linking	Sterilization	Thickness	Hydration Time	Company
Repliform™	Human Dermis	None	Amorphous Freeze-dried	~1.1 mm	10-40 minutes	Boston Scientific
Axis™	Human Dermis	None	Gamma Irradiation	~0.8 mm	Up to 30 minutes	Coloplast
Suspend™	Human Fascia Lata	None	Gamma Irradiation	~0.64 mm	Up to 30 minutes	Coloplast
Xenform™	Fetal Bovine Dermis	None	Ethylene Oxide	~1.0 mm	Less than 3 minutes	Boston Scientific
MatriStem™	Porcine Bladder Matrix	None	E-beam	~0.2 mm	20 minutes	ACell

Xenografts:

- **Xenform**TM (Boston Scientific): noncross-linked fetal porcine dermis. Matrix undergoes chemical viral inactivation as well as sterilization with ethylene oxide gas
- **MatriStem**TM (ACell): 6-layer acellular and noncross-linked matrix derived from porcine urinary bladder.

Allografts:

- **Repliform**TM (Boston Scientific Corporation), acellular cadaveric, noncross-linked dermal matrix, which is sterilized to ensure clinical safety.
- **Axis**TM (human dermis) and **Suspend**TM (human fascia lata) Coloplast
  - Both noncross-linked and sterilized using a proprietary process (Tutoplast) to prevent the transmission of pathogens.

Allograft Concerns

Transmission of bacterial or viral disease
Transmission of prions
Durability
Degradation of allograft
Inconsistent quality from some tissue banks
Cost
Depletion of tissue banks
Unpredictable host response

Slide Courtesy Ajay Singla

Ideal Material

Biocompatible
Acellular
Abundant collagen
Abundant elastin
Preserved extracellular matrix
High tensile strength
Durable
Free of Infection and erosion
Inexpensive

Slide Courtesy Ajay Singla

7:45 – 8:00

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Dirk De Ridder

- **What does research say about biological materials**

KATHOLIEKE UNIVERSITEIT LEUVEN

From bench to bedside in pelvic floor surgery is preclinical research relevant ?

Dirk De Ridder

Andrew Feola, Bia Mori, Maarten Albersen, Frank Van der Aa, Jan Deprest
Development and Regeneration, KU Leuven, Leuven, Belgium

Iva Urbankova, Lucie Hympanova, Ladislav Krofta
Charles University, Prague, Czech Republic

Edoardo Mazza
ETH Zurich, Switzerland

Antonio Fernandes, Rita Rynkevic
Oporto, Portugal

Sheila MacNeil
Sheffield, UK

Daniela Ulrich, Caroline Gargett,
Melbourne, Australia

Michel Cosson, Laurent De Landsheere
Lille, France

Jan-Paul Roovers,
Amsterdam, Netherlands

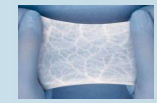
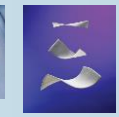
Disclosures: received support from AMS, FEG, BBGA and Clayton Lawyers
for independent research via Leuven Research Development Transfer Office

Implants

Xenografts
End 1990s
FDA approved for urogynaecology
CE marked

Non-cross linked
Small intestinal submucosa « SIS »
InteXen (LP)

Cross linked
Pelvicol
Pelvisoft

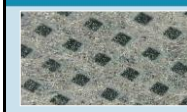



different host response, local side effects and durability ?

Question

- Do you think that biomeshes are a good alternative for mesh augmented repairs, now that synthetic mesh is out?
  - Yes, the scientific base is sound
  - Don't know
  - No, there are not enough data
  - New stem cell based technology will be the future

2005 Can we learn from experiments ?




Textile structure: Amid (1958) classification

Ob tape:
Siegel AL et al J Urol 2005
Yamada BS et al J Urol 2006
Adverse effects of microporous materials were predicted by a preclinical study in rats

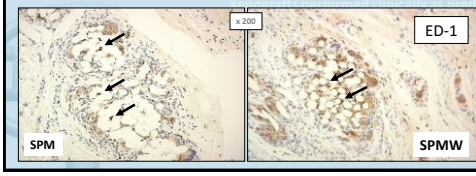
IVS multifilament sling was removed from market based on *Konstantinovic M et al, IUGJ 2006*

Xenografts performed clinically as predicted by experiments *Claerhout et al, Ozog et al, Konstantinovic et al, Zheng et al 2006-2010*

Amid type I (macroporous materials) are recommended *SCENIHR Report 2016*

2007 Can we learn from experiments ?





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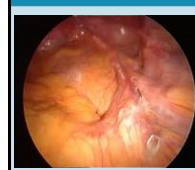
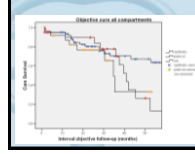
2010 Can we learn from experiments ?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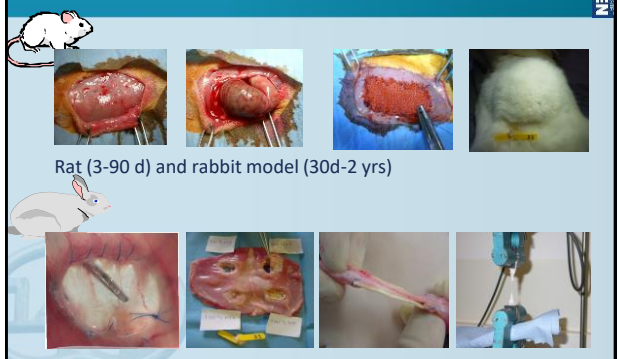
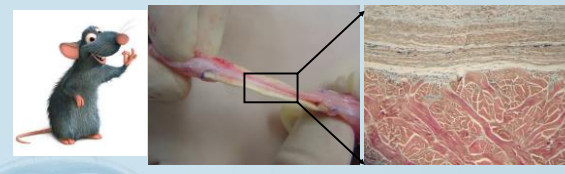
In vivo animal studies



Rat (3-90 d) and rabbit model (30d-2 yrs)

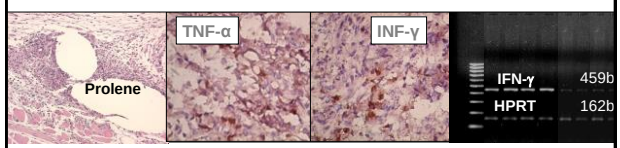
Xenografts – experimental data

Host response to acellular collagen matrix

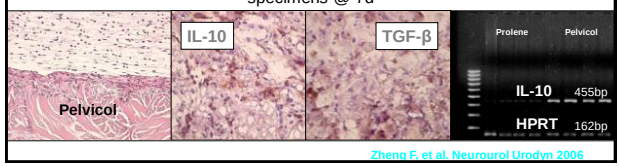


Weak inflammatory response
Less pro-inflammatory profile
Poor integration
Poor vascularization and collagen deposition

polypropylene provokes "pro-inflammatory" response = rejection
xenografts induce anti-inflammatory cytokines = "tolerance"

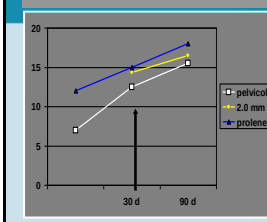


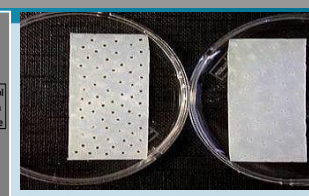
H& E stain | immunohistochemistry specimens @ 7d | PCR

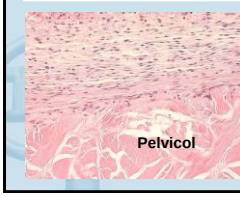


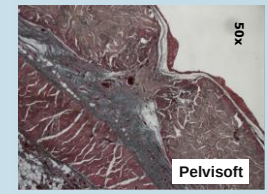
Zheng F, et al. Neurourol Urodyn 2006

Cross linked products



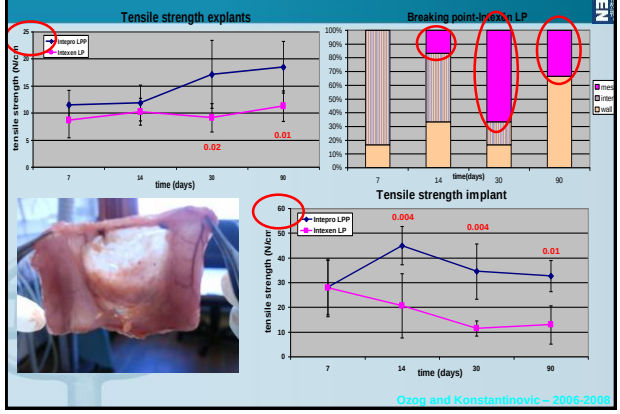






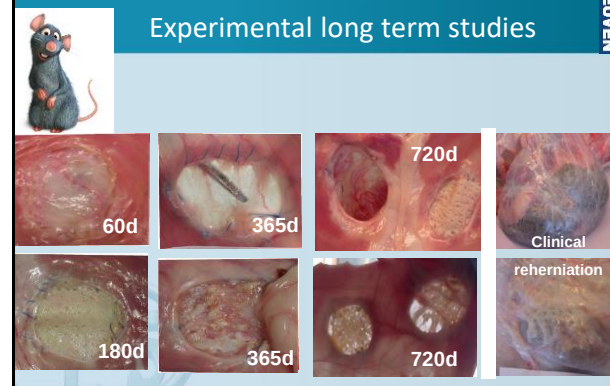
Zheng F, et al. Neurourol Urodyn 2005

Non-cross linked products



Ozog and Konstantinovic – 2006-2008

Experimental long term studies

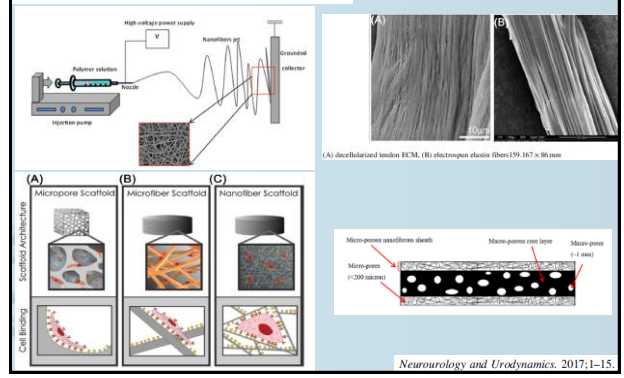


Improving materials

- Tissue engineering: non-textile matrices
  - Polylactic acid *(Roman Regueros, MacNeil & Deprest, 2014, 2016)*
  - Ureidopyrimidone *(Mori de Cunha, IUGA 2016)*
- New coatings for drug or cell delivery
  - Anti-inflammatory ibuprofen *(Canton, 2010)*
  - Antibiotics
    - Subclinical infection has been demonstrated ; clinical relevance uncertain *(Boulanger 2008; Marny 2011; Clave 2011; de Tayrac 2011; Vollebreght 2011)*
    - ampicillin: *Letouzey J Biomed Mater Res B 2011* – rifampicin: *Junge, Biomaterials 2005* – vancomycin *Harth, J Surg Res 2010*
  - Pro-angiogenics (VEGF, Heparin)
  - Estrogens *(Rizk 2008, 2009; Higgins AJOG 2009)*
  - Anti-oxidant ascorbic acid *(Mangir 2016)*
  - Cell carrier *(Ulrich, 2013)*

Biomimetic implants for pelvic floor repair

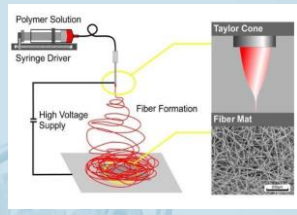
Mahshid Vashaghian Msc[1] | Sebastianus J. Zaat PhD[2] | Theodoor H. Smit PhD[3] | Jan-Paul Roovers MD, PhD[1]



Neurourology and Urodynamics. 2017;1–15.

Improving materials

- Tissue engineering: non-textile **electrospun** matrices
  - Polylactic acid *(Roman Regueros, MacNeil & Deprest, 2014, 2016)*
  - Ureidopyrimidone (Upy) *(Mori de Cunha, IUGA 2016)*



Microporous matrix

Promotes adhesion and proliferation of stem cells *(Shokrollah, 2010)*

Degradable

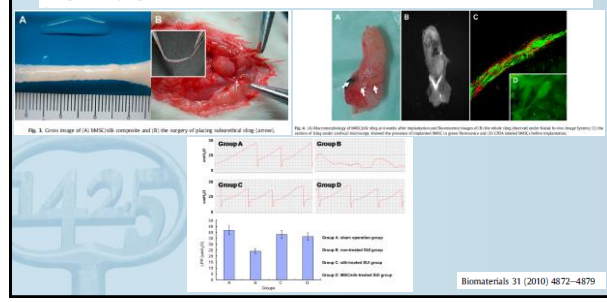
Can be rendered bioactive

www.bipupy.eu

Cell based slings/meshes

Mesenchymal stem cell seeded knitted silk sling for the treatment of stress urinary incontinence

Xiao Hui Zou [a,*], Yun Long Zhi [b], Xiao Chen [b], Hang Mei Jin [a], Lin Lin Wang [b], Yang Zi Jiang [b], Zi Yin [b], Hong Wei Ouyang [b,c,**]

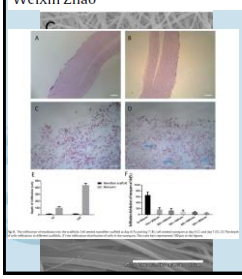


Biomaterials 31 (2010) 4872–4879

Cell base slings/meshes

Electrospun nanoyarn seeded with myoblasts induced from placental stem cells for the application of stress urinary incontinence sling: An *in vitro* study

Kaile Zhang [a,c,1], Xuran Guo [b,1], Yan Li [c,d,1], Qiang Fu [a,*], Xiumei Mo [b,*], Kyle Nelson [c], Weixin Zhao [c]



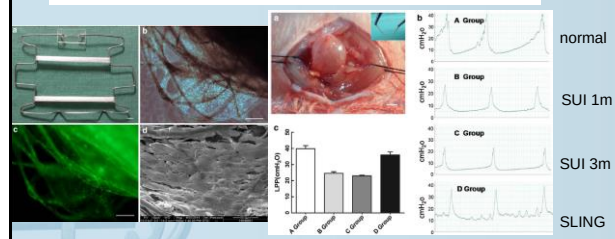
PSCs could be induced to myoblasts and revealed higher muscular cell markers and ECM expression. These myoblasts could become a potential cell source for tissue engineered sling. Furthermore, a novel electrospun nanoyarn was fabricated with dynamic liquid electrospinning. The *in vitro* study demonstrated that the nanoyarn could improve myoblasts proliferation, muscle development and ECM expression compared with nanofiber scaffold. The cooperation of myoblasts and nanoyarn scaffold could be a promising tissue engineered sling for our *in vivo* study in the future.

Colloids and Surfaces B: Biointerfaces 144 (2016) 21–32

Cell based slings/meshes

Adipose-derived stem cells seeded on polyglycolic acid for the treatment of stress urinary incontinence

Ying Wang[1] · Guo-wei Shi[1] · Ji-hong Wang[2] · Nai-long Cao[2] · Qiang Fu[2]



After sling operation in a rat of stress incontinence model, ADSCs-based tissue-engineered sling contributed to the restoration of sphincter structure and function.

World J Urol (2016) 34:1447–1455

Conclusions

Xenografts "ideal template" for remodelling ?

- Experimental evidence for induction different host response
- Non-cross linked materials
  - Poor early tensiometric resistance
  - Also disrupt more easily in the implant
- Cross linked
  - Stronger on tensiometry
  - Occasional degradation and loss of elasticity

Hybrids: electrospun scaffolds + Cells

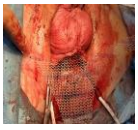
- Ongoing research

Ideal biomesh not designed yet

Thank you to all co-workers

Dirk.deridder@uzleuven.be and/or Jan.Deprest@uzleuven.be

Clinical evidence in the use of biological materials in female pelvic floor reconstruction



Rahmi Onur, MD.
Department of Urology,
Marmara University, Faculty of Medicine,
Istanbul-Turkey.

ICS 2017 FLORENCE

Affiliations to disclose†:

None

† All financial ties (over the last year) that you may have with any business organisation with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- ☐ Self-funded
- ☐ Institution (non-industry) funded
- ☒ Sponsored by: *Allergan*

ICS 2017 FLORENCE

Biological grafts are mostly preferred in case of…

A. Recurrent cystoceles
B. Advanced prolapse
C. Coexistent risk factors such as obesity, chronic constipation, asthma,.. etc
D. Patients not willing to receive synthetic mesh
D. All

ICS 2017 FLORENCE

Most of the RCT and metaanalyses related to use of graft augmentation in pelvic floor reconstruction revealed:

A. Higher subjective cure rates for prolapse treatment using adjuvant material
B. Similar mesh and biological graft extrusion rates
C. Increased short term objective anatomical cure rate
D. Better role in posterior repairs.

Question

ICS 2017 FLORENCE

Do you think that biomeshes are a good alternative for mesh augmented repairs, now that synthetic mesh is out?

- Yes, the scientific base is sound
- Don't know
- No, there are not enough data
- New stem cell based technology will be the future

Clinical evidence for use of biological grafts

- Is there enough evidence?
  (Evidence based use)
- Success rates
- Benefit / complication ratio?

→ Apical / Vault prolapse
Anterior repair
Posterior repair
SUI treatment

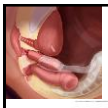
Apical prolapse: Abdominal sacrocolpopexy:

Author	n	Mesh type	Follow-up (mo)	Success (%)
Gregory et al (17)	28	Marlex/Mersilene	26.3	89
Culligan et al (16)	54	Polypropylene	12	91
Altman et al (18)	25	Prolene	7.4	71
Rust et al (19)	12	Mersilene	9-42	100
Addison et al (20)	56	Mersilene	6-126	89
Baker et al. (21)	59	Prolene	1-45	86
Tate et al. (22)	29	Polypropylene	60	93
Granese et al. (23)	131	Polypropylene	43 mo	94.9
Fox and Stanton (24)	29	Teflon	6-32	100
Snyder, Krantz (25)	147	Gore-Tex	60	73
Valaitis, Stanton(26)	43	Teflon	3-91	91

Success between 71-100%

- 74 % success rate even after 13 yrs
- Laparoscopic / Robotic Scx has similar success
- Exposure risk: 1-2 % with polypropylene

Hilger WS, et al, Am J Obstet Gynecol 2003, Murphy M Obstete Gynecol Cin N Amer 2009

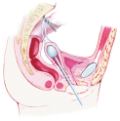


Apical prolapse treatment by graft use

Study	Graft/Mesh	No. Patients	Follow-up (mo)	Anatomic Cure	Comments
Latini et al[39]	Autologous fascia lata (AFL)	10	31	100%	No graft-related complications
Fitzgerald et al[40]	Cadaveric fascia lata (FD/IR-CFL)	53	17	17%*	40% reoperation rate
Flynn et al[41]	Cadaveric fascia lata (FD-CFL)	19	11	95%?	5% reoperation for apical prolapse 10% reoperation for anterior prolapse
Culligan et al[42]	Cadaveric fascia lata (SD/IR-CFL)	44 graft	12	68% graft	11% wound breakdown
	Polypropylene mesh (Type I)	45 mesh		91% mesh	15% wound breakdown 4% erosion
Gregory et al[43]	Cadaveric fascia lata (FD-CFL)	18 graft	21	61% graft	No erosion or wound breakdown in either group
	Mersilene mesh (type III)	19 mesh	26	89% mesh	
Afrisian et al[44]	PD (HMDI/IR-PD)	27 graft	7	71% graft	No erosion or wound breakdown in either group
	Polytetrafluoro-ethylene (Gore-tex)	25 mesh	7	76% mesh	

Success between 61-100%

Starkman J, et al, Curr Bladder Dys. Rep, 2007, 86-94.



The Use of Biological Materials in Urogynecologic Reconstruction: A Systematic Review

Ladin A. Yurteri-Kaplan, M.D.
Robert E. Gutman, M.D.
Washington, D.C.

Table 3. Sacral Colpopexy Outcomes for Apical Prolapse*

Author	Graft Type	No.	Follow-Up (mo)	Success Rate	Complications	Study Type
Cundiff et al., 2008[46]	Pelvicol (PD), Mersilene (PS), Gynemesh (PP), Gore-Tex (PT)	302	24	N/A	Erosion rates: PD 9.1%, NS; PS 7.5%, NS; PP 5.1%, NS; PT 19%, $p = 0.03$	RCT, secondary analysis
Culligan et al., 2005[47]	Tutoplast (CF), Trelex (PP)	89	12	CF: 68%, PP: 91%	Graft erosion: PP 2 vs. CF 0, NS	RCT
Deprest et al., 2009[48]	Xenograft (Surgisis SIS or Pelvicol: PD) vs. Gynemesh (PP)	104	33	PD: 79%, PP: 97%	Graft complication: 11% vs. 11%; erosion: PD 2 vs. PP 6, NS; Surgery for graft complication: PD 3% vs. PP 11%, NS	Prospective/ Retrospective cohort
Qsirou et al., 2008[49]	Pelvicol (PD), AF, synthetic mesh (PP/PS)	259	13	PD: 89%; AF: 93%; PP/PS: 99%	12%; erosion: PD 11, AF 1, PP/PS 0; 0.05; granulation: PD 9, AF 4, PP/PS 8, NS; VVF: PD 3, AF 0, PP/PS 0; NS; sinus tract: PD 1, AF 1, PP/PS 0	Retrospective series

PD, porcine dermis; RCT, randomized controlled trial; PP, polypropylene; CD, cadaveric dermis; PS, polyester; PT, polytetrafluoroethylene; CF, cadaveric fascia lata; AF, autologous fascia lata; SIS, porcine small intestine submucosa; VVF, vesicovaginal fistula; NS, not significant.
*Definitions of cure and surgical technique vary for each study.

Plast. Reconstr. Surg. 130 (Suppl. 2): 242S, 2012.)

Native tissue repair vs mesh repair

- Five randomized controlled trials
  - 4 out 5 trials favored mesh use in Abd. Scx.
- Native tissue repair was better in only one trial: 87% success with uterosacral ligament fixation vs 68% success with open sacrocolpopexy)
  - Superior efficacy and durability with Abd Scx & mesh
  - Lower rate of recurrent vault prolapse, reduced rate of residual prolapse and less dyspareunia with Abd. Scx

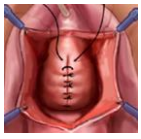
Siddiqui NY et al, Obstet Gynecol. 2015;125(1):44–55
Kontogiannis S, et al. Adv Ther 2016, 2139.
FDA Executive Summary, Brubaker L, et al

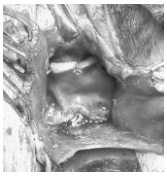
Role of biological grafts for apical prolapse

- Treatment of apical prolapse: Best with polypropylene mesh
- High success with less erosion rates: 2% as suggested by IUGA/ICS.
- *Why biological grafts not commonly used in abdominal sacrocolpopexy?*

❖ low success rate?
❖ High success rate by a much cheaper material (polypropylene mesh)

Anterior compartment: Graft or not to graft?





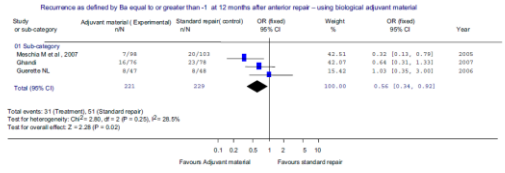
- Risk for failure : 30 %,
- Anterior colporraphy success: 37-57 %

- Graft use allows a broader base of support
- Not dependent on existing weakened tissue

Chen CC, et al. Clin Obstet Gynecol 2007, Weber AM, et al. Am J Obstet Gynecol 2001

Adjuvant materials in anterior vaginal wall prolapse surgery: a systematic review of effectiveness and complications

Richard Foon · Phillip Toozs-Hobson · P. M. Latthe



Int Urogynecol J (2008) 19:1697–1706

Success for biological graft reinforcement in anterior repair

- Porcine dermis vs anterior colporraphy alone: 93% vs 81%
- Kobashi et al., used cadaveric fascia lata for treatment of primary cystocele. No failures or complications were observed at a short follow-up.
- Frederick et al., examined 251 patients and at a short follow-up (6 months), cadaveric graft used for anterior prolapse showed 93% cure.
- Anterior colporrhaphy vs AC with small intestine submucosa (SIS) graft: Objective failure rate was significantly higher after the AC 33% compared to SIS group 14% (4/29).

Kobashi KC, et al. Urology 2000
Frederick R et al. J Urol 2005

Maher C, et al. Cochrane Database of Systematic Reviews (Online). 2013 (Issue 4)

Results of biologic grafts for the anterior compartment

Author	Graft	*n*	Follow-up (SD) (months)	Failure rate (> stage II)	Complications
Simsiman *et al.*, 2006 [33]	Porcine dermis (Pelvicol)	111	24 (10)	23%	15 erosions 3 ureteral kinking (with concomitant uterosacral suspension
Gandhi *et al.*, 2005 [34]	Cadaveric fascia lata (Tutoplast)	154	13	21% treatment 29% control	
Gomelsky *et al.*, 2004 [36]	Porcine dermis	70	24	12.9%	1 vaginal wound separation (with concomitant vault suspension)
Wheeler *et al.*, 2006 [37]	Porcine dermis (Pelvicol)	36	18.3 (7.9)	50%	41.7% overall 2.8% graft resorption 2.8% granulation tissue 16.7% urinary tract infection 2.8% readmission 11.1% postoperative fever 2.8% ureteral obstruction 2.8% hemorrhage
David-Montefiore *et al.*, 2005 [38]	Porcine dermis (Pelvicol)	47	24.6 (8.5)	4%	1 bladder injury (with vaginal hysterectomy) 1 rectal injury 1 urinary retention 4 de novo stress urinary incontinence 1 pararectal hematoma 1 urethrovaginal fistula

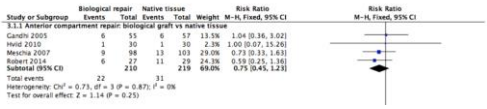
Cochrane Library

Biological tissue repair vs native tissue repair: 37 RCT

Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse (Review)

Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Marjoribanks J

Figure 5. Forest plot of comparison: 3 Biological repair versus native tissue repair, outcome: 3.1 Awareness of prolapse (1 to 3 years).



At one year review: only objective failure was high in native tissue group.

There was no evidence of a difference between the groups with respect to quality of life, recurrent prolapse, awareness of prolapse.

Cochrane Library

Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse (Review)

- If 10% of women were aware of prolapse after a native tissue repair, between 7% and 15% would be aware of prolapse after biological graft repair.

  (There was no evidence of a difference between the groups) (RR: 0.94, 95% CI 0.60 to 1.47, 7 RCTs, n = 587, I^2 = 59%).

- This suggests that if 30% of women had recurrent prolapse after a native tissue repair, then between 18% and 33% would have recurrent prolapse on examination after a biological graft repair.

Cochrane Library

Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse (Review)

Biological repair versus native tissue repair for vaginal prolapse

Population: women with vaginal prolapse
Settings: surgical
Intervention: biological repair
Control: native tissue repair

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Native tissue repair	Corresponding risk Biological repair				
Awareness of prolapse at 1 to 3 years	105 per 1000	102 per 1000 (68 to 151)	RR 0.97 (0.65 to 1.43)	777 (7 studies)	⊕⊕◯◯ low[1,2]	
Repeat prolapse surgery 1 to 2 years	43 per 1000	52 per 1000 (26 to 105)	RR 1.22 (0.61 to 2.44)	306 (5 studies)	⊕⊕◯◯ low[1,3]	
Recurrent prolapse at 1 year	295 per 1000	277 per 1000 (177 to 434)	RR 0.94 (0.60 to 1.47)	587 (7 studies)	⊕◯◯◯ very low[1,3,4]	
Bladder injury	Not estimable as only 1 event occurred (in the native tissue group)			137 (1 study)		
Bowel injury	Not estimable as only 1 event occurred (in the biological repair group)			137 (1 study)		
De novo dyspareunia (pain during sexual intercourse) review 1 to 3 years	177 per 1000	150 per 1000 (35 to 648)	RR 0.85 (0.20 to 3.67)	37 (1 study)	⊕◯◯◯ very low[3,4]	

RECONSTRUCTIVE

Plast. Reconstr. Surg. 130 (Suppl. 2): 242S, 2012.)

The Use of Biological Materials in Urogynecologic Reconstruction: A Systematic Review

Ladin A. Yurteri-Kaplan, M.D.
Robert E. Gutman, M.D.
Washington, D.C.

Summary: There are numerous randomized co...
logical materials in urogynecologic surgery. For p...
of a biological graft adds no benefit compared...
rectocele repair. Conflicting data exist regardin...

Adding biological graft for cystocele repair

Evidence: Conflicting

- ➢ Considerable variation in graft material and surgical technique.
- ➢ No benefit with porcine dermis compared with anterior colporrhaphy.
- ➢ The only other biologic graft that showed potential benefit was porcine small intestine submucosa.

Mesh, graft, or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery: two parallel-group, multicentre, randomised, controlled trials (PROSPECT)

The Lancet 2016

Cathryn MA Glazener, Suzanne Breeman, Andrew Elders, Christine Hemming, Kevin G Cooper, Robert M Freeman, Anthony RB Smith, Fiona Reid, Suzanne Hagen, Isobel Montgomery, Mary Kilonzo, Dwayne Boyers, Alison McDonald, Gladys McPherson, Graeme MacLennan, John Norrie (for the PROSPECT study group)*

Two pragmatic, parallel-group, multicentre, randomised controlled trials

Between 2010, and 2013, 1352 women allocated to treatment,

↓

(430 to standard repair alone, 435 to mesh augmentation)

&

(367 to standard repair alone, 368 to graft)

Mesh, graft, or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery: two parallel-group, multicentre, randomised, controlled trials (PROSPECT)

The Lancet 2016

Augmenting a primary transvaginal anterior or posterior prolapse repair with non-absorbable synthetic mesh or biological graft confers no symptomatic or anatomical benefit to women in the short term.

Similarly, in the first 2 years after surgery: No benefit to women having their first prolapse repair from the use of transvaginal synthetic mesh or biological graft to reinforce a standard anterior or posterior repair, either in terms of prolapse symptoms or in short term anatomical cure.

Conclusion: Biological grafts in anterior repair

- Mixed evidence: Conflicting results
- Variety of materials & techniques
- Short followup, non-standardised evaluation of results (i.e. definition of success, evaluation of success)
- Graft reinforcement in women with recurrent cystocele does appear to improve short-term outcomes.

Birch & Fynes, Curr Opin Obstet Gynecol 2002, Huebner M, Int J Gynecol Obstet

---

Posterior repair with graft reinforcement

- Biological graft use in posterior compartment (porcine dermis, porcine SIS, dermal allografts)
- A single RCT and 2 comparative cohort studies did not show improved outcomes with biological grafts.

* Results of biological grafts in the posterior compartment

Author	*n*	Graft	Mean follow-up (months)	Success rate
Oster and Astrup, 1981 [65]	15	Dermis, autologous	31.2	100%
Kohli and Miklos, 2003 [66]	43/30	Dermal allograft	12.9	93%
Altman *et al.*, 2005 [67]	32/29	Pelvicol	12	62%
Dell and O'Kelley, 2005 [68]	35	Pelvisoft	12	100%
Altman *et al.*, 2006 [69•]	32/23	Pelvicol	38	49%

Murphy M, Obstet Gynecol 2008, Paraiso MF et al. Am J Obstet Gynecol 2006,
*Modifed from Le et al, Curr Opin Obstet Gynecol 2007

Mesh in Pelvic Reconstructive Surgery

TABLE 4. Posterior Prolapse Surgery (Synthetic Mesh)

Study	Graft/Mesh	No. Patients	Follow-up	Anatomic Cure	Comments
Dwyer and O'Reilly[30]	Polypropylene	50	29 mo	100%	12% mesh erosion, 1 RV fistula
Milani et al[27]	Polypropylene	31	17 mo	100%	6.5% mesh erosion, 69% dyspareunia
Lim et al[34]	Composite polyglactin 910-polypropylene	90	6 to 12 wk, n = 31 to 6 mo	98.9% at 6 to 12 wk 87.5% at 6 mo	7.8% mesh erosion at 6 to 12 wk, 12.9% at 6 mo
Lim et al[35]	Composite polyglactin 910-polypropylene	78	36 mo	78%	30% mesh erosion, 27% de novo dyspareunia
de Tayrac et al[36]	Polypropylene to SSL	26	23 mo	92.3%	12% mesh erosion, 7.7% de novo dyspareunia
Sand et al[18]*	Polyglactin 910	65	24 mo	90%	No mesh-related complications
Watson et al[37]	Polypropylene	9	29 mo	Functional cure 89%	No mesh-related complications

Standard posterior colporraphy

- Success rate with traditional repair: 76%-96%
- Use of grafts: questionable
- Synthetic graft use : more complications
- Should we use ANY grafts?

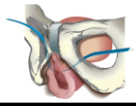
Study	N	Mean Follow-up (mo)	Anatomic Cure (%)	Vaginal Digitation (%)	Defecatory Dysfunction (%)	Fecal Incontinence (%)	Dyspareunia (%)	De novo Dyspareunia in Sexually Active Patients, n (%)
Mellgren et al								
Preoperative	25	12	96	8	100	8		2 (8)
Postoperative	25			0	88	8		
Weber et al								
Preoperative	53	12						14 (26)
Postoperative	53							
Sand et al†								
Preoperative	70	12	90					
Postoperative	67							
Maher et al								
Preoperative	38	12.5	89	100	100	3	37	1 (4)
Postoperative	38			16	13	0	5	
Paraiso et al†								
Preoperative	37	17.5	86	43	80		56	(20)
Postoperative	28			18	32		45	

*Prospective studies only.
†Two randomized controlled trials.

Ridgeway B, et al, Clin Obstet Gynecol 2008, De Ridder D, Curr Opin Urol 2008

Use of biological grafts for incontinence

- Transobturator and retropubic mid-urethral slings using cadaveric fascia lata, xenograft: similar success but expensive
- Autologous biological grafts: rectus fascia-fascia lata: for treatment of failures or in cases where synthetic mesh is contraindicated



Int J Urol. 2005 Sep;12(9):801-5.

Solvent-dehydrated cadaveric dermis: a new allograft for pubovaginal sling surgery.

Onur R[1], Singla A.

- Pubovaginal sling surgery using 2 x 12 cm cadaveric dermis.
- Outcome at 1 year assessed by the Urogenital Distress Inventory short form and standardized follow-up questionnaires.
- 80% patients were cured (20 patients: 17 dry, 3 improved)
- 76% percent of the patients indicated that urinary incontinence was no longer negatively affecting their daily life and were satisfied with the procedure.

Table 2. Sling Outcomes for Stress Urinary Incontinence*

Author	Graft Type	No.	Follow-Up (mo)	Success Rate
Paparella et al., 2010[15]	PelviLace TO (PD), Uretex TO (PP)	69	38 (27-50)	PD: 89%; PP: 88%
Amaro et al., 2009[23]	AF, TVT (PP)	41	12	AF: 57%; PP: 65%
Sharifiaghdas and Mortazavi, 2008[22]	AF, TVT (PP)	61	39	AF: 83%; PP: 88%
Basok et al., 2008[25]	CF, Intravaginal slingplasty (PP)	139	12	CF: 79%, PP: 71%
Bai et al., 2005[24]	AF, RPS, TVT (PP)	92	12	AF: 93%; RPS: 88%; PP: 87%
Arunkalaivanan and Barrington, 2003[16]	Pelvicol (PD), Gynecare TVT (PP)	142	12 (6-24)	Pelvicol: 76%; Gynecare: 74%
Giri et al., 2006[19]	Pelvicol (PD), RF	94	36	PD: 54%; RF: 80%
Frederick and Leach, 2005[24]	Tutoplast (CF)	251	24 (6-61)	45%
Kobashi et al., 2002[25]	Tutoplast (CF)	132	12 (6-28)	82%
Barrington et al., 2002[18]	Pelvicol (PD)	40	12 (6-18)	85%
Shippey et al., 2008[17]	PelviLace (PD), Gynecare TVT (PP)	109; PD 21, PP 88	22 (10-40)	PD: 76%; PP: 90%

Yurteri-Kaplan LA , et al, Plast Reconstr Surg. 2012

Use of biological materials in failed mesh slings for incontinence treatment

- Challenging clinical practice.
- Endoscopic bulking agents ?
- Re-do mid-urethral synthetic sling procedures ?
- Autologous fascial slings?
- Adjustable devices using meshes or balloons?
- Repeat colposuspension procedures?
- Artificial sphincter ?

Guidelines on **Urinary Incontinence**

M.G. Lucas, J.L.H.R. Bosch, F. Cruz, T.B. Madden, A. Nambiar, A. Neisius, R.S. Pickard, D.J.M.K. de Ridder, A. Tubaro, W.H. Turner

Guideline for the Surgical Management of Female Stress Urinary Incontinence: 2009 Update

5.2 Complicated SUI in women

This section will address surgical treatment for
failed, or those women who have undergone pr
Neurological lower urinary tract dysfunction is n
on Neurogenic Lower Urinary Tract Dysfunction
included in the next edition of these Guidelines

5.2.1 Failed surgery

Evidence summary	LE
The risk of treatment failure from surgery for SUI is higher in women who have had prior surgery for incontinence or prolapse.	1b
Open colposuspension and autologous fascial sling appear to be as effective for first-time repeat surgery as for primary surgery.	1b
The mid-urethral sling is less effective as a second-line procedure than for primary surgery.	2

Native Tissue Repair After Failed Synthetic Materials

A. Lenore Ackerman, Seth A. Cohen, and Shlomo Raz

Patients suffering from recurrent pelvic floor symptoms after mesh removal: practices of native tissue repair in vaginal reconstructive surgery.

55 yr-old woman: TAH + BSO: 12 years ago

- TAH + BSO: 12 yrs ago
  - Anter. repair + post. repair: 3 yrs
  - Abd. Scx: 1 yr

55 yr-old woman: presented with intermittent vaginal bleeding, progressive vaginal pain, dyspareunia, recurrent UTIs and SUI

On exam: 1 cm area of mesh extrusion at the apex
2 cm area of mesh extrusion at the anterior vaginal wall
1 cm mesh extrusion posteriorly

Management: Transvaginal exploration, complete removal of mesh products

Concomitant laparotomy + sacrocolpopexy mesh excision

Autologous fascia sacral colpopexy

55 yr-old woman: Repeat sacral colpopexy with autologous tissue

Now developed persistent SUI: requiring 5 pads/day.

SUI treatment using autologous fascia (pubovaginal sling)

55 yr-old woman: 9 mo later presented with anterior and posterior vaginal wall prolapse

Anterior colporraphy with plication of underlying perivesical fascia

Posterior native tissue repair

Conclusions

1- Use of biological grafts on apical prolapse

- ✓ Abdominal sacrocolpopexy with synthetic grafts: Better or similar results compared to biological grafts. Cheap, durable, long term success.
- ✓ Biologicals: in case of complications, failure, no more mesh use

Synthetic mesh use is more common!

Conclusions
2- Use of biological grafts for incontinence

- ✓ For index patient with no contraindication: MUS with mesh: long term durability with less morbidity
- ✓ Biological grafts can be suggested in patients with failed prior surgery, to patients not willing to receive synthetic material

Conclusions
3- Biological material for repair of posterior compartment

- ✓ Limited data for mesh augmentation in posterior repair.
- ✓ Use of biologicals in posterior wall did not reveal better results than native tissue repair.
- ✓ Same data for synthetic grafts

Native tissue repair is common!

Conclusions
4- Biological material for anterior repair

- Mixed evidence
- ✓ In primary cystocele: evidence is mixed for repair reinforced with or without augmentation of any type of graft
- ✓ Graft reinforcement in women with recurrent cystocele does appear to improve short-term outcomes
- ✓ Patient reported outcomes: similar for native and graft use

8:15 – 8:30

Discussion with Audience