

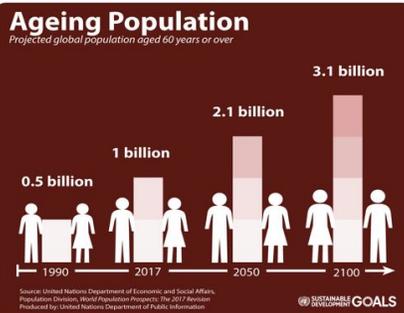
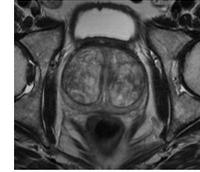
Prostatic Artery Embolization for Benign Prostatic Hyperplasia



Stephen T Kee, MD
Professor of Radiology

The prostate

- Walnut sized gland
 - ~25 cc
- Produces part of the fluid portion of semen
- Situated just under the bladder
 - Helps control flow of urine



$\frac{1}{4}$

Proportion of men over 70 who have moderate-severe BPH symptoms that impair quality of life

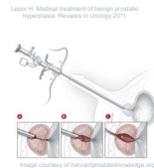
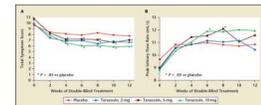
Many of these men are untreated or undertreated

IPSS Score	Symptom Severity
0-7	Mild
8-19	Moderate
20-35	Severe

Background

Traditional BPH treatments

- Medical therapy
 - Selective alpha-blockers
 - 5-alpha-reductase inhibitors
 - Modest (3-5 point) IPSS improvement
- Surgical therapy
 - TURP for prostates up to ~80-100 cc
 - Open prostatectomy for larger prostates
 - Risks of urinary incontinence, erectile dysfunction, retrograde ejaculation, urethral stricture
- Many men choose to avoid treatment



Prostate artery embolization for BPH

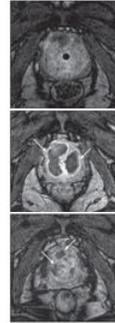
Rationale and technique

- The data
- UCLA experience
- Example cases
- Latest developments

PAE for BPH

Rationale

- Prostate is a hypervascular organ with blood supply from bilateral prostatic arteries
- Superselection and embolization of the prostatic arteries leads to partial ischemic necrosis
- Shrinkage of the gland follows, with improvement of LUTS
- Analogous to uterine fibroid embolization, splenic embolization, etc



PAE for BPH

Technique

- Femoral artery access
- Internal iliac artery angiograms to find prostatic artery on each side
 - Variable origin



PAE for BPH

Technique

- Femoral artery access
- Internal iliac artery angiograms to find prostatic artery on each side
 - Variable origin
- Small microcatheter to superselect prostatic artery on each side



PAE for BPH

Technique

- Femoral artery access
- Internal iliac artery angiograms to find prostatic artery on each side
 - Variable origin
- Small microcatheter to superselect prostatic artery on each side
- Confirm position with multiple views or cone-beam CT



PAE for BPH

Technique

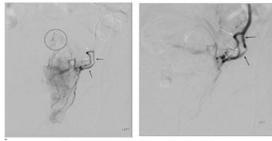
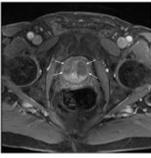
- Femoral artery access
- Internal iliac artery angiograms to find prostatic artery on each side
 - Variable origin
- Small microcatheter to superselect prostatic artery on each side
- Confirm position with multiple views or cone-beam CT
- Embolize with small particles (100-500 micron) to stasis



PAE for BPH

Potential advantages

- No limit on prostate size
- Outpatient procedure
- Conscious sedation
- Rapid recovery
- Less morbidity
 - No impotence
 - No incontinence
 - No Foley catheter
 - Minimal blood loss
- On-label indication with FDA since 2017

November, JUNE 2016

David Geffen School of Medicine UCLA Health System

Prostate artery embolization for BPH

Rationale and technique

The data

UCLA experience

Example cases

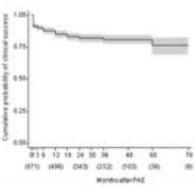
Latest developments

David Geffen School of Medicine UCLA Health System

PAE for BPH

Largest cohort study

- 630 consecutive patients
 - 67 in acute urinary retention (indwelling Foley)
 - Mean IPSS 23 (severe), QOL 4.2 (unhappy)
 - Prostate volume 81 cc
- Medium-term clinical success rate (1-3 years) was **82%**
- Long-term success rate (3-6.5 years) was **76%**
- Mean IPSS improvement of **12.1 points**
- Adverse events were mild
 - 0.3% major complication rate
 - No urinary incontinence or sexual dysfunction
- If PAE succeeds, it is durable in most patients**

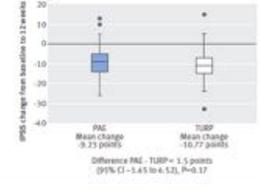


David Geffen School of Medicine UCLA Health System

PAE vs. TURP for BPH

2018 RCT

- High quality RCT
 - 99 patients with mod-severe LUTS
 - Mean age 66 years, mean IPSS ~18
 - Prostate volume ~50 mL
 - Good surgical candidates
- Randomized to PAE or TURP
 - Primary endpoint: IPSS change at 3 mo
- Result: No significant difference
 - PAE: **-9.2 points**
 - TURP: **-10.8 points**

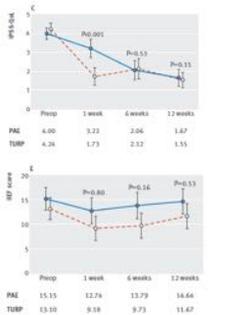


David Geffen School of Medicine UCLA Health System

PAE vs. TURP for BPH

2018 RCT: Secondary subjective measures

- QoL improvement similar
 - 2.33 for PAE, -2.69 for TURP (p=0.15)
- Erectile function unaffected
 - 0.98 for PAE, -1.84 for TURP (p=0.53)

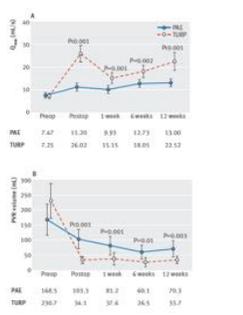


David Geffen School of Medicine UCLA Health System

PAE vs. TURP for BPH

2018 RCT: Secondary objective measures

- Peak flow improvement better with TURP
 - +5.2 for PAE, +15.3 for TURP (P<0.001)
- Postvoid residual improvement better with TURP
 - 88.4 for PAE, -200.0 for TURP (p=0.003)



David Geffen School of Medicine UCLA Health System

PAE vs. TURP for BPH

2018 RCT: Safety

- Less Hgb decrease at 24h for PAE
 - 0.4 for PAE, -1.4 for TURP (p=0.001)
- Less indwelling Foley time for PAE
 - 1.3 d for PAE, 3.3 d for TURP (p=0.001)
- Shorter hospital stay with PAE
 - 2.2 d for PAE, 4.2 d for TURP (p=0.001)
- Fewer adverse events for PAE
 - 36 vs 70 events (p=0.003)
 - One-third as many SAE

David Geffen School of Medicine | UCLA Health System

PAE vs. TURP for BPH

2018 RCT: Conclusions

- Similar subjective improvement for PAE and TURP
- Better objective measures with TURP
- Better safety profile with PAE

PAE should be considered in patients in whom the indication for surgery is primarily based on symptoms. For severe complications related to benign prostatic hyperplasia, TURP should be preferred.

David Geffen School of Medicine | UCLA Health System

PAE for BPH

2018 American cohort of large prostates

- 93 patients with prostate volume >80 mL
 - Mean IPSS 22.3, QoL 4.4
- PAE performed with PErFecTED technique
 - Proximal Embolization First, Then Embolize Distal
- Subjective outcomes at 12 months
 - Mean IPSS improvement of 15.0 points
 - Mean QoL improvement of 3.1 points
- No major complications
- PAE results improve with larger prostates and with meticulous technique

David Geffen School of Medicine | UCLA Health System

PAE guidelines

Updated multi-society consensus statement 2019

- Review of 2200 patients from 11 countries
- PAE is effective
 - IPSS improvement 10 to 18 points
 - QoL improvement 2 to 4 points
- PAE is safe
 - Major complication rate about 0.5%
 - Erectile function unchanged
 - Radiation dose similar to other complex embo procedures
- Specific clinical scenarios:
 - Effective (possibly more effective) in very large prostates
 - Catheter independence achieved in about 80%
 - Immediate cessation of hematuria

David Geffen School of Medicine | UCLA Health System

PAE guidelines

Updated multi-society consensus statement 2019

- Review of 2200 patients from 11 countries
- PAE is effective
 - IPSS improvement 10 to 18 points
 - QoL improvement 2 to 4 points
- PAE is safe
 - Major complication rate about 0.5%
 - Erectile function unchanged
 - Radiation dose similar to other complex embo procedures
- Specific clinical scenarios:
 - Effective (possibly more effective) in very large prostates
 - Catheter independence achieved in about 80%
 - Immediate cessation of hematuria

David Geffen School of Medicine | UCLA Health System

Prostate artery embolization for BPH

Rationale and technique
 Newest data
 UCLA experience
 Example cases
 Latest developments

David Geffen School of Medicine | UCLA Health System

PAE at UCLA

Patient selection

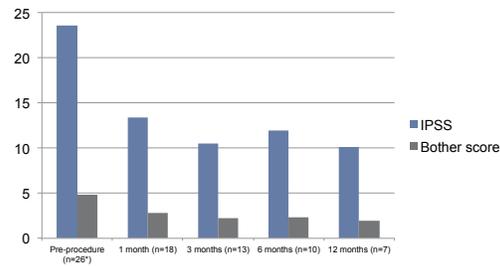
- Work closely with urology
 - Baseline evaluation
 - Work-up to rule out other causes of LUTS
 - Offer traditional therapy (medical and surgical)
 - Co-manage post-procedure
- First 60 patients treated
 - Severe LUTS (mean IPSS 23)
 - Prostate volume 40-400 cc
 - 4 with indwelling Foley
 - 3 with refractory hematuria

PAE at UCLA

Outcomes

- Overall clinical success 48/60 (80%)
 - Two patients with technical failure (severe atherosclerosis)
 - Ten patients technically successful but without significant improvement
 - Collateral prostate supply?
 - Bladder dysfunction?
 - 3/4 patients with indwelling Foley had it successfully removed
 - All 3 patients with hematuria had it resolve
- Mean IPSS improvement at 12 months = **13.5 points**
- Mean QOL improvement at 12 months = **2.9 points**

Outcomes following PAE for BPH at UCLA



PAE at UCLA

Outcomes

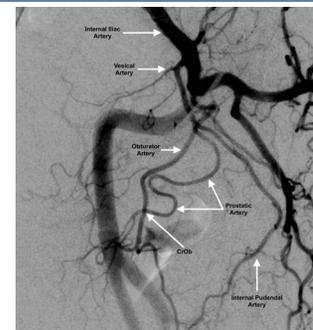
- All performed as outpatient procedure under conscious sedation
- 1 major adverse event
 - Groin pseudoaneurysm at access site, required thrombin injection, no sequelae
 - No bladder or rectal ischemia
 - No erectile dysfunction
 - No blood transfusion
- Minor adverse events (all self-resolved)
 - Dysuria in 8 patients
 - Bladder spasms or pelvic pain in 9 patients
 - Passage of sloughed tissue in 2 patients
 - Transient hematuria in 2 patients
 - Small self-limited penile skin ulcer in 1 patient

PAE studies at UCLA

- PAE predictors of success on CTA
 - PA size 1.5 mm or smaller showed IPSS improvement by 10.0 at 6 months
 - PA size >1.5 mm had IPSS improvement by 17.4 points at 6 months
 - No other predictors were significant
- PAE in giant prostatic enlargement (>200 cc)
 - IPSS improved by 16.7, QoL improved by 3.0
 - Safe and effective, no upper limit on size
- Survey-based assessment of ejaculatory function (n=28)
 - 16% had worsened EJD, 72% unaffected, 12% improved
 - 3 patients (12%) had severely affected EJD or anejaculation

Crossing obturator sign

- Look at 45 degree ipsilateral angiogram of internal iliac artery
- Prostatic artery crosses the obturator artery in 90% of cases
- Not applicable if obturator artery arises from external iliac



Crossing obturator sign

- Look at 45 degree ipsilateral angiogram of internal iliac artery
- Prostatic artery crosses the obturator artery in 90% of cases
- Not applicable if obturator artery arises from external iliac

Internal Iliac Artery
Vesical Artery
CRIB
Prostatic Artery
Obturator Artery
Internal Pudendal Artery

David Geffen School of Medicine
UCLA Health System

31

Crossing obturator sign

- Look at 45 degree ipsilateral angiogram of internal iliac artery
- Prostatic artery crosses the obturator artery in 90% of cases
- Not applicable if obturator artery arises from external iliac

Internal Iliac Artery
Vesical Artery
Obturator Artery
CRIB
Prostatic Artery
Middle Rectal Artery
Internal Pudendal Artery

David Geffen School of Medicine
UCLA Health System

32

Prostate artery embolization for BPH

Rationale and technique
Newest data
UCLA experience
Example cases
Latest developments

David Geffen School of Medicine
UCLA Health System

33

PAE at UCLA

Example 1: Poor surgical candidate

- 83 y/o male
- BPH with IPSS 15, QoL 5
- Prostate volume 340 cc (!)
- Failed medical therapy
- Urology consult: Not surgical candidate due to age and co-morbidities
 - CAD s/p stent x2
 - HTN, hyperlipidemia

David Geffen School of Medicine
UCLA Health System

PAE at UCLA

Example 1: Poor surgical candidate

- PAE performed 6/19/2018
 - Outpatient, moderate sedation
 - No Foley
 - No adverse events
- Good results at follow-up
 - IPSS down from 15 to 6
 - Bother score down from 5 to 2

David Geffen School of Medicine
UCLA Health System

PAE at UCLA

Example 2: Large prostate and median lobe

- 74 y/o otherwise healthy male
- BPH with episodic AUR and UTI
 - Foley in place
 - IPSS 16 (prior to Foley), QoL 5
 - Prostate volume 150 cc
 - Large median lobe bulging into bladder
- Failed medical therapy (Avodart/Flomax)
- Urology consult: Offered prostatectomy
 - Refused all surgery, concerned about side effects
 - Referred for PAE

David Geffen School of Medicine
UCLA Health System

PAE at UCLA

Example 2: Large prostate and median lobe

- 74 y/o otherwise healthy male
- BPH with episodic AUR and UTI
 - Foley in place
 - IPSS 16 (prior to Foley), QoL 5
 - Prostate volume 150 cc
 - Large median lobe bulging into bladder
- Failed medical therapy (Avodart/Flomax)
- Urology consult: Offered prostatectomy
 - Refused all surgery, concerned about side effects
 - Referred for PAE

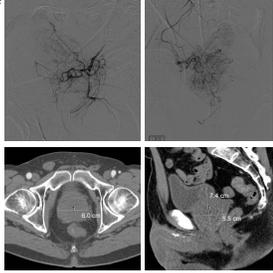


David Geffen School of Medicine
UCLA Health System

PAE at UCLA

Example 2: Large prostate and median lobe

- Successful PAE 3/28/2017
 - Outpatient procedure, no side effects
- Foley removed at 2 weeks
- 6 month follow-up
 - IPSS 2, QoL 0
 - CTA: PV 150 to 100 cc (-33%)
 - Median lobe shrinkage
- 12 month follow-up
 - IPSS 1, QoL 0



David Geffen School of Medicine
UCLA Health System

PAE at UCLA

Example 2: Large prostate and median lobe

- Successful PAE 3/28/2017
 - Outpatient procedure, no side effects
- Foley removed at 2 weeks
- 6 month follow-up
 - IPSS 2, QoL 0
 - CTA: PV 150 to 100 cc (-33%)
 - Median lobe shrinkage
- 12 month follow-up
 - IPSS 1, QoL 0



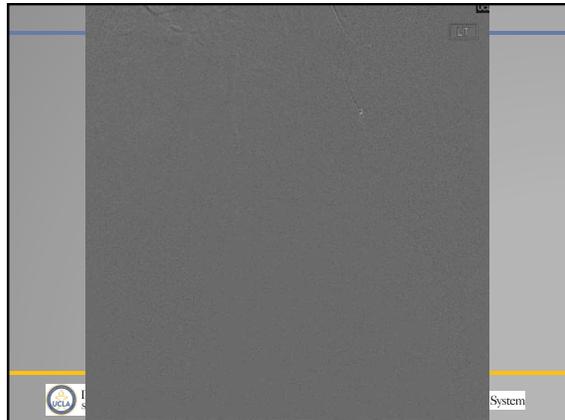
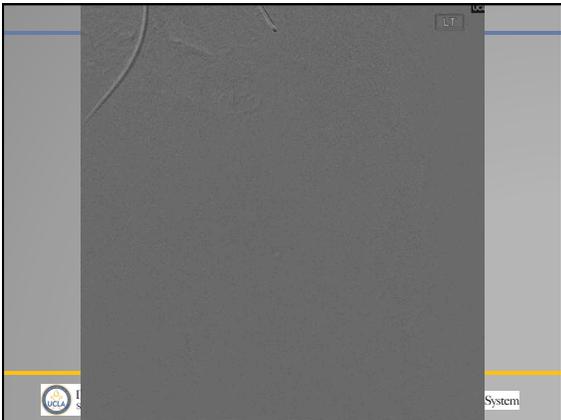
David Geffen School of Medicine
UCLA Health System

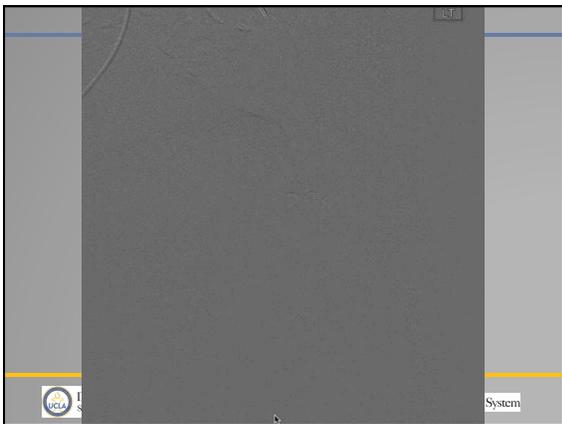
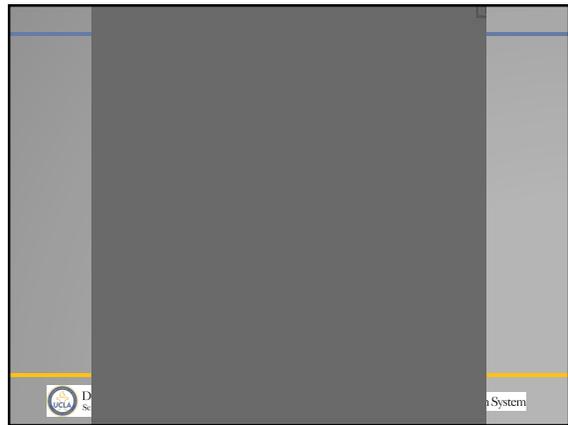
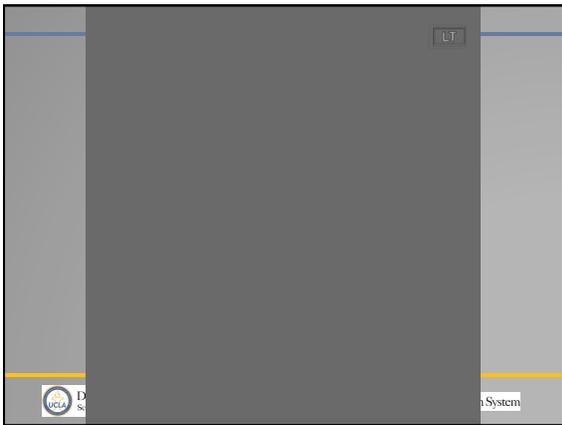
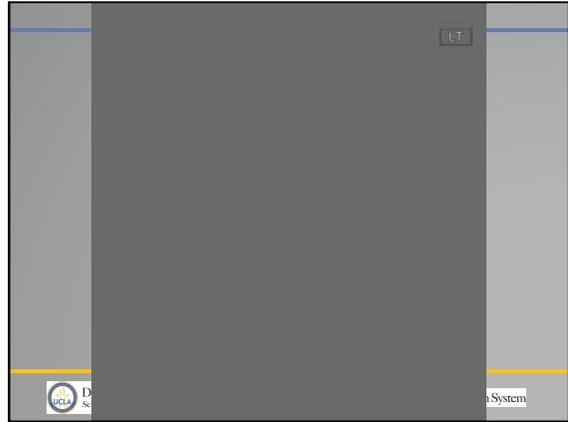
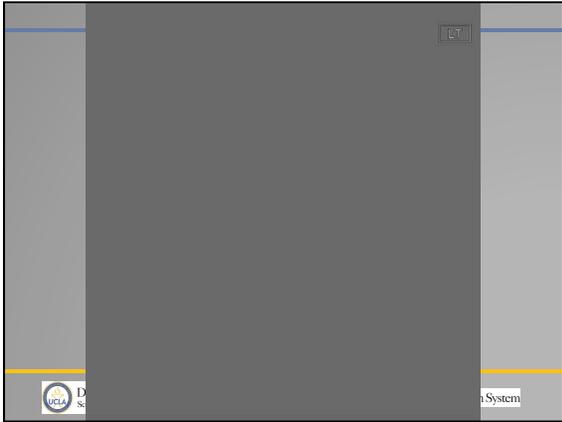
PAE at UCLA

Example 3: Collateral supply

- 69 y/o male with BPH and LUTS
 - IPSS 21, bother score 5
 - Prostate volume 105 cc
 - Failed medical therapy
 - Refuses TURP due to sexual dysfunction
 - Prostate too large for Rezum or Urolift
- Referred by urology for PAE

David Geffen School of Medicine
UCLA Health System

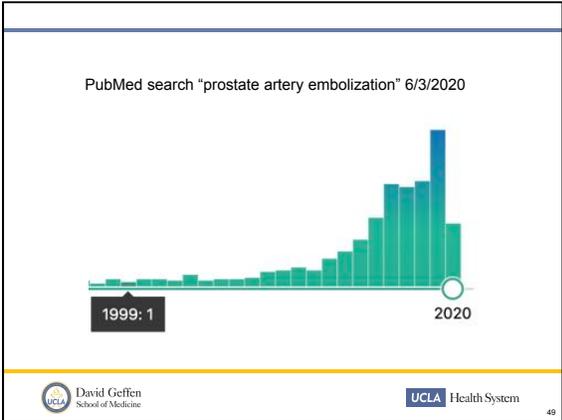




Prostate artery embolization for BPH

- Rationale and technique
- Newest data
- UCLA experience
- Example cases
- Latest developments**

UCLA David Geffen School of Medicine UCLA Health System 48



PAE vs TURP

- **Insausti 2020: Newest RCT of PAE vs TURP**
 - 23 PAE vs 22 TURP
 - Baseline similar with severe LUTS (IPSS 26)
 - PAE performed with 300-500 um BeadBlock
- PAE had similar (or superior) outcomes
 - IPSS improvement better with PAE (21 vs 18 points)
 - Mean Hgb at 1 month higher for PAE
 - Pain levels lower with PAE
 - Higher level of satisfaction for PAE
 - Fewer adverse events with PAE (3x difference)

Randomized Comparison of Prostatic Artery Embolization versus Transurethral Resection of the Prostate for Treatment of Benign Prostatic Hyperplasia

Trigo Insausti, MD, Ana Diaz de Otazola, MD, Anibal Gutierrez, PhD, Ferran Guadalupe, PhD, Isaac Gallegos, MD, Pedro Gil, MD, Tanya Britton, PhD, Ari Hassan, PhD, Ferran Llorens, PhD, and Sebastian Nappi, MD

Key findings: An important difference was found between the PAE and TURP groups: a significantly higher level of hemoglobin at 1 month with fewer transfusions in the PAE group.

David Geffen School of Medicine
UCLA Health System

PAE vs sham

- **Randomized, single blind controlled study of 80 men to PAE or sham**
 - Followed for 6 months then sham patients allowed to cross over
- **At 6 months:**
 - PAE had much better IPSS improvement (by 13.2) than sham
 - PAE had better QoL improvement (by 2.0) than sham
 - Adverse events similar in both groups

Randomized Clinical Trial of Prostatic Artery Embolization Versus a Sham Procedure for Benign Prostatic Hyperplasia

Andrés Rodríguez-Pérez, PhD, Andrés Rodríguez-Pérez, PhD, and Andrés Rodríguez-Pérez, PhD

David Geffen School of Medicine
UCLA Health System

Storage or voiding symptoms?

- **Two categories of LUTS**
 - **Storage (irritative):** Frequency, urgency, nocturia
 - **Voiding (obstructive):** Intermittency, weak stream, straining, incomplete emptying
- **Maclean 2020: PAE improves voiding symptoms more than storage symptoms**
 - Voiding IPSS reduced 13.4 to 5.4
 - Storage IPSS reduced 9.7 to 5.1
- **Moreira 2020: Similar results**
- **PAE improves all urinary symptoms**

Does Prostatic Artery Embolization (PAE) Improve Voiding Symptoms, Storage Symptoms, or Both?

Maclean, MD, et al.

Improvements in Voiding Versus Obstructive Symptoms of the International Prostate Symptom Score After Prostatic Artery Embolization in T2a Patients, in a Single Center

Moreira, MD, et al.

David Geffen School of Medicine
UCLA Health System

Median lobe: no-go?

- **Yu 2020: Median lobe that is taller than wide is a predictor of obstruction and poor clinical outcome**
 - Ball-valve obstruction
- **Maron 2020: No difference in outcomes between patients with severe or non-severe median lobe**
- **Jury still out**

Thickness-to-Height Ratio of Intravesical Prostatic Protrusion Predicts the Clinical Outcome and Morbidity of Prostatic Artery Embolization for Benign Prostatic Hyperplasia

Shen, C.H., Yu, M.B., MD, PhD, Carrizo, C.M., MD, PhD, MD, PhD, et al.

Effect of Median Lobe Enlargement on Early Prostatic Artery Embolization Outcomes

Maron, J., et al.

David Geffen School of Medicine
UCLA Health System

Ejaculatory function

- **Post-hoc analysis of prior RCT**
 - 40% of patients had reduced ejaculatory volume
 - 16% of patients had anejaculation
- **Histopathologic analysis**
 - Necrosis, fibrosis, hemorrhage
 - Ejaculatory ducts and seminal vesicles
- **More data needed**

Ejaculatory function after prostatic artery embolization: a retrospective of two prospective clinical trials

Shen, C.H., et al.

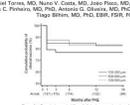
David Geffen School of Medicine
UCLA Health System

Microcatheters and particles

- Ayyagari 2019: Balloon occlusion microcatheter did not impact technical or clinical success
- Torres 2019: Randomized trial of different microsphere sizes
 - A: 100-300; B: 300-500; C: 100-300 then 300-500
 - No difference in clinical success at 18 months (77% vs 83% vs 83%)
 - Mild adverse events more common with 100-300 micron size (86% vs 41% vs 58%)

Case-Control Comparison of Conventional End-Hole versus Balloon-Occlusion Microcatheter Prostatic Artery Embolization for Treatment of Symptomatic Benign Prostatic Hyperplasia
 Raf Ayyagari, MD, Taylor Pomeroy, MD, Jameson Smith, MD, Julius Chapiro, MD, Steven Schreiber, MD, Ralph Devita, MD, and Jeffrey Paster, MD

Prostatic Artery Embolization for Benign Prostatic Hyperplasia: Prospective Randomized Trial of 100-300 µm versus 300-500 µm versus 100- to 300-µm + 300- to 500-µm Embospheres
 Daniel Torres, MD, Brian V. Coates, MD, John Pines, MD, PhD, Lee C. Pomeroy, MD, PhD, Andrew Hsu, MD, PhD, John Pines, MD, PhD, Travis Roberts, MD, PhD, John Pines, MD, PhD



Predictors of PAE difficulty

- du Pisanie 2019: Examined technical difficulty of PAE based on procedure time, fluoro time, contrast dose, radiation
 - Iliac tortuosity increased these by ~50%
 - Presence of atherosclerosis increased these by ~20%
 - Age alone not a predictor
 - Radial and femoral access similar
- Enderlein 2020: Prospective study of similar factors
 - Pelvic artery tortuosity increased FT and CV and reduced technical success rates
 - Superior vesical origin toughest
 - Obturator origin easiest

Predictors of Prostatic Artery Embolization Technical Outcomes: Patient and Procedural Factors
 Johannes de Pisanie, MD, Andrei Albotovschi, MD, MD, Kevin Conway, Jessica Smeeth, MD, Saveliy Ergin, MD, and An Isaacson, MD

Prostatic Artery Embolization—Anatomic Predictors of Technical Outcomes
 Georg Friedrich Enderlein, Thomas Lehmann, PhD, Friedrich Carl von Roonberg, PhD, MD, René Andriessen, PhD, MD, Marc Olivier Grimm, PhD, MD, Ulf Hergendorf, PhD, MD, and Tobias Fritsch, PhD, MD

Other studies

- Zhang 2020: Drug-eluting beads for PAE?
 - Study in beagles compared PAE with bland beads versus bleomycin-eluting beads
 - 10-15% greater ischemic volume using DEB
 - Bleomycin may increase ischemia and reduce prostatic volume
- de Assis 2019: PAE effect on ultrasound elastography of the prostate
 - PAE reduces elastic modulus by about 30%
 - Softens gland
 - Explains improvement in some patients who do not have prostate shrinkage

LABORATORY INVESTIGATION
Prostatic Artery Embolization for Benign Prostatic Hyperplasia: Bleomycin-Eluting versus Bland Microspheres in a Canine Model
 Jin Long Zhang, MD, Bing Yuan, MD, Mao Dong Wang, MD, Jun Jia Yu, MD, Feng Qian, MD, Tao Wang, MD, Liu Sheng, MD, Yan Wang, MD, Qin Hong Liu, MD, Yan Guang Shao, MD, Xia Di Wang, MD, Hong Guo Zhang, MD, Hong Ping Li, MD, Ju Yu Yan, MD, and Zhi Gang Song, MD

Effects of Prostatic Artery Embolization on the Dynamic Compliance of Benign Prostatic Hyperplasia as Assessed by Ultrasound Elastography: A Pilot Series
 Andre de Assis, PhD, Roger Hancock, PhD, Prostate and Urology, University of Toronto, Canada, George Haskali, MD, PhD, University of Toronto, Canada, and Prostate and Urology, University of Toronto, Canada

Future directions

- Pre-procedure imaging
 - Can high resolution MRA replace CTA?
 - Avoid radiation and contrast dye
 - Can imaging features predict response to PAE?
 - Transitional zone dominant BPH – others?
 - Can pre-procedure imaging predict bladder function?
 - One of the predominant reasons for PAE failure
- Randomized comparison of PAE to non-TURP surgeries
 - PAE vs Rezum or UroLift for prostates <80 cc
 - PAE vs prostatectomy for prostates >80 cc

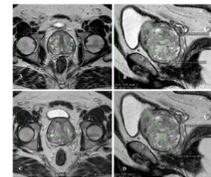
Final thoughts

- Prostate artery embolization is effective, and safe
 - New and minimally invasive way of treating BPH
 - May fill an important gap between medical and surgical therapy
 - Definitive option in poor surgical candidates, very large prostates, and refractory hematuria
- Increasing interest and need in an aging population
 - How can we partner with urology?
 - How can we get the word out to our patients?

Present research

- 93 patients who had MRI prior to PAE
- T2WI used to calculate the volume of the central gland and the whole prostate
- Central gland volume >45% of the whole prostate correlated with better outcomes

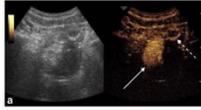
Prostate Zonal Volumes as a Predictor of Clinical Outcomes for Prostate Artery Embolization
 Andrew Hsu, MD, David Geffen School of Medicine, UCLA, and Prostate and Urology, University of Toronto, Canada; George Haskali, MD, PhD, University of Toronto, Canada; and Prostate and Urology, University of Toronto, Canada



Present research

Intra-Arterial and Intravenous Contrast-Enhanced Ultrasonography in Prostate Artery Embolization: A Case Series
Erolko Nettekun, MD, Anil Miralshur, MD, FRCP, DABR, Anguel Lira, MD, and Doreen Barakat, MD, MRCO, FRCR

- 8 patients had intra-arterial Definity contrast injected into PA while trans-vesical prostate US performed
 - Prostatic perfusion confirmed in all patients
 - Extra-prostatic perfusion seen in 4/20 interrogated arteries
- Intravenous CEUS used in 4 patients to confirm technical success
- CEUS may be able to reduce use of cone-beam CT



Present research

Adenomatous-Dominant Benign Prostatic Hyperplasia (ADBP) as a Predictor for Clinical Success Following Prostate Artery Embolization: An Age-Matched Case-Control Study
D. Kim, M.D., J. Kim, M.D., S. C. Hong, M.D., S. Kim, M.D., S. Kim, M.D., J. Kim, M.D., S. Kim, M.D.

- 24 patients had MRI prior to PAE
- 12 patients with adenomatous-dominant BPH (nodules in central gland) compared with 12 controls
 - More volume reduction in adenomatous group (34% vs 22%)
 - Better IPSS improvement in adenomatous group (13 points vs 9 points)
- Confounded by larger prostate volume in adenomatous group (125 cc vs 55 cc)

