# W18: Biological Materials in Female Pelvic Floor Reconstruction. What's New

Workshop Chair: Ajay Singla, United States

27 August 2013 09:00 - 12:00

| Start | End | Topic | Speakers |
|---|---|---|---|
| 09:00 | 09:30 | Biochemical evidence in tissue repair | • Ajay Singla |
| 09:30 | 10:00 | What does research say about biological materials | • Dirk de Ridder |
| 10:00 | 10:30 | Clinical evidence in use of biological materials | • Rahmi Onur |
| 10:30 | 11:00 | Break | None |
| 11:00 | 11:30 | Mesh complications | • Paulo Palma |
| 11:30 | 11:45 | FDA warning and case for concern | • Amit Chakrabarty |
| 11:45 | 12:00 | Discussion | All |

## Aims of course/workshop

The aim of this workshop is to familiarise 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.

# "Bio"-meshes

Dirk De Ridder

Jan Deprest

*Interdepartemental Center for Surgical Technologies*
*Faculty of Medicine,*
*Katholieke Universiteit Leuven, Leuven, Belgium*

Our laboratory has been supported by unconditional grants from Bard, Cook, Tyco, Ethicon, AMS

## Implants

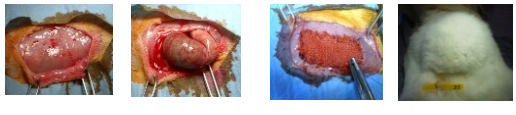
**Xenografts**
**End 1990s**
**FDA approved for urogynaecology**
**CE marked**


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

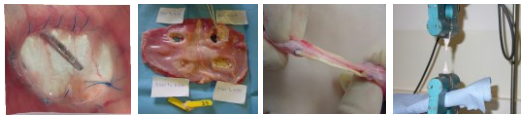
**Cross linked**
**Pelvicol**
**Pelvisoft**

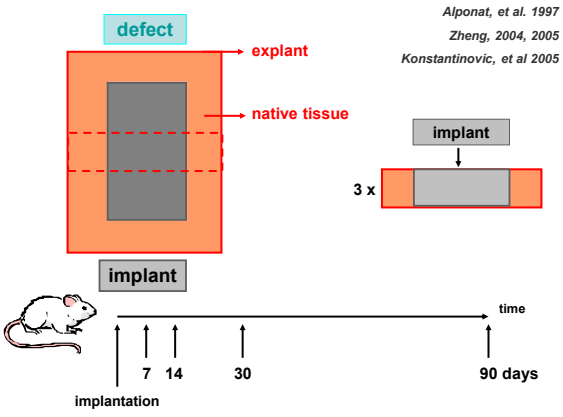

**different host response, local side effects and durability ?**

## In vivo animal studies



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

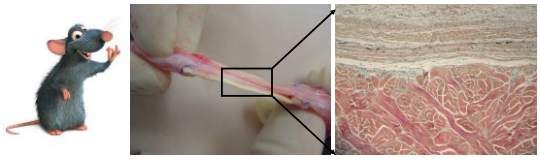





*Alponat, et al. 1997*
*Zheng, 2004, 2005*
*Konstantinovic, et al 2005*

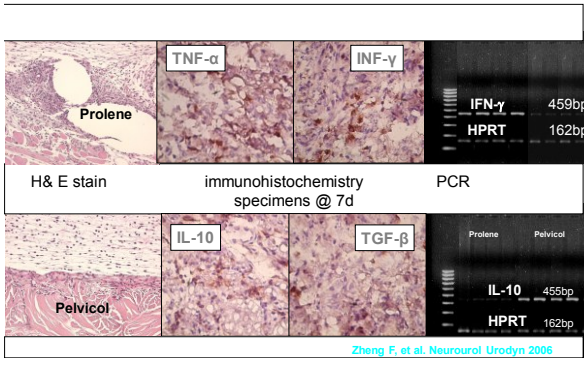
## Xenografts – experimental data

**Host response to acellular collagen matrix**



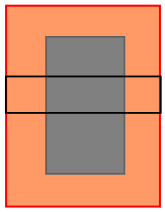
**Weak inflammatory response**
**Less pro-inflammatory profile**
**Poor integration**
**Poor vascularization and collagen deposition**

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

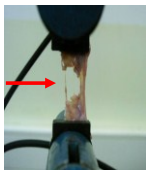


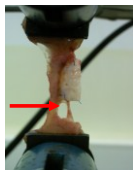

Zheng F, et al. Neurourol Urodyn 2006

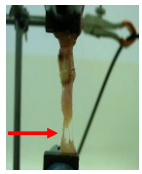
## Tensiometry of explant (in vivo)



4467 Instron tensiometer
Specimen: 1 x 5 cm
Crosshead speed: 2 cm/ min
Measurement:
maximum load to disrupt (N)
Location of disruption:
in mesh
or at interface





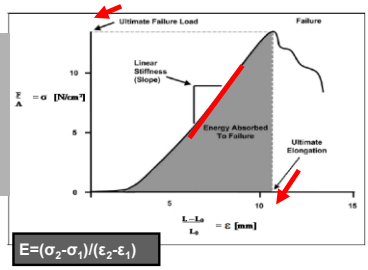


## Uni-directional stress/strain plot

elastic area
E is measure of slope

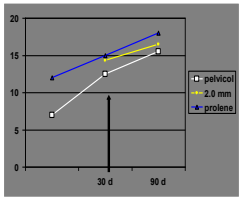
plastic area
permanent deformation

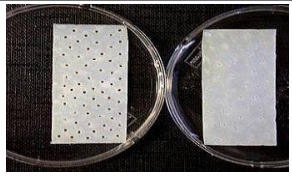
Main purpose: failure level
Determination of
Stress
Strain
Stiffness

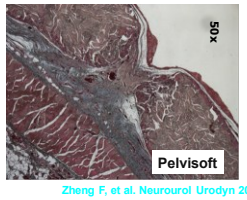



$E=(\sigma_2-\sigma_1)/(\varepsilon_2-\varepsilon_1)$

## Cross linked products



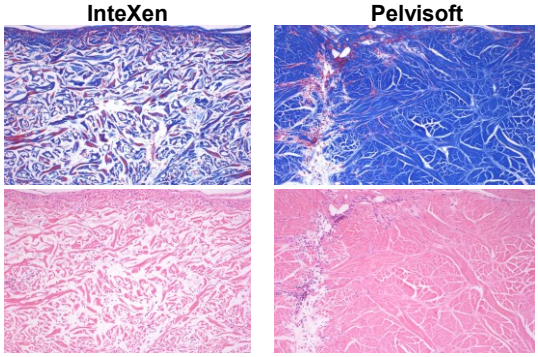



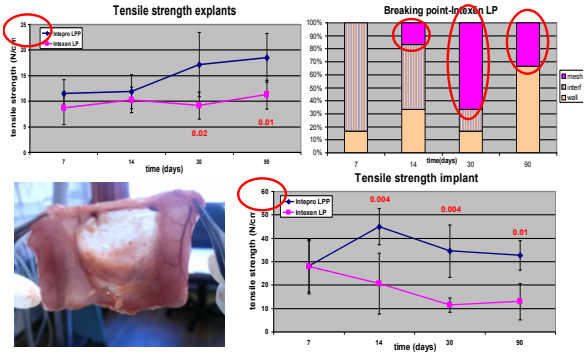

Zheng F, et al. Neurourol Urodyn 2005

## Structure of implant

InteXen | Pelvisoft

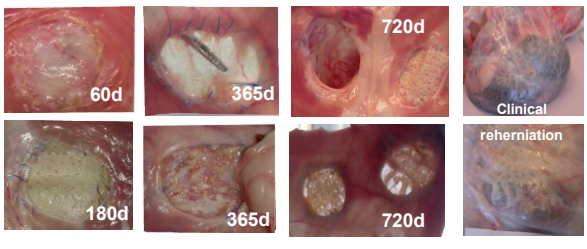


## Non-cross linked products

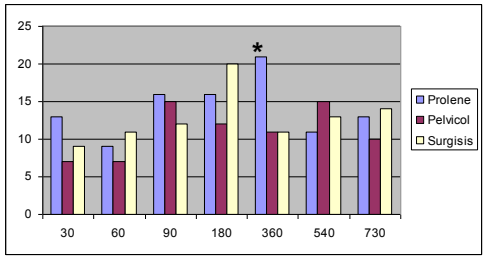



Ozog and Konstantinovic – 2006-2008

## Experimental long term studies



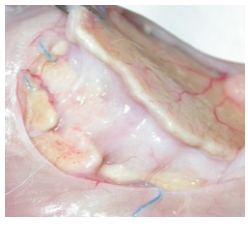
## Rabbits - explant strength

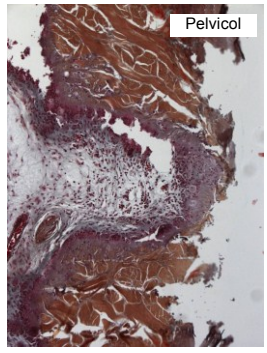



- Overall comparable performance
- reherniations in both bio-groups
- 25 % of SIS implants tear at the implant
- Loss of elasticity

*Claerhout et al, 2004, AJOG 2008*
*Trabuco et al, AJOG 2008*

## long term inflammatory changes






## Conclusions - 1

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

**Ideal biomesh not designed yet**

## Clinical data – anterior compartment

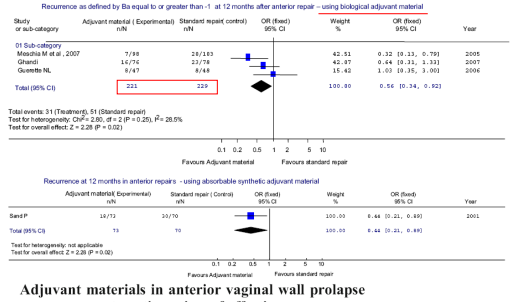
| | N | Product | Follow up |
|---|---|---|---|
| Leboeuf | 19 | Pelvicol | 15.0 mo |
| Urol 2004<br>Consec cases | 24 | Ant colp | |
| Chaliha | 14 | SIS | 24.0 mo |
| Int J Urogynaecol 2005<br>Case control study | 14 | Ant colp | |
| Meschia | 98 | Pelvicol | 12.0 mo |
| Urol 2007<br>Randomized trial | 101 | Ant colp | |

## Clinical data – anterior compartment

| recurrences | N | Product | Anterior Stage II | Anterior Stage III | Mid | posterior |
|---|---|---|---|---|---|---|
| Leboeuf | 19 | Pelvicol | - | 6.9% | 0% | 0% |
| Urol 2004<br>Consec cases | 24 | Ant colp | - | 0 % | 0 % | 0 % |
| Chaliha | 14 | SIS | At 6 mo significantly better for D and TVL | | | |
| Int J Urogynaecol 2005<br>Case control study | 14 | Ant colp | After 2 years no anatomic differences | | | |
| Meschia | 98 | Pelvicol | 7% | 2% | 3% | 3% |
| Urol 2007<br>Randomized trial | 101 | Ant colp | 19 % | 2% | 3% | 8% |

* Ba >-1

## Meta-analysis

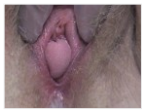


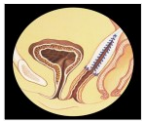

**Adjuvant materials in anterior vaginal wall prolapse surgery: a systematic review of effectiveness and complications**

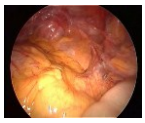
Richard Foon · Philip Toozs-Hobson · P. M. Latthe

Int Urogynecol J (2008) 19:1697–1706

## Sacrocolpopexy using xenografts







observational cohort study
*consecutive* laparoscopic sacropexies

- 50 xenografts
  (21 SIS , 29 pelvicol)
- 100 polypropylene
  50 before the cases
  50 after the cases

Follow up
- Yearly telephone interview (Kobashi, 1991)
- 95% clinical assessment for study (Claerhout, 08)
- POP-Q, QoL (Kings)

Claerhout et al, Europ Urol 2008

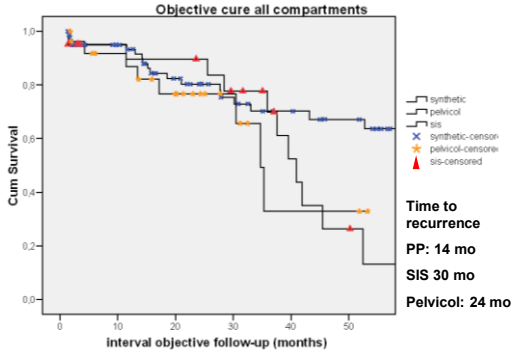
## Sacrocolpopexy using xenografts

| @ 32 months follow up | SIS 21 | Pelvicol 29 | Polypropylene 100 |
|---|---|---|---|
| Objective failure (C≥-1) | 22% | 19% | 3%* |
| Reoperation vault prolapse | 2 (10%) | 3 (10%) | 0 (0%)* |
| Infection/exposure | 2 (10%) | 2 (10%) | 6 (6%) |
| Reoperation GRC | 0 | 1 (3.5%) | 7 (7%) |

**Comparable demographics - no significant functional differences in prolapse, urinary, defecation and sexual function**

**(Deprest et al, submitted Obstet Gynecol 2008)**

## Sacrocolpopexy using xenografts




**Time to recurrence**

**PP: 14 mo**

**SIS 30 mo**

**Pelvicol: 24 mo**

## Clinical data – vault

| | N | Product | Follow up |
|---|---|---|---|
| Quiroz et al AJOG 2008 | 102 | Pelvicol | 1.1 yr |
| Consecutive cases Retrospective study | 134 | Polypr | 1.1 yr |
| | 23 | Fascia | 1.1 yr |
| Altman et al Urol 2006 | | | |
| Consecutive cases Retrospective study | 25 | Polypr | 7.1 mo |
| | 27 | Pelvicol | 7.1 mo |

## Clinical data – vault

| recurrences | N | Product | Follow up | Vault recurrence | anterior | posterior |
|---|---|---|---|---|---|---|
| Quiroz et al | 102 | Pelvicol | 1.1 yr | 11%* (8% reop) | 7 % | 3 % |
| Am J Obstet Gyn 2008 Consec cases | 134 | Polypr | 1.1 yr | 1% | 1% | 1% |
| Retrospective Mean follow up: 1.1 yr | 23 | Fascia | 1.1 yr | (1/15) | 0 | 0 |
| | | | | Stage II recurrence | | |
| Altman et al | 25 | Polypr | 7.1 mo | 24% | | |
| Urol 2006 Consec cases | 27 | Pelvicol | 7.1 mo | 29% | | |

## Clinical data – posterior compartment

| recurrences | N | Product | Follow Up | posterior Stage II* | Local problems |
|---|---|---|---|---|---|
| Paraiso et al | 37 | Posterior repair | 17.5 mo | | |
| Am J Obstet Gynecol 2006 | 37 | Site specific repair | | | |
| Randomized trial | 32 | +SIS augment | | | |

Conclusion

- No graft complications
- Faster and more severe failure with graft

* Bp ≥-2

## Conclusions - 2

- The results are at present conflicting
  - Even RCT material typically dubious in nature
  - Variety of materials and techniques
  - Inherent short follow up with new material
- Anterior: argument for graft augmentation
  - Underpowered for functional benefit
  - Same results with synthetic material (absorable) - €
- Middle and posterior: point not proven
  - Local complications not included
  - Point at importance of long term follow up for anatomical endpoint
  - Even arguments against…

**(These) materials should be used within trials**

**(?) PRIOR TO THEIR SALES (?)**

1 **Biomaterials in Female Pelvic Floor Reconstructive Surgery**

Ajay K Singla, MD, FACS, FICS
Associate Professor
Department of Urology and Gynecology
Wayne State University

2 **Total Female Population In U.S.**

- 20 million 30-39 years
- 21.4 million 40-49 years
- 15.8 million 50-59 years
- 10.7 million 60-69 years
- 
- Total procedures per year 180,000

3 **Incontinence - Incidence**

- 6.5 million women in US has SUI
- 10-35% of women 15-54 years age
- 30-50% of women over 60 years age
- 15-20% of women with recurrent SUI
- 15-20% of women with urge incontinence or other dysfunction following surgery
- De novo urge incontinence in 10%-30%
- Bladder outlet obstruction in 2.5%-24%

4 **Cost of Incontinence**

- $23.9 billion for evaluation & treatment
- $4.2 billion for Home Health Care associated with incontinence
- Total of $28.1 billion spent on incontinence in 1995 in United States
- 

5 **SUI Surgery Prevelance**

- prevalence of in-patient SUI surgery US [1]
  - 48,345/yr 1979
  - 135,000/yr 1998
  - 103,467/yr 2004

- ASC visits for SUI [2]
  - 15/100,000 1994
  - 34/100,000 2000

6 **Prevelance of Pelvic Organ Prolapse (POP) Surgery**

- prevalence of vaginal prolapse surgery US [1,2]
  - >200,000/yr
  - 29% reoperation rate within 4 yr

- Life time risk to undergo surgery for POP/SUI
  11.1% [2]

7 **Science Behind Biomaterial Use**

Pelvic organ support & Continence rely on:

- Endopelvic fascia
- Ligament support
- Pelvic floor muscles

8 **Biochemical basis for Pelvic floor support**

connective tissue fibroblast

collagen type I & III

compliance

elastin tensile strength & flexibility

fiber stabilization

cross linking proline & hydroxyproline amino acids

9 **Science Behind Biomaterial Use**

- Decrease in total collagen content in women with POP and SUI as compared to controls1
- Increase in matrix metalloproteinase (MMP) – a collagen degradation enzyme
- Decrease inhibitors of MMP expression in vaginal tissues
- Increase in degradation of elastin in women with POP and SUI
- Decrease in alpha1-antitrypsin mRNA level – elastin degradation inhibitor

10 **Historical Perspective**

- Goebel 1910 Pyramidalis Ms
- Price 1933 Rectus fascia (attached)
- Aldridge 1942 Rectus fascia strips (paired)
- McGuire 1978 Rectus fascia
- Blavais 1991 Fascial strip (free)
- Beck 1988 Fascia Lata
- Raz 1989 Vaginal wall
- Handa 1996 Cadaveric fascia Lata

11 **Types of biomaterials**

- Absorbable
  - Autograft (autologous)
  - Allograft
  - Xenograft
  - Absorbable synthetic mesh
- 
- Non-absorbable
  - Synthetic mesh

12 **Autograft**

- 
- Rectus fascia
- Fascia lata
- Rectus muscle
- Gracilis muscle
- Vaginal mucosa

13 **Allograft**

- Fascia lata
  - FasLata
  - Suspend

- Dermis
  - Urogen
  - Axis
  - Repliform
  - Dermal Allograft

14 **Xenograft**

- Porcine dermis
  - DermMatrix
  - Pelvicol
- Porcine SIS
  - Stratisis
  - FortaFlex
  - FortaPerm
- Bovine pericardium
  - Veritas

15 **Types of Synthetic Mesh**

- Absorbable
  - Vicryl (polyglactic acid)
  - Dexon (polyglycolic acid)
- Non-absorbable
  - Nylon
  - Silastic
  - Dacron (mersilene)
  - Marlex
  - Gore-Tex
  - Prolene

16 **Synthetic material**

- Pore size (macroporous vs microporous)
- Construction (monofilament vs multifilament)
- Weave (woven, knitted, thermal bonded)
- Flexibility or elasticity
- Additives or coatings (silicone, antibiotics, collagen)

Most meshes manufactured for sling surgery are:
Monofilament, loosely woven or knitted, elastic, macroporous polypropylene (standard of care)

17 **Classification of Synthetic Mesh**

- Type I – macroporous / monofilament
  - Atrium, Marlex, Prolene and Trelex

Type II – microporous / multifilament
Gore-Tex

Type III – macroporous with multifilament
Teflon, dacron (mersilene), woven polypropylene and PTFE

Type IV – Mesh with submicronic pores coated with silicone
silastic, cellgard, dura substitute

18 **History of Cadaveric fascia**

- More than 200,000 soft tissue allograft transplants done annually in US

- Cadaveric fascia has been in clinical use for 3 decades
- Ophthalmological uses
  - Orbital floor reconstruction
  -
- Orthopedic uses
  - Anterior cruciate ligament repair

19 **Donor Screening**

- HIV 1&2 Ab
- Hepatitis B Ag & Ab
- Hepatitis C Ab
- HTLV 1/11 Ab
- Syphilis
- HIV DNA by PCR
-

20 **Tissue Processing**

- Most common: Freeze dried (Incubation in 70% isopropyl alcohol→ Frozen→gamma irradiation @ 25 Kgy)
- Freeze dried ( Urogen, FasLata,Dermal allograft, Stratisis, Repliform
- Fresh Frozen (DermMatrix, Stratisis)
- Solvent dehydrated and gamma irradiated (suspend and axis tutoplast)
- Cryopreservation and amorphous freeze drying (Repliform)

21 **Processing and Strength**

- Sutaria and Staskin:
-
  - Comparison of tensile strength between freeze dried alone, freeze dried and gamma irradiated, solvent dehydrated-gamma irradiated
  - No stastical difference was noted using tensiometer

J Urol 163A 1194,2000

22 **Tissue strength**

- Lemer et. Al:
  - Maximum load to failure (MLF), stiffness assessed in autologous, freeze-dried, solvent dehydrated fascial grafts and dermal graft using tensiometer
  - MLF and stiffness equivalent in autologous and solvent dehydrated fascial graft and dermal allografts
  - Freeze dried allografts had lower MLF and were less stiff

Neurourol 18:497,1999

23 **Tissue Strength**

- Choe et.al:
-
  - Comparison of tensile strength (MLF) between allograft (freeze-dried gamma irradiated cadaveric fascia lata, cadaveric dermis), autologous (dermis, rectus fascia, vaginal mucosa) and synthetic (Gore-tex and prolene) mesh using tensiometer.
  -
  - Cadaveric fascia lata >cadaveric dermis >Gore-tex >prolene >human dermis >human rectus fascia >vaginal mucosa.

UROLOGY 58(3),2001

24 **Safety of Cadaveric tissue**

- Risk of HIV transmission from blood transfusion
  - 1/400,000 to 1/600,000
- Risk of HIV transmission from donor tissue
  - 1/1,667,600
- One documented case of HIV transmission from bone allograft in 1985

25 **Safety of Cadaveric tissue**

- Prions ("slow virus"):
  - Naturally occurring protein molecules located in CNS
  - PrPc prions are mutated due to infectious agent
  - Originally discovered after cannibalistic tribe in New Guinea found to die from progressive destructive brain disease.

26 **Prion diseases**

- Kuru Primates
- Creutzfeldt-Jacob Primates
- Scrapie Sheep
- BSE (mad cow) Cattle
- vCJD (injested tainted beef) Man
- Risk of transmission unknown

27 **Prion diseases**

- No known cure
- Inactivation is resistant to
  - Heat exposure
  - Gamma irradiation
- Alkaline treatment is thought to inactivate prions

28 **Bacterial Contamination**

- Study of 36 women undergoing cadaveric fascia lata sling
  - Cultures of allograft sent immediately prior to surgery:
  - 5/36 grew organisms
  - One developed superficial wound infection
  - Clinical significance of these findings unclear

Gerber, et.al,Urol 163A:735,2000

29 **DNA contamination**

- 4 different types of human fascia lata allograft, all processed by 4 different techniques extracted for DNA content.
- Total DNA concentrations ranged from 0.3 – 3.0 mcg/mg tissue

Sadhukhan et.al. J Urol 161A:396,1999

30 **Tissue Reaction**

- 30 female rabbit bladders exposed to
  - Synthetic sling vs. cadaveric fascia vs. control
  -
- Histologically examined at 6 and 12 weeks

31 **Tissue Reaction**

32 **Cadaveric fascia failure**

- 12 women failed cadaveric fascia (12%)
-
  - Allografts were freeze dried and irradiated
  - 3x10 cm strips used for PVS in 35 women
    »6 failed (1 week to 4 months)
  -
  - 6x 16 cm strips used for sacrocolpopexy (67)
    »6 failed (7–11 months)
  -

Fitgerald, et.al, Am. J. Obstet. Gynec.181:1339,1999

33 **Cadaveric fascia failure**

- Findings at re-operation:
-
  - Graft remnants found in 7 patients
    »Often thin and attenuated
-
  - No tissue found, only suture in 5 patients

34 **Cadaveric fascia failure**

- Histology:
  - Some areas with appropriate remodelling, linear orientation of fibrocytes within connective tissue, except high tensile strength
-
  - Other areas haphazardly arranged, non-inflammatory scar- like tissue, some areas with inflammatory response, still other areas with tissue degeneration.

35 **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
- Increased operative time and patient morbidity
- Unpredictable host response

36 **Synthetic Material**

- Type of Material:
- Monofilament
  - Prolene
- Multifilament
  - Mersilene
  - Gore-tex

*Bacteria enter into multifilament
*Macrophages and PMN's cannot

37 **Synthetic Material**

- Pore Size:
-
  - Larger pores > tissue bonding
  -
    - »Prolene > mersilene > marlex > Gore-tex

38 **Synthetic Material**

- Advantages:
  - Abundant – "off the shelf"
  - Decreased operative time
  - Durable – permanent
  - Cost – inexpensive
  - Independent of tissue re-modeling
  - Resistant to degradation
  - Long term preservation of tensile strength
- Risks:
  - Infection
    - »Prolene 0-3%, Mersilene & Gore-tex 5-23%
  - Erosion
  - Failure of remodeling

39 **Ideal Material**

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

40 **Applications In Urology**

- Sling surgeries in women for SUI
- Sling surgeries in men for SUI
- Pelvic floor reconstruction in women
- Urethral reconstruction in men
- Penile reconstructive surgeries
- Bladder reconstruction/replacement ?

41 **Future Sling Materials**

- Hybrid Sling Materials
-
  - Combination of allograft and synthetic material
  - Combination of xenograft and synthetic material
-
- Engineered Tissues
-

- Cells grown in tissue culture on matrix to create sling
- Myoblast taken from muscle biopsy from the patient

42

43 **Methodology**

- We evaluated 4 different sling materials
  - Small intestinal mucosa (SIS) (Cookbiotech)
  - Fascia lata (FL) (Coloplast Corp)
  - Fascia dermis (FD) (Coloplast Corp)
  - Pelvicol (P) (C.R.Bard)
- All currently used in patients clinically

44 **Methodology**

- Biomaterial was implanted intraperitoneally at the bladder neck of female Balb/c mice (n = 64)
- Animals were sacrificed at 2, 4, 8, or 12 weeks post-implantation
- Bladder and implants were extracted and fixed for histological analysis

45 **Methodology**

- Implant Histological Analysis:
  - Cell Count (cells/um$^2$)
  - Cell Morphology (aspect ratio)
  - Capsule formation (collagen deposition)
  - Capsule thickness (um)
  - Angiogenesis (CD31)
  -

46 **Capsule Thickness:**
**2 Weeks Implantation**

47 **Capsule Thickness:**
**12 Weeks Implantation**

48 **Cell Number**

- None of the implants displayed a significant change individually in cell number during the 12 weeks
- However, Pelvicol had significant decrease in cell number as compared to all other groups

49 **Cell Morphology**

- Aspect ratio correlates with cell morphology
  - Smaller round cells indicate inflammatory cells
  - Longer cells indicate a fibroblastic type of cell
- At specific time points there was significance between groups
- However, no implant had a significant change over the 12 weeks

50 **Capsule Thickness**

- Capsule thickness generally measures the severity of the inflammatory response
- SIS was the only group to show a significant decrease in capsule thickness over 12 weeks
- P had thinnest capsule at all time points
-
-
-

51 **Capillary Formation at 12 Weeks**

52 **Angiogenesis**

53 **Summary**

54 **Conclusion**

- Important for a graft to become incorporated as endogenous tissue and not lead to encapsulation
  - Angiogenesis allows for cells and nutrients to enter the matrix and ultimately implant survival.
  -
- At 12 weeks, SIS demonstrated minimal implant encapsulation and complete cell infiltration throughout the implant
  - Indicating improved biocompatibility as compared to the other tissues

55 **Conclusion**

- In comparing biological tissues for pelvic reconstruction we were able to assess the biocompatibility within the urological environment
- Through commercial processing, tissues are claimed to be devoid of cells
  - However, other antigens may be present which elicit inflammatory reactions, thus limiting the implant incorporation and use for long term urological therapies.
-

56 **In Vivo comparison of biomaterials in rabbit model**

- Cadaveric fascia lata
- Porcine SIS
- Porcine dermis
- Autologous
- Polypropylene mesh

57 **In Vivo comparison of biomaterials in rabbit model**

- Tensile strength (force required to break)
- Stiffness (force required to stretch sling)
- Shrinkage (% decrease in surface area)
- Distortion (ratio of the area of sling to the area of its minimal enclosing rectangle-rectangular fit factor)

58 **In Vivo comparison of biomaterials in rabbit model**

- At 12 weeks tensile strength and stiffness were greatly decreased from baseline in all materials except polypropylene mesh and autologous fascia.
- Polypropylene mesh gained stiffness with time.
- Autologous fascia and SIS experienced significant shrinkage at 12 weeks.

- Autologous fascia became highly distorted at 12 weeks.

59 **conclusions**

- Significance of tensile strength is unknown
- Stiffness is more important than tensile strength.
- The stretching of a sling with time is more likely scenario than breakage and may be responsible for the recurrence of incontinence
- Low tensile strength may explain difficulty in manipulating sling tension for recurrent incontinence
- Stiffness of mesh increased with incorporation of surrounding tissue
- The biomechanical results support the use of polypropylene mesh for sling surgery relative to other non-autologous materials.

60 **NICE Review**

61 **Objective Failure Rate**

62 **Objective Failure Rate**

63 **Failure rate for anterior prolapse**

- No mesh – 28.8%
- Synthetic non-absorbable mesh – 8.5%
- 
- "The objective failure when using non-absorbable synthetic mesh was significantly lower than without mesh/graft"

64 **Low Rate of Erosion**

65 **Erosions**

- Clearly a risk – 10% in literature
- With better surgical technique/more care with the vaginal wall dissection current studies demonstrate a much lower incidence – 2-5%

66 **How well do we do with traditional prolapse repairs?**

- Randomized trial
- Median follow up of 23 months
- Findings – Success rates
  - Anterior plication – 30%
  - Plication with absorbable mesh – 42%
  - Ultralateral plication – 46%
- Many of these did not require further repair
- But - What will happen at 5 or even 10 years?

67 **Why such a high failure rate?**

- Tissue Factors
  - Multiple studies show differences in tissue between women with prolapse and those without – vaginal tissue, skin and other sites
- 

68 **Why such a high failure rate**

- Tissue Factors
  - Multiple studies show differences in tissue between women with prolapse and those without – vaginal tissue, skin and other sites
- 
- Thus – are we really helping by suturing weakened, possibly defective tissue back

together?

■

69 **Paradigm of General Surgery: Hernia Repairs**

- For decades inguinal and abdominal wall hernias were repaired by suturing native tissue to native tissue
- ■
- More recently many have started to use synthetic mesh with improved results
- Can we follow this paradigm?

70 **Mesh Repair - Kits**

71 **Outcomes**

- National Institute for Health and Clinical Excellence (NICE) report
  - Provides national clinical guidelines in the United Kingdom
- Examined surgical repair of vaginal prolapse using mesh
- 199 page document
- Evaluated 446 reports - 49 studies selected
- 4569 patients in total

72 **Poor Surgical Outcome with Allograft**

73

74

75

76

77

78 **Failure of Allograft**

- Variable host response
- Method of tissue processing
- Site of harvest
- Quality of harvested graft

79 **Small intestinal submucosa (SIS)**

- Prepared from submucosa of small intestine of pigs and is replaced by host tissue in 90-120 days
- SIS contains
  - Collagen
  - Growth factors
    - Transforming growth factor- alpha
    - Fibroblast growth factor-2
    - Glucosaminoglycans
    - Glycoprotein
- Minimal tissue reaction
- Biocompatible
- High tensile strenghth

80 **SIS in Pubovaginal Sling**

Literature Review

- Total Patients 152
- Follow-up time 4 yrs
- Cured 142 (93.4%)
- Improved 3 (1.98%)
- Failed 7 (4.06%)

81 **Our Experience with SIS**

- 
- Total patients 22
- PVS (4-PLY) 15
- PVT (8-PLY) 6
- Male Sling (4-PLY) 1

82 **Our Experience with SIS**

- PVS
  - Cured 12
  - Improved 2
  - Failed 1
- PVT
  - Cured 3
  - Improved 1
  - Failed 2
- Male Sling
  - Cured/Improved 1

83 **What Do I Use**

- Hypermobility
  - Polypropylene mesh (TOT)
  - ISD
    - First time – SIS pubovaginal sling
    - Re do - Autologous fascia
  - POP
    - vaginal – allograft
    - sacrcolpopexy – polypropylene mesh

84 **FDA Regulation**

- FDA classify all implantable devices into 3 regulatory classes based on the degree of regulation necessary to provide device safety and effectiveness. (1976 amendment)
- Sling materials are included in class II devices and are subject to general controls and special controls. It requires data from human clinical trials, post-market surveillance, patient registries. (1990 amendmend)

85

- Biomaterial – Any natural or synthetic substance that incorporates or integrates into patients tissues.
- Biocompatibility – Ability of a material to perform with an appropriate host response in a specific situation.
  - It needs to be integrated properly into the tissues
  - Generate an appropriate inflammatory response
  - Maintain mechanical integrity (hold shape)
  - 
- 

86

87

88 **Criteria for Ideal Synthetic Sling**

1. The material should be chemically inert.
2. Not to be modified by tissue fluids.
3. Not induce inflammatory response or antibodies.
4. Not be carcinogenic.
5. Not induce allergy or hypersensitivity.
6. Be able to resist mechanical stress.
7. Be manufactured in the required shape.
8. Be able to be sterilized.
9. Resistant to infection.
10. Be resistant to adhesions.
11. Have a better in vivo response than autologous tissue.
12. Cost effective

1.

# Clinical evidence in use of biological materials for pelvic organ prolapse surgery

**Rahmi Onur, MD. Department of Urology,**
**Firat University, Elazig-Turkey.**

## Mesh use in POP surgery

2010 : 300.000 women, underwent POP repair surgeries in US
appr. in 100.000 women mesh used for repair

3 out of 4 mesh POP procedures were performed transvaginally

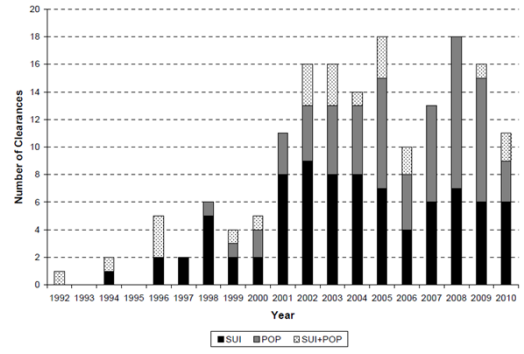
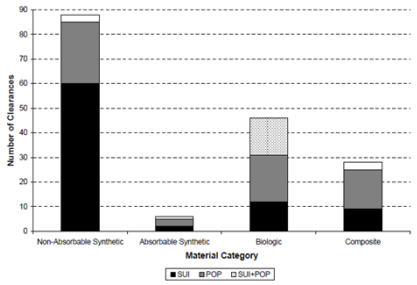



**Figure 1** – ***Urogynecologic Surgical Mesh 510(k) Clearances by Year (1992-2010).*** *This stacked column graph shows the number of cleared urogynecologic surgical mesh submissions each year from 1992-2010, broken down by indication—SUI, POP, or both (SUI+POP). As the graph indicates, after the year 2000, there was an increase in the number of clearances across all indications. (Please see Appendix I for a larger version of this graph.)*

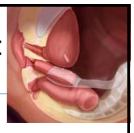



## Should we use biological or synthetic materials in pelvic floor ?

- Is there enough evidence?
- Evidence based literature data?
- Benefit / complication ratio?
- Which mesh?
  - Biological, synthetic?
  - Absorbable, Nonabsorbable?
  - Composite?

Apical / Vault prolapse
Anterior repair
Posterior repair
Combined

## 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 ranges between 71-100%
- 74 % success rate even after 13 yrs
- 67 women who underwent ASC with cadaveric fascia lata :92 % success ( f-u: 6-11 months)
- Laparoscopic Scx has similar success at experienced hands
- Exposure less than 1% with polypropylene, > 3% wit polyethylene grafts

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

*The Use of Synthetic Mesh in Pelvic Reconstructive Surgery*

CLINICAL OBSTETRICS AND GYNECOLOGY
Volume 51, Number 1, 136–152
© 2008 Lippincott Williams & Wilkins

ERI RIDGEWAY, MD, CHI CHIUNG GRACE CHEN, MD, and MARIE FIDELA R. PARAISO, MD

- RCT: Polypropylene mesh is superior compared with cadaveric fascia lata in sacral colpopexy

  Objective cure rates: 91 % vs 68 %.

- Higher success rates with mesh (89%) compared with allograft or xenograft use (61%)

Ridgeway B, et al, Clin Obstet 2008, Culligan PJ et al, Obstet Gynecl, 2005, Nygaard IE, et al, Ocbstet Gynecl, 2004

## Transvaginal repair of apical and vault prolapse

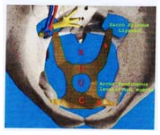
- Benson et al: 88 women: 30 mo follow-up

| | Bilateral sacrospinous vault suspension & paravaginal repair | sacrocolpopexy & paravaginal repair |
|---|---|---|
| optimal result: | 29 % | 58 % |
| unsatisfactory results: | 33 % | 16 % |

Benson JT, et al, Am J Ocbstet Gynecl, 1996

## Transvaginal vs Abdominal repair of apical and vault prolapse

- Lo and Wang: 138 women:
  Maher et al: 95 women



| | Unilateral sacrospinous vault suspension | Abd. sacrocolpopexy |
|---|---|---|
| optimal result: | | |
| Lo & Wang: | 80.3% | 94.2% |
| Maher et al: | 91 % | 94 % |

Lo & Wang, J Gynecol Surg 1998, Maher et al, Am J Obstet Gynecol 2004

## Vaginal repair of vault prolapse by mesh

- Posterior intravaginal slingplasty: to reinforce atrophied uterosacral ligaments

| Author | n/n (follow-up) | Used material | Technique | Mean follow-up (months) | Cure rate, anat. (no vault prolapse) |
|---|---|---|---|---|---|
| Petros, 2001 [49] | 71 | Nylon | Posterior IVS | 1.5 to 54 | 94.0% |
| Farnsworth, 2002 [13] | 91 | Nylon ($n=49$) Polypropylene ($n=44$) | Posterior IVS | 12 | 91.0% |
| Lo et al., 2005 [51] | 15 | Polypropylene | SSLS | 34.8 | 100.0% |
| Rutman et al., 2005 [52] | 50 | Polypropylene | SULC complex | 6 | 92.0% |
| Shah et al., 2004 [53] | 29 | not mentioned | H-shaped mesh | 25.14 | 93.1% |
| Biertho et al., 2004 [55] | 34 | Polypropylene | Posterior IVS | 12 | 91.2% |
| Jordaan et al., 2005 [56] | 42/33 | Polyglactin and Prolene (Vypro) | Posterior IVS | 13 | 71.0% |

71- 100 % success

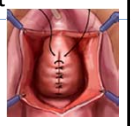
Modified from Huebner M, et al. Int J Gynecol Obstet 2006, 285

## Use of mesh in apical prolapse

- Abd Scx with mesh: lower rate of recurrent vault prolapse, reduced rate of residual prolapse and less dyspareunia compared to vaginal sacrospinous colpopexy
- Abd. Scx: Safe and efficacious
- Transvaginal surgery with mesh to correct vaginal apical prolapse is associated with a higher rate of complication

FDA Executive Summary

## Use of grafts in Anterior compartment



Why grafts are used?

- Limited success with classical anterior repair
- Intrinsic attenuated tissue – or – even no native tissue
- Risk for failure within 4 yrs: 30 %
- Risk of reoperation as high as 29%
- Anterior colporraphy success: 37-57 %

- Graft use allows a broader base of support
- Eliminates the need to be dependent on existing weakened tissue

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

## Anterior repair reinforced by absorbable mesh/graft

| Author | Mesh type | Follow-up (mo) | Success(%) |
|---|---|---|---|
| Chaikin et al | Cadaveric fascia | 6 | 100 |
| Groutz et al | Cadaveric fascia lata | 19 | 100 |
| Gandhi et al | Cadaveric fascia | 13 | 79 |
| Chung et al | Cadaveric dermis | 24 | 84 |
| Salomon et al | Porcine dermis | 18 | 81 |
| Clemons et al | Alloderm | 18 | 59 |

International Journal of Gynecology and Obstetrics (2006) 92, 279–288

## Anterior repair reinforced by absorbable mesh/graft

| Author | Operation | Result |
|---|---|---|
| Sand (2001) | anterior repair vs ant. Repair + polyglactin mesh | Higher success than traditional repair |
| Meschia (2007) | anterior colporraphy vs anter. colp. + porcine dermis (Pelvicol) | No difference at 1 year- f-u |
| Gandhi (2005) | Anterior colporraphy w/wo (solvent dehydrated cad. fascia lata) | similar success at 13th mo |
| Gomelski | Porcine dermis | 91 % 24 mo f-u: cure |

## Anterior colporraphy +/- absorbable graft

Weber AM, Walters MD, Piedmonte MR, Ballard LA. (Am J Obstet Gyn 2001) :

109 patients: appr. 2 years- follow-up, POP-Q evaluation of recurrence

- Standard ant. colporraphy: 30 % satisfactory outcome
  ant. colporr. + polyglactin mesh: 42 % ”
  ultralateral colporraphy: 46 % ”
- Addition of mesh: No benefit

186 women: trocar-guided mesh repair vs 182 women underwent colporraphy

At year 1: no prolapse (objective and subjective outcome)

Restoration of anterior vaginal wall to POP-Q stage 0 to 1

82.3% in mesh group vs 47.5% in no-mesh group ( p<0.001)

with regard to vaginal bulging

75.4% in mesh group vs 62.1% in no-mesh group ( p<0.001)

| | mesh repair | vs | colporraphy |
|---|---|---|---|
| Symptoms of SUI | more | | less |
| New SUI | 12.3 % | p=0.05 | 6.2% |
| Obstructive symptoms | less | | more |
| Dyspareunia | 7.3% | | 2% |
| Pelvic pain | 7 | | 1 |
| Duration of surgery | 52.6 min | p<0.001 | 33.5 min |
| Bladder perforation | 3.5% | p<0.001 | 0.5% |
| Reoperation for mesh exposure | 3.2% | | - |

## Anatomic superiority with use of mesh in anterior compartment

| RCT | N | Follow-up (months) | Anatomic Cure | | p |
|---|---|---|---|---|---|
| | | | Mesh | Traditional | |
| Sivaslioglu (2008) | 90 | 12 | 91% Ant | 72% | p<0.05 |
| Nguyen (2008) | 75 | 12 | 87% Ant | 55% | p<0.05 |
| Carey (2009) | 139 | 12 | 81% Ant/Post | 65.6% | p=0.07 |
| Nieminen (2010) | 202 | 36 | 87% Ant | 59% | p<0.0001 |
| Iglesia (2010) | 65 | 9.7 | 40.6 All | 29.6 | p=0.28 |
| Withagen (2011) | 194 | 12 | 90.4 All | 54.8 | p<0.001 |
| Altman (2011) | 389 | 12 | 82.3 Ant | 47.5 | p=0.008 |

## Comparative studies: EFFICACY

Jia X, et al. BJOG, 2008

**Table 1.** Efficacy of anterior repair, summary of crude event rates (95% CI, any study design) by type of mesh/graft

| | No mesh, *n/N* (%, 95% CI) | Absorbable synthetic mesh, *n/N* (%, 95% CI) | Biological graft, *n/N* (%, 95% CI) | Nonabsorbable synthetic mesh, *n/N* (%, 95% CI) |
|---|---|---|---|---|
| Subjective failure | 19/179 (10.6, 6.9–16.0) | 5/112 (4.5, 1.9–10.0) | 36/486 (7.4, 5.4–10.1) | 1/55 (1.8, 0–6.5) |
| Objective failure | 184/640 (28.8, 25.4–32.4) | 63/273 (23.1, 18.5–28.4) | 186/1041 (17.9, 15.7–20.3) | 48/548 (8.8, 6.7–11.4) |
| De novo prolapse | — | — | 8/58 (13.8, 7.2–24.9) | 8/45 (17.8, 9.3–31.3) |
| Further operation needed* | 2/85 (2.4, 0.6–8.2) | 16/174 (9.2, 5.7–14.4) | 9/280 (3.2, 1.7–6.0) | 3/234 (1.3, 0.4–3.7) |
| Persistent urinary symptoms | 9/10 (90.0, 59.6–98.2) | 5/49 (10.2, 4.4–21.8) | 13/14 (92.9, 68.5–98.7) | 17/44 (38.6, 25.8–53.4) |
| Persistent bowel symptoms | — | — | — | — |
| Persistent dyspareunia | — | — | — | — |

—, no studies reported this outcome.
*Surgery for prolapse (recurrent or de novo).

29% failure 23% failure 18% failure 9% failure

***•A trend in the crude objective failure rates with procedures not using mesh/graft having highest failure:***

***no mesh > absorbable synthetics > biological > non-absorbable meshes***

## Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review

Hasan Abed · David D. Rahn · Lior Lowenstein · Ethan M. Balk · Jeffrey L. Clemons · Rebecca G. Rogers ·

Int Urogynecol J (2011) 22:789–798

- 110 studies: 11785 women
- Similar exposure rates with use of biological or synthetic grafts ( 10.1% vs 10.3%)

**Table 1** Comparison of rates of adverse events between non-absorbable synthetic and biological graft

| Adverse event graft type | Number of studies | Total number of adverse events/total number of patients | Summary adverse event rate[a] (95% confidence interval) (%) | *P* difference (subgroups) |
|---|---|---|---|---|
| Graft erosion | | | | |
| All grafts | 110 | 982/11,785 | 10.3 (9.7, 10.9) | |
| Non-absorbable synthetic | 91 | 897/10,440 | 10.3 (9.7, 11.0) | NS |
| Biologic | 19 | 85/1,345 | 10.1 (8.3, 12.3) | |
| Wound granulation tissue formation | | | | |
| All grafts | 16 | 92/1,762 | 7.8 (6.4, 9.5) | |
| Non-absorbable synthetic | 9 | 49/1,113 | 6.8 (5.2, 8.9) | NS |
| Biologic | 7 | 43/649 | 9.1 (6.8, 12.1) | |
| Dyspareunia | | | | |
| All grafts | 70 | 350/5,638 | 9.1 (8.2, 10.0) | |
| Non-absorbable synthetic | 54 | 284/4,566 | 8.9 (8.0, 10.0) | NS |
| Biologic | 16 | 66/1,072 | 9.6 (7.6, 12.1) | |

## Use of graft reinforcement in anterior repair

- Mixed evidence
- In primary cystocele: evidence is mixed for repair reinforced with prostheses in anterior repair
- Prosthetic reinforcement in women with recurrent cystocele does appear to improve short-term outcomes
- A role for the use of grafts in anterior vaginal wall prolapse: relatively low rate of complication with acceptable outcomes

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

## 4th International Consultation for Incontinence Committee for Pelvic Organ Prolapse review

- Insufficient data to make any definitive conclusion with regard to the role of biological or synthetic prosthetic materials in primary or recurrent prolapse surgery

- Many of the studies: retrospective case series
- definition of prolapse is different
- no standard procedure used
- lack of consensus on the definition of anatomic cure
- poor usage of validated questionnaires

Herschorn S, Curr Opin Urol 2007

## Posterior repair with graft reinforcement

- Who should receive ?

- recurrent rectoceles
- advanced prolapse
- deficient rectovaginal fascia and weak tissue
- coexistent risk factors such as obesity, chronic constipation

## Standard posterior colporraphy

- Succes rate with traditional repair: 76%-96%
- Use of grafts: questionable
- Synthetic graft use : more complications
- Should we use biological-absorbable 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 | 52 | 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 | | | 10 | 32 | | 45 | |

* Prospective studies only.
† Two randomized controlled trials.

## Graft augmented posterior colporraphy

| Study | N | Mean Follow-up (mo) | Anatomic Cure (%) | Graft Type | Defecatory Dysfunction (%) | Vaginal Digitation (%) | De novo Dyspareunia in Sexually Active Patients n (%) | Mesh Erosion (%) |
|---|---|---|---|---|---|---|---|---|
| Milani et al | | | | | | | | |
| Preoperative | 63 | | 94 | Prolene | 45 | | 4 (6) | 13 |
| Postoperative | | | | | 30 | | | |
| Altman et al | | | | | | | | |
| Preoperative | 32 | 38 | 62 | Acellular porcine dermis | 100 | | | |
| Postoperative | 23 | | | (Pelvicol) | < 50 | | | |
| Sand et al† | | | | | | | | |
| Preoperative | 73 | 12 | 92 | Polyglactin | | | | |
| Postoperative | 65 | | | | | | | |
| Paraiso et al† | | | | | | | | |
| Preoperative | 31 | 17.5 | 54 | Acellular porcine small intestinal | 97 | 51 | | |
| Postoperative | 26 | | | Submucosa (Fortagen) | 21 | 7 | (6) | |

## Posterior repair with graft reinforcement

- xenograft use in posterior compartment (porcine dermis, porcine SIS)
- 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

## Posterior repair with graft reinforcement

- 9 studies with 417 women: 2 RCT, 2 non-randomised comparative studies, case series, abstract
- 3 studies used absorbable synthetics, 3 used biological graft, 1 used combined, 2 used synthetic meshes
- No RCTs or comparative studies compared different types of meshes
- Median follow-up was 12 mo
- Objective failure was compared:

**No mesh : 12.7% faiure** **Absorbable graft: 8.6%**
**Biological graft: 20.43%** **Synthetic mesh: 6.5%**

Jia X et al, BJOG 2008

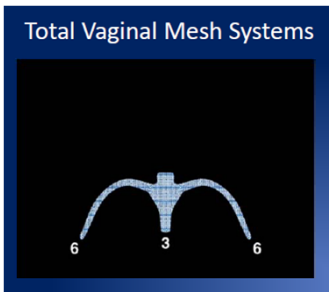
## Posterior repair with graft reinforcement

- Graft augmented posterior repair: 60-100% success rates. but risk of erosion, dyspareunia, difficulty in defecation, etc..
- 1 RCT showed anatomic benefit for posterior repair with mesh, 3 RCT did not show any benefit.
- Transvaginal posterior repair with mesh does not appear to provide any added benefit

## Posterior repair with graft reinforcement

- The need for graft reinforced repairs of posterior prolapse is less clear than for anterior prolapse and abdominal Scx
- There are no comparative studies to guide any recommendation on the use of meshes in posterior repair when compared with native tissue

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



## The use of graft materials in vaginal pelvic floor surgery

M. Huebner*, Y. Hsu, D.E. Fenner

Combined procedures- cystocele and rectocele repair

| Author | n/n at follow-up | Used material | Mean follow-up (months) | Cure rate, anat. stage 0, 1, anterior vs. posterior | Adverse effects | Erosion anterior vs. posterior |
|---|---|---|---|---|---|---|
| Sand et al., 2001 [15] | 161/143 | Polyglactin 910 | 12 | 75% 91.2% | | 0% |
| Milani et al., 2004 [42] | 63 | Polypropylene | 17 | 100% 93.8 | DND 12.5%, IN 3.2%, DYS 63% (increase) | 13% 6.5% |
| Cosson et al., 2005 [44] | 687 | Prolift | 3.6 | 94.7 | DNSUI 5.4% | 6.7% ST |
| Dwyer et al., 2004 [45] | 97 | Polypropylene | 29 | 91.5% ant. 93.9% post. 88.2% comb. | DND 2.6%, DNU 2.6%, one rectovag. fistula, 2 postop. Hemorrhages >500 ml | 9.0% |
| Adhoute et al., 2004 [46] | 52 | Polypropylene | 27 | 95% 100% | | 3.8% |
| Borrell Palanca et al., 2004 [47] | 31 | Polypropylene | 23.5 | 100% | DNU 9.7%, UR 3.2% | 3.2% |
| Canepa et al., 2001 [48] | 16 | Polypropylene | 24.3 | 93.8% | DND 0%, DNU 12.5% | |

DND: de novo dyspareunia, IN: Infection, DYS: dyspareunia (general), DNSUI: de novo stress urinary incontinence, DNU: de novo urgency, UR: urinary retention, ST: surgically treated.

International Journal of Gynecology and Obstetrics (2006) 92, 279–288

## Perioperative experience of pelvic organ prolapse repair with the Prolift® and Elevate® vaginal mesh procedures

- Median operative times for anterior/apical repairs with fixation to the SSL with Prolift and Elevate were shorter than reports of abdominal (221–225 min) and robotic (226–328 min) sacrocolpopexy.
- No rectal injury but 3 ( 2.4%) bladder injuries with Prolift
- Pelvic hematoma: 4.8%
- Less hospital stay with Elevate (…less postoperative pain?)
- Voiding dysfunction requiring catheterization 7.1% with Prolift

## Vaginal prolapse repair using the Prolift™ kit:

European Journal of Obstetrics & Gynecology and Reproductive Biology 158 (2011) 104–109

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

| | |
|---|---|
| Total prolapse (ant+post) | 54 |
| Mesh in 2 patches | 46 |
| Monoblock (in one patch) | 8 |
| Concomitant surgical procedures | |
| SUI* | 53 |
| Hysterectomy | 2 |
| Other* | 7 |
| Anesthesia | |
| General anesthesia | 13 |
| Epidural anesthesia | 87 |
| Mean operating time (min) | 39.8 ± 14.8 |
| Anterior prolapse | 28.4 ± 8.4 |
| Posterior prolapse | 25.1 ± 7.3 |
| Total prolapse | 48.4 ± 11.9 |
| Mean hospital stay (days) | 2.6 |
| Per-operative complications | |
| Bleeding (>300 ml) | 3 |
| Bladder or rectum damage | 0 |
| Immediate post-operative complications | |
| Hematoma, ecchymosis | 3 |
| Urinary tract infection | 4 |
| Acute urine retention | 2 |
| Reoperation | 1 |

Recurrence with Prolift

| Total Prolift™ | 2 | 6 | 12 months |
|---|---|---|---|
| Anterior level | 1 | 1 | 2 |
| Middle level | 1 | 0 | 0 |
| Posterior level | 0 | 1 | 2 |
| Total recurrence | 2 | 2 | 4 |

4 out of 54 failure

## Transvaginal mesh repair for POP: Benefit/risk

Published literature suggest that mesh use for POP repair

- is effective, restores anatomy
- improve QoL measures
- relatively safe
- serious AEs are low

* Important option for treatment of complicated cases

## Mesh related adverse events

FDA : Manufacturer and User Device Experience (MAUDE) database

- 2005- 2010: Database was set, 3719 events were reported
- 2874 ( out of 3719) events within last 3 years.
- 1503 events out of 2874 cases were related to POP repairs
- 2007-2010: reported events were 5 times more than the events reported between 2005-2007.

## Several safety concerns & conclusions

1- Patients who undergo POP repair with mesh are subject to mesh-related complications

2- Mesh-associated complications are not rare
( 110 studies: 11,785 women, 10 % of women experienced mesh erosion within 12 months of surgery ).

3- Mesh contraction may cause vaginal shortening, tightening, and /or pain

Abed et al, Int Urogynecol J, 2011

## Several safety concerns & conclusions

4- New onset SUI has ben reported to occur more frequently following mesh augmentation in anterior repair than traditional repair without mesh

5- Transvaginal apical or posterior repair with mesh does not provide additional benefit in treatment

6- An anatomic benefit of anterior repair + mesh. However, improvement in QoL did not differ significantly when compared to traditional repair

Sand PK, Am J Obstet Gynecol 2001, Nieminen K, Am J Obstet Gynecol 2010, Altman D, N ew Eng J Med 2011

| RCT | N | Follow-up (months) | Anatomic Cure | | p |
|---|---|---|---|---|---|
| | | | Mesh | Traditional | |
| Sivaslioglu (2008) | 90 | 12 | 91% Ant | 72% | p<0.05 |
| Nguyen (2008) | 75 | 12 | 87% Ant | 55% | p<0.05 |
| Carey (2009) | 139 | 12 | 81% Ant/Post | 65.6% | p=0.07 |
| Nieminen (2010) | 202 | 36 | 87% Ant | 59% | p<0.0001 |
| Iglesia (2010) | 65 | 9.7 | 40.6 All | 29.6 | p=0.28 |
| Withagen (2011) | 194 | 12 | 90.4 All | 54.8 | p<0.001 |
| Altman (2011) | 389 | 12 | 82.3 Ant | 47.5 | p=0.008 |

U.S. Department of Health & Human Services

FDA U.S. Food and Drug Administration

Medical Devices

FDA Safety Communication: UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse

Date Issued: July 13, 2011

FDA Public Health Notification: Serious Complications Associated with Transvaginal Placement of Surgical Mesh in Repair of Pelvic Organ Prolapse and Stress Urinary Incontinence

**V. SUMMARY OF KEY FINDINGS**

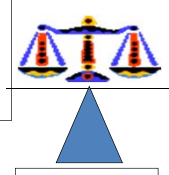
Based on evaluation of adverse event reports and assessment of the scientific literature, the FDA has NOT seen conclusive evidence that using transvaginally placed mesh in POP repair improves clinical outcomes any more than traditional POP repair that does not use mesh, and it may expose patients to greater risk.

## Limitations of existing literature

- Majority of studies focus on ideal pelvic support for effectiveness measure which is not necessary for most women to achieve symptomatic relief
- Results are mixed: both primary and repeat procedures
- Multiple compartment repairs simultaneously
- Adverse events are not reported in standardized method
- Poorly designed, underpowered, incomplete evaluation, documentation ( few RCT, validated instruments, surgical technique, etc..)
- very few studies extend past 2 years.

-is effective, restores anatomy
- improve QoL measures
- relatively safe
- serious AEs are low

* Important option for treatment of complicated cases



-Patients who undergo POP repair with mesh are subject to mesh-related complications

- Mesh exposure, erosion or mesh contraction may cause vaginal shortening, tightening, and /or pain

- No QoL difference

- No conclusive evidence to use mesh

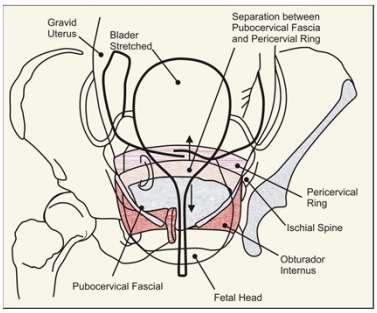
Biomaterial use in POP surgery

ICS 2013 Barcelona

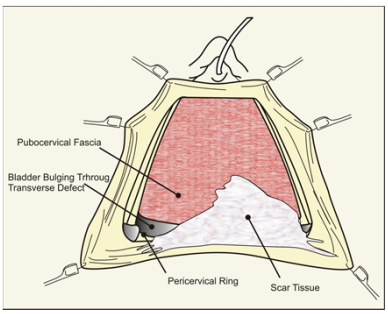
# Complications of biological Implants

Paulo Palma, M.D., Ph.D.
Professor of Urology
University of Campinas,
São Paulo, Brazil

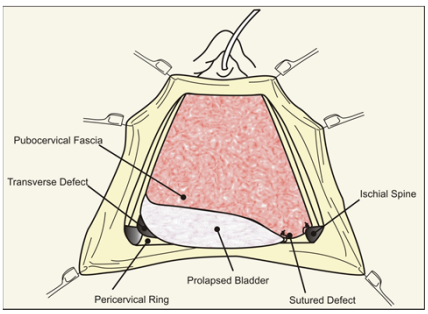
## Childbirth & Prolapses



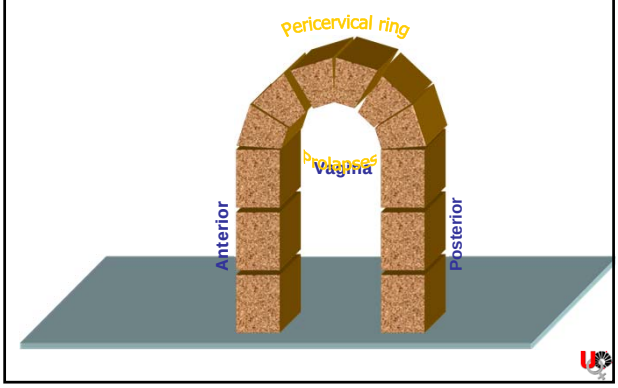

## Anatomical basis



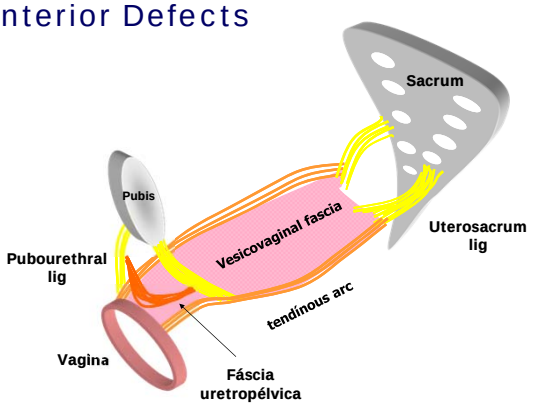

## Anatomical basis



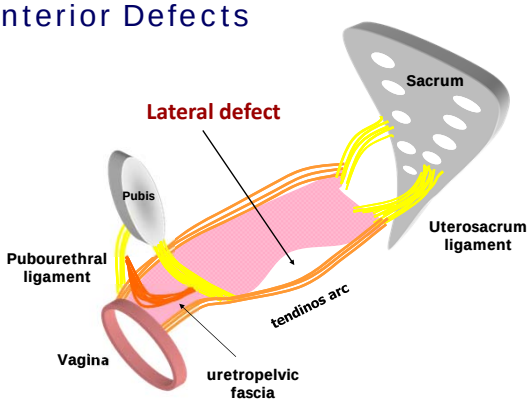

## Level I Defect



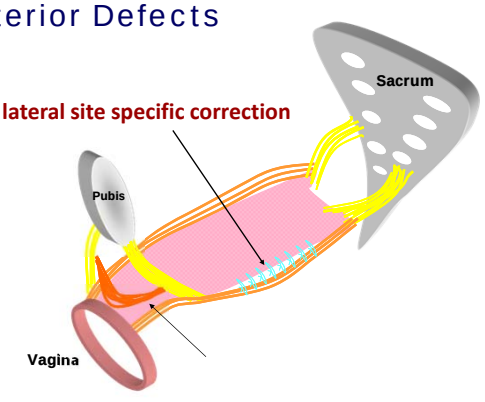

## Anterior Defects



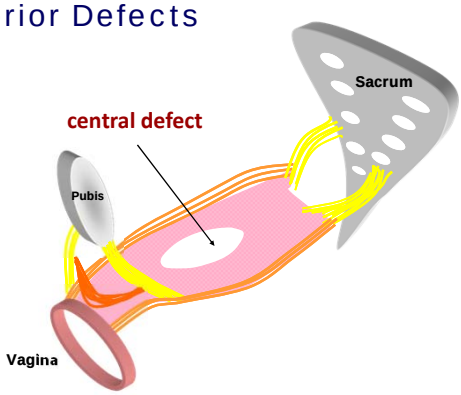
## Anterior Defects



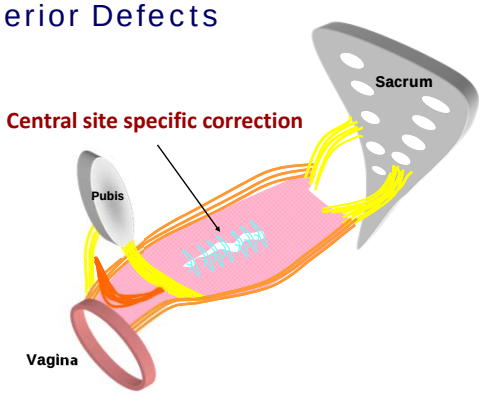

## Anterior Defects



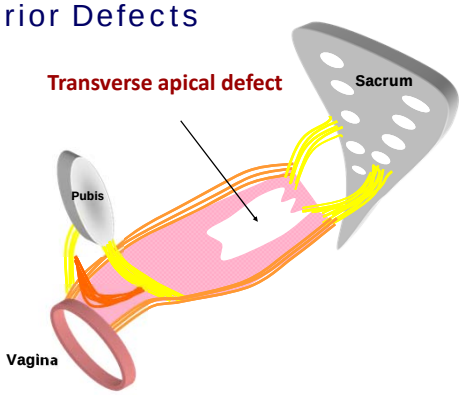

## Anterior Defects



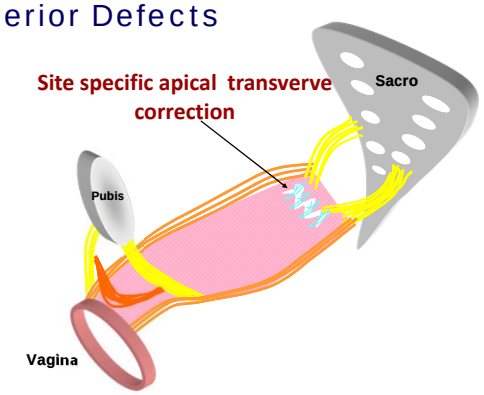

## Anterior Defects



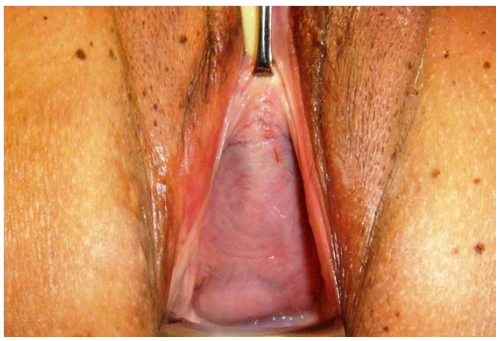

## Anterior Defects



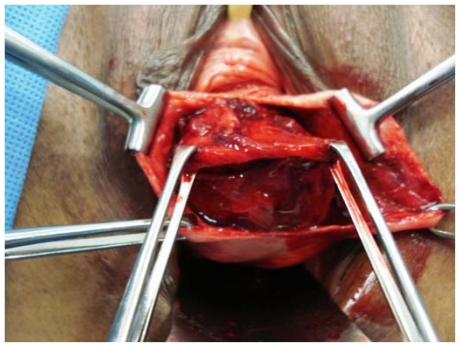

## Anterior Defects



## Transverse Anterior Defect



## Transverse Anterior Defect



## Mesh for POP repair

- High failure rates after conventional techniques
- Reinforce the native tissues (“neoligaments”)
- Achieve improved functional and anatomical outcomes
- Anterior vaginal mesh: reduces the prolapse recurrence
- Posterior and apical vaginal mesh: no level I evidence to support the use

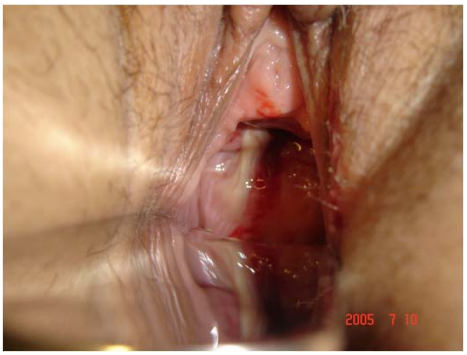
## Complications (2008-2011)

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

- Erosion
- Infection
- Pain
- Urinary problems
- Recurrence of prolapse and/or incontinence
- **Shrinkage of polypropylene meshes[1,2]**

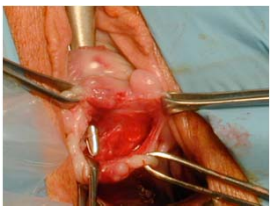
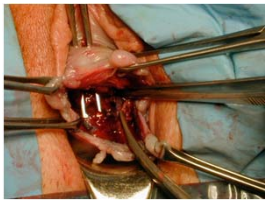
1. Garcia-Urena MA et al. Am J Surg 2007
2. Gauruder-Burmester A et al. Int Urogynecol J Pelvic Floor Dysfunct 2007

## SIS: abscess

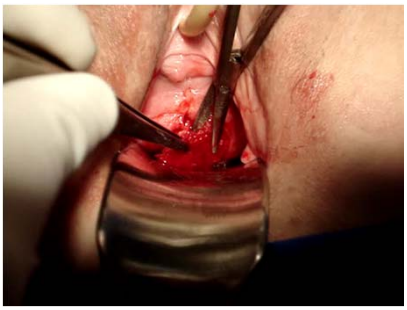



## SIS: Asseptic abscess

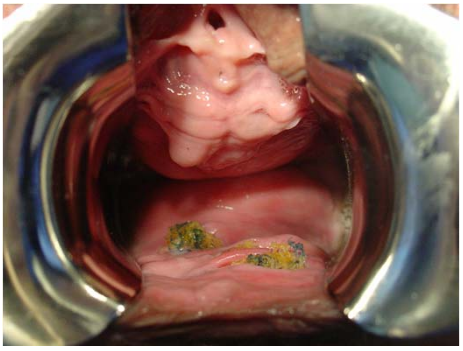
## Urethrovaginalvaginal fistula

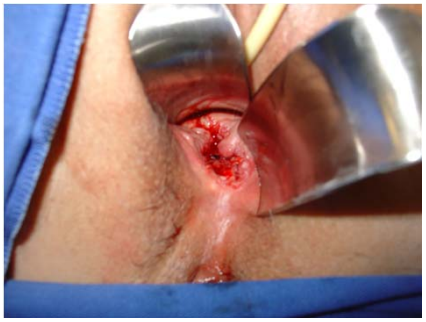
## Partial removal of mesh



## Posterior Gynemesh exposure

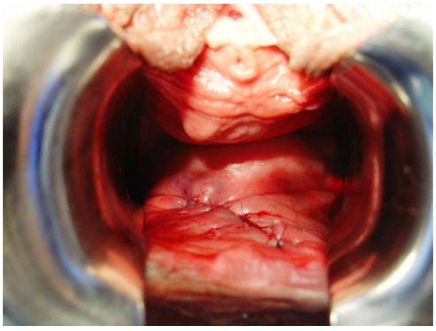


## Posterior Gynemesh exposure



## Posterior Gynemesh exposure

## Posterior Gynemesh exposure



## Mesh contraction

What are the clinical concerns?

## Mesh contraction

### Major Symptoms

- Severe vaginal pain (worsened by movements)
- Dyspareunia

### Minor Symptoms

- Vaginal discharge/spotting
- Awareness of prolapse
- Male partner discomfort

## Vaginal examination

- Prominent tense focal areas of mesh
  - arm / body
- Painfull prominent mesh areas
- Prominent tender band
- Vaginal tightness
- Foreshortened vagina
- Mesh erosion

## Vaginal examination

Palpation of each side and arms of the mesh

↓

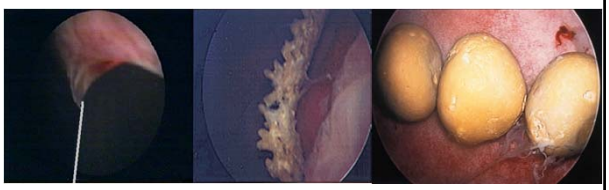
Ask if she experienced pain like during sexual intercouse or movements

↓

Localize trigger points

## Perfurations

- 3,5%



## Obstruction (BOO)

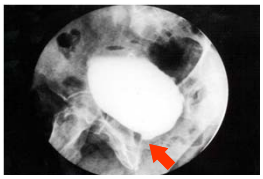
- BOO under diagnosed
- Incidence 2.7 – 23%
- Anatomical or functional
- Detrusor overactivity

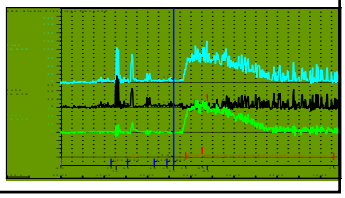
## Etiology

- Anti-incontinence procedures 20%
- Genital prolapes 16%
- Primary obstruction of the bladder neck 6%

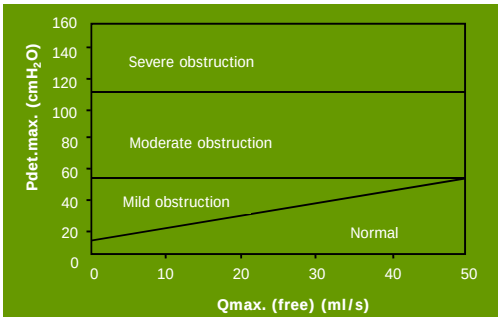
## Diagnosis

➢Residuals
➢Urodinamics + VUCG
➢Videourodynamic





## Nomograma



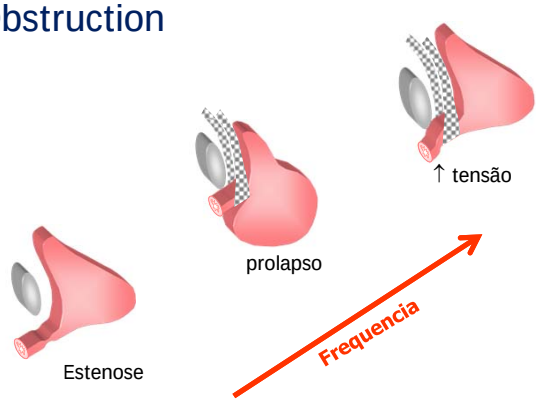

Blaivas & Groutz, 2001

## BOO

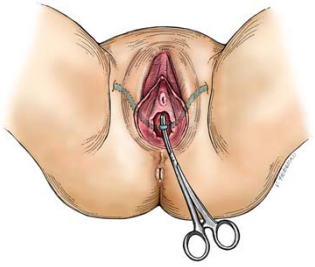
1.Functional

2.Anatomic

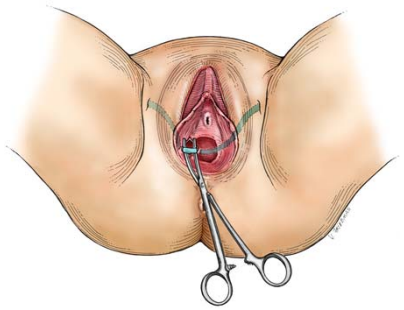
## Obstruction



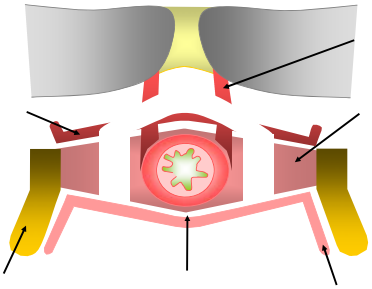

## Tape incision



## Partial removal



## Urethrolisys



## Urethrolisys :

### Results

**436 slings: 20 BOO (1995 - 2003)**

**Autologous: 18 / 210 (8,5 %)**

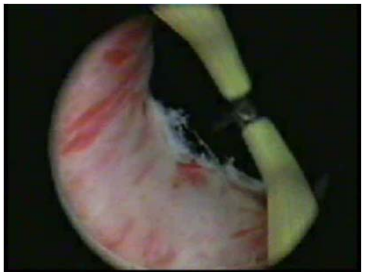
**Synthetic: 2 / 226 (0,6 %)**

**Diagnosis: from 3 m to 8 yrs. (mean: 9 m)**

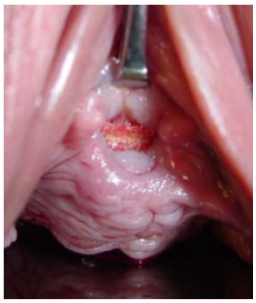
**$Q_{max}$: 9,9 ml/s $P_{detQmax}$: 48 $cmH_2O$ (mean)**

Palma et al; Eur. Urol, 2004

## TUIBN



## Healing abnormalities



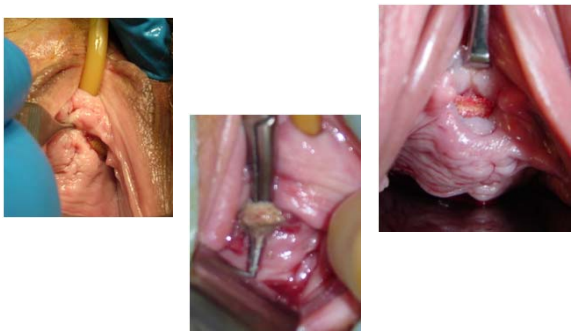
- Geralmente exposições sem granulação
- Ocorre em 6-14% casos
- Maioria assimtomatica
- Tratada conservadoramente consultório ou CC
- Influencia resultado?

## Classification of healong abnormalities

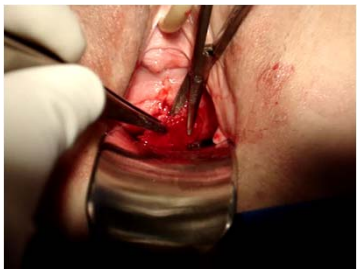
| | Simple | Comple |
|---|---|---|
| Tempo pós-op | < 12 weeks | > 12 weeks |
| Granulatio inflammation | Absent | Present |
| Localization | incision | Other |
| organ | Vagina | viscus |

IUGA grafts symposium, 2005

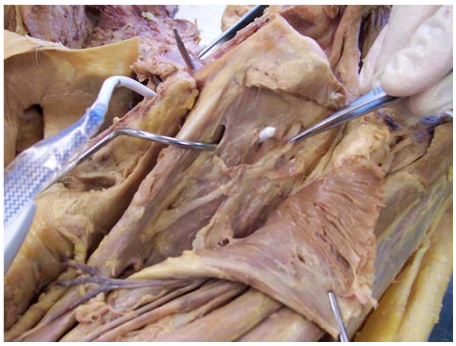
## Sling : healing abnormalities



## Partial removal



## Inside- out?



## Complications- TOT

| | Ob Tape | Monarc | TVT-O |
|---|---|---|---|
| Erosão | 99 | 4 | 2 |
| Infecção | 22 | 1 | 1 |
| Neuropatia | 0 | 1 | 3 |
| Dor | 0 | 1 | 8 |
| Sangramento | 1 | 1 | 3 |
| L. Bexiga | 2 | 0 | 1 |
| L. Uretra | 0 | 0 | 3 |

Maude DB review. Hamilton Boyles, et. al. ICS 2005.

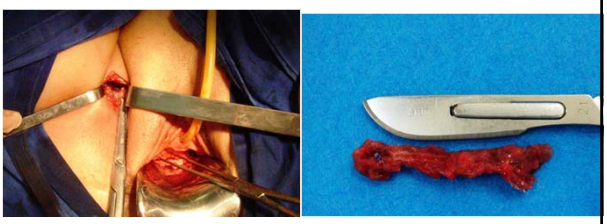
## Leg pain

- 40% TVT-0

**Teo R, Moran P, Mayne C, Tincello D: Randomized trial of TVTand TVT-O for the treatment of urodynamic stress urinary incontinence in women.**

**2008 neurourology and urodymanics 27:572-3**

## Persistent pain

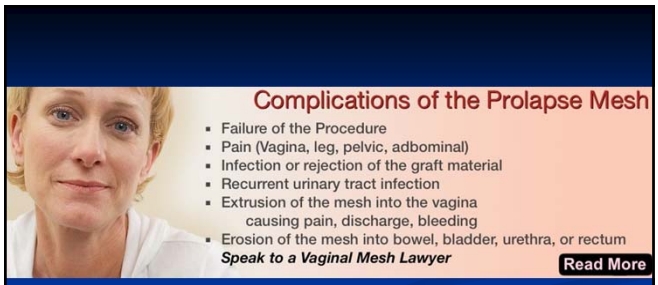


## Conclusions

- **Mesh exposure 6-14% (experience)**
- **Conservative management first**
- **Partial removal**
- **Impact on the outcome?**
- **Severe complications -**
- **New techniques & better meshes**

# Addressing Concerns over MESH used for repair of Pelvic Organ Prolapse

Amit Chakrabarty, MD, FRCS.
Urologic Clinics of North Alabama
www.ucna.com



FDA & Center for Diseases and Radiologic Health
**Urogynecologic Surgical Mesh:**
**Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse**

- In October 2008 the FDA released a Public Health Notification
  - to inform clinicians and patients of the adverse events related to the urogynecological use of surgical mesh
  - and advise how to mitigate these risks and counsel patients
- FDA continued to monitor the outcomes of such mesh repairs
- MAUDE reports for 3 years (Jan 1,2008 to Dec 31, 2010)
  - 2874 MDRs (including reports of injury, death and malfunction)
    - 1503 POP repairs
    - 1371 SUI repairs

- The FDA also conducted a systematic review of the scientific literature to learn more about the safety and effectiveness of POP and SUI using surgical mesh.
- July 13, 2011, FDA released an update on safety and effectiveness of transvaginal placement of surgical mesh for pelvic organ prolapse(POP) on their website as a Public Health Notification
- http://www.fda.gov/MedicalDevices/safety/AlertsandNotices/ucm262435.htm
- Did not include mesh used in treatment of Stress urinary incontinence or that used for abdominal or laparoscopic repair of pelvic organ prolapse

The FDA determined that

- serious adverse events are NOT rare, contrary to what was stated in the 2008 PHN, and
- transvaginally placed mesh in POP repair does NOT conclusively improve clinical outcomes over traditional non-mesh repair

- The FDA convened an advisory panel meeting of outside experts in September 2011 to discuss these findings and the types of clinical studies necessary to better assess the risks and benefits of using mesh to treat POP and SUI
- Advised on post marketing studies (522) on single incision mesh and slings.

**2008 FDA Recommendations**

As stated in the Oct. 20, 2008 Public Health Notification, the FDA continues to recommend that health care providers should:

- Obtain specialized training for each mesh placement technique, and be aware of the risks of surgical mesh.
- Be vigilant for potential adverse events from the mesh, especially erosion and infection.
- Watch for complications associated with the tools used in transvaginal placement, especially bowel, bladder and blood vessel perforations.
- Inform patients that implantation of surgical mesh is permanent, and that some complications associated with the implanted mesh may require additional surgery that may or may not correct the complication.
- Inform patients about the potential for serious complications and their effect on quality of life, including pain during sexual intercourse, scarring, and narrowing of the vaginal wall in POP repair using surgical mesh.
- Provide patients with a copy of the patient labeling from the surgical mesh manufacturer if available.

**2011 additional FDA Recommendations**

In addition, the FDA also recommends that health care providers:

- Recognize that in most cases, POP can be treated successfully without mesh thus avoiding the risk of mesh-related complications.
- Choose mesh surgery only after weighing the risks and benefits of surgery with mesh versus all surgical and non-surgical alternatives.
- Consider these factors before placing surgical mesh:
  - Surgical mesh is a permanent implant that may make future surgical repair more challenging.
  - A mesh procedure may put the patient at risk for requiring additional surgery or for the development of new complications.
  - Removal of mesh due to mesh complications may involve multiple surgeries and significantly impair the patient's quality of life. Complete removal of mesh may not be possible and may not result in complete resolution of complications, including pain.
  - Mesh placed abdominally for POP repair may result in lower rates of mesh complications compared to transvaginal POP surgery with mesh.
- Inform the patient about the benefits and risks of non-surgical options, non-mesh surgery, surgical mesh placed abdominally and the likely success of these alternatives compared to transvaginal surgery with mesh.
- Notify the patient if mesh will be used in her POP surgery and provide the patient with information about the specific product used.
- Ensure that the patient understands the postoperative risks and complications of mesh surgery as well as limited long-term outcomes data.

## FDA UPDATE 01/04/2012

- The FDA continues to assess the safety and effectiveness of urogynecologic surgical mesh devices, through:
- Review and analysis of published literature, Medical Device Reports (adverse event reports) submitted to the agency, and post-approval study reports.
- Epidemiological research on safety and effectiveness of surgical mesh, as a part of our effort to better understand possible adverse events associated with surgical mesh for SUI and POP.
- Collaborations with professional societies and other stakeholders to fully understand the postmarket performance of urogynecologic surgical mesh devices, as well as the occurrence of and signs and symptoms associated with specific adverse events.
- Collecting and reviewing all available information about currently marketed urogynecologic surgical mesh devices.
- Mandating postmarket surveillance studies ("522 studies") by manufacturers of urogynecologic surgical mesh devices.

## On January 03, 2012, the FDA issued

- 88 postmarket study orders to 33 manufacturers of urogynecologic surgical mesh for POP; and
- 11 postmarket study orders to seven manufacturers of single-incision mini-slings for SUI.
- The manufacturers will be required to submit study plans to the FDA that address specific safety and effectiveness concerns related to surgical mesh devices for POP and single-incision mini-sling devices for SUI. Data from the studies will enable the agency to better understand the safety and effectiveness profiles of these devices.

## Why mesh?

- PROS: Improves anatomical results from surgery
- CONS: associated with risks like erosion, sexual dysfunction, urinary tract injury, pain etc
- All except erosion are not unique to mesh surgeries
- Certain meshes used in the past and possibly responsible for several of the complications included in the FDA warning have been removed from the US marketplace

## Reoperation rates

- Rates of reoperation for failure of primary repair have been reported to be as high as 29%[1]
- The contributions to risk of reoperation are multifactorial
- However, recent studies recognize the contribution of genetic and hereditary factors to the risk of reoperation[2]
- Partially contributing to the high recurrence rate is the use of native tissue in primary repair. This has led to an increase in the use of biomaterials[3]

1. Olsen, A.L., Smith, V.J., Berstrom, J.O., Colling, J.C., Clark, A.L. *Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence.* Obstet Gynecol 1997, 89(4): 501-6.
2. Dallenbach, P., Nancoz, C.J., Eperon, I., Dubuisson, J.B., Boulvain, M. *Incidence and risk factors for reoperation of surgically treated pelvic organ prolapse.* Int Urogynecol J 2011, Advance publication.
3. Aboushwareb .T., Mekenzi, P., Wezel, F., Southgate, J., Badlani, G. *Is tissue engineering and biomaterials the future for lower urinary tract dysfunction (LUTD)/pelvic organ prolapse (POP)?* Neurourol and Urodyn 2011, 30: 775-82.

## Studies

- Nieminen et al.
- Randomized controlled trial with Low-weight polypropylene
- Patients:105, Follow up 24 months
- Recurrence 89 vs. 59% (Anterior repair)
- 8% Erosion, dyspareunia lower in mesh group

Nieminen, K., Hiltunen, R., Heiskanen, E., Takala, T., Niemi, K., and Heinonen, P. (2008) Symptom resolution and sexual function after anterior vaginal wall repair with and without polypropylene mesh. Int. Urogynecol. J. Pelvic Floor Dysfunct. 19, 1611–1616

## Studies

- Lukban et al, March 2012
- Elevate anterior and apical
- 1 year prospective outcomes
- 92.5 and 89.2 % posterior wall and apical cure rates
- Extrusion rate of 6.5%

Lukban JC, Rovers WR, VanDrie DM, Erickson T, Zylstra S, Patel M, Moore RD Int Urogynecol J March 2012

Society of Urodynamics
and Female Urology
(SUFU)
stand on the
FDA recommendations

## FDA recommendations that SUFU strongly agrees

- Surgeons require rigorous training in pelvic floor anatomy and pelvic floor surgery as well as proper patient selection for pelvic floor prolapse reconstructive procedures
- Prior to utilization of mesh in pelvic floor repair, surgeons should be properly trained in specific mesh implantation techniques
- Prior to utilization of mesh the surgeon should be competent in recognizing intraoperative and post operative complications as well as comfortably and competently managing these adverse events eg those involving urinary and gastointestinal tracts
- Prior to implantation of surgical mesh for the treatment of pelvic organ prolapse, the surgeon and patient MUST have a proper informed consent discussion regarding the risks, benefits, alternatives and indications for the use of mesh

## FDA recommendations that SUFU acknowledges

- Recognize that many cases of POP can be treated successfully without mesh
- Choose mesh surgery only after weighing the risks and benefits of surgery with mesh vs all other alternatives
- Consider that surgical mesh is a permanent implant which can make future POP repairs more challenging, can cause bothersome complications which require additional surgery and can be difficult or impossible to remove
- Inform patients about treatment alternatives that do not require mesh placement
- Notify patients when mesh will be used and provide patients wit information about mesh
- Ensure that the patient understands about the risks of mesh surgery and the limited long-term outcomes data

American College of Obstetricians and Gynecologists (ACOG)
&
the American Urogynecologic Society (AUGS)
stand on the
FDA recommendations

**American College of Obstetricians and Gynecologists and the American Urogynecologic Society Recommendations**

- Outcome reporting for prolapse surgical techniques must clearly define success, both objectively (anatomic results) and subjectively (patient satisfaction or symptomatic return of bulge causing bother or requiring reoperation). Complications and total reoperation rates (for recurrence or complications) should be reported as outcomes.
- Pelvic organ prolapse vaginal mesh repair should be reserved for high-risk individuals in whom the benefit of mesh placement may justify the risk, such as individuals with recurrent prolapse (particularly of the anterior compartment) or with medical comorbidities that preclude more invasive and lengthier open and endoscopic procedures.
- Surgeons placing vaginal mesh should undergo training specific to each device and have experience with reconstructive surgical procedures and a thorough understanding of pelvic anatomy.
- Compared with existing mesh products and devices, new products should not be assumed to have equal or improved safety and efficacy unless clinical long-term data are available.
- The American College of Obstetricians and Gynecologists and the American Urogynecologic Society 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.
- Rigorous comparative effectiveness randomized trials of synthetic mesh and native tissue repair and long-term follow-up are ideal.
- Patients should provide their informed consent after reviewing the risks and benefits of the procedure, as well as discussing alternative repairs.

**<u>Time to Rethink</u>:**
**An Evidence-Based Response from Pelvic Surgeons to the "FDA Safety Communication: UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse"**

In summary we believe:

1. The FDA should more accurately reflect the reality that in the surgical management of advanced prolapse, all treatment options involve risks. The UPDATE portrays transvaginal mesh repairs as uniquely hazardous, providing no broader context regarding the significant risks and/or higher recurrence rates associated with its alternatives.

There is ample published evidence (arguably more robust for TVM than its alternatives) upon which physicians and patients can have a detailed informed consent process leading to an individualized decision.

2. Training guidelines and credentialing criteria lie at the core of these reported complications and need to be better defined as a collaborative effort between societies, hospital systems, and the medical device industry.

3. Transvaginal mesh, when used judiciously in experienced hands, is an essential tool for a large number of expert, high-volume surgeons, only a fraction of which have co-signed this document. All of the co-signed surgeons are committed, above all else, to advancing the safest and most effective surgical procedures.

We are deeply concerned that the current process could, as an unintended consequence result in a major setback to those core goals for many providers successfully utilizing mesh and observing high rates of satisfaction and superior outcomes. This large segment of highly dedicated surgeons, using mesh in a thoughtful and selective manner in properly counseled patients, could suffer unjustified and arbitrary medical-legal exposure if the current process fails to incorporate a full and accurate perspective on these complex issues and challenging surgical conditions that we treat on a daily basis.

American Urological Society
(AUA)
stand on the
FDA recommendations

AUA strongly agrees with the FDA that a thorough informed consent should be conducted prior o the use of mesh products for pelvic organ prolapse. The AUA agrees with the FDA statement that surgeons who wish to utilize mesh techniques for pelvic organ prolapse should:

- undergo rigorous training in the principles of pelvic anatomy and pelvic surgery
- be properly trained in specific mesh implantation techniques
- be able to recognize and manage complications associated with vaginal mesh

## MRG Study December 2011

- 181 respondents, of which 130 were current users of synthetic surgical mesh in urogynecologic treatments and 51 were synthetic surgical mesh nonusers
- Users: 72 Gynecologists, 40 Urologists, 18 Urogynecologists
- Non Users: 44 Gynecologists, 7 Urologists
- Survey results:
  - procedure volumes remained flat in 2011, due in large part to shaken confidence and increased patient concern.
  - 2012, the number of transvaginal pelvic floor repair (PFR) procedures and sacral colpopexy/hysteropexy procedures using either a synthetic mesh or a biologic graft will increase by 2 percent.
- Some companies and mesh brands have been substantially more successful than others at building physician loyalty despite the recent adverse events and proposed regulatory changes.
- While little differentiation seems to exist between brands of biologic meshes, physicians do demonstrate strong brand preferences among synthetic meshes,
- Base their choice on specific factors that include mesh material or weight, patient profiles and training programs offered by synthetic mesh providers.

## AUGS voices opposition to restrictions on mesh

**Publish date: APR 01, 2013**

- "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,"
- "A ban on mesh would have a chilling effect on research in this area and would severely limit the advancement of science and future innovations that could significantly help women. We recommend preserving all surgical options, including transvaginal mesh for pelvic organ prolapse, adopting recently published credentialing guidelines, standardizing the informed consent process, and establishing a robust mechanism to track both surgeons and products being implanted to fully assess safety and efficacy,"

AUGS President Anthony G. Visco, MD

## AUGS latest recommendations

- A complete restriction on the use of surgical mesh was not the stated intent of the January 2011 FDA safety communication regarding mesh.
- 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 National Institutes of Health, American College of Obstetricians and Gynecologists, 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, AUGS recommends the implementation of credentialing guidelines so that mesh procedures are performed by qualified surgeons.

## Abstract at International Continence Society (ICS) Glasgow, UK, 2011

**CAN CARDIAC STENT & INTRAOCULAR LENS TECHNOLOGY BE APPLIED TO PELVIC FLOOR REPAIR WITH MESH?**

**AUTHOR LIST:** Amit Chakrabarty, MD (Urologic Clinics of North Alabama, Huntsville, AL); Kumaresan Ganabathi, MD (Clarion Health Complex, Clarion, PA); J. Steven Alexander, MD (Gynecology Center, Fort Wayne, IN); Philip Hoekstra, MD (MMPC, Grand Rapids, MI)

## CONCLUSIONS

This is the first multi-institutional study looking at the efficacy and safety of surgical mesh treated with PC that was used to repair pelvic prolapse. Our data suggests that this device is a safe and effective treatment for anterior prolapse. Though no statistical inferences can be made with such limited numbers in the study group, short term data suggests that PC treated mesh use in repair of anterior prolapse is very effective and demonstrates a marked reduction in adverse events, particularly dyspareunia and mesh exposure This is in line with similar successes of other PC coated medical devices implanted in the body. Longer term studies with more subjects are needed to prove the improved performance of the Perigee PC system.

# DOES PELVIC MESH TREATED WITH PHOSPHORYLCHOLINE IMPROVE OUTCOMES? AN EARLY EXPERIENCE?

**Amit Chakrabarty MD etal,**

**European Journal of Obstetrics and Gynecology, December 2012**

**Objectives:** Implantable devices treated with Phosphorylcholine (PC) have been successfully used in cardiac, ophthalmic, and other applications. This surface modification has resulted in a reduction in the host inflammatory responses. This pilot study tested the safety and efficacy of PC treated polypropylene mesh grafts implanted for the treatment of pelvic organ prolapse.

**Study Design:** Surgeons from 5 U.S. sites collected data on subjects implanted with Perigee IntePro Lite + PC. Pre-procedure data collected included demographics and prolapse severity. At follow-up, subjects were assessed for anatomical outcomes (success ≤ Stage I POPQ or Baden Walker), symptomatic improvement, and complications, particularly mesh exposure.

**Results:** A total of 40 subjects were enrolled with 80% (32/40) of them completing at least 5-7 months of follow-up. Mean patient age was 60 years (range 36 - 78 years) and the mean BMI was 28 (range 20 to 40). There were no cases of mesh exposure/extrusion or granuloma formation. The anatomical success rate was 100% at 5-7 months (32/32).

**Conclusions:** This is the first publication on pelvic mesh treated with PC. There were no adverse events attributed to this surface modification. However, as the numbers are small, the results are not statistically significant. PC surface modification of pelvic mesh shows promise in its application for the reduction of mesh related complications.

## INFORMED CONSENT

**UROLOGIC CLINICS OF NORTH ALABAMA**
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**Information for patients who are scheduled to undergo pelvic floor repair surgery with vaginal mesh**

The FDA Safety Communication in July of 2011 has issued an UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse. Though various natsonal organizations consisting of surgeons who do these procedures do not agree with all their opinions, I would like to educate you with their recommendations. Dr. Chakrabarty and his staff want you to carefully read the followwg, clarify any concerns that you have and weigh the benefits against the associated risks before you consider undergoing the surgery that involves placement of a vaginal mesh.

**Recommendations for Patients before Surgery:**

- Be aware of the risks associated with surgical mesh for transvaginal repair of Pelvic Organ Prolapse.
- Know that having a mesh surgery may put you at risk for needing additional surgery due to mesh-related complications. In a small number of patients, repeat surgery may not resolve complications.
- Ask your surgeon about all POP treatment options, including surgical repair with or without mesh and non-surgical options, and understand why your surgeon may be recommending treatment of POP with mesh.

**In addition, ask Dr. Chakrabarty these questions before you agree to have surgery in which surgical mesh will be used:**

- Are you planning to use mesh in my surgery?
- Why do you think I am a good candidate for surgical mesh?
- Why is surgical mesh being chosen for my repair?
- What are the alternatives to transvaginal surgical mesh repair for POP, including non-surgical options?
- What are the pros and cons of using surgical mesh in my particular case? How likely is it that my repair could be successfully performed without using surgical mesh?
- Will my partner be able to feel the surgical mesh during sexual intercourse? What if the surgical mesh erodes through my vaginal wall?
- If surgical mesh is to be used, how often have you implanted this particular product? What results have your other patients had with this product?

- What can I expect to feel after surgery and for how long?
- Which specific side effects should I report to you after the surgery?
- What if the mesh surgery doesn't correct my problem?
- If I develop a complication, will you treat it or will I be referred to a specialist experienced with surgical mesh complications?
- If I have a complication related to the surgical mesh, how likely is it that the surgical mesh could be removed and what could be the consequences?
- If a surgical mesh is to be used, is there patient information that comes with the product, and can I have a copy?

**Recommendations for Patients after surgery:**

- Continue with your annual and other routine check-ups and follow-up care. There is no need to take additional action if you are satisfied with your surgery
- and are not having complications or symptoms.
- Notify your health care provider if you have complications or symptoms, including persistent vaginal bleeding or discharge, pelvic or groin pain or pain
- with sex, that last after your follow-up appointment.
- Let your health care provider know you have surgical mesh, especially if you plan to have another surgery or other medical procedures.
- Talk to your health care provider about any questions you may have.
- If you had POP surgery, but do not know whether your surgeon used mesh, ask your health care provider at your next scheduled visit.
- To read the whole FDA report please ask for a copy or visit online http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm262435.htm
- If you would like a copy of the patent labeling from the manufacturer of the product used in your repair, please inform us and we will obtain a copy for you.
- I have read and understood the two pages of this document, and had an opportunity to ask the doctor all questions concerning the rationale of the procedure, its risks, benefits, alternatives and risks of those alternatives and give my consent for repair of my vaginal prolapse with synthetic or porcine mesh. I have been offered a copy of this consent.

_____ _____
(Signature of the patient/guardian) (Date)

_____ _____
(Witness)

**Notes**