Managing urinary morbidity after brachytherapy

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Themes

- Can we predict urinary morbidity?
- Prevention of urinary morbidity
- Dealing with urinary morbidity
  - Storage LUTS
  - Urinary retention (urethral, s/p catheters and ISC)
  - TURP /TUIP
  - Stress incontinence management post brachytherapy

Brachytherapy urinary morbidity results

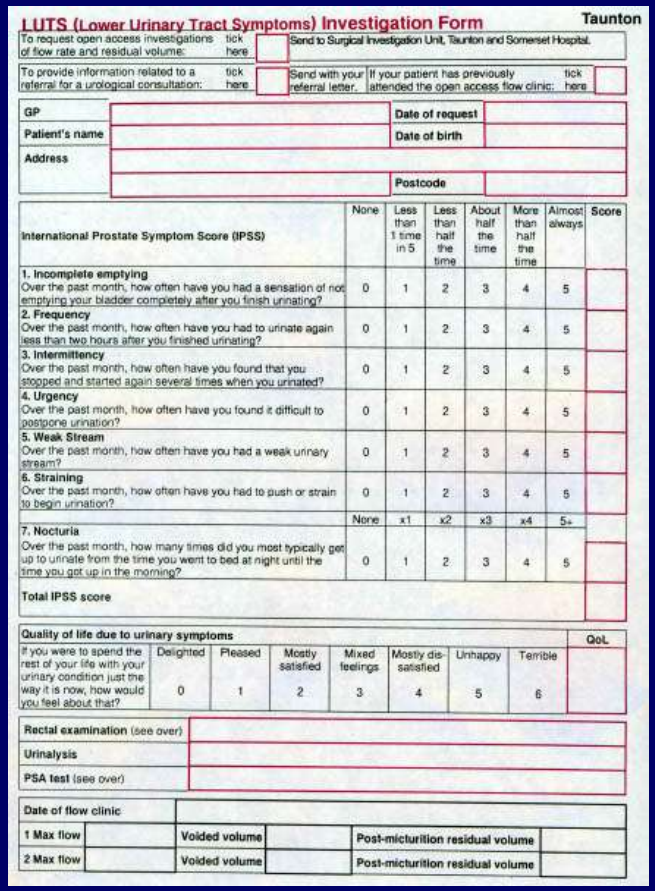
Complication	Number of Studies	Median (%)
Flare in I-PSS	>30	20-30
Urinary retention	26	10-20
Urgency /urge incontinence	>30	6
Incontinence	17	<3
Urethral stricture	7	<3
Impotence	19	20-80

Adapted from Vicini

BPH is a progressive disease

The factors that predict progression

1. Symptoms
2. Bother
3. Flow rate
4. Age
5. Prostatic volume
6. PSA
7. Residual volume
8. Inflammation



LUTS (Lower Urinary Tract Symptoms) Investigation Form — Taunton

To request open access investigations of flow rate and residual volume: tick here ☐ — Send to Surgical Investigation Unit, Taunton and Somerset Hospital.

To provide information related to a referral for a urological consultation: tick here ☐ — Send with your referral letter. If your patient has previously attended the open access flow clinic: tick here ☐

GP		Date of request	
Patient's name		Date of birth	
Address		Postcode	

International Prostate Symptom Score (IPSS)	None	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Score
1. Incomplete emptying — Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
2. Frequency — Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
3. Intermittency — Over the past month, how often have you found that you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency — Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream — Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining — Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	x1	x2	x3	x4	5+	
7. Nocturia — Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5	
Total IPSS score							

Quality of life due to urinary symptoms	Delighted	Pleased	Mostly satisfied	Mixed feelings	Mostly dissatisfied	Unhappy	Terrible	QoL
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6	

Rectal examination (see over)	
Urinalysis	
PSA test (see over)	

Date of flow clinic					
1 Max flow		Voided volume		Post-micturition residual volume	
2 Max flow		Voided volume		Post-micturition residual volume	

Published Predictors for Urinary symptoms

Author	Prost vol	TZ vol	Age	IPSS –O	AUR	Prostat e dose	Urethra Dose	Bladder dose	Needles	ERBT	Nuclide
Van Gellekom (2005)	+	0	0	0	0	+	-	0	0	0	0
Gutman (2006)	-	0	0	+	+	-	-	0	0	+	0
Niehas (2006)	-	0	0	+	+	-	-	0	0	+	-
Allen (2005)	-	0	-	+	0	-		0	0	0	+
Wallner (2002)	-	0	0	0	0	0	+	0	0	0	0
Wust (2004)	-	0	+	0	0	+	-	0	+	+	0
Hinerman-Mulroy (2004)	-	+	0	0	-	-	-	0	0	0	0
Merrick 2003	+	+	0	0	0	0	0	0	0	0	0
Salem (2003)	+	0	0	0	0	-	+	0	-	0	0
Williams (2004)	-	0	-	+	0	-	-	+	-	0	0
Geblum (1999)	+	0	0	+	0	-	0	0	0	-	-
Kelly (2006)	+	0	-	+	+	-	0	0	0	0	0
Steggerda (2008)	+		+	+	0	-	-	+	-	0	0

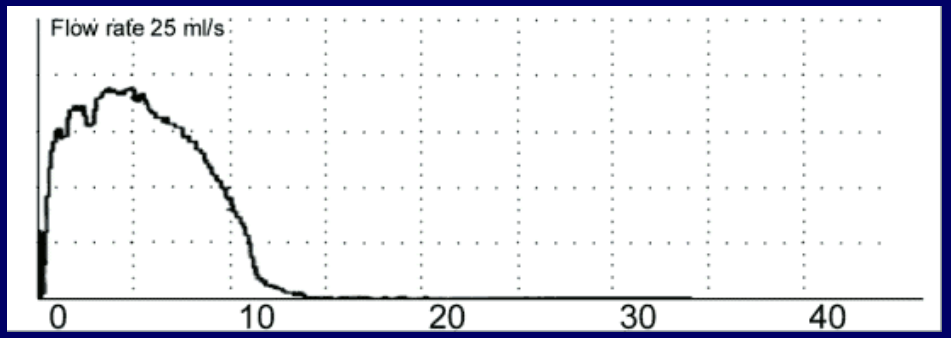
Published Predictors for Urinary symptoms
(other than acute urinary retention or need for TURP)

Author	Prost vol	TZ vol	Age	IPSS –O	AUR	Prostate dose	Urethra Dose	Bladder dose	Needles	ERBT	Nuclide
Van Gellekom (2005)	+	0	0	0	0	+	-	0	0	0	0
Gutman (2006)	-	0	0	+	+	-	-	0	0	+	0
Niehas (2006)	-	0	0	+	+	-	-	0	0	+	-
Allen (2005)	-	0	-	+	0	-		0	0	0	+
Wallner (2002)	-	0	0	0	0	0	+	0	0	0	0
Wust (2004)	-	0	+	0	0	+	-	0	+	+	0
Hinerman-Mulroy (2004)	-	+	0	0	-	-	-	0	0	0	0
Merrick 2003	+	+	0	0	0	0	0	0	0	0	0
Salem (2003)	+	0	0	0	0	-	+	0	-	0	0
Williams (2004)	-	0	-	+	0	-	-	+	-	0	0
Geblum (1999)	+	0	0	+	0	-	0	0	0	-	-
Kelly (2006)	+	0	-	+	+	-	0	0	0	0	0
Steggerda (2008)	+		+	+	0	-	-	+	-	0	0

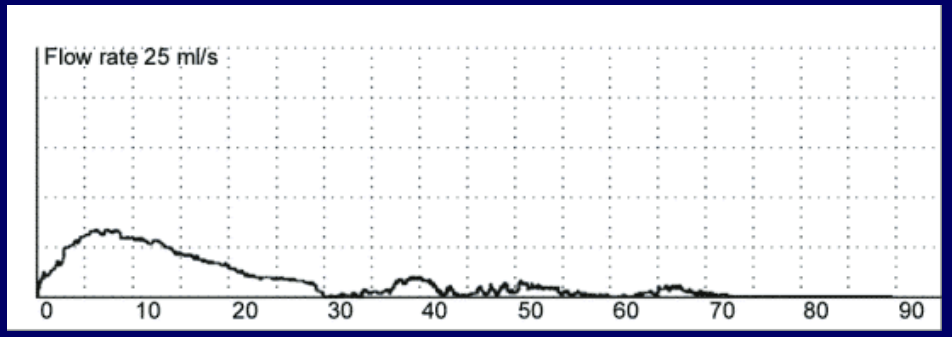
Predicting urinary morbidity

- IPSS
- Prostate volume
- Flow rate
- Urodynamics
- Seed placement

- Patients with high IPSS are frequently offered alternative treatments

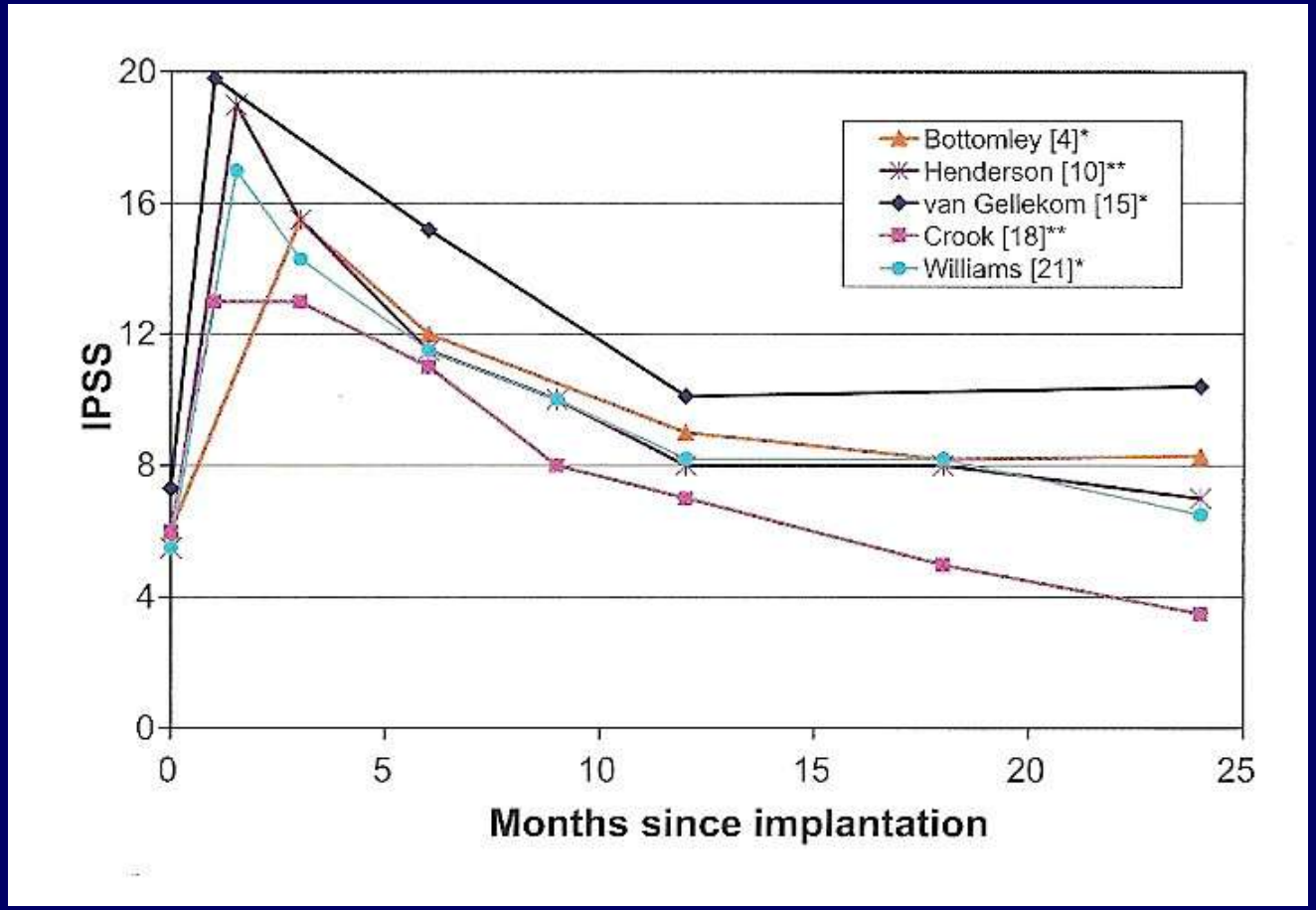


Unobstructed



Obstructed

IPSS post seed implantation



Steggerda et al, European Urology, 2008, 723-731

Prophylactic tamsulosin in patients undergoing prostate 125I brachytherapy

- Single-institution, double-blind, placebo-controlled, randomized trial, comparing prophylactic tamsulosin versus placebo
- Outcome measures acute retention and AUA symptom score
- All patients started the medication 4 days before PI and continued for 60 days.
- 126 patients enrolled, 58 tamsulosin arm and 60 in placebo group
- Urinary retention rate
  - 17% (10 patients) in the placebo group
  - 10% (6 patients) in the tamsulosin group ($p = 0.3161$).
- Intolerable urinary symptoms were reported equally (10 patients in each group) with 70% occurring in the first 2 weeks after PI.
- There was a significant difference in mean AUA score in favour of tamsulosin at week 5 after PI ($p<0.03$)
- Prophylactic tamsulosin (0.8 mg/day) before prostate brachytherapy did **not** significantly affect urinary retention rates, but had a positive effect on urinary morbidity at week 5 after PI.

Elshaikh MA et al, Int J Radiat Oncol Biol Phys, 2005, 1; 62(1):164-9

Cr

The bottom line

- Numerous nonrandomized studies and one randomized study support the proposition that the occurrence of LUTS secondary to RT is effectively mitigated by alpha1-adrenoreceptor blockade.

Crawford ED, Kavanagh BD, Am J Clin Oncol. 2006 Oct;29(5):517-23.

Corticosteroid use to prevent the development acute urinary retention after prostate brachytherapy

- Randomized trial to assess the efficacy of intraoperative steroid use in decreasing acute urinary retention after transperineal radioactive iodine-125 implantation for prostate cancer. Mierzwa et al, Cancer 2008 Nov 1;113(9):2605-9.
- A retrospective review on 400 consecutive patients. Androgen deprivation was given to 146 patients for 3 months before the implant and 280 received a 2-week course of dexamethasone (4 mg twice daily for 1 week then 2 mg twice daily). Multivariate analysis. Sacco, DE et al. BJU Int 2003 Mar;91(4):345-9.

Irritative symptoms, urgency and urge incontinence post brachytherapy

Bladder overactivity post brachytherapy

- ?mechanical damage
- ?placement close to urethra

- Men after brachytherapy have a much higher incidence of detrusor overactivity, prostatic and urethral strictures and prostatic urethral stones Blavias et al, BJU Int. 2006 98(6):1233-7
- Urgency and urge incontinence 6.4% Crook, J.Urol, 179, 141-146, 2008

The effect of antimuscarinic treatments in overactive bladder; An update of a systematic review and meta-analysis

Chapple et al, European Urology,2008,,54, 543-562

- 83 trials included
- Antimuscarinics safe more effective than placebo
- Tolerability good
- No RCTs post brachytherapy in literature
- Dry mouth most common adverse effect
- Significant differences between antimuscarinics in rates of withdrawal and rates and ranges of adverse events and efficacy outcome

The bottom line!

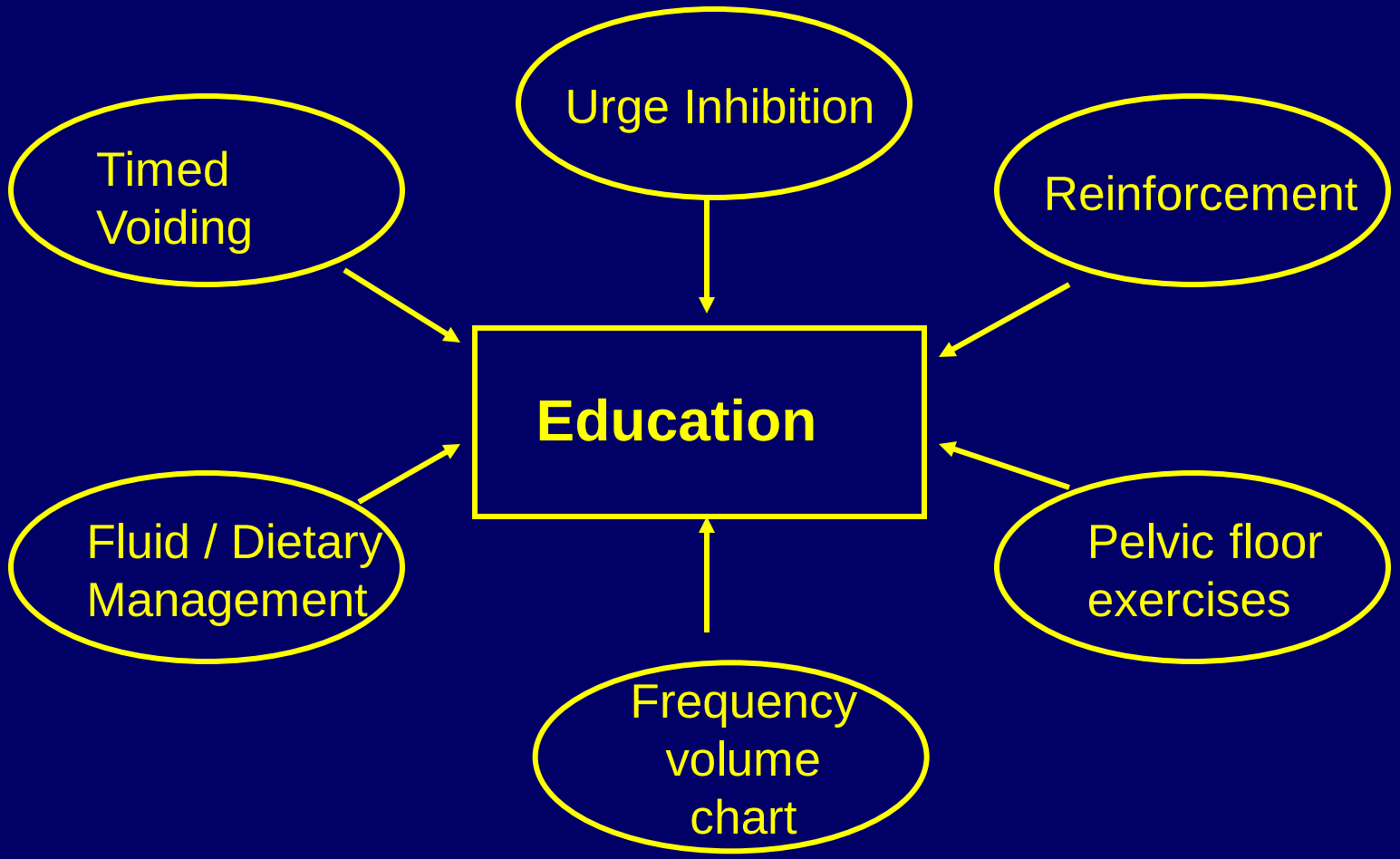
4th International Consultation in Incontinence
Antimuscarinics/Mixed Action Drugs

Drug	Level of evidence	Grade of recommendation
Darifenacin	1	A
Fesoterodine	1	A
Solifenacin	1	A
Tolterodine	1	A
Trospium	1	A
Oxybutynin	1	A
Propiverine	1	A

Fourth International Consultation On Incontinence (ICI) Paris 2008 - Drug Treatment Committee Highlights, in press
Karl-Erik Andersson, MD, PhD, and Christopher Chapple, MD, Committee Chairs

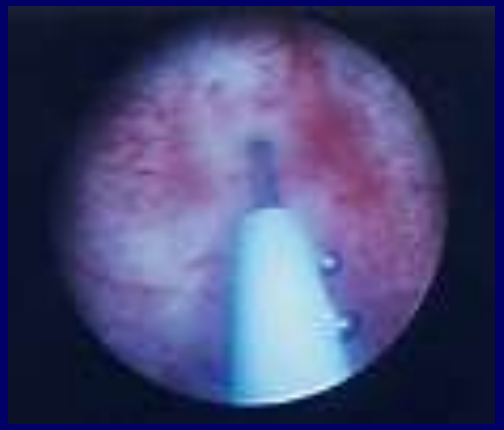
Does medication help?

A little, but patients need lifestyle modification



Botulinum Toxin (BoNT) /1

- Produced by the gram positive anaerobic and spore forming *Clostridium botulinum*
- Seven different neurotoxins (A–G) produced by *Clostridium botulinum*
- Only A and B in therapeutic use
- Four types of BoNT are on the market



Recommendations on the Use of Botulinum Toxin in the Treatment of Lower Urinary Tract Disorders and Pelvic Floor Dysfunctions: A European Consensus report.

Apostalides et al, Eur Urol, 2009, 55,100-102

- Use of botulinum neurotoxin type A recommended in
  - Intractable neurogenic detrusor overactivity (NDO)
  - Idiopathic detrusor oveactivity (IDO)
- Caution is recommended in IDO, because of the risk of voiding difficulty and duration of effect.
- The depth and location of should be within the detrusor muscle outside the trigone (grade c)
- Recommend larger placebo controlled trials to evaluate efficacy

Results of BoNT in detrusor overactivity

- 300 mU (Neurogenic); 200mU (Idiopathic)
- ↑ max cystometric capacity >150%
- ↓ max detrusor pressure by 60%
- Improves symptoms (subjective and objective)
  - Frequency / Urgency / Incontinence
- Effective for average of 8/12
  - 2nd injection works as well as the first
  - Not clear if this will be so for multiple repeats

Popat, J Urol,174;984-9. 2005

Management of acute retention

- Catheter and TWOC
- Suprapubic catheter
- ISC
- TURP
  - Literature rate 1-5%
  - Incontinence rate post TURP 18%
  - Higher incidence 2 years after implantation
  - No correlation with prostate volume or prostate or urethral dose of radiation

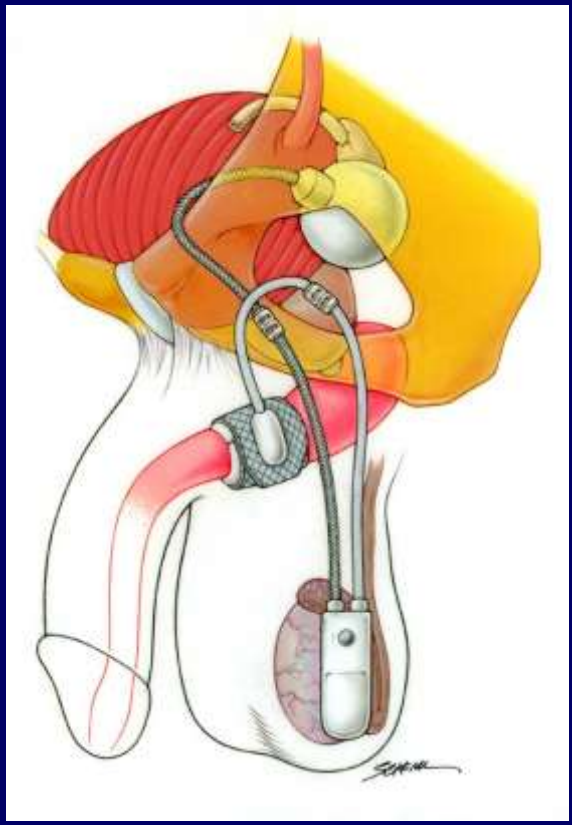
Kollmeirer et al; J.Urol.2005173:808-812

Timing of TURP

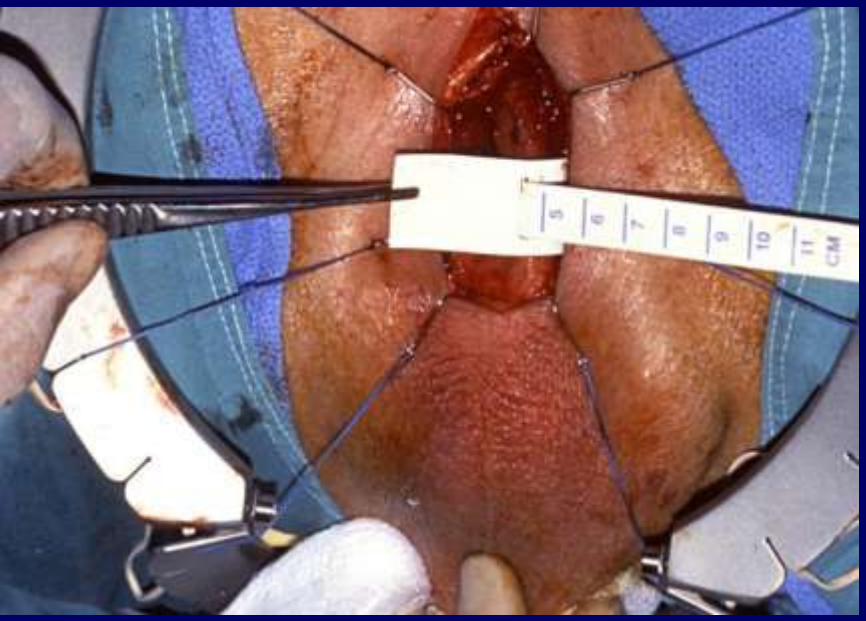
- Kollmeier 2005
- 2050 patients, 38pts (2%) required one or more TURPs
- 18% urinary incontinence
- Post TURP incontinence higher 2 years post brachytherapy
- ?related to radiation induced fibrosis

Kollmeier et al, J Urol, 2005, 173; 808-812

The patient has developed stress incontinence post TURP



Artificial urinary sphincter insertion



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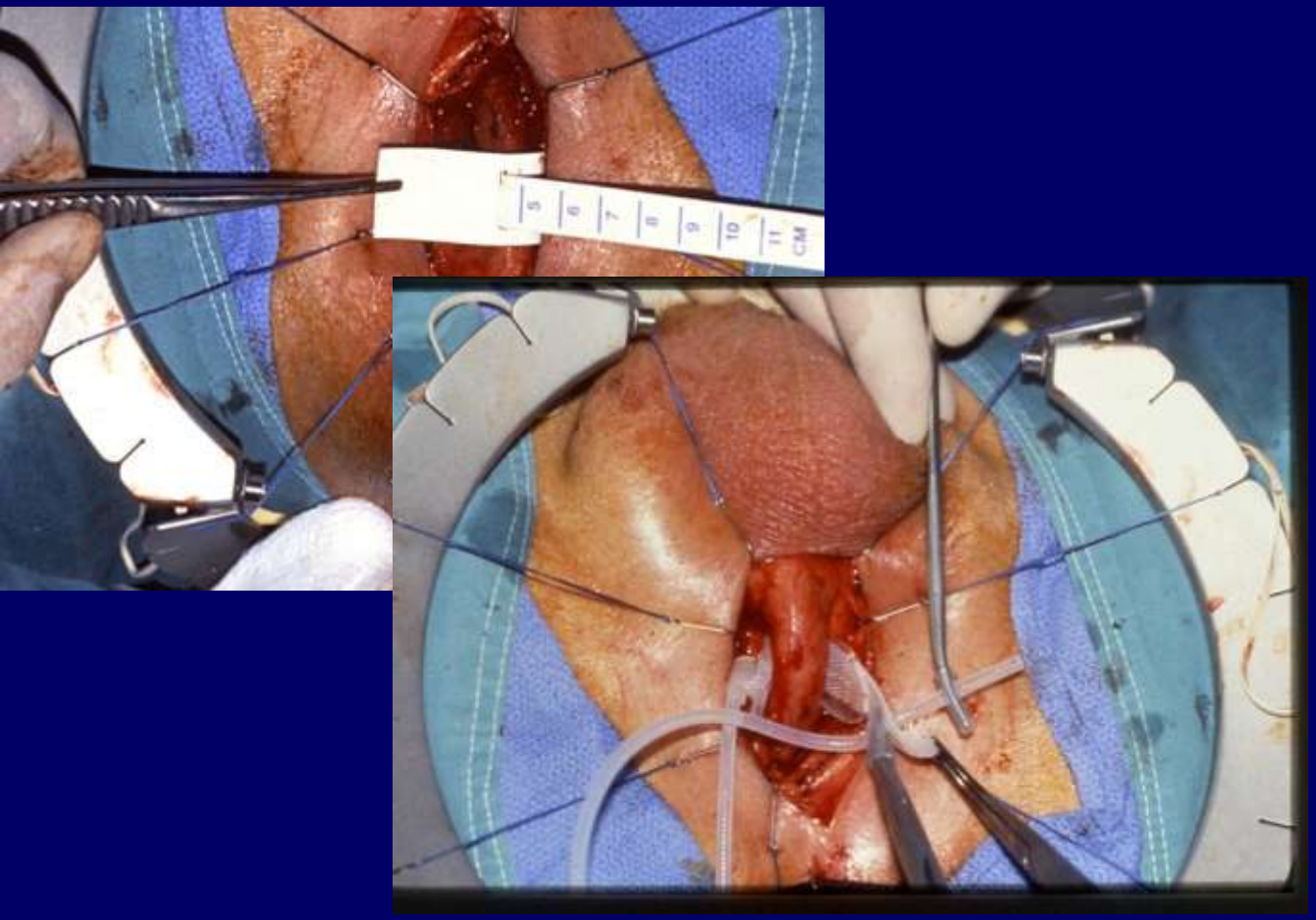

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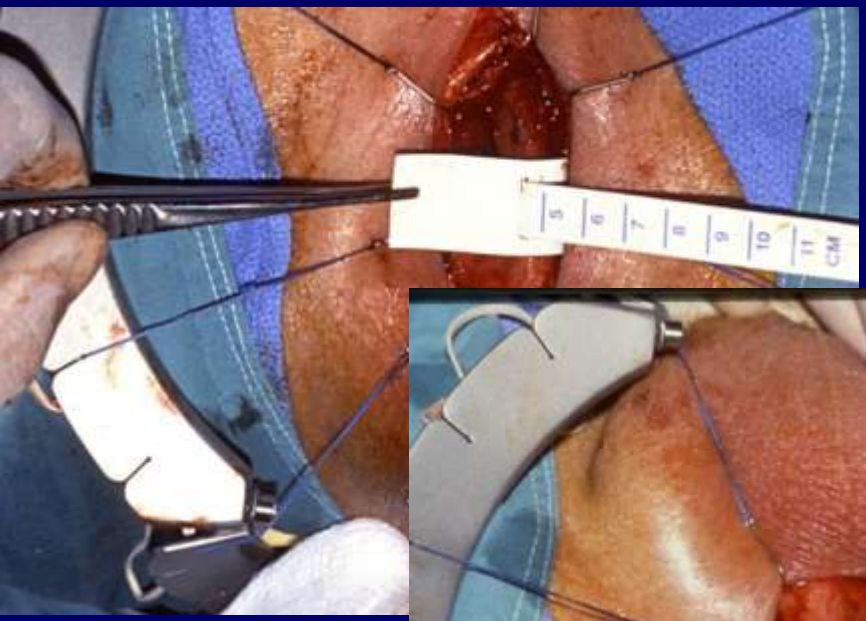

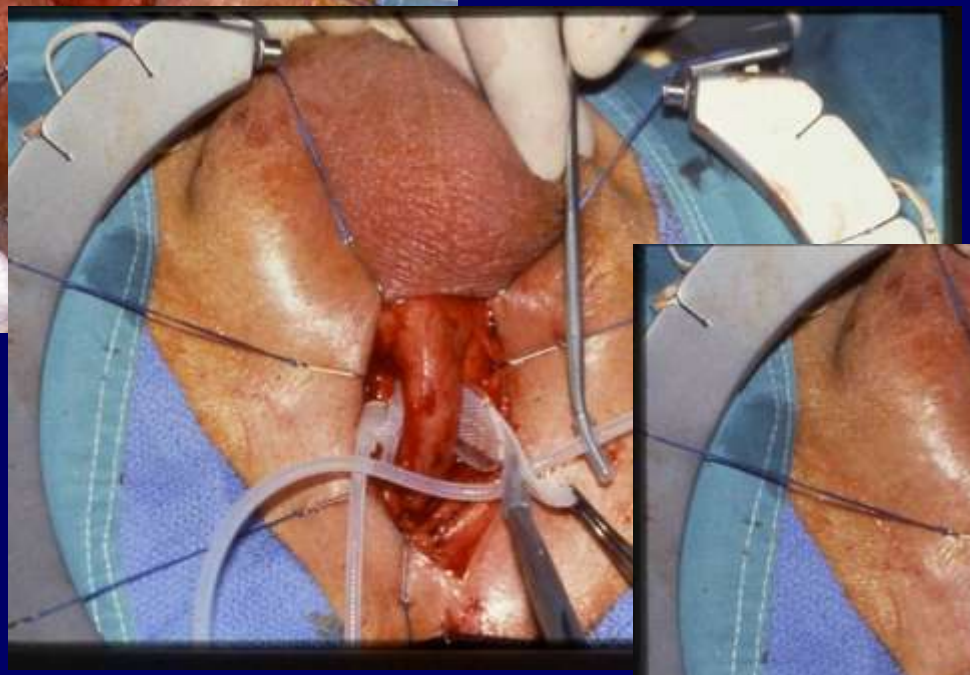

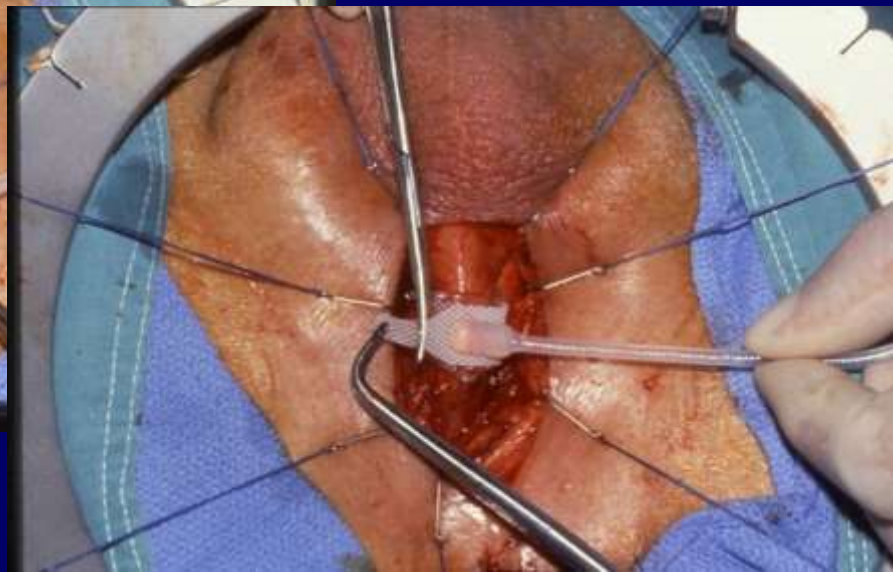

AUS Continence Rates

	Continence rate at 10 years %
Overall	89
Post prostatectomy	91
Neuropaths	86
Explants	37
Post radiotherapy	?

Complications of AUS

- Device failure – 3% per year
- Infection - 4% in the first year
- Erosion - late erosion /infection 4% per year
  - ?post brachytherapy

Conclusions

- Irritative and obstructive symptoms are common with brachytherapy
- Symptoms return to baseline within 1 year
- Prophylactic use of tamsulosin improves lower urinary tract symptoms
- High pretreatment IPSS predicts high post implant IPSS
- If in doubt pre-implant urodynamics may help
- Early TURP when required seems appropriate
- On occasion salvage procedures may be required!

Extras

Previous transurethral resection of the prostate is not a contraindication to high-dose rate brachytherapy for prostate cancer.

- 32 patients with previous TURP and 106 with no previous TURP Luo HL,et al, . BJU Int. 2009 Dec;104(11):1620-3. Epub 2009 Jul 16.

Does neoadjuvant hormonal therapy improve urinary function when given to men with large prostates undergoing prostate brachytherapy?

- 395 men with 50 cc or greater glands were treated with 3 months of neoadjuvant hormonal therapy (204) or implantation alone (191).
- Urinary function was assessed by the IPSS, retention rate and TURP
- Mean prostate volume in neoadjuvant hormonal therapy cases was 72.9 cc, which decreased to 54.3 cc after 3 months ($p < 0.001$). Mean prostate volume in cases without hormonal therapy was 60.6 cc ($p < 0.001$).
- Urinary retention 16 of 191 men (8.4%) without vs 25 of 204 (12.3%) with hormones therapy ($p = 0.207$).
- The median duration of urinary retention was 42 days (range 2 to 243).
- No difference in the retention rate in patients with hormonal therapy with an initial score of 15 or greater vs less than 15 (2 of 25 or 8% vs 11 of 102 or 10.8%, $p = 0.614$).
- Transurethral prostate resection was done in 11 of 191 men (5.8%) without vs 12 of 204 (5.9%) with hormonal therapy ($p = 0.958$). There was no difference in biochemical failure in the 2 groups

Stone et al. J Urol. 2010 Feb;183(2):634-9. 2009 Dec 16.