HE WHO ASKS A QUESTION IS A FOOL FOR FIVE MINUTES; HE WHO DOES **NOT ASK A QUESTION** REMAINS A FOOL FOREVER.

EVEN IF YOU'RE ON THE RIGHT TRACK, YOU'LL **GET RUN OVER IF YOU** JUST SIT THERE.

- WILL ROGERS-

- CHINESE PROVERB -

COURAGE IS RESISTANCE TO FEAR, MASTERY OF FEAR, NOT ABSENCE OF FEAR.

- MARKTWAIN -



# BPH REVIEW: OLD AND NEW (BENIGN PROSTATIC HYPERPLASIA)

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### $\mathsf{BPH}$

- Prostate definition (from the Greek); 'to stand before/alone'
- 8% in  $4^{th}$  decade  $\rightarrow$  90% in  $9^{th}$  decade
- Refers to size and histology, not symptoms
- Lower Urinary Tract Symptoms (LUTS)
  - Irritation, obstruction or a mix
  - 5,000 men 65+; 45% report moderate to severe LUTS
  - 30,000 men (USA, UK, Sweden): 75% sometimes LUTS / 45% often LUTS
- Bladder Outlet Obstruction (BOO)
  - Most commonly from BPH (neurologic #2 most common cause)
  - Can lead to bladder wall changes which can lead to upper tract changes
- Average size → 25 gm (cc)



#### Table 1. Differential Diagnosis of LUTS (Lower Urinary Tract) Symptoms

Benign prostatic hyperplasia

Bladder calculi

Bladder cancer

Bladder irritants (e.g., caffeine)

Diabetes mellitus

Medication use

Anticholinergics (incomplete emptying)

Antidepressants, such as tricyclics

(frequency, incomplete emptying)

Antihistamines (incomplete emptying)

Bronchodilators (straining)

Diuretics (frequency)

Opioid analgesics (incomplete emptying)

Sympathomimetics (straining,

(incomplete emptying)

Neurogenic bladder

Obstructive sleep apnea

(nocturia)

Overactive bladder

Polyuria (isolated nocturnal,

24-hour polyuria)

Prostate cancer

**Prostatitis** 

Urethral or bladder neck

strictures

**Urethritis/sexually** 

transmitted infections

Urinary tract infections



### **BPH**

- Pathophysiology
  - Not well understood
  - Size ‡ symptoms
  - o Alpha Adrenergic Receptors at prostatic urethra-bladder neck
    - ✓ Stimulation of sympathetic nerve fibers above = contraction of smooth muscle; urinary obstruction
    - ✓ That's why alpha blockers work
- Risk Factors
  - o Mild correlation: age, African American, obesity, DM, ETOH



## **BPH Evaluation**

- Primary Care
  - o International Prostate Symptom Score (IPSS) sheet
  - Review EtoH diet, caffeine, any other risk factors
  - o RX (see Table 1)
    - ✓ Obstructive
      - > Anticholinergics, Antihistamines, Opioids
    - ✓ Irritative
      - > Diuretics
      - ➤ B Blocker, Beta Blockers, Calcium Channel Blockers
- DRE
  - Not just nodules but sphincter tone
- UA
- PSA if 10-year life expectancy
- No imaging needed unless sign/symptoms of upper GU tract issues (flank pain, hematuria)

# International Prostate Symptom Score (IPSS)

Over the past month	Not at all	Less than one time in five	Less than half the time	About half the time	More than half the time	Almost always
Incomplete emptying®	0	1	2	3	4	5
Frequency	0	1	2	3	4	5
Intermittency	0	1	2	3	4	5
Urgency	0	1	2	3	4	5
Weak Stream	0	1	2	3	4	5
Straining	0	1	2	3	4	5
Sleeping	0	1	2	3	4	5
Add Symptom Scores:						

	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
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

Total International Prostate Symptom score =

1 – 7 mild symptoms | 8 – 19 moderate symptoms | 20 – 35 severe symptoms Regardless of the score, if your symptoms are bothersome you should notify your doctor.

<sup>\*</sup> In the true sheet the symptoms terms are described

# Overview BPH Treatment Options

- Observation
- Dietary Modifications
- Medication
  - Alpha Blockers
  - 5-ARI (Finasteride, Dutasteride)
  - PDE (daily Cialis)
  - o OAB RX in combination with above
- Minimally Invasive Surgical Therapy (MIST)
  - TUM I Historical
  - o TUNA /
  - o Rezum (Steam Vapor)
  - o UroLift
  - o iTIND (Temporary Inserted Nitinol Device)
- Other
  - Prostatic Artery Embolization (PAE)

- Definitive Surgery
  - o TURP
  - o TUIP
  - o HoLAP
  - PVP (Green Light)
  - HoLEP/ThuLEP
  - Open Simple or Robotic Prostatectomy
  - Aquablation



## **BPH Treatment MILD-MODERATE Symptoms**

- Conservative management is the preferred approach for patients with mild symptoms and without complicating factors.
- Watchful waiting is based on patient education, lifestyle interventions and disease monitoring.
- Lifestyle modifications for mild symptoms
  - o Beverage's without alcohol, caffeine, carbonation, acidic.
    - √ Convert all beverages to water
  - Highly seasoned foods.
  - o Decreasing evening fluid intake / time voiding schedule / limit salt / losing weight
  - Limiting medications known to cause lower urinary tract symptoms (see Table 1 on page 4)
    - ✓ Anticholinergics, Antihistamines, Antidepressants, Diuretics, Bronchodilators (straining), Opioids
- Patients should be followed up regularly (q 6 mos.) detect worsening of symptoms, or the occurrence of complications.



#### **BPH Treatment**

#### **Medications**

- Consider if prostate symptom score over 8, despite lifestyle changes
- Alpha adrenergic (Alpha Blockers)
  - Less constrictions of muscle of bladder neck
  - o Originally from HPTN RX (now rarely used due to 1 incidence CVA & CAD)
  - Now selective RX
    - √ Flomax (Tamsulosin)
    - ✓ Rapaflo (Silodosin)
    - ✓ Uroxatral (Alfuzosin)
  - o IPSS Score ↓ 4-6 points
- Side Effects
  - Hypotension/dizziness
    - ✓ Don't use with PPD 5 inhibitors (Viagra, etc.): hypotension
      - Cataract surgery may have "Floppy Iris" so stop at least 2 weeks prior
      - > But Cialis 5mg does not cause hypotension unless other underlying factors.
  - o ED, retrograde ejaculation, decrease libido





#### **BPH Treatment**

#### **Medications**

- 5α Reductase Inhibitors (ARI)
  - o Testosterone and DHT in prostate are blocked, yet hormonal effects still work
  - Finasteride (ProScar) / Dutasteride (Avodart)
  - o IPSS score ↓ 4-6 points
  - o Unclear how much size decreases, all agree no increase in size
  - Side Effects
    - ✓ Breast swelling / tenderness
    - ✓ 50% ↓ PSA seen after 6m use; so double the PSA value
      - Does not change prostate cancer risk
- Combo of 5 Alpha Reductase Inhibitors + Alpha Blockers
  - Work better than separately
  - o IPSS score ↓ 6-7 points; not as good many surgeries
- Supplements do not work / ? Side effects
  - Saw Palmetto





### Table 2. Medical Therapies for Benign Prostatic Hyperplasia

Medication	Daily Dosage	Cost*	Adverse effects	Comments
Nonselective alpha bloc	kers	•		
Doxazosin (Cardura)	1 mg; titrate to maximum of 8 mg daily	\$20 (\$80)	Orthostatic Hypotension	Requires blood pressure monitoring and dose titration; less expensive
Terazosin	1 mg; titrate to maximum of 20 mg daily	\$10 (NA)	Orthostatic Hypotension	
Selective Alpha Blockers	5			
Alfuzosin (Uroxatral)	10 mg	\$20 (\$400)		Low risk of retrograde ejaculation, hypotension; no blood pressure monitoring or dose titration
Silodosin (Rapaflo)	8 mg	NA (\$170)	Retrograde ejaculation	
Tamsulosin (Flomax)	o.4mg; titrate to maximum of o.8 mg daily	\$30 (\$190)	Decreased ejaculation; highest risk of intraoperative floppy iris syndrome	

## Table 2. Medical Therapies for Benign Prostatic Hyperplasia

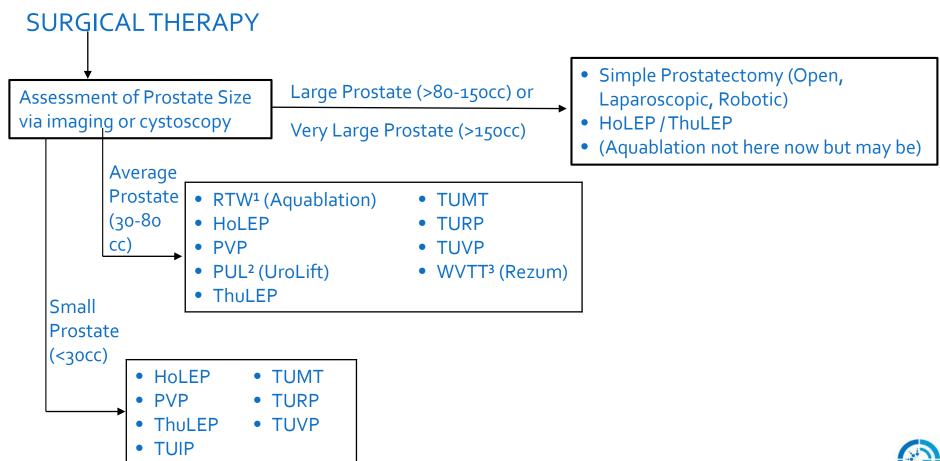
Medication	Daily Dosage	Cost*	Adverse effects	Comments			
5-alpha reductase inhibitors							
Dutasteride (Avodart)	o.5 mg	NA (\$155)	Ejaculation disorder, decreased libido, erectile dysfunction	No dose titration; three to six months to take effect; decreases prostate-specific antigen by 50%; combination therapy with an alpha blocker recommended in patients with an enlarged prostate			
Finasteride	5mg		Ejaculation disorder, decreased libido, erectile dysfunction	No dose titration; three to six months to take effect; decreases prostate-specific antigen by 50%; combination therapy with an alpha blocker recommended in patients with an enlarged prostate			
Anticholinergic agents							
Fesoterodine (Toviaz)	4 to 8 mg	NA (\$210)	Dry mouth and eyes, constipation	Assess postvoid residual urine before starting, for patients with predominantly irritative symptoms			
Oxybutynin extended release (Ditropan XL)	10 mg	\$40 (\$175)	Dry mouth and eyes, constipation	Assess postvoid residual urine before starting, for patients with predominantly irritative symptoms			
Solifenacin (Vesicare)	5 mg	NA (\$240)	Dry mouth and eyes, constipation	Assess postvoid residual urine before starting, for patients with predominantly irritative symptoms			
Tolterodine extended release (Detrol LA)	4 mg	\$150 (\$265)	Dry mouth and eyes, constipation	Assess postvoid residual urine before starting, for patients with predominantly irritative symptoms			
Beta 3 Agonist							
Myrbetriq (3 Beta)	25mg-50mg	Depends on insurance up to \$400/mo	Minimal	Assess postvoid residual urine before starting, for patients with predominantly irritative symptoms 13			

# **BPH Surgical Therapy**

- Treatment; guideline recommendations (2021)
  - Failure / Patient Refusal of medical therapy
  - Refractory urinary retention
  - Recurrent urinary tract infection
  - o Persistent hematuria
  - Bladder stones
  - Renal insufficiency
  - o Guidelines of prostate size for surgery purposes (average size 25gm)
    - ✓ Small <30gm
    - ✓ Average 30-80 gm
    - ✓ Large 80-150 gm
    - ✓ Very Large >150 gm
    - ✓ 1700 patients reviewed 20% over >75gm; 9% over 100gm



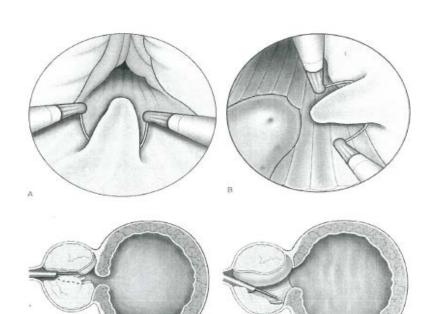
#### Table 3 Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia

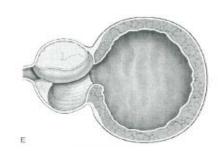




# BPH Surgical Treatment (OLD) The Transurethral Resection of the Prostate (TURP)

- A resectoscope loop introduced into the bladder surgically removes prostate tissue
- Gold Standard; started in 1920's so hundreds of studies done
- Surgery with the most proven long-term outcomes.
- Negatives
  - o Dilutional hyponatremia is possible at time of surgery
  - o 70% Retro-ejaculation
  - o 5-7% Retention
  - o Incontinence o% 5%
  - o Stricture 4%
  - o BNC 2%
  - o ED 1% 10%
  - o Inpatient Procedure
  - o Higher cost
  - Longer hospital stay (2-3 days)



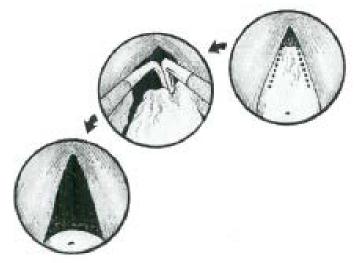


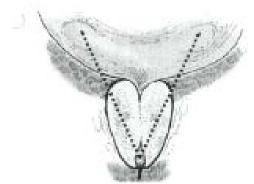


# Surgical BPH Treatment (Old)

(Transurethral Incision Prostate)

- Small cuts are made in the prostate at 5 and 7 o'clock to reduce urethral constriction
- Pros:
  - Better for small (<30-g) prostates</li>
  - Outpatient procedure
  - Less blood loss and shorter hospital stay than with TURP
  - o Reduced ejaculatory problems
  - o "High-riding" bladder neck
  - o IPSS scores high with smaller prostates
  - o Complication rate <TURP
- Cons:
  - Higher rate of repeat procedures compared with TURP
  - Lack of large, high-quality studies w/long-term outcomes







# Surgery BPH Treatment (Old)

#### VaporTrode Electrode Current Vaporization

- Device using many configurations of rollerball
- Works on contact using rollerball





- Low Bleeding Rate
- Outpatient
- Cath

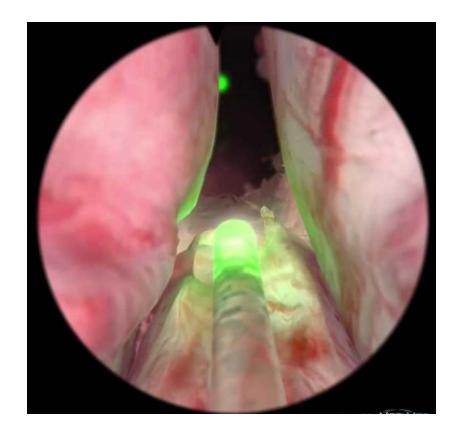
- <80 gm
- Retrograde ejaculation
- Dysuria
- Few long term studies



# **BPH Treatment (Old)**

#### **Green Light Laser**

- Holmium YAGLaser vaporizes prostate tissue (non-contact)
- Pros:
  - Continually upgrade of fiber
  - o OP procedure
  - Shorter catheterization
  - o Less bleeding\*
- Cons:
  - Slower and less prostatic tissue removed than with TURP
  - Bladder Neck Scar
  - o Irritative Symptoms for up to 12 weeks

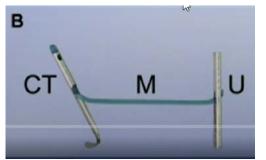


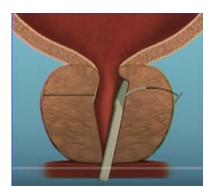


New BPH Surgical Treatment

Prostatic Urethral Lift (UroLift)

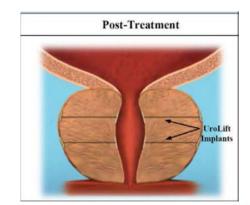
- UroLift®
  - Permanent implants that retract lateral lobe obstructive tissue
  - Lifts the obstruction out of the way
    - ✓ Creates a "new" anterior channel
  - o Components:
    - ✓ Nitinol capsular tab
    - ✓ Stainless steel urethral tab
  - o Positive
    - ✓ MR compatible
    - ✓ No ED / Retrograde Ejaculation
    - ✓ Outpatient; oral or IV sedation
    - ✓ IPSS + 8 at 5 years
  - Negatives
    - ✓ Cath 50%, 1-2 days
    - ✓ Not really office, more like ASC
    - ✓ Retreatment in 14% at 5 years
    - ✓ Can't use on median lobes + / -













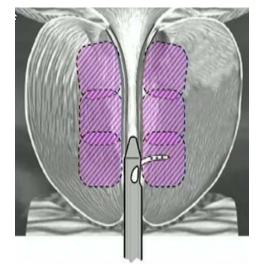
New BPH Surgical Treatment

Water Vapor Thermal Therapy (Rezum)

- FDA approved 2015: average size prostate (30-80gm)
- Radiofrequency thermal therapy in the form of steam
  - Caused cell (tissue necrosis death and delayed tissue sloughing)
  - Single use device with a needle and 12 emitters creates at 1.5-2.0 cm lesion
- Positives
  - Office based procedure
  - Use on median lobe
  - o Comparable with UroLift long term studies (up to 5 years).
- Negatives
  - o High retreatment rate
  - Not as good as TURP especially retreatment and IPSS
  - o Lots of irritative symptoms for the first 2 weeks



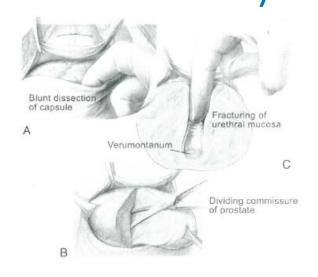








## Surgical BPH Treatment Both Old & New Old Retropubic Simple Prostatectomy



- Larger glands >250gm
- Ret Ejaculation 90%
- ED: 3-5%
- BNC 5%
- Catheter 3-7 days

# New Robotic Simple Prostatectomy



- Larger glands >100gm; doing for all size but usually above 200
- Longer Operation Time
- Complications similar to open but few large studies
- High Cost
- Length of Stay shorter than open
- Catheter 3-7 days

# Surgical BPH Treatment Both Old & New

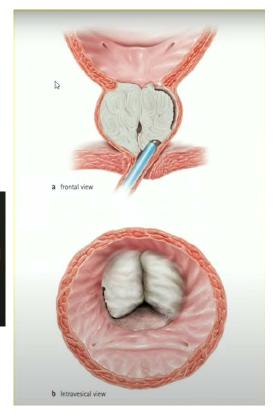
#### Holmium Laser Enucleation of the Prostate (HoLEP)

#### HoLEP

- o First described 1995 but new Holmium laser fiber are more efficient
- All prostate sizes, configurations
- o Adenoma separated from prostate capsule
- o Enucleated tissue morcellated in the bladder
- o 1000 Patient Study 2018
  - ✓ Size range 9-391 gm
  - ✓ Pre IPSS 20 / at 5 year ↓ to 5
  - ✓ Pre-flow 8 / at 3 years ↑ to 22 (cc/sec)
  - ✓ Long term incont 1-2%
  - ✓ Urethral stricture 2-7%
- o Pro
  - ✓ Any size prostate
  - ✓ No incision
  - ✓ Get tissue for pathology
- o Con
  - ✓ Long time to do / learn
  - ✓ Morcellation piece of the surgery still an issue (time / side effects)









# Very New BPH Treatment

# iTIND Device (Temporarily Implanted Nitinol Device)



- Works similar to TUIP: incisions at 5/7 o'clock
- Second-generation iTIND device with three struts and one anchoring leaflet.
- FDA Approved 2020
- 3 Struts at 12, 5, 7 o'clock that stay in 3-7 days
  - o Has string during time in
- Good local, no Cath, ED preserved, device removed in office
- Bad 5 to 7 day implant with string coming out of penis, no high neck; minimal data

#### **Prostate Embolization**

- Interventional Radiology
- Outpatient (maybe)
- Short Cath Time
- Not recommended per AUA (little long-term data)
  - o Interventional Radiology Community Disagrees
  - More randomized trials then Rezum, UroLift or Aquablation and has equivalent efficiency / side effects
  - "Jury Still Out"

# Very New BPH Surgical Treatment

#### Aquablation (AquaBeam) System

- Ultrasound Guided
- Robot assisted water jet
- 2015 First Trial
- 2017 FDA approved
- 2020 Medicare approve BUT still has "t" code for (experimental) CPT
- 3 main components: see circles

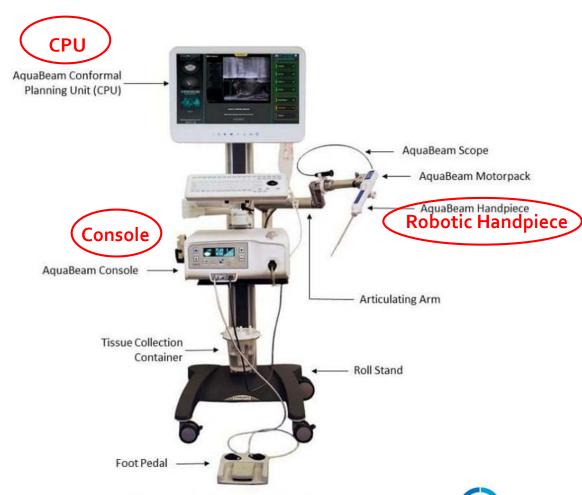
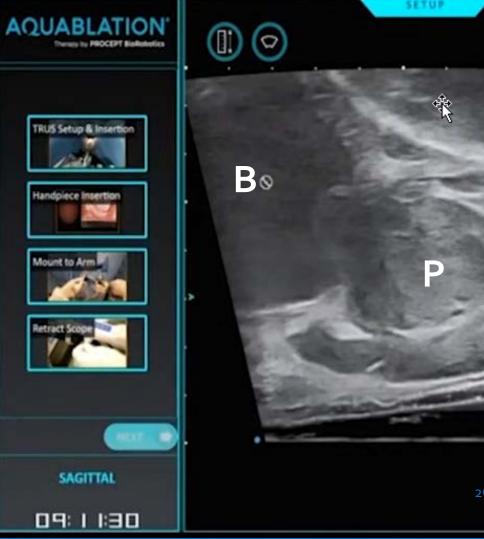


Figure 1 AQUABEAM System

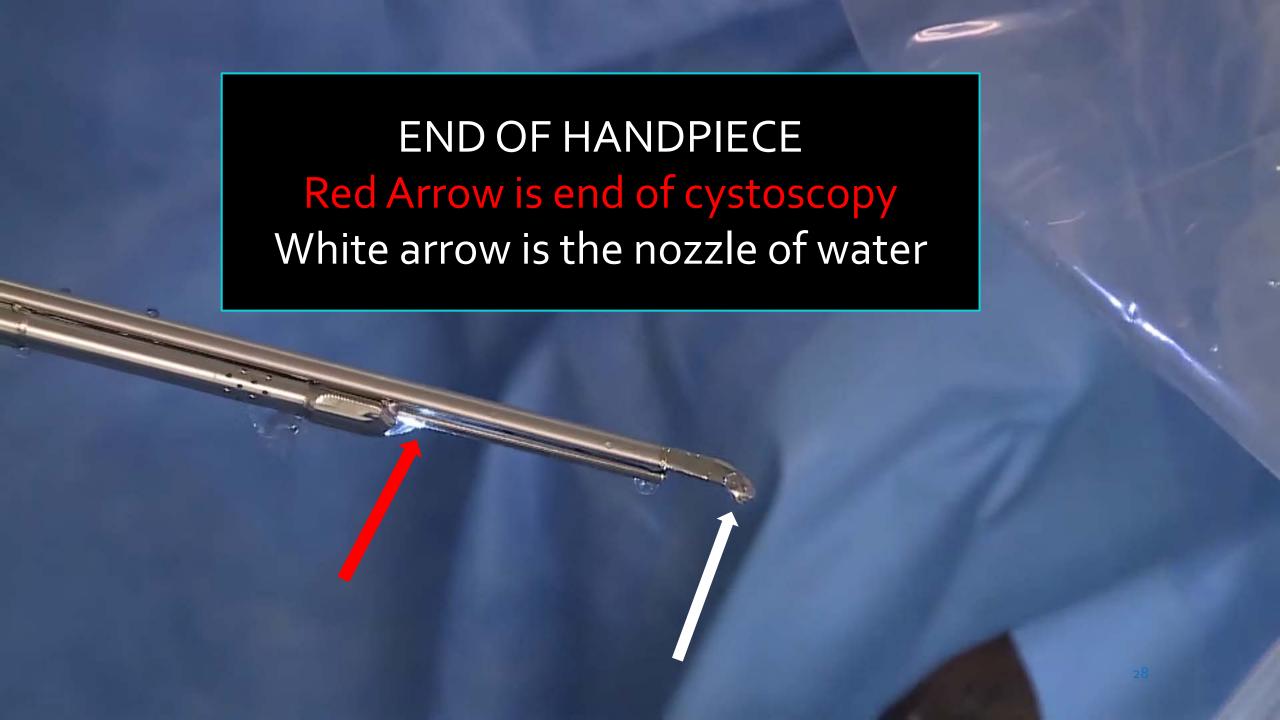


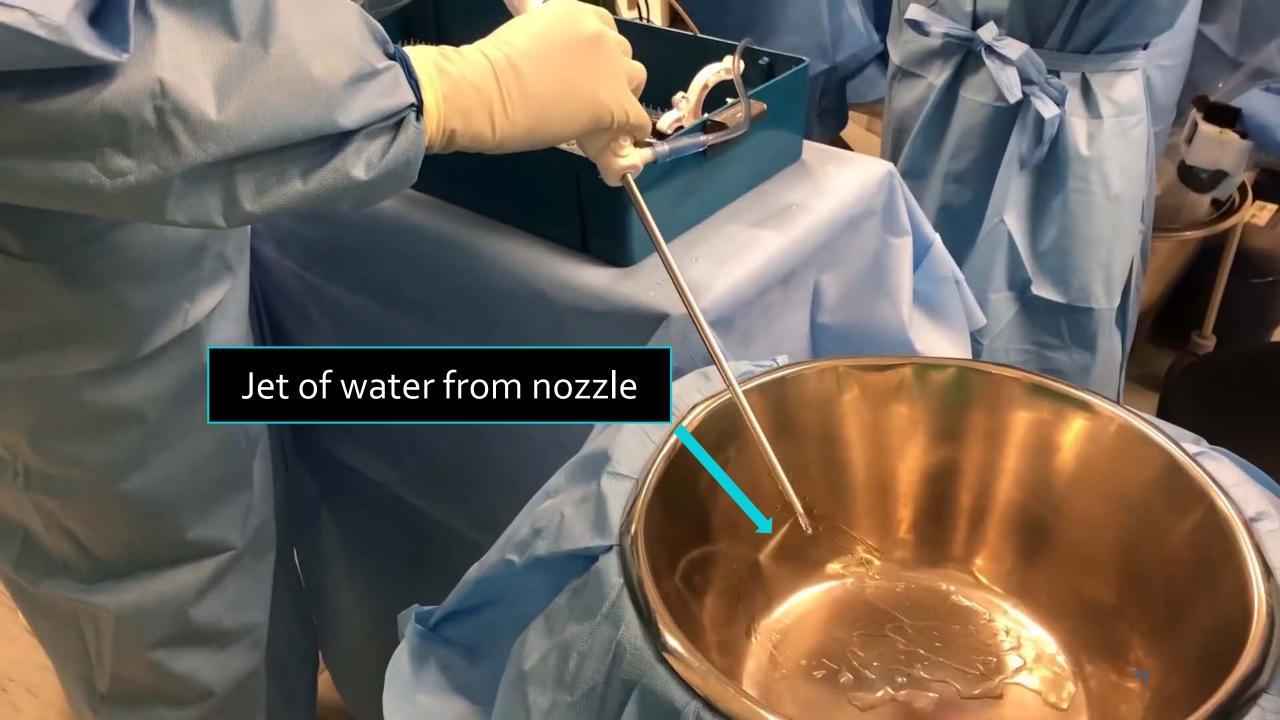


#### **TRUS Insertion**











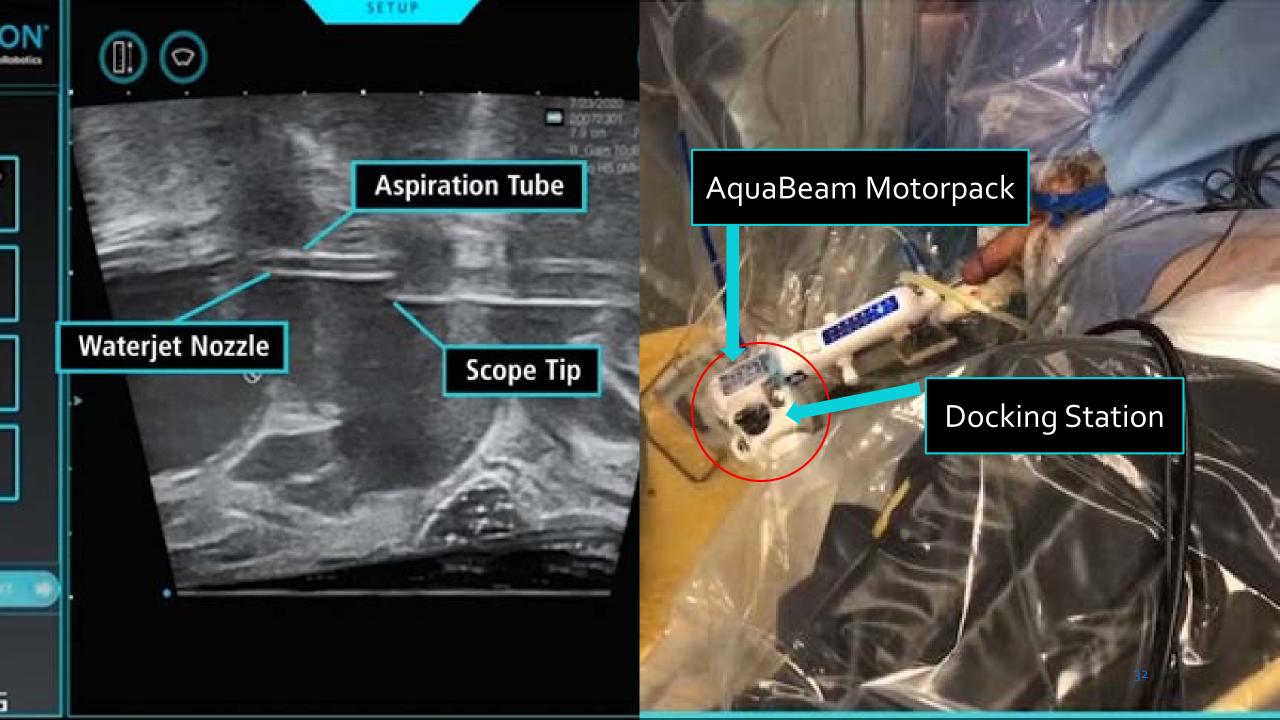
#### **Handpiece Insertion**

**Shadow from handpiece in Prostate** 

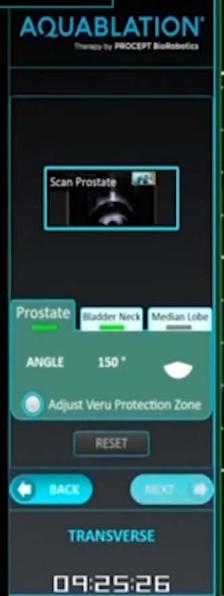


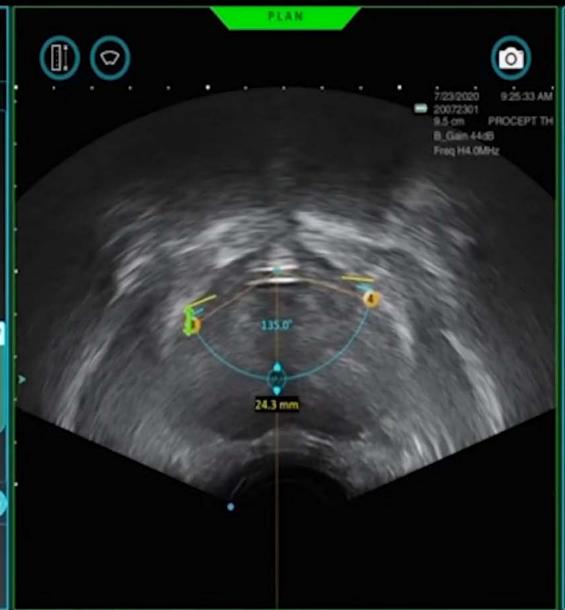






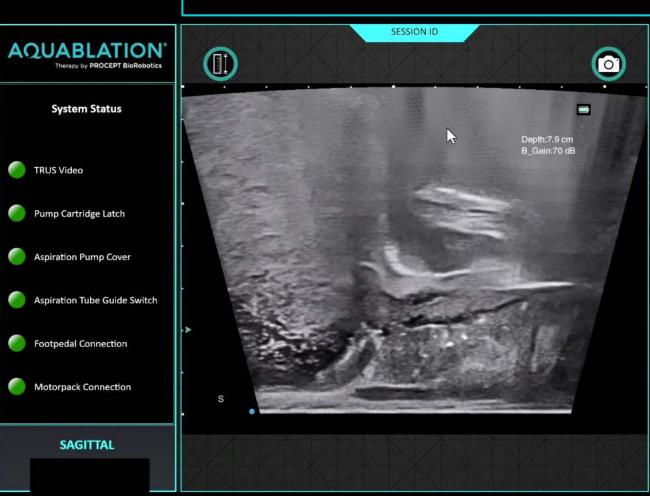
#### **Angle Planning**







### Post Treatment







## AQUABLATION CLOT EVACUATION AND FOCAL BLADDER NECK CAUTERY





#### Surgical BPH Treatment (New vs. Old Gold Standard)

5 Year Results Aquablation vs TURP 30-80 grams Randomized, multi-center, blinded

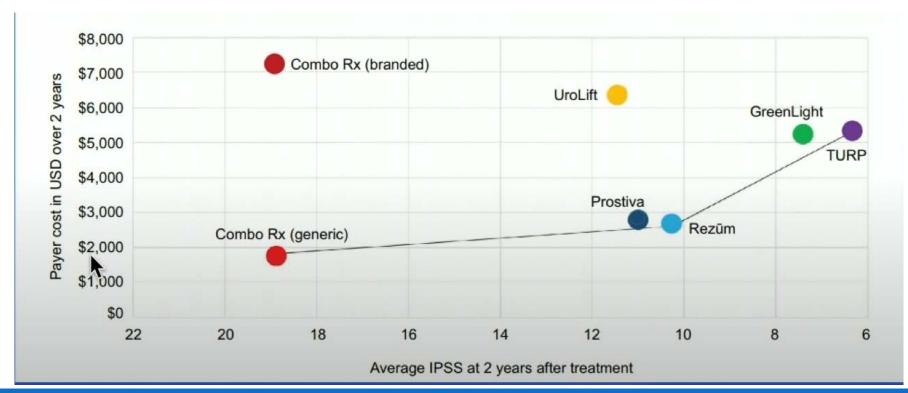
	Aquablation	TURP	
Patients	58	32	
IPSS (improvement)	15	13	
Change Qmax (Peak Flow Rate) (improved)	125% (11cc/sec)	89% (6cc/sec)	
Sexually Active	80%	82%	
No Ejaculation	10%	75%	
Retreatment at 5 year (Rx or Sx)	6%	12%	
Procedure Time Minutes	40	36	
Length of Stay / Foley In	1.4 / 1 day	1.4 / 1 day	

# Surgical BPH Treatment Aquablation (AA) Future

- <u>Then</u>: AA was in MIST (Minimally Invasive Surgical Therapies) category (prostate size <80gm)
  - Showing better efficacy than other MIST and comparable with TURP
- <u>Now</u>: AA with new 5-year data and doing surgery on all prostate sizes, it is proving comparable to HoLEP and simple prostatectomy (open or robotic)
- <u>Future</u>: Guideline will acknowledge it is appropriate for prostate glands small through very large (30 to >150 gm)

# Two Year Comparison of Cost vs Efficacy of Various Treatments by IPSS

Attribute	Statistic	ComboRx		Rezūm®	UroLift®	Prostiva®	Greenlight®	TURP
		Medicare Part D price	Branded price					
Cost	Mean at 2 years	\$1,736	\$7,082	\$2,582	\$6,386	\$2,855	\$5,099	\$5,181
IPSS	Mean at 2 years	18.9	18.9	10.2	11.4	10.9	7.4	6.4
Cost-effectiveness of	ICER at 2 years	\$97	-\$518	Base comparator	-\$3,058	-\$352	\$900	\$686
Rezūm versus other <sup>a</sup>	Dominated	No	Yes	NA	Yes	Yesb	No	No
Cost-effectiveness of	ICER at 2 years	\$276	-\$1,523	\$6,863	-\$240	\$509	\$83	Base comparator
TURP versus other	Dominated	No	Yes	No	Yes	No	No	NA





## My BPH Evaluation Pathway

- IPSS
- UA (C/S)
- PSA\* / DRE
- Bladder Scan by Ultrasound
- Renal US or CT
- Urocuff Test
- Flexible Local Cystoscopy + Transrectal Ultrasound of Prostate for Volume (TRUS) (+ / - biopsy of prostate)

## Bladder Scan



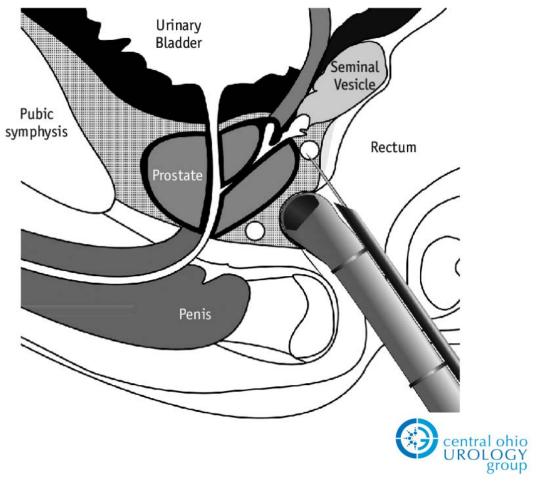




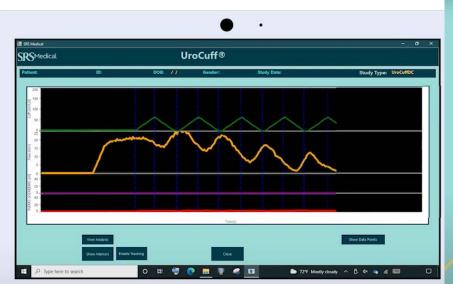
## Transrectal Ultrasound (TRUS)

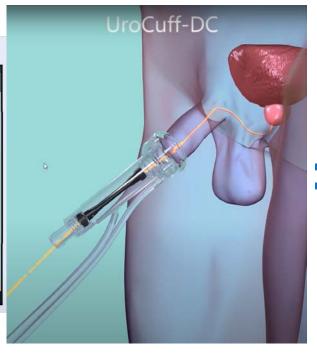


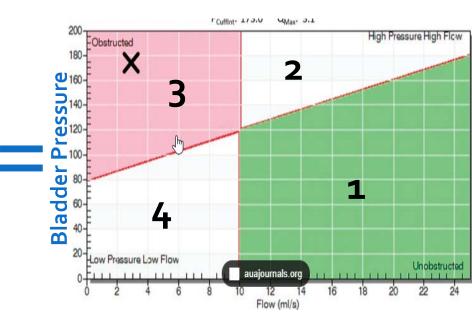
For prostate volume (cc's, gm, cm<sup>3</sup>) For prostate biopsy



#### **UroCuff Test**







 Noninvasive test for pressure flow for these patients with LUTS: 1 Green – unobstructed → 2 White = High Pressure High Flow → 3 Pink = Obstructed → 4 White = low pressure low flow



#### BPH Treatment – My Discussion with Patients

- Treatment
  - Conservative Management
  - $\circ RX$

<u>Positive:</u> <u>Negative:</u>

No SX 3-6 pills/day

Potential Long-Term S/E

Lab changes possible

Need close F/U

Poor Compliance (70% stop after 6-12 months)

Patients over age 60 take an average 7 meds

- MIST (Minimally Invasive Surgical Therapies)
  - ✓ See Table 3
  - ✓ Size and Prostate Shape Matters
    - > Help determine which treatment
    - > Study 1700 men: 20% over 75 gm; 9% over 100gm
  - ✓ Most show 8 points improvement in IPSS; 3 pts improvement in urine flow rate



## BPH Treatment – My Discussion with Patients

- More Invasive Therapies
  - See Table 3
  - All Sizes over 100 gm (large)
    - ✓ TURP\* (probably need 2)
    - √ HoLEP
    - ✓ Aquablation\*
  - Over 150gm (very large)
    - √ HoLEP
    - ✓ Aquablation\*
    - √ Simple open or robotic prostatectomy
    - ✓ PAE\*
  - My Aquablation experience
    - √ ~ 65 70 cases since 6/2020
    - ✓ Size 4ogm to 26ogm
    - ✓ Comparable S/E profile to TURP. Unofficially, 80-90% either off catheter or off RX.



## Final Thoughts



- Think LUTS when you think of BPH
  - Remember IPSS Sheet
  - o Conservative therapy for mild-moderate cases; successful 50% of the time.
    - ✓ Hard for patient to achieve / maintain
- When I see patients:
  - o 1 need directive evaluation (upper and lower GU tract evaluation)
  - o 2 discussion
    - ✓ Is a procedure really worse than adding 1-4 RX to someone or an avg of 7 RX/day
    - ✓ Is RX a "fur-lined trap"?
    - ✓ Surgery; Lots of Choices
    - ✓ Determining factors
      - > Size/Shape Prostate and patient comorbidities
      - > Willingness for surgery treatment

"Change is the only constant in Life" (the original quote) – Heraclitus 500BC





