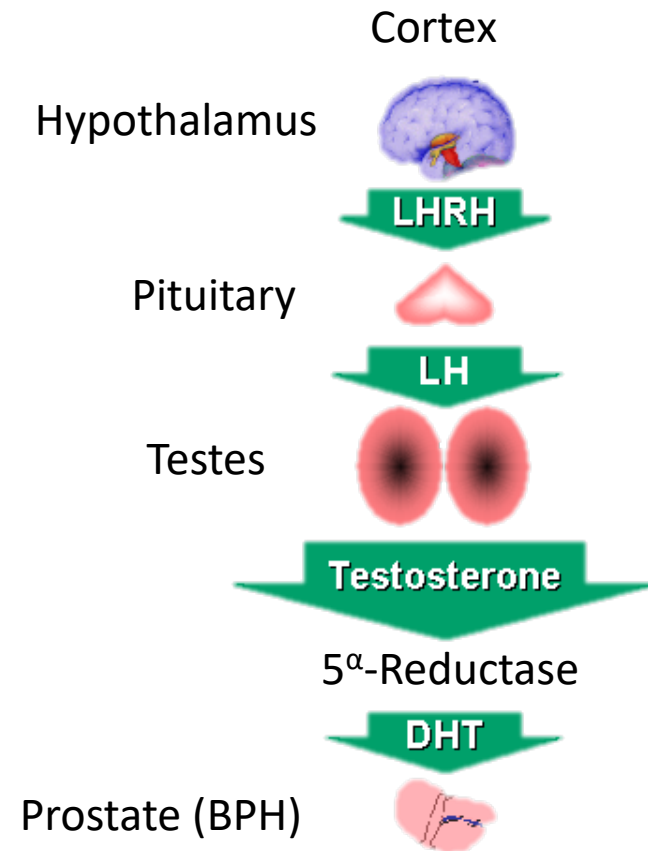


# An Ever-Growing Problem for Men- Benign Prostatic Hypertrophy

Lee Hammontree, *M.D.*

UCA | UROLOGY CENTERS  
OF ALABAMA

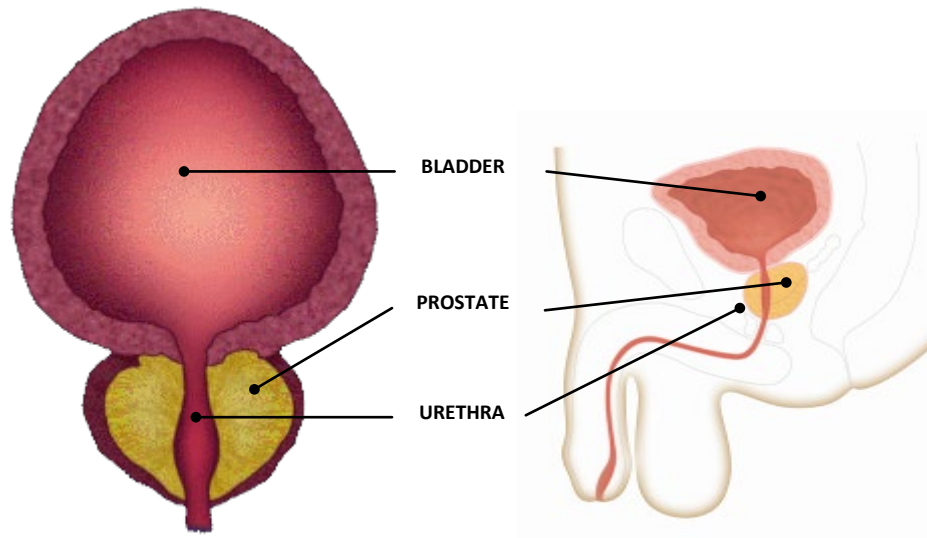
# ● Hormonal Regulation of the Prostate



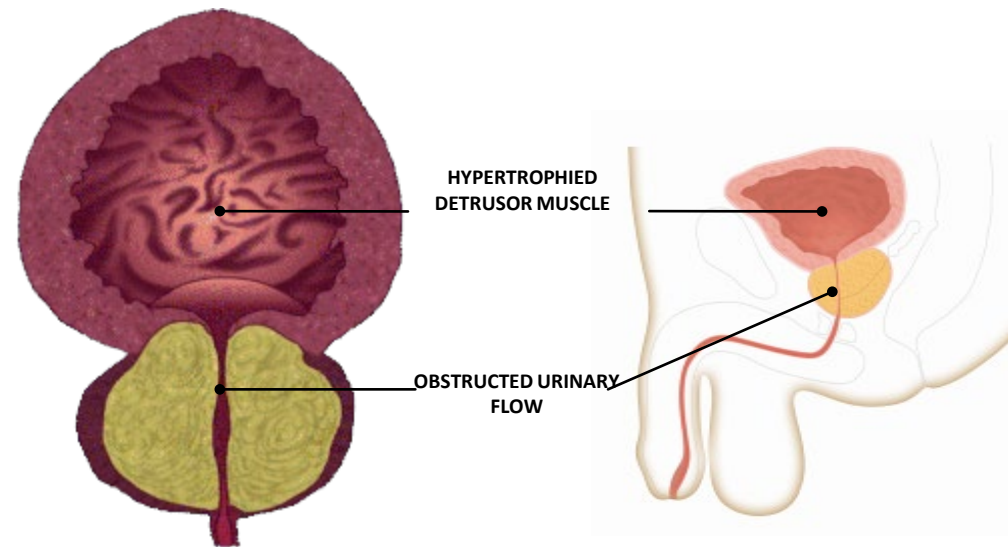
# Normal vs. Enlarged Prostate

- As the prostate enlarges, pressure can be put on the urethra
- Causes urinary problems
- In general, the size of the prostate does not correlate to severity of symptoms

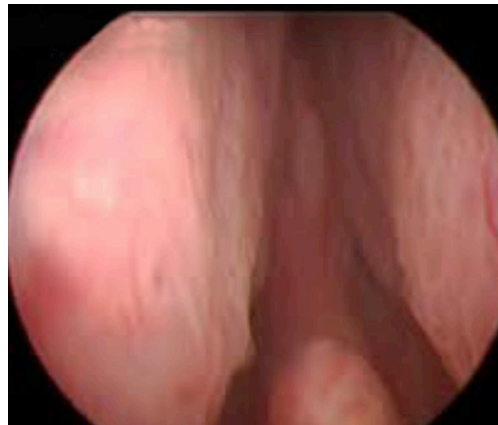
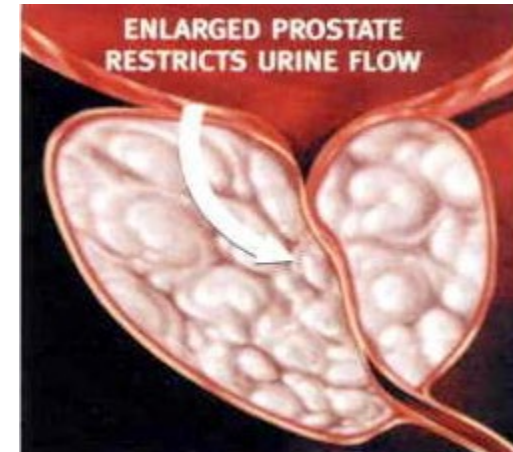
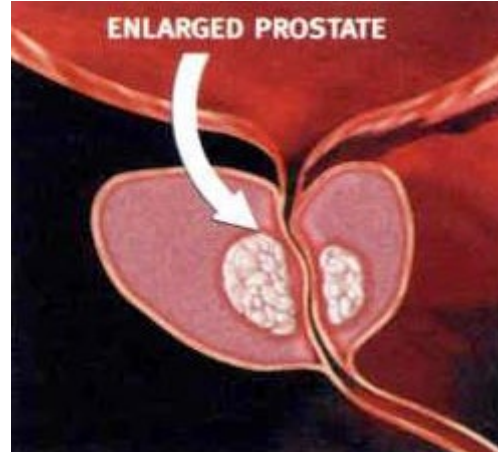
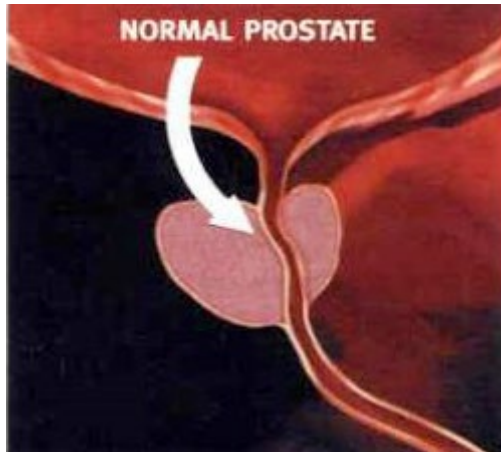
**Normal Prostate Anatomy**



**Enlarged Prostate (BPH) Anatomy**

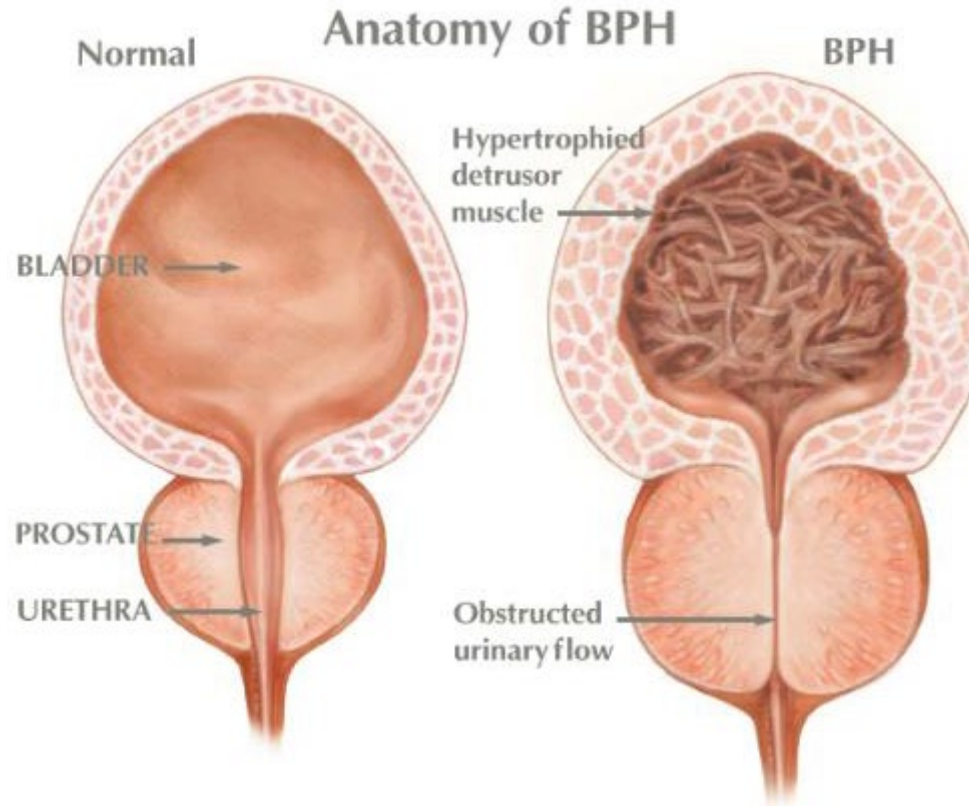


# BPH Disease Progression



Images courtesy Dr. Steven Gange

## What Happens if BPH is Not Treated?

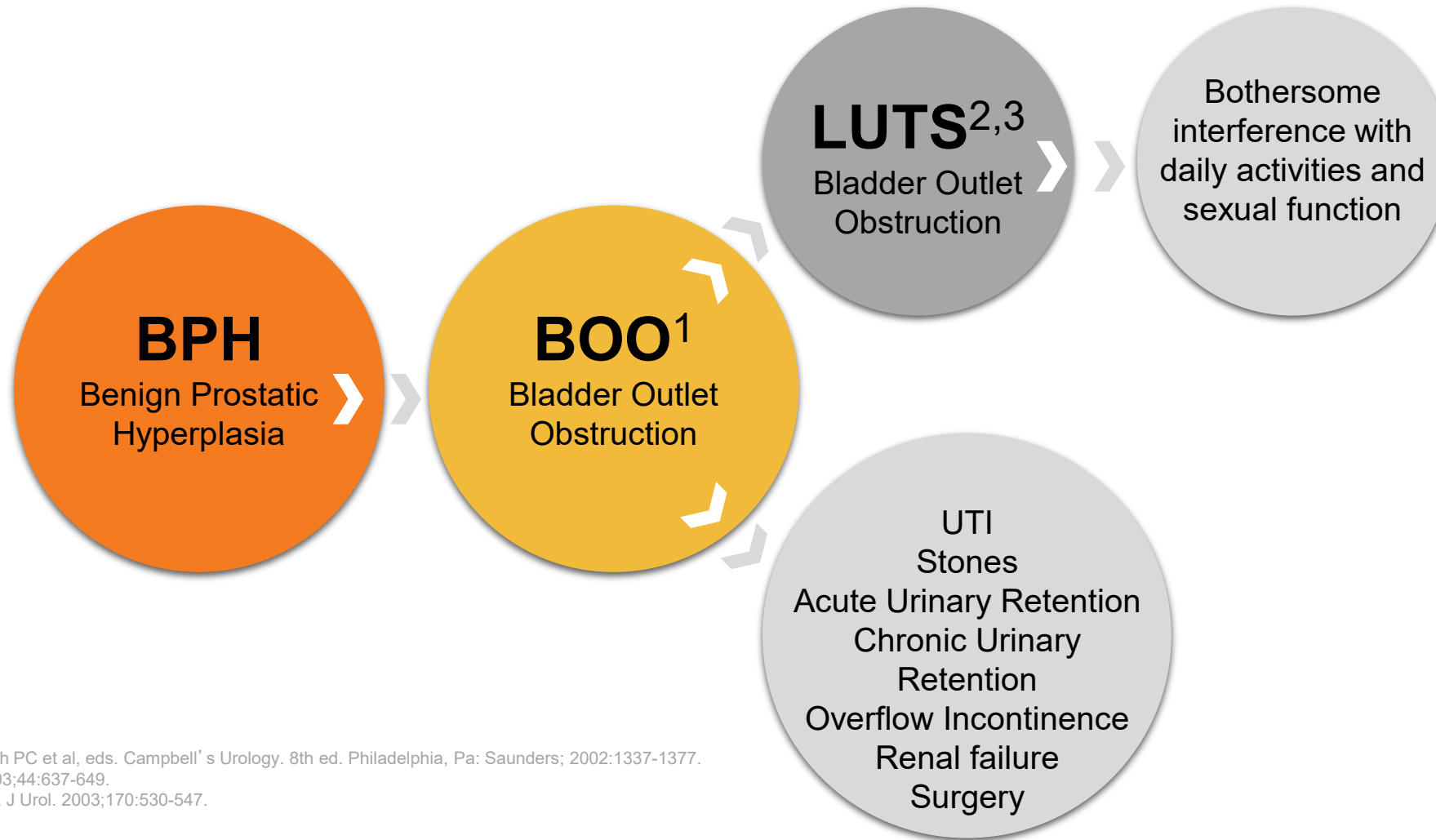


**Not treating enlarged prostate can lead to bladder deterioration**

- But If Your Bladder Works Too Hard:



# Histologic BPH Leads to BOO, LUTS and Clinical Consequences



1. Lepor H, Lowe FC. In: Walsh PC et al, eds. Campbell's Urology. 8th ed. Philadelphia, Pa: Saunders; 2002:1337-1377.

2. Rosen R et al. Eur Urol. 2003;44:637-649.

3. AUA Guidelines Committee. J Urol. 2003;170:530-547.

# BPH is Important

Top 10 Diagnosed Diseases in 2006 for Men 50 years and older

Rank	Disease	1-year prevalence (%) (n = 963,452 person-years)
1	Coronary Artery Disease/Hyperlipidemia	51.3
2	Hypertension	45.2
3	Diabetes Mellitus Type 2	17.5
4	<b>Enlarged Prostate</b>	<b>13.5</b>
5	Osteoarthritis	13.3
6	Arrhythmias	8.8
7	Cataract	8.6
8	Gastroesophageal reflux disease	8.4
9	Bursitis	8.0
10	Prostate Cancer	7.8

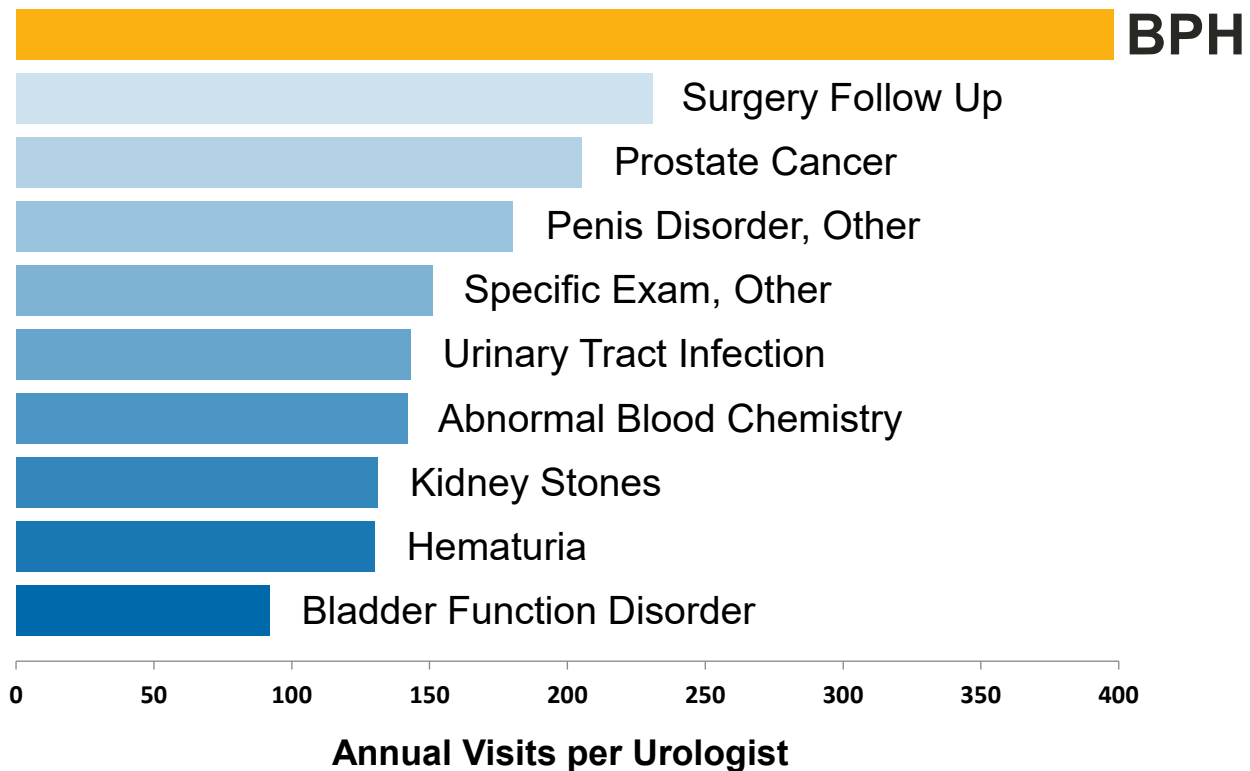
Issa MM et al. Am J Manag Care. 2006;12(suppl):S83–S89.





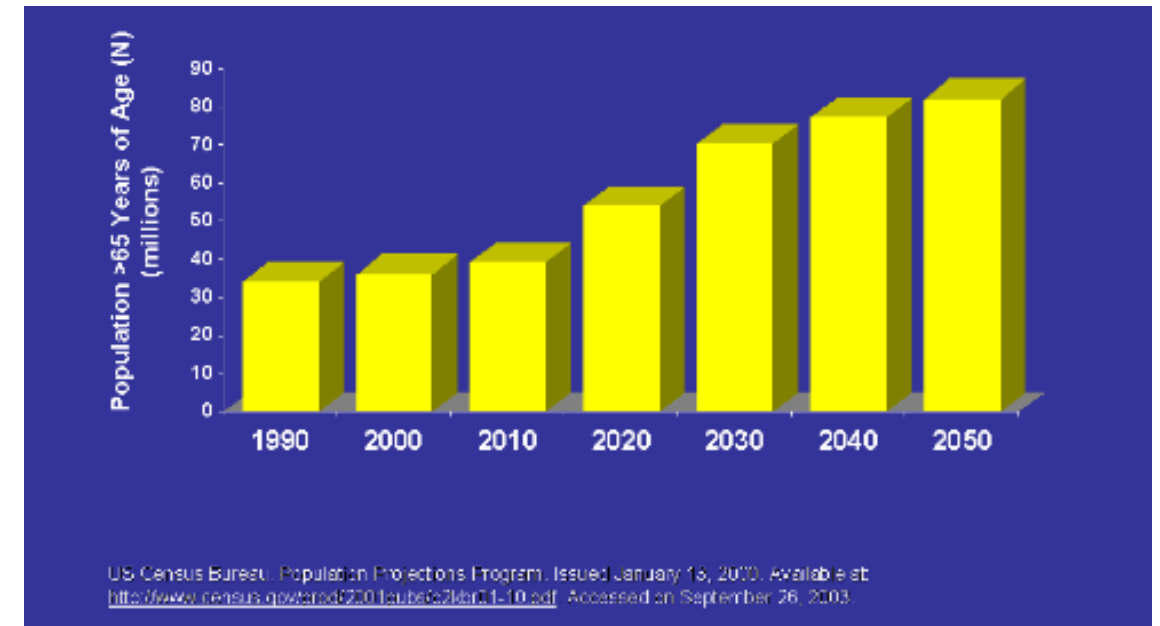
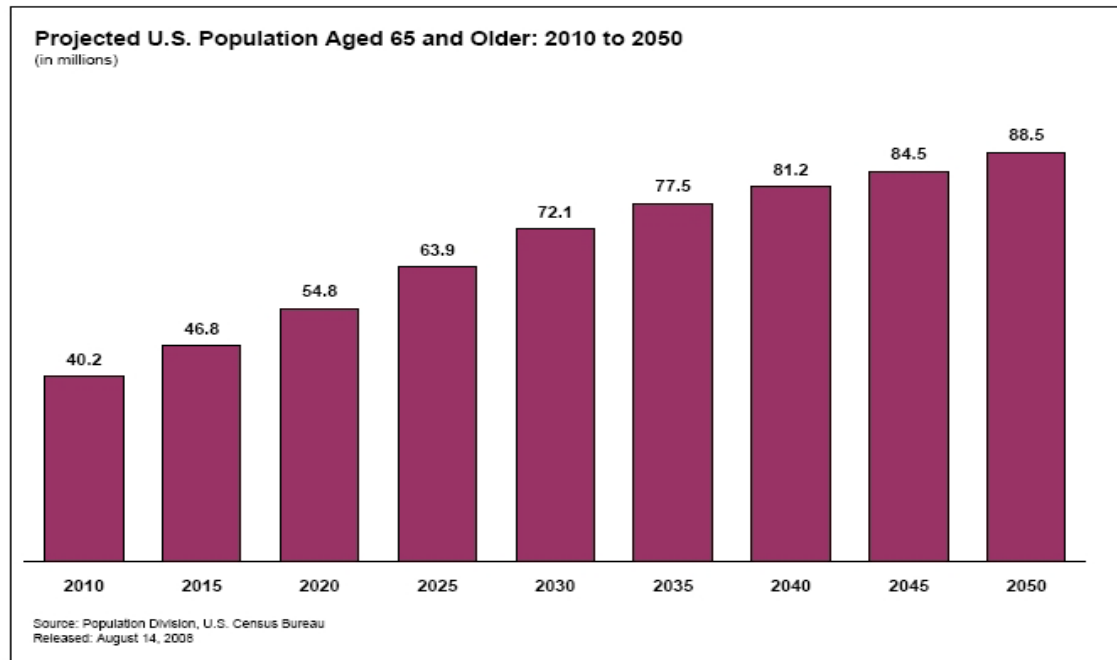
# The Current State of Urology

## Top 10 Reasons for Visits to Urologists<sup>1</sup>

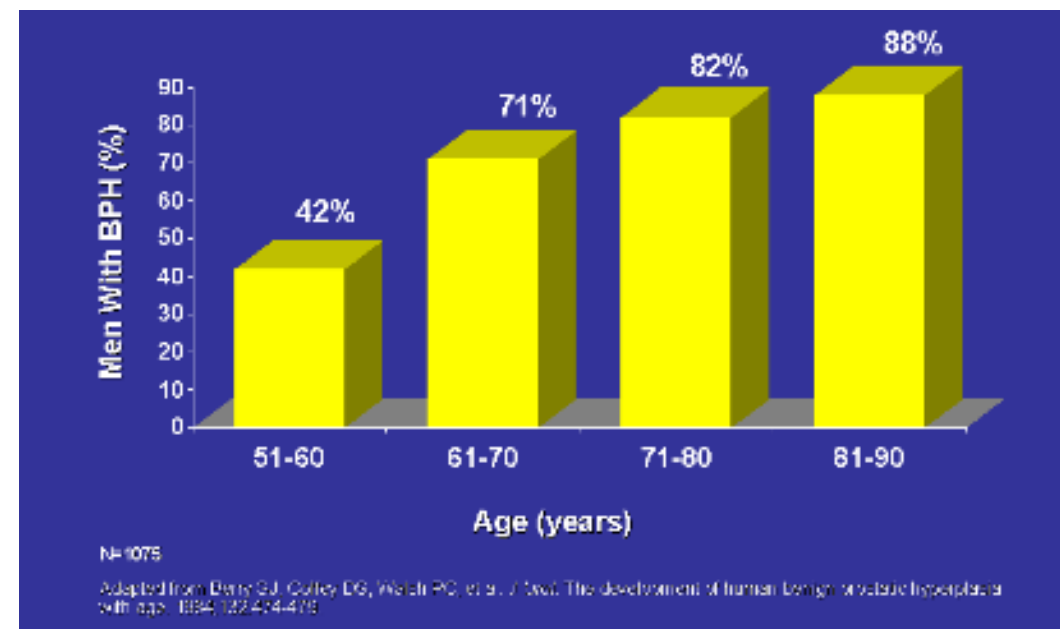
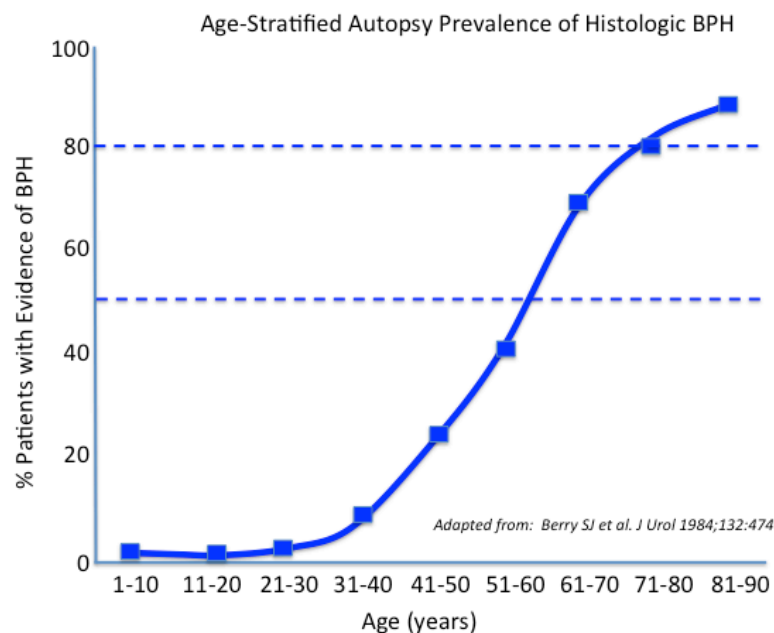


1. IMS Health NDTI Urology Specialty Profile, July 2012 - June 2013

# Aging of the US Population



# ● Prevalence of BPH by Age





# • Symptoms of BPH

## **Obstructive Symptoms**

- Hesitancy
- Weak urine stream
- Intermittency
- Dribbling at the end of urination
- Sensation of incomplete emptying of bladder

## **Irritative Symptoms**

- Nocturia
- Frequency
- Urgency



## ● Distinguishing BPH From Other Causes of LUTS

### **BPH must be distinguished from**

- Prostate cancer<sup>1</sup>
- Prostatitis<sup>2</sup>
- Urinary tract infection<sup>1</sup>
- Urethral stricture<sup>1</sup>
- Bladder dysfunction<sup>1</sup>
- Bladder stones<sup>1</sup>
- Overactive bladder<sup>3</sup>
- Bladder Cancer<sup>1</sup>

1. AUA Practice Guidelines Committee. J Urol. 2003; 170:530-547

2. Krieger JN et al. Urology. 1996;48: 715-722

3. Mostwin JL. Urology. 2002(suppl 5A): 22-27

# • Confounding Co-Morbidities

- Parkinson's Disease
- Dementia
- CVA
- Multiple Sclerosis
- Diabetic Neuropathy
- Spinal Cord Injury
- Advanced age



# • Patient Evaluation

- Medical history
  - Review of patient complaints
  - Patient self-administered questionnaire
    - Use of AUA-SI/IPSS
- Focused physical examination
  - General physical examination, including DRE
  - Neurologic examination
- Laboratory studies
  - Urinalysis
  - PSA assay in appropriate men
  - Urine cytology when appropriate
    - Multiple risk factors
    - Irritative symptoms predominate



## ● When to Refer to a Urologist

- DRE reveals palpable nodules or irregularities<sup>1</sup>
- PSA level 2.5ng/mL (in younger or high-risk men) or yearly increase >0.4ng/mL in PSA level over a 3-year period<sup>1</sup>
  - Higher PSA cutoff point (4.0ng/mL) may be justified in older (<70 years)
- Inadequate response to medication/Intolerable side effects
- Refractory LUTS
- Complications<sup>2</sup>
  - Renal failure
  - Bladder or urethral stones
  - UTI
  - Hematuria
  - Urinary retention

1. Barry MJ et al. In: *Primary Care Medicine*. 4<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Wilkins; 200: 742-747

2. *Clinical Practice Guideline Number 8: Benign prostatic hyperplasia: diagnosis and treatment*. Rockville, Md: US DHHS: 1994. AHCPR Publication NO. 94-0582



# • The Urologist's Evaluation

- History/Physical
- UA +/- PSA
- Uroflowmetry
- Post-void residual volume (PVR)
- Cystoscopy
- TRUS measurement of prostate volume

# AUA Symptom Index Score

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. 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. Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
	None	1 time	2 times	3 times	4 times	5 or more times
7. 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 Symptom Score						

Adapted from AUA Practice Guidelines Committee. *J Urol*. 2003;170:530-547.

# ● The Most Important Question

How much do your urinary symptoms bother you?

- Enough to take daily medicine?
- Enough to consider surgery?

# ● Treatment Options for BPH

- Watchful waiting/Observation
- Pharmacologic therapy
  - Alpha blockers
  - 5AR Inhibitors
  - Tadalafil daily
  - saw palmetto
- Surgical intervention
  - In office, non-heat based tx (Urolift)
  - In office, heat based tx (Rezum)
  - VLAP (laser TURP)
  - TURP
  - TUVF (“Button” procedure)
  - Robotic subtotal prostatectomy

# ● Pharmacologic Approaches to BPH Treatment

- Phyto therapy (Saw palmetto)
  - Herbal product available OTC
  - Approximately 60% subjective response
  - Main problem is potency of the purchased product since the FDA classifies as a “food product”
  - Takes 2 months to work
  - \$6-20 per month
- Alpha-adrenergic blockade
  - Relaxes smooth muscle of prostate/bladder neck
  - Rapidly improves urinary flow and symptoms
  - No long-term issues with medication but about 33% of patients develop significantly decreased effectiveness within several years

# ● Pharmacologic Approaches to BPH Treatment

- 5-alpha reductase inhibitors
  - Reduces prostate size over 5-6 months
  - More gradual symptom improvement
  - Only works in large prostates
  - Lowers serum PSA levels by 40-50%
    - This is often helpful diagnostically in patients with elevated PSA's and prior negative biopsies. If PSA does not fall 40-50%, the rise is likely NOT due to BPH

# “Combination Therapy” Alpha blocker + 5 AR Inhibitor

MTOPS (Medical Therapy of Prostatic Symptoms) Study<sup>1</sup> (finasteride vs doxazosin vs combination vs placebo)



## Results

- 1 year: doxazosin = combo > finasteride > placebo
- 3 year: combo > doxazosin or finasteride > placebo
- Finasteride and combo decreased risk of invasive tx by 64% and 67%, doxazosin did not
- Finasteride and combo both worked much better with larger prostates (>30g)

1. McConnell JD et al. (2003) The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. N Engl J Med 349: 2387–2398

# BPH Drug Side Effects

***“..PFS (Post-Finasteride Syndrome) is an emerging clinical problem..”<sup>9</sup>***

	Long Known Potential Side Effects <sup>1</sup>	Newly Discovered Potential Side Effects
<b>Alpha Blockers</b> 	<ul style="list-style-type: none"><li>• Lightheadedness</li><li>• Headaches</li><li>• Fatigue</li><li>• Ejaculatory dysfunction</li><li>• Insomnia</li><li>• Nasal congestion</li></ul>	<ul style="list-style-type: none"><li>• Intraoperative floppy iris syndrome first described 8 years after tamsulosin introduction<sup>2</sup></li><li>• Increased risk of stroke<sup>3</sup></li><li>• Increased risk of dementia<sup>4</sup></li></ul>
<b>5-ARI</b> 	<ul style="list-style-type: none"><li>• Diminished ejaculate</li><li>• Erectile dysfunction</li><li>• Decreased libido</li><li>• Gynecomastia</li></ul>	<ul style="list-style-type: none"><li>• Depression and self-harm<sup>5</sup></li><li>• Increased risk of metabolic syndromes<sup>6,7</sup></li><li>• Increased risk of dementia<sup>8</sup></li></ul>

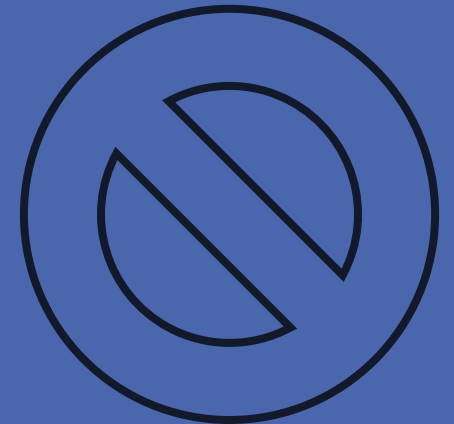
1. AUA Guideline, 2003, 2010, 2. Chang DF, Campbell JR, J Cataract Refract Surg. 2005 Apr; 31(4): 664-673, 3. Lai et al, CMAJ. 2016 Mar 01; 188(4): 255-260, 4. Duan et al, Pharmacoepidemiol Drug Saf. 2018 Mar; 27(3): 340-348, 5. Welk et al, JAMA Intern Med. 2017 May 1; 177(5): 683-691, 6. Traish et al, Horm Mol Biol Clin Investig. 2017 Jun 21; 30(3): 1-16, 7. Wei et al, BMJ. 2019 Apr 10; 365:l12049 8. Welk et al, J Neurol Sci. 2017 Aug 15; 379: 109-111, 9. S. Diviccaro, et al. Neurobiology of Stress 12 2020



# Do BPH Drugs Address Bladder Outlet Obstruction (BOO)?

- The effect of BPH medications on BOO is limited
- The increase in flow is significantly greater than placebo but is still modest<sup>1</sup>
- Bladder muscle (detrusor) overactivity is prevalent in patients with BOO
- Appears to persist after watchful waiting or treatment with medical therapy<sup>2</sup>

ONLY  
**~15-23%**  
INCREASE  
IN FLOW<sup>1</sup>



1. Tubaro, Drugs Aging 2003; 20 (3): 185-195; 2. De Nunzio, J Urol 2003 Feb. 169: 535-539

# Men are Bothered by LUTS, Even When on Rx Therapy



**1 in 3**

men are satisfied with the effectiveness of their medication<sup>1</sup>

**65%**

of men age > 50 seeing a urologist are interested in an alternative to medication for BPH<sup>1</sup>

**82%** OF MEN

over 50 wake up at least 1x per night to urinate on a regular basis



Content based on a survey of 2,000 US men and women conducted by NeoTract in 2017  
©2017 NeoTract, Inc. All rights reserved. MAC00602-01 Rev A

1. Prostate Research Study, Harris Interactive Group 2007



## ● Expert Opinion<sup>1</sup>

\* 100 Urologists and practice administrators were asked:

What percentage of your practice's BPH patients do you think **should** receive advanced BPH therapies?

### # Respondents

A. 0-5%      0

B. 6-10%      9

C. 11-20%      28

D. 21-30%      32


E. > 30%      31

**3 out of 5** of those surveyed thought  
**≥ 20% of BPH patients should**  
**receive advanced treatment**

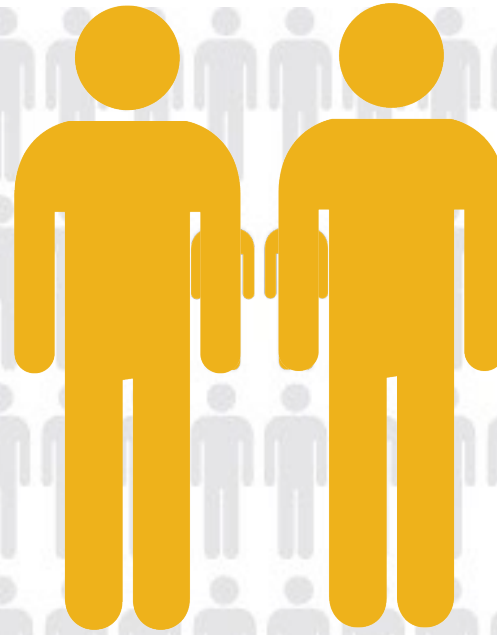
1. UroGPO Conference Survey, November 30, 2018



# BPH Can Be Frustrating for Both Urologists and Patients



2%<sup>1</sup>



1. 2% of men get an advanced BPH procedure. Data on file. NeoTract US Market Model estimates for 2019 based on IQVIA Health Drug and Procedure data.

# ● Urologists and Patients Have Different Points of View

**88%**

of urologists report discussing BPH procedures with moderate to severe BPH patients early after their BPH diagnosis<sup>1</sup>



**23%**

of patients said their doctor suggested minimally invasive procedures as an alternative to medication<sup>2</sup>

1. Data on file: VOC Tracking Study 2019, n = 153 urologists (US)

2. Data on file: Mens Health Survey 2018, n = 203

# ● Current State BPH Patient Population

## Redefining Minimally Invasive BPH Treatment



Watchful Waiting

**34%**

4.3 Million  
Patients



Medical Therapy

**64%**

7.9 Million  
Patients



Surgery/Procedure

**2%**

248,000  
Patients

Many patients  
are looking for  
alternative  
treatments to  
medications.

NeoTract US Market Model estimates for 2020 based  
on IQVIA Health Drug and Procedure data

# Untreated BOO: The Case for Early Intervention

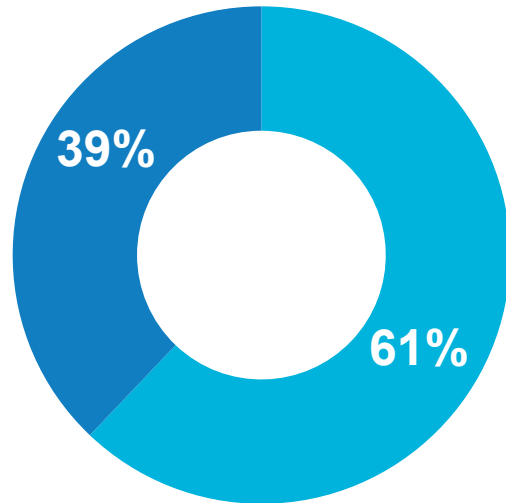
**UNTREATED BOO**

May lead to **irreversible bladder damage**<sup>1</sup>

**SURGERY PROVIDES**

**Maximum** disobstruction

But irreversible bladder damage may have already occurred<sup>1,2</sup>



6 months after open prostatectomy,  
**only 61% of patients** have  
**complete resolution** of LUTS.<sup>1,3</sup>

1. Tubaro, Drugs Aging 2003; 20 (3): 185-195; 2. Flanigan, J Urol 1998 July; 160: 12-17; 3. Tubaro, J Urol 2001 July; 166: 172-176

# History: BPH Procedures

## 1. Remove prostate tissue

- Enucleation: Simple, HoLEP, Robotic simple
- Resection: TURP, TUIP, Bipolar
- Vaporization: PVP laser, HoLAP, Button

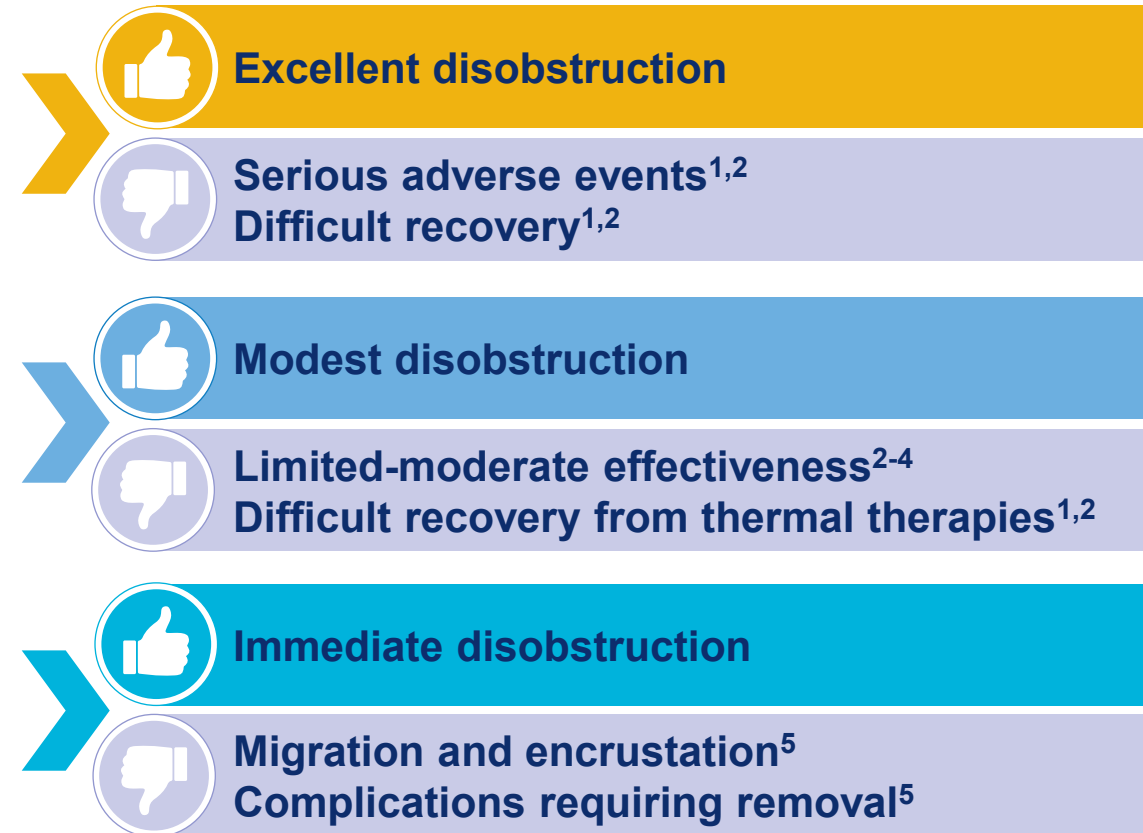
## 2. Injure/heat/ablate prostate tissue

- Thermal: Microwave, TUNA
- Chemical: Ethanol, Toxins

## 3. Open the prostate

- Stents

1. Miano, Med Sci Mont 2008; 14(7): RA94-102; 2. AUA Guidelines 2003;  
3. Lusuardi, Res and Reports Urol 2014; 6: 67-70; 4. Marberger, Eur Urol 2013;  
63: 496-503; 5. Peyton, Can J Urol 2015; 22 (Suppl 1): 75-81





# • Surgical Treatment

- Minimally Invasive
- Heat based therapies
  - Rezum - Steam injection
- Non-heat based therapies
  - Prostatic Urethral Lift (PUL)
- Invasive
  - VLAP - Visual Laser Ablation of the Prostate (Laser TURP)
  - TUVP – TransUrethral Vaporization of the Prostate
  - TURP – TransUrethral Resection of the Prostate
  - Robotic subtotal prostatectomy

# ● Transurethral Resection of the Prostate TURP

- TURP = The “Gold Standard”
- Requires general or spinal anesthesia
- Must be off anti-coag/anti-platelet meds
- 0-2 night hospitalization with catheter
- 90% overall success
- Tissue is available for pathologic examination

# Transurethral Vaporization of the Prostate TUVP

- Requires general or spinal anesthesia
- Must be off anti-coag/anti-platelet meds
- Similar to a TURP in rapidity of effectiveness and overall success (>90%)
- Less bleeding, quicker recovery, less pain, typically overnight stay
- Tissue not available for pathologic examination

# ● Resectoscopes



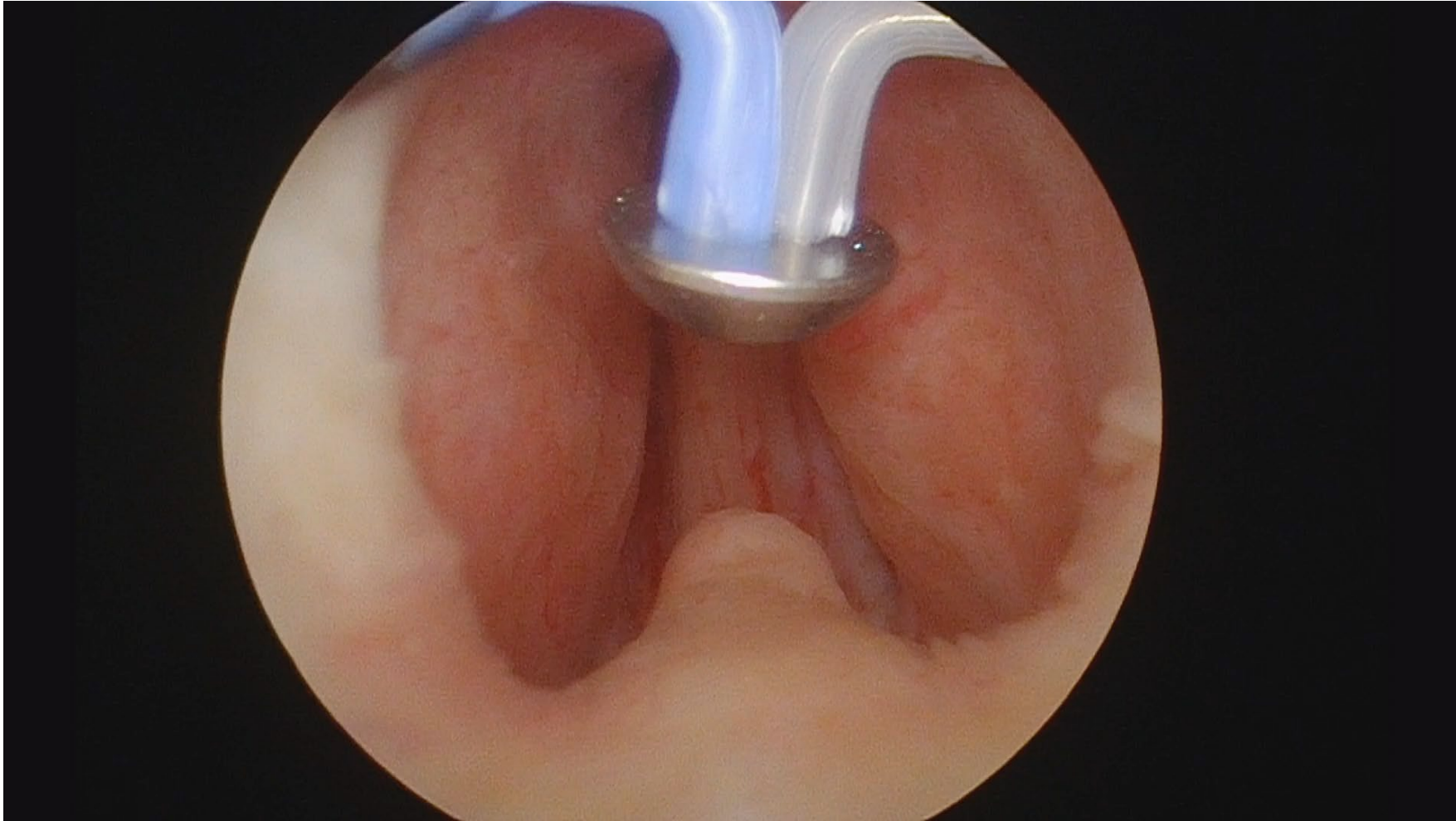
*TURP Loop*



*TUVP Button*



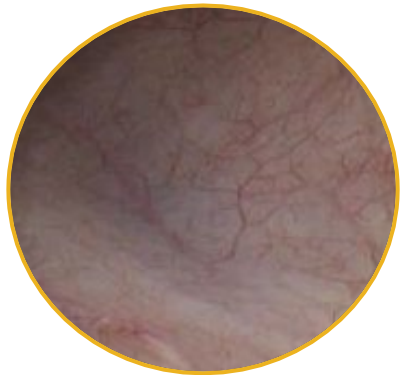
# • TUV



Roehrborn Urol Clin N Am 2016

“Large clinical need for an effective treatment... less invasive than surgery” – AUA<sup>1</sup>

### From healthy bladder to permanent damage



**Healthy  
Bladder**



**Bladder  
Worsens**



**Permanently  
Damaged**

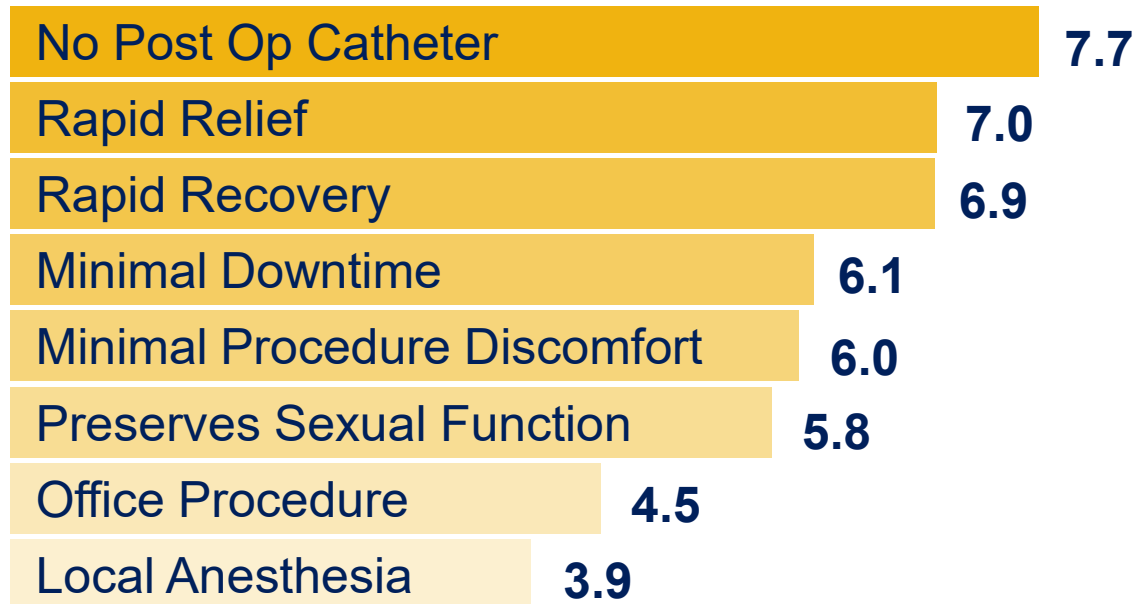
“

*“Since many men discontinue medical therapy, yet proportionately few seek surgery, there is a large clinical need for an effective treatment that is less invasive than surgery. With this treatment class, perhaps a significant portion of men with BOO who have stopped medical therapy can be treated prior to impending bladder dysfunction.”*

1. AUA Guideline 2018, amended 2019

# ● How Do Men Define “Minimally Invasive”?

## Men's Perceptions of Importance When Considering a Minimally Invasive Procedure for BPH<sup>1</sup>



**10 = Most Important**

## Prostatic Urethral Lift Advantages

- Typically no catheter required after treatment<sup>2</sup>
- Rapid symptom relief and recovery<sup>2,3</sup>
- Preservation of sexual function<sup>\*2,4</sup>
- In-office procedure

*\*No instances of new, sustained erectile or ejaculatory dysfunction*

1. NeoTract-sponsored Men's Health Survey, November 2018. n = 1,000 men (88% of respondents were over age 45 years of age). Respondents compared items to each other by placing them in order of importance.; 2. Roerbom J Urology 2013; 3. Shore Can J Urology 2014 Local Study; 4. McVary J Sex Medicine 2014

# What Would a Solution Look Like from the Urologist's Point of View?



## What Urologists Wanted

## What the PUL Offers



**Rapid relief with minimal side effects**

- Most side effects resolve within 2-4 weeks
- **No impact** on sexual function<sup>\*1,2</sup>
- **No/Reduced** need for post op catheter



**Performed in office and outpatient setting**

- **Routinely**



**Straightforward procedure**

- Reliable, **reproducible**



**Durable**

- 2-3% procedural retreatment per year (vs 1-2% TURP)<sup>3</sup>



**Broad reimbursement coverage**

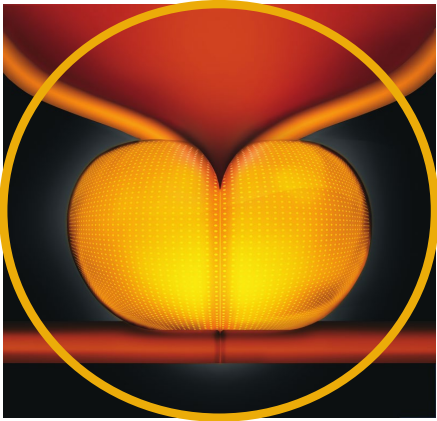
- Covered by Medicare and all major private insurers when medical criteria are met

\*No instances of new, sustained erectile or ejaculatory dysfunction in the FDA pivotal study

1. McVary, J Sex Med 2014; 2. Roehrborn, J Urology 2013 LIFT Study; 3. Bachmann A, Tubaro A, Barber N, et al. J Urol 2015 GOLIATH

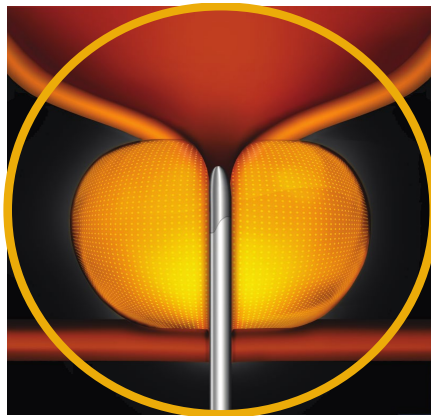


# How the PUL Works



## Enlarged Prostate

An enlarged prostate can narrow or even block the urethra.



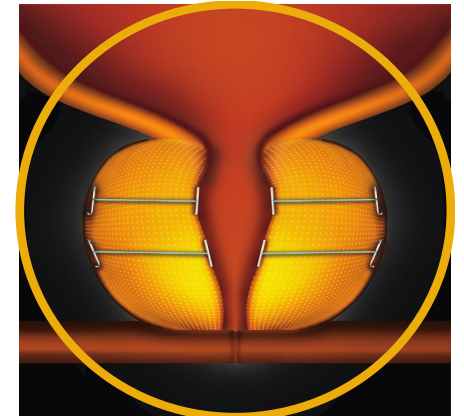
## Step 1

The Delivery Device is placed through the obstructed urethra to access the enlarged prostate.



## Step 2

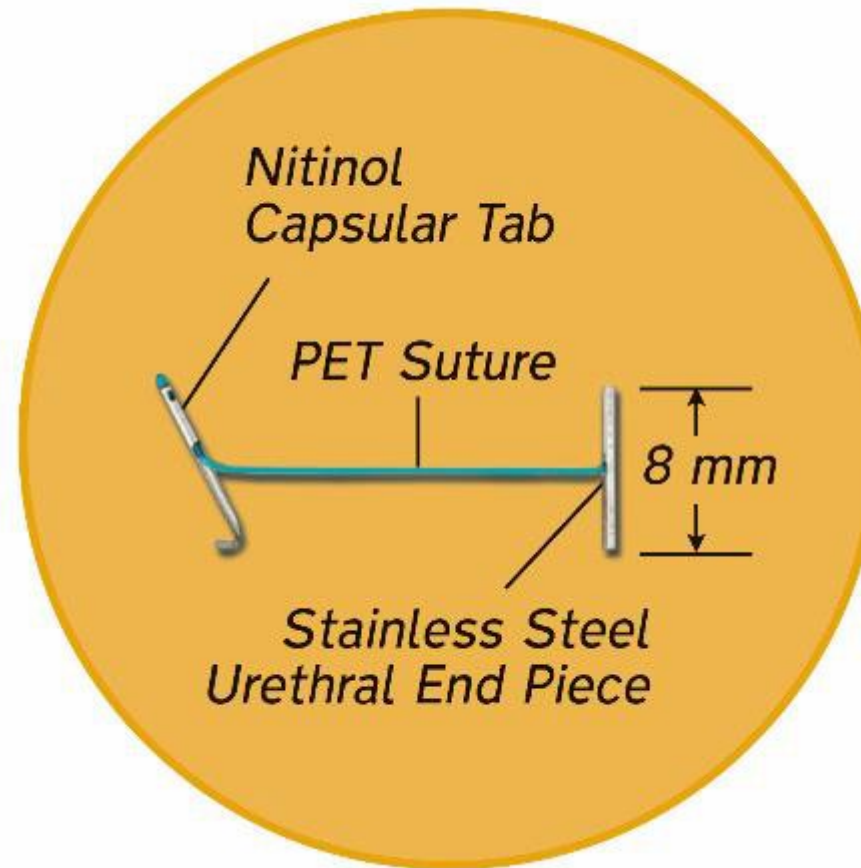
Small Implants are permanently placed to lift and hold the enlarged prostate tissue out of the way and increase the opening of the urethra.



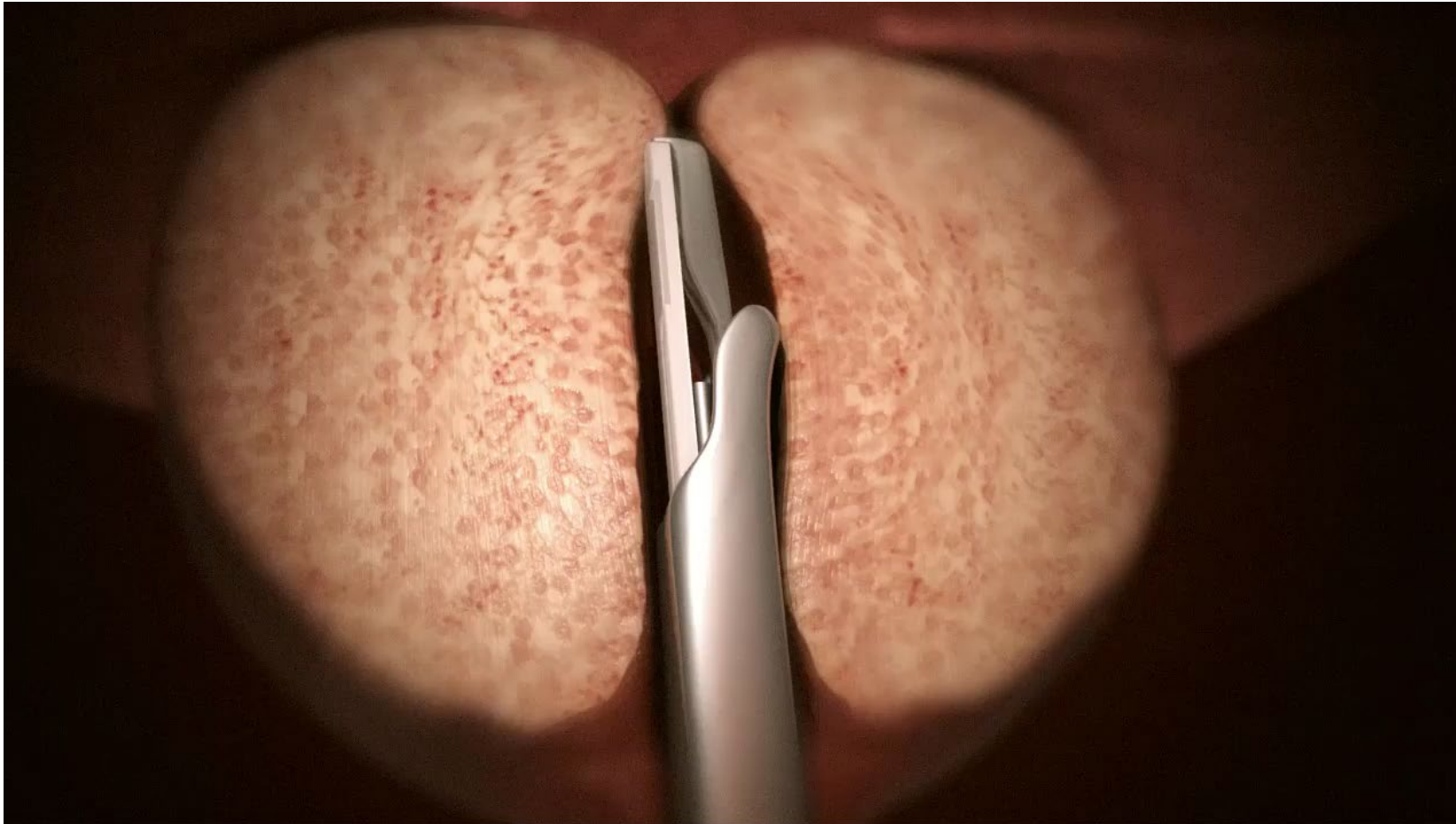
## Step 3

The Delivery Device is removed, leaving an open urethra designed to provide symptom relief.

# UroLift® Permanent Implant

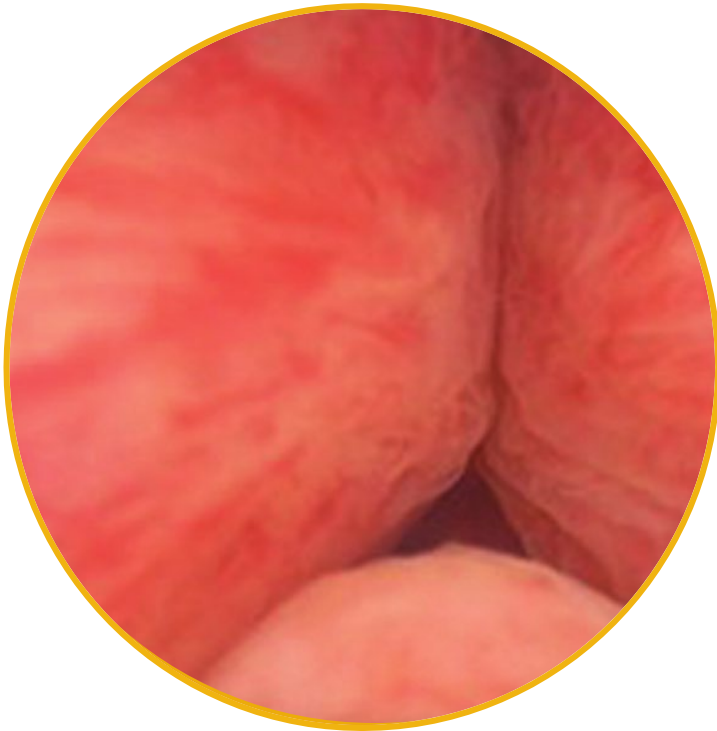


# UroLift® Animation

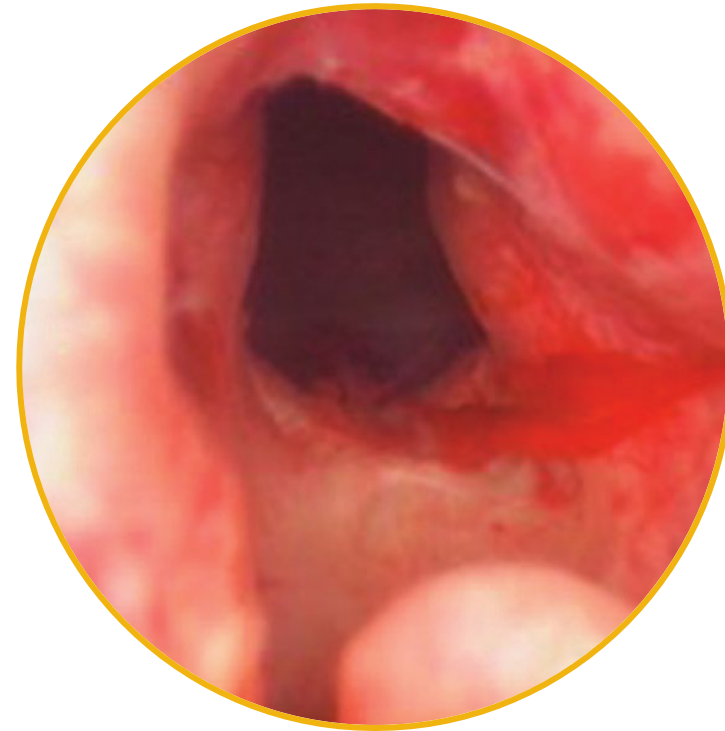


# ● PUL Treatment Images

**Before Treatment:**  
Obstructed Channel



**After Treatment:**  
Open Channel

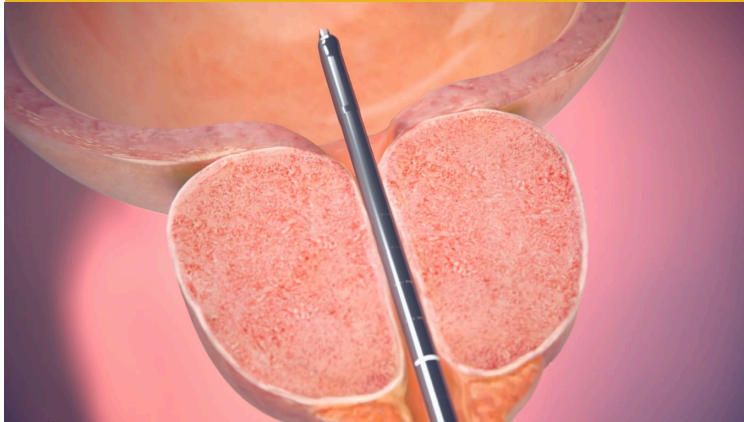


Images representative of a typical effect  
Individual results may vary



# Visual Demonstrations

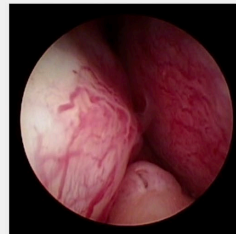
## The PUL System Animation Video



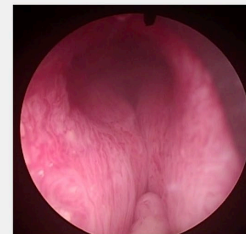
[Click here to view](#)

## Procedure Video

UROLIFT



Before

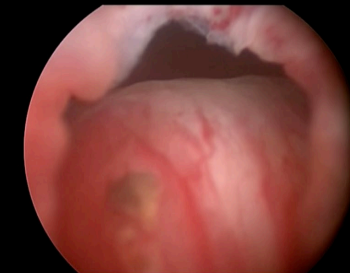


After

[Click here to view](#)

## Obstructive Median Lobe Video

### Median Lobe Technique Case Video #1




















[Click here to view](#)



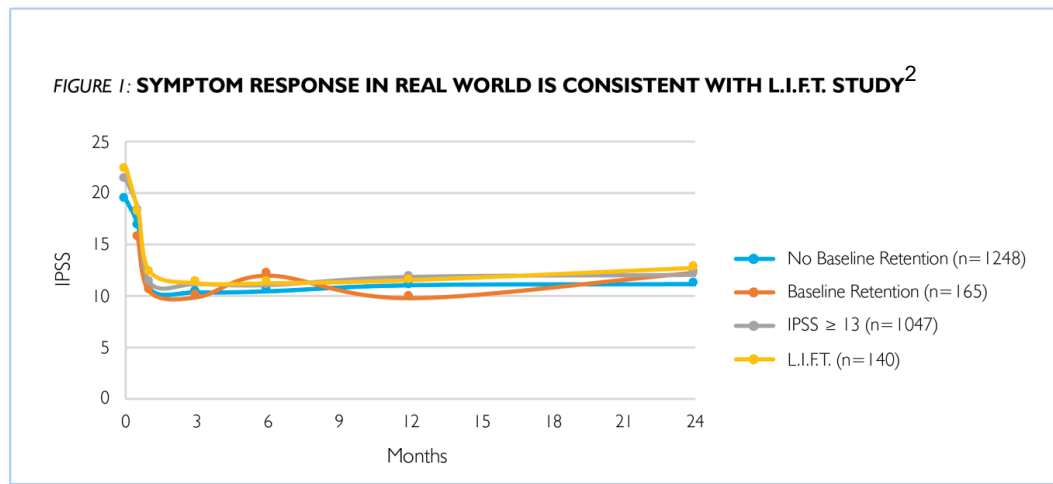


# Extensive, Peer-Reviewed Clinical Data Support the PUL procedure

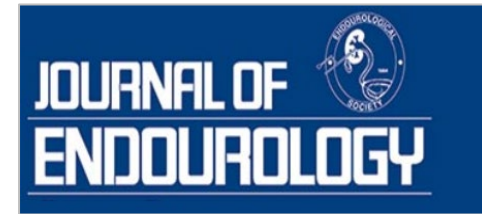
			 Prospective Crossover Study	 European Association of Urology BPH6: Randomized to TURP				
 Safety & Feasibility	 European Association of Urology 'Real-World' European Registry	 LIFT Randomized Controlled Trial	 Sexual Function  LOCAL Study	 3 Year LIFT	 2 Year Crossover	 5 Year LIFT	 MedLift	 Real World Retrospective
2011	2012	2013	2014	2015	2016	2017	2018	2019
 Preservation of Sexual Function	 2 Year Durability		 2 Year LIFT			 2 Year BPH6	 German 'Real-World' Study	

# The PUL System has Extensive Clinical Data Support

- Five year durability<sup>1</sup>
- Proven in the real world
- Consistent results across studies and in clinical practice



1. Roehrborn et al. Can J Urol 2017; 2. Eure et al J Endourol 2019



# The Prostate Urethral Lift: Part of the Standard of Care

## AUA GUIDELINE HIGHLIGHTS:

- Urologists “should consider” PUL....
- Patients “*should be made aware that surgical treatment can cause ejaculatory dysfunction (EjD) and may worsen ED.*”
- “*In men so concerned about new onset of ED and/or EjD, PUL likely does not pose additional risk.*”

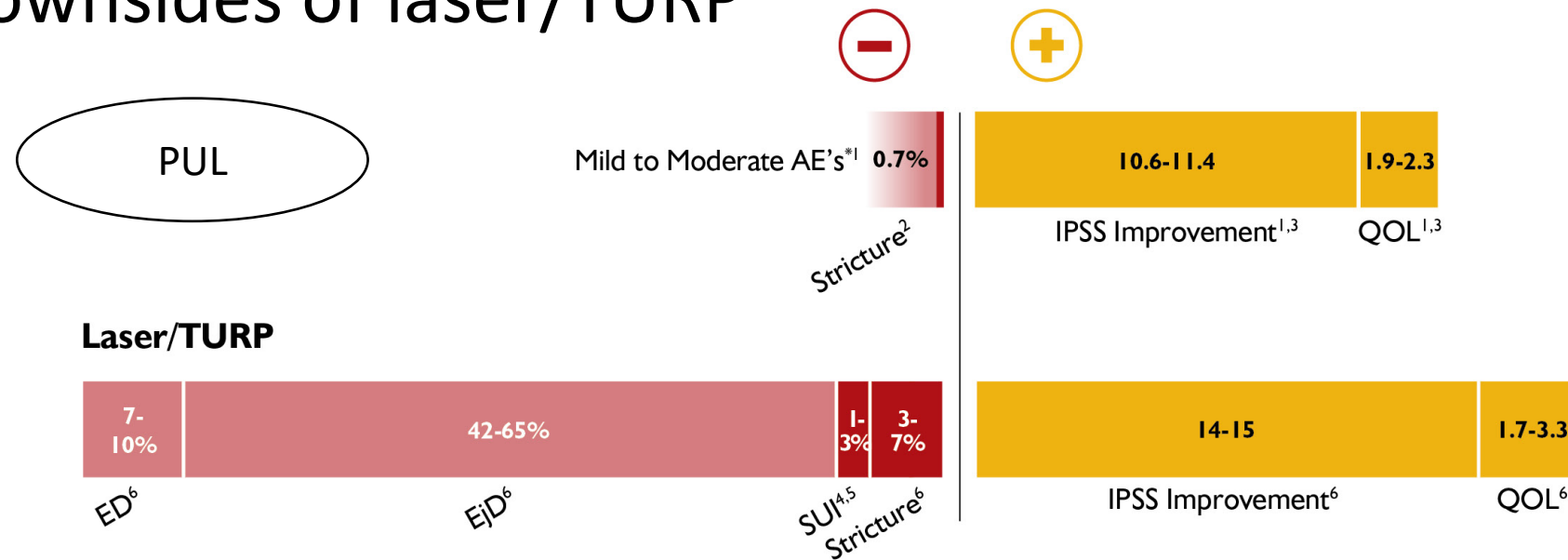


American  
Urological  
Association



# ● Safe and Effective

Significant improvement without the significant permanent downsides of laser/TURP



SUI – Stress Urinary Incontinence    ED – Erectile Dysfunction  
EjD – Ejaculatory Dysfunction    QOL – Quality of Life

Indicated for the treatment of symptoms of an enlarged prostate up to 100cc in men 45 years or older. As with any medical procedure, individual results may vary. Most common side effects are temporary and include hematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence.<sup>1</sup> Rare side effects, including bleeding and infection, may lead to serious outcomes and may require intervention. Consult the Instructions for Use (IFU) for more information. There was no occurrence of new onset, sustained erectile or ejaculatory function in the L.I.F.T. study.

1. Roehrborn, J Urol 2013; 2. Roehrborn, Urol Practice 2015; 3. Sonksen, Eur Urol 2015; 4. Cindolo et al. Int Urol Nephrol 2017; 5. Noordhoff et al. Neurourol Urodyn 2019; 6. AUA BPH Guidelines 2003, 2010

# US BPH Patients have Access to PUL in All Sites of Care

Covered by Medicare, and all national and major commercial plans, when medical criteria are met



Dedicated Category 1 CPT and HCPCS codes with all sites of care (e.g. office, ASC, outpatient hospital)



0-Day global period vs. 90-days for all other BPH procedures



Established physician and facility payments in all sites of care



Geisinger



Humana



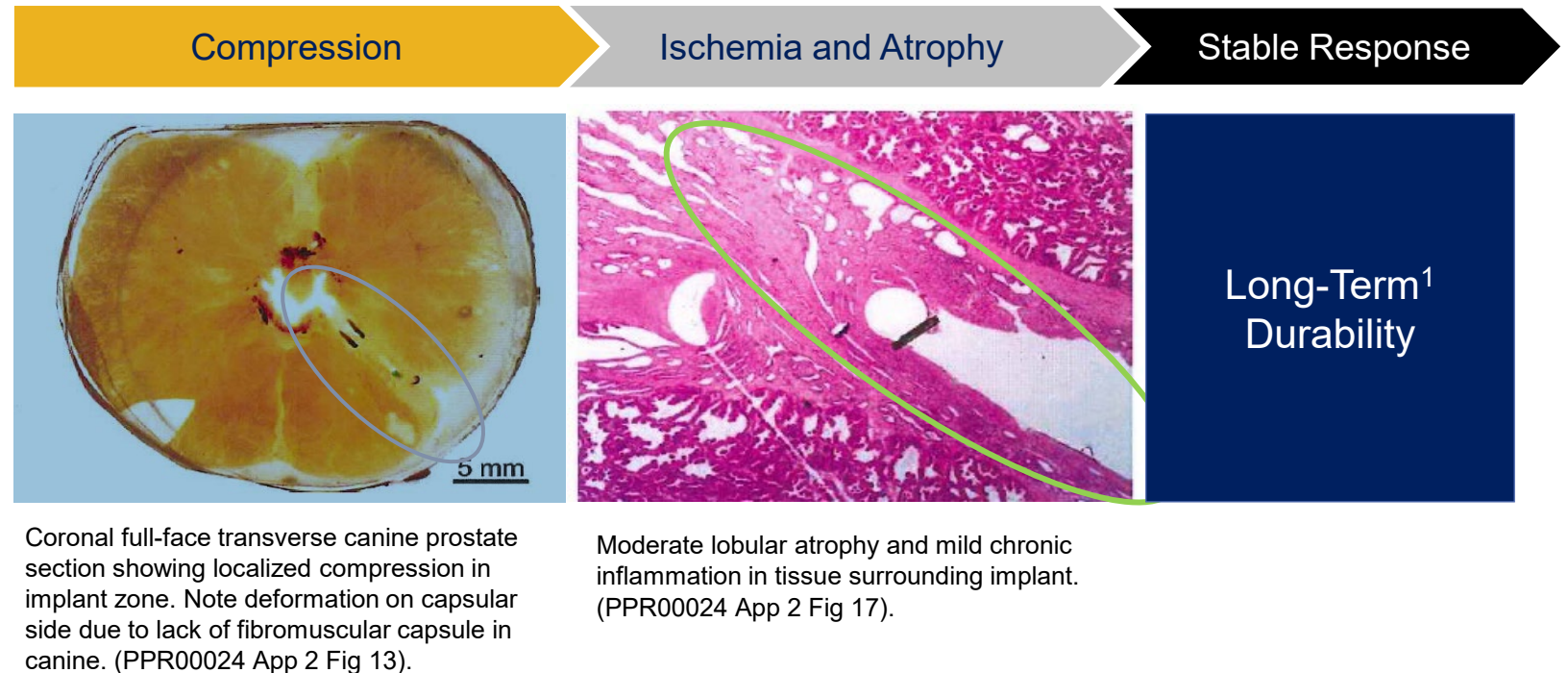
Anthem





# *Pre-Clinical Animal Study Explains Durability*

The combination of the mechanical effect of pulling back the prostate **and** tissue atrophy, together, sustain results.



1. Roerborn et al Can J Urol 2017

# ● Post-Treatment Expectations

- Symptom improvement may start within 2 weeks, may continue to improve up to 3 months
- Some irritation such as pain upon urinating, small amount of blood in urine, pelvic discomfort or urgency for some time after the procedure
- Typically return to preoperative activity level within 5-9 days
- Symptom relief seems durable beyond 5 years.

# Rapid Return to Work and Pre-Op Activities: L.O.C.A.L. Study Results

- 86% achieved high quality recovery<sup>1</sup> within 1 month
- Satisfaction (via Patient General Impression Index):
  - 90% reported improvement in their condition

Perioperative Assessments	Mean	SD
Return to work (days)	2.8	3.7
Return to preoperative activity* (days)	5.1	5.8
Work Productivity at 1 Month		
Work missed	0%	0%
Overall work impairment	3%	9%
Impairment in activity	8%	19%

<sup>1</sup>High quality recovery defined as  $\geq 80$  on the Quality of Recovery VAS

Shore et al. Can J Urol 2014; 21(1): 7094-7101.

# PUL vs TURP:

## No Difference in Quality of Life

- Despite predicted differences in IPSS and Qmax, improvement in quality of life was not different.
- Important to evaluate with patients risks vs returns for each treatment option.

	Change at 1 year		Difference p-value
	PUL	TURP	
IPSS	-11.4	-15.4	0.02
Qmax [mL/sec]	+4.0	+13.7	<0.001
QoL	-2.8	-3.1	0.4 Not Significant

Sonksen et al. Eur Urol 2015

# ● Summary

## Patient Selection:

### Men With BPH Who...

- ✓ Want increased symptom relief
- ✓ Want off BPH medications
- ✓ Would prefer a less invasive solution
- ✓ Want to preserve sexual function
- ✓ Are concerned about surgery

### Candidates for TURP or Laser Who...

- ✓ Are concerned about complications
- ✓ Want to preserve sexual function
- ✓ Want a more rapid return to daily life

# THANK YOU

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UCA | VAN SCOTT  
CANCER CENTER

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CENTER