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Shock waves may change future of ED therapy

Procedure offers promise of disease modification vs. symptomatic treatment

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

Study	No. of patients	Key finding
Ramasamy et al (<i>J Sex Med</i> 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 (<i>Urology</i> Sept. 26, 2017 [Epub ahead of print])	637	SWT significantly improved patients' IIEF and Erection Hardness Score



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

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 University.

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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



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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

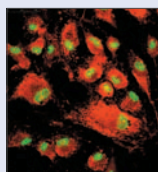
Devices are being studied in clinical trials, and shock wave therapy to treat ED is already being marketed. Aventura, FL-based Sexual MD Solutions markets the GAINSWave therapy brand to enhance sexual performance and optimize erection quality through a network of more than 100 trained providers. According 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

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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.

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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/mm²; 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.



IRWIN GOLDSTEIN, MD

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

"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 Direx-Group'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**



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Cialis and Viagra, who have received shock waves, appear to go back to respond to PDE-5 inhibitors."

RANJITH RAMASAMY, MD