

# Bulking Agents for Stress Urinary Incontinence

Dr. J. Matthew Andrews B.Sc, M.Sc, MD, FRCSC

Clinical Assistant Professor

Memorial University



# Disclosures

- Lecturer
  - Astellas Pharma Canada
  - Pfizer
- Advisor
  - Sanofi

# Armamentarium against SUI

## **Non-Surgical**

- Observation
- Continence Pessary
- Vaginal Inserts
- Pelvic Floor Muscle Exercises

## **Surgical**

- Bulking Agents
- Midurethral sling (synthetic)
- Autologous Fascia Pubovaginal Sling
- Burch colposuspension
- Artificial Urinary Sphincter

# AUA / SUFU Guideline 2017

- In index patients considering surgery for stress urinary incontinence, physicians may offer the following options: (Strong Recommendation; Evidence Level: Grade A)
  - Midurethral sling (synthetic)
  - Autologous fascia pubovaginal sling
  - Burch colposuspension
  - Bulking agents

# AUA / SUFU Guideline 2017

- In patients with stress urinary incontinence and a fixed, immobile urethra (often referred to as 'intrinsic sphincter deficiency') who wish to undergo treatment, physicians should offer: (Expert Opinion)
  - Pubovaginal slings
  - Retropubic midurethral slings
  - Urethral bulking agents

# Bulking agents – Patient Selection

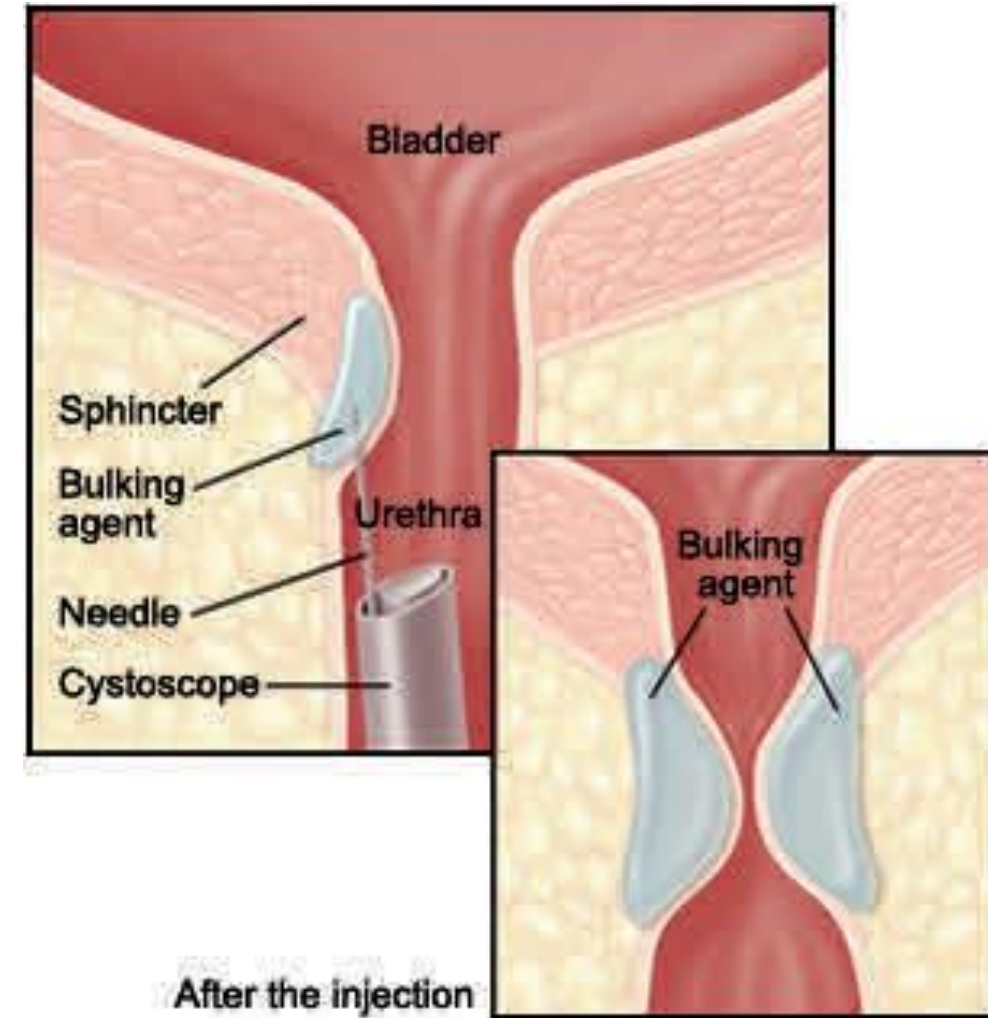
- First described as early as 1904
  - Injection of periurethral paraffin wax for SUI
- Viable option for SUI in select patient population
- Alternative option for:
  - Salvage procedures post-failure of MUS
  - Patients with contraindication to MUS

**Table 1. Indications for periurethral bulking for female stress urinary incontinence (SUI)**

Indication	Key points
Patient choice	<ul style="list-style-type: none"><li>• Low to moderate volume SUI</li><li>• Accepts lower likelihood of success versus surgery</li></ul>
Young patient who desires future pregnancy	As above
Poor bladder emptying	Lower risk of permanent urinary retention vs. surgery
Poor candidate for surgical intervention	<ul style="list-style-type: none"><li>• High anesthetic risk</li><li>• Stenotic introitus</li><li>• Advanced age</li><li>• Severe obesity</li><li>• Anticoagulated</li></ul>

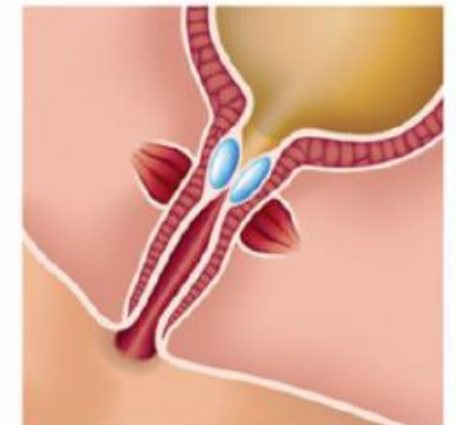
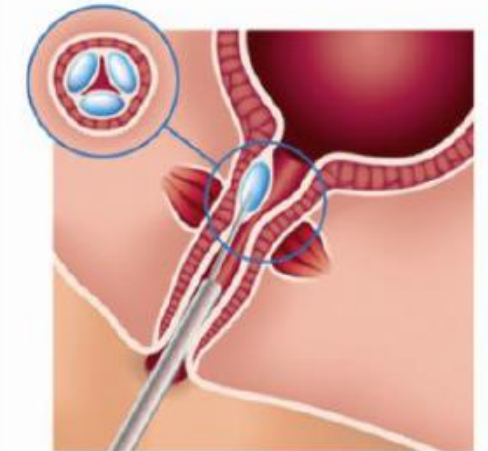
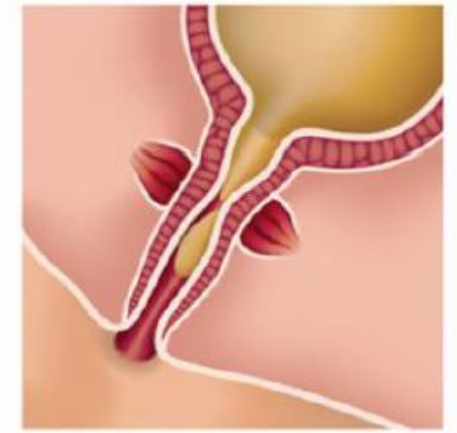
# Mechanism of action

- Augment or restore mucosal coaptation without obstructing urination
- Injected into the submucosal space to elevate the urethral mucosa
  - increases coaptation and urethral resistance
- Inject at bladder neck or proximal urethra

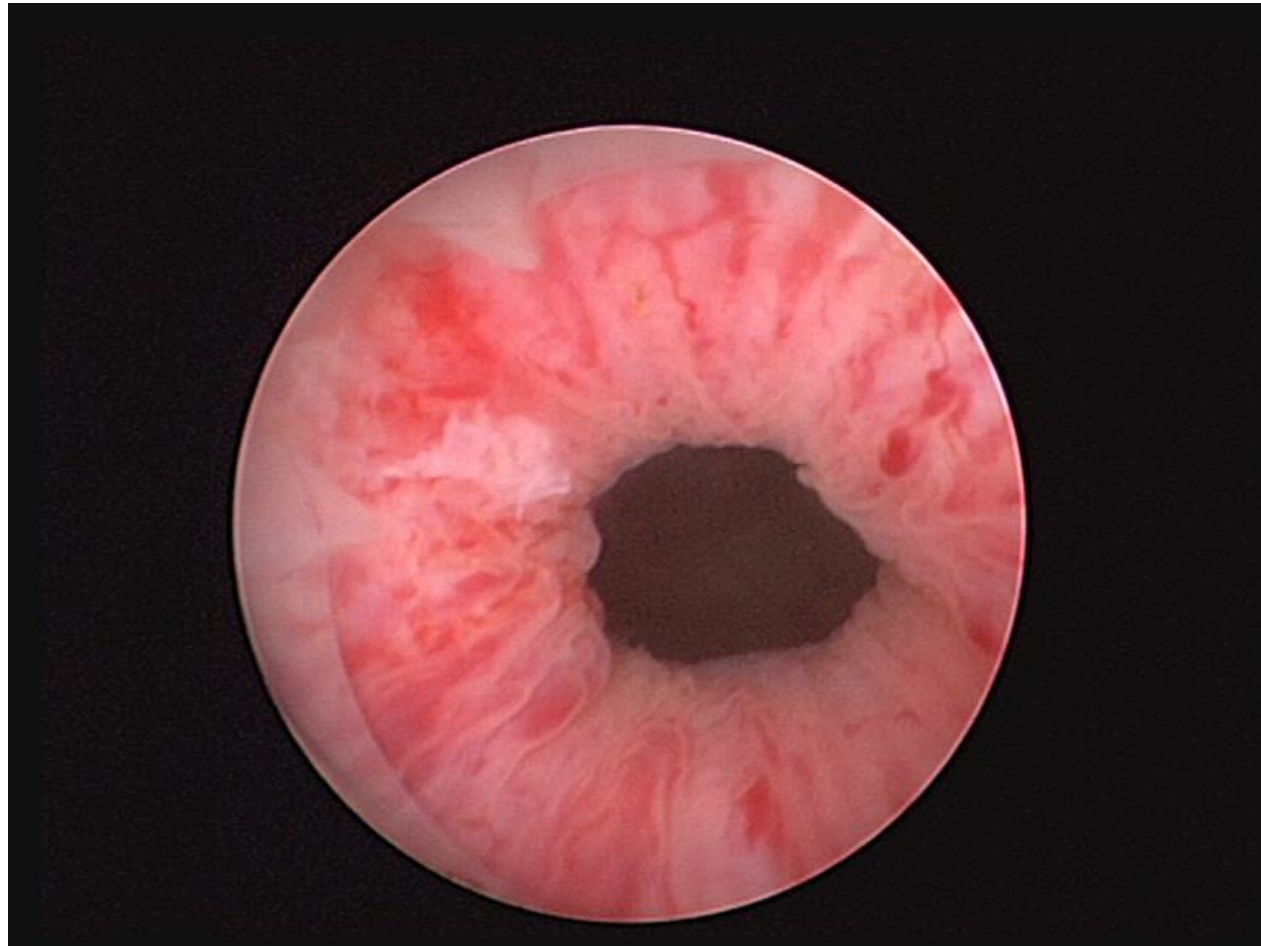


# Technique Aspects

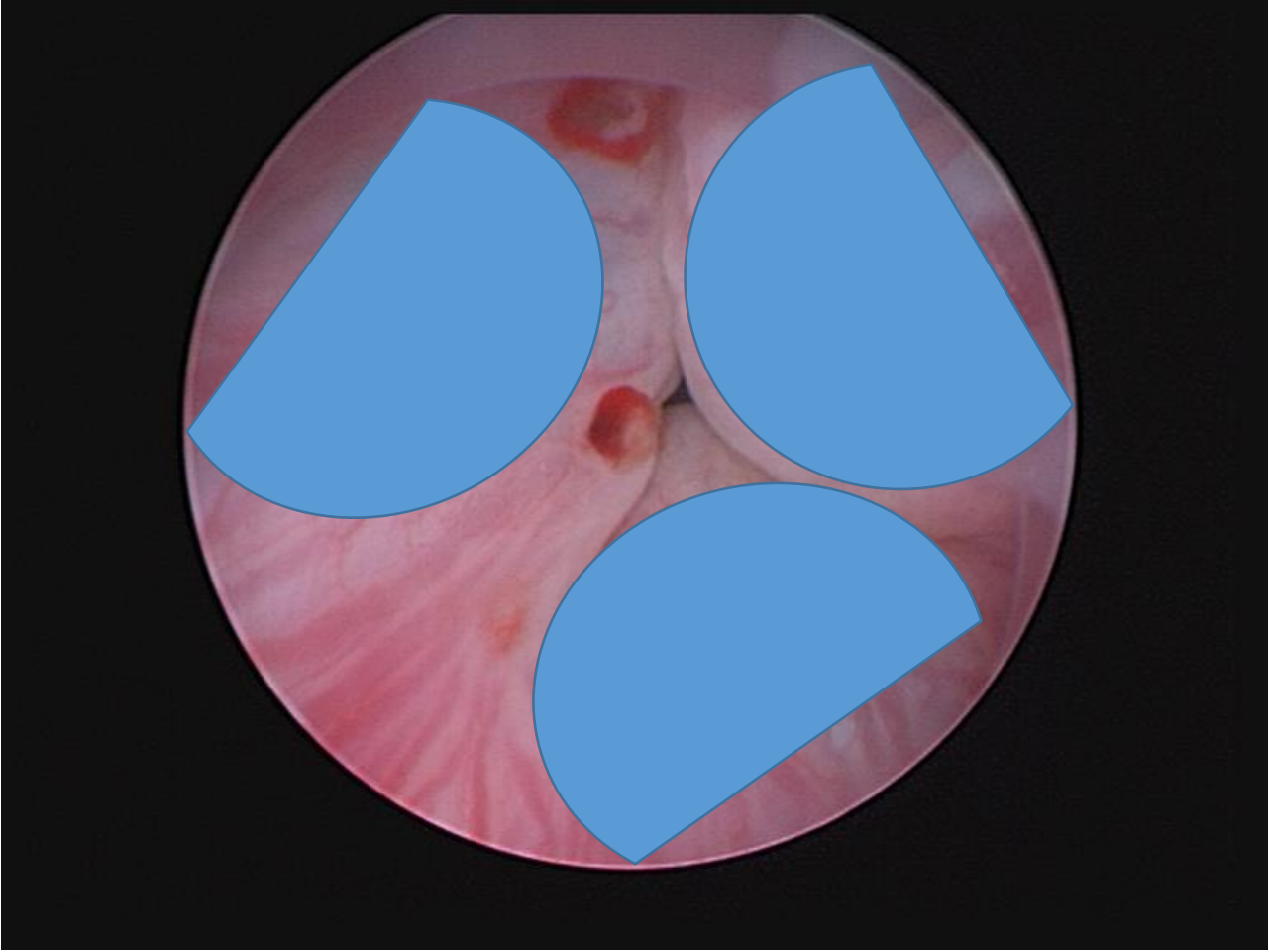
- Outpatient setting
- Anesthesia: **Local** vs IV sedation vs general
- Peri-urethral or trans-urethral injections
- Cystoscope with 0 degree lens
- 23-gauge 120mm needle
- 3 - 4 equally spaced submucosal injections at level of proximal urethra and/or bladder neck
- Minimize passage of scope across bladder neck
- Drain bladder with small in/out catheter
- Repeat injections in 1-3 mths if incontinence persists

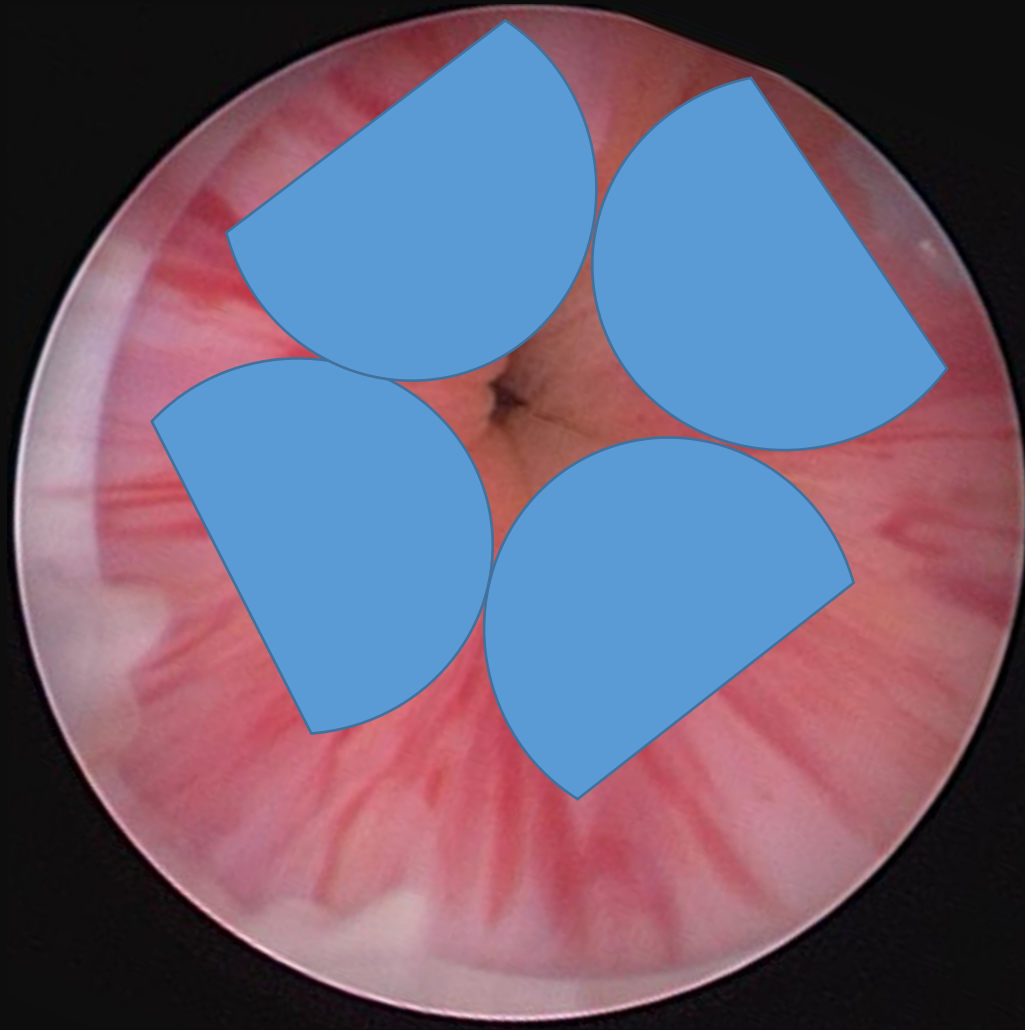












# Ideal Bulking Agent

- Easy to inject
- Non-immunogenic, non-carcinogenic,
- Biocompatible
- Non-migratory
- Cost-effective
- Non-inflammatory
- Sufficient durable clinical improvement

# Available agents

	Bulking agent	Material	Particle size (Mm)
<b>Cross-linked collagen</b>	Contigen®	Bovine collagen	N/a
	Permacol®	Collagen piglet	
<b>Particulate combination Gels</b> (Mini-particles suspended in a carrier gel)	Zuidex®	Dextranomer hyaluronic acid	80 - 200
	Deflux®	Dextranomer hyaluronic acid	80 - 250
	Macroplastic®	Polydimethylsiloxane	73 – 100
	Durasphere EXP®	Carbon coated beads	90 – 212
	Opsys®	Polyacrylate polyalcohol copolymer	300
	Coaptite®	Calcium hydroxylapatite	75 - 125
<b>Silicon elastomer</b>	Uryx / Tegress®	Vinyl alcohol copolymer implants	N/a
	Urolastic®	Crosslinked vinyl dimethyl polydimethylsiloxane	
<b>Homogenous hydrogel</b>	Bulkamid®	Hydrogel Polyacrylamide (PAHG) <b>97.5% water and water 2.5% cross-linked polyacrylamide</b>	N/a

Withdrawn from market for safety or commercial reasons

# Efficacy

- Clinical data on bulking agents is limited and heterogenous
- Majority of literature focuses on subjective improvement rather than objective improvement measures
- Long term follow-up is lacking
- Cochrane review 2017<sup>1</sup>
  - 14 trials – small, moderate quality
  - Insufficient data to allow for meta-analysis or clinical decision making
  - Select agents shown to be more effective than pelvic floor muscle therapy, but less effective than open surgical management for SUI
- Overall, efficacy ranges 50-70% for early subjective improvement<sup>2</sup>
  - Not sustainable and lacks durability over time
- Inadequate data to recommend one injectable agent over another

<sup>1</sup> Kirchin V et al. Cochrane Database of Systematic Reviews 2017, Issue 7.

<sup>2</sup> Kocjancic et al. Neurourol Urodyn. 2019

# Hyaluronic acid and Dextranomer microspheres

- Viscous gel
- Biocompatible
- **Zuidex<sup>®</sup>** (Periurethral injection)– **removed from market**
  - High complication rate
  - Lower success rates compared to Collagen (53% vs 66.5%)<sup>1</sup>
- **Deflux<sup>®</sup>** (Transurethral injection)
  - Lightner et al. Urol 2010
    - 4/35 pts developed pseudoabscess requiring operative management
    - Failed for 23/35 pts with ISD

<sup>1</sup>Lightner et. al. Urol 2009



# Polyarcylamide hydrogel (PAHG) - Bulkamid<sup>®</sup>

- Injectable hydrogel consisting of **97.5%** water and **2.5%** cross-linked polyacrylamide
- Homogeneous (no micro-particles)
- Non-degradable and non-migratory
  - Exchanges water, salts and organic molecules with host tissue
- Pivotal study<sup>1</sup>
  - 345 women with SUI, randomized 2:1
  - PAHG non-inferior to collagen
  - At 12 mths, 53% improved, 47% cured
  - 77% required repeat injections



<sup>1</sup>Sokol et al. JUrol 2014

# Safety

- ~ 1/3 of patients experience some complication<sup>1</sup>
  - Majority low grade, transient, noninvasive tx (ie. ABX, catheter)
- Potential adverse events<sup>2</sup>
  - **Urinary tract infection**
  - **Injection site pain**
  - Urinary retention
  - Hematuria
  - Periurethral abscess
  - De novo urgency urinary incontinence
  - Bulking agent extrusion
  - Delayed hypersensitivity reaction
  - Granuloma formation

<sup>1</sup> Kocjancic et al. Neurourol Urodyn May 2019

<sup>2</sup> Mamut & Carlson CUAJ 2017

# Contraindications

- Hypersensitivity to the agent
- Active urinary tract infection



# Patient Counselling



- Minimally invasive
- Low tx morbidity
- Improved coaptation

- Efficacy & durability inferior to surgical slings for SUI
- Repeat injections may be required

# Summary

- Viable option for select patients
  - Non candidates for more invasive surgical interventions
  - Multiple prior failed surgeries
- Efficacy is modest at best
- Not as effective as slings
- Repeat injections are the norm