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Shock waves may change future of ED therapy

Procedure offers promise of disease modification vs. symptomatic treatment

Lisette Hilton | UT CORRESPONDENT

It's hard to argue against an erectile dysfunction treatment that is potentially disease modifying, is noninvasive, and seems to do no harm. The treatment, low-intensity shock wave therapy, has yet to earn the FDA's approval but is widely used in other countries. Early results from ongoing U.S. trials are promising.

A shock wave is a wave of energy that travels faster than the speed of sound. Urologists commonly apply the energy, during shock wave lithotripsy, to break up kidney stones.

But when directed at a scarred penis, the therapy is different.

Linear shock waves used for erectile dysfunction use about one-tenth of the energy of traditional shock wave machines for kidney stones. And rather than break something down, as is the case with stones, shock waves make the penis healthier, according to Ranjith Ramasamy, MD, director of male reproductive urology at the University of Miami.

"Stay tuned. It's exciting," said Arthur L. Burnett, MD, MBA, professor of urology at Johns Hopkins Uni-

Please see **SHOCK WAVES,** on page 17

SHOCK WAVE THERAPY (SWT) FOR ED: WHAT META-ANALYSES SHOW

Study	No. of patients	Key finding
Ramasamy et al *(J Sex Med* 2017; 14:27-35)	602	IIEF score significantly improved 6.40 points from baseline in men receiving SWT vs. 1.65 points in those receiving sham therapy
Li et al *(Urology* Sept. 26, 2017 [Epub ahead of print])	637	SWT significantly improved patients' IEEF and Erection Hardness Score

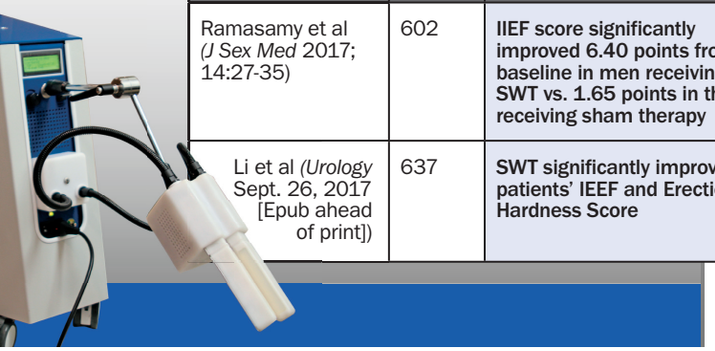

Image of device (MoreNova) courtesy of Ranjith Ramasamy, MD, and colleagues

Inside

How to reduce opioid use in post-op patients

The opioid crisis in the United States is widespread and affects many patients—including those undergoing major urologic procedures. In this interview, urologist Francis J. McGovern, MD, of Harvard Medical School, Massachusetts General Hospital, Boston, discusses the scope of the problem, outlines opioid-sparing strategies, and explains what the future holds in this area.

Q&A | OPIOID SPARING

Francis J. McGovern, MD

For the full article, please turn to page 10

UBM

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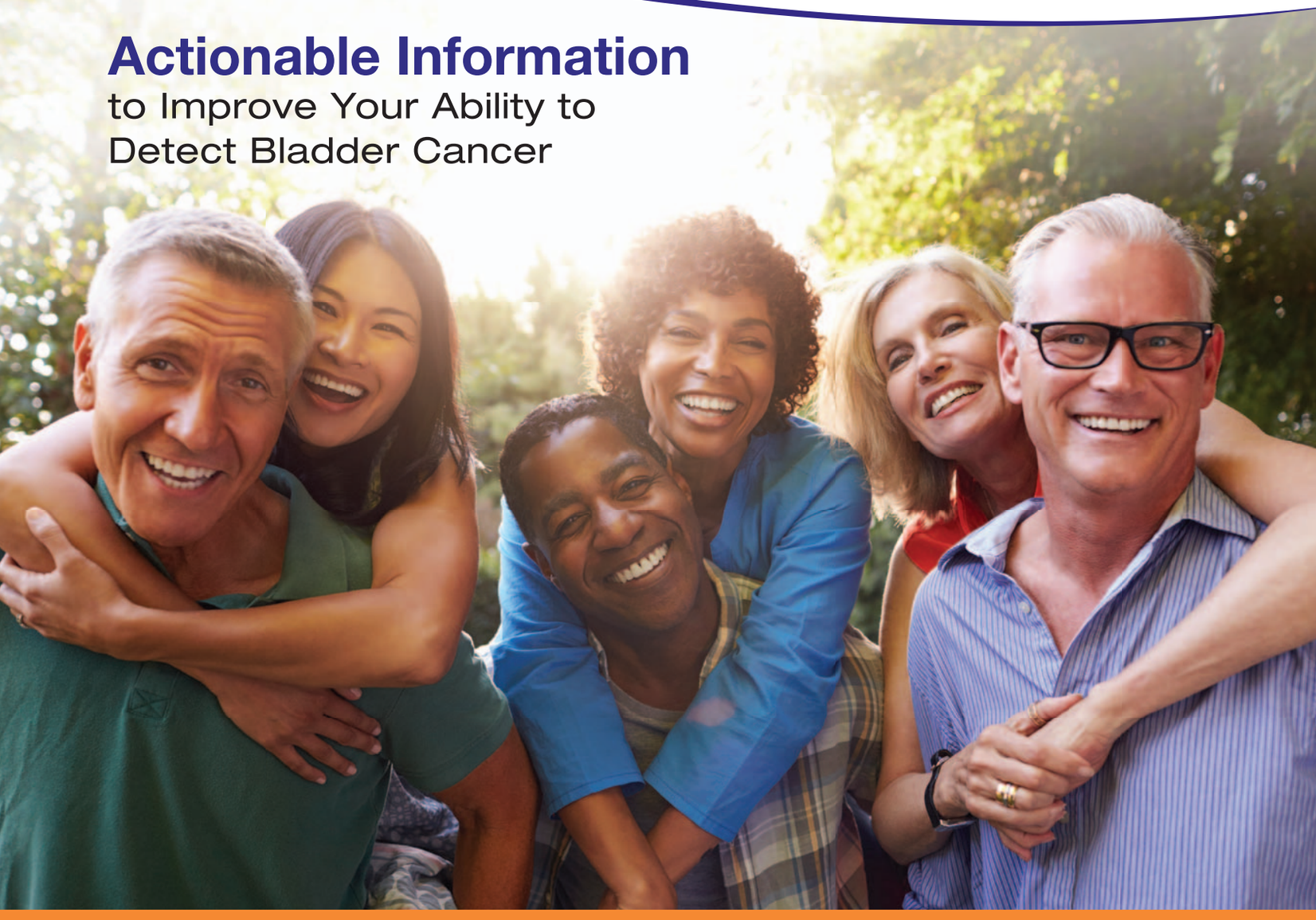

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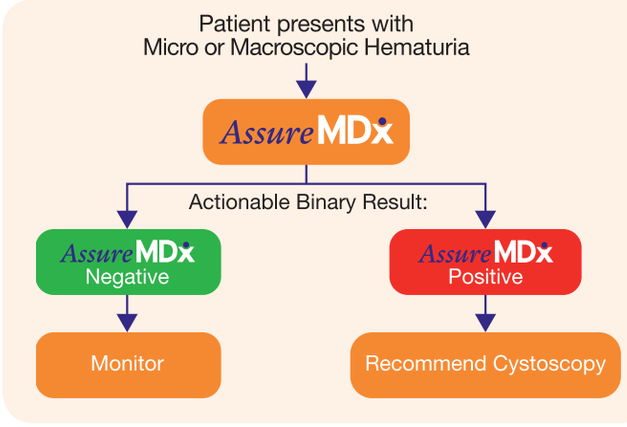

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Reference: 1. van Kessel KE, Van Neste L, Lurkin I, Zwarthoff EC, Van Crienkinge W. Evaluation of an Epigenetic Profile for the Detection of Bladder Cancer in Patients with Hematuria. *J Urol.* 2016 Mar;195(3):601-7 **2.** van Kessel KE, et al. Validation of a DNA Methylation-Mutation Urine Assay to Select Patients with Hematuria for Cystoscopy. *J Urol.* 2017 Mar;197(3 Pt 1):590-595.

Disclaimer: MDxHealth is regulated under the Clinical Laboratory Improvement Amendments (CLIA) and the College of American Pathologists as an accredited laboratory to perform high complexity clinical testing. The AssureMDx for Bladder Cancer test was developed and its performance characteristics determined by MDxHealth. This test is intended for use as an aid to clinicians for patient management decisions. Use outside of this indication has not been validated by MDxHealth. The test results should be interpreted in conjunction with other laboratory and clinical data available to the clinician. MDxHealth is certified by DEKRA for ISO 9001:2008 Quality Management System. This test is performed by MDxHealth, Inc., 15279 Alton Parkway, Suite 100, Irvine, California 92618. CLIA# 05D2033858; CAP# 8015399

IR-ADVS-0004

SNS vs. botulinum: Caveats, considerations

Gopal H. Badlani, MD

Dr. Badlani, a *Urology Times* editorial consultant, is professor of urology at Wake Forest Baptist Medical Center, Winston-Salem, NC.

AUA/SUFU clinical guidelines for OAB, updated in 2014, suggest third-line treatment options of: intradetrusor onabotulinumtoxinA (100 U) *Standard* (Evidence Strength Grade B), peripheral tibial nerve stimulation (PTNS) *Recommendation* (Evidence Strength Grade C), or sacral neuromodulation (SNS) *Recommendation* (Evidence Strength Grade C).

The 24-month ROSETTA trial data suggest that UUI episode reduction was the same for botulinum toxin and sacral neuromodulation, but treatment satisfaction and endorsement favored botulinum toxin (see page 4).

There are some caveats to this conclusion: A higher dose (vs. guidelines) of 200 U was used in the botulinum toxin arm. The 24-month data are true for the SNS group but are <1 year in 35% to 70% of patients who underwent a second injection of botulinum toxin. Finally, 30% of patients in both arms opted for a secondary treatment.

The practical considerations for choosing one of these three treatments include: Patient age, mobility, mentation, and hand dexterity are important, as each of these arms need a good understanding of possible side effects, ability to self-cath, and learn programming. In a recent study of women with refractory urge incontinence, younger patients experienced greater absolute continence, symptom improvement, and fewer UTIs than older patients *(Am J Obstet Gynecol* Oct. 11, 2017 [Epub ahead of print]). A similar study found older women with multiple comorbidities and decreased functional and health-related quality of life had decreased treatment response and satisfaction with botulinum toxin versus sacral SNS *(J Urol* 2017; 198:890-6).

Insurance approval is improving for both botulinum toxin and SNS but is an issue for PTNS. SNS also has a caution regarding MRI if needed for associated neurologic conditions (less of a concern with the new generator) and requires two OR visits, whereas long-term success is a plus with SNS.

Office-based use of botulinum toxin has appeal for patients, but the need for repeated injections at variable intervals and the possible need for CIC are deterrents. The interval between injections is impressive in this trial, and if the retention rate is not increased, then an initial higher dose may be worthwhile.

Ultimately, there is a physician bias in suggesting one of these options.

Gopal H. Badlani, MD

Feedback Send your comments to Dr. Badlani c/o *Urology Times,* at **UT@advanstar.com**

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Mission

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Sacral neuromodulation, botulinum show equal efficacy

Satisfaction ratings in UUI patients appear to favor botulinum toxin at 2 years

Andrew D. Bowser, ELS
UT CORRESPONDENT

In patients with refractory urgency urinary incontinence (UUI), sacral neuromodulation (InterStim) and onabotulinumtoxinA (Botox) produce similar reductions in mean daily UUI episodes, according to 24-month follow-up data on patients treated in a randomized trial.

Investigators in the ROSETTA (Refractory Overactive Bladder: Sacral NEuromodulation versus BoTulinum Toxin Assessment) trial in 2016 reported that botulinum toxin at 6 months of treatment resulted in a "small daily improvement in UUI episodes" that was statistically significant *(JAMA* 2016; 316:1366–74).

"At this point, we have two equally efficacious treatments."

CHRISTOPHER J. CHERMANSKY, MD

Now, in long-term follow-up data on ROSETTA, NIH investigators reported at the International Continence Society annual meeting in Florence, Italy that the two treatments provide similar reductions in mean daily UUI episodes at 24 months. However, botulinum toxin treatment was more likely to provide complete resolution of episodes 6 months after treatment, and it was associated with higher patient satisfaction and treatment endorsement ratings over the 24 months, reported first author Christopher J. Chermansky, MD, assistant professor of urology at the University of Pittsburgh School of Medicine.

"Even though the primary outcome was the same with respect to UUI episode reduction, there was this difference in treatment satisfaction and treatment endorsement that favored botulinum toxin over sacral neuromodulation," Dr. Chermansky told *Urology Times*.

As previously reported in 6-month ROSETTA results, botulinum toxin was associated with higher rates of urinary tract infection, while sacral neuromodulation required revisions and removals in some patients.

"At this point, we have two equally efficacious treatments," Dr. Chermansky said.

As the prevalence of UUI increases in an aging population, so does the use of third-line treatment options, including botulinum toxin, sacral neuromodulation, and percutaneous tibial nerve stimulation, when more conservative measures do not provide relief. However, little data exist to guide treatment choice in third-line therapies. In one systematic review, researchers found that current evidence was insufficient to recommend one treatment over another *(Evid Rep Technol Assess* 2009; 187:1-120).

Subsequently, ROSETTA investigators used a comparative effectiveness design to assess whether botulinum toxin was superior to sacral neuromodulation in reducing UUI episodes in women with symptoms refractory to conservative measures.

ROSETTA results

A total of 381 women were randomized to either sacral neuromodulation or intradetrusor injection of botulinum toxin, 200 U. As previously reported, there was a greater reduction at 6 months in the mean number of daily UUI episodes favoring the botulinum toxin group (–3.9 vs. –3.3 episodes per day; p=.01).

In the follow-up report presented at the ICS meeting, which included 24-month follow-up data for 293 of the women enrolled in ROSETTA, there was no difference in mean number of daily UUI episodes at 24 months (–3.9 episodes per day for botulinum toxin vs. –3.5 episodes per day for sacral neuromodulation, p=.15).

Although complete resolution and >75% reduction of UUI episodes was more commonly seen in the botulinum toxin group at 6 months, this difference was not maintained over 24 months. Yet, the botulinum toxin group had higher satisfaction and treatment endorsement scores sustained to 24 months (mean difference of –9.2 for treatment satisfaction and –11.2 for treatment endorsement on the Overactive Bladder Satisfaction of Treatment questionnaire).

Among the women receiving botulinum toxin, 72% requested a second injection, and the clean intermittent catheterization rate was 6%. Also, the UTI rate at 24 months was 18% in the botulinum toxin group, compared with 8% for sacral neuromodulation (p≤.05). Sacral neuromodulation revision and removals occurred in 3% and 9%, respectively. Additionally, 58% of these patients required at least one reprogramming, and only 17% required three or more reprogrammings.

Researchers aren't sure what could account for the higher satisfaction and treatment endorsement rates in the botulinum toxin arm, though one possibility is the long interval between botulinum toxin injections at the 200-unit dose.

"If they are coming in on average just once a year for their repeat injection, there may be satisfaction with that," Dr. Chermansky said.

Dr. Chermansky is a clinical trial study site principal investigator for Allergan. UT

Clinical Updates

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Robotic nephrectomy linked to greater OR times, costs

Robot-assisted laparoscopic radical nephrectomy requires slightly longer operating times and results in increased costs compared with traditional laparoscopic surgery, according to a large, multiyear analysis by researchers at the Stanford University School of Medicine, Stanford, CA.

However, the two approaches have comparable patient outcomes and lengths of hospital stay, the study showed. Findings were published in *JAMA* (2017; 318:1561-8).

"We found that, although there was no statistical difference in outcome or length of hospital stay, the robotic-assisted surgeries cost more and had a higher probability of prolonged operative time," said senior author Benjamin Chung, MD.

The discrepancy may be due to the time needed for robotic operating room setup or due to a surgeon being in the earlier part of his or her learning curve, resulting in a subsequent increase in operating room and instrumentation costs, the authors speculated.

Foot stimulation may offer at-home OAB treatment

3-hour stimulation found more efficacious than 30-minute session in preliminary study

Richard R. Kerr
CONTENT CHANNEL DIRECTOR

Boston—New research may pave the way for a form of nerve stimulation for refractory overactive bladder (OAB) that is home based and less invasive than current neuromodulation approaches.

In a preliminary study presented at the AUA annual meeting in Boston, University of Pittsburgh researchers reported that the FootStim, which stimulates transcutaneous afferent nerves in the foot, showed symptom improvement that was comparable to that seen with percutaneous tibial nerve stimulation (PTNS). The study, designed to determine an ideal stimulation duration, found that 3 hours of daily stimulation per week led to better improvement in overall OAB symptoms than 30 minutes of daily stimulation.

FootStim uses skin surface adhesive pad electrodes applied to the sole of the foot to deliver electrical pulses to branches of the tibial nerve. No needles are required. In an initial study published in 2014, the researchers sought to determine the impact of FootStim in healthy human subjects with no OAB. In eight subjects who underwent FootStim for 90 minutes, the authors reported a post-stimulation effect that resulted in an increase in bladder capacity of approximately 200 cc *(J Urol* 2014; 191:1009-13).

"This prompted us to continue our pursuit of FootStim as a treatment for OAB," said principal investigator Christopher Chermansky, MD, assistant professor of urology at the University of Pittsburgh School of Medicine, who worked on the study with Changfeng Tai, PhD, and colleagues.

At the AUA annual meeting, Dr. Chermansky presented results from 38 women with refractory OAB who had 3.7 leaks per day at baseline. Nineteen of the patients underwent FootStim for 30 minutes every evening over the course of 7 days, while the other 19 patients underwent 3 hours of treatment over the same period. All patients went through a 2-week washout of OAB drug therapy prior to initiation of the study.

The study was performed over 3 weeks. Week 1 was used to obtain baseline voiding parameters, FootStim was applied during week 2, and week 3 was used to monitor the post-stimulation effect. Stimulation parameters included pulse frequency of 5 Hz and pulse width of 0.2 milliseconds; intensity of stimulation was set by patients at two to four times the minimal stimulation necessary to cause the great toe to twitch. A responder was defined as having a statistically significant improvement in one or more measured voiding parameters.

Results showed that after 3 hours of daily stimulation per week, urge incontinence episodes decreased significantly from 3.7 to 2.8 leaks per day (p=.04), and a statistically significant improvement in urgency frequency was observed as well. With 30 minutes of daily stimulation, only the urge incontinence episodes decreased significantly—from 5.1 to 4.3 leaks per day (p=.03).

In the 3-hour group, 84% of patients (16 of 19) responded to at least one voiding parameter, versus 63% (12 of 19) in the 30-minute group. There were no adverse events, including redness, rash, or foot cramp, in either group. In both groups, foot stimulation effects persisted for about 4 days.

"Although this is an observational cohort study, testing different stimulation durations (3 hours or 30 minutes) did serve as a test to define the ideal stimulation duration," Dr. Chermansky said.

"We saw improvements in urgency urinary incontinence with both groups, with either 3 hours or 30 minutes per week. Yet, FootStim for 3 hours better improved the other OAB symptoms. Our results are comparable to PTNS," he added, "but unlike PTNS, FootStim was able to be done at home."

Dr. Chermansky said additional testing of FootStim is underway at the University of Pittsburgh with a 12-week randomized, sham-controlled trial in women with OAB

Study funding included a Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction Foundation neuromodulation grant and a Coulter Foundation grant at the University of Pittsburgh. UT

"We saw improvements in urgency urinary incontinence with both groups, with either 3 hours or 30 minutes per week. Yet, FootStim for 3 hours better improved the other OAB symptoms."

CHRISTOPHER CHERMANSKY, MD

Interstitial Cystitis/BPS | *Low complication, 30-day readmission rates observed*

Repeat hydrodistention found safe in treating IC

Wayne Kuznar
UT CORRESPONDENT

Boston—Repeated hydrodistention as therapy for interstitial cystitis (IC) has a low complication rate and does not decrease bladder capacity over time.

The procedure is also associated with symptomatic improvement, according to a retrospective review of patients who underwent two or more hydrodistentions at a single institution. The study was presented at the AUA annual meeting in Boston.

The use of cystoscopy and hydrodistention varies widely between providers, and the effect on symptoms is not clear from the literature, said first author Peter Kirk, a fourth-year medical student at the University of Michigan, Ann Arbor. The long-term effects are also not well understood. Working with Anne Pelletier Cameron, MD, and colleagues, his group measured changes in bladder capacity, development of ulcers, complications, and changes in symptoms of all patients undergoing hydrodistention for nonulcerative IC between 2006 and 2016 at the University of Michigan.

"We wanted to know if repeatedly stretching the bladder leads to scarring of the tissue and decreased bladder capacity over time, or if you follow these people over time, do you see people switching from nonulcerative IC to ulcerative IC," he said. "Part of our analysis is driven by the fact that there's not a lot of literature that rigorously assesses how patients respond to it."

In its 2011 guideline, the AUA states that "Short-duration low-pressure hydrodistention may be undertaken if first- and second-line

Please see **HYDRODISTENTION,** page 6

IC/BPS: One-fourth of patients have Hunner lesions

Cystoscopy recommended in patients over age 50 and men, researcher advises

Wayne Kuznar
UT CORRESPONDENT

Boston—About one-fourth of patients with interstitial cystitis/bladder pain syndrome (IC/BPS) have Hunner lesions in the bladder visible on cystoscopy.

Their urologic symptoms are indistinguishable from those of patients without Hunner lesions, according to H. Henry Lai, MD, and colleagues.

In addition, "IC patients with Hunner lesions may be less likely to have certain systemic manifestations, such as irritable bowel syndrome and anxiety," said Dr. Lai, associate professor of surgery and anesthesiology, Washington University, St Louis. He presented his data at the AUA annual meeting in Boston.

The rate of Hunner lesions found is substantially higher than that reported in the literature.

"We probably have a selected group of patient for which Hunner lesions may be enriched," Dr. Lai told *Urology Times*. "I think generally the experience is that about 10% of patients may have Hunner lesions, based on some of the published studies from the U.S. and Canada."

Since patients with Hunner lesions respond to specific treatments (such as triamcinolone injection, fulguration, or cyclosporine) and because Hunner lesions may represent a distinct phenotype among patients with IC/BPS patients, "one should consider cystoscopy to look for Hunner lesions, particularly for patients over the age of 50 or in men," he said.

The authors hypothesized that IC/BPS patients with Hunner lesions may represent a different phenotype from patients without Hunner lesions. For their study, they compared urologic symptoms (urgency, frequency, nocturia, urologic pain, bladder hypersensitivity, and sexual dysfunction) and nonurologic features (severity and distribution of systemic pain, comorbid functional pain syndromes, anxiety, and depression) between patients with and those without Hunner lesions visible on office cystoscopy without hydrodistention.

All patients completed a battery of questionnaires in which urologic features were assessed, such as the Interstitial Cystitis Symptom and Problem Indexes (ICSI, ICPI), Pelvic Pain and Urgency/Frequency Questionnaire, numeric ratings (0 to 10) of pain, urgency, and frequency, RICE Questionnaire, and the AUA Symptom Index. Nonurologic measures included the Hospital Anxiety and Depression Scale (HADS), psychologic stress, the Body Pain Map, Brief Pain Inventory, Poly-Symptomatic Poly-Syndromic Questionnaire, and comorbid pain conditions (irritable bowel syndrome [IBS], fibromyalgia, and chronic fatigue syndrome).

A Hunner lesion was defined as "a circumspect, reddened mucosal area that can have vessels radiating toward a central scar and/or a fibrin deposit of coagulum attached to this area." It often bleeds (like a waterfall) with bladder distention.

Hunner lesions found in 27%

Forty-one of 150 patients (27%) were found to have Hunner lesions. Those with Hunner lesions were about 15 years older on average than those without (57.3 vs. 42.3 years; $p<.001$). Those with Hunner lesions also reported less intense urologic pain scores (5.3 vs. 6.5; $p=.021$) as well as less bladder pain on the ICSI (3.0 vs. 3.5; $p=.034$) and increased nighttime frequency on the ICSI (3.5 vs. 2.6; $p=.034$).

A lower percentage of patients with Hunner lesions had anxiety on the HADS (22.0% vs. 43.1%; $p=.017$), and a lower percentage had IBS (15.0% vs. 36.1%; $p=.013$).

There was no difference between the groups in daytime frequency, urgency, depression, fibromyalgia, and chronic fatigue syndrome.

"I personally don't find that patients have a lot of discomfort during cystoscopy. You may not want to do it in every single patient," said Dr. Lai. "The older ones are probably more likely to be the ones in whom you'll find Hunner lesions. I would suggest cystoscopy to look for Hunner lesions or other conditions in the differential diagnosis in patients over the age of 50, in men, or in those with hematuria or at risk for bladder cancer." UT

HYDRODISTENTION

continued from page 5

treatments have not provided acceptable symptom control."

Ninety-seven patients (98% female) underwent multiple cystoscopy and hydrodistention for nonulcerative IC over the 10-year period. Some 63% had comorbid pain disorders. Their mean age was 35.7 years and mean body mass index was 27.1 kg/m^2. Patients had as many as 18 hydrodistentions, with the median number being three. The median time between distentions was 245 days.

Treatments for IC included anticholinergics in 39%, tricyclic antidepressants in 37%, gabapentin/pregabalin in 20%, pentosane polysulfate (Elmiron) in 33%, phenazopyridine (Pyridium) in 39%, hydroxyzine in 11%, intravesical instillation in 38%, and an implanted neurostimulator in 6%.

No significant changes in capacity

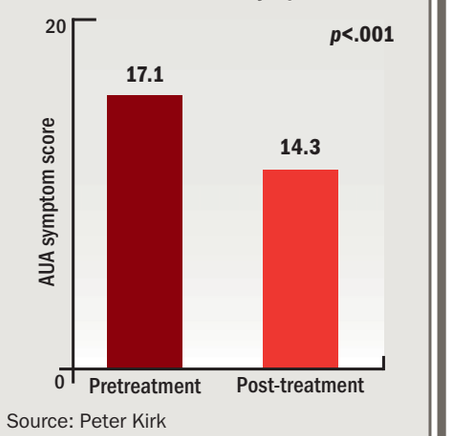
"We didn't see any significant changes in bladder capacity over time. We saw a really low complication rate and a really low 30-day readmission rate," Kirk said. "We also saw only a single patient in our cohort develop new ulceration that wasn't seen at their initial cystoscopy and hydrodistention."

The complication rate with hydrodistention was <1%. The rate of 30-day readmission was 2%. The mean initial anesthetic bladder capacity was 723.9 cc, which was not significantly different from the final capacity of 753.1 cc ($p=.15$).

Among patients who completed AUA symptom questionnaires before and after hydrodistention, the symptom score improved from 17.1 before treatment to 14.3 post-hydrodistention ($p<.001$) and the quality of life score improved from 4.3 to 3.6 ($p<.001$).

"One of the things we want to do in the future, and what we're working on, is building this database out to try to understand how we can predict who will benefit from hydrodistention," Kirk told *Urology Times*. "We're working to do multivariable modeling techniques to try to understand what the contributions of various clinical and demographic factors are in terms of being able to predict symptomatic response." UT

UT Figure Effect of hydrodistention on AUA symptom score



Source: Peter Kirk

Prostate Cancer | *Persistence on AS greater in men receiving testing*

Genomic testing linked to higher surveillance uptake

Wayne Kuznar
UT CORRESPONDENT

Boston—In men with clinically low-risk prostate cancer managed in community-based urology practices, utilization of active surveillance (AS) as initial management is higher among those who undergo genomic testing.

Persistence on AS is also greater in those having genomic testing, according to the results of an interim analysis in an observational cohort of men.

Investigators led by Gregg Eure, MD, examined the impact of a 17-gene assay (Oncotype DX) on the management of patients with clinically low-risk prostate cancer from 26 community-based urology practices that were using AS at the time. They presented their analysis at the AUA annual meeting in Boston and published the findings in *Urology* (2017; 107:67-75).

Based on an interim analysis of the first 297 participants, "We found that it's very helpful in the low-grade, low-stage men who are considering AS to help the physician and the patient with a shared decision," Dr. Eure told *Urology Times*.

"The individual risk refinement provided by genomic testing demonstrates the impact of the GPS in identifying appropriate patients and supporting more AS decisions in clinically low-risk prostate cancer."

GREGG EURE, MD

The 17-gene assay is a validated, biopsy-based commercial gene expression assay that, when combined with clinical features, provides an individual estimate of disease aggressiveness at the time of prostate cancer diagnosis. From the assay, a Genomic Prostate Score (GPS) that predicts 10-year risk is derived.

The 26 community practices that contributed patients were all active users of AS. The investigators compared AS rates and persistence in the group of 297 that had GPS testing at these practices and a baseline group of 247 patients that did not receive GPS testing from the same practices.

"These were the same physicians and the same manner of diagnosis and counseling. The only variable that did change going forward was the addition of the GPS scores," said Dr. Eure, chairman of research, Urology of Virginia, Virginia Beach. "Patients were told of their diagnosis, counseled, and given their GPS score, and follow-up visits were made within the next several weeks, followed by a decision made to pursue AS or not."

One-year results were available in 258 of the 297 tested patients.

Results 'durable out to 1 year'

The utilization of AS in GPS-tested men increased, "and that result is durable out to 1 year. At 1 year, men who were tested with GPS were more likely to choose AS and stay on it than men who don't have the benefit of the test," Dr. Eure said.

The higher utilization and persistence on AS resulted in a 21% absolute increase (34% vs. 55%) and a 62% relative increase in the proportion of GPS-tested men on AS at 1 year post-diagnosis compared with baseline. The net increase of patients on AS at 1 year was observed across age groups and racial groups.

"We thought we were maxed out on our AS acceptance but using GPS improved that," said Dr. Eure. "The individual risk refinement provided by genomic testing demonstrates the impact of the GPS in identifying appropriate patients and supporting more AS decisions in clinically low-risk prostate cancer."

Dr. Eure is a consultant/adviser for Genomic Health, Inc. and has a financial or other relationship with several pharmaceutical companies. Several of his co-authors are employees of and have an investment interest with Genomic Health, and several co-authors have disclosures related to Genomic Health and/or pharmaceutical companies. UT

CCP score further risk stratifies surveillance candidates

High-risk results more frequently associated with T3, T4 disease at RP

Wayne Kuznar
UT CORRESPONDENT

Boston—Use of a cell cycle progression (CCP) genomics test (Prolaris) can further stratify risk in men who are candidates for active surveillance (AS) based on clinical criteria, and therefore may have a role in decision-making in men with early-stage prostate cancer, researchers say.

Among a cohort of men undergoing radical prostatectomy (RP) at a large community-based practice for whom CCP scores were available, high-risk results were more frequent in men with pathologic stage T3 or T4 disease at RP, first author Patrick Hurley, MD, reported at the AUA annual meeting in Boston.

As more men are being chosen for AS, the appropriate clinical question is whether they are being accurately staged, said Dr. Hurley, a urologist at Comprehensive Urology in Novi, MI. Confirmatory tests for men considering AS include a re-biopsy, multiparametric magnetic resonance imaging (mpMRI), and genomic tests. Patients have concerns about re-biopsy, and mpMRI may not be available in the community setting. Also, the post-biopsy accuracy of MRI when the patient has had biopsy hemorrhage is uncertain, he said.

"There is growing interest regarding the extent to which prostate cancer genomic tests can further risk stratify men who are being considered for AS," he said.

The CCP score is a signature of 31 CCP genes; the score is the average expression level of the CCP genes normalized to 15 housekeeping genes. The study he presented at the AUA annual meeting assessed the utility of the combined risk score, which is the CCP score combined with the CAPRA-S to provide a 10-year estimate of prostate cancer-specific mortality. A low-risk score for the study was defined as a combined risk score <3%. High risk was defined as a combined risk score ≥3%.

Patients undergoing CCP testing between July 2013 and April 2016 at Comprehensive Urology had their CCP scores linked with treatment and pathologic information from the Michigan Urological Surgery Improvement Collaborative (MUSIC) prostate cancer registry.

> **"Patients with a low-risk score had <15% chance of having adverse pathology, suggesting they may be good candidates to remain safely on AS."**
>
> PATRICK HURLEY, MD

Some 651 patients had a CCP test result at biopsy, from which 408 had grade group 1 and grade group 2 disease and were therefore considered candidates for AS. Of these, 118 underwent RP as primary treatment. The frequency of adverse pathology was compared between men with high-risk versus low-risk CCP scores. In addition, the rate of adverse pathology was assessed in the 54 patients deemed appropriate for AS via the MUSIC appropriateness criteria, defined as one to three cores positive and no cores containing 3+4 disease with >50% cancer.

High-risk score linked to adverse pathology

Patients in grade group 1 or 2 who had a high-risk score had a much greater chance of having adverse pathology than those with a low-risk score. Gleason grade 4 or 5 cancer was present in 20.3% of the high-risk group compared with 10.2% in the low-risk group (*p*=.14). Patients in the high-risk group also had triple the rate of T3 or T4 cancer versus those in the low-risk group (36.2% vs. 12.2%; *p*=.004).

"Possibly more importantly, patients with a low-risk score had <15% chance of having adverse pathology, suggesting they may be good candidates to remain safely on AS," said Dr. Hurley.

In examining pathology in the group appropriate for AS by MUSIC criteria, the high-risk group via the CCP test had a much higher rate of Gleason 4 or 5 cancer than the low-risk group (21.7% vs. 3.2%; *p*=.73) as well as double the rate of stage T3 or T4 disease (17.4% vs. 9.7%; *p*=.44).

Urologists seemed to be influenced by the CCP test results in choosing patients for AS, Dr. Hurley said. Among patients in grade groups 1 and 2, half of the patients with a low CCP score were chosen for AS, whereas only 14% with a high CCP score were chosen for AS.

"If they were in grade group 1 (Gleason 6 only), there didn't seem to be any difference, likely because they were going to go on AS anyways," he said.

"For the patients who are candidates for AS, whether through the MUSIC appropriateness criteria or grade group 1, they were the ones with low-risk scores and low rates of adverse pathology, suggesting that likely they're safe to remain on AS," Dr. Hurley concluded.

One of Dr. Hurley's co-authors is a consultant/adviser for Myriad Genetics, Inc. The study received funding from Blue Cross and Blue Shield of Michigan and a grant from the National Cancer Institute. UT

UT Table **Cell cycle progression score: High risk vs. low risk**

	Patients with high-risk score	Patients with low-risk score	*p* value
Gleason grade 4 or 5	20.3%	10.2%	.14
Gleason grade 4 or 5 (MUSIC criteria)	21.7%	3.2%	.73
Rate of T3 or T4 cancer	36.2%	12.2%	.004
Rate of T3 or T4 cancer (MUSIC criteria)	17.4%	9.7%	.44

Source: Patrick Hurley, MD

Early data on PCa tracer promising

An easy-to-produce prostate cancer tracer has been developed, with phase I study findings published online in the *Journal of Nuclear Medicine* (Oct. 6, 2017).

Known as 68Ga-THP-PSMA, the new tracer, which was developed with support from the National Institute for Health Research Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London, can be made very quickly and easily in a radio-pharmacy, researchers say.

"The tracer [co-author Jennifer Young] has developed will give more patients access to potentially lifesaving scans. The low-cost and relatively straightforward production process means that smaller hospitals and not just the biggest specialist hospitals can produce it for their patients," said co-author Philip Blower, of King's College London.

Theragnostics provided funding for the study.

Immediate post-TURBT mitomycin instillation reduces recurrence risk

Benefit observed even in patients receiving adjuvant instillations, data indicate

Badar M. Mian, MD

Dr. Mian is associate professor of surgery in the division of urology at Albany Medical College, Albany, NY.

Mitomycin C (MMC) instillation within 24 hours after transurethral resection (TURBT) of non-muscle invasive bladder cancer (NMIBC) significantly reduces the risk of recurrence and delays the time to recurrence.

According to a prospective multicenter randomized phase III trial conducted in the Netherlands, this benefit was noted even in those patients who subsequently received adjuvant MMC based on risk category. The findings were published online in *European Urology* (July 10, 2017).

In this report by Bosschieter et al, patients were preoperatively randomized to receive 40 mg MMC in 50 mL saline, either immediately (within 24 hours after TURBT) or in a delayed fashion (2 weeks after TURBT). The efficacy endpoints were defined as recurrence risk, time to recurrence, and progression risk, while safety endpoints measured were incidence and severity of adverse effects.

Of the 2,844 patients, 1,384 (49%) were assigned to an immediate instillation and 1,460 (51%) to a delayed instillation group. A total of 601 patients were excluded due to not meeting the study criteria, thus leaving 2,243 patients eligible for intention-to-treat analysis. After TURBT, patients were categorized as low risk (LR): primary, solitary pTa/pT1 grade 1–2 tumor; intermediate risk (IR): primary, solitary pTa/pT1 grade 3 tumor or recurrent, solitary pTa/pT1 grade 1–3 tumor; or high risk (HR): all multiple tumors and/or carcinoma in situ, independent of stage or grade. The LR group received no further adjuvant MMC, the IR group received three weekly and five monthly instillations, and the HR group received three weekly and 11 monthly instillations. Cystoscopy was performed every 3 months for 1 year and then every 6 months.

Significantly lower recurrence risk seen

The recurrence risk in the entire cohort was significantly lower at 27% in the immediate instillation group compared to 36% in the delayed instillation group ($p<.001$). Further, the difference in time to recurrence after 3 years of follow-up significantly favored an immediate instillation, with 34% reduction in the relative risk of recurrence (hazard ratio: 0.66) compared to delayed instillation. The 3-year cancer progression rate was lower with immediate instillation (2.7%) compared to delayed instillation (5.5%). However, the trial was not powered or designed to evaluate the risk of progression.

When analyzing each risk group separately, no difference was noted in the risk of recurrence in the LR group from immediate versus delayed instillation (43% vs. 46%). However, immediate instillation significantly reduced the risk of recurrence in both the IR (20% vs. 32%) and HR group (28% vs. 35%).

Adverse effects were recorded in 258 of 1,048 patients (25%) in the immediate instillation group and 257 of 1,195 patients (22%) in the delayed instillation group ($p=.08$). Most common adverse effects were skin rash (5.4%) and irritative voiding symptoms (5.0%). In six patients (0.57%) in the immediate instillation group, MMC extravasation was reported, which was managed conservatively.

For the entire study population, MMC instillation appears to be more effective when given immediately post-TURBT and appears to have a relatively favorable side effect profile. Because the protocol was devised in 1998, the risk categorization used in this report are somewhat different than the contemporary risk categories and the results of sub-group analysis may not be translatable. Also, a second TURBT or reporting muscle in the specimen (which are now quite standard) for high-risk cases was not required in this trial.

It is postulated that the beneficial effect of post-TURBT MMC may be due to eradicating floating tumor cells, overlooked small tumors, or residual tumor at the resection site. Our clinical paradigm has shifted to bacillus Calmette-Guérin (not used in this trial) as the primary adjuvant therapy, and the increasing use of enhanced visualization technology (blue light cystoscopy, narrow band imaging) to allow more complete resection. One must question whether the benefits of MMC instillation will still be maintained in patients managed using these modalities.

It appears that for all NMIBC patients, an immediate single instillation of MMC within 24 hours after TURBT reduces the recurrence rate and prolongs time to recurrence, regardless of whether adjuvant MMC instillations were given. UT

Q&A

FRANCIS J. McGOVERN, MD

Dr. McGovern was interviewed by *Urology Times* Editorial Consultant **Stephen Y. Nakada, MD,** the Uehling Professor and founding chairman of urology at the University of Wisconsin, Madison.

OPIOID SPARING

How to reduce opioid use in post-op patients

The opioid crisis in the United States is widespread and affects many patients—including those undergoing major urologic procedures. In this interview, urologist Francis J. McGovern, MD, discusses the scope of the problem, outlines opioid-sparing strategies, and explains what the future holds in this area. Dr. McGovern is assistant clinical professor of surgery at Harvard Medical School, Massachusetts General Hospital, Boston.

Q: ***What is the scope of the problem of opioid abuse?***

A: The scope of the problem in the United States is very, very serious and it's widespread. The first statement I'd like to make is that pain is not a vital sign. In 1996, the American Pain Society trademarked the slogan "Pain: The Fifth Vital Sign." Soon to follow, health regulatory agencies agreed with this declaration and it contributed to a significant rise in the use of narcotics. The United States alone uses more narcotics than all other countries on the planet combined. In 2016, there were over 50,000 deaths in the United States from drug overdose, and 30,000 of those deaths are directly attributed to opioids. In the 1960s, heroin was the most common gateway to opioid addiction. That has been surpassed by prescription opioids.

U.S. studies have shown that 20% of the opioid prescription deaths can be traced back to a patient's specific prescribing physician. In that same study, 54% of the opioids were obtained from a relative or friend. But when they traced back one step further, 80% of that 54% were, again, traced back to the prescribing pattern of a doctor.

At Massachusetts General Hospital, we are now seeing collaboration with other departments within the department of surgery to address opioid use. We're all trying to get a better sense for prescribing patterns, establishing norms, and looking at ways to prevent or reduce the need for opioids.

Q: ***How did you get involved in this area?***

A: It's been a surgical evolution. At Mass General Hospital, I have a very active urologic/oncologic surgery practice. I'm often operating 4 days a week. As operating surgeons, we all know that complications significantly affect patient outcomes. Every surgeon wants their patients to do well.

Back in 2000, I chaired a committee at our hospital on the development of clinical pathways for major urologic surgery. During the development of these pathways, we dissected every aspect of care: pre-op, intra-op, and post-op. Efforts were made to standardize the pathways for all major urologic procedures.

What is the scope of the problem of opioid abuse?
STEPHEN Y. NAKADA, MD

The scope of the problem in the United States is very, very serious and it's widespread.
FRANCIS J. McGOVERN, MD

We're currently using these pathways and when we first executed them, we learned that this gave us a window into clearly seeing the issues that were contributing to post-op complications and increased length of stay. We learned that there are basically two main categories of surgical complications. One is directly attributed to surgical operative events. I would put bleeding, anastomotic leaks, anastomotic disruption, and infections in this category.

But then there's a second, broader category of complications that can be traced to side effects from medications, particularly opioids. Medical literature is now categorizing this as ORADES (Opioid-Related Adverse Drug Events). These are opioid-related side effects including confusion, respiratory issues, ileus, and retention. These are just a few of the very common complications we see. By reducing opioid need, we would also significantly improve patient care, reduce complications, and reduce length of stay.

I credit our outstanding residents for pointing out that most of what they do in their shifts when they're not in the operating room involves taking care of the side effects of opioids in post-op patients. This therefore became low-hanging fruit for improvement. It's all been done in an effort to improve care, get more optimal results, and reduce length of stay.

Q: ***Please discuss the key strategies to avoiding opioids.***

A: First, we should all be implementing an Enhanced Recovery After Surgery (ERAS) pathway or an ERAS-type pathway. Five of the twenty steps in ERAS involve opioid reduction. Second, we should collaborate with our anesthesia colleagues, instead of working in two separate silos of surgery and anesthesia. We get our best outcomes when we have a discussion about each patient. Third, develop an individualized pain control plan for each patient's needs.

Dr. Nakada, you may operate on a patient for a large kidney mass who has chronic obstructive pulmonary disease. This factor is critical in the development of an individualized pain plan. That patient may benefit greatly from a multimodality pain control strategy, such as the use of general anesthesia, epidural and local blocks, and non-narcotic medications such as gabapentin and Tylenol. We know a patient who already has some compromised respiratory function will have further suppression with narcotics, so we want to minimize the opioids.

In a course that I gave with my anesthesia colleague, Tony Anderson, MD (currently at Stanford Medical Center), at the AUA annual

Please see **OPIOID USE,** page 12

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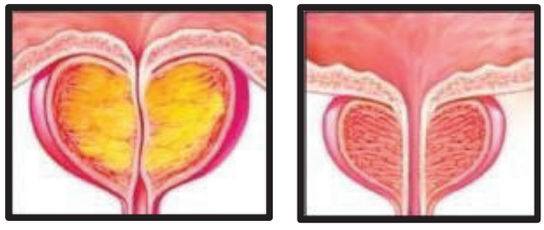

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OPIOID USE

continued from page 10

meeting in Boston, we coined the pneumonic "ALARM." "A" is for general anesthesia, "L" and "A" are for local anesthesia, "R" is for regional anesthesia, and "M" is for multimodality. Oftentimes, the strategy for optimal pain management doesn't come from just one segment but from a multi-modality approach.

I would also point out that if you're going to make an incision, to think about using a block. Blocks are very easy, are tolerated extremely well, and can reduce the need for opioids in the post-anesthesia care unit. The next strategy is to educate the patient, the family members, nurses—particularly recovery room nurses—as well as the floor nurses and the resident team on the benefits of minimizing the use of opioids. Also important is for the team to include this teaching with any Visiting Nurse Association referral that is arranged at discharge.

Q: ***What are some of the barriers to success?***

A: This is a significant paradigm shift. The challenge is to change patterns of long-standing behavior. For example, everyone who comes into contact with the patient needs to be on board with the pain management process. You may have an anesthesiologist who always likes to use a high dose of narcotics or a recovery room nurse who always likes to give several doses of narcotics.

We try to address this professionally by utilizing communication and education. When my residents deliver a patient to the recovery room now and greet the nurse or the anesthesiologist, they will say, "We specifically gave this patient a block and the patient should not require much in the way of narcotics." We have seen a significant decrease in the use of opioids in the post-op course since we started to implement this process at Massachusetts General Hospital.

Q: ***What should a practicing urologist, who may be a novice to this, do at this point?***

A: Every practicing urologist, whether they're at a major institution or at a small hospital, can speak with their anesthesia team and their pain experts. For most of my career, I would look at my surgical plan and delegate the decision on the pain management to my anesthesia colleagues. We get a better outcome when we collaborate with our anesthesia and nursing colleagues and work together. I strongly recommend for all of us to develop the surgical plan in parallel with the pain management plan.

Q: ***Are there any caveats to this approach?***

A: We've seen significant reductions in length of stay and increased patient satisfaction with this process, but there's always room for improvement. Hopefully, new technologies and new innovations will get us to the point where we have medications that can replace or help minimize our need to use any opioids. But until we're there, we need to do further research and development.

Please discuss the key strategies to avoiding opioids.
STEPHEN Y. NAKADA, MD

We should all be implementing an Enhanced Recovery After Surgery (ERAS) pathway or an ERAS-type pathway.
FRANCIS J. McGOVERN, MD

Q: ***Could you expand a little on the future opportunities in research and development in this area?***

A: This area is in its early stages. I asked my colleagues in other surgical departments at Mass General if they knew how much narcotic an average patient needs for a surgical procedure after they go home. I discovered that nobody had an answer. I asked my resident team how much narcotic the average patient having a radical prostatectomy would utilize and, again, there was a wide variability in the answers.

At Mass General, we currently have submitted an IRB that is awaiting approval. This will basically allow us to send patients home with a calendar to record how much narcotic they took on post-op day 1 2, 3, 4, 5. The data will be reported at their post-op visit. We will use this information to help us quantitate the use of these medications so that we can establish a set of standards. The point is not to have all patients live by the same number but to understand the norm. This will help us identify patients that are outliers in using an excessive amount of pain medication, which may indicate a post-op clinical problem. Our hope is this data will help us to write for an appropriate number of pills without giving patient an excess amount.

We also need to find ways of research and development into education for patients and families that should begin before surgery—even intra-op or immediately post-op—so that we have everyone on board for the patient's well-being and safe recovery. There will be great opportunities for research in this area because it's often the anchor of what's holding patients back from a speedy, safe recovery. UT

Urologists identify risk factors for opioid overdose

Risk factors for opioid dependence or overdose (ODO) include younger age, inpatient surgery and increasing hospitalization duration, baseline depression, tobacco use, and chronic obstructive pulmonary disease, according to a study published in the *Journal of Urology* (2017; 198:1130-6).

In addition, insurance provider, Medicaid or Medicare enrollment, and noninsured status were factors associated with ODO risk. The investigators also correlated ODO rates to specific urologic surgical procedures, with stone procedures (0.15%) or major renal surgery (0.12%) having the highest rates, and major pelvic surgery (0.03%) and inguinal/scrotal procedures (0.05%) having the lowest rates.

"Using these risk factors, we can identify patients at the highest risk for ODO, and tailor specific pain and follow-up regimens for them that carry the least consequences," explained lead investigator Gopal N. Gupta, MD, of the Loyola University Medical Center, Chicago. "Perhaps the greatest and most rapid impact can be made if physicians reduce over prescription of opioids and seek alternative pain management strategies. Vigilant monitoring of aberrant behavior such as early refill requests, treatment noncompliance, and reports of lost or stolen prescriptions will improve the recognition of signs of abuse."

Using data from 2007 to 2011 for more than 675,000 patients from the Healthcare Cost and Utilization Project for California that included information on patient discharge, outpatient surgeries, and emergency department records, the authors were able to link surgical records to postoperative diagnoses of ODO occurring within 1 year of surgery.

Comparing patients in whom ODO did or did not occur, those who overdosed were younger (median age 50 vs. 62 years), more likely to be Caucasian (63.4% vs. 57.3%) or African-American (9.5% vs 3.6%), and less likely to have undergone ambulatory surgery (18.0% vs. 57.8%) compared to patients who did not overdose. Patients who overdosed were more likely to have been diagnosed with depression (15.0% vs. 3.4%) or be a tobacco user (28.2% vs. 15.7%), and less likely to have cancer (17.2% vs. 22.8%).

For patients younger than 65 years of age who were on Medicare or Medicaid, and individuals who self-paid for insurance, the risk of ODO was 2.1 to 3.0 times higher than patients with private insurance. Medicare patients 65 years old or older were not found to be at increased risk for ODO.

In an accompanying commentary *(J Urol* 2017; 198:990-2), Michael S. Leapman, MD, of the Yale School of Medicine, New Haven, CT, and Steven A. Kaplan, MD, of the Icahn School of Medicine at Mount Sinai, New York, wrote, "As attitudes toward opioids are rapidly changing, a balance must be struck between highly restrictive and overzealous prescribing. In light of sobering national statistics of misuse, all clinicians are tasked to embrace responsible prescribing. A middle ground appears possible that reeducates toward demystifying dosing strategies, maximizing patient safety, and preserving a clinician's judgment."

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- Are not eligible for cisplatin-containing chemotherapy, or
- Have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

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ALK=anaplastic lymphoma kinase; EGFR=epidermal growth factor receptor; PD-L1=programmed death-ligand 1.

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Important Safety Information

Serious Adverse Reactions

Please refer to the full Prescribing Information for important dose management information specific to adverse reactions.

- **Immune-related pneumonitis.** Immune-mediated pneumonitis or interstitial lung disease have occurred. Fatal cases have been observed in patients with urothelial carcinoma (UC) and non-small cell lung cancer (NSCLC). Permanently discontinue TECENTRIQ for Grade 3 or 4 pneumonitis
- **Immune-related hepatitis.** Immune-mediated hepatitis and liver test abnormalities, including a fatal case of hepatitis in a patient with UC, have occurred. Permanently discontinue TECENTRIQ for Grade 3 or 4 immune-mediated hepatitis
- **Immune-related colitis.** Immune-mediated colitis or diarrhea, including a fatal case of diarrhea-associated renal failure in a patient with UC, occurred. Permanently discontinue TECENTRIQ for Grade 4 diarrhea or colitis
- **Immune-related endocrinopathies.** Immune-related thyroid disorders, adrenal insufficiency, hypophysitis, and type 1 diabetes mellitus, including diabetic ketoacidosis, have occurred. Permanently discontinue TECENTRIQ for Grade 4 hypophysitis
- **Other immune-related adverse reactions.** Meningoencephalitis, myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome, ocular inflammatory toxicity, and pancreatitis, including increases in serum amylase and lipase levels, have occurred. Permanently discontinue TECENTRIQ for any grade of meningitis or encephalitis, or any grade of myasthenic syndrome/myasthenia gravis or Guillain-Barré syndrome. Permanently discontinue TECENTRIQ for Grade 4 or any grade of recurrent pancreatitis
- **Infection.** Severe infections, such as sepsis, herpes encephalitis, and mycobacterial infection leading to retroperitoneal hemorrhage, have occurred. Fatal cases have been observed in patients with UC and NSCLC
- **Infusion-related reactions.** Severe infusion reactions occurred. Permanently discontinue TECENTRIQ in patients with Grade 3 or 4 infusion reactions
- **Embryo-fetal toxicity.** TECENTRIQ can cause fetal harm in pregnant women. Advise patients of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TECENTRIQ and for at least 5 months after the last dose
- Advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months after the last dose

Most Common Adverse Reactions

The most common adverse reactions in cisplatin-ineligible UC (rate ≥20%) were fatigue (52%), decreased appetite (24%), diarrhea (24%), and nausea (22%).

The most common adverse reactions (rate ≥20%) in previously treated UC were fatigue (52%), decreased appetite (26%), nausea (25%), urinary tract infection (22%), pyrexia (21%), and constipation (21%).

The most common adverse reactions in NSCLC (rate ≥20%) included fatigue (46%), decreased appetite (35%), dyspnea (32%), cough (30%), nausea (22%), musculoskeletal pain (22%), and constipation (20%).

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

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This is a brief summary of information about TECENTRIQ. Before prescribing, please see full Prescribing Information.

1 INDICATIONS AND USAGE

1.1 Locally Advanced or Metastatic Urothelial Carcinoma

TECENTRIQ (atezolizumab) is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:

- are not eligible for cisplatin-containing chemotherapy, or
- have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials *[see Clinical Studies (14.1)]*.

1.2 Metastatic Non-Small Cell Lung Cancer

TECENTRIQ is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving TECENTRIQ *[see Clinical Studies (14.2)]*.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Immune-Related Pneumonitis

Immune-mediated pneumonitis or interstitial lung disease, defined as requiring use of corticosteroids and with no clear alternate etiology, occurred in patients receiving TECENTRIQ. Monitor patients for signs with radiographic imaging and for symptoms of pneumonitis. Administer steroids at a dose of 1 to 2 mg/kg/day prednisone equivalents for Grade 2 or greater pneumonitis, followed by corticosteroid taper. Withhold TECENTRIQ until resolution for Grade 2 pneumonitis. Permanently discontinue TECENTRIQ for Grade 3 or 4 pneumonitis *[see Dosage and Administration (2.2)]*.

Across clinical trials, 2.6% (51/1978) of patients developed pneumonitis. Fatal pneumonitis occurred in two patients.

Urothelial Carcinoma

In 523 patients with urothelial carcinoma who received TECENTRIQ, pneumonitis occurred in six (1.1%) patients. Of these patients, there was one patient with fatal pneumonitis, one patient with Grade 3, three patients with Grade 2, and one patient with Grade 1 pneumonitis. TECENTRIQ was held in all cases. Pneumonitis resolved in three patients. The median time to onset was 2.6 months (range: 15 days to 4.2 months). The median duration was 15 days (range: 6 days to 3.1+ months). Immune-mediated pneumonitis occurred in 5 (1.0%) patients.

NSCLC

In 1027 patients with NSCLC who received TECENTRIQ, pneumonitis occurred in 38 (3.7%) patients. Of these patients, there was one patient with fatal pneumonitis, two patients with Grade 4, thirteen patients with Grade 3, eleven patients with Grade 2, and eleven patients with Grade 1 pneumonitis. TECENTRIQ was held in 24 patients and 21 patients were treated with corticosteroids. Pneumonitis resolved in 26 of the 38 patients. The median time to onset was 3.3 months (range: 3 days to 18.7 months). The median duration was 1.4 months (range: 0 days to 12.6+ months).

5.2 Immune-Related Hepatitis

Immune-mediated hepatitis, defined as requiring use of corticosteroids and with no clear alternate etiology, occurred in patients receiving TECENTRIQ treatment. Liver test abnormalities occurred in patients who received TECENTRIQ. Monitor patients for signs and symptoms of hepatitis. Monitor AST, ALT, and bilirubin prior to and periodically during treatment with TECENTRIQ. Administer corticosteroids at a dose of 1–2 mg/kg/day prednisone equivalents for Grade 2 or greater transaminase elevations, with or without concomitant elevation in total bilirubin, followed by corticosteroid taper. Withhold TECENTRIQ for Grade 2 and permanently discontinue TECENTRIQ for Grade 3 or 4 immune-mediated hepatitis *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

Across clinical trials (n=1978), Grade 3 or 4 elevation occurred in ALT (2.5%), AST (2.3%), and total bilirubin (1.6%).

Urothelial Carcinoma

In patients with urothelial carcinoma (n=523), Grade 3 or 4 elevation occurred in ALT (2.5%), AST (2.5%), and total bilirubin (2.1%). Immune-mediated hepatitis occurred in 1.3% (7/523) of patients. Of these cases, one patient died from hepatitis, five patients had Grade 3, and one patient had Grade 2 hepatitis. The median time to onset was 1.1 months (range: 0.4 to 7.7 months). TECENTRIQ was temporarily interrupted in four patients; none of these patients developed recurrence of hepatitis after resuming TECENTRIQ.

NSCLC

In patients with NSCLC, Grade 3 or 4 elevation occurred in ALT (1.4%), AST (1.3%), and total bilirubin (0.6%). Immune-mediated hepatitis occurred in 0.9% (9/1027) of patients. Of these nine patients, one patient had Grade 4, four patients had Grade 3, three patients had Grade 2, and one patient had Grade 1 immune-mediated hepatitis. The median time to onset was 28 days (range: 15 days to 4.2 months). TECENTRIQ was temporarily interrupted in seven patients; none of these patients developed recurrence of hepatitis after resuming TECENTRIQ.

5.3 Immune-Related Colitis

Immune-mediated colitis or diarrhea, defined as requiring use of corticosteroids and with no clear alternate etiology, occurred in patients receiving TECENTRIQ. Monitor patients for signs and symptoms of diarrhea or colitis. Withhold treatment with TECENTRIQ for Grade 2 diarrhea or colitis. If symptoms persist for longer than 5 days or recur, administer 1–2 mg/kg prednisone or equivalent per day. Withhold treatment with TECENTRIQ for Grade 3 diarrhea or colitis. Treat with IV methylprednisolone 1–2 mg/kg per day and convert to oral steroids once the patient has improved. For both Grade 2 and Grade 3 diarrhea or colitis, when symptoms improve to Grade 0 or Grade 1, taper steroids over ≥ 1 month. Resume treatment with TECENTRIQ if the event improves to Grade 0 or 1 within 12 weeks and corticosteroids have been reduced to the equivalent of ≤ 10 mg oral prednisone per day. Permanently discontinue TECENTRIQ for Grade 4 diarrhea or colitis *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

Across clinical trials, colitis or diarrhea occurred in 19.7% (389/1978) of all patients.

Urothelial Carcinoma

In 523 patients with urothelial carcinoma who received TECENTRIQ, colitis or diarrhea occurred in 98 (18.7%) patients. Ten patients (1.9%) developed Grade 3 or 4 diarrhea. Four patients (0.8%) had immune-mediated colitis or diarrhea with a median time to onset of 1.7 months (range: 1.1 to 3.1 months). Immune-mediated colitis resolved with corticosteroid administration in three of these patients, while the other patient died without resolution of colitis in the setting of diarrhea-associated renal failure.

NSCLC

In 1027 patients with NSCLC who received TECENTRIQ, colitis or diarrhea occurred in 198 (19.3%) patients. Twelve patients (1.2%) developed Grade 3 colitis or diarrhea. Five patients (0.5%) had immune-mediated colitis or diarrhea with a median time to onset of 21 days (range: 12 days to 3.4 months). Of these patients, one had Grade 3, two had Grade 2, and two had Grade 1 immune-mediated colitis or diarrhea. Immune-mediated colitis or diarrhea resolved with corticosteroid administration in four of these patients, while the fifth patient died due to disease progression prior to resolution of colitis.

5.4 Immune-Related Endocrinopathies

Immune-related thyroid disorders, adrenal insufficiency, and type 1 diabetes mellitus, including diabetic ketoacidosis, have occurred in patients receiving TECENTRIQ. Monitor patients for clinical signs and symptoms of endocrinopathies.

Hypophysitis

Hypophysitis occurred in 0.2% (1/523) of patients with urothelial cancer receiving TECENTRIQ. Monitor for signs and symptoms of hypophysitis. Administer corticosteroids and hormone replacement as clinically indicated. Withhold TECENTRIQ for Grade 2 or Grade 3 and permanently discontinue for Grade 4 hypophysitis *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

Thyroid Disorders

Thyroid function was assessed routinely only at baseline and the end of the study. Monitor thyroid function prior to and periodically during treatment with TECENTRIQ. Asymptomatic patients with abnormal thyroid function tests can receive TECENTRIQ. For symptomatic hypothyroidism, withhold TECENTRIQ and initiate thyroid hormone replacement as needed. Manage isolated hypothyroidism with replacement therapy and without corticosteroids. For symptomatic hyperthyroidism, withhold TECENTRIQ and initiate an anti-thyroid drug as needed. Resume treatment with TECENTRIQ when symptoms of hypothyroidism or hyperthyroidism are controlled and thyroid function is improving *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

Across clinical trials, hypothyroidism and hyperthyroidism occurred in 3.9% (77/1978) and 1.0% (20/1978) of patients, respectively.

Urothelial Carcinoma

In 523 patients with urothelial carcinoma who received TECENTRIQ, hypothyroidism occurred in 2.5% (13/523). One patient had Grade 3 and twelve patients had Grade 1–2 hypothyroidism. The median time to first onset was 5.4 months (range: 21 days to 11.3 months). Thyroid stimulating hormone (TSH) was elevated and above the patient's baseline in 16% (21/131) of patients with a follow-up measurement.

Hyperthyroidism occurred in 0.6% (3/523) of patients with urothelial carcinoma. Of the three urothelial carcinoma patients, one patient had Grade 2 and two patients had Grade 1 hyperthyroidism. The median time to onset was 3.2 months (range: 1.4 to 5.8 months). TSH was decreased and below the patient's baseline in 3.8% (5/131) of patients with a follow-up measurement.

NSCLC

In 1027 patients with NSCLC who received TECENTRIQ, hypothyroidism occurred in 4.2% (43/1027). Three patients had Grade 3 and forty patients had Grade 1–2 hypothyroidism. The median time to onset was 4.8 months (range 15 days to 31 months.) TSH was elevated and above the patient's baseline in 17% (54/315) of patients with follow-up measurement.

Hyperthyroidism occurred in 1.1% (11/1027) of patients with NSCLC. Eight patients had Grade 2 and three patients had Grade 1 hyperthyroidism. The median time to onset was 4.9 months (range: 21 days to 31 months). TSH was decreased and below the patient's baseline in 7.6% (24/315) of patients with a follow-up measurement.

Adrenal Insufficiency

Adrenal insufficiency occurred in 0.4% (7/1978) of patients across clinical trials, including two patients with Grade 3, four patients with Grade 2, and one patient with Grade 1. Adrenal insufficiency resolved in two patients.

For symptomatic adrenal insufficiency, withhold TECENTRIQ and administer methylprednisolone 1–2 mg/kg per day IV followed by oral prednisone 1–2 mg/kg per day or equivalent once symptoms improve. Start steroid taper when symptoms improve to ≤ Grade 1 and taper steroids over ≥ 1 month. Resume treatment with TECENTRIQ if the event improves to ≤ Grade 1 within 12 weeks and corticosteroids have been reduced to the equivalent of ≤ 10 mg oral prednisone per day and the patient is stable on replacement therapy, if required *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

Diabetes Mellitus

New onset diabetes with ketoacidosis has occurred in patients receiving TECENTRIQ. Diabetes mellitus without an alternative etiology occurred in one (0.2%) patient with urothelial carcinoma and three (0.3%) patients with NSCLC.

Initiate treatment with insulin for type 1 diabetes mellitus. For ≥ Grade 3 hyperglycemia (fasting glucose >250–500 mg/dL), withhold TECENTRIQ. Resume treatment with TECENTRIQ when metabolic control is achieved on insulin replacement therapy *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

5.5 Other Immune-Related Adverse Reactions

Other immune-related adverse reactions including meningoencephalitis, myasthenic syndrome/myasthenia gravis, Guillain-Barré, ocular inflammatory toxicity, and pancreatitis, including increases in serum amylase and lipase levels, have occurred in ≤ 1.0% of patients treated with TECENTRIQ.

Meningitis / Encephalitis

Monitor patients for clinical signs and symptoms of meningitis or encephalitis. Permanently discontinue TECENTRIQ for any grade of meningitis or encephalitis. Treat with IV steroids (1–2 mg/kg/day methylprednisolone or equivalent) and convert to oral steroids (prednisone 60 mg/day or equivalent) once the patient has improved. When symptoms improve to ≤ Grade 1, taper steroids over ≥ 1 month *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

Motor and Sensory Neuropathy

Monitor patients for symptoms of motor and sensory neuropathy. Permanently discontinue TECENTRIQ for any grade of myasthenic syndrome/myasthenia gravis or Guillain-Barré syndrome. Institute medical intervention as appropriate. Consider initiation of systemic corticosteroids at a dose of 1–2 mg/kg/day prednisone *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

Pancreatitis

Symptomatic pancreatitis without an alternative etiology occurred in 0.1% (2/1978) of patients across clinical trials. Monitor patients for signs and symptoms of acute pancreatitis. Withhold TECENTRIQ for ≥ Grade 3 serum amylase or lipase levels (> 2.0 ULN), or Grade 2 or 3 pancreatitis. Treat with 1–2 mg/kg IV methylprednisolone or equivalent per day. Once symptoms improve, follow with 1–2 mg/kg of oral prednisone or equivalent per day. Resume treatment with TECENTRIQ when serum amylase and lipase levels improve to ≤ Grade 1 within 12 weeks or symptoms of pancreatitis have resolved, and corticosteroids have been reduced to ≤ 10 mg oral prednisone or equivalent per day. Permanently discontinue TECENTRIQ for Grade 4 or any grade of recurrent pancreatitis *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

5.6 Infection

Severe infections, including sepsis, herpes encephalitis, and mycobacterial infection leading to retroperitoneal hemorrhage occurred in patients receiving TECENTRIQ. Monitor patients for signs and symptoms of infection and treat with antibiotics for suspected or confirmed bacterial infections. Withhold TECENTRIQ for ≥ Grade 3 infection *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

Across clinical trials, infections occurred in 38.4% (759/1978) of patients.

Urothelial Carcinoma

In 523 patients with urothelial carcinoma who received TECENTRIQ, infection occurred in 197 (37.7%) patients. Grade 3 or 4 infection occurred in sixty (11.5%) patients, while three patients died due to infections. Urinary tract infections were the most common cause of Grade 3 or higher infection, occurring in 37 (7.1%) patients.

NSCLC

In Study 3, a randomized trial in patients with NSCLC, infections were more common in patients treated with TECENTRIQ (43%) compared with those treated with docetaxel (34%). Grade 3 or 4 infections occurred in 9.2% of patients treated with TECENTRIQ compared with 2.2% in patients treated with docetaxel. Two patients (1.4%) treated with TECENTRIQ and three patients (2.2%) treated with docetaxel died due to infection. Pneumonia was the most common cause of Grade 3 or higher infection, occurring in 7.7% of patients treated with TECENTRIQ.

5.7 Infusion-Related Reactions

Severe infusion reactions have occurred in patients in clinical trials of TECENTRIQ. Infusion-related reactions occurred in 1.3% (25/1978) of patients across clinical trials, 1.7% (9/523) of patients with urothelial carcinoma, and 1.6% (16/1027) of patients with NSCLC. Interrupt or slow the rate of infusion in patients with mild or moderate infusion reactions. Permanently discontinue TECENTRIQ in patients with Grade 3 or 4 infusion reactions *[see Dosage and Administration (2.2) and Adverse Reactions (6.1)]*.

5.8 Embryo-Fetal Toxicity

Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD–L1/PD–1 pathway can lead to increased risk of immune-related rejection of the developing fetus resulting in fetal death. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, advise the patient of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TECENTRIQ and for at least 5 months after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

- Immune-Related Pneumonitis *[see Warnings and Precautions (5.1)]*
- Immune-Related Hepatitis *[see Warnings and Precautions (5.2)]*
- Immune-Related Colitis *[see Warnings and Precautions (5.3)]*
- Immune-Related Endocrinopathies *[see Warnings and Precautions (5.4)]*
- Other Immune-Related Adverse Reactions *[see Warnings and Precautions (5.5)]*
- Infection *[see Warnings and Precautions (5.6)]*
- Infusion-Related Reactions *[see Warnings and Precautions (5.7)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Urothelial Carcinoma

Cisplatin-Ineligible Patients with Locally Advanced or Metastatic Urothelial Carcinoma

The safety of TECENTRIQ was evaluated in Study 4, a multicenter, open-label, single-arm trial that included 119 patients with locally advanced or metastatic urothelial carcinoma who were ineligible for cisplatin-containing chemotherapy and were either previously untreated or had disease progression at least 12 months after neoadjuvant or adjuvant chemotherapy *[see Clinical Studies (14.1)]*. Patients received 1200 mg of TECENTRIQ intravenously every 3 weeks until either unacceptable toxicity or disease progression. The median duration of exposure was 15.0 weeks (range 0, 87 weeks).

The most common adverse reactions (≥ 20%) were fatigue (52%), decreased appetite (24%), diarrhea (24%), and nausea (22%). The most common Grade 3–4 adverse reactions (≥ 2%) were fatigue, urinary tract infection, anemia, diarrhea, blood creatinine increase, intestinal obstruction, ALT increase, hyponatremia, decreased appetite, sepsis, back/neck pain, renal failure, and hypotension.

Five patients (4.2%) who were treated with TECENTRIQ experienced one of the following events which led to death: sepsis, cardiac arrest, myocardial infarction, respiratory failure, or respiratory distress. One additional patient (0.8%) was experiencing herpetic meningoencephalitis and disease progression at the time of death. TECENTRIQ was discontinued for adverse reactions in 4.2% (5/119) of patients. The adverse reactions leading to discontinuation were diarrhea/colitis (1.7%), fatigue (0.8%), hypersensitivity (0.8%), and dyspnea (0.8%). Adverse reactions leading to interruption of TECENTRIQ occurred in 35% of patients, the most common (≥ 1%) were intestinal obstruction, fatigue, diarrhea, urinary tract infection, infusion related reaction, cough, abdominal pain, peripheral edema, pyrexia, respiratory tract infection, upper respiratory tract infection, creatinine increase, decreased appetite, hyponatremia, back pain, pruritus, and venous thromboembolism. Serious adverse reactions occurred in 37% of patients. The most frequent serious adverse reactions (≥ 2%) were diarrhea, intestinal obstruction, sepsis, acute kidney injury, and renal failure.

Immune-related adverse reactions requiring systemic corticosteroids or hormone replacement therapy occurred in 19.3% (23/119) patients, including 12.6% (15/119) patients who required systemic corticosteroid therapy and 6.7% (8/119) patients who required only hormone replacement therapy.

Six patients (5.0%) received an oral prednisone dose equivalent to ≥40 mg daily for an immune-mediated adverse reaction *[see Warnings and Precautions (5)]*.

Table 1 summarizes the adverse reactions that occurred in ≥ 10% of patients and Table 2 summarizes Grade 3–4 selected laboratory abnormalities that occurred in ≥ 1% of patients treated with TECENTRIQ in Study 4.

Table 1: All Grade Adverse Reactions in ≥ 10% of Patients with Urothelial Carcinoma in Study 4

	TECENTRIQ N = 119	
Adverse Reaction	All Grades (%)	Grades 3–4 (%)
General Disorders		
Fatigue[a]	52	8
Peripheral edema[b]	17	2
Pyrexia	14	0.8
Gastrointestinal Disorders		
Diarrhea[c]	24	5
Nausea	22	2
Vomiting	16	0.8
Constipation	15	2
Abdominal pain[d]	15	0.8
Metabolism and Nutrition Disorders		
Decreased appetite[e]	24	3
Musculoskeletal and Connective Tissue Disorders		
Back/Neck pain	18	3
Arthralgia	13	0
Skin and Subcutaneous Tissue Disorders		
Pruritus	18	0.8
Rash[f]	17	0.8
Infections		
Urinary tract infection[g]	17	5
Respiratory, Thoracic, and Mediastinal Disorders		
Cough[h]	14	0
Dyspnea[i]	12	0

[a] Includes fatigue, asthenia, lethargy, and malaise
[b] Includes edema peripheral, scrotal edema, lymphedema, and edema
[c] Includes diarrhea, colitis, frequent bowel movements, autoimmune colitis
[d] Includes abdominal pain, upper abdominal pain, lower abdominal pain, and flank pain
[e] Includes decreased appetite and early satiety
[f] Includes rash, dermatitis, dermatitis acneiform, rash maculo-papular, rash erythematous, rash pruritic, rash macular, and rash papular
[g] Includes urinary tract infection, urinary tract infection bacterial, cystitis, and urosepsis
[h] Includes cough and productive cough
[i] Includes dyspnea and exertional dyspnea

Table 2: Grade 3–4 Laboratory Abnormalities in Patients with Urothelial Carcinoma in Study 4 in ≥ 1% of Patients

Laboratory Test	Grades 3–4 (%)
Hyponatremia	15
Hyperglycemia	10
Lymphopenia	9
Anemia	7
Increased Alkaline phosphatase	7
Increased Creatinine	5
Hypophosphatemia	4
Increased ALT	4
Increased AST	4
Hyperkalemia	3
Hypermagnesemia	3
Hyperbilirubinemia	3

Previously Treated Patients with Locally Advanced or Metastatic Urothelial Carcinoma

The safety of TECENTRIQ was evaluated in Study 1, a multicenter, open-label, single-arm trial that included 310 patients in a single arm trial with locally advanced or metastatic urothelial carcinoma who had disease progression during or following at least one platinum-containing chemotherapy regimen or who had disease progression within 12 months of treatment with a platinum-containing neoadjuvant or adjuvant chemotherapy regimen *[see Clinical Studies (14.1)]*. Patients received 1200 mg of TECENTRIQ intravenously every 3 weeks until unacceptable toxicity or either radiographic or clinical progression. The median duration of exposure was 12.3 weeks (range: 0.1, 46 weeks).

The most common adverse reactions (≥ 20%) were fatigue (52%), decreased appetite (26%), nausea (25%), urinary tract infection (22%), pyrexia (21%), and constipation (21%). The most common Grade 3–4 adverse reactions (≥ 2%) were urinary tract infection, anemia, fatigue, dehydration, intestinal obstruction, urinary obstruction, hematuria, dyspnea, acute kidney injury, abdominal pain, venous thromboembolism, sepsis, and pneumonia.

Three patients (1.0%) who were treated with TECENTRIQ experienced one of the following events which led to death: sepsis, pneumonitis, or intestinal obstruction. TECENTRIQ was discontinued for adverse reactions in 3.2% (10/310) of the 310 patients. Sepsis led to discontinuation in 0.6% (2/310) of patients. Adverse reactions leading to interruption of TECENTRIQ occurred in 27% of patients; the most common (> 1%) were liver enzyme increase, urinary tract infection, diarrhea, fatigue, confusional state, urinary obstruction, pyrexia, dyspnea, venous thromboembolism, and pneumonitis. Serious adverse reactions occurred in 45% of patients. The most frequent serious adverse reactions (> 2%) were urinary tract infection, hematuria, acute kidney injury, intestinal obstruction, pyrexia, venous thromboembolism, urinary obstruction, pneumonia, dyspnea, abdominal pain, sepsis, and confusional state.

Immune-related adverse reactions requiring systemic corticosteroids or hormone replacement therapy occurred in 11.0% (34/310) patients, including 8.4% (26/310) patients who required systemic corticosteroid therapy and 2.6% (8/310) patients who required only hormone replacement therapy.

Eighteen patients (5.8%) received an oral prednisone dose equivalent to ≥40 mg daily for an immune-mediated adverse reaction *[see Warnings and Precautions (5)]*.

Table 3 summarizes the adverse reactions that occurred in ≥ 10% of patients while Table 4 summarizes Grade 3–4 selected laboratory abnormalities that occurred in ≥ 1% of patients treated with TECENTRIQ in Study 1.

Table 3: All Grade Adverse Reactions in ≥ 10% of Patients with Urothelial Carcinoma in Study 1

	TECENTRIQ N=310	
Adverse Reaction	All Grades (%)	Grades 3–4 (%)
Gastrointestinal Disorders		
Nausea	25	2
Constipation	21	0.3
Diarrhea	18	1
Abdominal pain	17	4
Vomiting	17	1
General Disorders		
Fatigue	52	6
Pyrexia	21	1
Peripheral edema	18	1
Infections		
Urinary tract infection	22	9
Metabolism and Nutrition Disorders		
Decreased appetite	26	1
Musculoskeletal and Connective Tissue Disorders		
Back/Neck pain	15	2
Arthralgia	14	1
Renal and urinary disorders		
Hematuria	14	3
Respiratory, Thoracic, and Mediastinal Disorders		
Dyspnea	16	4
Cough	14	0.3
Skin and Subcutaneous Tissue Disorders		
Rash	15	0.3
Pruritus	13	0.3

Table 4: Grade 3–4 Laboratory Abnormalities in Patients with Urothelial Carcinoma in Study 1 in ≥ 1% of Patients

Laboratory Test	Grades 3–4 (%)
Lymphopenia	10
Hyponatremia	10
Anemia	8
Hyperglycemia	5
Increased Alkaline phosphatase	4
Increased Creatinine	3
Increased ALT	2
Increased AST	2
Hypoalbuminemia	1

NSCLC

The safety of TECENTRIQ was evaluated in Study 3, a multicenter, international, randomized, open-label trial in patients with metastatic NSCLC who progressed during or following a platinum-containing regimen, regardless of PD–L1 expression *[see Clinical Studies (14.2)]*. Patients received 1200 mg of TECENTRIQ (n=142) administered intravenously every 3 weeks until unacceptable toxicity or either radiographic or clinical progression or docetaxel (n=135) administered intravenously at 75 mg/m^2 every 3 weeks until unacceptable toxicity or disease progression. The median duration of exposure was 3.7 months (range: 0–19 months) in TECENTRIQ-treated patients and 2.1 months (range: 0–17 months) in docetaxel-treated patients.

The most common adverse reactions (≥ 20%) in patients receiving TECENTRIQ were fatigue (46%), decreased appetite (35%), dyspnea (32%), cough (30%), nausea (22%), musculoskeletal pain (22%), and constipation (20%). The most common Grade 3-4 adverse reactions (≥2%) were dyspnea, pneumonia, hypoxia, hyponatremia, fatigue, anemia, musculoskeletal pain, AST increase, ALT increase, dysphagia, and arthralgia.

Nine patients (6.3%) who were treated with TECENTRIQ experienced either pulmonary embolism (2), pneumonia (2), pneumothorax, ulcer hemorrhage, cachexia secondary to dysphagia, myocardial infarction, or large intestinal perforation which led to death. TECENTRIQ was discontinued due to adverse reactions in 4% (6/142) of patients. Adverse reactions leading to interruption of TECENTRIQ occurred in 24% of patients; the most common (>1%) were pneumonia, liver function test abnormality, upper respiratory tract infection, pneumonitis, acute kidney injury, hypoxia, hypothyroidism, dyspnea, anemia, and fatigue. Serious adverse reactions occurred in 37% of patients. The most frequent serious adverse reactions (> 2%) were pneumonia, dyspnea, pleural effusion, pyrexia, and venous thromboembolism.

Table 5 summarizes adverse reactions that occurred in at least 10% of TECENTRIQ-treated patients and at a higher incidence than in the docetaxel arm. Table 6 summarizes selected laboratory abnormalities worsening from baseline that occurred in ≥10% of TECENTRIQ-treated patients and at a higher incidence than in the docetaxel arm.

Table 5: Adverse Reactions Occurring in ≥10% of TECENTRIQ-Treated Patients with NSCLC and at a Higher Incidence than in the Docetaxel Arm (Between Arm Difference of ≥5% [All Grades] or ≥2% [Grades 3–4]) (Study 3)

	TECENTRIQ (n=142)		Docetaxel (n=135)	
Adverse Reaction	**All grades**	**Grade 3–4**	**All grades**	**Grade 3–4**
	Percentage (%) of Patients			
General Disorders				
Pyrexia	18	0	13	0
Infections				
Pneumonia	18	6	4	2
Metabolism and nutrition disorders				
Decreased appetite	35	1	22	0
Musculoskeletal and connective tissue disorders				
Arthralgia	16	2	9	2
Back pain	14	1	9	1
Psychiatric Disorders				
Insomnia	14	0	8	2
Respiratory, thoracic and mediastinal disorders				
Dyspnea	32	7	24	2
Cough	30	1	25	0

Table 6: Selected Laboratory Abnormalities Worsening from Baseline Occurring in ≥10% of TECENTRIQ-Treated Patients with NSCLC and at a Higher Incidence than in the Docetaxel Arm (Between Arm Difference of ≥5% [All Grades] or ≥2% [Grades 3–4]) (Study 3)

	Percentage of Patients with Worsening Laboratory Test from Baseline			
	TECENTRIQ		**Docetaxel**	
Test	All grades %	Grade 3–4 %	All grades %	Grade 3–4 %
Hyponatremia	48	13	28	8
Hypoalbuminemia	48	5	49	1
Alkaline Phosphatase increased	42	2	24	1
Aspartate aminotransferase increased	33	2	15	0
Alanine aminotransferase increased	31	2	9	1
Creatinine increased	19	1	14	2
Hypokalemia	18	2	11	4
Hypercalcemia	13	0	5	0
Total Bilirubin increased	11	0	5	1

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. Among 275 patients in Study 1, 114 patients (41.5%) tested positive for treatment-emergent (treatment-induced or treatment-enhanced) anti-therapeutic antibodies (ATA) at one or more post-dose time points. Among 135 patients in Study 3, 73 patients (54.1%) tested positive for treatment-emergent ATAs at one or more post-dose time points. Among 111 patients in Study 4, 53 patients (47.7%) tested positive for treatment-emergent ATAs at one or more post-dose time points. In Study 1, Study 3, and Study 4, the presence of ATAs did not appear to have a clinically significant impact on pharmacokinetics, safety or efficacy.

Immunogenicity assay results are highly dependent on several factors, including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medications and underlying disease. For these reasons, comparison of incidence of ATAs to TECENTRIQ with the incidence of antibodies to other products may be misleading.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. There are no available data on the use of TECENTRIQ in pregnant women. Animal studies have demonstrated that inhibition of the PD–L1/PD–1 pathway can lead to increased risk of immune-related rejection of the developing fetus resulting in fetal death *[see Data]*. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, advise the patient of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Animal reproduction studies have not been conducted with TECENTRIQ to evaluate its effect on reproduction and fetal development. A literature-based assessment of the effects on reproduction demonstrated that a central function of the PD–L1/PD–1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to a fetus. Blockage of PD–L1 signaling has been shown in murine models of pregnancy to disrupt tolerance to a fetus and to result in an increase in fetal loss; therefore, potential risks of administering TECENTRIQ during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the blockade of PD–L1/PD–1 signaling in the offspring of these animals; however, immune-mediated disorders occurred in PD–1 and PD–L1 knockout mice. Based on its mechanism of action, fetal exposure to atezolizumab may increase the risk of developing immune-mediated disorders or altering the normal immune response.

8.2 Lactation

Risk Summary

There is no information regarding the presence of atezolizumab in human milk, the effects on the breastfed infant, or the effects on milk production. As human IgG is excreted in human milk, the potential for absorption and harm to the infant is unknown. Because of the potential for serious adverse reactions in breastfed infants from TECENTRIQ, advise a lactating woman not to breastfeed during treatment and for at least 5 months after the last dose.

8.3 Females and Males of Reproductive Potential

Contraception

Females

Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment with TECENTRIQ and for at least 5 months following the last dose.

Infertility

Females

Based on animal studies, TECENTRIQ may impair fertility in females of reproductive potential while receiving treatment *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of TECENTRIQ have not been established in pediatric patients.

8.5 Geriatric Use

Of the 310 previously-treated patients with urothelial carcinoma treated with TECENTRIQ in Study 1, 59% were 65 years or older. Of the 142 patients with NSCLC treated with TECENTRIQ in Study 3, 39% were 65 years or older. No overall differences in safety or efficacy were observed between patients ≥ 65 years of age and younger patients.

Of the 119 cisplatin-ineligible patients with urothelial carcinoma treated with TECENTRIQ in Study 4, 83% were 65 years or older and 41% were 75 years or older. The overall response rate in patients 65 years or older was 23% (23/99) and in patients 75 years or older was 29% (14/49). Grade 3 or 4 adverse reactions occurred in 53% (52/99) of patients 65 years or older and 51% (25/49) of patients 75 years or older. No overall differences in safety or efficacy were observed between patients ≥ 75 years of age and younger patients.

8.6 Renal Impairment

Based on a population pharmacokinetic analysis, no dose adjustment of TECENTRIQ is recommended for patients with renal impairment *[see Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

Based on a population pharmacokinetic analysis, no dose adjustment of TECENTRIQ is recommended for patients with mild hepatic impairment. TECENTRIQ has not been studied in patients with moderate or severe hepatic impairment *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

There is no information on overdose with TECENTRIQ.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Inform patients of the risk of immune-related adverse reactions that may require corticosteroid treatment and interruption or discontinuation of TECENTRIQ, including:

- Pneumonitis: Advise patients to contact their healthcare provider immediately for any new or worsening cough, chest pain, or shortness of breath *[see Warnings and Precautions (5.1)]*.
- Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice, severe nausea or vomiting, pain on the right side of abdomen, lethargy, or easy bruising or bleeding *[see Warnings and Precautions (5.2)]*.
- Colitis: Advise patients to contact their healthcare provider immediately for diarrhea or severe abdominal pain *[see Warnings and Precautions (5.3)]*.
- Endocrinopathies: Advise patients to contact their healthcare provider immediately for signs or symptoms of hypophysitis, hyperthyroidism, hypothyroidism, adrenal insufficiency, or type 1 diabetes mellitus, including diabetic ketoacidosis *[see Warnings and Precautions (5.4)]*.
- Meningoencephalitis, Myasthenic syndrome/Myasthenia Gravis, and Guillain-Barré syndrome: Advise patients to contact their healthcare provider immediately for signs or symptoms of meningitis, myasthenic syndrome/myasthenia gravis, or Guillain-Barré syndrome *[see Warnings and Precautions (5.5)]*.
- Ocular Inflammatory Toxicity: Advise patients to contact their healthcare provider immediately for signs or symptoms of ocular inflammatory toxicity *[see Warnings and Precautions (5.5)]*.
- Pancreatitis: Advise patients to contact their healthcare provider immediately for signs and symptoms of pancreatitis *[see Warnings and Precautions (5.5)]*.
- Infection: Advise patients to contact their healthcare provider immediately for signs or symptoms of infection *[see Warnings and Precautions (5.6)]*.
- Infusion-Related Reactions: Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion-related reactions *[see Warnings and Precautions (5.7)]*.
- Rash: Advise patients to contact their healthcare provider immediately for signs or symptoms of rash *[see Dosage and Administration (2.2)]*.

Embryo-Fetal Toxicity

Advise female patients that TECENTRIQ can cause fetal harm. Instruct females of reproductive potential to use effective contraception during treatment and for at least 5 months after the last dose of TECENTRIQ *[see Use in Specific Populations (8.1, 8.3)]*.

Lactation

Advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months after the last dose *[see Use in Specific Populations (8.2)]*.

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SHOCK WAVES

continued from page 1

versity School of Medicine, Baltimore. "But it would be good to study it enough to make sure we're providing good care to patients."

Beyond addressing symptoms

ED is extremely prevalent, according to Irwin Goldstein, MD, director of San Diego Sexual Medicine and director of sexual medicine at Alvarado Hospital in San Diego.

"It's ridiculously and horribly bothersome and distressing. It affects mood. It affects ego. It's frustrating to the partner, and the man feels not a man anymore," he said.

"It's almost curative. [If approved,] we can offer something that can heal the penis and maybe allow natural responses."

ARTHUR L. BURNETT, MD, MBA

While ED causes vary, a common cause, and the focus for shock wave therapy, is when the erectile tissue becomes so scarred that during the process of muscle relaxation, the subtunical space can't close because the tissue is no longer expandable.

"The erectile tissue can't expand against the tunica, thereby closing down the subtunical space, thereby compressing the subtunical venules," Dr. Goldstein said. "Then, during an erection, blood will leave, like air does when there's a nail in a tire."

Symptomatic treatment with phosphodiesterase type-5 (PDE-5) inhibitors has long been the first-line treatment among urologists and other providers since their launch in the late 1990s. If oral agents aren't successful, men have the options of prostaglandin E1 injection therapy, a vacuum erection device, intraurethral suppository treatment, or a penile implant.

Symptomatic treatment often works, but medication leaves a big ED treatment void: disease modification. That's important, Dr. Goldstein says, because pharmacologic treatments can stop working with age, and many men don't want to take medications for the rest of their sexual lives.

"We need ways to get rid of the scar tissue and return muscle back to the patient," Dr. Goldstein said.

It's time physicians recognize that while PDE-5 inhibitors remain a treatment for ED, the medications don't enable a man to be natural and functional with natural erectile ability, according to Dr. Burnett.

"I think [shock wave therapy] does address that. It's almost curative. [If approved,] we can offer something that can heal the penis and maybe allow natural responses," Dr. Burnett said.

Three options on the table

Low-intensity shock wave therapy is currently one of three experimental disease modification strategies to help restore erectile tissue health. The other two are stem cell infusion and the use of platelet-rich plasma (PRP).

Dr. Goldstein said his site will begin recruiting in December for a trial looking at use of stem cells for erectile dysfunction. The treatment, which uses mesenchymal stem cells, requires liposuction to obtain needed fat cells and a trip to the operating room for the stem cell infusion. PRP, he said, is widely used in sports medicine and orthopedics. The problem is, the therapy is largely uncontrolled in the U.S.

"It's the Wild West. But that shouldn't distract from the fact that PRP is a fabulous material. It should be undergoing FDA trials with a robust placebo arm, but it isn't," Dr. Goldstein said.

Enter shock wave therapy

The movement to make shock wave therapy a credible and widespread ED option is well on its way.

In a systematic review and meta-analysis published in 2017, Dr. Ramasamy and colleagues analyzed the use of low-intensity extracorporeal shock wave therapy in seven randomized controlled trials, with a total of 602 patients. They found among men with an average age of 60.7 years and an average follow-up of 19.8 weeks, International Index of Erectile Function score significantly improved an average 6.40 points from baseline in men receiving shock wave treatment, compared to an average 1.65 points in those receiving sham therapy (*J Sex Med* 2017; 14:27-35).

"Some [responses] are more dramatic than others. But every man has improvement in the quality of their erections."

BRUCE SLOANE, MD

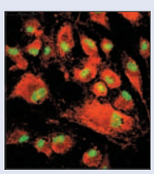
Devices are being studied in clinical trials, and shock wave therapy to treat ED is already being marketed. Aventura, FL-based Sexual MD Solutions markets the GAINSWave therapy brand to enhance sexual performance and optimize erection quality through a network of more than 100 trained providers. According to the company, certified GAINSWave providers must follow specific protocols and are required to use a medical device that is FDA cleared for other indications, including localized improvement of blood flow.

Bruce Sloane, MD, a urologist in private practice in Philadelphia, whose solo practice focuses on men's health, offers the GAINSWave procedure and said it has shown good results in treating ED.

"I've had some men in their 30s who are diabetic and men in their 80s. Some [responses] are more dramatic than others. But every man has improvement in the quality of their erections," said Dr. Sloane, who had treated about 50 patients when interviewed by *Urology Times*. "I have a couple men with severe erectile dysfunction who were only getting erections after penile injection therapy. I treated them with 12 sessions of the

Please see **SHOCK WAVES,** on page 18

EXPERIMENTAL DISEASE MODIFICATION STRATEGIES FOR ED



STEM CELL INFUSION: Studies using mesenchymal stem cells are aimed at finding an ED cure. One avenue of research involves obtaining adipose-derived stem cells via liposuction.

PLATELET-RICH PLASMA: Widely used in sports medicine and orthopedics, it is largely uncontrolled in the U.S. Placebo-controlled FDA trials are needed.

LOW-INTENSITY SHOCK WAVE THERAPY: One theory posits that shock waves create injury, creating new blood vessels to help treat vasculogenic ED; a second theory is that shock wave therapy improves ED by recruiting stem cells. Early U.S. results are promising.

Images: Vshivkova; Romaset/Shutterstock.com

SHOCK WAVES

continued from page 17

GAINSWave therapy, and they now only have to use medication. They're off the injections."

How does it work?

There are two theories about how shock waves work to treat ED, according to Dr. Ramasamy. One relates to neo-angiogenesis at penile tissue; the shock waves create injury and, therefore, create new blood vessels that will help treat vasculogenic erectile dysfunction. The second theory is that shock wave therapy improves ED by recruiting stem cells, which helps with growth of new corporal and penile tissue.

Dr. Goldstein said he thinks low-intensity shock wave therapy works by activating stem cells.

"The shock wave provides an energy to the stem cells, and the stem cells get activated and grow—growing muscle, blood vessels," said Dr. Goldstein, whose practice is among the U.S. sites conducting a placebo-controlled trial on use of low-intensity shock wave therapy for ED with the Dornier device.

Finding that ideal protocol

Just how to use it for ED—how many shocks to deliver, how often, and for how long—remains largely unanswered. Urologists and others in the U.S. need data to make low-intensity shock wave therapy clinically useful and safe, Dr. Goldstein said.

Without clear protocols, the danger exists that the therapy might not be as effective or effective at all, according to Dr. Burnett.

"You still want to be credible. You want to offer therapy that patients feel good about spending their resources and money to obtain," Dr. Burnett said.

At the moment, there is no single gold-standard protocol.

In a recently published meta-analysis looking at low-intensity extracorporeal shock wave therapy for ED, Chinese researchers analyzed nine studies, including 637 patients, from 2005 to 2017. They found that low-energy extracorporeal shock wave therapy could significantly improve patients' International Index of Erectile Function and Erection Hardness Score, and therapeutic efficacy could last at least 3 months (*Urology* Sept. 26, 2017 [Epub ahead of print]). They also reported that lower energy density, at an average 0.09 mj/mm^2; 3,000 pulses per treatment; and total treatment courses of less than 6 weeks resulted in better therapeutic efficacy.

The number of treatments needed varies, according to Dr. Sloane, who said the basic GAINSWave protocol is six or 12 treatments, depending on ED severity.

"Men who have not tried Cialis and Viagra respond very well, and men who have tried and failed Cialis and Viagra, who have received shock waves, appear to go back to respond to PDE-5 inhibitors."

RANJITH RAMASAMY, MD

"The shock wave treatment is about 30 minutes and completely pain free."

IRWIN GOLDSTEIN, MD

"If a man needs six treatments, we'll do two a week for 3 weeks. And the treatments are about 15 minutes each," Dr. Sloane said.

Dr. Ramasamy, who has been part of a clinical trial using shock wave therapy with DirexGroup's FDA-cleared MoreNova device, said men in the study are receiving a total of 1,800 shocks.

"It's a randomized trial with two arms. It's either every other day, for a total of six sessions, or every day, for a total of five sessions. The total number of shocks delivered is basically the same in both arms, and treatments last about 10 minutes each. Then, we follow patients at 1 month, 3 months, and 6 months," he said.

In preliminary data, Dr. Ramasamy said men who receive the everyday treatment appear to respond better than those receiving the every-other-day treatment.

"Men would be able to have sex as early as the following week [after treatment]," he said.

Dr. Ramasamy and colleagues have recruited 44 patients so far and will recruit a total of 80.

Dr. Goldstein said his study's protocol is to administer low-intensity shock wave therapy once a week for 6 weeks. He tells patients they can have sex the same day or night as treatment.

"The shock wave treatment is about 30 minutes and completely pain free," Dr. Goldstein said.

As for the need for maintenance treatments, that's not clear, according to Dr. Ramasamy.

"No one truly understands how long the effect of these shock waves lasts and what the long-term effect is. Right now, we have very good data at 3 months and very few patients at 6 months," Dr. Ramasamy said.

Shock wave therapy appears to be safe.

"Patients tolerate it very well," Dr. Ramasamy said. "There's minimal pain. Sometimes, subjects have redness on the skin. But at the doses that we're using there is very minimal change that happens to the penis, itself."

Ideal candidates

Low-intensity shock wave therapy for ED appears to be most suited for men who have mild erectile dysfunction and who are either responsive or nonresponsive to PDE-5 inhibitors, according to Dr. Ramasamy.

"Men who have not tried Cialis and Viagra respond very well, and men who have tried and failed Cialis and Viagra, who have received shock waves, appear to go back to respond to PDE-5 inhibitors," he said. "I don't think it's appropriate for the man with severe diabetes, severe venous insufficiency, or men who have had previous pelvic surgeries, such as radical prostatectomy or radical cystectomy."

Dr. Goldstein said he agrees that it's doubtful shock wave therapy will rescue men in the severe group.

"But, if we follow this over time, we might allow people to never become severe," Dr. Goldstein said.

The next big advance in ED treatment?

If the FDA approves shock wave therapy for ED, Dr. Goldstein said he thinks all urology practices will offer the treatment.

Using the device and performing the treatment requires little in the way of a skill set. Nurses can deliver the treatment. But everyone in the room needs to wear heavy-duty ear protection because the sound from the device can be loud and physically damaging, especially to those administering low-intensity shock wave therapy, Dr. Goldstein said.

The only disposable required to use the technology is ultrasound gel, which when rubbed on the penis helps to transmit the shock waves, according to Dr. Sloane.

"The point is, this will become a pretty widespread treatment of aging men. Most people will have pretty good erectile function until age 40, 45, 50. Then, after age 40 or 45, you have a direct falling," Dr. Goldstein said. "So if you can change the slope a tiny bit, make it less steep with just getting your penis shocked, would you do that? When this comes out and it's shown to be efficacious, I will be one of the people getting shock wave therapy."

Dr. Burnett is an investigator for Medispec. Dr. Ramasamy is an investigator for Direx. Dr. Goldstein is a consultant to and researcher for Dornier; researcher for Tissue Genesis; a member of the speakers' bureau for Coloplast, Dornier, and Mist Pharmaceuticals; and provides writing support for Pfizer. UT

Speak Out

What one thing about MOC would you change if you could?

"The thing I found really onerous was the data collection. They have you create an Excel spreadsheet of every last thing you do over 6 months: every surgery, every office visit, every urinalysis, every ultrasound done in the office, every injection, and code for it, etc.

They say, 'Just transfer it from your EMR—put it right here, boom!' We weren't able to do that. I have electronic medical records, but they didn't sync up, and a lot of the doctors who have been practicing as long as I have are still on paper.

It gave them information about my practice pattern, but I really think it was just data collection for them. Why in the world would they need to know every urinalysis I do?

The examination, the studying up, and reviewing everything—I think that's good. I didn't like it, but I think it accomplished its purpose. It brushed me up nicely and I feel better for it. So even though I didn't enjoy it and it took a lot of time, I think it's a reasonable thing to do."

Frederick Snoy, MD
Albuquerque, NM

"I just recertified in the past year. There is a lot of pressure and a lot of weight placed on the examinations. A lot of it isn't necessarily applicable to what we do every day in the office.

Even though I don't see pediatric urology patients, I have to take an exam that has pediatric urology questions. I have seen suggestions that they are looking at perhaps trying to tailor the test more specifically to people's practices. If you don't see peds, perhaps that won't be a part of your exam. That would make a lot of sense.


Dr. Rubens

I did prepare, and it took a lot of time. I took a University of Chicago course on CDs. I think there were 50 CDs I would listen to while I was driving.

I know the role is to try to keep us up to date on our learning and our ability to continue to practice safe medicine and to keep up with the times. It would be nice, however, if there wasn't really a big exam that had a whole lot of weight associated with it."

Brandon Rubens, MD
Cary, NC

"I think they are already in the process of making this change, but the frequency in which we have to do things is cumbersome. Every 2 years, you have to go online at the American Board of Urology website and enter some patient information or answer questions about the way you practice. Every 2 years, you have to do some sort of module. It doesn't take long, but you usually have to do something in June and repeat the process in October.


Dr. Stefaniak

It's not anything important to how we practice. They pick a topic, such as erectile dysfunction, and you're supposed to pull charts to review how you handled that topic—like, did you ask the patient x, y, and z? Did you do this? Did you do that? They'll want you to pull five patient charts on that diagnosis, and I don't know that people are actually pulling more than one or two. It's basically busy work that's not helpful; it's a hoop you have to jump through just to say you did it. Every 2 years is a little bit much. At a recent recertification course, they said that would probably change to every 4 years soon. That would be helpful."

Heather Stefaniak, MD
Green Bay, WI

ABU: Life-long learning will be relevant, less burdensome

The American Board of Urology (ABU) recognizes that after initial certification, many diplomates find the maintenance of certification (MOC) program to be onerous, burdensome, and not relevant to their practice. The trustees, chair of MOC (Michael Ritchey, MD), and executive secretary of the ABU (Gerald Jordan, MD) have carefully evaluated the MOC process, have listened to diplomates' concerns, and have instituted what we are referring to as a life-long learning (LLL) program rather than MOC. More detail on the history of MOC and the ABU evolution of an LLL program is available on the ABU website *(www.abu.org)*.


Dr. Carter

The ABU believes that urologists strive to keep abreast of our rapidly changing field after initial certification. The LLL program is designed to help diplomates achieve that goal by assessing their performance as their practice changes over time. The ABU views the LLL program as a partnership with diplomates to assist them in identifying potential areas of weakness and to then provide them with the feedback to remediate those areas.

Last year we made the decision to revert to a modular examination, recognizing that many urologists "self" specialize as their practice evolves after training. The current examination will consist of a core general urology module required by all (40 questions), and one of four modules (35 questions) in a specific area of practice (oncology, andrology, female urology/voiding dysfunction, calculi/obstruction/laparoscopy). A large percentage of questions come from the AUA self-assessment study program exam and are based on AUA guidelines.

An additional change is in the method of scoring that in the past could result in "failure." The ABU believes that an LLL program consists of many components and is more than a single examination. Beginning this year, the ABU will use the knowledge assessment exam given in October to identify those diplomates who have knowledge gaps and direct them to focused CME in areas that need attention. The ABU is able to make this change because of multiple sources of information provided by our diplomates, including submission of billing logs.

Although billing logs are time consuming for all involved, they provide insight into diplomates' practice and assessment of their practice standards. These will now be used to verify that diplomates are taking the modular exam that best fits their practice, allowing an improved assessment of their required knowledge base. In addition, the practice logs allow the trustees to be certain that diplomates have a sufficient case load to maintain their skills.

Most importantly, we have the opportunity to provide feedback to the diplomate. In the very near future, the ABU will launch a web portal individualized for the diplomate, informing them of where they stand in the LLL process and easing the process of log submission.

Another major change will be the frequency of assessments during a 10-year cycle. In the past, we have required completion of some element of the process every 2 years. In the near future, this will change to a total of two assessments over a decade. These assessments will occur at years 4 and 7-9, and will decrease the time required to participate in LLL.

These changes require continuous learning on the part of those who practice and continuous evolution of the process for assessing the knowledge, judgment, and skills of the practicing physician. The ABU is committed to an LLL program that diplomates find relevant and less burdensome. We will always welcome diplomates' feedback on this evolving program.

H. Ballentine Carter, MD
President, American Board of Urology

How to get reimbursed for BPH water vapor ablation

Until introduction of new code in 2019, follow one of two coding pathways for payment

Coding Q&A

Ray Painter, MD, Mark Painter

Urologist **Ray Painter, MD**, is president of Physician Reimbursement Systems, Inc., in Denver and is also publisher of *Urology Coding and Reimbursement Sourcebook*. **Mark Painter** is CEO of PRS Urology SC in Denver.

Q How do I code for convective water vapor ablation for lower urinary tract symptoms/BPH (Rezūm System)?

A Up front, we must disclose that Physician Reimbursement Services has contracted with NxThera to provide support for offices that have billed for Rezūm. In this article, we will provide the basics as we know them at this point.

Until recently, you could find an article published by the AUA Coding and Reimbursement Committee recommending the use of CPT Code 53852 (Transurethral destruction of prostate tissue; by radiofrequency thermotherapy) online. That article was removed from the AUA website in August. A search of *www.auanet.org* for Rezūm at the time this article was written did not return any information. However, there is an archival post on the AUA website referencing Rezūm *(bit.ly/Rezumclearance)*.

The recently published public transcript from the September meeting of the CPT Editorial Panel was released officially on Oct. 13, 2017 and can be found at *bit.ly/CPTpanelsummary*. Item 21 on this report indicates that the panel decided to "add a code 538X3 to report water vapor or steam thermotherapy for destruction of prostate tissue." Once released for use Jan. 1, 2019, this will become the correct way to report Rezūm.

How to report Rezūm prior to Jan. 1, 2019 will likely be a topic of discussion, with different answers depending upon the payer. In the end, coverage and payment of this procedure will depend upon review of the clinical evidence by payers that is presented by urologists and patients that feel the procedure is the best clinical pathway to treat a patient's BPH.

At this point, we see two possible coding pathways:

- Continue to report code 53852 (Transurethral destruction of prostate tissue; by radiofrequency thermotherapy).
- Report Rezūm with unlisted code 53899 (Unlisted procedure, urinary system insert "Rezūm Transurethral destruction of prostate tissue; by radiofrequency thermotherapy" or "Rezūm water vapor or steam thermotherapy for destruction of prostate tissue") in box 19 of the claim form to assure prompt payment.

You will need to consult your payer prior to providing this service to determine the correct approach for the payer and to make sure the service is covered. Consulting a payer should consist of reviewing current posted coverage policies and following instructions provided. If the coverage is unclear or there is no information posted, we recommend calling the payer for coverage and payment requirements.

Other points to consider:

- Payers may continue to request the use of code 53852 for ease of adjudication, or a payer may develop an edit on the unlisted code that allows processing of the service with the unlisted code without review of each claim.
- Payers may also choose to require the unlisted code and require a review of each case submitted.
- Payers may choose to consider Rezūm as a non-covered service, allowing the practice to bill the patient directly for the service under the practice's current fee schedule rate.
- If the payer does *not* provide any instructions or information on current coverage and/or proper reporting of Rezūm, it is left to the practice to choose to continue to report code 53852 unless the AUA or the American Medical Association publishes a coding recommendation indicating otherwise, or to use 53899 as noted above.

You will need to consult your payer prior to providing this service to determine the correct approach.

Note: For payers that do not provide information on coverage or payment, remember that you will need to follow contractual instructions if contracted with the payer, which may or may not allow for collection of payment from the patient prior to claim adjudication, and likely will require appeal or submission of supporting materials for proper claim adjudication. For those payers with whom you are not contracted, collection from the patient is allowed; however, practice processes used for other services should be followed. UT

Send coding and reimbursement questions to Ray Painter, MD, and Mark Painter c/o *Urology Times*, at UT@advanstar.com.

Questions of general interest will be chosen for publication. The information in this column is designed to be authoritative, and every effort has been made to ensure its accuracy at the time it was written. However, readers are encouraged to check with their individual carrier or private payers for updates and to confirm that this information conforms to their specific rules.

Business of Urology

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1. Hamstra, DA et al. Sexual Quality of Life Following Prostate Intensity Modulated Radiotherapy (IMRT) with a Rectal/Prostate Spacer: Secondary Analysis of a Phase III Trial. Practical Radiation Oncology, doi: 10.1016/j.prro.2017.07.008. Published online: July 19, 2017. 67% SpaceOAR vs. 38% Control (p=0.049)
2. Hamstra, DA et al. Continued Benefit to Rectal Separation for Prostate Radiation Therapy: Final Results of a Phase III Trial. Int J Radiat Oncol Biol Phys. 2017 Apr 1;97(5):976-985.

How to choose between Roth, traditional accounts

Traditional plans often best when your tax bracket is projected to be lower in retirement

Money Matters

Jeff Witz, CFP,
David Zemon

Jeff Witz, CFP, (top) is educational program director and **David Zemon** is a wealth manager at MEDIQUS Asset Advisors, Inc. in Chicago. They can be reached at 800-883-8555 or witz@mediqus.com or zemon@mediqus.com.

Q What is the difference between a traditional and Roth account? Are there advantages to using one versus the other?

A Saving for retirement is important, and there are plenty of account options available to assist in this goal. Traditional and Roth individual retirement accounts as well as traditional and Roth 401(k)s are among the more commonly used retirement savings vehicles. However, due to IRS income phase-out limits, many physicians are not eligible to contribute to a Roth IRA and cannot take advantage of the tax benefits associated with contributing to a traditional IRA.

Viable alternatives for physicians are traditional and Roth 401(k) and 403(b) plans. These accounts are often available to physicians through their employers and are not subject to the same income limits.

Unbeknownst to many investors, 401(k)s and 403(b)s are nearly identical retirement savings vehicles. Both have the same contribution limits and the same tax-deferred or tax-free benefits. The primary difference is that a 401(k) plan is only offered through a for-profit company whereas a 403(b) plan is offered through a non-profit organization.

Financial Tips

- Due to IRS income phase-out limits, many physicians are not eligible to contribute to a Roth IRA and cannot take advantage of the tax benefits associated with contributing to a traditional IRA; viable alternatives are traditional and Roth 401(k) and 403(b) plans.
- 401(k)s and 403(b)s are nearly identical retirement savings vehicles; the primary difference is that a 401(k) plan is only offered through a for-profit company whereas a 403(b) plan is offered through a non-profit organization.
- If you expect to be in a lower tax bracket in retirement than you are now, contributing to a traditional plan may be the best option.
- As a general rule, when smaller-sized mutual funds gain in popularity due to stellar performance, they also gain in asset size.

The mechanics of traditional 401(k) and 403(b) plans are fairly straightforward. You can usually make a pre-tax contribution of up to $18,000 each year ($24,000 if you are over age 50), and your employer may contribute additional money through either a fixed percentage or a match. Contributions are typically invested in mutual funds and/or exchange-traded funds, and grow tax-deferred (meaning you do not pay capital gains tax on any sales made that generate a gain). Once you reach age 59½, you can take qualified distributions from the account. But since contributions were made pre-tax, you must pay ordinary income tax on any amount withdrawn from the plan.

Roth 401(k)s and 403(b)s work in similar fashion to traditional plans; however, instead of contributing pre-tax dollars, you contribute post-tax dollars.

There are no income limits that prohibit contributing to these plans, nor are there income limits that reduce the tax benefits. However, be aware that for high-income individuals earning over $270,000 per year, the maximum amount your employer can contribute is limited.

Roth 401(k)s and 403(b)s work in similar fashion to traditional plans; however, instead of contributing pre-tax dollars, you contribute post-tax dollars. This means federal and state taxes have already been withheld. Since you have already paid taxes on the contribution side, the funds grow tax-free, and withdrawals made during retirement are tax-free as well.

There are some nuances to consider, however. First, the matching employer contributions must still be made in a traditional 401(k), not a Roth 401(k). You will still owe tax on withdrawals of amounts contributed by the employer into the traditional 401(k). There are no income limits impacting eligibility to contribute to a Roth 401(k) or 403(b), but as with traditional plans, there may be a limit on how much your employer is allowed to contribute.

Whether to use a traditional or Roth account is not always an easy decision since it essentially requires you to predict the future. As a general rule of thumb, if you expect to be in a lower tax bracket in retirement than you are now, contributing to a traditional plan may be the best option. This is a common scenario for physicians. However, if you own or plan to own businesses or properties that will continue to generate income in retirement equal to or greater than you are earning now, contributing to a Roth 401(k) or 403(b) account makes sense.

Q Should the size of a mutual fund be a factor in deciding whether to invest?

A Mutual funds range in size from tens of millions of dollars to hundreds of billions of dollars. As a fund grows, the list of companies that it invests in also tends to grow. This can be an advantage since it creates greater stock diversification, which may reduce price fluctuations within the fund. Remember that all funds start out small in size. A new fund has the ability to build a portfolio that reflects the manager's view of attractive investments. A new, smaller fund is not burdened by tax issues related to previously held investments.

Some funds like being small and don't want to become large. To preserve this perceived investing advantage, some funds actually close to new investors once they attain a certain size. As a general rule, when smaller-sized mutual funds gain in popularity due to stellar performance, they also gain in asset size. The unknown variable is how that fund will manage its growth. UT

Send us your questions

Send your questions about estate planning, retirement, and investing to Jeff Witz, CFP, c/o *Urology Times*, at UT@advanstar.com.

Questions of general interest will be chosen for publication. The information in this column is designed to be authoritative. The publisher is not engaged in rendering legal, investment, or tax advice.

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Are you taking steps to prevent data breaches?

Training staff to recognize phishing attacks is one step you can take now

In 2015, I wrote a series of articles outlining privacy and security concerns for urologists in light of emerging evidence that health care organizations were being targeted for sensitive data *(www.modernmedicine.com/tag/protecting-patient-data).* Since then, the problem has continued if not worsened, and urologists need to be ever more vigilant to protect the private information under their custodianship. In this article, I will review some recent developments in this area and some steps that urologists can take to minimize their risk.

Breaches on the rise

The public's attention was recently turned to breaches of private and sensitive information when the large credit bureau Equifax disclosed the exposure of private information on over 140 million Americans that may have been due to the actions of a single individual. According to the Identity Theft Resource Center *(bit.ly/USbreaches),* the number of reported data breaches tracked in the U.S. is on track for an all-time high in 2017 and an increase of 29% over 2016. One-third of those breaches in 2016 involved health/medical organizations, second only to the general business category, the center reports. Hacking is the leading cause of breach (63%) and has more than doubled as a percent of breaches since 2014 *(bit.ly/Breachcause).* This continued rise in activity could be due to hacking becoming easier, or to an increased awareness on the part of health care organizations of their responsibility to report, according to some industry experts *(bit.ly/Healthbreaches).*

A data breach could literally bankrupt a small medical practice. Like medicine, IT is highly specialized, and your IT employee or partner should understand the risks and prevention strategies specific to your business and your specialty.

The U.S. Department of Health and Human Services Office for Civil Rights (OCR), as required by the HITECH Act, publishes breaches of unsecured protected health information affecting 500 or more individuals on its portal/website *(bit.ly/Breachlist).* This author's analysis of the incident data contained therein (health care-related breaches) reveals the following information related to data through September 2017 (annualized):

- The most common type of covered entity reporting a breach is health care provider (80.1%). This category includes physician and hospital organizations, and is increasing as a percent of entities reporting a breach. Health plans (13.7%) and business associates (5.7%) were the next largest types.
- Hacking/IT incidents were identified as the most common type of breach (43.0%) followed by unauthorized access/disclosure (34.5%), theft (15.7%), and loss (4.3%).
- Somewhat surprising: The electronic medical record was only identified as the source of the breached information in 6.6% of cases, a fraction that has remained steady in the last 3 years. The most common location of breached information was email (23.6%), followed by a network server (21.7%), paper/film (14.0%), other portable device (4.6%), laptop (4.3%), and desktop computer (2.6%).

There are 12 organizations that can easily be identified as urology entities from the name of the covered entity in the HHS/OCR data (less than 1% of health care provider entities) since 2009. This includes one organization reporting a hacking incident involving a network server and 300,000 individuals in 2016, and four separate reports in 2017 (all unresolved at this writing) involving 300,036 individuals; two of those incidents also involved hacking a network server, and one was an unauthorized disclosure via email (939 individuals).

What are the consequences of suffering a data breach in your organization? Assuming you self-report as required by law, you may look forward to an investigation by the OCR that could result in civil monetary penalties, a corrective action plan, a resolution agreement, or even resolution without further action. The civil monetary penalties associated with a confirmed breach are significant and stipulated in law *(bit.ly/Breachlaw).* There are other potential costs: legal fees, damage to reputation, credit monitoring, and even civil litigation *(bit.ly/Cybersecurityhealthcare).* A breach could literally bankrupt a small medical practice.

What you can do

What lessons can urologists learn and apply from this information and these statistics? This is a very real risk to any organization, and as with any risk mitigation strategy, there are some general principles to follow:

Know the law, the rules, and the consequences. If you are a small organization, you should have access to an attorney with contemporary knowledge of this subject matter.

Engage an IT professional with experience in health care information technology. Like medicine, IT is highly specialized, and your employee or partner should understand the risks and prevention strategies specific to your business and your specialty. For example, is your urodynamic machine secure? This is a small example of specialty-specific issues that need to be considered.

Hold your vendors responsible for their contribution to your risk. Be certain that you have business associate agreements in place and reviewed regularly—this alone can constitute a violation.

Review common areas of vulnerability. The data reveal that most of the breaches originate in email. Have you formally trained your staff how to recognize a phishing attack? Do they know what procedures to follow to send pro-

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Practice Pointers

- According to the Identity Theft Resource Center, 33% of U.S. data breaches in 2016 involved health/medical organizations, second only to the general business category.
- Data from the Health and Human Services Office for Civil Rights (OCR) indicate that hacking/IT incidents were the most common type of breach over the reporting period.
- If your practice suffers a data breach, consequences (assuming you self-report as required by law) may include an investigation by the OCR that could result in civil monetary penalties, a corrective action plan, a resolution agreement, or resolution without further action.
- One way to mitigate risk of a data breach is to consider insuring for matters out of your control.

The Bottom Line

Robert A. Dowling, MD

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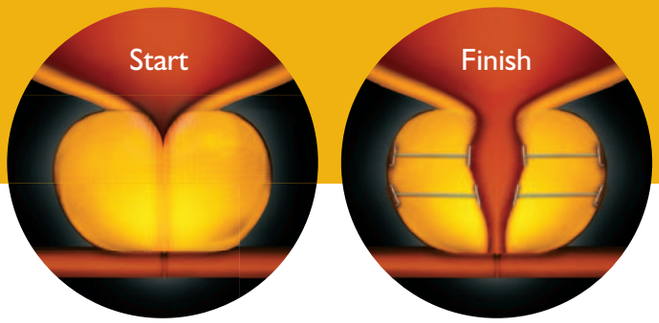

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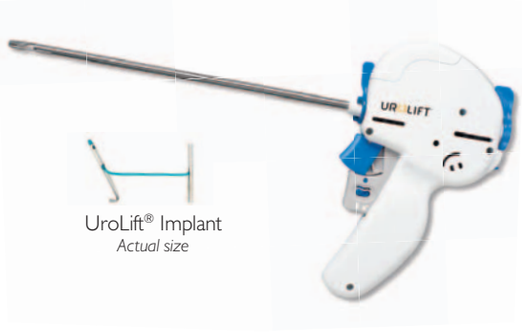

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1. Shore, Can J Urol 2014
2. Sonksen, Eur Urol 2015
3. AUA BPH Guidelines 2003
4. Roehrborn, J Urology 2013
5. McVary, J Sex Med 2014
6. CG Roehrborn, Can J Urol 2017

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If disaster strikes, is your practice prepared?

Business recovery insurance, 'recovery box' for valuables are key preventive tools

Practice Management

Lisette Hilton

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Hurricanes and wildfires may have claimed recent headlines, but natural and other disasters that can devastate physicians' practices, hospitals, and entire regions take many forms—from blizzards, earthquakes, floods, and fires, to terrorist attacks, explosions, epidemics, and data breaches.

In essence, no one (and no practice) is immune.

A month after Hurricane Harvey's aftermath, Houston-based urologist Steven Canfield, MD, says his practice is still having to reschedule operating room times to help out with the hurricane-induced OR shortage.

Dr. Canfield, chief of urology at Memorial Hermann-Texas Medical Center in Houston, says Houston medical centers and medical schools had learned their lessons about hurricane preparedness after severe flooding from Tropical Storm Allison in 2001. Texas Medical Center, for example, has since installed a flood gate network, above-ground electrical vaults and generators, and water pump systems to protect its infrastructure.

But while the preparation and timely implementation of storm surge protections kept the University of Texas (UT) Health Science Center and Texas Medical Center from severe flooding, Harris Health System's two flagship hospitals and community practices in Houston were impacted. As a result, so were affiliated physicians and patients, says Dr. Canfield.

"Ben Taub Hospital flooded," Dr. Canfield said. "LBJ General Hospital, where the UT Medical School provides coverage and where I also practice, didn't flood but sustained storm damage—to the point that a number of ORs have been shut down since, and about 100 inpatient rooms have been affected, leading to a mandatory cancellation of elective surgeries requiring postoperative admission."

Flooding near downtown Houston following Hurricane Harvey. About 100 inpatient rooms in Harris Health System were affected, said Houston urologist Steven Canfield, MD. (Image: IrinaK/Shutterstock.com)

Patient triage addresses critical cases

Dr. Canfield and colleagues have tried to triage cases, so that more critical cancer and other urgent patients are taken care of before patients scheduled for elective surgeries and less urgent cases.

"Some of those smaller cases, unfortunately, include patients with chronic kidney stones for example, who certainly are suffering but would not be as critical as a cancer patient," Dr. Canfield said.

Hurricane Irma, which battered South Florida Sept. 10, took its toll on physicians and patients at the University of Miami Health System, including Sylvester Comprehensive Cancer Center in Miami, according to Chad Ritch, MD, a urologist on staff there.

Staff prepared in the week leading up to the storm by trying to make sure that the sickest patients were stabilized and those who could be discharged were sent home or to other facilities, to avoid a critical mass in the hospital during and after the storm, according to Dr. Ritch.

"In our clinics, we had to reschedule a lot of patients who were coming in for procedures while making sure to see the more critical patients before the clinic shut down," he said.

The health system and clinics shut down Thursday and Friday before the storm, and remained closed Monday and Tuesday after.

"Post-storm, we were set up to have an emergency response team, from each department, in the hospital. So from urology, we had a doctor on call who stayed in the hospital, as well as a resident because we're a teaching facility," Dr. Ritch said. "Our team A were the people who stayed in the hospital from the morning of the hurricane to the day after, 7 a.m. to 7 a.m. Then, post-storm, we had our B-team, so to speak, who came in the following day after the storm. Then, of course, we had backups in case people were trapped and couldn't get out from where they were."

Dr. Ritch said he learned the importance of being able to prioritize which patients needed to be rescheduled urgently and figuring out which cases could be canceled or rescheduled.

"A lot of it had to do with informing patients and letting them know the plan, so they didn't feel like they were left in the dark," he said.

A New Orleans-based urologist in private practice on Aug. 29, 2005 when Hurricane Katrina hit, Neil Baum, MD, was shut down for 12 weeks because of the natural disaster. Dr. Baum said he was on top of the world before the category 3 hurricane hit New Orleans, and, basically, unable to work at his practice in the days, weeks, and months after.

Dr. Baum, who today is professor of clinical urology at Tulane University School of Medi-

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tected health information via email? Paper/film is another area of risk. Do you have shredding practices firmly in place? Is there an opportunity to stop printing on paper altogether for certain functions? Is that fax machine printing instead of sending directly to a file folder? Do your physicians still insist on "printing the last progress note"?

Consider insuring for matters out of your control. The cyber insurance industry is in its infancy *(bit.ly/Cyberinsurance),* and the benefit/cost ratio is still being established. Your business insurance policy may include limited coverage for costs associated with a data breach, and you should understand what remaining risks exist.

Have a data backup plan in place and practice restoring it. This is not a simple matter, but it is an important strategy in the event of loss or loss of access (ransomware, for example).

Bottom line: Health care organizations are increasingly at risk for hacking attacks and breaches of sensitive information. Practicing in the modern era involves recognizing these risks, an active strategy of prevention and preparedness, and partnership with expert professionals in law and health information technology. UT

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cine, said he was so distraught about Katrina's devastation that he wrote a book to help others, "Disaster Planning for the Clinical Practice."

Because of a mandatory evacuation, Dr. Baum couldn't go back to his practice until November that year. He returned to a sixth-floor office with spotty elevator service, scarce drinkable water, and no air conditioning—conditions that made it challenging for patients to get to the practice and for Dr. Baum to deliver care.

"Fortunately, I had electronic medical records. Patients [had evacuated] far and wide across the country, and I was able to contact other physicians in other parts of the country to help take care of my patients," Dr. Baum said.

Colleagues without electronic health records, he recalls, told him their records had turned to paste from water damage.

How to prepare for the next disaster

Urologists must prepare for disasters by having disaster plans in place and reviewing those plans at least annually, according to Dr. Baum.

"Disaster planning should not take place in a vacuum. To work effectively, it must be integrated into the practice routine and operating procedures," he said.

These are key disaster preparedness plan considerations, according to Dr. Baum:

- Get business interruption insurance, and keep in mind that payouts, if you get them, might take several months.
- Have up-to-date access to your data. Clouds have made it easier to store data off site. But even when important data is stored on clouds, urologists should have a hard disk of that data that's up to date and can go with them should they need to evacuate.
- Have a phone tree for all your employees, vendors, drug reps, and other people who are important for the practice to run. The phone tree, or listing, should be updated at least quarterly and include alternate numbers, when possible.
- Remove medications and things that are refrigerated from your refrigerators when you evacuate. "I lost thousands of dollars worth of very valuable medications because I didn't do this," Dr. Baum said.
- Put all practice valuables in a "recovery box," which you'll take with you if you have to leave before an impending crisis. The box should have copies of medical records, business records, medical licenses, diplomas, tax returns, insurance documents, and the practice procedural manual. The phone tree should be in there, as well as a visual and written list of your inventory, including pictures and sales receipts for devices and computer equipment. The documentation will help you recover the value of what was inside the practice.
- You might want to take a few supplies if you think you'll have to practice off site after a disaster. Dr. Baum said he moved his office to Baton Rouge for a while after Katrina, and it helped that he had taken stethoscopes, blood pressure cuffs, and other basic medical supplies to work at the temporary office.
- Appoint an emergency management team, if your practice is large, or an emergency captain, if your practice is small. The team or captain would be charged with coordinating what needs to be done before, during, and after a disaster.

Finally, don't forget about you.

"Personally speaking, we also have to be prepared," Dr. Ritch said. "You can get caught up in taking care of your patients and forget to get your own water, gasoline, and all these things. If you're not prepared and can't do your job, that affects your ability to take care of people." UT

Cost considerations in the management of bladder cancer

Areas of improvement can help cut high expenditures associated with care, improve outcomes

Daniel J. Lee, MD ■ Sam S. Chang, MD

Concerns over high costs, poor outcomes, and poor access to health care in the United States have prompted legislation that emphasizes value and quality of care over quantity. The goal of health care delivery under these legislative changes will be to improve the value and efficiency of care, measuring the outcomes achieved relative to the cost. (Also see, "New payment models emphasize outcomes, value," page 30.)

Quality and cost concerns are particularly relevant in the diagnosis and management of urothelial carcinoma of the bladder (UCB). UCB has the highest lifetime treatment cost of all cancers,[1] with estimated expenditures of approximately $187,000 per case and, in 2010, a cost of approximately $4 billion to treat.[1,2] There is significant variation among providers in the clinical management of UCB, with concerns that compliance with treatment guidelines should be optimized to help improve patient outcomes.[3-5]

In addition, more care does not necessarily mean better care. In an analysis of the Surveillance, Epidemiology and End Results (SEER)–Medicare database, there was no association between survival and the intensity or frequency of the surveillance protocols for bladder cancer.[4] Moreover, we have to consider the potential consequences that changes in legislation, billing, and reimbursement can have on our practice patterns. As an example, changes to the reimbursement of in-office cystoscopy provided unintended incentives that increased the utilization of in-office cystoscopy by over 640%, decreasing the overall cost efficiency of cystoscopy with an increase in redundant office-based procedures and decrease in diagnostic yield.[6]

There can be significant reductions in unnecessary costs if ultrasound is used as a first-line diagnostic modality in place of CT scans.

Bladder cancer care delivery represents an opportunity to provide smarter care and improve outcomes while reducing wasteful spending. We will review the evidence and identify potential areas of improvement that can help reduce costs associated with UCB management while improving outcomes.

Bladder cancer diagnosis

The goal for bladder cancer screening is to detect tumors at an earlier stage. Studies of screening for bladder cancer have had conflicting results; some have found a survival[7,8] and potential cost-effectiveness benefit[9-11] with screening, while others have not.[12-15] Current guidelines do not recommend routine screening for bladder cancer in an asymptomatic population because screening would result in increased exposure to unnecessary diagnostic procedures without a relative benefit.[15,16]

The management of low-grade, low-risk non-muscle-invasive bladder cancer (NMIBC) represents an area of possible cost reduction. Expectant management of low-grade NMIBC with active surveillance has been successfully implemented with low risks of progression.[17-19] Because the risk of progression is low, there may be significant overtreatment of low-grade NMIBC that can expose patients to excess harm and increased costs without much benefit.[16] Implementation of active surveillance for low-grade, low-risk disease may help decrease the risks of overtreatment and overdiagnosis and in turn decrease the overall costs of bladder cancer care.[16]

In patients with asymptomatic microhematuria, AUA guidelines recommend cystoscopy and upper tract imaging, with a multiphasic computed tomography (CT) scan as the most sensitive and specific test to detect an upper tract urothelial carcinoma.[20] However, a recent cost-effectiveness analysis by Halpern et al[21] found that the use of ultrasound and cystoscopy could substantially reduce costs, decrease radiation exposure, and not compromise detection of cancer. Halpern et al found that the use of renal ultrasound with cystoscopy had an incremental cost per cancer detected of about $50,000, while the incremental cost per cancer detected was about $6.5 million with a CT scan and cystoscopy, and that replacing the renal ultrasound with a CT scan detected just one more malignancy per 10,000 patients evaluated. These findings suggest that there can be significant reductions in unnecessary costs if ultrasound is used as a first-line diagnostic modality in place of CT scans.

Management of NMIBC

The management of NMIBC has been well-established,[16] with the central tenets being: a complete initial resection of cancer, close surveillance for progression and recurrence with cystoscopy, and use of intravesical immunotherapy or chemotherapy with a maintenance regimen. However, multiple studies have shown extremely low rates of compliance with level I evidence and national guidelines.

For example, a meta-analysis of seven randomized trials found that instillation of chemotherapy after transurethral resection of a bladder tumor (TURBT) was associated with about a 40% risk reduction in bladder cancer recurrence.[22] However, several studies in the SEER–Medicare database have found that instillation of chemotherapy immediately after TURBT occurs extremely rarely.[23] In addition, 40% of providers did not perform at least one cystoscopy, cytology, or course of immunotherapy for their patients within 2 years of initial diagnosis. Surgeon compliance with guidelines accounted for almost half of the variation in compliance with post-TURBT intravesical chemotherapy.[24] Likewise, despite level I evidence that bacillus Calmette-Guérin (BCG) instillations with a maintenance protocol can significantly lower

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the risk of recurrence and progression,[25] less than half of patients with NMIBC received a single dose of induction or maintenance BCG.[26]

The completeness of the initial TURBT resection also shows significant variation in its quality. In one study of a high-volume tertiary care center, 74% of patients referred from an outside urologist found residual tumor in the patients who underwent a second TURBT, 30% of whom were upstaged to muscle invasion.[27] This can have important implications, as delays beyond 3 months between diagnosis of muscle invasion and definitive treatment can significantly affect survival.[28] Improving compliance with level I evidence and national guidelines can improve bladder cancer outcomes while decreasing the costs associated with disease progression or recurrence.

Blue-light, or fluorescence, cystoscopy (BLC) was developed to enhance a complete resection during TURBT and improve cancer detection. Several studies have found significant reduction in recurrence of about 40% with BLC compared to standard white-light cystoscopy.[29] The use of BLC can significantly decrease the overall costs of NMIBC treatment,[29-33] primarily powered from a 20%-60% decrease in the number of TURBTs. The total costs of a TURBT at an academic medical center can range from $3,000 to $6,000,[34] so the utilization of BLC to improve complete resections has the potential to improve cancer outcomes and decrease costs.

In high-volume facilities, there can be potential cost savings associated with the robotic procedure if the length of stay and complication rates can be significantly decreased.

However, significant up-front expenditures have to be considered in the utilization of photodynamic visualization, including Foley catheters for instillation, increased surveillance for patients that are up-staged with BLC, and any new equipment costs for BLC compatibility. Many of the current studies differ in their cost assumptions and follow-up, so future research will be required to help clarify the true cost-effectiveness.

Muscle-invasive bladder cancer management

The gold-standard treatment for localized muscle-invasive bladder cancer (MIBC) is a radical cystectomy with urinary diversion, with neoadjuvant chemotherapy if the patient is eligible. However, there are multiple areas in the treatment and management of MIBC where patients are not receiving guideline-concordant care. Only about 20% of patients with MIBC undergo radical cystectomy,[35-37] with only about 13% of patients undergoing neoadjuvant chemotherapy.[38]

There also appears to be a significant barrier to accessing available providers who would perform a cystectomy, as patients who traveled long distances had lower odds of undergoing a radical cystectomy.[37] Patients who underwent a radical cystectomy had improved overall and disease-specific survival compared to those who underwent other alternative treatments.[37] Improved compliance with guidelines for the management of MIBC can improve the health-related outcomes associated with bladder cancer.

Minimally invasive approaches to radical cystectomy were developed in the hopes of reducing the morbidity associated with radical cystectomy. Three randomized controlled trials[39-41] and three systematic meta-analyses[42-44]

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have compared the outcomes of the standard open cystectomy to the robot-assisted approach, with the final findings of the multicenter RAZOR study yet to be published. In general, these randomized controlled trials and meta-analyses have found that the robot-assisted cystectomy was associated with decreased blood loss but longer operative times. Associations with length of stay and postoperative complications differed with each study and cohort.

Cost identification analysis was performed comparing the costs of robot-assisted cystectomy with open cystectomy in three separate studies of large-volume centers (about 200-300 cases per year).[45-47] In two of these analyses, robot-assisted cystectomy was associated with a shorter length of stay than open cystectomy, and also conferred a significant decrease in hospitalization costs by 60%-70% and overall costs by 19%-38%.[46,47] The direct equipment costs were higher with robot-assisted cystectomy in these studies of large-volume centers, but overall offset by the improvement in length of stay and complications. However, it is important to remember that these studies are of high-volume centers with expertise in robotic cystectomy, as both studies had operative times that were equivalent or faster than the open cystectomies.

Two population-based analyses confirmed the findings that robot-assisted cystectomies add about $4,000 per case compared to open, primarily because of increased supply costs.[48,49] However, the cost difference with robotic cystectomy would disappear in high-volume centers (>19 cases per year) or when performed by high-volume surgeons (>7 cases per year).[49] Robot-assisted cystectomies are consistently associated with higher direct costs than open procedures with more equipment purchases, maintenance, and disposable instruments. However, ownership of a robotic platform can increase utilization for other urologic, surgical, or gynecologic procedures that can then marginalize the additional equipment costs.

In high-volume facilities, there can be potential cost savings associated with the robotic procedure if the length of stay and complication rates can be significantly decreased. Future studies that analyze the cost per quality-adjusted life year will help clarify the potential value for a robot-assisted approach.

Postoperative length of stay is an important factor in the patient's quality of life and costs of bladder cancer care. Enhanced recovery after surgery (ERAS) protocols aim to standardize perioperative care and reduce variation. Although there is some variation in ERAS protocols between institutions, different randomized trials and meta-analyses have found that overall, ERAS protocols are associated with decreased overall complication rates, length of stay, and a faster return of bowel function.[50] A cost-effectiveness analysis at a high-volume tertiary center found that the implementation of an ERAS protocol produced an overall average 30-day cost savings of about $4,500 per procedure.[51]

Postoperative ileus is the most common complication that can affect length of stay. Alvimopan (Entereg) is a mu-opioid receptor antagonist that has been shown to significantly improve time to return of bowel function after cystectomy, decrease the postoperative ileus rate by more than 50%, and decrease the postoperative length of stay.[52] The published wholesale price for alvimopan is $62.50, with maximum cost of about $937.50 for 15 doses.[53] In one cost-consequence analysis, utilization of alvimopan was associated with a cost reduction of more than $2,300 per patient.[54] Most of the cost savings resulted from a shorter length of stay (by almost 3 days), decreased utilization of gastrointestinal medications, and decreased parenteral nutrition use. The routine use of ERAS protocols with alvimopan utilization can significantly decrease postoperative length of stay and complication rates associated with cystectomy and thereby significantly decrease the overall costs of bladder cancer management.

Conclusion

There has been an increasing emphasis on improving the value of health care by improving the quality or outcomes of care while decreasing the costs. The management and treatment of bladder cancer is costly, but certain areas of improvement can have a dramatic impact on outcomes and costs. Cost-saving measures, such as the use of front-line renal ultrasound with cystoscopy instead of a CT scan, can help decrease costs while not compromising outcomes. Quality improvement measures, such as improving compliance with guideline-concordant care in the management of NMIBC and MIBC can decrease recurrence and progression rates, improve outcomes, and prevent unnecessary costs.

Finally, the implementation of newer processes such as blue-light cystoscopy, ERAS protocols, and alvimopan can significantly decrease costs and improve the health outcomes of patients undergoing a cystectomy. Future studies that focus on cost-effectiveness relative to quality of life after cystectomy will be essential to determine other potential areas of improvement. UT

New payment models emphasize outcomes, value

The United States has the highest per capita health care expenditures in the world, accounting for approximately 17% of the national gross domestic product in 2015.[1] In fact, from 1980 to 2010, the cumulative difference in health care spending between the United States and Switzerland, the country with the second-highest per capita health care expenditures, amounts to approximately $15.5 trillion.[2] Over the last two decades, health care costs have continued to increase dramatically, and at current rates, have been estimated to increase about 40% over the next 25 years.[3]

Despite the high costs, health care outcomes are often much worse than those of other countries; the United States currently ranks 42nd in life expectancy and 56th in infant mortality rates.[4] There is also significant geographic variation in the quality of health care, as some states have life expectancies and infant mortality rates that are worse than countries ranked in the 100s.[4]

Given the poor health outcomes, significant barriers to access care, and rising health care costs, legislation and payment models have shifted dramatically in an attempt to transition from a fee-for-service model that incentivizes high-output health care to one that emphasizes value and quality of care. Passage of the Patient Protection and Affordable Care Act (ACA) and the Medicare Access and CHIP Reauthorization Act (MACRA) represents a long-standing adjustment to value-based compensation that incorporates quality outcomes, cost savings, patient satisfaction, and preventive care. In fact, the Centers for Medicare & Medicaid Services has a goal of tying 50% of traditional payments to quality metrics by 2018.[4]

By linking payments to outcomes, these alternative payment models provide incentives to coordinate care, ensure quality care provision, and prevent overtreatment or improper care. It has been estimated that up to $425 billion of the health care expenditures in 2011 were from failures in care delivery, care coordination, and improper overtreatment.[5] With these legislative changes, the goal of health care delivery will be focused on improving the value and efficiency of care, measuring the outcomes achieved relative to the cost.[6]

References

1. GBoDHFC Network. Evolution and patterns of global health financing 1995-2014: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. *Lancet* 2017; 389:1981-2004.
2. "Health Expenditure and Financing" Organisation for Economic Cooperation and Development. *http://stats.oecd.org/Index.aspx?DataSetCode=SHA* . Accessed July 15, 2017.
3. GBoDHFC Network. Future and potential spending on health 2015-40: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. *Lancet* 2017; 389:2005-30.
4. "Oncology Care Model"; Center for Medicare and Medicaid Innovation. *http://innovation.cms.gov/initiatives/Oncology-Care/* . Accessed July 15, 2017.
5. Berwick DM, Hackbarth AD. Eliminating waste in US health care. *JAMA* 2012; 307:1513-6.
6. Porter ME. What is value in health care? *N Engl J Med* 2010; 363:2477-81.

References

1. Riley GF, Potosky AL, Lubitz JD, et al. Medicare payments from diagnosis to death for elderly cancer patients by stage at diagnosis. *Med Care* 1995; 33:828-41.
2. Mariotto AB, Yabroff KR, Shao Y, Feet al. Projections of the cost of cancer care in the United States: 2010-2020. *J Natl Cancer Inst* 2011; 103:117-28.
3. Skolarus TA, Ye Z, Montgomery JS, et al. Use of restaging bladder tumor resection for bladder cancer among Medicare beneficiaries. *Urology* 2011; 78:1345-9.
4. Hollenbeck BK, Ye Z, Dunn RL, et al. Provider treatment intensity and outcomes for patients with early-stage bladder cancer. *J Natl Cancer Inst* 2009; 101:571-80.
5. Karl A, Adejoro O, Saigal C, et al. General adherence to guideline recommendations on initial diagnosis of bladder cancer in the United States and influencing factors. *Clin Genitourin Cancer* 2014; 12:270-7.
6. O'Neil B, Graves AJ, Barocas DA, et al. Doing More for More: Unintended Consequences of Financial Incentives for Oncology Specialty Care. *J Natl Cancer Inst* 2016; 108.
7. Messing EM, Madeb R, Young T, et al. Long-term outcome of hematuria home screening for bladder cancer in men. *Cancer* 2006; 107:2173-9.
8. Messing EM, Young TB, Hunt VB, et al. Hematuria home screening: repeat testing results. *J Urol* 1995; 154:57-61.
9. Ellwein LB, Farrow GM, Friedell GH, et al. An assessment of the impact of urine cytology screening using a computer-based model of bladder cancer. *Urol Clin North Am* 1984; 11:585-98.
10. Svatek RS, Sagalowsky AI, Lotan Y. Economic impact of screening for bladder cancer using bladder tumor markers: a decision analysis. *Urol Oncol* 2006; 24:338-43.
11. Lotan Y, Svatek RS, Sagalowsky AI. Should we screen for bladder cancer in a high-risk population?: A cost per life-year saved analysis. *Cancer* 2006; 107:982-90.
12. Thériault GP, Tremblay CG, Armstrong BG. Bladder cancer screening among primary aluminum production workers in Quebec. *J Occup Med* 1990; 32:869-72.
13. Friedman GD, Hiatt RA, Quesenberry CP. Problems in assessing screening experience in observational studies of screening efficacy: example of urinalysis screening for bladder cancer. *J Med Screen* 1995; 2:219-23.
14. Lotan Y, Elias K, Svatek RS, et al. Bladder cancer screening in a high risk asymptomatic population using a point of care urine based protein tumor marker. *J Urol* 2009; 182:52-7; discussion 8.
15. Chou R, Dana T. Screening adults for bladder cancer: a review of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med* 2010; 153:461-8.
16. Chang SS, Boorjian SA, Chou R, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. *J Urol* 2016; 196:1021-9.
17. Pruthi RS, Baldwin N, Bhalani V, et al. Conservative management of low risk superficial bladder tumors. *J Urol* 2008; 179:87-90; discussion
18. Tiu A, Jenkins LC, Soloway MS. Active surveillance for low-risk bladder cancer. *Urol Oncol* 2014; 32:33.e7-10.
19. Soloway MS, Bruck DS, Kim SS. Expectant management of small, recurrent, noninvasive papillary bladder tumors. *J Urol* 2003; 170:438-41.
20. Davis R, Jones JS, Barocas DA, et al. Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline. *J Urol* 2012; 188:2473-81.
21. Halpern JA, Chughtai B, Ghomrawi H. Cost-effectiveness of Common Diagnostic Approaches for Evaluation of Asymptomatic Microscopic Hematuria. *JAMA Intern Med* 2017; 177:800-7.
22. Sylvester RJ, Oosterlinck W, van der Meijden AP. A single immediate postoperative instillation of chemotherapy decreases the risk of recurrence in patients with stage Ta T1 bladder cancer: a meta-analysis of published results of randomized clinical trials. *J Urol* 2004; 171:2186-90, quiz 435.
23. Chamie K, Saigal CS, Lai J, et al. Quality of care in patients with bladder cancer: a case report? *Cancer* 2012; 118:1412-21.
24. Chamie K, Saigal CS, Lai J, et al. Compliance with guidelines for patients with bladder cancer: variation in the delivery of care. *Cancer* 2011; :5392-401.
25. Lamm DL, Blumenstein BA, Crissman JD, et al. Maintenance bacillus Calmette-Guerin immunotherapy for recurrent TA, T1 and carcinoma in situ transitional cell carcinoma of the bladder: a randomized Southwest Oncology Group Study. *J Urol* 2000; 163:1124-9.
26. Huang GJ, Hamilton AS, Lo M, et al. Predictors of intravesical therapy for nonmuscle invasive bladder cancer: results from the Surveillance, Epidemiology and End Results program 2003 patterns of care project. *J Urol* 2008; 180:520-4; discussion 4.
27. Herr HW. Role of re-resection in non-muscle-invasive bladder cancer. *ScientificWorldJournal* 2011; 11:283-8.
28. Gore JL, Lai J, Setodji CM, et al. Mortality increases when radical cystectomy is delayed more than 12 weeks: results from a Surveillance, Epidemiology, and End Results-Medicare analysis. *Cancer* 2009; 115:988-96.
29. Burger M, Grossman HB, Droller M, et al. Photodynamic diagnosis of non-muscle-invasive bladder cancer with hexaminolevulinate cystoscopy: a meta-analysis of detection and recurrence based on raw data. *Eur Urol* 2013; 64:846-54.
30. Burger M, Zaak D, Stief CG, et al. Photodynamic diagnostics and noninvasive bladder cancer: is it cost-effective in long-term application? A Germany-based cost analysis. *Eur Urol* 2007; 52:142-7.
31. Otto W, Burger M, Fritsche HM, et al. Photodynamic diagnosis for superficial bladder cancer: do all risk-groups profit equally from oncological and economic long-term results? *Clin Med Oncol* 2009; 3:53-8.
32. Garfield SS, Gavaghan MB, Armstrong SO, et al. The cost-effectiveness of blue light cystoscopy in bladder cancer detection: United States projections based on clinical data showing 4.5 years of follow up after a single hexaminolevulinate hydrochloride instillation. *Can J Urol* 2013; 20:6682-9.
33. Malmström PU, Hedelin H, Thomas YK, et al. Fluorescence-guided transurethral resection of bladder cancer using hexaminolevulinate: analysis of health economic impact in Sweden. *Scand J Urol Nephrol* 2009; 43:192-8.
34. Svatek RS, Hollenbeck BK, Holmäng S, et al. The economics of bladder cancer: costs and considerations of caring for this disease. *Eur Urol* 2014; 66:253-62.
35. Schrag D, Mitra N, Xu F, et al. Cystectomy for muscle-invasive bladder cancer: patterns and outcomes of care in the Medicare population. *Urology* 2005; 65:1118-25.
36. Gray PJ, Fedewa SA, Shipley WU, et al. Use of potentially curative therapies for muscle-invasive bladder cancer in the United States: results from the National Cancer Data Base. *Eur Urol* 2013; 63:823-9.
37. Gore JL, Litwin MS, Lai J, et al. Use of radical cystectomy for patients with invasive bladder cancer. *J Natl Cancer Inst* 2010; 102:802-11.
38. Fedeli U, Fedewa SA, Ward EM. Treatment of muscle invasive bladder cancer: evidence from the National Cancer Database, 2003 to 2007. *J Urol* 2011; 185:72-8.
39. Nix J, Smith A, Kurpad R, et al. Prospective randomized controlled trial of robotic versus open radical cystectomy for bladder cancer: perioperative and pathologic results. *Eur Urol* 2010; 57:196-201.
40. Bochner BH, Sjoberg DD, Laudone VP, Group MSKCCBCST. A randomized trial of robot-assisted laparoscopic radical cystectomy. *N Engl J Med* 2014; 371:389-90.
41. Parekh DJ, Messer J, Fitzgerald J, et al. Perioperative outcomes and oncologic efficacy from a pilot prospective randomized clinical trial of open versus robotic assisted radical cystectomy. *J Urol* 2013; 189:474-9.
42. Li K, Lin T, Fan X, et al. Systematic review and meta-analysis of comparative studies reporting early outcomes after robot-assisted radical cystectomy versus open radical cystectomy. *Cancer Treat Rev* 2013; 39:551-60.
43. Tang K, Xia D, Li H, et al. Robotic vs. open radical cystectomy in bladder cancer: A systematic review and meta-analysis. *Eur J Surg Oncol* 2014; 40:1399-411.
44. Ishii H, Rai BP, Stolzenburg JU, et al. Robotic or open radical cystectomy, which is safer? A systematic review and meta-analysis of comparative studies. *J Endourol* 2014; 28:1215-23.
45. Smith A, Kurpad R, Lal A, et al. Cost analysis of robotic versus open radical cystectomy for bladder cancer. *J Urol* 2010; 183:505-9.
46. Martin AD, Nunez RN, Castle EP. Robot-assisted radical cystectomy versus open radical cystectomy: a complete cost analysis. *Urology* 2011; 77:621-5.
47. Lee R, Chughtai B, Herman M, et al. Cost-analysis comparison of robot-assisted laparoscopic radical cystectomy (RC) vs open RC. *BJU Int* 2011; 108:976-83.
48. Yu HY, Hevelone ND, Lipsitz SR, et al. Comparative analysis of outcomes and costs following open radical cystectomy versus robot-assisted laparoscopic radical cystectomy: results from the US Nationwide Inpatient Sample. *Eur Urol* 2012; 61:1239-44.
49. Leow JJ, Reese SW, Jiang W, et al. Propensity-matched comparison of morbidity and costs of open and robot-assisted radical cystectomies: a contemporary population-based analysis in the United States. *Eur Urol* 2014; 66:569-76.
50. Tyson MD, Chang SS. Enhanced Recovery Pathways Versus Standard Care After Cystectomy: A Meta-analysis of the Effect on Perioperative Outcomes. *Eur Urol* 2016; 70:995-1003.
51. Nabhani J, Ahmadi H, Schuckman AK, et al. Cost Analysis of the Enhanced Recovery After Surgery Protocol in Patients Undergoing Radical Cystectomy for Bladder Cancer. *Eur Urol Focus* 2016; 2:92-6.
52. Lee CT, Chang SS, Kamat AM, et al. Alvimopan accelerates gastrointestinal recovery after radical cystectomy: a multicenter randomized placebo-controlled trial. *Eur Urol* 2014; 66:265-72.
53. Kraft M, Maclaren R, Du W, et al. Alvimopan (entereg) for the management of postoperative ileus in patients undergoing bowel resection. *P T* 2010; 35:44-9.
54. Kauf TL, Svatek RS, Amiel G, et al. Alvimopan, a peripherally acting μ-opioid receptor antagonist, is associated with reduced costs after radical cystectomy: economic analysis of a phase 4 randomized, controlled trial. *J Urol* 2014; 191:1721-7.

NDA submitted for non-metastatic castration-resistant PCa agent

Janssen Biotech, Inc. has submitted a new drug application to the FDA for apalutamide, an investigational, next-generation oral androgen receptor inhibitor for men with non-metastatic castration-resistant prostate cancer (CRPC). The submission is based on phase III data from the pivotal ARN-509-003 (SPARTAN) clinical trial, which assessed the safety and efficacy of apalutamide versus placebo in men with non-metastatic CRPC who have a rapidly rising PSA despite receiving continuous androgen deprivation therapy. The primary endpoint of the study was metastasis-free survival. SPARTAN study results will be presented at a future medical meeting, according to Janssen Biotech.

Priority review granted for advanced renal cell carcinoma agent

The FDA has determined Exelixis, Inc.'s supplemental new drug application for cabozantinib (CABOMETYX) for patients with previously untreated advanced renal cell carcinoma (RCC) to be sufficiently complete to permit a substantive review. The FDA granted priority review of the filing and assigned a Prescription Drug User Fee Act action date of Feb. 15, 2018. The application is based on data from CABOSUN, a randomized phase II trial conducted by The Alliance for Clinical Trials in Oncology as part of Exelixis' collaboration with the National Cancer Institute's Cancer Therapy Evaluation Program. CABOMETYX was previously approved by the FDA on April 25, 2016 for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy.

Study to evaluate 3-D printing of kidney, prostate models

Stratasys announced that a new clinical study is being conducted with the New York University School of Medicine, New York, aimed at advancing diagnosis and treatment of complex kidney and prostate tumors through imaging and 3-D printing. The 2-year clinical trial is specifically targeted at analyzing how patient-specific multi-colored physical tumor models, printed on the Stratasys J750 3-D printer, can potentially change and improve the quality of patient care. Under the randomized, controlled study, researchers are 3-D-printing kidney and prostate cancer models for a sample of the participating 300 patients—measuring the specific impact each has on pre-surgical planning versus traditional 2-D visualization approaches. Subjects are separated into three treatment categories to analyze and compare conventional preoperative 2-D imaging, augmented reality models, and next-generation 3-D printed models. The study is expected to continue into 2018, according to Stratasys.

FDA accepts supplemental NDA for bladder cancer detection agent

The FDA has accepted the supplemental new drug application for Photocure ASA's Cysview on a priority review basis. Photocure said it is looking to expand the label of Cysview to include its use in the outpatient setting to detect the recurrence of bladder cancer using a flexible cystoscope, the detection of carcinoma in situ, and the repeat administration of Cysview. The filing is a combination drug-device application with the KARL STORZ D-LIGHT C PDD Flexible Videoscope System. With the FDA granting a priority review, a decision is expected in the first half of 2018.

Imaging modality leads to changes in prostate cancer management

Results of a recent interim analysis showed that 61.2% (52/85) of prostate cancer patients had their clinical management changed when results of fluciclovine (^{18}F) positron emission tomography/computed tomography imaging were added to the standard-of-care diagnostic workup. Results from the phase III FALCON trial were presented at the American Society for Radiation Oncology annual meeting in San Diego. The study is evaluating the clinical impact of fluciclovine (^{18}F) PET/CT imaging on patient management decisions in men with biochemically recurrent prostate cancer, according to Blue Earth Diagnostics. Fluciclovine F 18 injection (Axumin) is an FDA-approved molecular imaging agent for use in PET imaging in men with suspected prostate cancer recurrence based on elevated PSA levels following prior treatment. It is not currently approved in the United States for treatment planning in men with biochemically recurrent prostate cancer.

Treatment underway for patients in clinical trial of BPH treatment

The first patients have been treated in the WATER II Study (Waterjet Ablation Therapy for Endoscopic Resection of prostate tissue). The WATER II study is a U.S. investigational device exemption clinical trial evaluating the safety and efficacy of Aquablation, delivered with PROCEPT BioRobotics' AQUABEAM System, in large prostates (80 mL to 150 mL) for the treatment of BPH. The study will enroll 100 patients at up to 20 sites in the U.S. and Canada, with patient follow-up out to 12 months. The WATER II Study is a follow-up study to the successful WATER Study, which showed a superior safety profile for Aquablation with very strong efficacy outcomes comparable to transurethral resection of the prostate for the treatment of BPH in prostates 30 mL to 80 mL, according to PROCEPT BioRobotics.

Urinary incontinence agent's new drug application accepted by FDA

Following the launch of the phase II clinical study of its leading compound Litoxetine IXA-001 in Europe and Canada, Ixaltis has announced the FDA's acceptance FDA of the company's investigational new drug application. The open application will allow Ixaltis to conduct a clinical study in the U.S. with the objective of assessing the safety, tolerability, and efficacy of Litoxetine as treatment for men and women suffering from mixed urinary incontinence, according to the company.

PCa treatment improves metastasis-free survival in phase III trial

The phase III PROSPER trial evaluating enzalutamide (XTANDI) plus androgen deprivation therapy (ADT) versus ADT alone in patients with non-metastatic castration-resistant prostate cancer (CRPC) met its primary endpoint of improved metastasis-free survival, Pfizer Inc. and Astellas Pharma Inc. recently announced. The preliminary safety analysis of the PROSPER trial appears consistent with the safety profile of enzalutamide in previous clinical trials. Based on the results of PROSPER, the companies intend to discuss the data with global health authorities to potentially support expanding the label for enzalutamide to cover all patients with CRPC.

Patents available for external urine collection catheter

ASG Services Inc. announced the availability of two U.S. and international patents for the manufacture and global sale and distribution of Ur24, an external urine collection catheter. The system's Human Apparatus attaches to the urethra and is made of a medical-grade, pliable silicone gel and when attached to the urethra, urine can be directed to flow into a collection container that is part of the Urine Collection Apparatus. A combination of one-way valves known as the "breather" allows air into the Human Apparatus, and a low-pressure vacuum then directs the urine to flow into the awaiting Urine Collection Apparatus container, according to AGS Services. Ur24 will be a Class II FDA product that will not require clinical trials, the company said.

Products & Services

MEDICAL EQUIPMENT

Careers

NEW JERSEY

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Careers

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WASHINGTON

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DEPARTMENT OF UROLOGY

The Department of Urology at the University of Washington seeks a full-time urologist, with training in urological oncology, at the assistant or associate professor level, without tenure due to funding, to join an established and high volume urological cancer program at UW Medicine and the Seattle Cancer Care Alliance. This position requires the applicant to possess an MD degree (or foreign equivalent), to have completed an accredited residency in Urology (or foreign equivalent), and to be Board-certified or eligible for certification in Urology with subspecialty training in urologic oncology (or foreign equivalent).

We seek candidates who demonstrate a commitment to building and sustaining an inclusive climate for all faculty and students. At the University of Washington, diversity is integral to excellence. We value and honor diverse experiences and perspectives, strive to create welcoming and respectful learning environments and promote access, opportunity and justice for all.

The Department of Urology has an established and high volume urologic practice, a large clinical population from the state of Washington and four neighboring states, active research programs, and an extremely strong academic urology faculty. Candidates should be capable of developing and growing a urologic cancer practice, including some aspects of general urology. The candidate will be required to perform open and robotic-assisted surgery and collaborate with other surgeons and medical/radiation oncologists within and across UW Medicine and its affiliated entities.

The University of Washington faculty engage in teaching, research, and service. Thus, the candidate must demonstrate clinical excellence and a commitment to teaching residents, fellows, and students; interested applicants may propose a research program. The University of Washington, a recipient of the 2006 Alfred P. Sloan award for Faculty Career Flexibility, is committed to supporting the work-life balance of its faculty.

All candidates must be eligible for and able to maintain a Washington State medical license. In order to be eligible for University sponsorship for an H-1B visa, graduates of foreign (non-U.S.) medical schools must show successful completion of all three steps of the U.S. Medical Licensing Exam (USMLE), or equivalent as determined by the Secretary of Health and Human Services. Salary and benefits are commensurate with experience and responsibilities. The position is open until filled.

Interested applicants should submit a letter of interest and CV to:

Serena Newhall
Manager of Human Resources and Faculty Affairs
University of Washington, Department of Urology Box 356510, 1959 NE Pacific Street, Seattle, WA 98195.
206-221-5869 **serenn2@uw.edu**

University of Washington is an affirmative action and equal opportunity employer. All qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, gender expression, national origin, age, protected veteran or disabled status, or genetic information.

Careers

WASHINGTON

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MedPAC advocates for MIPS termination

Proposed alternative would create pool for value payments

Bob Gatty
UT Washington Correspondent

Bob Gatty, a former congressional aide, covers news from Washington for *Urology Times*.

If members of the Medicare Payment Advisory Commission (MedPAC) have their way, the new Merit-based Incentive Payment System (MIPS) will be sent into oblivion, never to be heard of again.

During a meeting in Washington Oct. 5, MedPAC members, who include physicians, health care executives, and other policy experts, essentially said MIPS should be trashed as commission analysts offered the framework of a possible alternative.

MIPS is one of two payment systems established by the Medicare Access and CHIP Reauthorization Act. The second consists of Advanced Alternative Payment Models (APMs), which major urology organizations have been working to develop.

Within MIPS, physician pay depends on performance in four categories: Quality, Cost, Improvement Activities, and Advancing Care Information.

According to critics at MedPAC, the MIPS program is overly complex because of the various reporting options and exemptions. Ultimately, Medicare gives clinicians a score based on performance and either increases or reduces their payment based on that score.

"It is extremely unlikely that physicians will understand their score or what they need to do to improve it," said David Glass, MedPAC principal policy analyst.

An alternative approach suggested by Glass and MedPAC senior analyst Kate Bloniarz, which they called the Voluntary Value Program, would withhold a small percentage of clinicians' fee schedule dollars to be placed in a pool to be used for value payments for those in a "sufficiently large entity," such as those affiliated with a single hospital or one geographic area. Other physicians could choose to participate in an Advanced APM.

The sentiment to kill MIPS was part of a discussion at the Oct. 5 meeting; it remains to be seen if a formal recommendation to that effect is presented to Congress, and then, of course, it is up to lawmakers to determine if that recommendation is to be enacted.

IPAB on the ropes

Meanwhile, on another front, the House Ways and Means Committee voted Oct. 4 to repeal the controversial Independent Payment Advisory Board (IPAB), which was created by the Affordable Care Act and slammed as a "death panel" by Republicans. The purpose of the IPAB, which has never been implemented, is to provide the administration and Congress with cost-cutting recommendations if Medicare spending reaches a certain threshold. The IPAB has been strongly opposed by major urology organizations.

Approval of the repeal legislation by the Ways and Means Committee is an important first step, especially since the measure is backed by 43 Democratic co-sponsors. It still must be passed by the full House and Senate before going to President Trump, who insiders believe will gladly sign it.

"While the repeal of IPAB will not have any practical effect on how urologists in independent practice approach treatment, it will restore accountability for spending on Medicare to elected officials," said Neal D. Shore, MD, president of LUGPA.

"We look forward to continuing our dialogue with lawmakers to ensure Americans have access to appropriate Medicare coverage under legislation that promotes quality care with fair reimbursement for physicians," Dr. Shore told *Urology Times*. "LUGPA strongly supports repealing IPAB, as this unelected board has the power to initiate cuts to Medicare without congressional consent and thus compromise patient access to care."

DoD research funding in jeopardy

A third issue important to urologists has been moving in Congress, this one involving funding for critical medical research programs at the Department of Defense.

The AUA has been working in support of an amendment to the National Defense Authorization Act (NDAA) for fiscal year 2018 that would nullify provisions in that bill narrowly defining how research funding can be used.

"Undoubtedly, this language would impact existing funding for prostate, kidney, and bladder cancers and other painful urologic disorders such as interstitial cystitis," the AUA said in a "Policy and Advocacy Brief" on its website. "If enacted, it could jeopardize funding for urologic research activities that have broader relevance to the U.S. military, including the health and well-being of military families and veterans, and the efficiency of the military health care system."

"It is extremely unlikely that physicians will understand their [MIPS] score or what they need to do to improve it."

DAVID GLASS
MEDPAC PRINCIPAL POLICY ANALYST

The amendment to remove the restrictive language was sponsored by Sen. Dick Durbin (D-IL).

"At a time in America when we need medical research—for breast cancer, for brain disease, Alzheimer's—for all of the things that are facing us, why would we cut back on medical research?" Durbin asked. "It's a serious mistake."

"It is absolutely critical that we maintain funding for research into causes, treatments, and therapies for diseases that affect those who serve on the battlefield, their spouses, and dependents," said Sen. Lisa Murkowski (R-AK), a co-sponsor of the Durbin amendment. "Medical research in the Defense Department is another way we demonstrate to those who place their lives on the line that the American people have their back."

However, the Senate approved the NDAA, including its restrictive language, despite the objection of the AUA and more than 140 medical research associations and many veterans groups. The NDAA version approved by the House did not include those restrictions, and at press time, a House-Senate conference was expected to iron out that and other differences between the two measures. UT

Fast Facts

The National Defense Authorization Act for fiscal year 2018's provisions on research funding:

- narrowly define how research funding can be used
- are opposed by the AUA and more than 140 medical research associations and many veterans groups
- could be nullified by a proposed amendment

How incidental radiology findings can lead to malpractice litigation

Practices should have policy in place for routing, communicating findings

A 60-year-old male presents to the local emergency room in the early morning hours with complaints of nausea, abdominal pain radiating to the chest, and dysuria. He reports a prior history of kidney stones. A cardiac workup is negative, and both urology and general surgery are consulted.

The urologist and general surgeon agree to obtain an ultrasound to look for both kidney and gall stones. The ultrasound comes back showing cholelithiasis, and the surgeon reports this to the urologist. In the meantime, the patient's urinalysis results are positive and antibiotics are ordered for a urinary tract infection. The patient is admitted, undergoes laparoscopic cholecystectomy, and is discharged home quickly.

The use of diagnostic imaging in the emergency department has surged in recent years, and so too, have incidental findings.

Nearly 30 months later, the patient is seen for a routine physical exam by his primary care physician, who palpates a firm abdominal mass. An ultrasound is performed that shows a large right kidney mass, with comparison to a previous ultrasound showing it had nearly doubled in size. Further workup reveals metastatic perinephric leiomyosarcoma, which the patient eventually died from.

What previous ultrasound, you might be wondering? The missing piece in the case above is that of the incidental radiology finding. At the time of evaluation in the emergency department, the ultrasound also showed a cystic lesion adjacent to the right kidney and recommended a computed tomography scan with contrast for correlating clinical concern.

The ultrasound report with this incidental finding was routed electronically to the urology attending, among others. A nurse going through the radiology in-basket in the urology office looked at the report, but noted that the patient had never been seen in the clinic by a urologist, and assumed the report was routed incorrectly. Thus, the consulting urologist was never made aware of this finding.

Malpractice Consult

Brianne Goodwin, JD, RN

Ms. Goodwin is manager of clinical risk and patient safety at Cambridge Health Alliance, Cambridge, MA.

This is a classic, and not-infrequent, example of the patient who falls through the cracks with an incidental radiology finding. Whose responsibility is the communication of the incidental finding? Should the urologist have accepted the word of the general surgeon regarding cholelithiasis, or should she have read the report on her own? Was the finding present on the preliminary report, or only the final report? Did the urologist's confirmation of a UTI and prescribing of antibiotics provide a false sense of issue resolution, and contribute to non-review of the ultrasound? Was the incidental finding embedded in a multi-page report, making it hard to find? Did the emergency physician know of this result and not communicate it to the urologist? All of these questions are critical when developing facts in a lawsuit and when putting organizational policy into place.

If asked in court why you did not follow up on a particular finding, pointing to an institutional policy is more of a defense than having no reason at all.

The use of diagnostic imaging in the emergency department has surged in recent years, and so too, have incidental findings. For example, one study found that there was a fourfold increase in emergency department use of CT scans to evaluate respiratory symptoms over a 9-year span *(bit.ly/Testsincrease)*.

Not surprisingly, not all incidental findings are communicated to patients. One 2011 study found that 33.4% of CT scans performed in an ED had an incidental finding; only 9.8% of these were reported to the patient *(Emerg Med Int;* 2011:624847).

Mishandling of an incidental finding can lead to a medical malpractice lawsuit, whether the finding itself turned out to be malignant or whether the monitoring of that finding would have increased surveillance and caught another lesion inadvertently *(bit.ly/Incidentalfindingliability)*.

Develop, follow policy

There are many schools of thought on the best ways to manage incidental findings, and the best answer for one organization may not be the best for another. What is important is that health care organizations develop a policy on how incidental findings are routed and communicated, and systematically audit that the policy is being followed. If asked in court why you did not follow up on a particular finding, pointing to an institutional policy is more of a defense than having no reason at all.

If you are in receipt of a radiology report documenting an incidental finding, you should not assume that another provider has dealt with it unless you see clear documentation of this in the medical record. If it is a finding outside of your specialty, it would be prudent to communicate this information to the patient's primary care or admitting physician, with a note in the chart to memorialize the communication. If the patient is not established in your organization, make sure the patient has a copy of the radiology report and document that he or she has been told how to best follow up. This way, if the patient chooses to do nothing with this information, you have helped to insulate yourself from litigation.

Incidental radiology findings are low-hanging fruit that organizations should develop processes for handling proactively. Although a great number of these findings are benign and will remain benign, the small number that turn into cancers or other growths requiring surgical intervention or significant medical treatment have the potential to become low-hanging fruit for a plaintiff's attorney. UT

THE NEW WAVE IN BPH TREATMENT

For many BPH sufferers, the road to relief goes through the central zone.

A significant number of men who present with symptoms of LUTS secondary to BPH have a median lobe and/or an enlarged central zone.[1,2] An enlarged central zone increases the prostatic urethral angle and contributes to bladder outlet obstruction.[2]

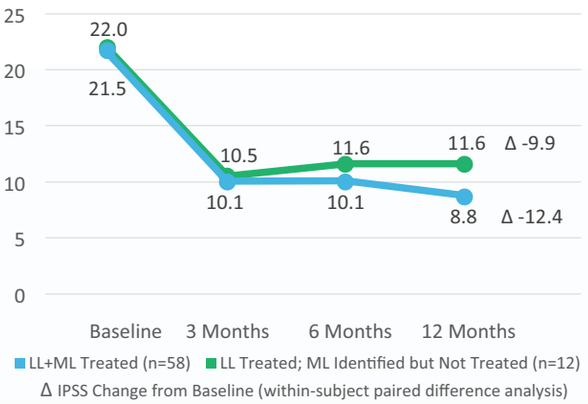
Rezūm gives you the flexibility to treat all areas of an enlarged prostate, so you can customize your BPH treatment to suit each patient's unique anatomy.

This in-office/outpatient therapy does not require general anesthesia, preserves sexual and urinary functions,[1] and eliminates the need for drug therapies and their associated side effects.

Contact us at info@rezum.com to learn more about how Rezūm is transforming the BPH treatment experience for physicians and their patients.

Rezum Pivotal Study

IPSS: Median Lobe (ML) Identified – Treated vs Not Treated



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[1] Roehrborn CG, Gange SN, Gittelman MC et al. Convective Thermal Therapy: Durable 2-Year Results of Randomized Controlled and Prospective Crossover Studies for Treatment of Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia. *J Urol*. June 2017. [2] Ku JH, Ko DW, Cho JY, Oh S-J. Correlation Between Prostatic Urethral Angle and Bladder Outlet Obstruction Index in Patients with Lower Urinary Tract Symptoms. *Urology*. 2010;75(6):1467–1471. doi:10.1016/j.urology.2009.08.049.

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