NAVIGATING FEMALE STRESS URINARY INCONTINENCE IN THE ERA OF MESH

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DISCLOSURES

- Advisory Board and/or Speaker and Investigator
  - Allergan
  - Contura
  - Medtronic
- AUA Guidelines
  - Stress incontinence, Chair, 2015-2017
  - Microhematuria, Member 2018-present

OVERVIEW

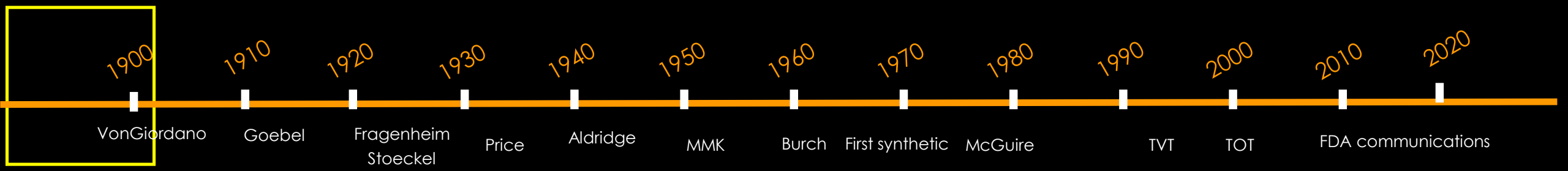
- Perspective and impact
- Brief history of slings and mesh
- Current status (in US and abroad)
  - FDA communications
  - Patients, surgeons, industry, attorneys
- What next?

PREVALENCE

- Up to 40% of women have SUI
- Lifetime risk of surgery for POP or SUI
  - 11% on 1995
  - 20% in 2011
- Procedures
  - Increased 27% in US between 2000-2009
    - 2004 28,000
    - 2013 14,490
  - In UK:
    - 2000-01 8458
    - 2008-09 13219
    - 2012 11845

A LITTLE HISTORY

Author	Technique
Von Giordano, 1907	Gracilis muscle
Goebel, 1910	Pyramidalis
Fragenheim, 1917	Rectus fascia flap
Stoeckel, 1917	Plication of muscle around bladder neck
Price, 1933	Fascia lata fixed to rectus muscle

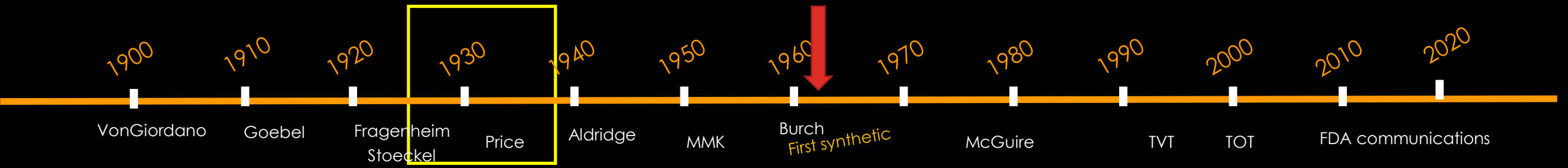


COMMON BELIEF

Muscle around bladder neck would acquire sphincter-like function

A LITTLE MORE HISTORY

Author	Technique
Aldridge, 1942	2 strips fascia beneath urethra
Narik, Palmrich, 1962	External oblique aponeurosis attached to pubic tubercle
Williams, 1962	*First synthetic sling (mersiline)*



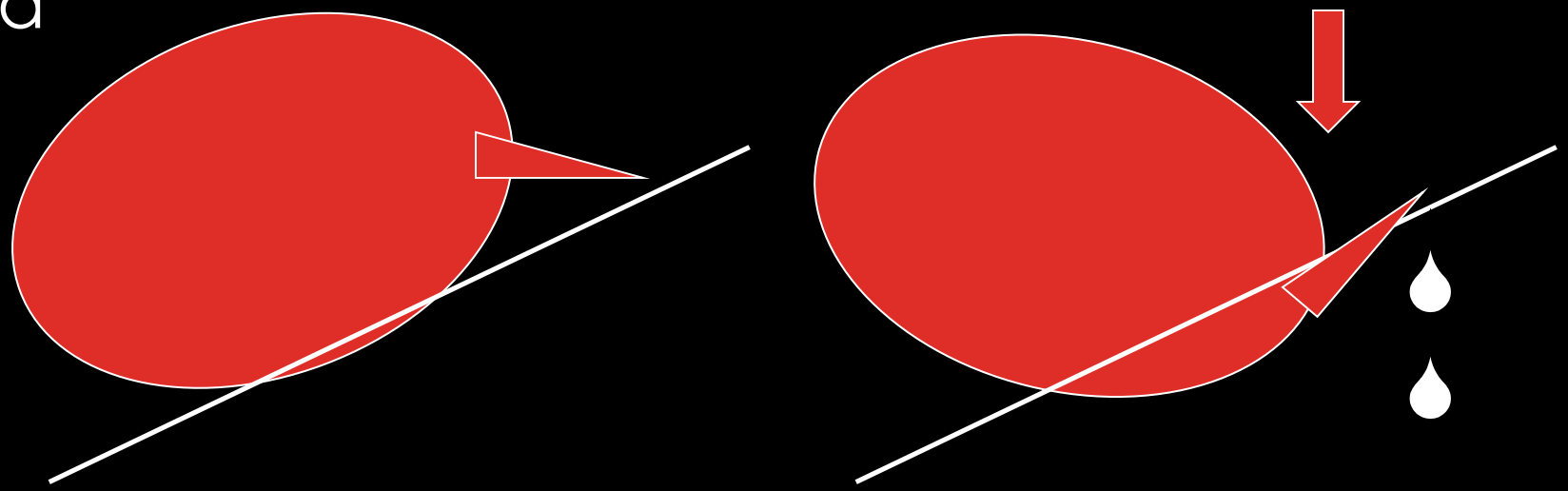
SLINGS FELL OUT OF FAVOR

- Efficacy reasonable for the time
- Complications high
  - Fistulas
  - Obstruction
  - Urethral sloughing
  - Abscesses
- Gave way to bladder neck suspensions

SEVERAL THEORIES

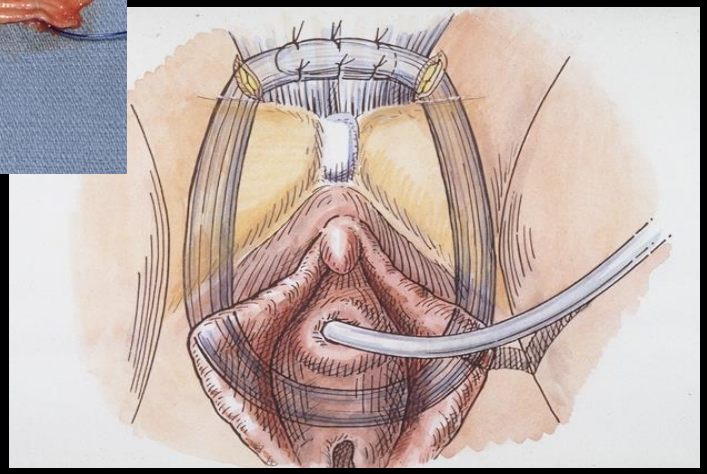
- Pressure distribution and differential
- Compressibility of urethra

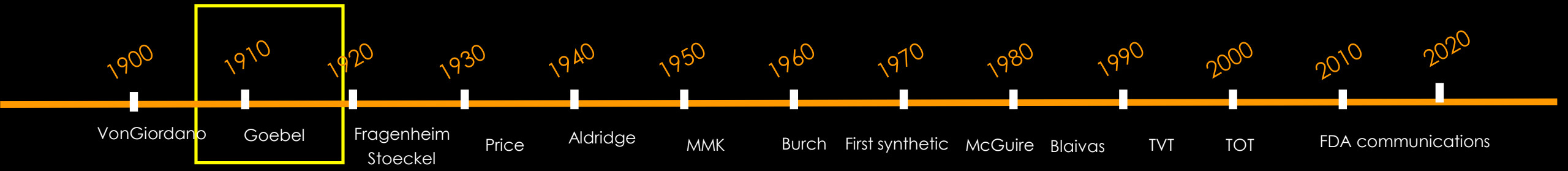
- Early success reported
- But, eventually….



REVIVAL OF THE SLING

- McGuire autologous sling
- Blaivas modification





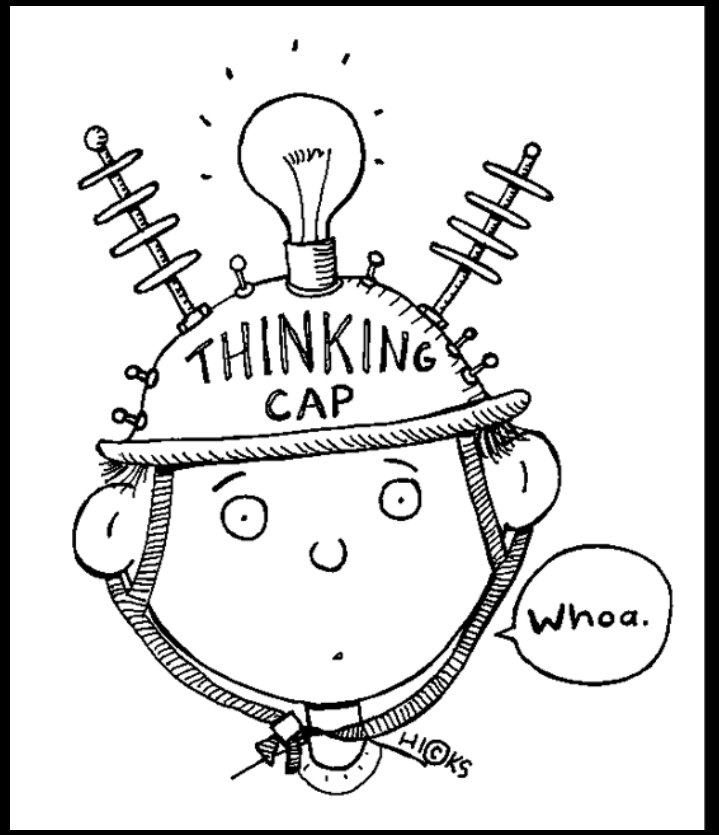
"EARLY" LONG-TERM RESULTS

Author	n	Result	Follow up
Siegel	20	80% no SUI	15.4 years
Morgan	247	85% of 88 "cured"	4.25 years
Chaikin	20	95% of 20 "cured"	10 years
Rodrigues	126	74.4% "cured"	5.86 years

Siegel SB, et al. J Urol 1997;460,abstract 1798.
Morgan JE, et al.: Am J Obstet Gynecol 1985;151.
Chaikin DC, et al.: J Urol 1998;160.
Rodrigues P, et al.: Neurourol Urodyn 2004;627.

BUT TECHNICALLY CHALLENGING

- Generally limited to a few specialists of the time
- Could it be easier?
- Back to the continence mechanism…



ANOTHER THING…

- Many continent women have proximal urethral mobility

and

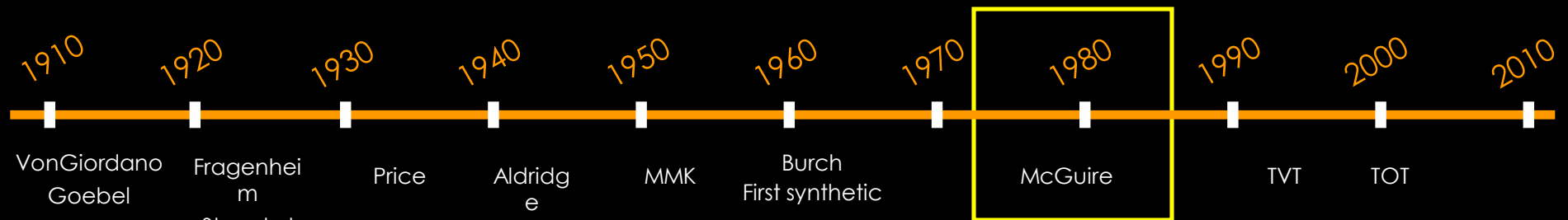
- Many successful anti-incontinence procedures do nothing to proximal urethral mobility

THE INTEGRAL THEORY

Continence dependent upon:

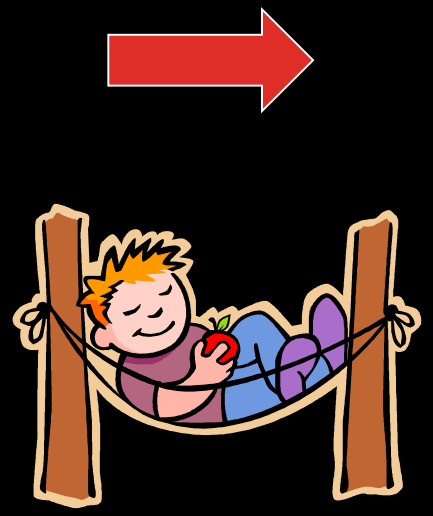
- Fixation of *midurethra* to pubic bone
- Physiologic backboard
- Support of stretch receptors at proximal urethra

Petros, Ulmsten: Acta Obstet Gynecol Scand Suppl 1990;153:7-31.



THE HAMMOCK THEORY

- Anterior vaginal wall
- Levator ani
- Pubourethral ligaments



- Suburethral support

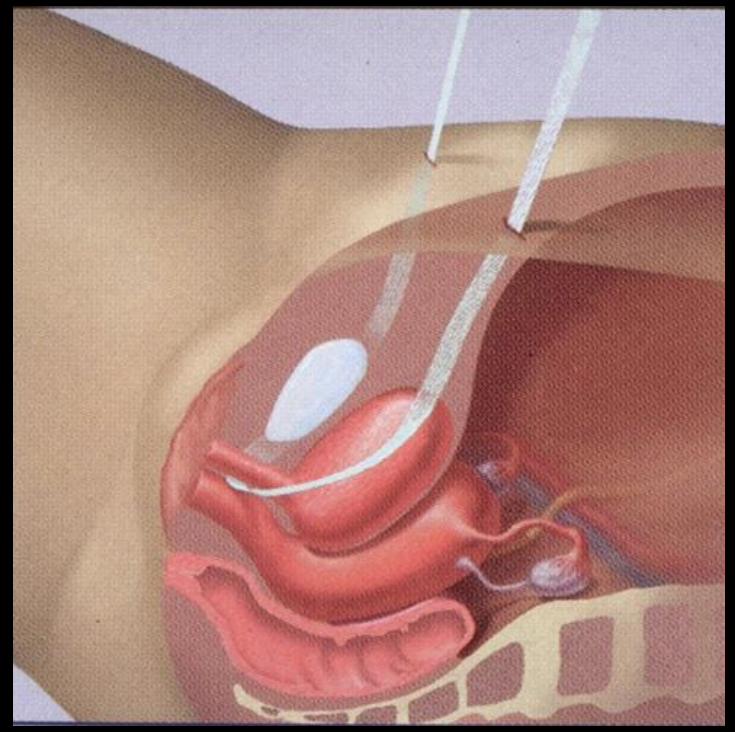
and

- Musculofascial compression

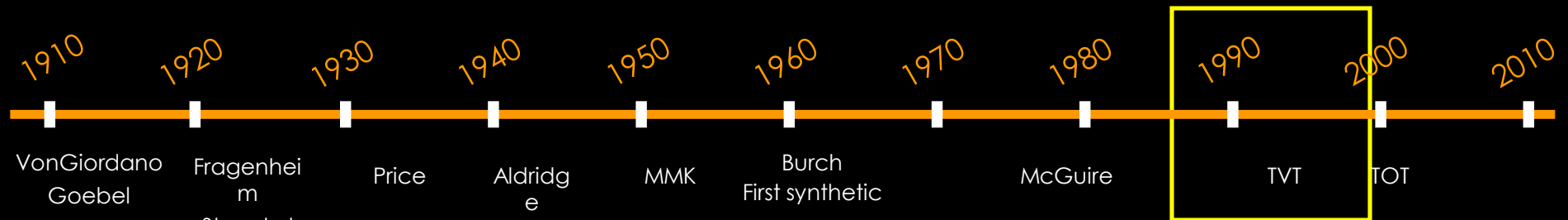
Delancey, 1994

MIDURETHRAL SLING: A POPULAR CHOICE

- Type I polypropylene mesh
- Loosely at midurethra



- Simple
- Efficacious
- Safe



MECHANISM OF ACTION

- Ultrasound
- Rotation of proximal urethra
- Midurethral kinking
- Compression of urethra between sling and symphysis

Sarlos d, et al: Int Urogynecol J 2003;14:395-8.

EARLY TVT™ REPORTS

Authors	n	F/U (mos)	Cured % (n)	Improved % (n)	Retention % (n)
Ulmsten et al., 1998	131	≥12	91 (119)	7 (9)	3 (4)
Wang & Lo, 1998	70	3-18	87 (61)	4 (3)	17 (12)
Olsson & Kroon, 1999	51	36	90 (46)	6 (3)	Few
Wang, 2000	39	19	90 (35)*	-	-
Nilsson, et al, 2001	90	48-70	84.7 (72)	10.6 (9)	0
Haab, 2001	46	12-24	86.9 (40)	10.9 (5)	0
Jeffry et al., 2001	88	25	91 (80)	9 (8)	4 (4)

*Cured/improved reported together

WARD AND HILTON

- Randomized prospective trial
- n=344 with 2 year follow up

Technique	n	Objective cure	Objective cure with intent to treat
TVT™	175	81%	63%
Colposuspension	169	80%	51%

Ward KL, Hilton P: Am J Obstet Gynecol 2004;190(2)324-31.

TVT™ "EARLY" LONG-TERM RESULTS

Author	F/U	n	"Success" (%)
Chene, 2006	At 5 years	82	79.2
Ankardal, 2006	At 5 years	707	73
Doo, 2006	67 (60-76)	134	76.9
Kuuva, 2006	Mean 6 years	129	74% by stress test
Tsivian, 2004	55 (48-65)	52	78.9

TVT™ LONG-TERM DATA

- 1- and 5-year follow up
- n=134

	1-year	5-year
Cure/improved	97.7%	94.9%
Cure	90.1%	76.9%

Doo, et al; Eur Urol 2006;50:333-8.

TVT™ : MULTICENTER STUDY

- N=689, 24 month follow up
- 41 hospitals, 54 surgeons

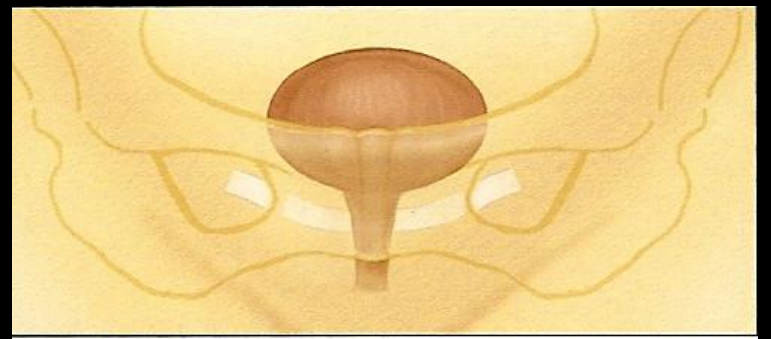
	2 mos	6 mos	12 mos	24 mos
No leakage	68.30	71.90	71.90	67.70
Improved	23.00	22.80	24.90	28.30
No change	7.60	4.20	2.60	3.60
Worse	1.10	1.10	0.60	0.40

Schraffordt Koops, et al: Int Urogynecol J 2007;18:437-42.

Overall success: 96.00%

OTHER ITERATIONS

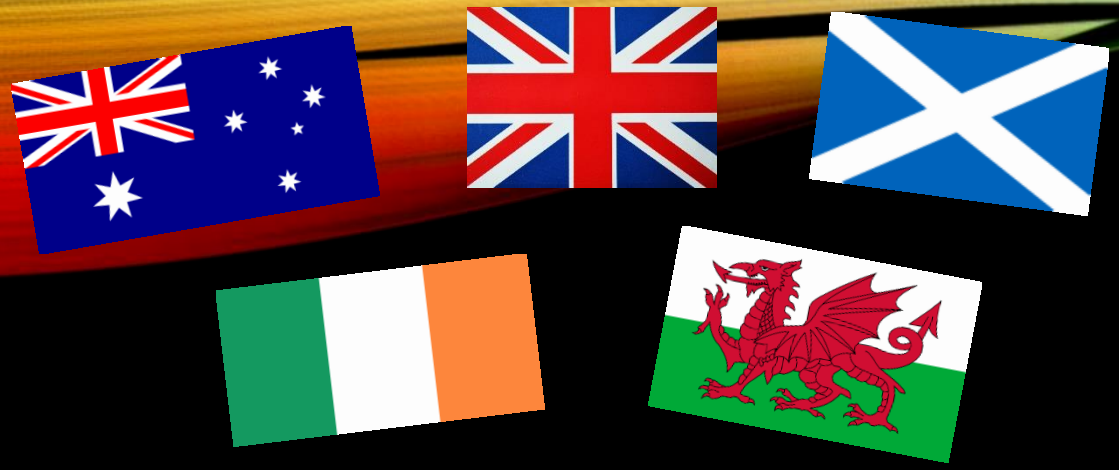
- Transobturator
  - Avoid retropubic space
- Single incision slings
  - Avoid passage "anywhere"



Transobturator Sling Placement

FAST FORWARD

Global status



INTERNATIONALLY

YEAR	AUSTRALIA	UNITED KINDGOM
1998	Mesh approved	
2006	First complication reported	
2014		Scotland suspension on mesh
11/28/17	POP mesh and mini-slings halted MUSs remained on registry	
7/10/18		"Pause" on all TV mesh (England, Wales, Ireland)
9/12/18		Halt on all mesh (Scotland)
12/1/18	Mesh reclassified IIb→III (med-high→high risk) Previously approved must reapply by 12/20	

UPDATED 2019 NICE GUIDELINES

- NICE
  - Highly regarded
  - Evidence-based by independent committees including professionals, lay members
- Slings remain an option, but not first line
- Patients should be advised
  - Permanent
  - May not be reversible
- Empowers patients to make informed choice

ENGLAND

- NHS not compelled to abide by guidelines
- ***Pause remains in effect***
- Slings must be done by specialists
- Outcomes be reported to database
- Possible re-look in 2020 once national registry established

CANADA

- TV mesh continues to evolve
- Complications may occur
- Must be aware of complications
- Surgery may or may not correct condition
- Surgeons need adequate training
- POP may be successfully treated with native tissue repair
- SIS is novel and may have higher risk

CANADIAN POSITION STATEMENT

- Literature supports RMUS and TMUS
- Rare, but serious complications can occur
- May or may not be correctable even with surgery
- Patients must be informed
- Surgeons should be adequately trained
- Must be able to recognize and address

Welk B, et al.: Ca Urol Assoc 2017;11(6Suppl2):S105-107

IN THE US…

IN THE BEGINNING…2001

- FDA classified TV mesh for POP as class II
- Similar to abdominal hernia mesh
- Approved without premarket evaluation
- Only 501k process necessary

FDA ON MESH

YEAR	ACTION
10/20/08	**FDA notification re: serious complications with TV mesh for POP and SUI**
7/13/11	Update for POP only
9/8/11	**Panel convened to assess POP and SUI mesh**
1/3/12	Post market surveillance ("522") ordered for POP, mini-sling
3/27/13	Updated communication regarding slings
4/29/14	Proposal to reclassify POP mesh, require premarket assessments, 510K for tools
1/5/16	**POP mesh reclassified II→III (high risk)**
1/6/17	(final order requiring 510k for devices)
7/13/18	Last posterior compartment mesh pulled
2/12/19	**Panel convened to assess *specifically POP mesh***

FDA PANEL CONCLUSIONS

February 12, 2019

- 36 month safety and outcomes
- Must be superior to native tissue repairs to be supported

APRIL 16, 2019

FDA MANDATE:

Distribution of all transvaginal mesh ***for prolapse*** repair halted

EFFECTIVE IMMEDIATELY

SUFU RESPONSE

- Corresponded with FDA
- Partnering with AUA, AUGS, ACOG, SGS
  - ICS, IUGA on international front

- ***Must maintain differentiation of TV POP mesh from midurethral slings (and transabdominal POP mesh)*
- Acknowledge risks
- Preserve choices for patients

LEGAL CLIMATE IN US

- After 2008 statement, 100 cases filed[1]
- After 2011, 32,296/year[2]
- By 2015, 74,514[3]
- Distribution:
  - 63% SUI
  - 14% POP
  - 23% POP and SUI

[1]Perkins, et al. Curr Bladder Dysfunct Rep 2015; 10 (1): 39-45
[2]Litigation USJPoM, 2015
[3]Souders et al. Female Pelvic Med Reconstr Surg 2018; 24: 21-25


MERV'S
MANURE
SAM'S
FANS

SO, WHERE NEXT?

Back to more invasive options?

Less effective choices?

Efficacy and safety must be known

SO, WHAT ARE OUR OPTIONS?

Non-surgical	Surgical
Pelvic floor muscle exercises	Urethral bulking injection
Physical therapy	Sling
Continence pessary	Burch
Vaginal inserts	Clinical trials

CURRENT LITERATURE

- Large meta-analysis
- 175 RCTs with 21,598 patients
- 21 treatment comparisons
- Outcomes measures:
  - 105 on “cure”
  - 120 on “improved”

COCHRANE

- 8 reviews of RCTs regarding 9 procedures
- Lack of standardization in procedures and assessement
  - →Interpretation difficult
- Primary outcomes: Cure and improvement
- Again, no standardization, so hierarchy applied
  - Cure: PROMS, composite scores, pads, UDS
  - Improved: subjective, satisfaction, pads, UDS

OTHER PROBLEMS

- Small sample sizes
  - (n=15-655, mean 91)
- Short follow up
  - (1-126 months, mean 12 months)
- Only 41 studies had ≥3 years follow up

STILL…TO DATE,

Best studied technique

Most robust assessment

CURRENT LITERATURE

	Cure	Improved
Pubovaginal sling	89.4	67.7
Retropubic MUS	89.1	97.0
Colposuspension	76.7	63.8
Transobturator MUS	64.1	76.1

ODDS RATIO VERSUS RMUS

Procedure	Cured		Improved	
	Odds ratio	***Evidence***	***Odds ratio***	***Evidence***
Pubovaginal sling	1.06	Low	0.69	Low
Colposuspension	0.85	Very low	0.65	Low
Transobturator MUS	0.74	Moderate	0.76	Moderate

RETROSPECTIVE STUDIES

Britain

- >92K women over 8 years
- 9.8 % periprocedural complications (up to 5 years)
- 5.9% readmitted within 5 years

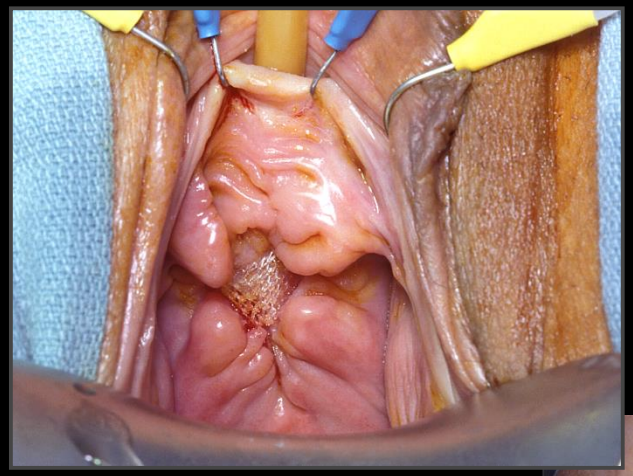
Scotland

- >16K women between April 1997 and March 2016
- Immediate complications, readmission, reoperation low

Keltie K et al.: Sci Rep 2017;7:12015

ADVERSE EVENTS

- De novo urgency
- Vaginal extrusion
- Urinary tract erosion
- LUTS/Retention
- Visceral or neurologic injury
- Hemorrhage
- Pain



MUS COMPARISON

Transobturator

- Highest reoperation
- Groin pain

Retropubic

- Suprapubic pain
- Vascular complications
- Urinary tract perforation
- LUTS

AUA/SUFU SUI GUIDELINES

COUNSELING (statements 7-10)

- Consider bother
- Should include following options
  - Non surgical
  - Surgical
- Should discuss complications
  - Risks, benefits, alternatives
  - Include specific to mesh

TREATMENT (statements 11-16)

- Nonsurgical
  - Continence pessary
  - Vaginal inserts
  - Pelvic floor muscle exercises
- Surgical
  - Urethral bulking
  - Midurethral slings (synthetic)
  - Pubovaginal sling
  - Burch colposuspension

AUA/SUFU SUI GUIDELINES

OUTCOMES ASSESSMENT (23-24)

Communicate early

- Pain
- Voiding problems
- UTI
- Dysparuenia
- Mesh concerns
- If so, bring in

Formal follow up within 6 mos

- Further intervention may be indicated
- Patient subjective outcome
  - Specifics (pain, voiding problems, etc.)
- Physical exam
- PVR
- Questionnaires optional

ALL AGREE…

- Must be performed by specialists
- Surgeons must be properly trained
- Complications must be considered
- Complications and alternatives must be presented to patients
- Must keep data for long term assessment

MOVING FORWARD

- Informed consent critical
  - Non-surgical options
  - Non-mesh alternatives
- Must keep long-term data
- Improve outcomes reporting
  - Patient-centered outcomes
  - Optimal measures
  - Randomized trials
  - Registries

CONCLUSION

- Guidelines generally in agreement
- Full range of options for SUI should be offered
- Do not discount potential complications
- Discuss risks, benefits, and alternatives
- Fully informed patients should have a choice