
New Less Invasive Management of BPH

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- Faculty: Dean Elterman, MD MSc FRCSC
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- Relationships with commercial interests:
 - Grants/Research Support: Boston Scientific, Pfizer, Clarion
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 - Consulting: Medtronic, BSCI, Coloplast, Axonics
 - Investigator: BSCI, Meditate, Neotract, Medtronic, Axonics, Procept Biorobotics

Learning Objectives:

To review CUA guidelines for treatment of BPH-LUTS

To review new technologies as alternatives to surgical interventions for BPH-LUTS

To discuss patient selection for various treatment modalities

BPH is a significant Men's Health disease

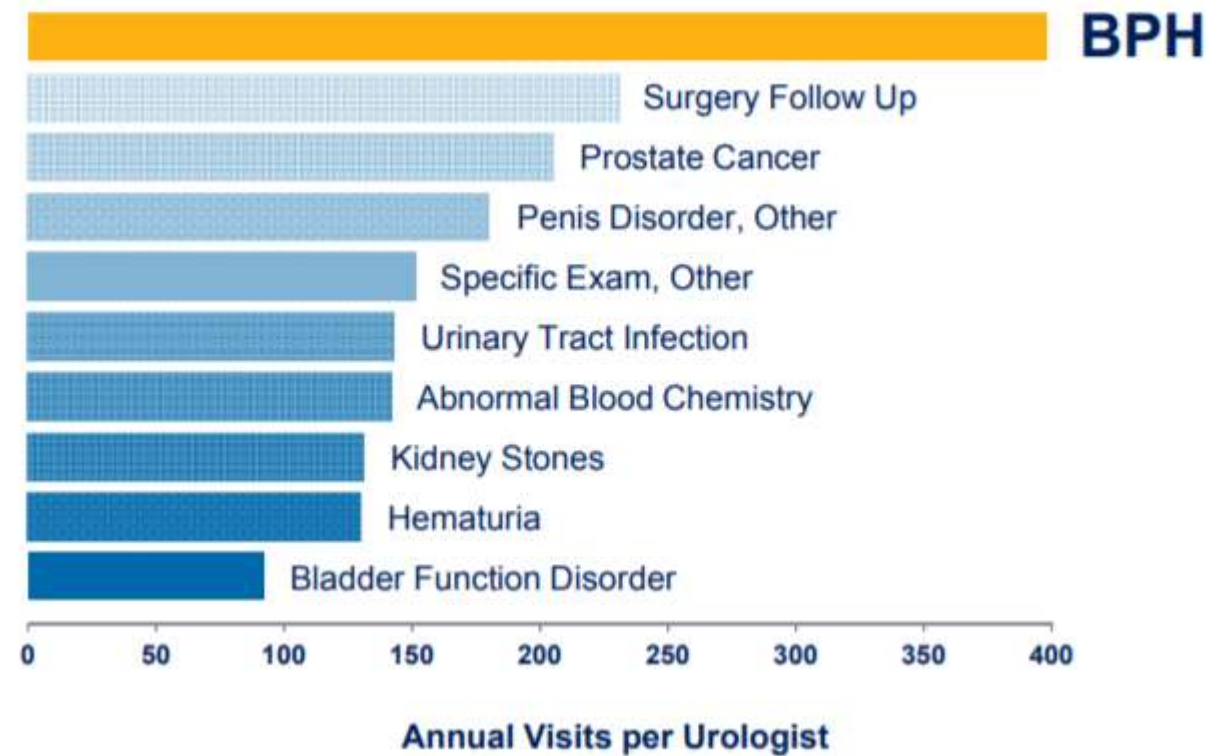
38M

Men in US with BPH pathology¹

\$4B

Annual BPH treatment costs in US ¹

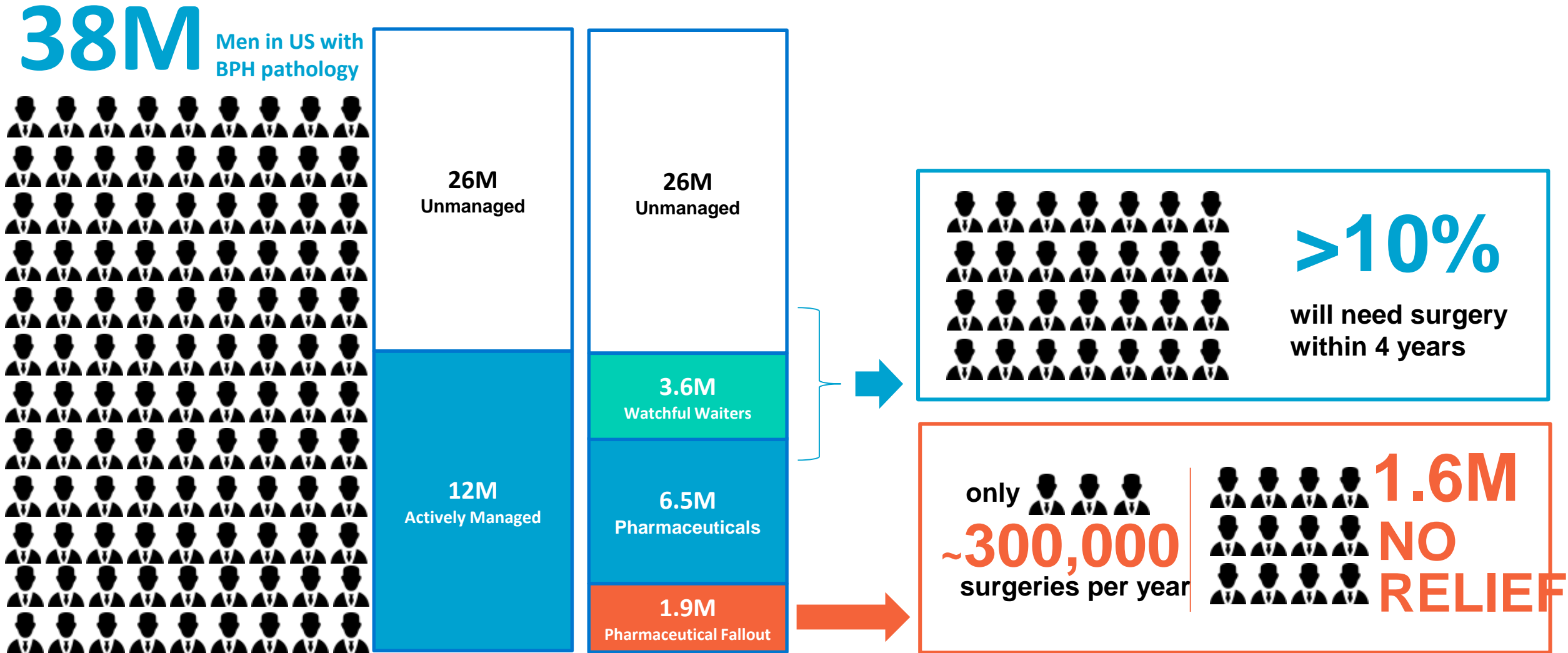
BPH is the #1 reason men visit a urologist²



¹Vuichoud, C, Loughlin, K. Benign prostatic hyperplasia: epidemiology, economics and evaluation. Can J Urol. 2015 Oct;22 Suppl 1:1-6.

²IMS Health NDTI Urology Specialty Profile, July 2012-June 2013

Surgical Market is Underserved & Expected to Grow

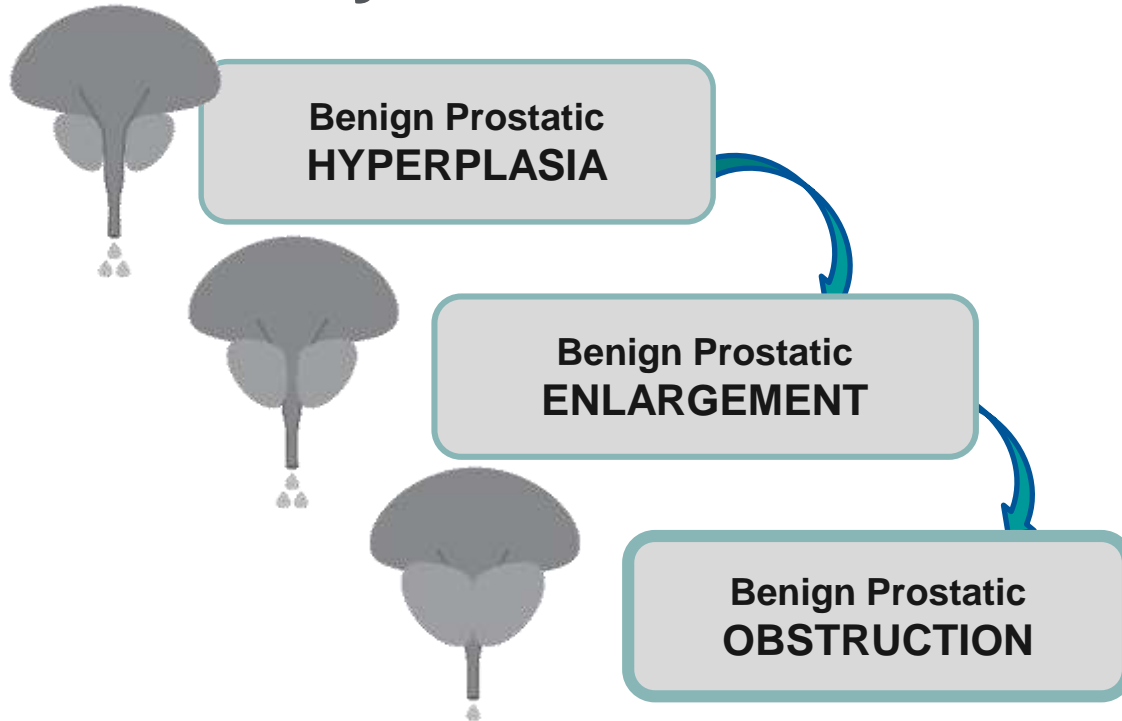


Vuichoud, C, Loughlin, K. Benign prostatic hyperplasia: epidemiology, economics and evaluation. Can J Urol. 2015 Oct;22 Suppl 1:1-6.

Emberton, M, et al. Understanding patient and physician perceptions of benign prostatic hyperplasia in Europe; the Prostate Research on Behaviour and Education (PROBE) Survey. Int J Clin Pract, January 2008, 62, 1, 18-26

Male LUTS Have Traditionally Been Associated With Benign Prostatic Hyperplasia (BPH)

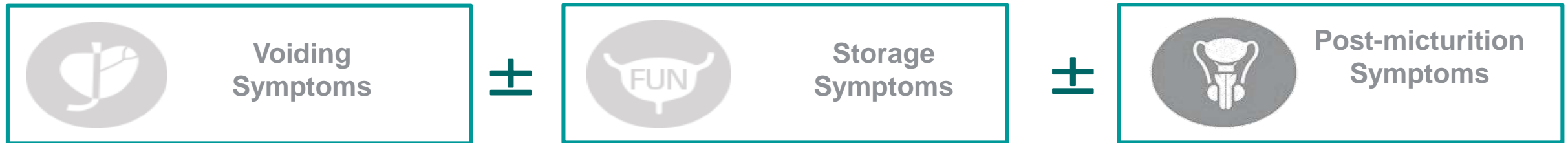
How has our understanding of BPH evolved into what we know today?



Only **25-50%** of men with BPH report voiding LUTS, as symptoms do not present until prostatic enlargement has progressed to cause obstruction.

Individualized Treatment Plans Are An Important Aspect Of Male LUTS Management

Male LUTS can present differently in each patient:

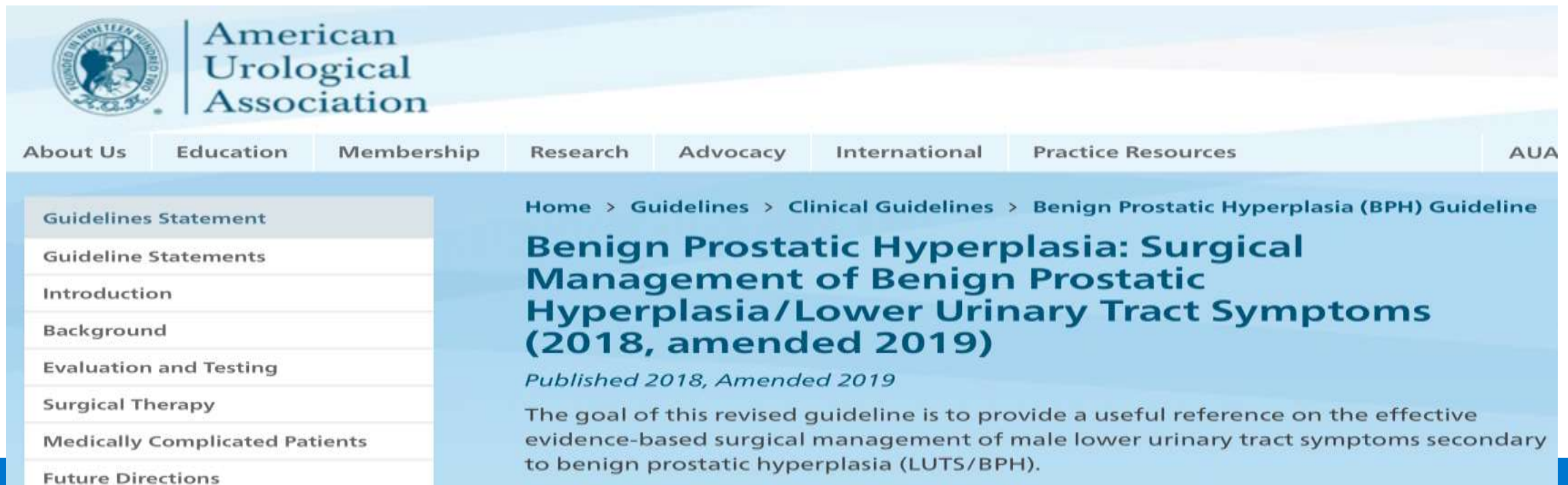


“Therapeutic decision-making should be guided by the severity of the symptoms, the degree of bother, and patient preference.”

- CUA Guidelines, 2010

Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH): 2018 update

J. Curtis Nickel, MD¹; Lorne Aaron, MD²; Jack Barkin, MD³; Dean Elterman, MD⁴; Mahmoud Nachabé, MD²; Kevin C. Zorn, MD⁵



The screenshot shows the American Urological Association (AUA) website. The header includes the AUA logo and the text "American Urological Association". Below the header is a navigation menu with the following items: About Us, Education, Membership, Research, Advocacy, International, Practice Resources, and AUA. The main content area displays the breadcrumb trail: Home > Guidelines > Clinical Guidelines > Benign Prostatic Hyperplasia (BPH) Guideline. The title of the guideline is "Benign Prostatic Hyperplasia: Surgical Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms (2018, amended 2019)". Below the title, it states "Published 2018, Amended 2019". The introductory text reads: "The goal of this revised guideline is to provide a useful reference on the effective evidence-based surgical management of male lower urinary tract symptoms secondary to benign prostatic hyperplasia (LUTS/BPH)."

American Urological Association

About Us | Education | Membership | Research | Advocacy | International | Practice Resources | AUA

Home > Guidelines > Clinical Guidelines > Benign Prostatic Hyperplasia (BPH) Guideline

Benign Prostatic Hyperplasia: Surgical Management of Benign Prostatic Hyperplasia/Lower Urinary Tract Symptoms (2018, amended 2019)

Published 2018, Amended 2019

The goal of this revised guideline is to provide a useful reference on the effective evidence-based surgical management of male lower urinary tract symptoms secondary to benign prostatic hyperplasia (LUTS/BPH).

Guidelines Statement
Guideline Statements
Introduction
Background
Evaluation and Testing
Surgical Therapy
Medically Complicated Patients
Future Directions

Medical Treatment of BPH-LUTS

- α -adrenergic antagonists (α -blocker)
 - For patients with signs and symptoms of BPH
- 5α -reductase inhibitors (5ARIs)
 - For patients with symptomatic BPH and prostate enlargement
- Combination therapy (α -blocker + 5ARIs)
 - For patients with symptomatic BPH and prostate enlargement
- Phosphodiesterase type 5 (PDE5) inhibitors
 - For patients with signs and symptoms of BPH
 - For patients with erectile dysfunction and signs and symptoms of BPH
- PLUS BLADDER MEDS

Medical Management of BPH

α –Blockers – Common Side-Effects

- Fatigue/asthenia (physical weakness, lack of energy)
- Runny nose/rhinitis
- Dizziness: due to CNS effect (3%)
- Syncope/Hypotension (5%)
- Headache (2%)
- GI upset
- Retrograde ejaculation (3%)
- Priapism

Medical Management of BPH

5 α –Reductase Inhibitors: Side-Effects

- Erectile Dysfunction
 - (most common S/E on MTOPS, PLESS and PCPT)
- Decreased libido
- Ejaculatory disorder
- Breast tenderness/swelling

Surgical Treatment of BPH

Peri-Op Complications

- Retention
- UTI/Sepsis
- Bleeding
- Clot retention
- UO injury
- Rectal injury
- TUR Syndrome

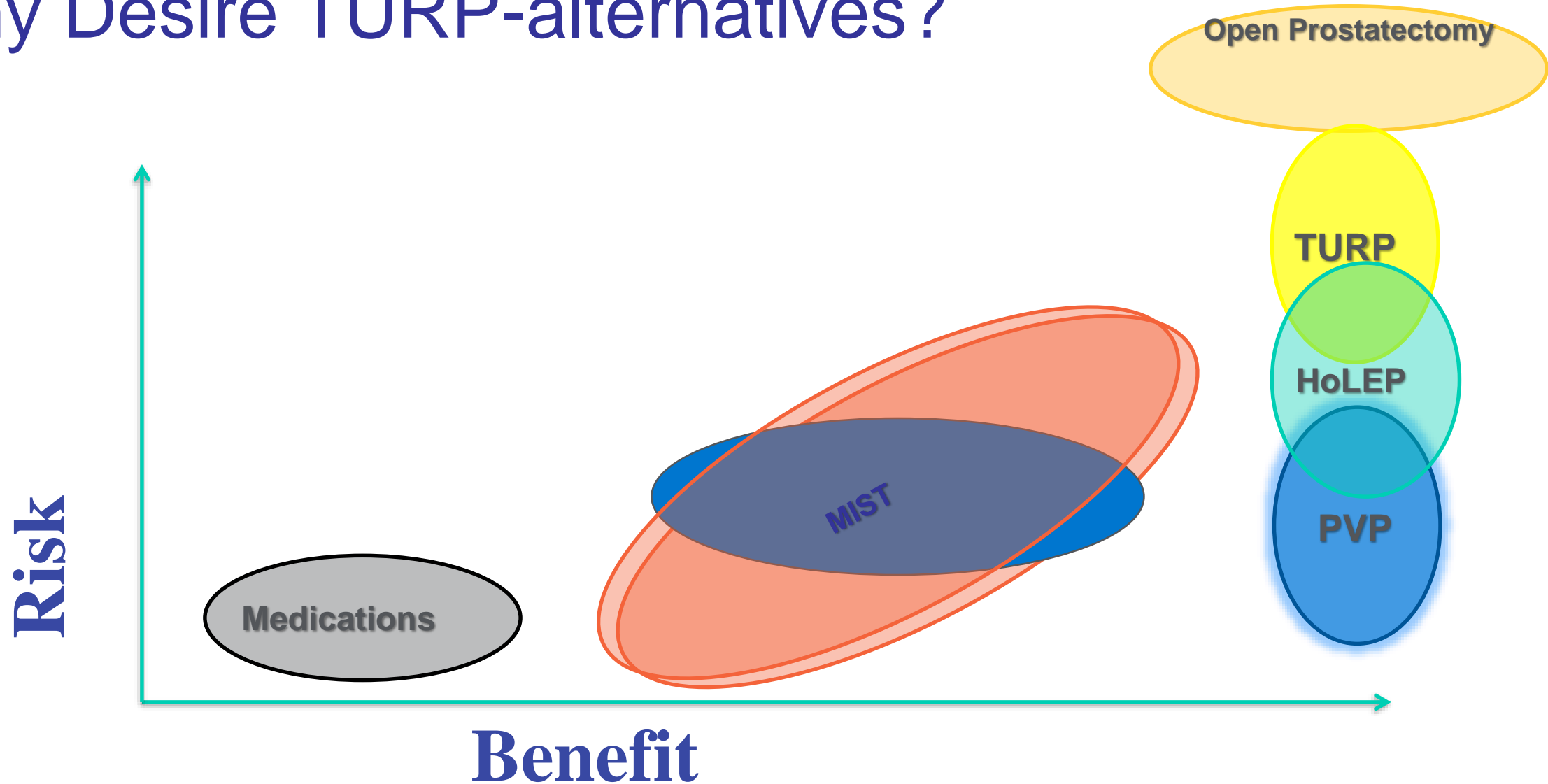
Late Post-Op Complications

- Delayed bleeding
- BN contracture
- Urethral stricture
- Meatal stenosis
- Incontinence
- ED

Indications for BPH Surgery

- 1) Recurrent or refractory urinary retention
- 2) Recurrent urinary tract infections (UTIs)
- 3) Bladder stones
- 4) Recurrent hematuria
- 5) Renal dysfunction secondary to BPH
- 6) *Symptom deterioration despite medical therapy*
- 7) *Patient preference*

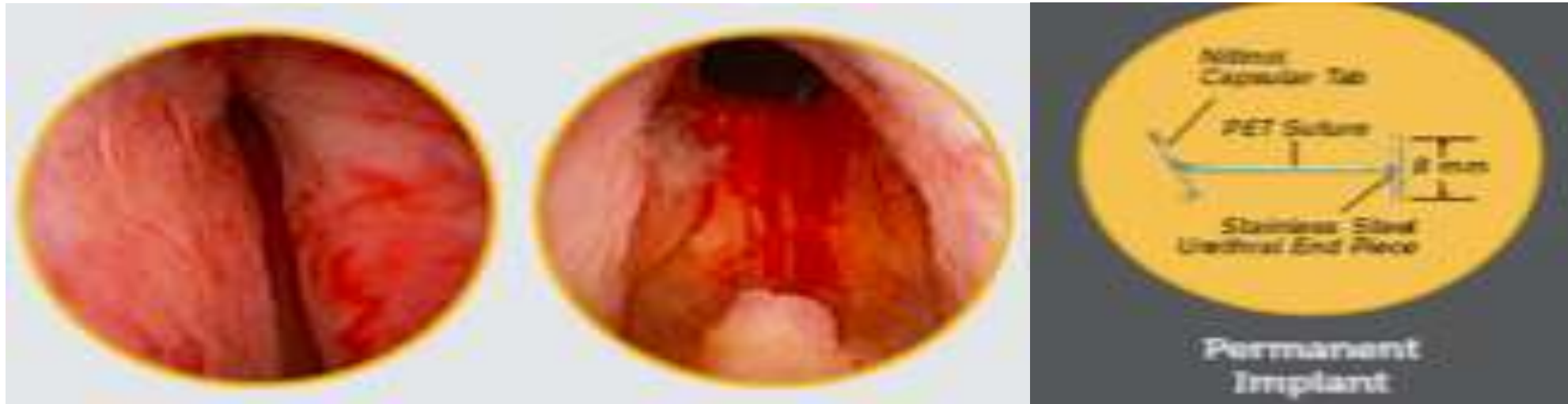
Why Desire TURP-alternatives?



BPH Therapy Wish List

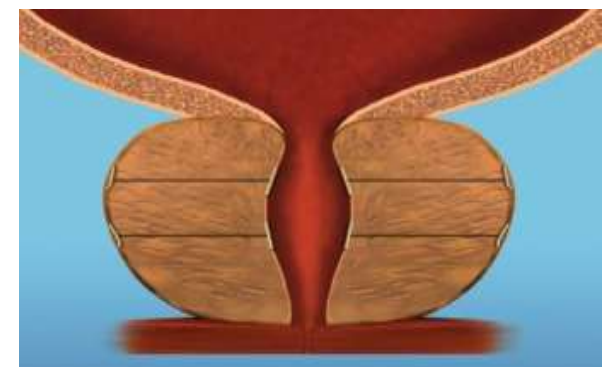
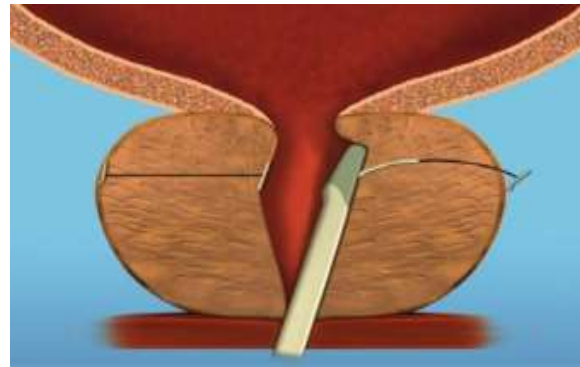
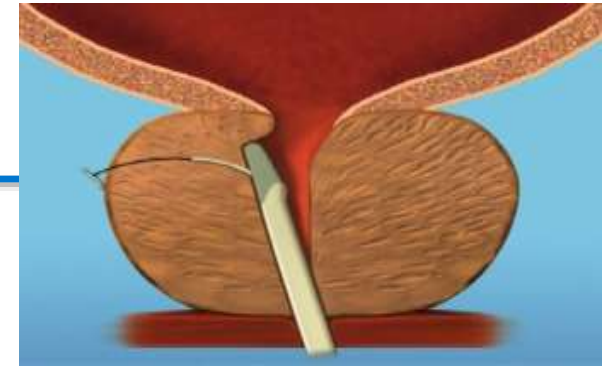
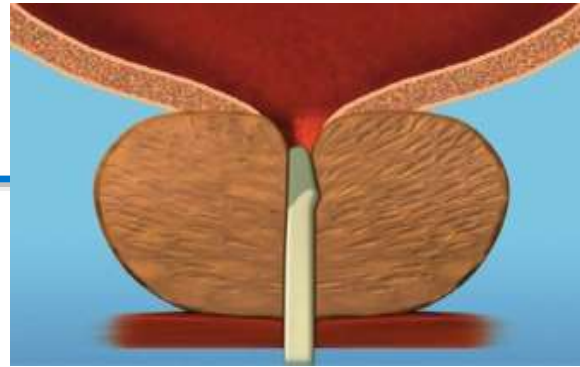
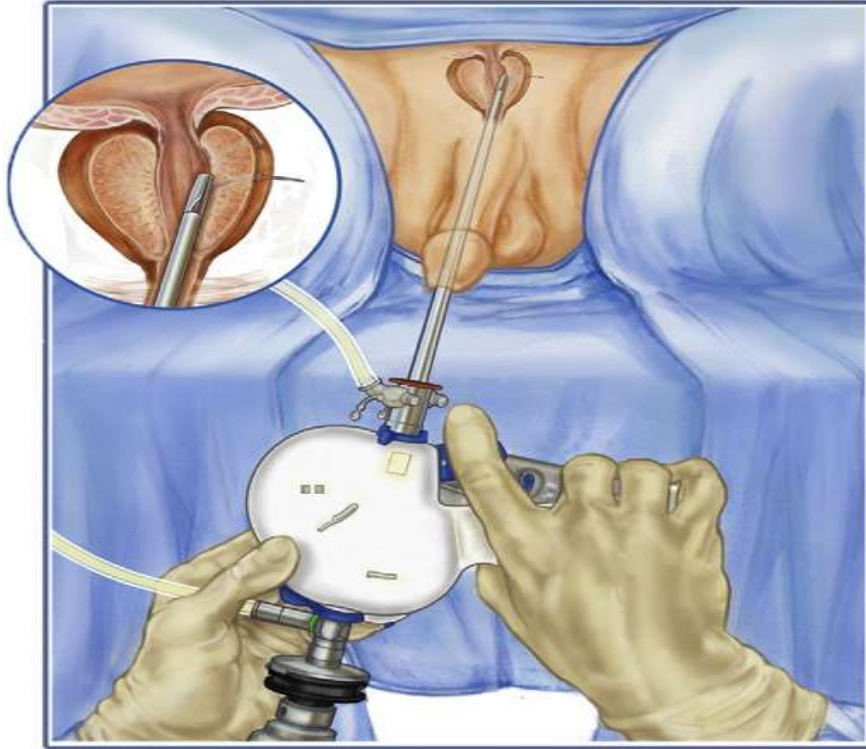
- **Improves symptoms / resolves retention**
- **Easy and painless for patient and MD**
- **Rapid symptom relief and recovery**
- **Safe**
- **Durable**

UroLift System

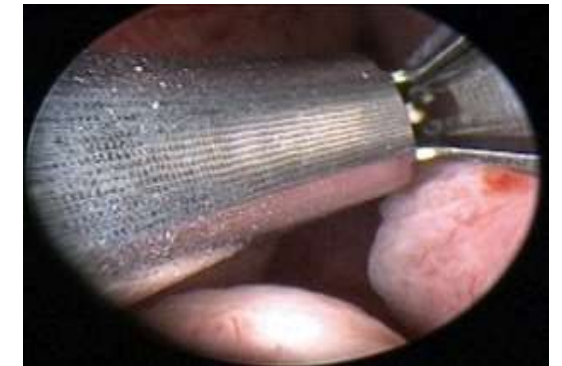


UROLIFT®

The Prostatic Urethral Lift

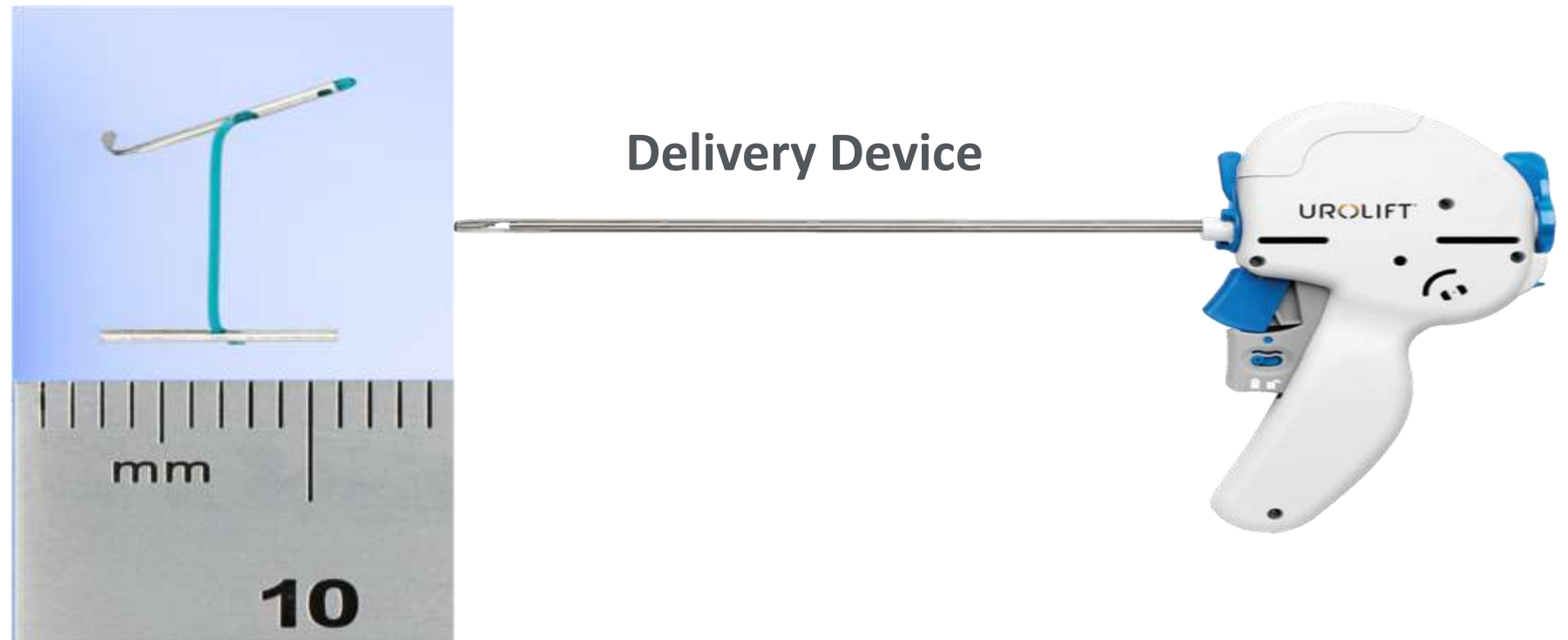


- Compress encroaching lateral lobe
- Deliver UroLift[®] implant to hold in place
- Typically ~4 implants delivered (<40-50mL)



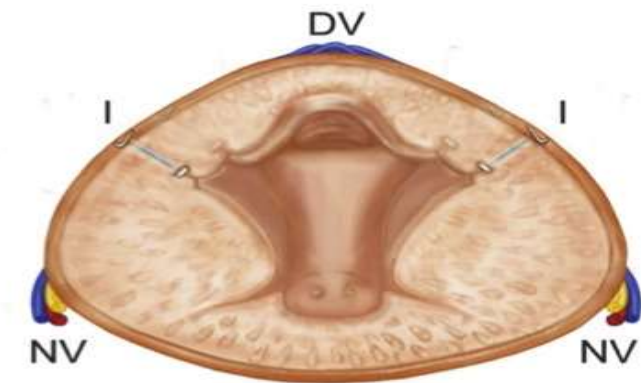
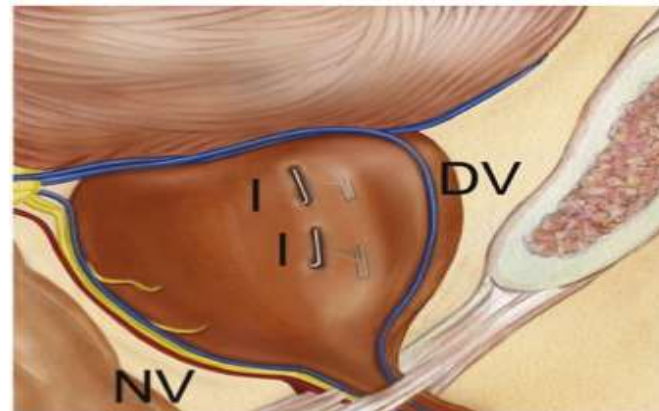
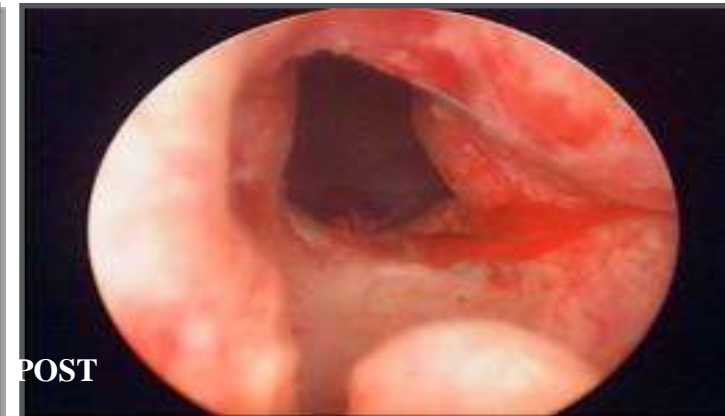
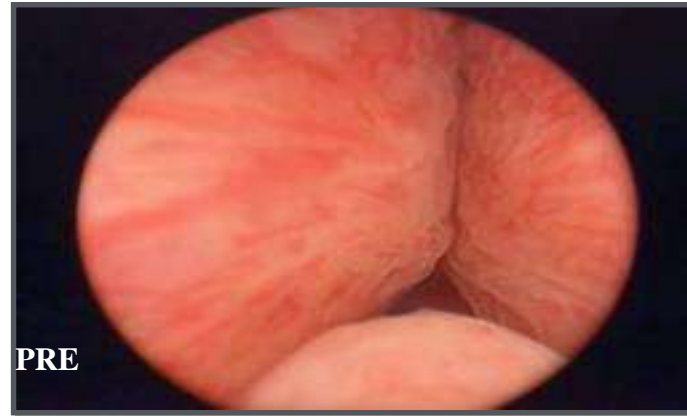
The UroLift Implant

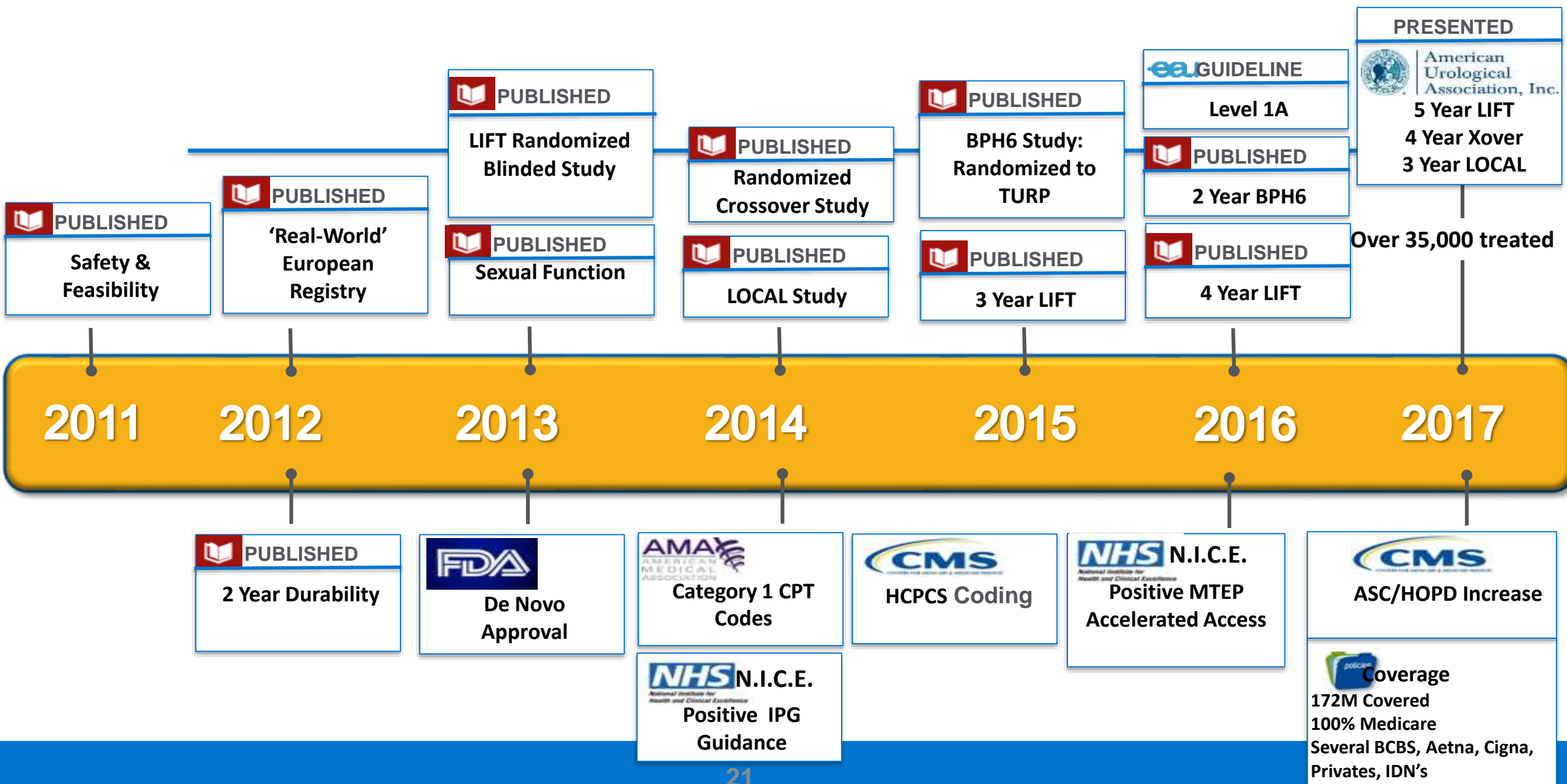
- Permanent Transprostatic Tissue Retractor
 - Implant sized *in situ* to prostate lobe
 - Nitinol, PET, Stainless Steel



Immediate UroLift Effect

- Mechanically opens prostatic urethra
- Result is visible under cystoscopy
- Implants are anterolateral, away from NV bundles or dorsal venous complex

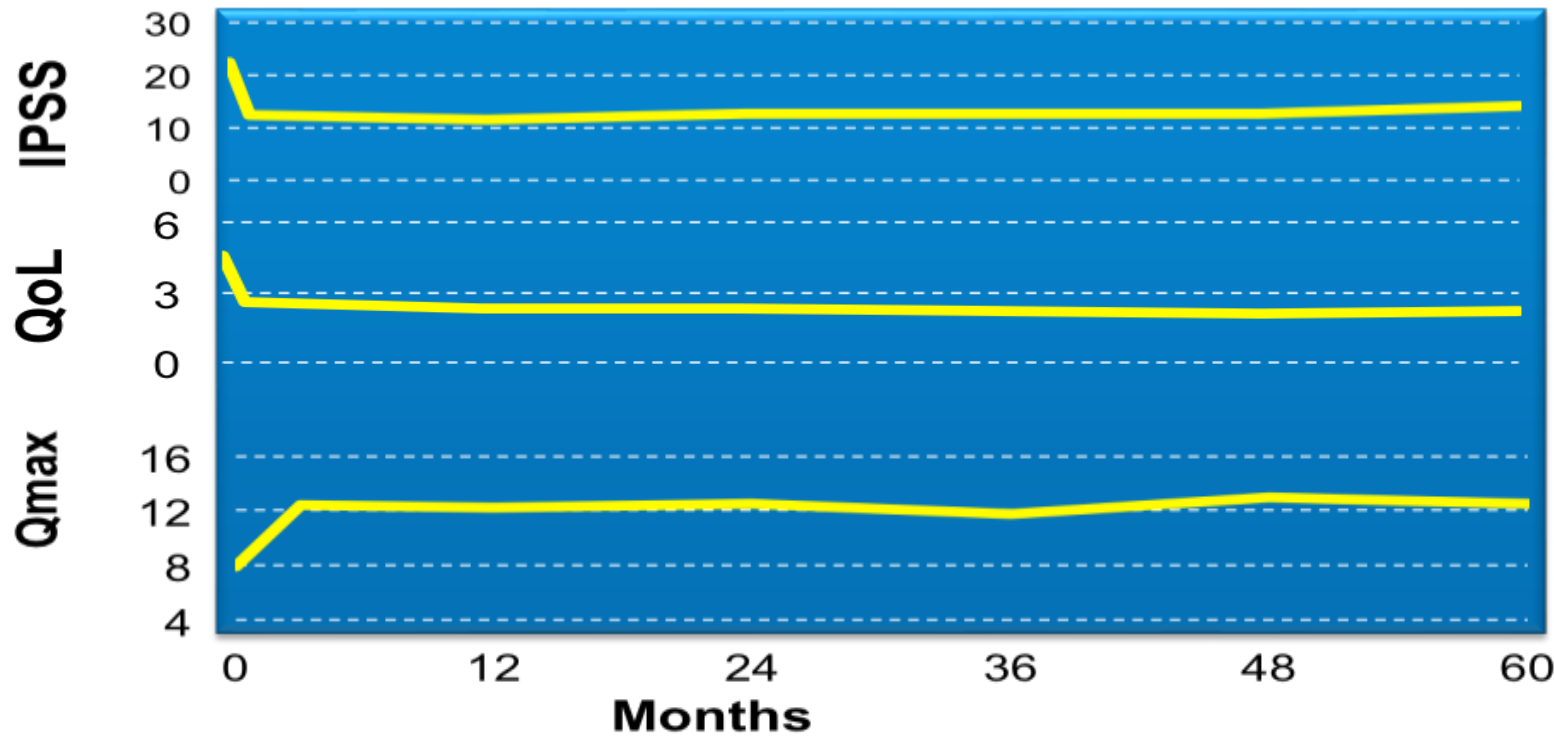




5-Year Durability



Symptom relief is achieved rapidly, within two weeks, and at one month is very similar to what can be expected at five years



13.6% Retreatment thru 5 Years^{1,2}
4.3% Add'l PUL
9.3% TURP or PVP

UroLift ReTx = ~ 2% to 3% per year
TURP ReTx = ~1% to 2% per year



Gold Standard

1. Roehrborn, EAU 2017, London
 2. Roehrborn et al. Urology Clinics 2016
 3. Data on File at NeoTract

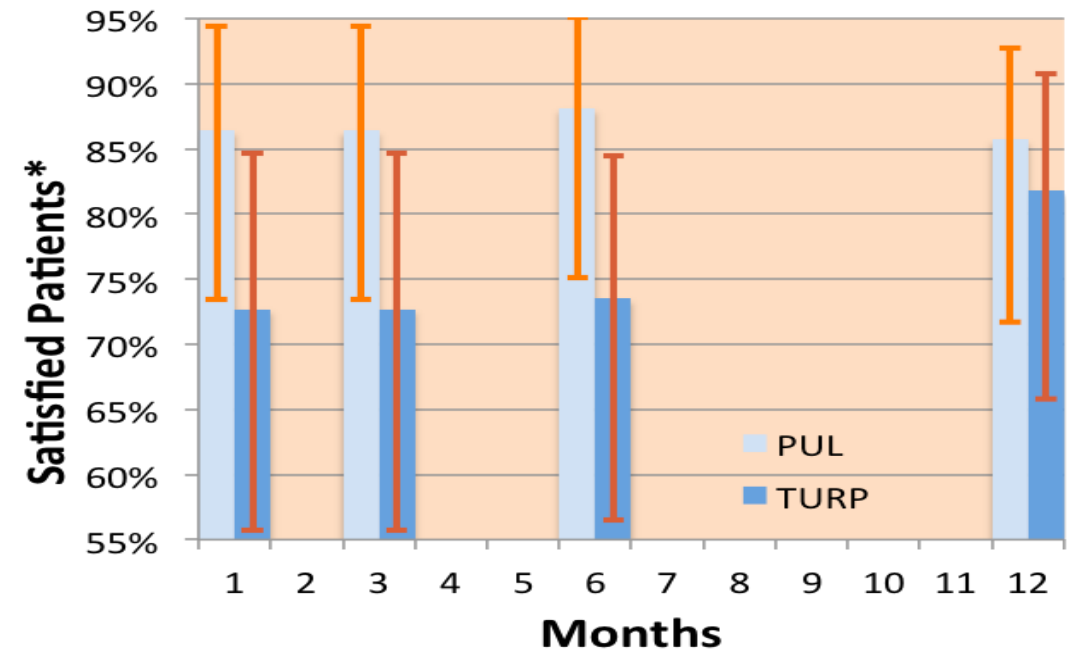
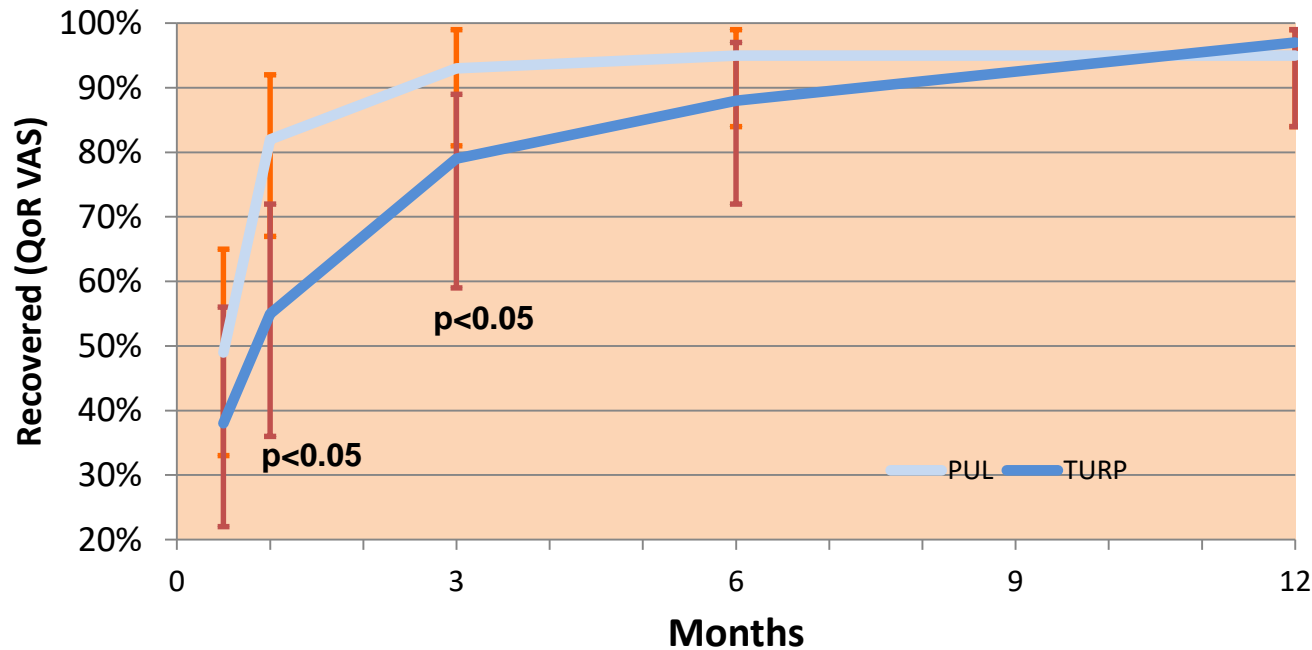
BPH6: UroLift vs TURP Randomized Study

- *UroLift remains superior to TURP in overall BPH6 at 2 years.*

	PUL	TURP	p value
Composite Primary Endpoint	46%	22%	0.05
#1) LUTS ($\geq 30\%$ IPSS reduction)	62%	91%	0.01
#2) Recovery ($\geq 70\%$ VAS @ 1 mo)	82%	53%	<0.01
#3) Erectile Function (<6 SHIM reduction)	97%	94%	NS
#4) Ejaculatory Function (MSHQ-EjD #3 \neq 0)	100%	64%	<0.01
#5) Continence (ISI<5)	83%	75%	NS
#6) Safety (no Clavien-Dindo II+)	92%	79%	NS

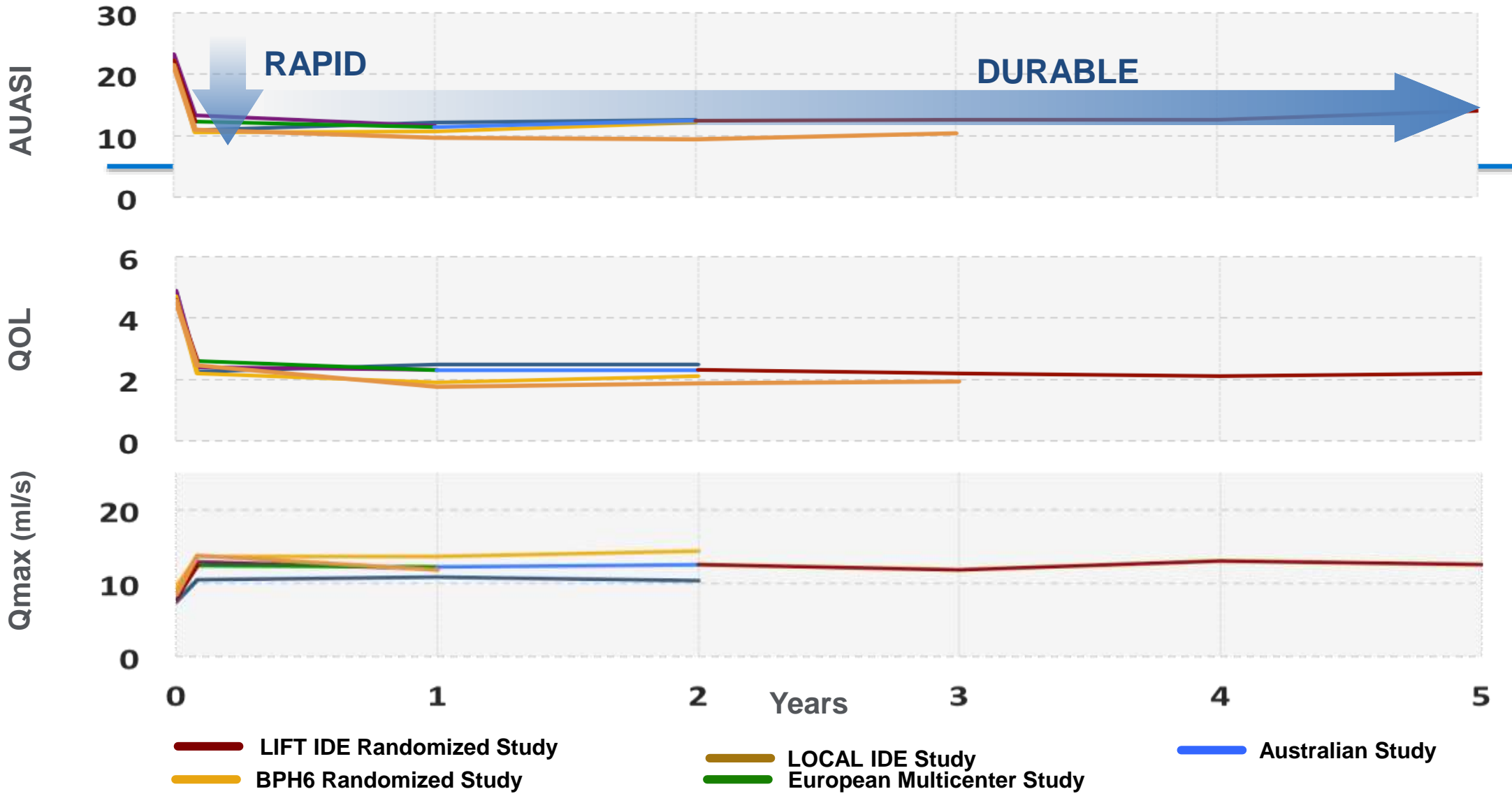
Patient Recovery and Satisfaction

- UroLift patients recover more quickly
 - TURP catches up only between 6 to 12 months
- UroLift patients satisfied sooner and to greater extent



*would recommend procedure

Reproducible Results



Roehrborn AUA2017; Gratzke BJUI 2017; Gange AUA2017; McNicholas Eur Urol 2013; Chin Urology 2012

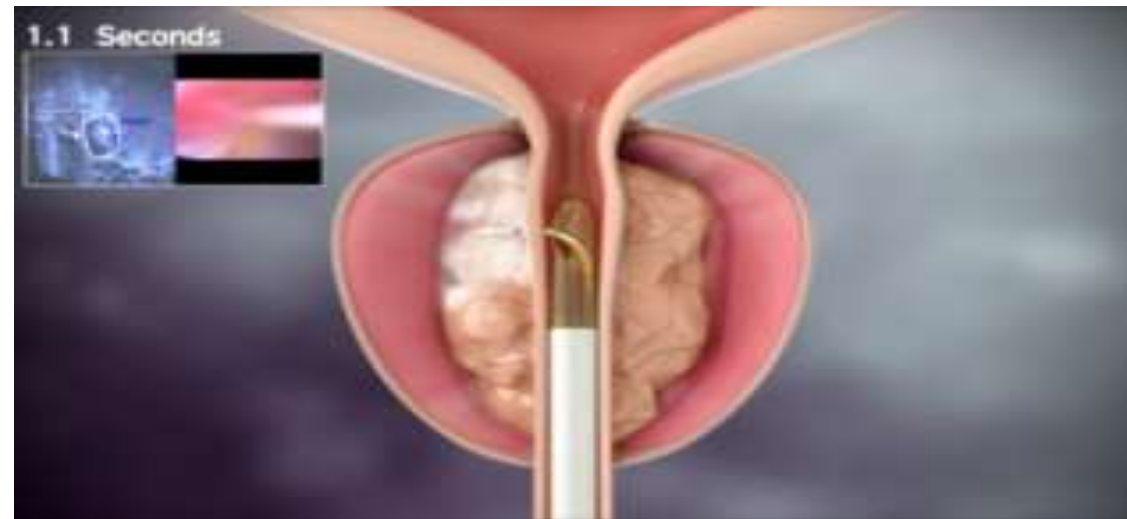
Minimally Invasive Safety Profile

Most common AE were mild to moderate and typically resolved by 2-4 weeks.

	PUL Subjects	Control Subjects
Dysuria	34%	17%
Hematuria	26%	5%
Pelvic pain	18%	5%
Urgency	7%	0%
Urge Incontinence	4%	2%
UTI	3%	2%

No incidence of de novo sustained ejaculatory or erectile dysfunction.

Rezum: Convective RF Thermal Therapy Ablation



Rezūm – Fundamentally Different

- Rezūm is a fundamentally different way of applying thermal energy to effectively treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (BPH).
- Unique in 3 ways:
 - Heat Source
 - Heat Transfer
 - Contained within Prostate Anatomy
- Results in convectively delivered, targeted and precise dose of thermal energy

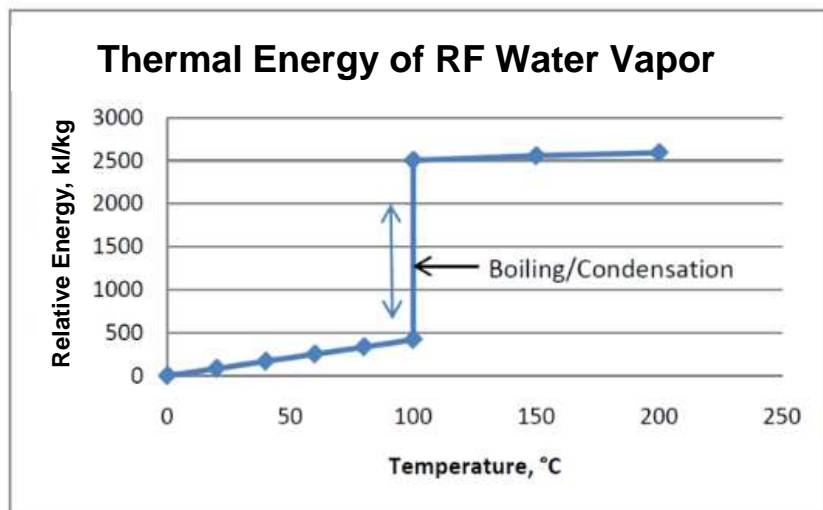
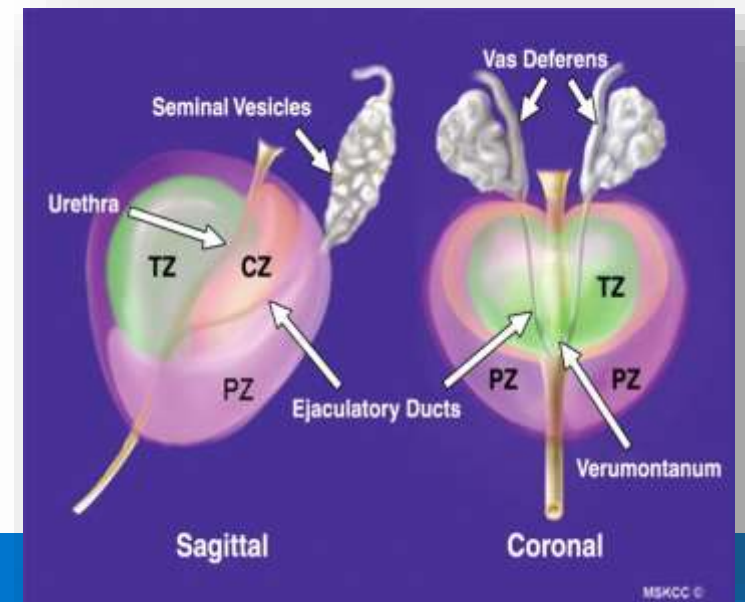
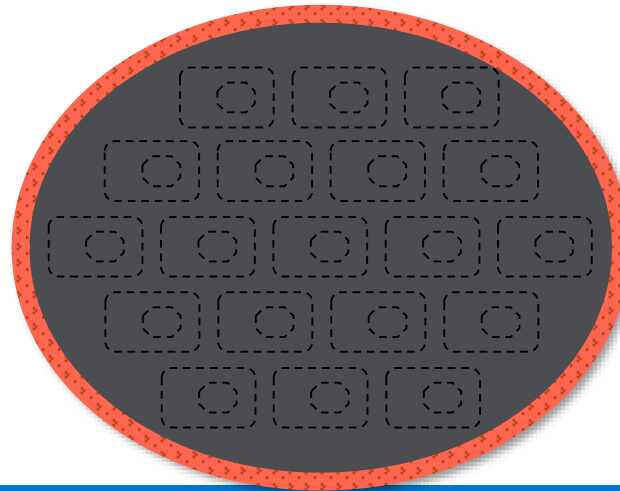


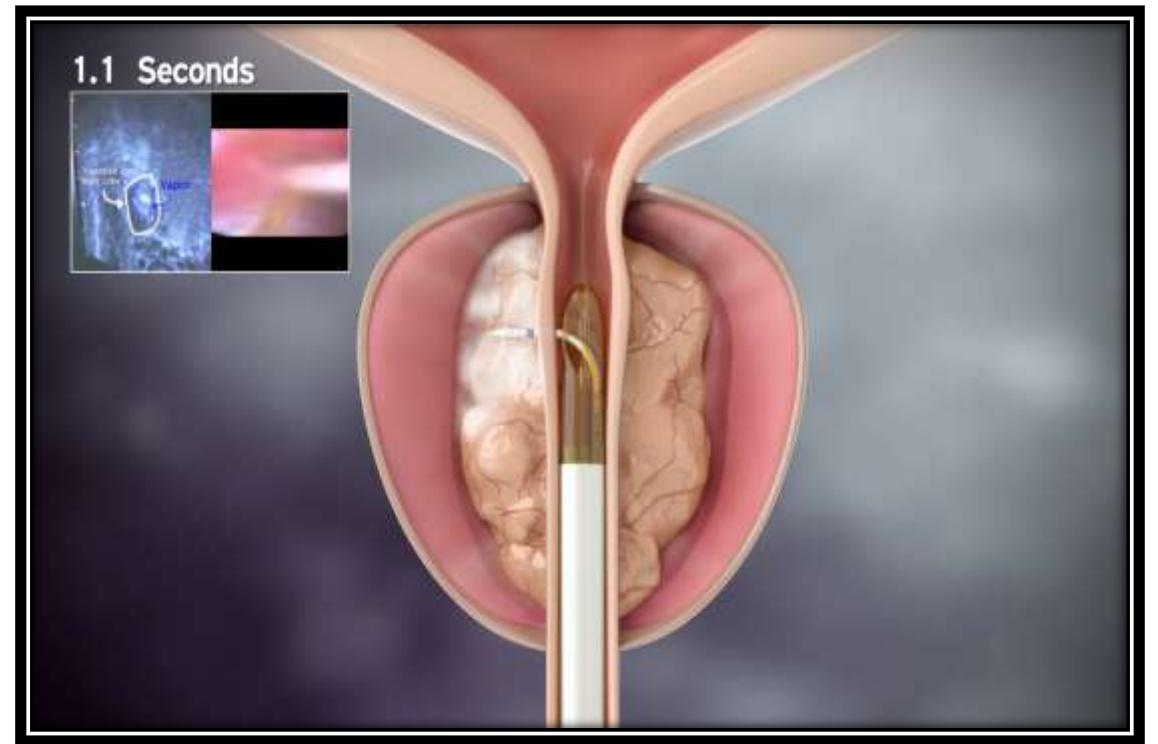
Figure 1. Relative Energy of water.



Overview of Rezūm

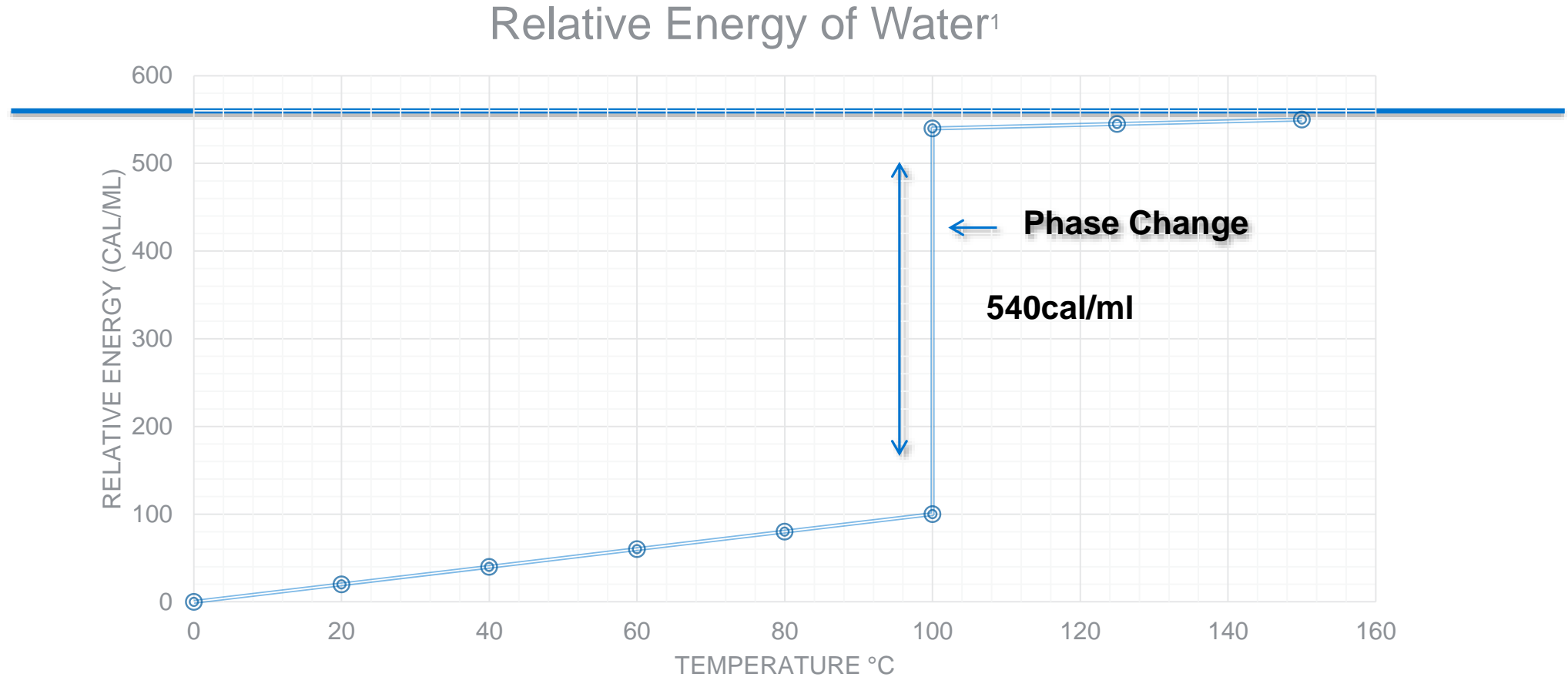


Generator and Hand-held Delivery Device



Water Vapor Delivery into Transition Zone

Unique Heat Source - Water Vapor Energy



540cal/ml of stored thermal energy is released during phase change from water vapor to water².

Thermal Effects on Tissue

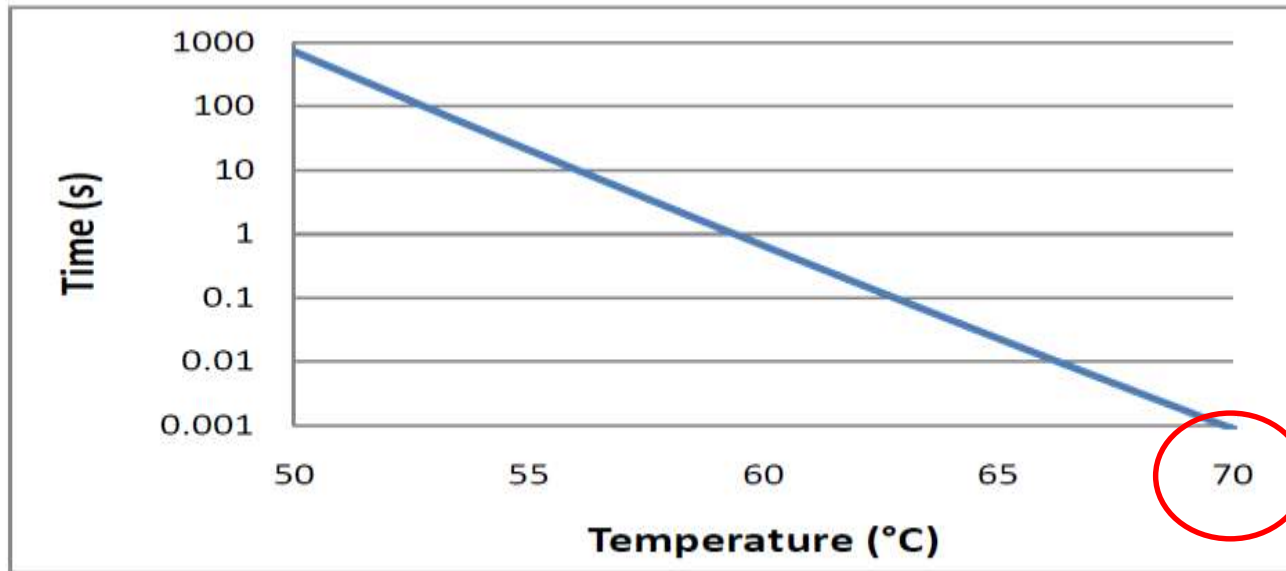
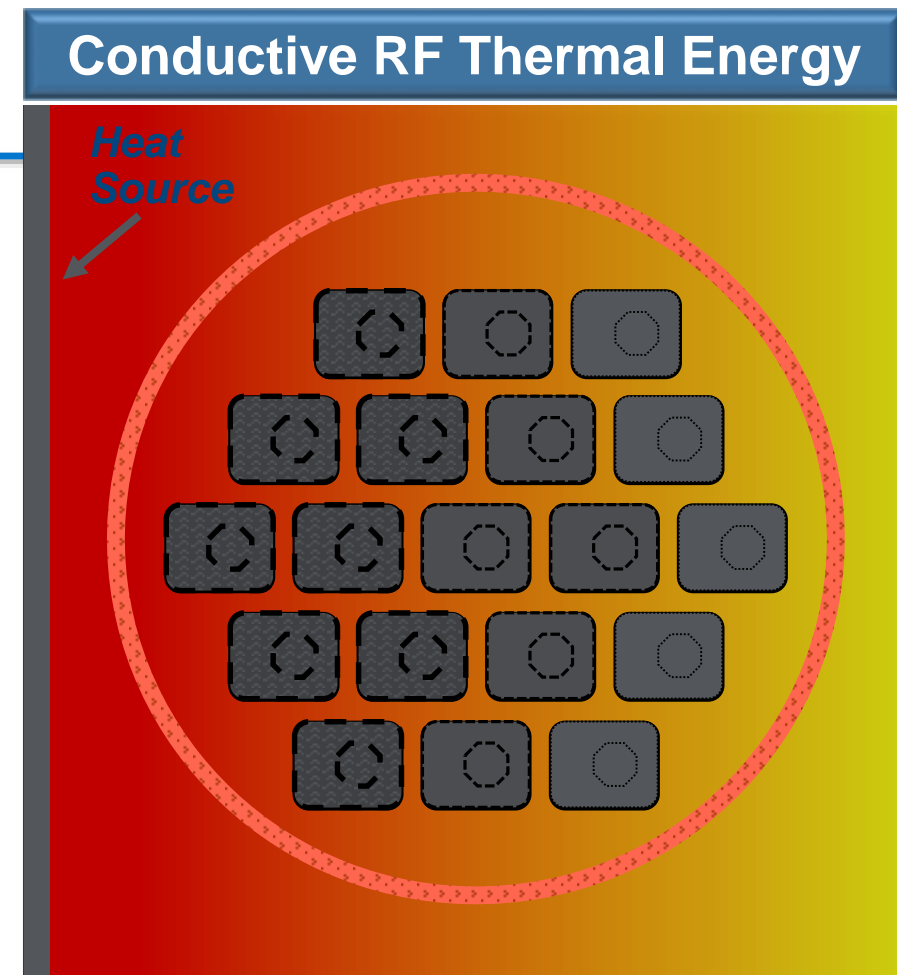
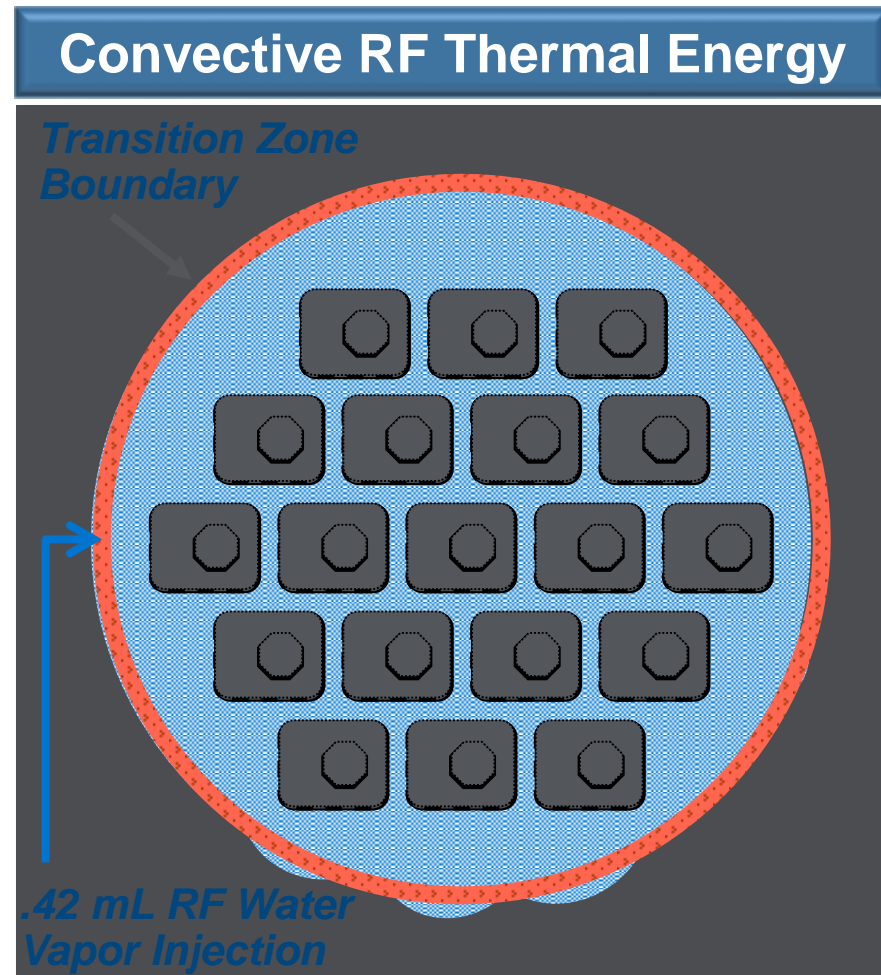


Figure 3. Graph of temperature vs. the time needed to cause tissue ablation (necrosis).¹

At >70°C cell death is immediate and irreversible

During a Rezūm treatment, 103°C water vapor is convectively delivered into 37°C prostate tissue, increasing the temperature of tissue within each treatment area to approximately 70°C+ over the course of each 9 second treatment, resulting in instantaneous cell death².

Unique Heat Transfer- Convection vs Conduction



- 0.42ml RF vapor convectively dispersed through interstices
- Condensation uniformly releases 208cal stored thermal energy
- Cell membranes gently denatured causing cell death

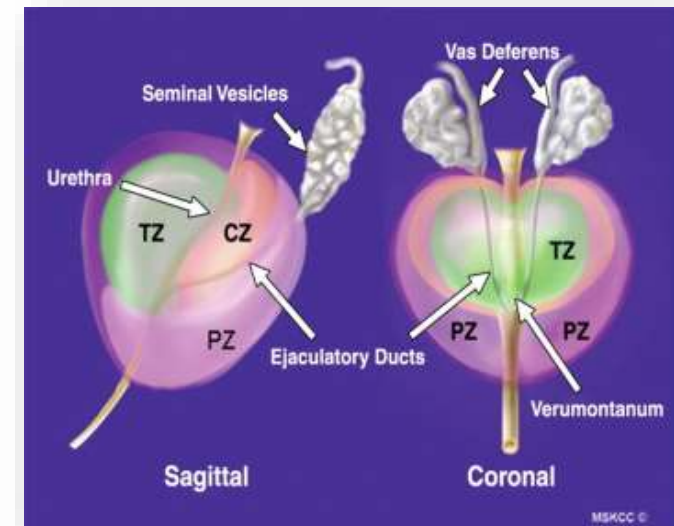
- Conductive heat transfer cell to cell
- Non-uniform heat gradient results in cells near source being heated substantially more than those far away
- Conductive heating of prostate capsule may occur

Uniquely Contained within Prostate Anatomy

- The prostate is made up of 3 primary zones, each contained within anatomically distinct densified tissue often referred to as a pseudocapsule
- Water vapor cannot penetrate the zonal boundaries and therefore stays within the zone it is injected

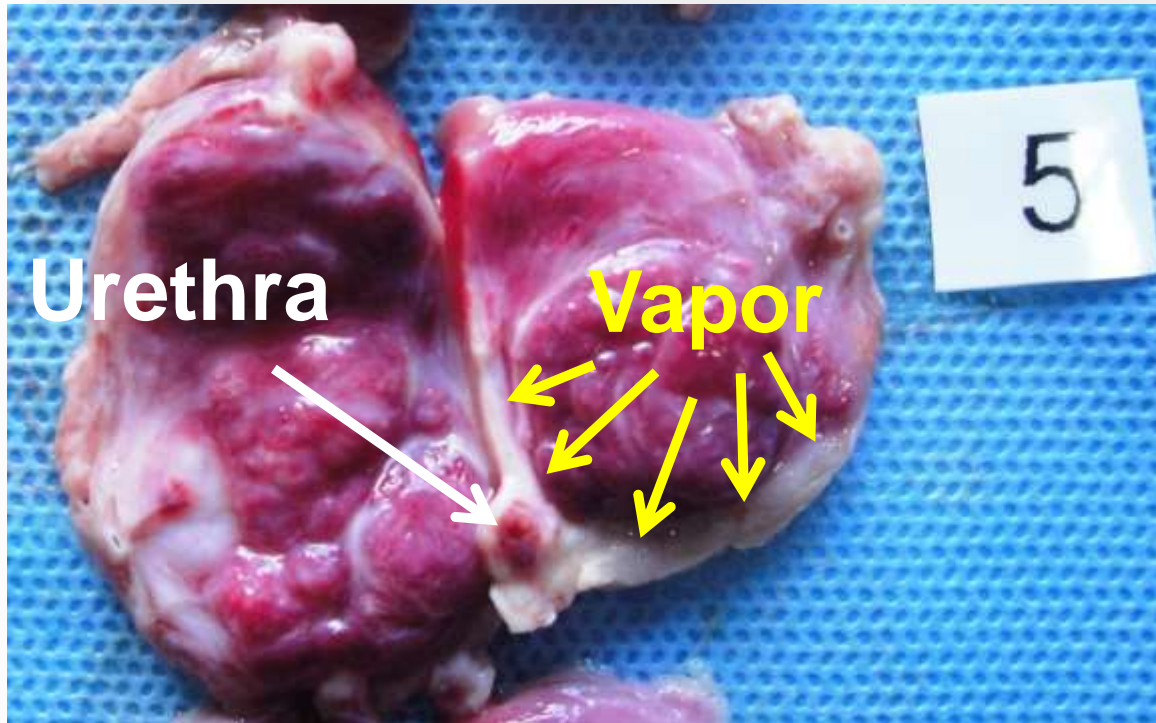
Zones of the Prostate

1. Transition Zone (TZ)
2. Central Zone (CZ)
3. Peripheral Zone (PZ)



Using anatomy to deliver targeted treatments

Uniquely Contained within Prostate Anatomy



Zonal Treatment

Complete ablation of the thin peripheral zone and absence of treatment in the large transition zone*

*Image from Reviv prostate cancer feasibility study

Rezūm is not indicated for treatment of prostate cancer.

Uniquely Contained within Prostate Anatomy

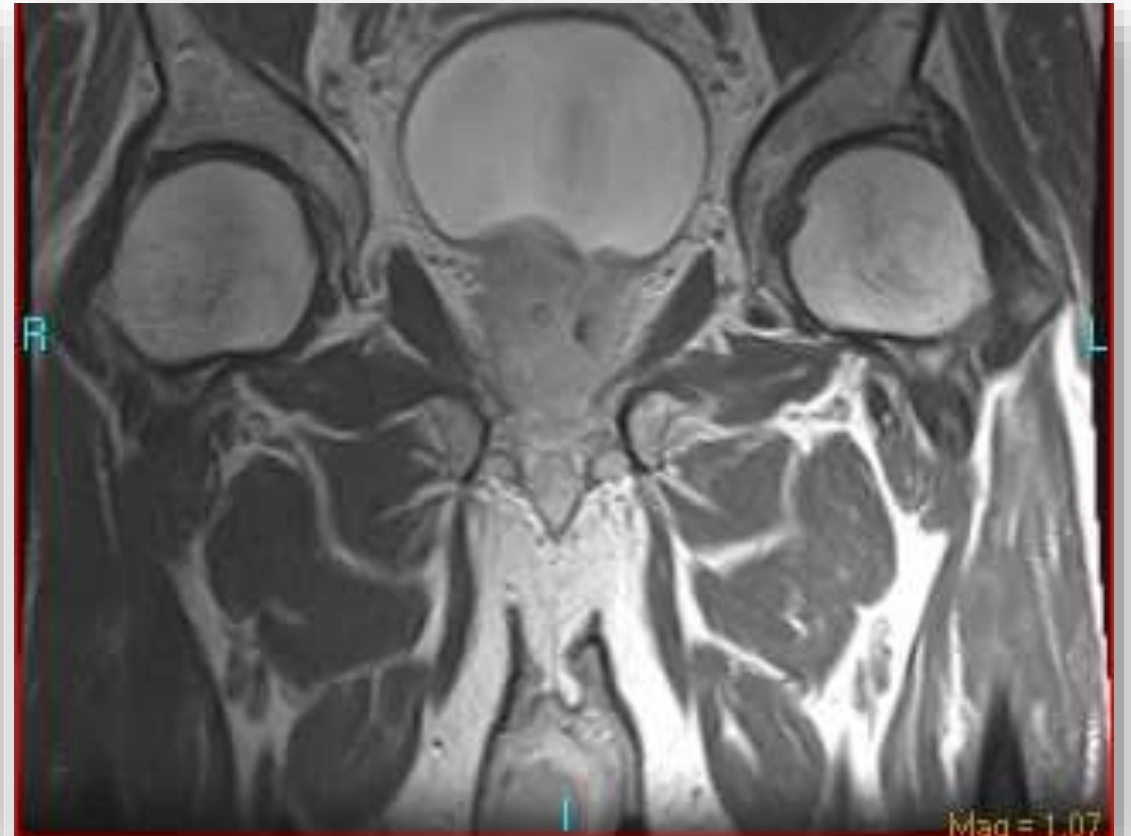
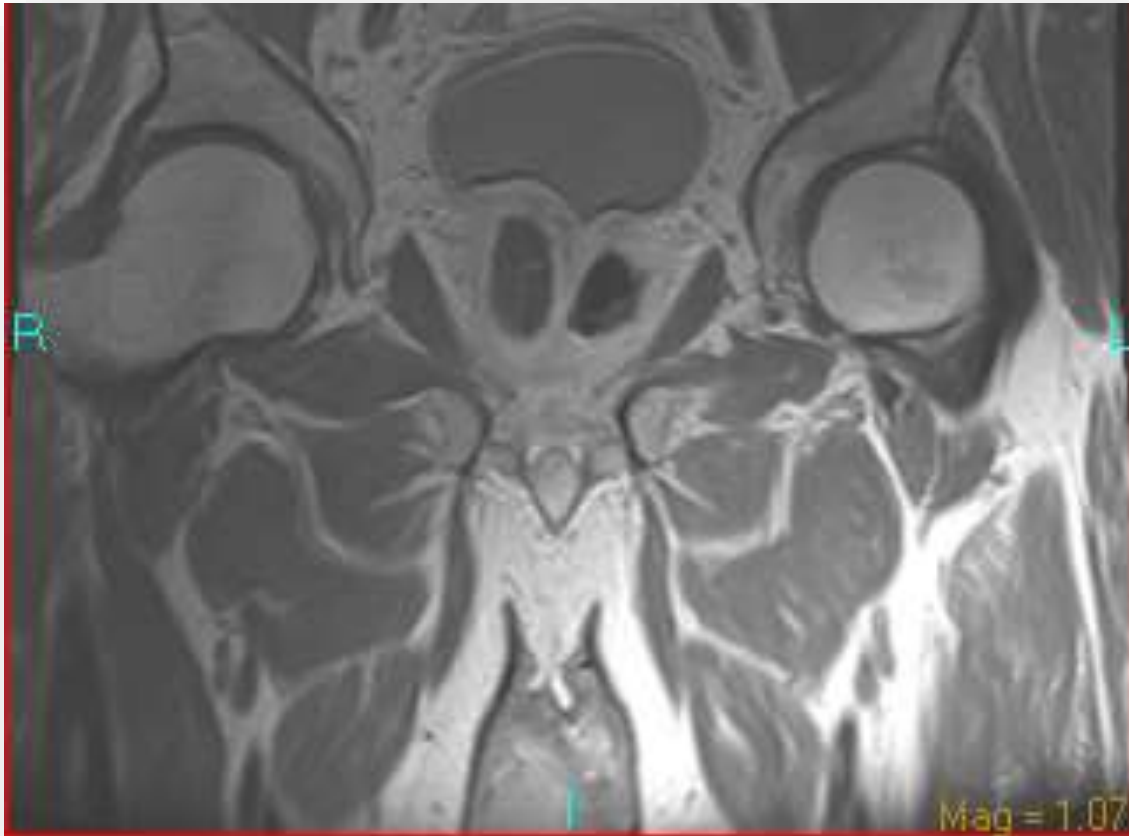


Images from Michael Hoey, PhD Chief Technology Officer, NxThera Inc. Rezum Pilot Study.

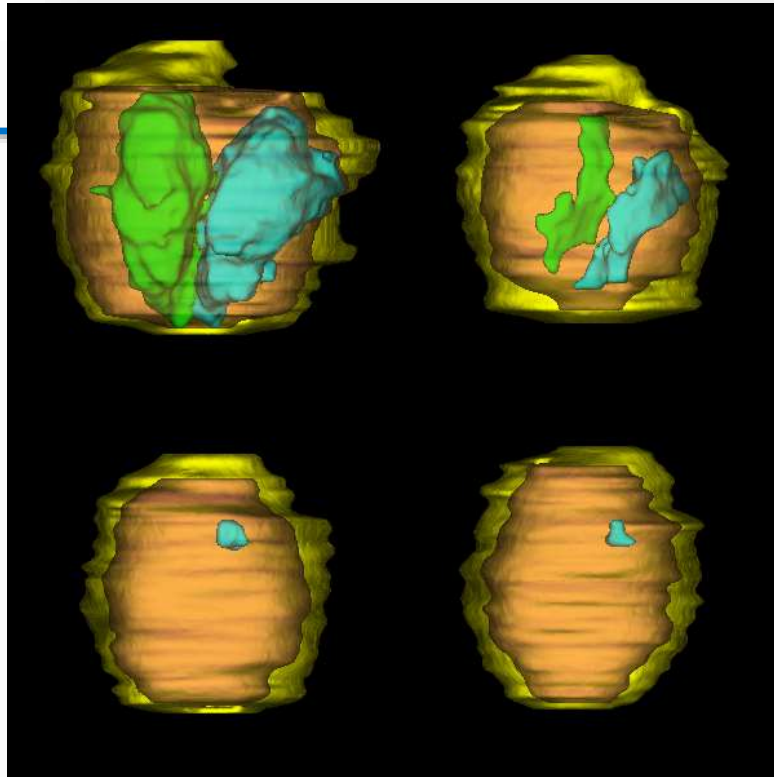
Rezūm Pilot Study

1 week post-procedure

3 months post-procedure



MRI Study- Significant Lesion Creation/Resolution and Volume Reduction



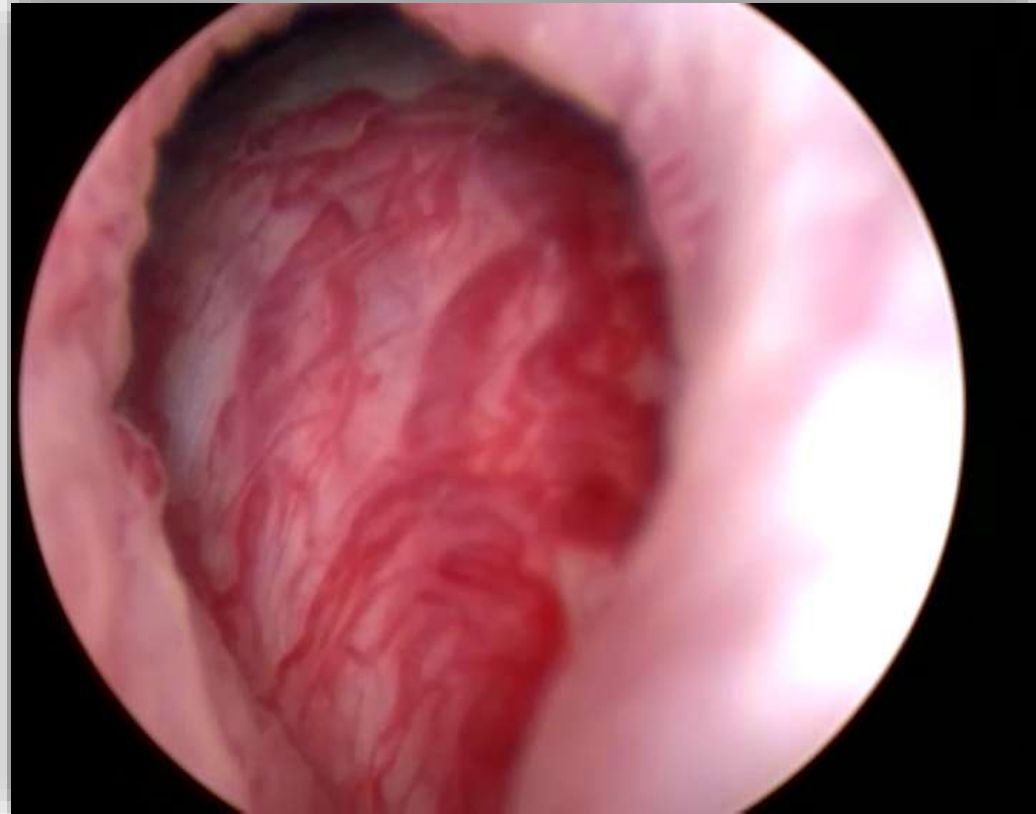
6-Month Measurements vs. 1 Week	
Lesion resolution	99.5%
Transition zone volume reduction	-52.7%
Prostate volume reduction	-46.2%

Entire Study Group

	Time	N	Mean (cm ³)	Mean Δ (cm ³)	Mean % Δ
Lesion Volume	1 Week	59	8.5		
	1 Month	57	3.5	-5.0	-58.8%
	3 Months	55	0.7	-7.8	-91.8%
	6 Months	54	0.3	-8.2	-96.5%
Transition Zone Volume	1 Week	59	40.1		
	1 Month	57	33.1	-7.0	-17.5%
	3 Months	55	28.0	-12.1	-30.2%
	6 Months	54	24.8	-15.3	-38.2%
Prostate Volume	1 Week	59	67.8		
	1 Month	57	58.5	-9.3	-13.7%
	3 Months	55	51.7	-16.1	-23.7%
	6 Months	54	47.2	-20.6	-30.4%

Clinically Significant Tissue Volume Reduction

Pre-Treatment

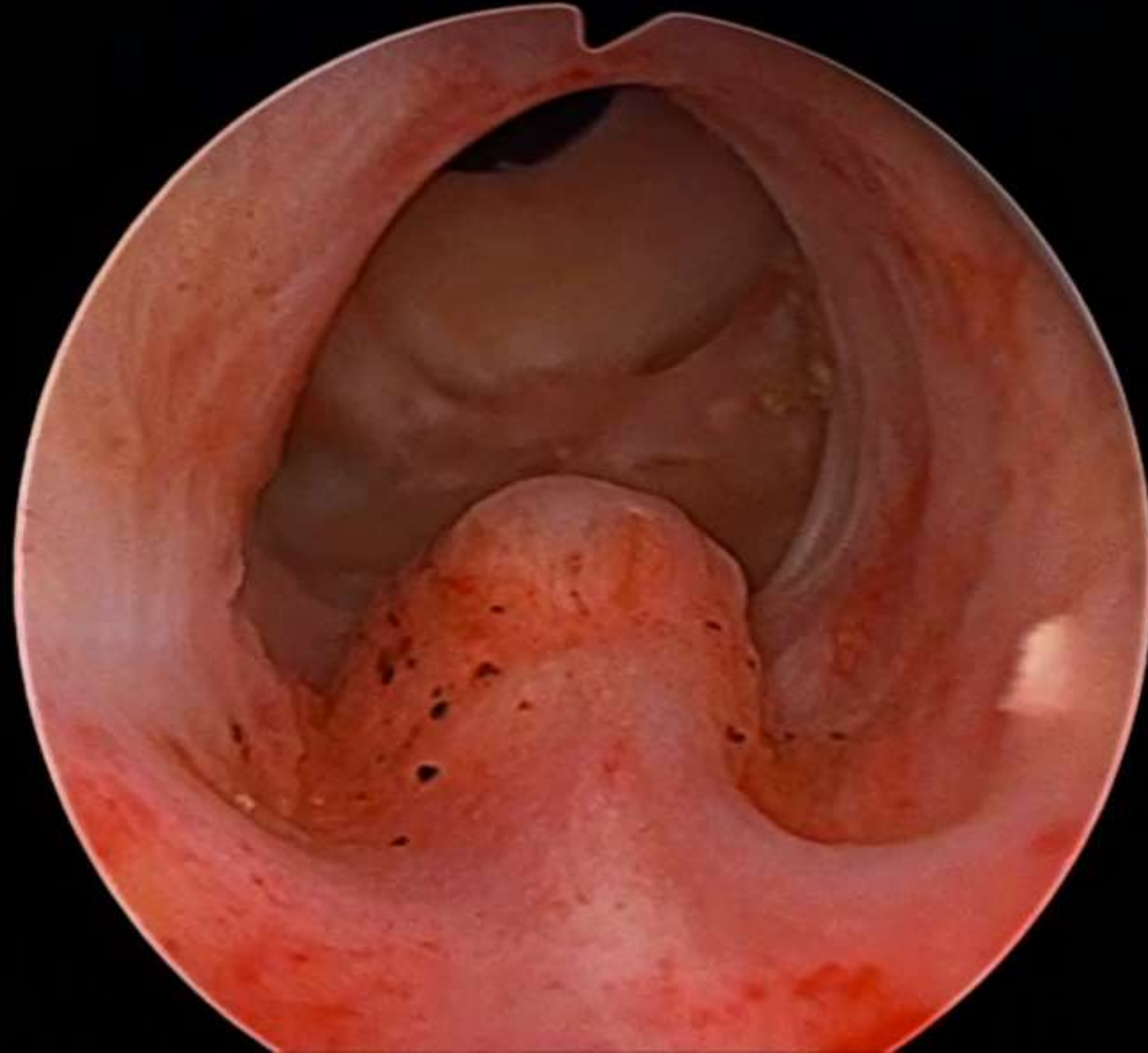


52cm³ prostate – 3Tx/RLL; 4Tx/LLL; 2 Tx/ML

6-Month



Rezüm – Cystoscopy 10 Months



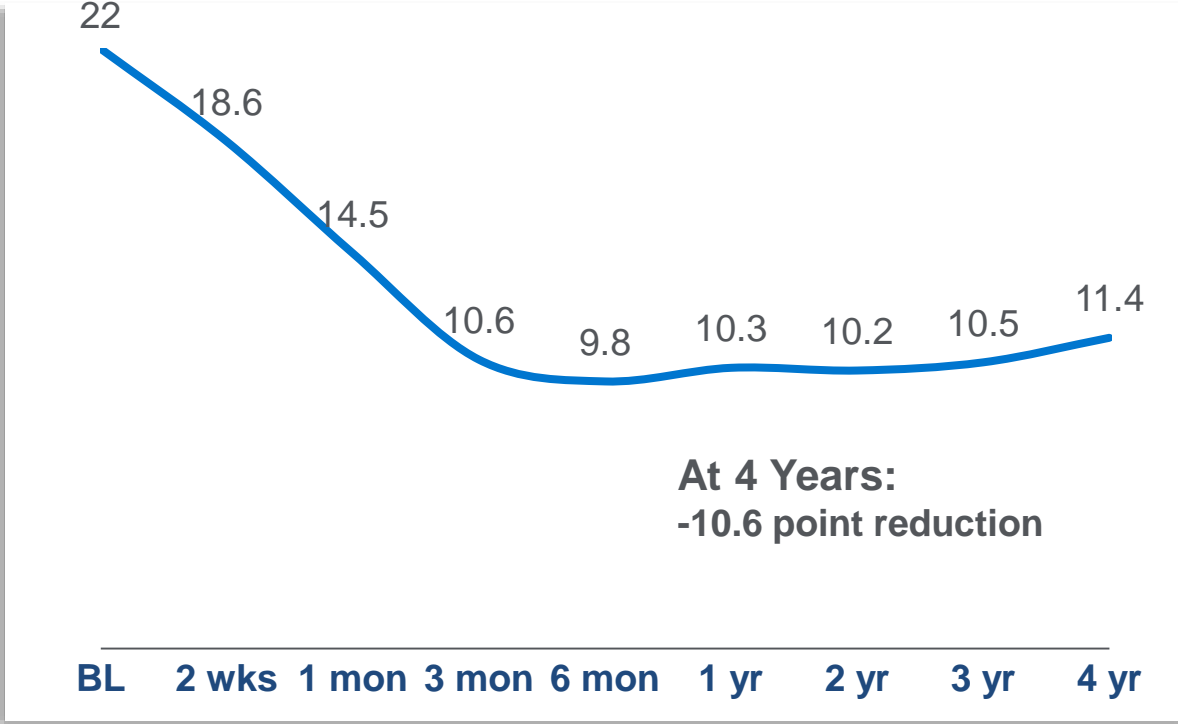
Rezum II Pivotal Study – 4 Year Data (sustained durability)

IPSS and Qmax were significantly improved from baseline

IPSS

4 Year Data

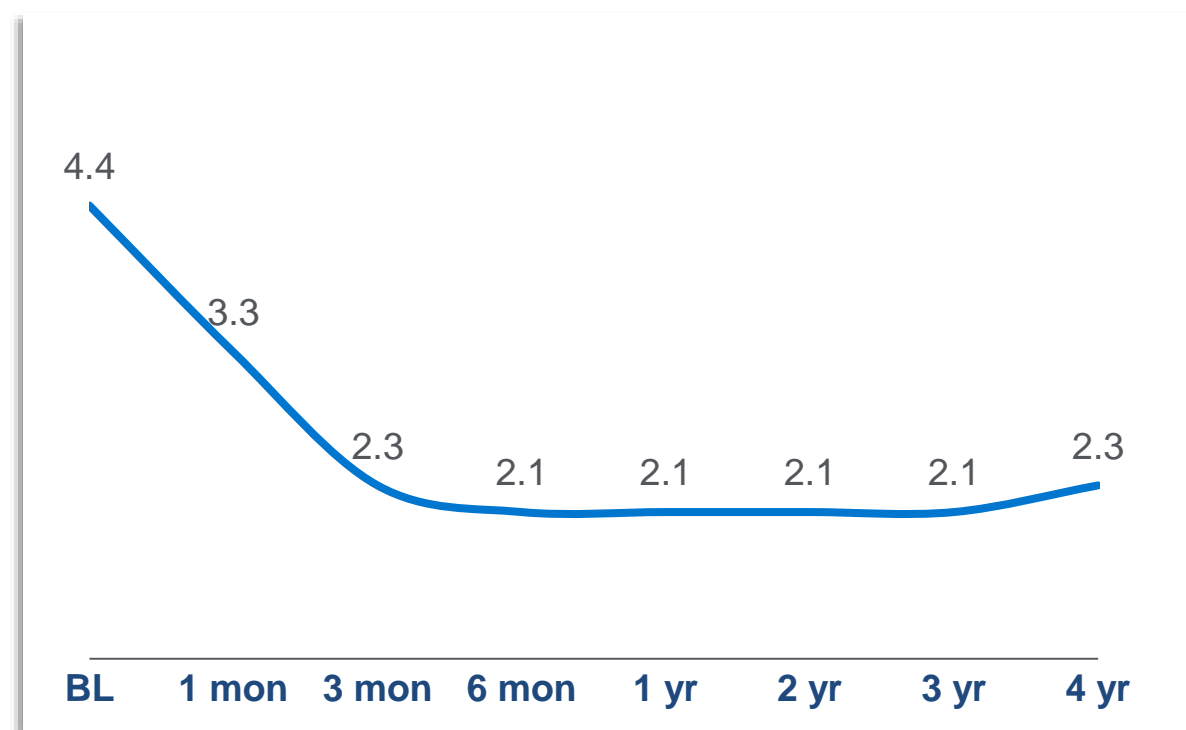
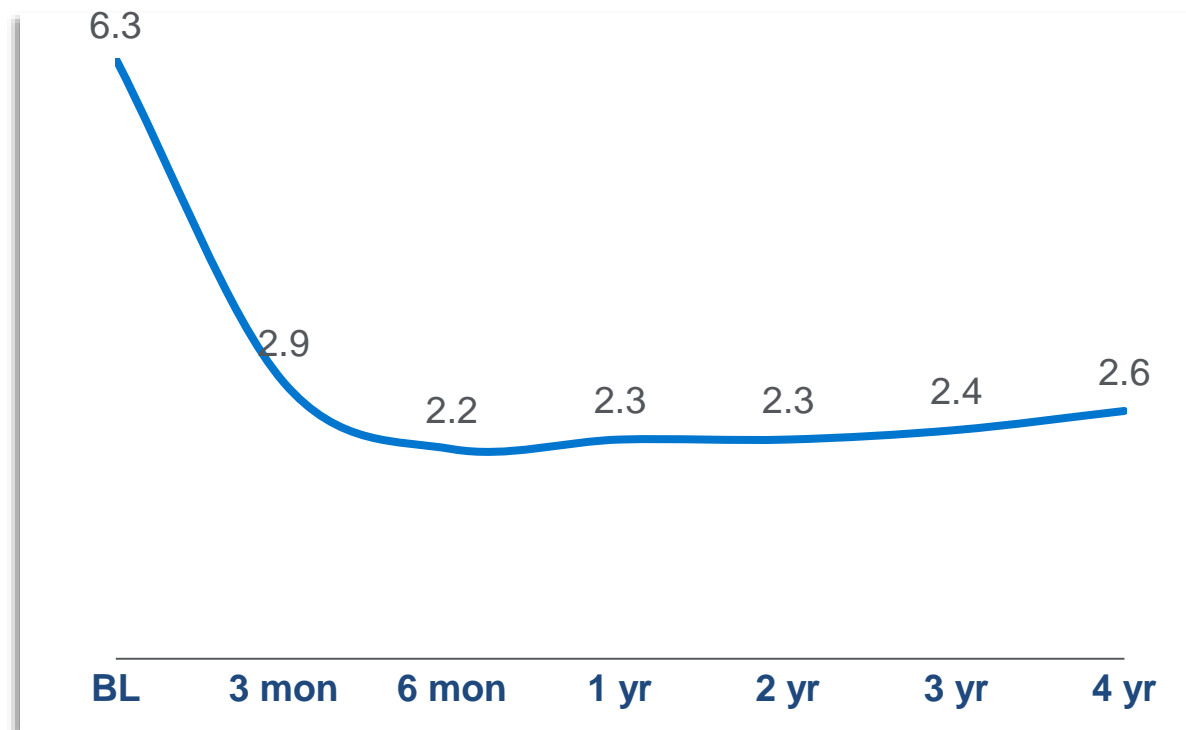
Qmax (mL/sec)



Quality of life and BPH II remained significantly improved

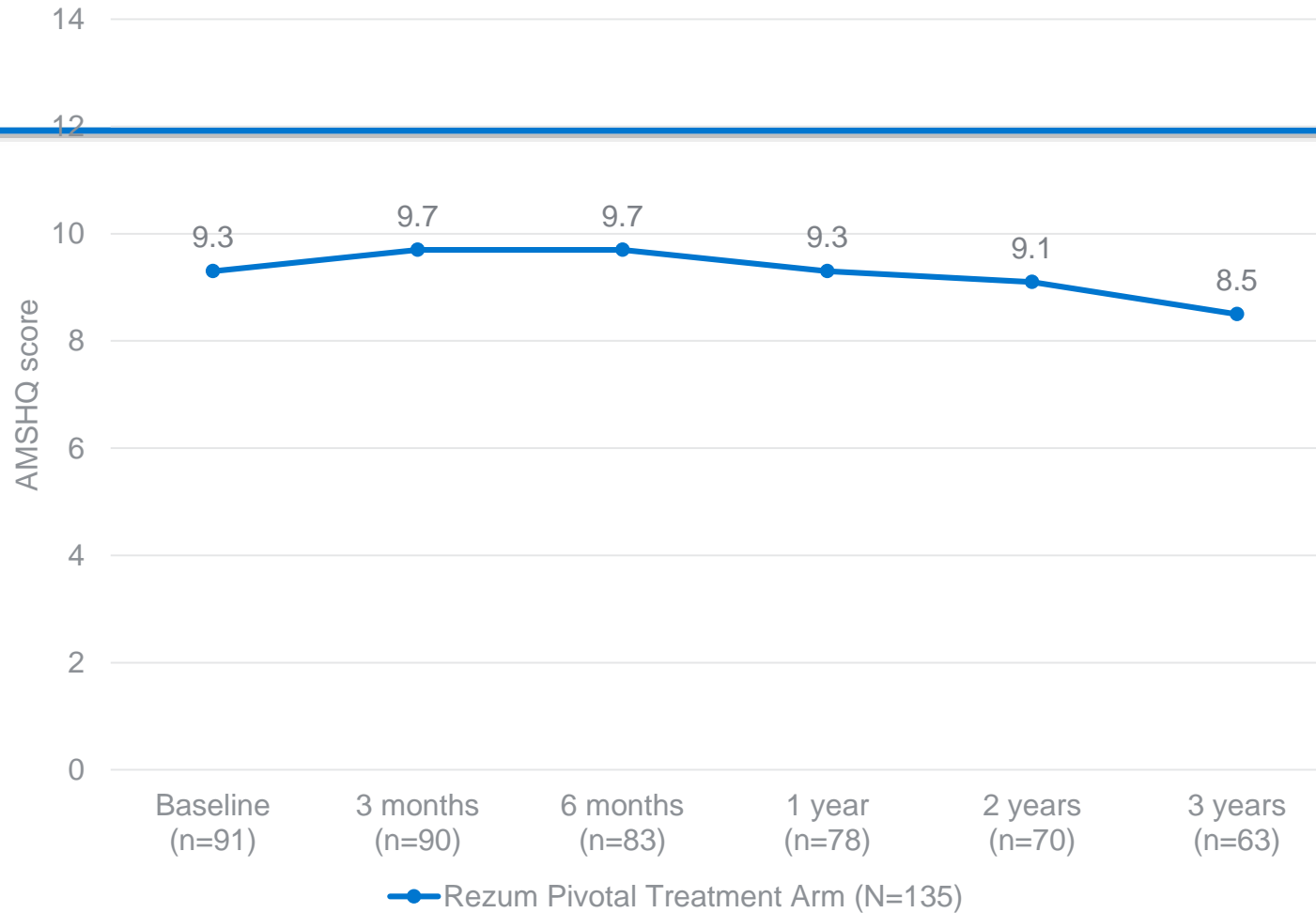
BPH II (Impact Index) 4 Year Data

QoL (Quality of Life)



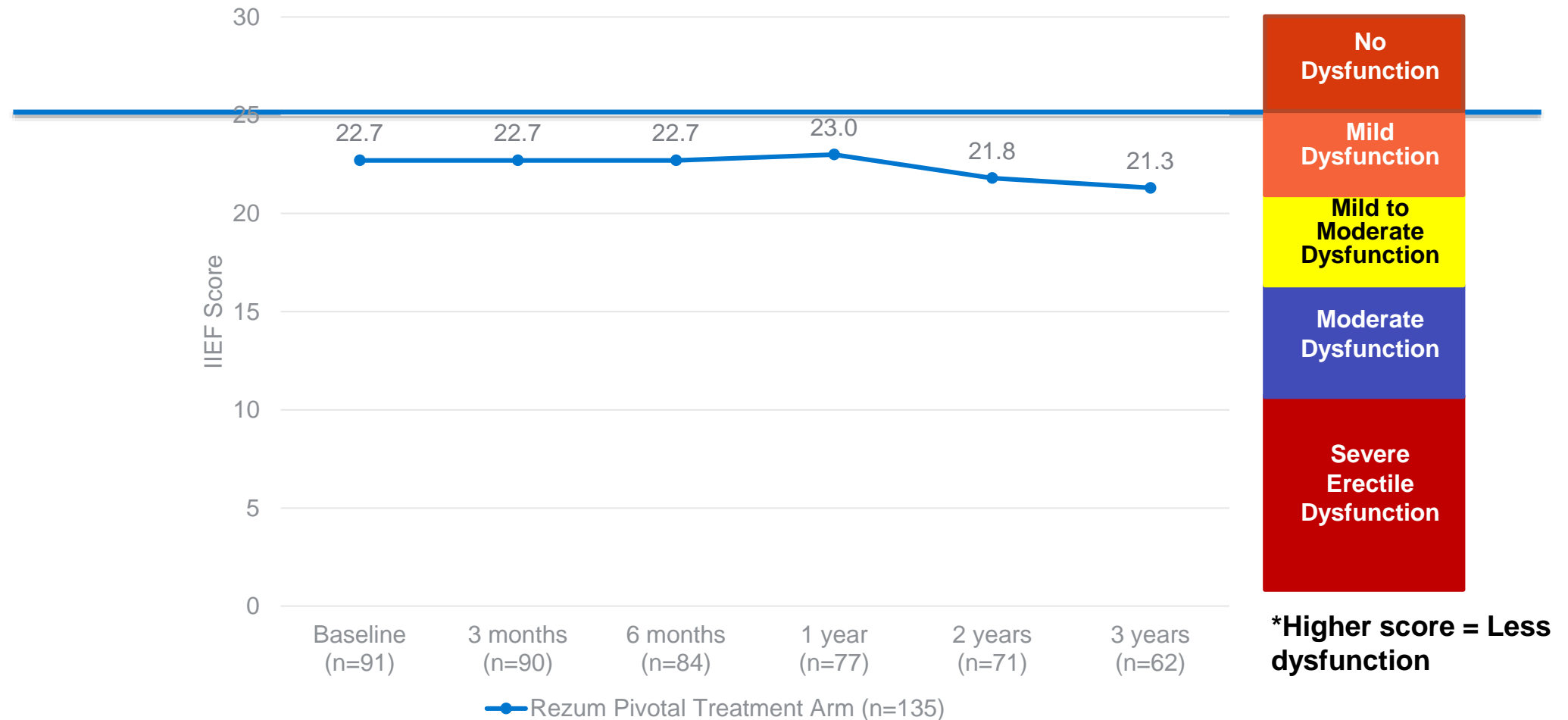
Rezūm II Pivotal Study

MSHQ-Function – No change in ejaculatory function



Rezūm II Pivotal Study

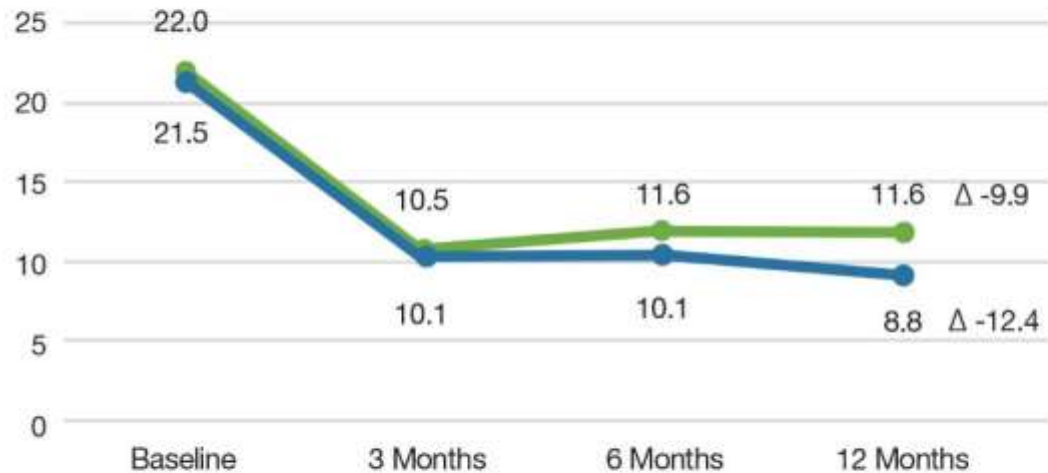
IIEF-EF Treatment Arm – No change in sexual function



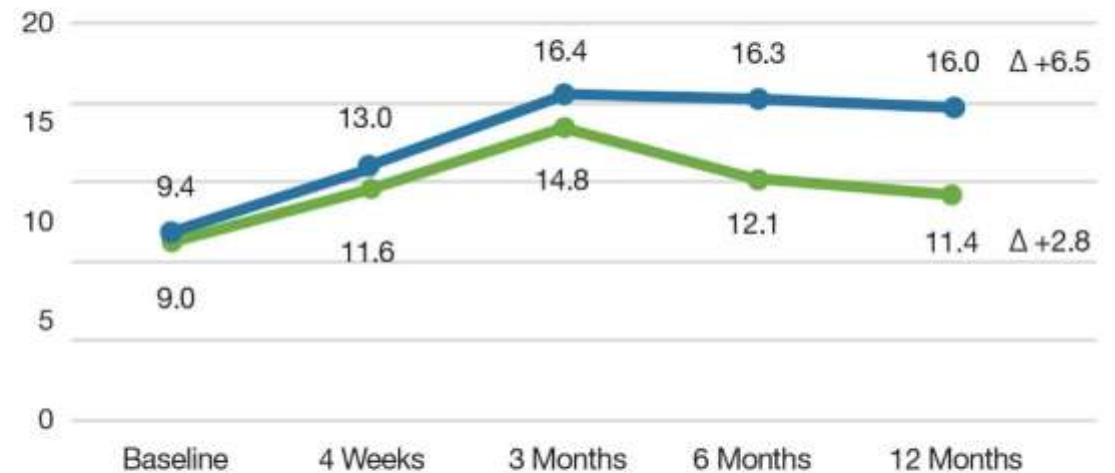
Rezūm II Pivotal Study – IPSS and Qmax with Median Lobe

Additional clinically meaningful improvement gained by treating the Median Lobe

**IPSS: Median Lobe Identified -
Treated vs Not Treated**



**QMax: Median Lobe Identified -
Treated vs Not Treated**

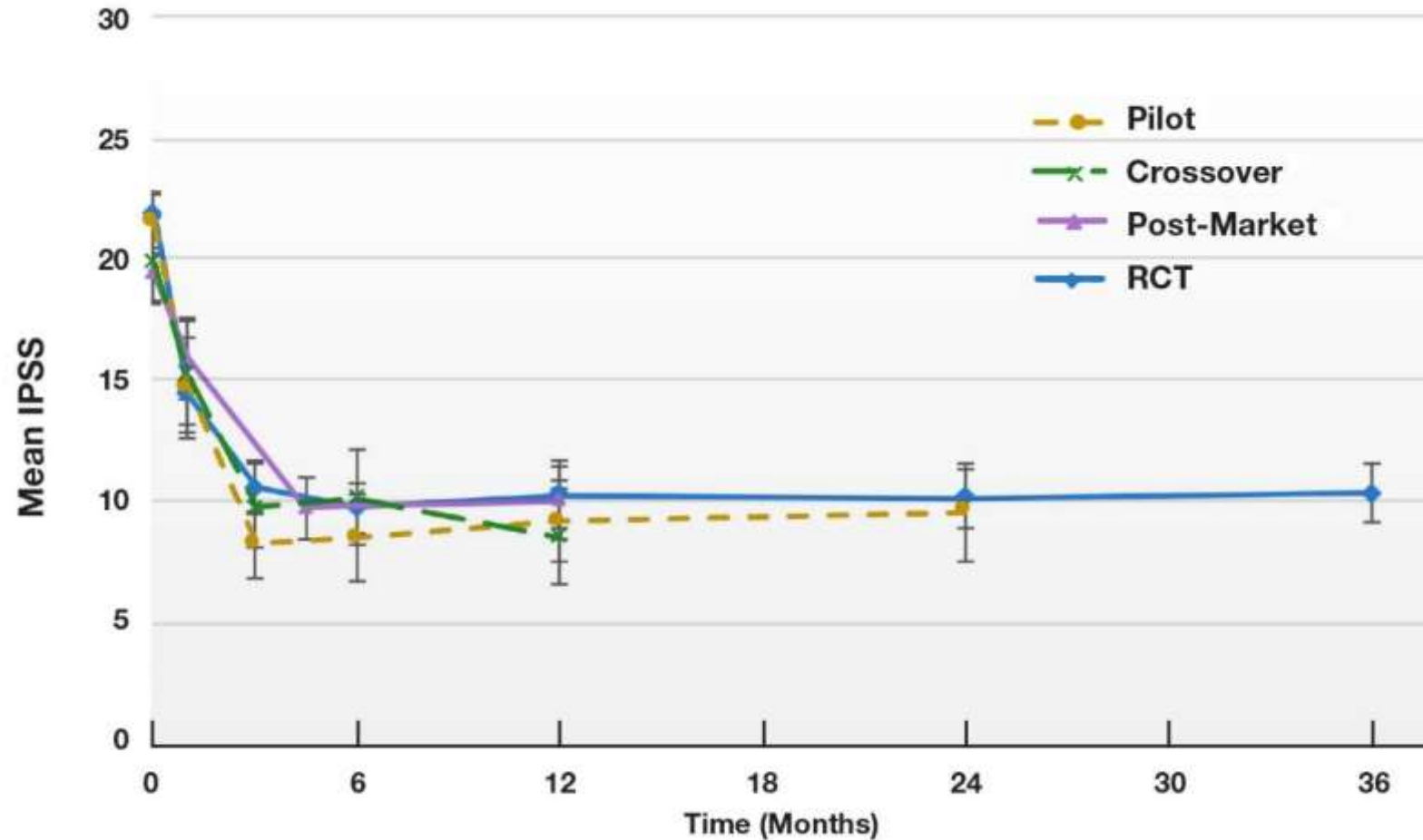


● LL and ML Treated (n=58)
 ● LL Treated, ML Identified but Not Treated (n=12)

Δ IPSS Change from Baseline (within-subject paired difference analysis)

Rezūm Studies – Mean IPSS Change

Consistent and durable across all studies



⁶Dixon CM, Cedano ER, Mynderse LA, Larson TR. Transurethral convective water vapor as a treatment for lower urinary tract

symptomatology due to benign prostatic hyperplasia using the Rezūm® system: evaluation of acute ablative capabilities in the human prostate. *Res Rep Urol.* 2015;7:13-18. <https://doi.org/10.2147/RRU.S74040>

¹¹Roehrborn CG, Gange SN, Gittelman MC, et al. Convective water vapor energy (WAVE) ablation therapy: Durable two-year results and prospective blinded crossover study for treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. *J Urol.* 2017;197:1507-16. doi: 10.1016/j.juro.2016.12.045.

¹²Darson MF, Alexander EE, Schiffman ZJ. Procedural techniques and multicenter postmarket experience using minimally invasive convective RF thermal therapy with Rezūm System for treatment of LUTS due to BPH. *Res Rep Urol.* 2017;9:159-69.

⁹McVary KT, Roehrborn CG. Three-year outcomes of the prospective, randomized controlled Rezūm System study: Convective radiofrequency thermal therapy for treatment of lower urinary tract symptoms due to benign prostatic hyperplasia. *Urology.* 2018 Jan;111:1-9.

This graph is a visual representation of IPSS reductions from 3 Rezūm clinical studies. The Rezūm Pilot¹, Rezūm Pivotal² and Rezūm Postmarket³ listed above. Also included are the 3 year IPSS data from the Rezūm Pivotal Study⁴.

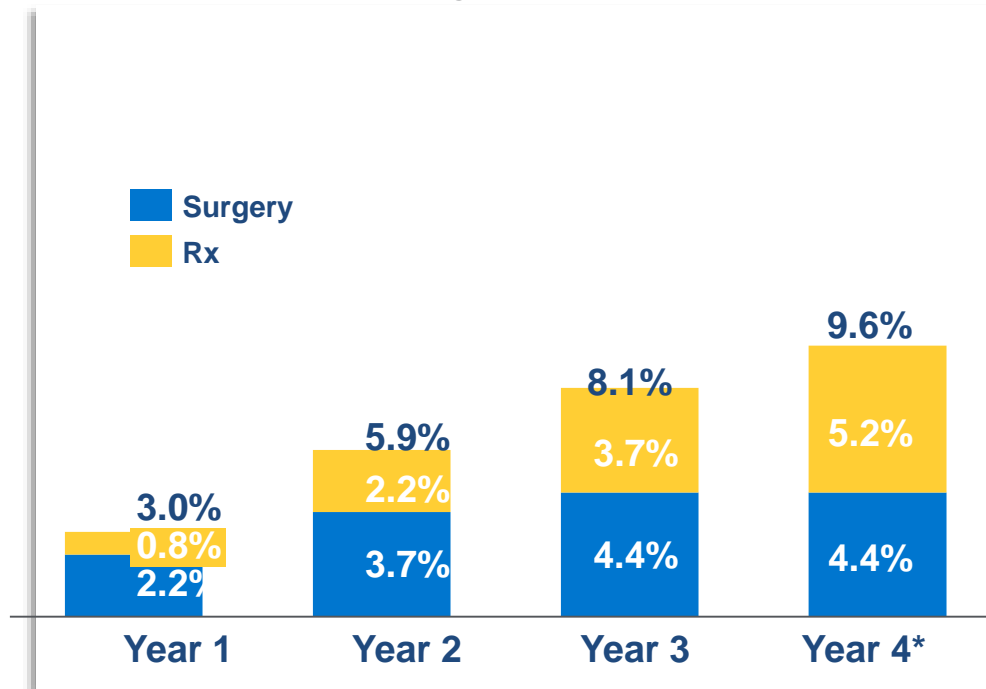
Adverse Events

**57% of Treatment and Crossover patients did not report any AEs.
Related AEs were typically mild to moderate in severity and resolved within 3 weeks.**

Most Common Device and/or Procedure Related Adverse Events	Treatment and Crossover Subjects (N=188) Number of Events (% Occurrence)	Resolved
Dysuria	34 (18.1%)	33
Hematuria, Gross	22 (11.7%)	22
Hematospermia	12 (6.4%)	12
Urinary Frequency	11 (5.9%)	9
Urinary Retention	11 (5.9%)	11
Urinary Urgency	9 (4.8%)	7
Total – All study reported device and/or procedure AEs	Number of Events (Number of Patients, %)	Resolved
	209 (81, 42.9%)	185

Rezūm Retreatment Rates

Rezūm™ Therapy Retreatment Rates^{9,10}



Maintaining Reporting Standards

- 4 year Surgical retreatment rates of 4.4% are consistent with 3-year results
- At 4 years, two additional patients started BPH medication for a total of 5.2% returning to medication

Rezūm Summary and Conclusions

- Statistically significant and clinically meaningful improvements through 4 years¹
 - IPSS 22.0 to 11.4
 - Qmax 9.9 to 13.7
 - QOL 4.4 to 2.3
- **Preservation of sexual function**
 - No de novo erectile dysfunction²
- Adverse events are generally mild and transient³
 - Frequency, Dysuria, Urgency
- Rezūm is an alternative for a broad range of patients with symptomatic BPH including those with **a median lobe/enlarged central zone**²
- Given the overall clinical evidence, safety, efficacy, durability, transient AE's and preservation of sexual function, **perhaps Rezūm can be considered as a first-line therapy for BPH**

Rezūm™ Procedure

HOW I DO IT

The Rezūm system – a minimally invasive water vapor thermal therapy for obstructive benign prostatic hyperplasia

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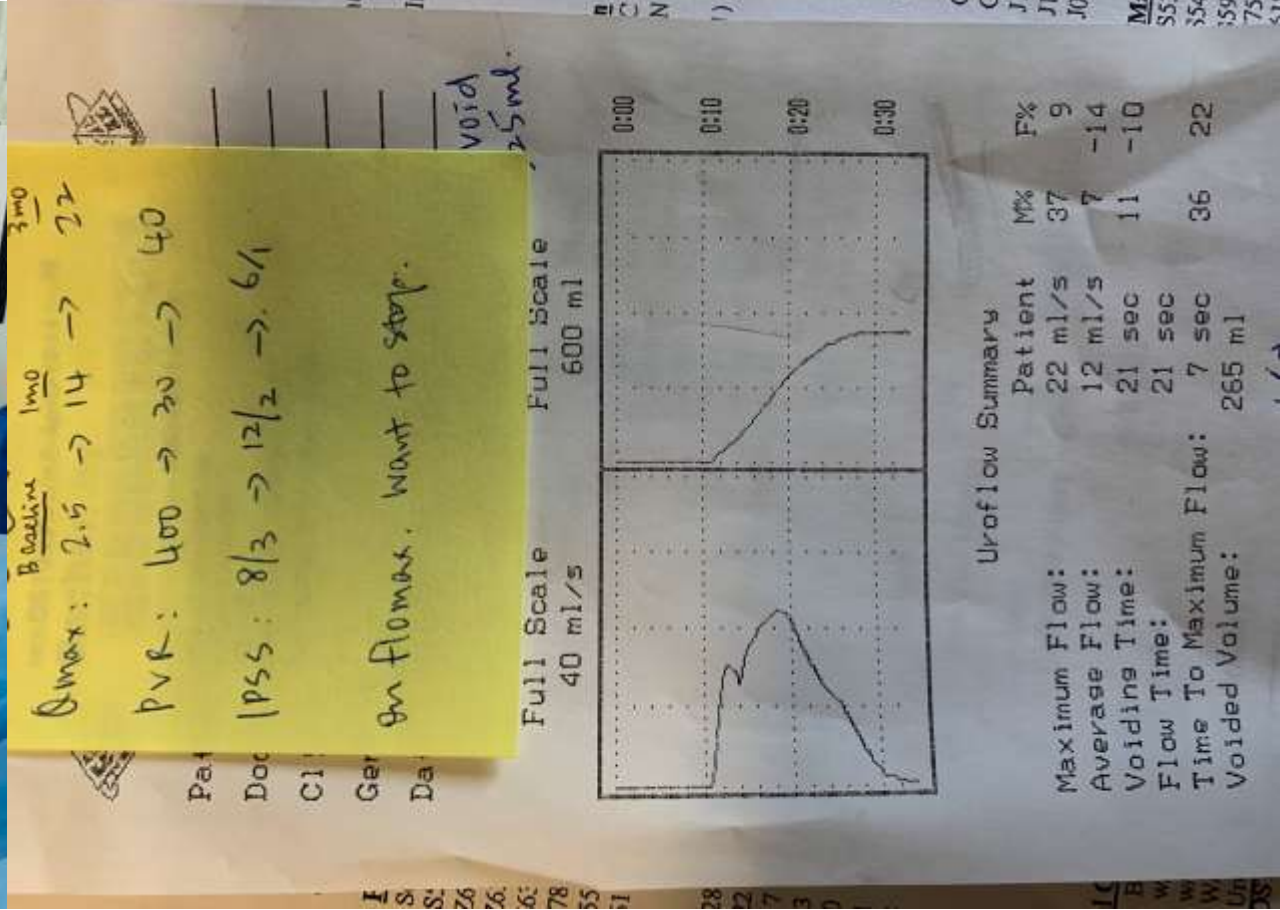
UroLift and Rezum Patient Selection

- Men who have elected to discontinue or who have chosen not to take BPH medications
- Men who are not receptive to other minimally invasive or surgical BPH procedures
- Men who have indicated they aren't bothered enough by symptoms to elect a surgical procedure

Rezüm in Canada – My Experience (First in Canada)



Rezüm in Canada – My Experience



Men's Health Summit 2020



UHN

Toronto General
Toronto Western
Princess Margaret
Toronto Rehab



THANK YOU

QUESTIONS?

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