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SEXUAL MEDICINE EXPERTS DISCUSS

The Sexual Side Effects of BPH Therapy

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Introduction

On June 24, 2015 an expert panel was convened to discuss the sexual side effects of therapies for benign prostatic hyperplasia (BPH). More than ever, men suffering from lower urinary tract symptoms (LUTS) are reluctant to compromise their ability to enjoy an active and satisfying sex life. The advent of minimally invasive treatment alternatives such as the UroLift® System, which lifts or holds the enlarged prostate tissue out of the way so it no longer blocks the urethra, is bringing new hope to patients who seek a way to relieve their urinary symptoms and preserve their sexual function. Members of the panel were:



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GOLDSTEIN:

To begin our discussion I want our panel of sexual medicine experts to compare the available BPH therapies. Please rate the current BPH surgical therapies keeping in mind the level of overall attractiveness as well as the possibility of complications from the therapy that affect quality of life as well as the potential exposure to adverse effects from the patient's perspective. Please rate each therapy as 1 (most attractive) to 5 (least attractive). Let's start with the tissue removal surgeries: open prostatectomy, traditional TURP and laser assisted TUR.

Carrion: Open prostatectomy would have to be a 5, the least attractive. I don't think I have done one for five years. I would have to put the classic gold standard TURP at 3.5 to 4 and laser at 2 to 3. I think something like a GreenLight laser has a degree of hemostatic advantage. I would say TUIP is 2.5, but you can occasionally have issues with hemostasis as well as retrograde ejaculation.

Perito: I agree with open prostatectomy being least attractive, and it has been years for me as well. If you had a choice, open would definitely be your last choice. I agree with 3.5 to 4 for TURP. Laser might have the only advantage of not being as bloody, that's it. I would have to give TUIP a 2 but there is a possibility that you will render the patient with retrograde ejaculation.

Baum: I think an open prostatectomy is more like a 6 or 7 out of 5! The results can be achieved with therapies that are much more attractive. The postoperative course to resume normal activities after an open prostatectomy is usually weeks to several months. The risks and complications make it a very unattractive procedure and most men, even with >100gm glands, will opt for less invasive procedures.

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GOLDSTEIN:

Now let's look at heat treatments, like microwaves, TUNA, steam or others.

Perito: I would give it a 3.5 to 4 you don't know what you have until several weeks later. Number two, my patients invariably experienced lengthy irritative symptoms postoperatively because of the cavitory defects we have created, and that's why I've completely abandoned all my TUNA and microwave therapy.

Carrion: I give it a 3 because, even though it can be done in the office, the recovery is extremely variable and can be difficult. Not to mention long-term efficacy is very poor.

Wilson: I think that is a very important point. Even though these therapies have a big advantage over resection because they can be done without anesthesia and without hospitalization, they have two big disadvantages. First, the postoperative morbidity is sometimes months long; and second, the improvement in symptom score is not much better than with oral medications.

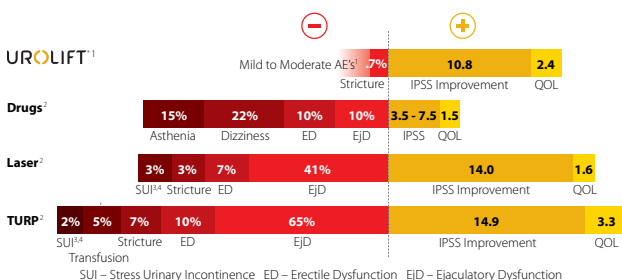
Baum: In addition, although these treatments are less invasive, the results are less durable. So on a difficulty scale for the patient, I give it a 3. However, on the durability scale, I think it is a 5. These procedures have not stood the test of time, especially long term follow up.

GOLDSTEIN:

How about the UroLift® System?

Perito: I'd rate it at 1.5 to 2. The only reason I rate it above 1 is that it is transurethral, and simply conducting a cystoscopy can be experienced as invasive by patients. I do this in my hospital to eliminate the discomfort of extensive cystoscopy, although I know others routinely use local anesthesia in the office. As far as having minimal adverse effects on the patient, however, UroLift is the clear leader. It is really the least invasive, particularly with no sexual dysfunction or incontinence reported among the thousands of procedures already accomplished.

L.I.F.T. Randomized Study Results Compared to AUA Guidelines at 1 Year



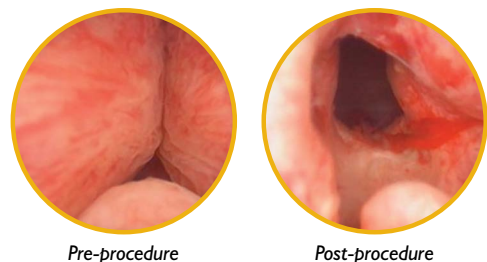
1. L.I.F.T. IDE Study. Roehrborn. J Urology 2013; 2. AUA BPH Guidelines 2003, 2010; 3. Naspro, Eur Urol 2009; 4. Montorsi, J Urol 2008

*Most common adverse events reported include hematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence. Most symptoms were mild to moderate in severity and resolved within two to four weeks after the procedure.

Carrion: I put UroLift at 1.5. I think the morbidity and the risk is truly minimal, but we have seen occasional bleeding on one patient due to mucosal abrasion, and he needed a catheter.

Wilson: Passing a rigid cystoscope on a male patient under local anesthesia is a skill that today's younger urologists never had to master. The advent of the flexible cystoscope in the early '90s rendered this skill set obsolete. Turning the corner of the deep bulbar urethra can be uncomfortable and the prostatic mucosa is easily abraded. I recommend that younger urologists do their initial procedures with significant sedation or general/spinal anesthesia to hone their technique. Old geezers like me probably remember how to pass a rigid cystoscope under local – like riding a bike after a 20 year absence.

Baum: UroLift is the game changer! It is less than 1. The learning curve is 10 to 15 cases and once the doctor has developed comfort with the procedure, it can easily be accomplished in the office setting under local anesthesia. The results are immediate, the likelihood of requiring a postoperative catheter is minimal, and sexual function is preserved. Once the doctor becomes comfortable with the procedure, even anti-coagulated patients can be treated.



(Images courtesy of Dr. Peter Chin, Wollongong, NSW, Australia)

GOLDSTEIN:

What do you think the level of overall attractiveness is for alpha-blockers?

Carrion: I think alpha-blockers are 2.5 to 3. Clearly this is a well-known and documented therapy that serves millions, but there are issues with it. In Tampa, we're close to MacDill Air Force Base, and senior pilots are prohibited from alpha-blocker therapy because of the side effects that can impair their ability to fly an aircraft. When you consider the risk of orthostatic hypotension in a number of occupations, these drugs are contraindicated.

Perito: I consider alpha-blockers an obligatory initial therapy for BPH, but I rate them as a 3 to 4, especially in my patient population. The more selective the alpha-blocker, the more effective, but with increasing selectivity the more retrograde ejaculation they're going to have. Ejaculatory dysfunction is catastrophic to a lot of my patients; not just some, a lot.

Cohen: I think Flomax or Tamsulosin would probably get somewhere in the range of 2 to 2.5, depending on the age of your patients. When dealing with a predominantly geriatric population, orthostatic hypotension can be an issue.

Wilson: Because of the 7 in front of my own age, I have the advantage of having tried most of the BPH oral medications. I didn't like any of them. The alpha-blockers were poorly tolerated and Cialis gave me a hearing loss, which fortunately reversed with cessation of the medication and high dose steroids. I never tried the 5-alpha-reductase inhibitors because the benefits didn't seem to outweigh the risks.

GOLDSTEIN:

What about the rest of the panel? Please share your thoughts of overall invasiveness of 5-alpha-reductase inhibitors (Finasteride and Dutasteride).

Perito: I give them a 5 because of the potential for post-Finasteride syndrome that can last up to 40 months after you've stopped taking it, and because of the resulting decreased ejaculate and libido. 5-ARIs are prescribed to decrease prostatic volume, but this is a therapeutic outcome that doesn't matter to the patient. They don't care if they get a decrease in prostate size, they care about their voiding symptom relief. I personally have never seen a significant decrease in symptom score while taking this medication. And what's worse, the length of therapy and the side effects from a sexual, hormonal central nervous system standpoint is completely unacceptable.

Carrion: I would put it around 4.5 and echo most every point Paul made.

Wilson: As both a BPH patient of these therapies and a urologist, my evaluation of this class of drugs convinced me the rewards weren't worth the risk of an adverse event. I am surprised at how popular they are with non-urologist physicians. I guess it is the advertised prostate shrinkage that encourages primary care physicians to prescribe these medications. They must believe the structural diminishment of the prostate is superior to the simple improvement in symptoms provided by the other oral therapies.

Goldstein: I have particular concern with these drugs because it is not widely understood how vast the systemic effects can be. I believe the perception of the urologic community is that the 5-alpha-reductase is entirely specific to the enzymatic conversion of testosterone to dihydrotestosterone, forgetting its role in other chemical pathways. Would you agree?

Carrion: Yes.

Perito: Absolutely.

Goldstein: It is worth noting that 5-ARI inhibits the enzyme by destroying the enzyme – this is why it can be irreversible. To reverse its lethal side effects, the enzyme must be

resynthesized by the body. A 5-ARI adverse event is one of the few drug side effects that a urologist will deal with that affects all aspects of the sexual experience. Desire, erectile function and ejaculatory/orgasmic function are all impacted.

GOLDSTEIN:

Let's move to PDE-5 inhibitors, specifically 5 mg Tadalafil. What's your overall attractiveness rating?

Carrion: I would put it at a 2 due to the known adverse event profile of the class, not just Tadalafil.

Perito: I give it a 1, because of the ancillary benefit of erections. I think the only side effect that you might see would be reflux, and that tends to not preclude usage because they're so happy with their added sexual function.

Cohen: I'd give Cialis a 1 to 1.2 at the worst. I have not really seen any side effects with 5-milligram daily dosage other than better erections and that's not a side effect, but rather a bonus.

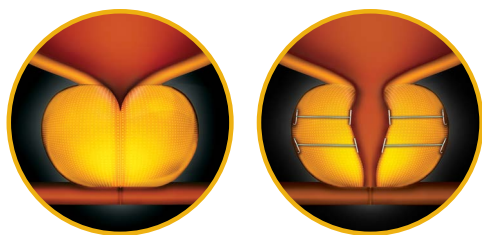
Wilson: Low-dose Cialis for two weeks gave me a temporary sensorineural hearing loss. It is rare but recognized adverse event of PDE inhibitors and is usually permanent. I give it a 3 because of this risk.

GOLDSTEIN:

I'd like to move away from a discussion of the drug therapies and focus on UroLift®'s place in our armamentarium of BPH/LUTS therapy. Will UroLift replace some currently existing BPH LUTS treatments - either surgical or medical treatments? Another way of asking the question is whether "use-rate" of any of the current therapies to be lowered because of UroLift?

Carrion: I think certain treatments will absolutely decrease, particularly TUIP, TUNA, microwave and even laser. I don't think the individual undergoing an open prostatectomy is affected, and I think a TURP is more and more being reserved by most urologists for that larger gland that really needs a classic TURP. UroLift® is uniquely minimally invasive. It is technically quite reproducible, very user-friendly, and it's easy to teach the technique to urologists in training. The most important attribute of UroLift is the lack of side effects such as sexual dysfunction.

Perito: I have to hand it to the NeoTract engineers that figured out that all that you really need is to create an anterior channel through the prostatic urethra to significantly impact voiding symptoms. We're taught that you need to be able to drive a car through the cavitated prostatic fossa, but now we know with UroLift that you don't. Once urologists understand that, we're going to see all these other therapies—microwave, TUIP and laser therapy—being set aside. UroLift is just a less invasive yet effective approach.

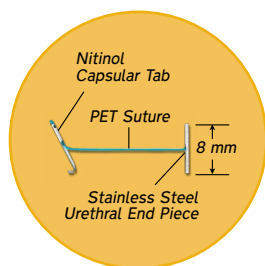


Pre-procedure

Post-procedure

Cohen: In the current era of “Dr. Google,” it seems patients know the data sometimes better than we do and they know they do not want sexual dysfunction as a result of their BPH therapy. UroLift® therapy also eliminates the need to prepare for a formal surgical procedure under anesthesia. We don’t have to obtain preoperative medical clearance, get a full diagnostic workup and wait for a surgical OR time. Contrast that with the ability to stay in the office or come back next week for a walk-in, walk-out UroLift procedure. It may well change the gold standard of BPH procedures because of the number of potential candidates and the safety and efficacy of the therapy.

Baum: I believe once a critical mass of patients in the community learns about UroLift, this will be the treatment of choice. I’m not sure how many urologists discuss the sexual side effects of alpha-blockers with their patients. I never thought it was necessary to have this discussion with my patients as I didn’t think middle-aged men would be concerned about this side effect. However, when the men have a choice between normal ejaculation and no ejaculation, 100% opt for normal ejaculation. Preservation of sexual function makes UroLift very attractive as a treatment option for men with symptomatic BPH.



UroLift® Permanent Implant

GOLDSTEIN:

Because of my long experience with the concerns of my patients with iatrogenic erectile or ejaculatory dysfunction following LUTS-directed treatment, I feel there is a need to reclassify all LUTS treatments as those that preserve sexual function versus those that do not preserve sexual function. What is your opinion?

Cohen: I hope our urologic colleagues are already adopting that line of thinking. When we talk about LUTS, we also are aware of the concomitant sexual dysfunction. As patients are

becoming much more sexually aware, we realize we need to be too. We need to be educating our patients about the negative effects some procedures can have on sex and we need to tell them there is a procedure that preserves sexual function.

Carrión: I also think it’s an outstanding concept. We do bring it up, but then my clinical practice is a little bit biased because it’s very heavily focused on sexual medicine so I know it is important to the great majority of my patients.

GOLDSTEIN:

Do you know of any other LUTS treatment beyond the medical ones of testosterone and Cialis and the surgical one of UroLift® that preserve sexual function?

Cohen: No.

Perito: I want to ask all of you one question, how many guys have come to your office after they’ve had a TURP and they tell you that their doctor never told them that they would have dry ejaculate?

Cohen: All the time.

Wilson: Before we had all these different BPH therapies and only had TURP, we never disclosed the ejaculation problem because there were no alternative therapies that were not accompanied by this problem. We urologists concluded, “Who cares, they are past the child fathering age.”

Perito: I think this points to a culture in urology that needs to shift its thinking. It appears to be a misunderstanding that if you’re not making babies, who cares about ejaculatory function. My current practice algorithm goes like this: first Tadalafil, and if you fail that, you get a UroLift. We did 120 UroLift procedures last year. So, concern with preserving sexual function is absolutely the way this office goes. And if a patient fails UroLift, he unfortunately moves onto options that are known to carry the risk of compromising sexual function.

What I tell patients is, “I’m going to burn no bridges and I’m going to spare your ejaculatory function. Let’s take the sex preservation route first.” Now, can we talk our peers into thinking that way? Not all of them. There are still going to be guys who don’t even tell their patients the risk of retrograde ejaculation with TURP.

Baum: I think the fact that UroLift preserves sexual function will make it more attractive than other treatments.

GOLDSTEIN:

If you have ever implanted UroLift® prior to IPP placement, please describe your experience.

Perito: I have done somewhere between 12 and 15 and the time between procedures was anywhere from two days to months, with no complications or infections regardless of

the gap. I discovered you could perform IPP as soon as you ascertained the patient's hematuria had ceased.

Wilson: Paul, this is a great idea. When I practiced general urology, I used to make my patients wait three months if I did a TURP before the IPP because I was afraid the IPP would precipitate urinary retention. Many of these patients lost interest in the IPP with such a long wait and went "back on the couch." The fact that UroLift® is so minimally invasive lends itself to a quick prophylactic opening of his channel to prevent his obstructive BPH from causing problems after the IPP.

GOLDSTEIN:

Did you treat the LUTS first because you were worried that they would go into retention post IPP?

Perito: I offer UroLift before IPP because I want to offer my patient a complete men's health package for LUTS and sexual function. Several of them were on alpha-blockers and were dissatisfied with the ejaculatory issues. I say, "We're going to get you off the meds with their associated side effects and cost. By combining UroLift and IPP, we will take care of your voiding symptoms, and cure your impotence without impacting your ejaculation."

Carrion: We have a smaller N of two, both with concurrent LUTS and ED. The IPP surgery ranged from 1 to 2 months after UroLift. Both had really uneventful courses. The moral of the story is probably, had we used another surgical BPH modality, there's no way we would have considered penile prosthetic insertion after such a short time interval.

Cohen: I did one UroLift patient after IPP but I don't have any patients that received UroLift prior to implant. I do see many patients presenting for ED and LUTS combined. On LUTS workup, uroflow and bladder scans show retention of urine. I believe it is important to take care of a urinary problem prior to their IPP. When I discuss this with a motivated IPP patient, he sometimes gets upset – the patient may want to fix his ED first. The fact is, now we can treat the LUTS with UroLift and place an IPP two to four weeks after. It's going to change the way we have been treating severe ED with concomitant LUTS.

Wilson: I believe you could do IPP as soon as you were satisfied the patient was past the danger of hematuria. The voiding symptoms can so quickly improve, some patients may not need to wait a month or two.

Perito: Another important fact is that UroLift can be safely done on patients who have an IPP. Probably half of the men I have treated with UroLift already had an implant, since that's the nature of my practice. There was no deleterious effect to the implant and no complication to the UroLift treatment itself.

GOLDSTEIN:

Based on the UroLift® experience that you have, how much training do you feel a first-time user needs to have to successfully implant the UroLift?

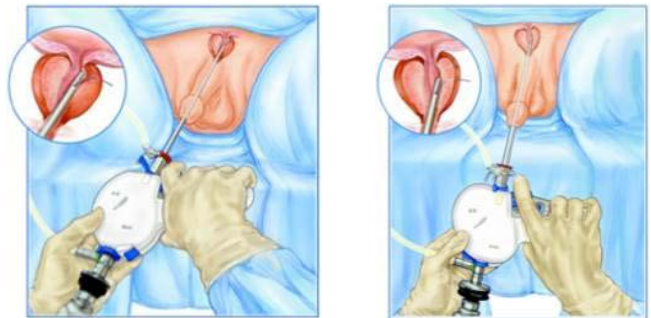
Cohen: I would say two to three patients and you are feeling comfortable with the device. It's not complicated but a main point to remember is making sure that anterior channel is there because urologists were never trained to shave out an anterior channel to cure BPH.

Carrion: It's always going to be variable, but with consistent technique I would say after several cases you will have the device part down.

Perito: We've held a number of training programs, and I think your first ones should be done under anesthesia where you're not having the stress of a patient that might be feeling it or wondering what you are doing.

Cohen: I had a chance to see Steve Gange in Utah. On that operative day, he did 10 UroLift cases, all in his office and all without general anesthesia. He's so masterful; he makes it look so easy. His anesthesia technique is oral Xanax and chilled urethral lidocaine, and it really does work. Most patients can tolerate the procedure just fine, but if you have a patient who you know is going to freak out it's probably better to administer light sedation.

Carrion: We still do them under general at Tampa General Hospital and VA, but I definitely want to entertain the local anesthetic technique because I think that is the bright future for this therapy.



Baum: I think you could go to a training center such as I did with Dr. Perito. I was comfortable after getting hands-on experience, then coming home and doing several cases in an OR setting. It would not behoove the neophyte surgeon to try and do just one case after going to training. I think it's best to have several cases scheduled, utilize the company trainer and start with the smallest glands first -- those that only require four implants -- before tackling larger glands that require six or more.

GOLDSTEIN:

How long after patients undergo a UroLift® procedure do they show improved symptoms and then eventually when do they return to full activity?

Perito: Usually somewhere between one and two weeks, my patients suddenly realize they are feeling good. Most are back to full activity three to four days after the procedure.

Carrion: Most of the patients in our series have experienced a substantial upward swing in their voiding function within seven to 14 days. We do ask that they take it easy for 72 hours, but other than that, no real activity restrictions.

Cohen: My only exception to that was a gentleman with overactive bladder. The UroLift® addressed his obstruction, but we later placed him on a low-dose anticholinergic to address his OAB and he responded well with that combination.

GOLDSTEIN:

What is your estimation of your UroLift® patient's satisfaction?

Perito: Interestingly, my results pretty much fall right in with the published results, and that is saying a lot, since I am treating a much broader population.

Baum: Nearly all are happy and would recommend the procedure to others. I have several patients who serve as my patient advocates and are available to speak to other potential patients about their UroLift experience. I have also videotaped several patients after the procedure and will show the video testimonial on the computers in each exam room after they watch the UroLift patient education video NeoTract produced. This helps provide real-life experience to patients who are considering the procedure.

GOLDSTEIN:

What is the major driver of your patients for choosing UroLift®?

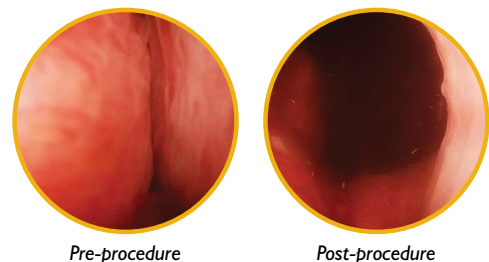
Carrion: Many have issues with medication compliance and they want a treatment without the daily pill. Because my practice is weighted toward sexual medicine, they come to me seeking a solution to their BPH that preserves sexual function.

Perito: I would have to say that half of my patients are on an alpha-blocker and want to get off of it. And since most have ED, they are seeking a full global solution to their problems. That's what I provide in my practice, and the UroLift for BPH is definitely a part of that solution.

Cohen: It will be interesting to see how general urologists counsel their patients when they have this solution in their hands. So many patients complain about the side effects of the 5-alpha-reductase and the alpha-blockers. I think it's going to change the paradigm when they start to tell their patients that there is a different solution that preserves sexual function.

Wilson: Unfortunately, I believe that more than half of our patients on alpha-blockers abandon the therapy because of cost, ineffectiveness or side effects. The vast majority of these patients were prescribed by primary care physicians. Most of those patients never return to their prescribing physician to ask about another therapy. And, if they did, the primary care physician has no other weapons to combat the LUTS. So along with urologist education, we must also educate the consumer and his regular family care physician.

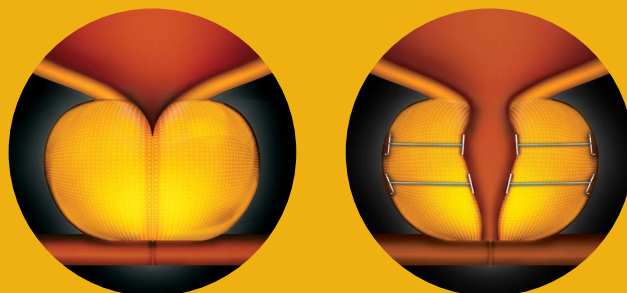
Baum: The major driver is the relief of symptoms with preservation of sexual function and minimal postoperative morbidity. At the end of the day, this is what makes patients happy. The UroLift also excites my staff because they have few phone calls from patients after the procedure. And best of all, a happy doctor who enjoys being on the cutting (or no-cutting, in the case of UroLift) edge of new technology.



Pre-procedure

Post-procedure

(Images courtesy of Dr. Justin Chee, Melbourne, VIC, Australia)



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Most common adverse events reported include hematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence. Most symptoms were mild to moderate in severity and resolved within two to four weeks after the procedure.

1. Data on file at NeoTract; 2. Roehrborn, Journal of Urology 2013; 3. Shore, Canadian Journal Urology 2014; 4. Sonksen, European Urology 2015; 5. No instances of de novo, sustained erectile or ejaculatory dysfunction. McVary, Journal of Sexual Medicine 2014.

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