Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Irwin Goldstein, MD
Director, San Diego Sexual Medicine
Director, Sexual Medicine, Alvarado Hospital, San Diego, CA
Clinical Professor of Surgery, University of California at San Diego
Past President, International Society for the Study of Women's Sexual Health
Past President, Sexual Medicine Society of North America
Editor-in-Chief, *Sexual Medicine Reviews*
Editor Emeritus, *The Journal of Sexual Medicine*
Editor Emeritus, *International Journal of Impotence Research*

dr.irwingoldstein@gmail.com

Clinical principles of shockwave therapy in medicine

What is the difference between genuine shockwaves and "imitation shockwaves"

How does shockwave therapy activate stem cells

Animal data

Clinical data for ED

Shockwaves in everyday life

Lightning

Ultrasonic Flight

A shockwave is a type of propagating disturbance that moves faster than local speed of sound (767 mph in air; 3355 mph in water) in medium

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy uses acoustic wave energy as mechanical force to enact biologic tissue change.

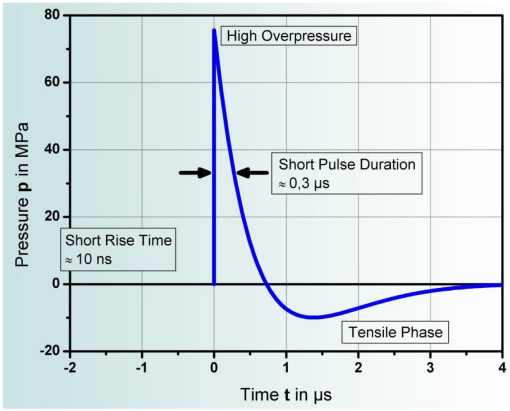
High-intensity shock waves are used in lithotripsy because the shockwave energy can break stones into smaller fragments,

Medium-intensity waves have been theorized to have anti-inflammatory benefits in the orthopedic setting to treat tendonitis and bursitis.

Low intensity shock waves exhibit angiogenic properties to manage chronic wounds, peripheral neuropathy, cardiac ischemic tissue

Introduction – Shock Waves

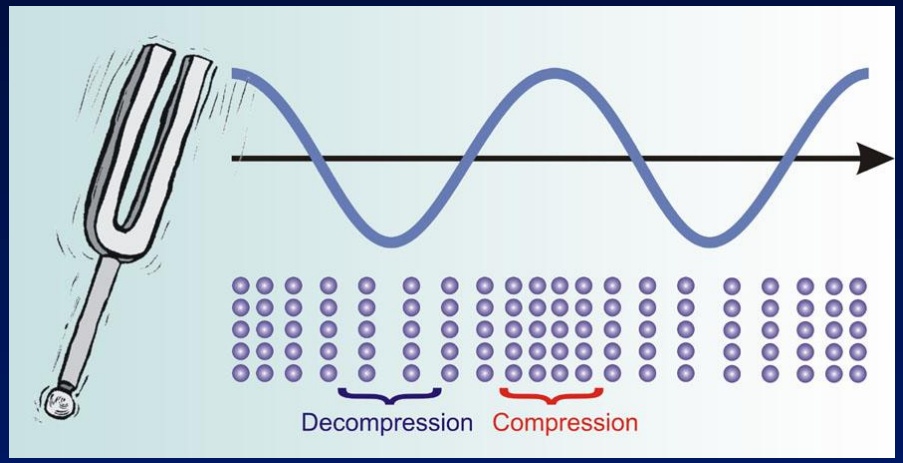
- A shockwave is a **very short acoustic pulse**.
- Very short time from ambient pressure to maximum pressure
- Typical peak pressure range: 5-100 MPa
  Negative pressure: typically -5 MPa

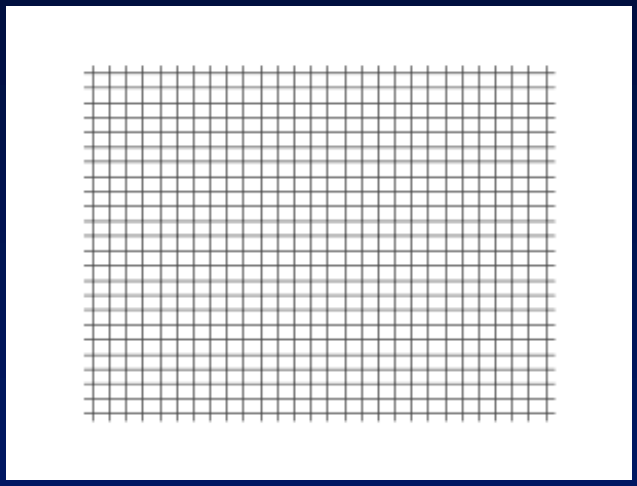


Introduction – Acoustic Waves

Shock waves* are *acoustic waves.

Well known example of acoustic waves are sound waves.





Acoustic waves propagate through a medium by alternating decompression and compression of the medium → vibration.

Acoustic waves are pressure and density variations of a medium.

Introduction – Shock Waves

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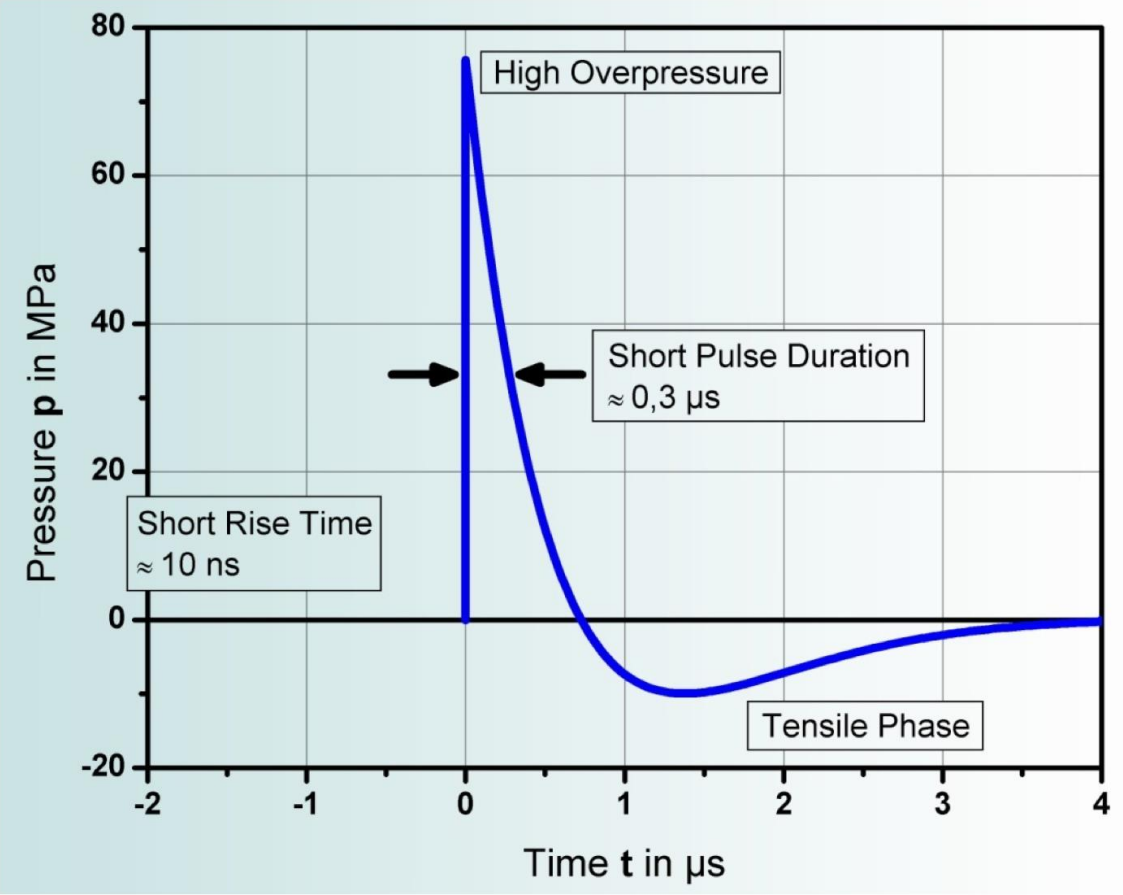
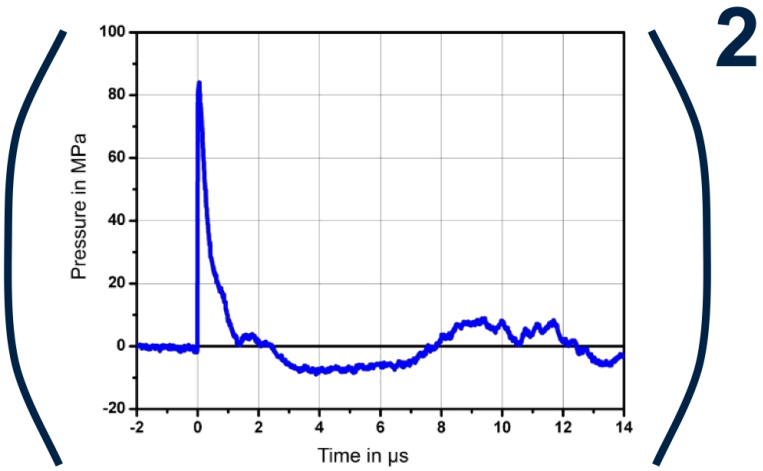
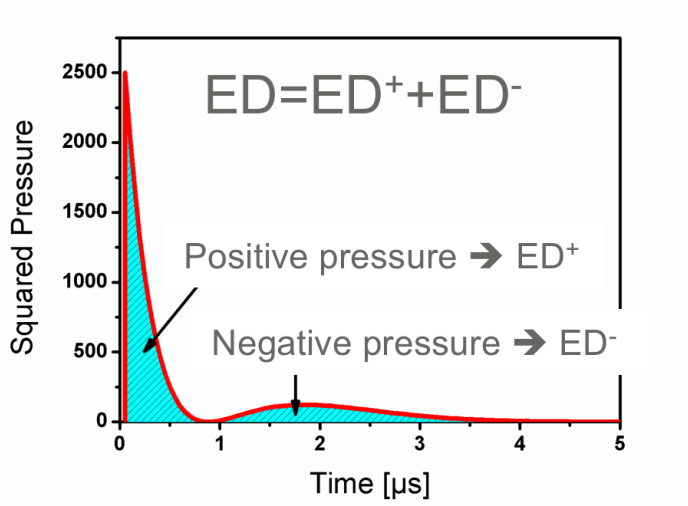


Shock wave parameter: Energy Density

The Energy Density is the total energy experienced by one mm^2 of the tissue as the entire shockwave passes through.

The measured pressure pulse p(t) is squared and integrated over time. The area under the squared pressure curve corresponds to Energy Density:





$$ED = \frac{1}{Z}\int_t p^2(t)dt \qquad Z = \rho \cdot c$$

c Speed of sound

ρ Density of the medium

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave

⇩

Mechanical Response

⇩

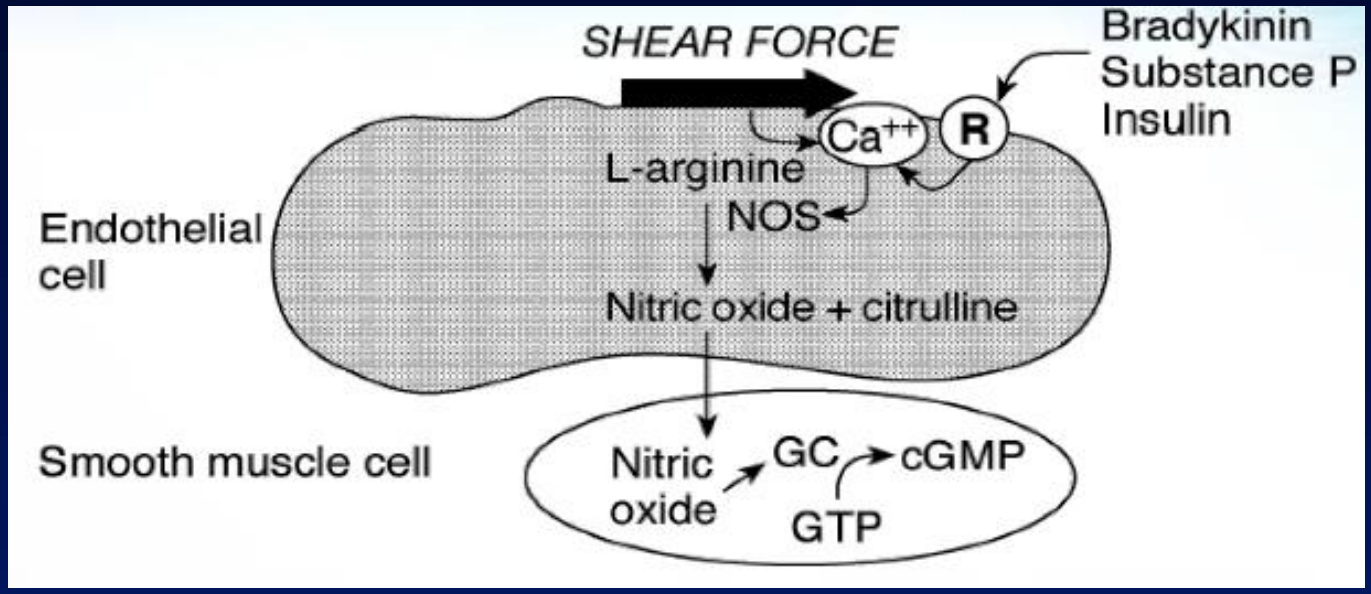
Biochemical Response

⇩

Clinical Response

⇩

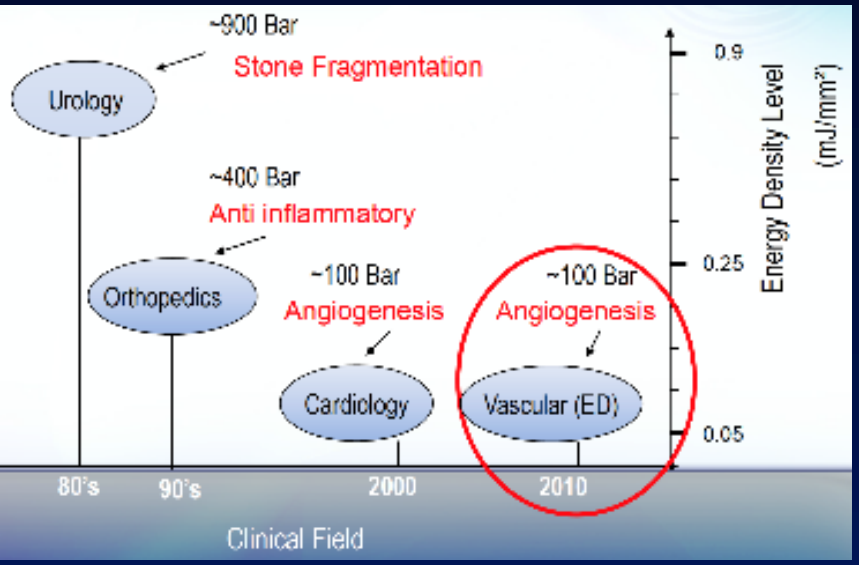
⇧ Erectile Function



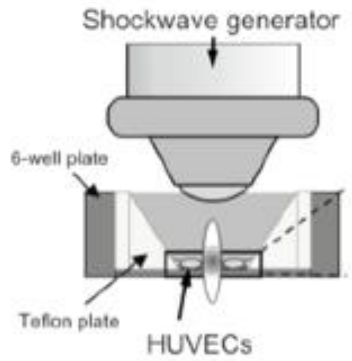
Analogy to blood flow imparting physical forces – shear stress - onto endothelial cell to cause a biochemical response (NO release)

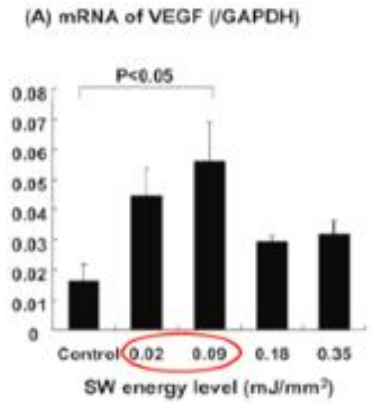
Shockwave therapy induces a mechanical – biochemical response – resulting in a clinical response

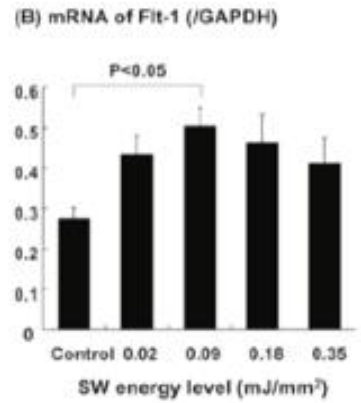
Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction



Threshold of biological effect: angiogenesis?





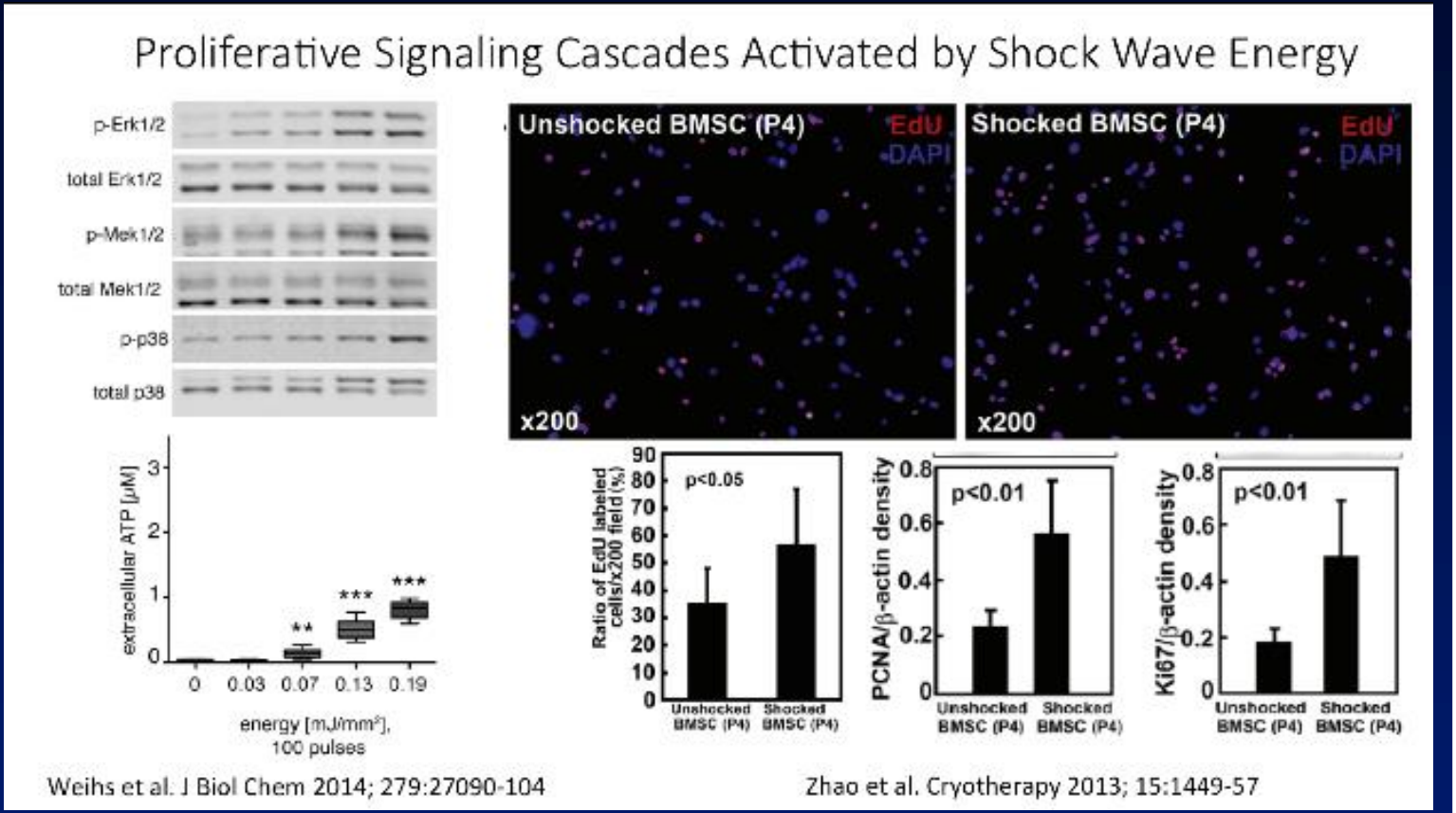


500 SWs at different ED were applied to HUVEC cells. VEGF and Flt-1 mRNA were analyzed 24h after treatment.

- Highest VEGF up-regulation observed at 0.09mJ/mm^2
- VEGF up-regulation already present at the lowest dose 0.02mJ/mm^2

- **0.9 mJ/mm^2 for stone fragmentation VERSUS 0.02 – .09 mJ/mm^2 for angiogenesis (2 - 10% lithotripsy levels)**
- **Angiogenic Growth Factors are induced by low intensity shockwave**
- **There is an optimal energy window for this response**

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction



Dose response of shock wave energy activating signaling pathways involved in cell proliferation

Shockwave therapy induces a mechanical – biochemical response – resulting in a clinical response

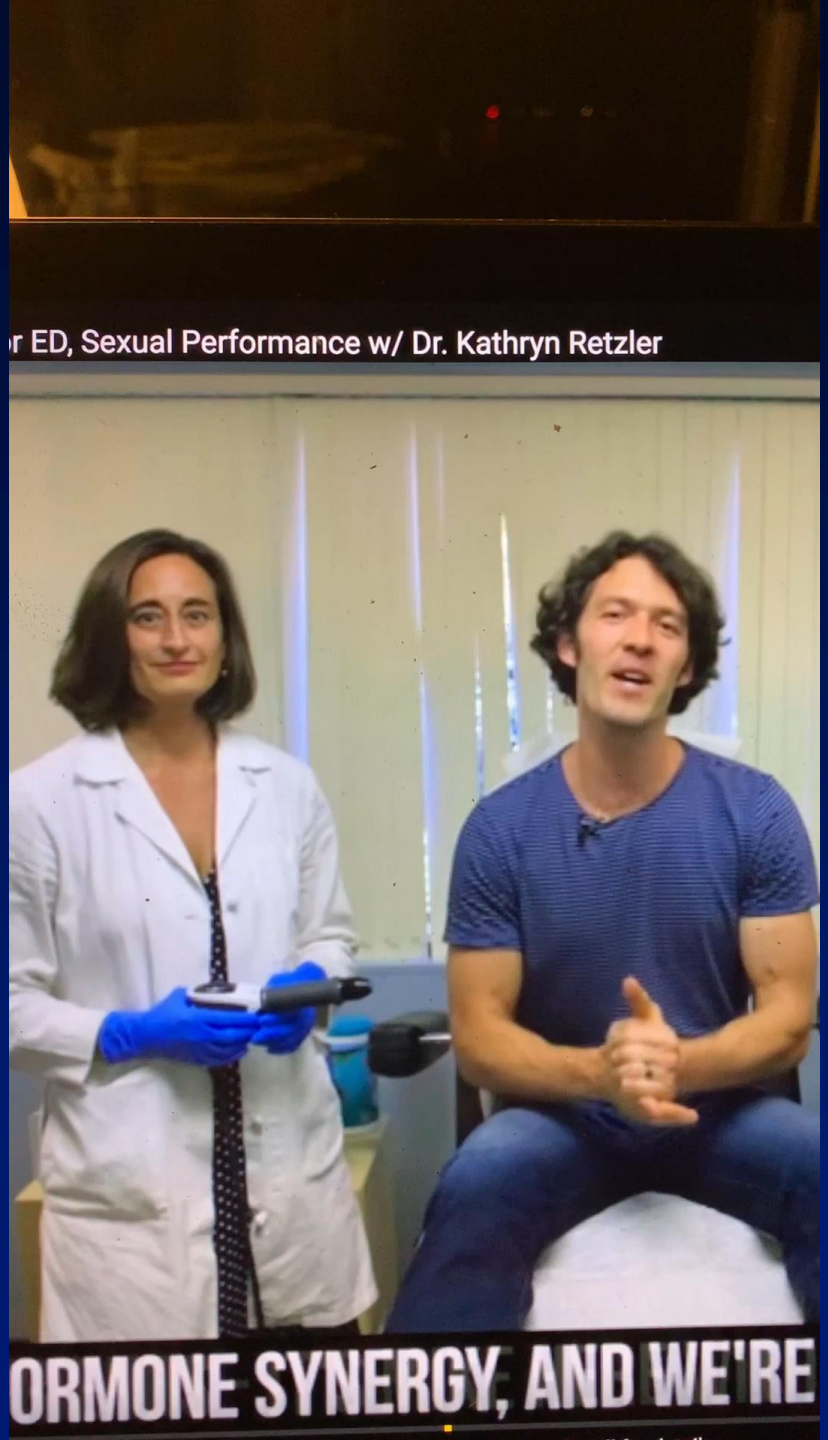
Clinical principles of shockwave therapy in medicine

What is the difference between genuine shockwaves and "imitation shockwaves"

How does shockwave therapy activate stem cells

Animal data

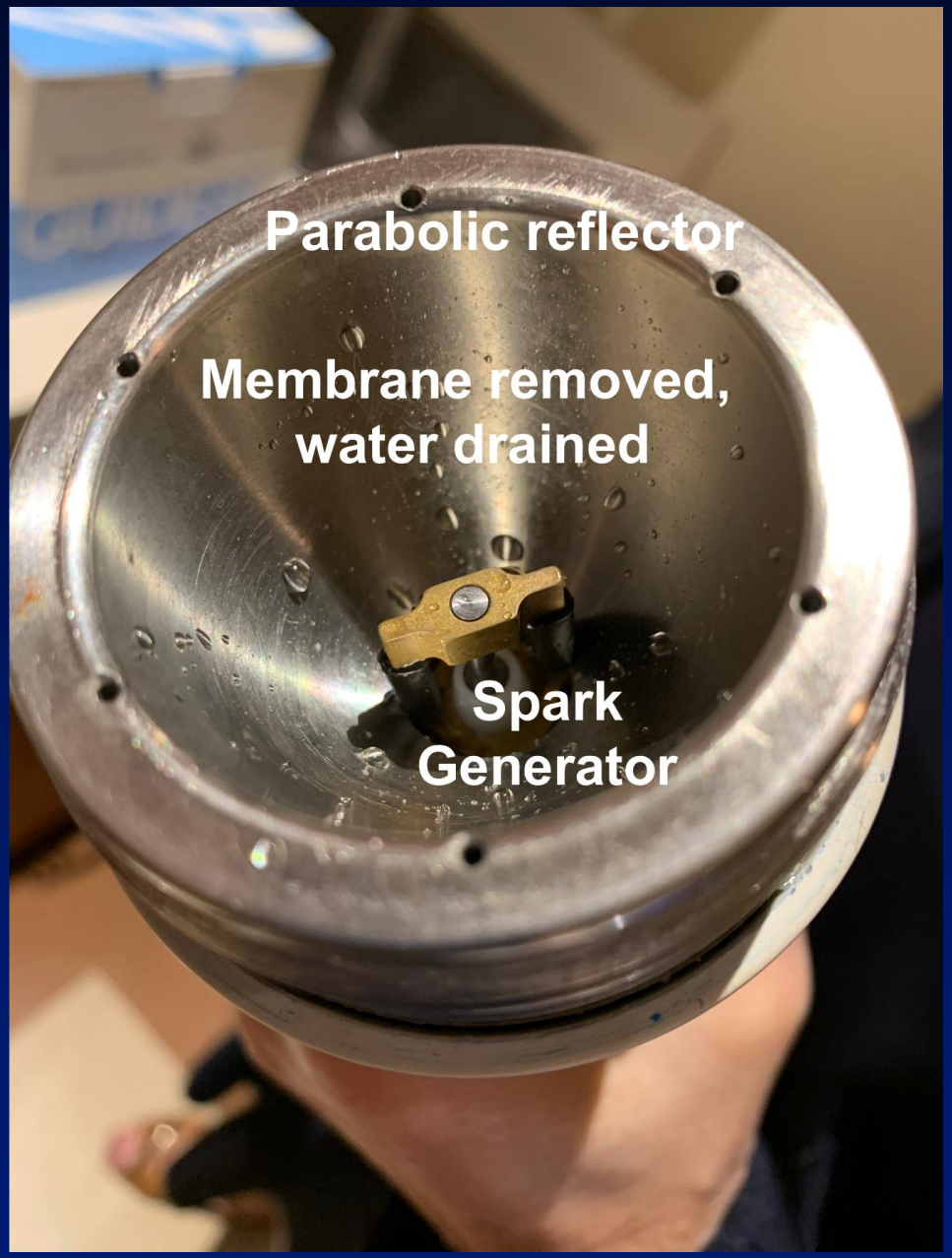
Clinical data for ED

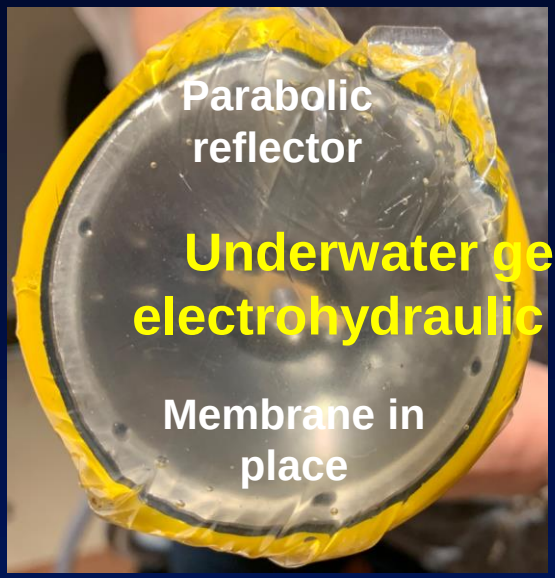

r ED, Sexual Performance w/ Dr. Kathryn Retzler
ORMONE SYNERGY, AND WE'RE

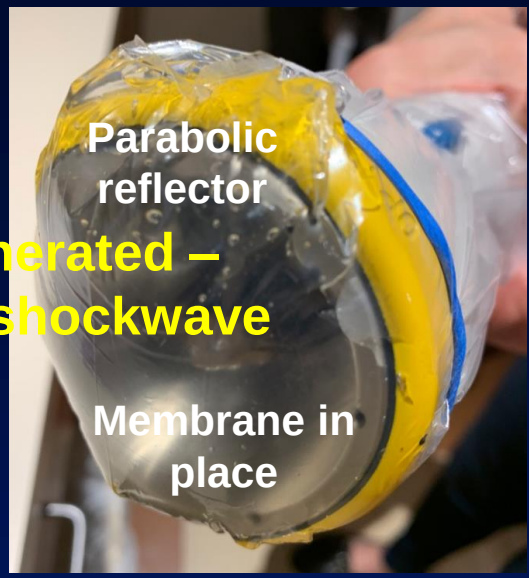
Shockwave Generators in Medicine:

- Electrohydraulic technology (EH)
  - Spark in water
- Electromagnetic technology (EMSE)
  - Coil with membrane
- Piezoelectric technology (PE)
  - Multiple piezo elements

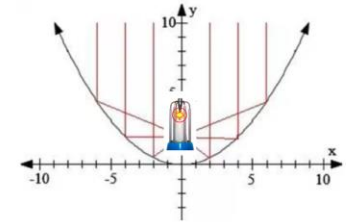
Urogold 100 MTS – Electrohydraulic Shockwaves

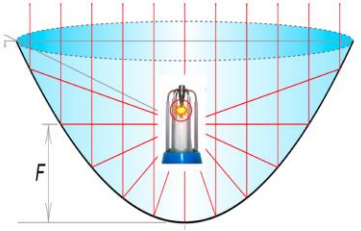






Electrohydraulic Shockwaves

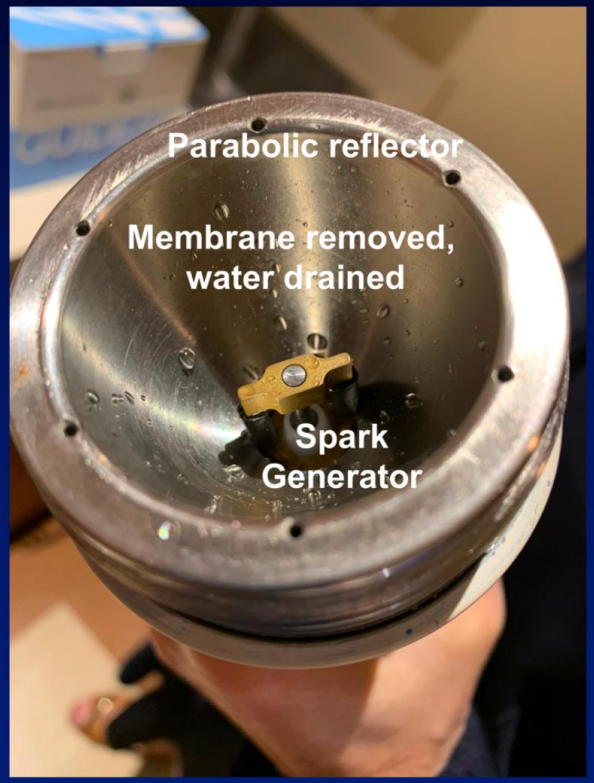


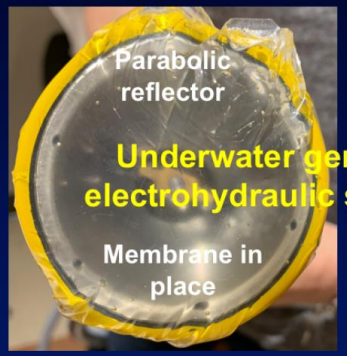


- **Underwater spark gap discharge creates a spherical shockwave**
- **Shockwave is reflected by parabola - unfocused**

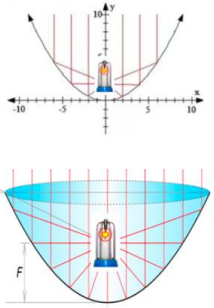
Urogold 100 MTS – Electrohydraulic Shockwaves

Urogold 100 MTS – Electrohydraulic Shockwaves





Electrohydraulic Shockwaves



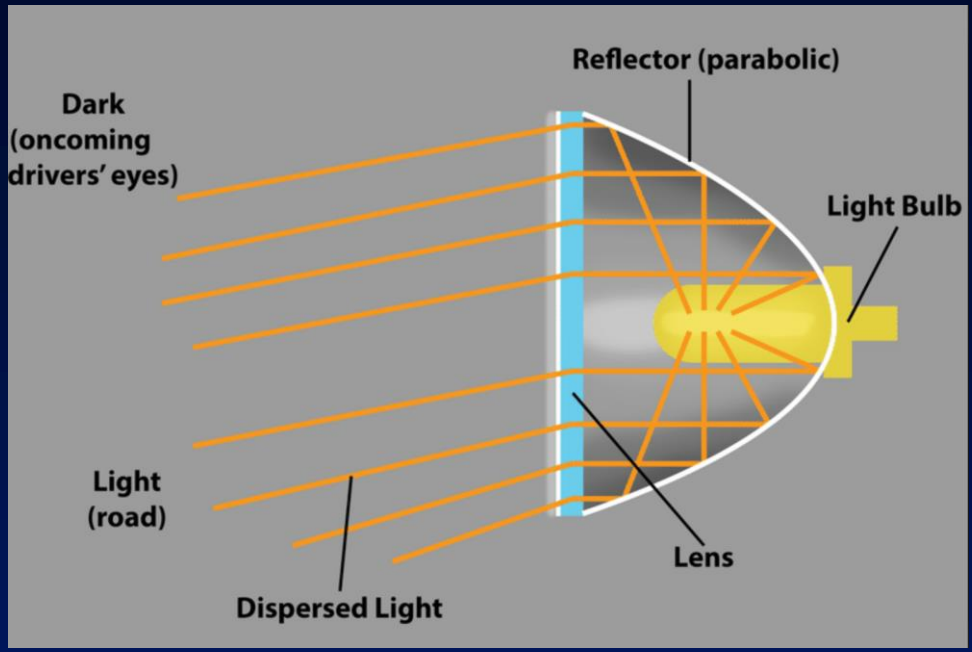
- Underwater spark gap discharge creates a spherical shockwave
- Shockwave is reflected by parabola - unfocused

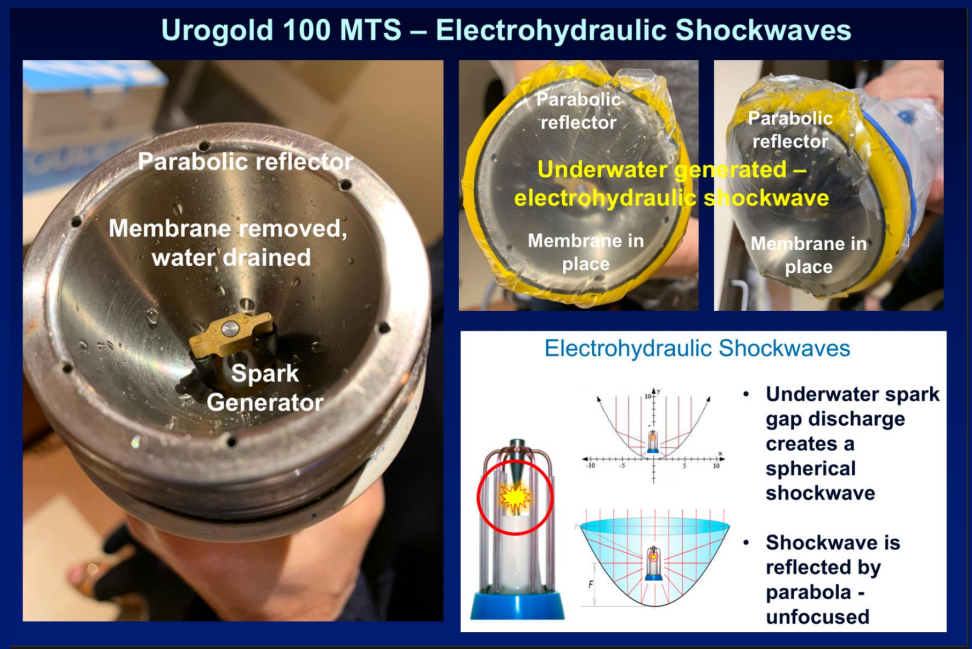
Urogold 100 MTS – Electrohydraulic Shockwaves

Parabolic reflector

Shockwave energy that originates from a point source at the focus is reflected into a parallel collimated beam, **leaving the parabola parallel to the axis of symmetry.**

This reflective property is the basis of many practical uses of parabolic reflectors (headlight).

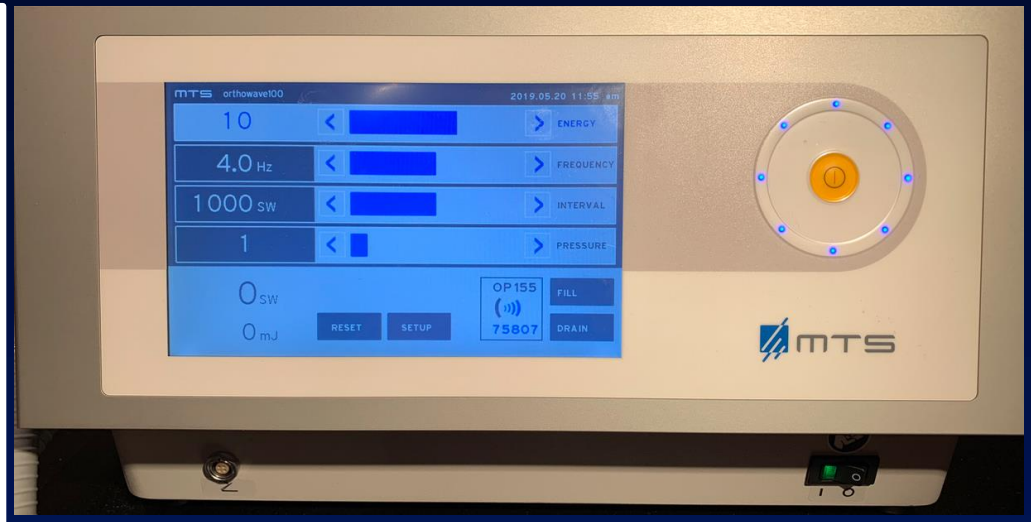


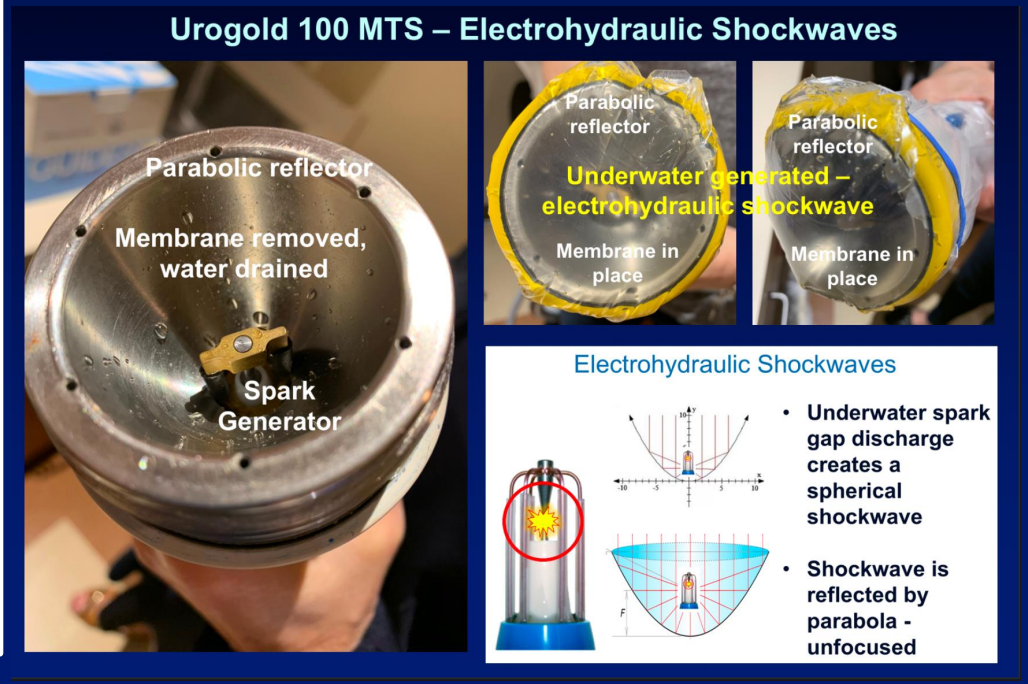


Urogold 100 MTS – Electrohydraulic Shockwaves

Urogold 100 MTS possible advantages:

1. not focused = less pain with treatments
2. not focused = higher treatment efficacy rate
3. not focused = lower re-treatment rate
4. not focused = treatments do not require anesthesia
5. not focused = larger surfaces can be treated faster and easier





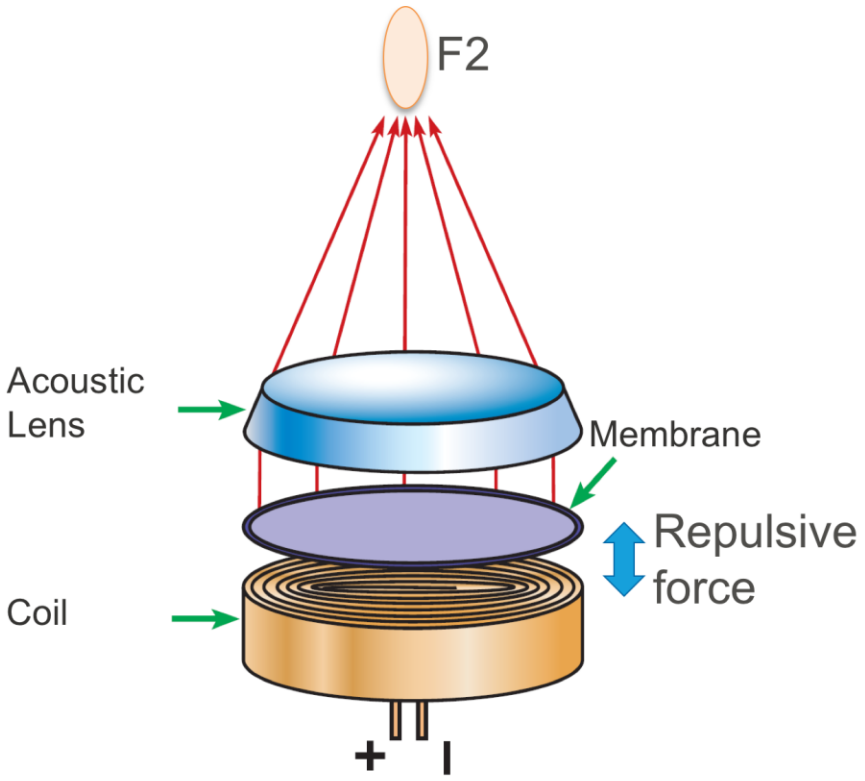
Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Electrohydraulic Shockwaves

MTS

MEDISPEC

Electromagnetic Shockwaves



- High current pulse in coil creates a magnetic field, and induces an opposing field in the overlying membrane
- Membrane is repelled, creating a pressure wave, which is focused by a lens into focal point F2

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

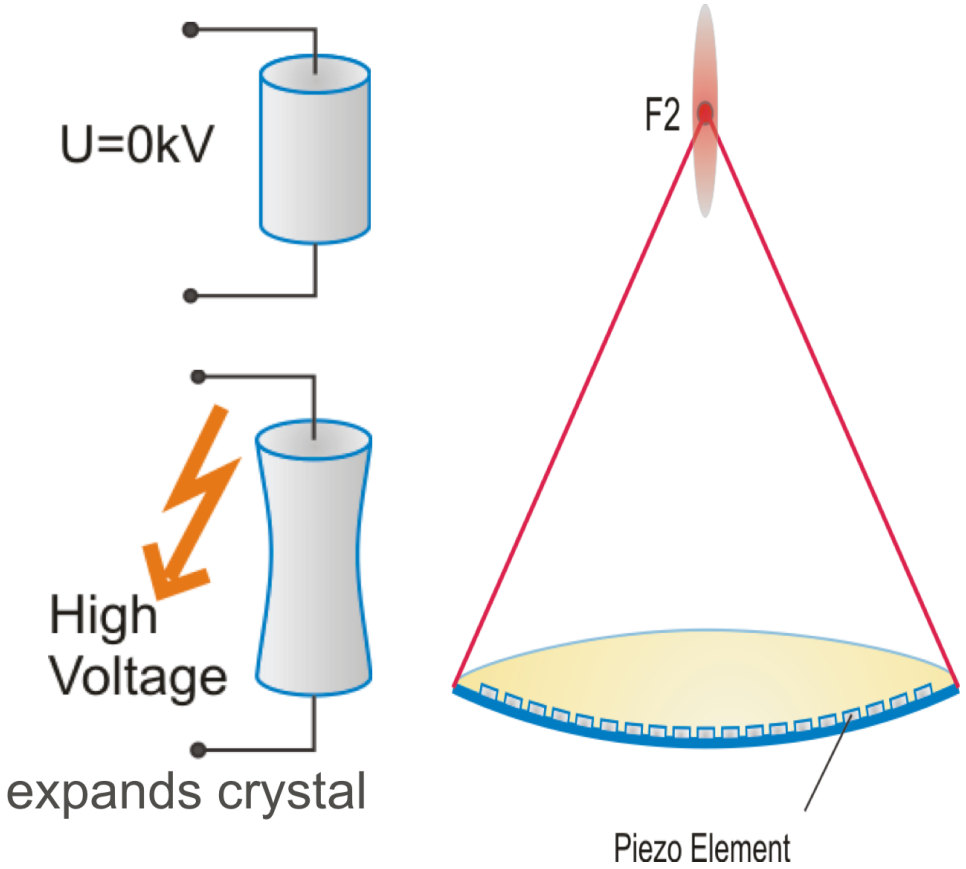
Electromagnetic Shockwaves

STORZ MEDICAL

Dornier MedTech

DiREX
DIREXGROUP

Piezoelectric Shockwaves



- Piezoelectric crystals rapidly expand with high voltage
- Excitation of multiple crystals creates a pressure wave
- Flexible shape of focus area, based on different crystal arrangements

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Piezoelectric Shockwaves

RICHARD WOLF

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

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How does shockwave therapy activate stem cells

Animal data

Clinical data for ED

Tissue Regeneration Technologies (TRT)

Effects of Low-Energy Shockwave Therapy on the Erectile Function and Tissue of a Diabetic Rat Model

Xuefeng Qiu, MD,*‡ Guiting Lin, MD, PhD,*‡ Zhongcheng Xin, MD, PhD,† Ludovic Ferretti, MD,* Haiyang Zhang, MD,* Tom F. Lue, MD,* and Ching-Shwun Lin, PhD*

*Knuppe Molecular Urology Laboratory, Department of Urology, School of Medicine, University of California, San Francisco, CA, USA; †Andrology Center, Peking University First Hospital, Beijing, China

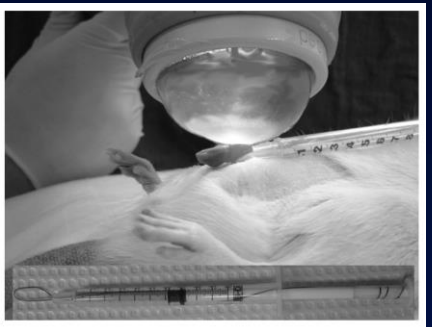


Figure 1 Shockwave application to the rat penis. Under anesthesia, the penis was drawn out of the prepuce, held in place with a loop made of suture line and syringe (shown in inset), applied with ultrasound gel, and treated with shockwave.

Shockwave Treatment

Four weeks post-STZ injection, rats in the DM+SW group were treated with shockwaves as depicted in Figure 1 and explained in the following. Under anesthesia, each rat was placed in a supine position, its lower abdomen shaved, and its penis drawn out of the prepuce and held in place with a loop made of suture line and syringe. After application of ultrasound gel (Aquasonic, Parker Laboratories, Inc, Fairfield, NJ, USA) on the penis, a shockwave applicator (DermaGold, MTS Europe GmbH, Konstanz, Germany) was placed in contact with the penis, and a total of 300 shocks were delivered at energy level of 0.1 mJ/mm2 and frequency of 120/minute. This procedure was repeated three times a week for 2 weeks, and the entire treatment course is comparable with clinical shockwave treatment for ED patients. Due to the fact that DermaGold is clinically approved to treat superficial wounds, its delivered shock- wave is expected to penetrate a few centimeters (probably the thickness of a rat penis) in the contacted area.

J Sex Med 2012

Tissue Regeneration Technologies (TRT)

Low-energy Shock Wave Therapy Ameliorates Erectile Dysfunction in a Pelvic Neurovascular Injuries Rat Model

Huixi Li,[1,2] Melanie P. Matheu,[3] Fionna Sun,[1] Lin Wang,[1,2] Melissa T. Sanford,[1] Hongxiu Ning,[1] Lia Banie,[1] Yung-chin Lee,[1,4] Zhongcheng Xin,[2] Yinglu Guo,[2] Guiting Lin,[1] and Tom F. Lue[1]

Low-energy Shockwave Treatment

For the in vivo experiment, LESW therapy was started 48 hours postoperatively. Shockwave was delivered to the pelvic region with a special probe that was attached to a compact electrohydraulic unit with a focused shockwave source (DermaGold, MTS Europe GmbH, Konstanz, Germany).

J Sex Med 2016;13:22–32

Tissue Regeneration Technologies (TRT)

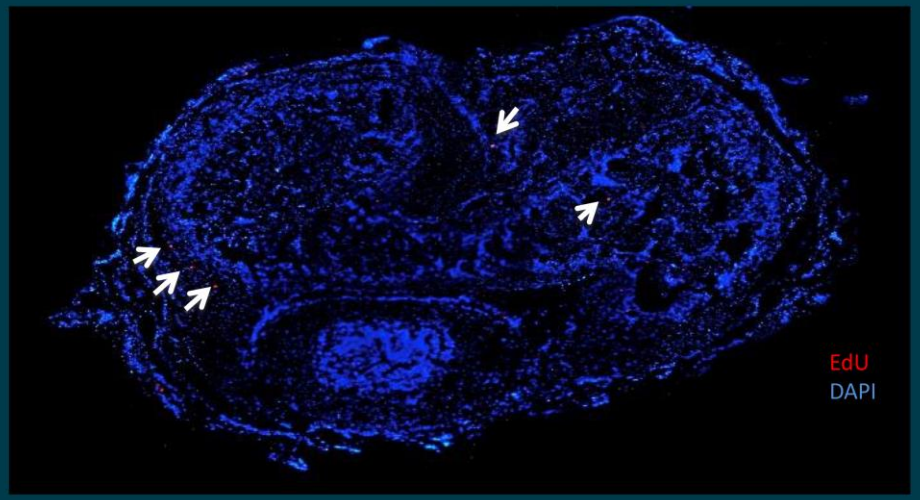
THE JOURNAL OF
SEXUAL MEDICINE

BASIC SCIENCE

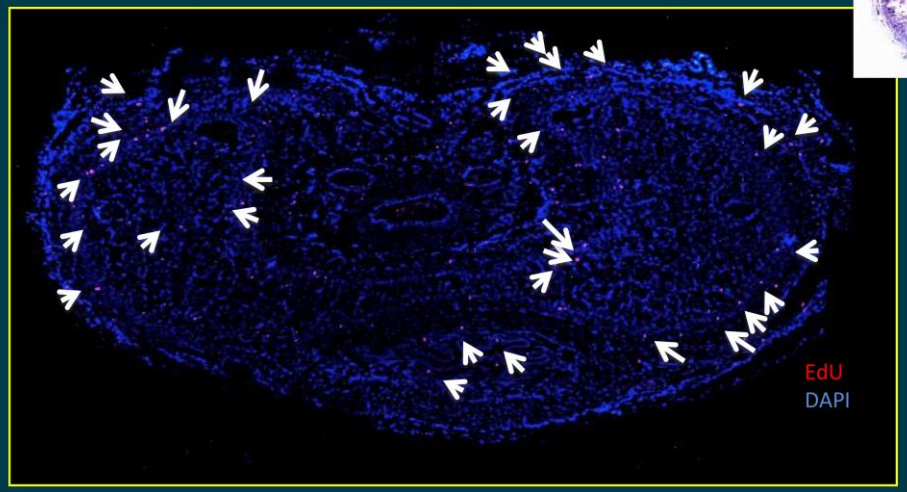
In Situ Activation of Penile Progenitor Cells With Low-Intensity Extracorporeal Shockwave Therapy

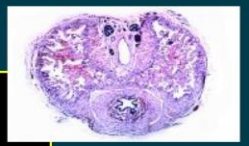
Guiting Lin, MD, PhD,[1] Amanda B. Reed-Maldonado, MD,[1] Bohan Wang, MD,[1,2] Yung-chin Lee, MD,[1,3] Jun Zhou, MD,[1,4] Zhihua Lu, MD,[1,5] Guifang Wang, MD,[1] Lia Banie, BS,[1] and Tom F. Lue, MD[1]

EdU+ cells in rat penis



EdU+ cells in rat penis after Li-ESWT





Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy induces numerous physiologic responses

Physiological Effect	Based on	Study Source
Shear stress	Shockwave exert a "cavitation effect" (inside and outside of cells) inducing localized stress on cell membranes that resembles shear stress	Maisonhaute E, Prado C, White PC. Surface acoustic cavitation understood via nanosecond electrochemistry. *Ultrason Sonochem* 2002;
NO synthesis	Shockwave cause nonenzymatic nitric oxide synthesis from L - arginine and hydrogen peroxide.	Gotte G, Amello E, Russo S. Short-time non-enzymatic nitric oxide synthesis from L-arginine and hydrogen peroxide induced by shock waves treatment. FEBS Lett 2002.
VEGF and flt-1 upregulation	SW upregulates VEGF and its receptor, Flt-1, in endothelial cells in vitro and VEGF in the ischemic myocardium in vivo.	Nishida T, Shimokawa H, Oi K, Tatewaki H. Extracorporeal cardiac shock wave therapy markedly ameliorates ischemia -induced myocardial dysfunction in pigs in vivo. *Circulation* 2004
Endothelial Progenitor Cells recruitment	Shock Wave Therapy recruits systemically infused Endothelial Progenitor Cells on a rat model of chronic limb ischemia.	Aicher A, Heeschen C, Sasaki K. Low-Energy Shock Wave for Enhancing Recruitment of Endothelial Progenitor Cells - A New Modality to Increase Efficacy of Cell Therapy in Chronic Hind Limb Ischemia. *Circulation.* 2006
Anti-inflammatory	Modulation of neuronal NOS catalytic activity, NO production, NF-κB activation, isoform NOS and TNF-alpha mRNA expression	Ciampaa AR, Marlinghause E, Suzukia H. Nitric oxide mediates anti-inflammatory action of extracorporeal shock waves. FEBS Lette 2005
Neovascularization	SW therapy induces neovascularization at tendon via upregulation of endothelial nitric oxide synthesis, VEGF, and proliferating cell antigen.	Wang CJ, Wang FS, Yang KD. Shock wave therapy induces neovascularization at the tendon-bone junction. A study in rabbits. *J Orthop Res* 2003
Local perfusion increased	Myocardial perfusion in the ischemic myocardium was improved only where the SW's were applied.	Fukumoto Y, Shimokawa H et al 2006
Vasodilatation	Shockwaves acutely reduces arterial perfusion pressure on artificially perfused rabbit	Seemann O, Rassweiler J, Chvapil M. The effect of single shock waves on the vascular system of artificially perfused rabbit kidneys. *J Stone Dis.* 1993

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Shockwave therapy induces numerous physiologic responses

hypothesis

Mechanical stimulation of SWT causes **release of microvesicles**.

The released microvesicles and their specific **micro RNA cargo** are **responsible for SWT effects**.

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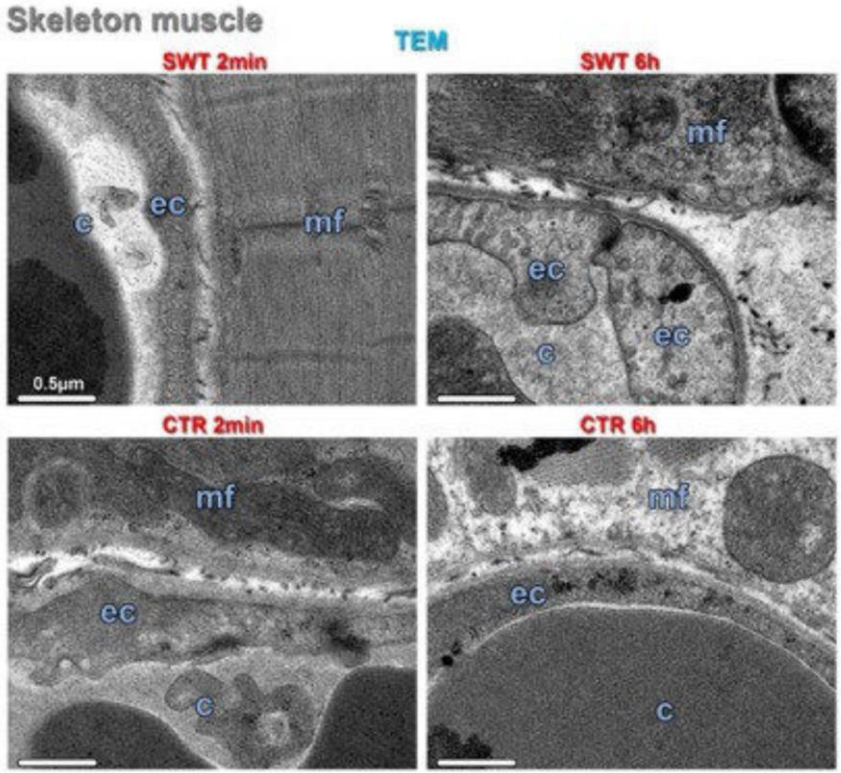
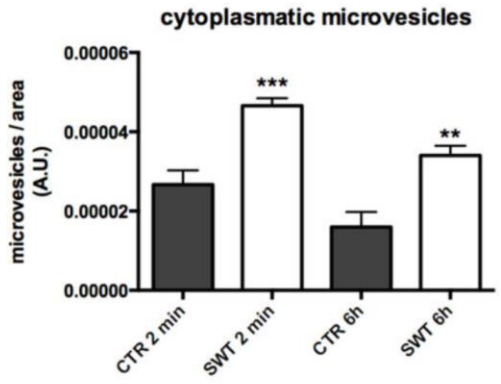
Shockwave therapy induces numerous physiologic responses

microvesicle release after SWT





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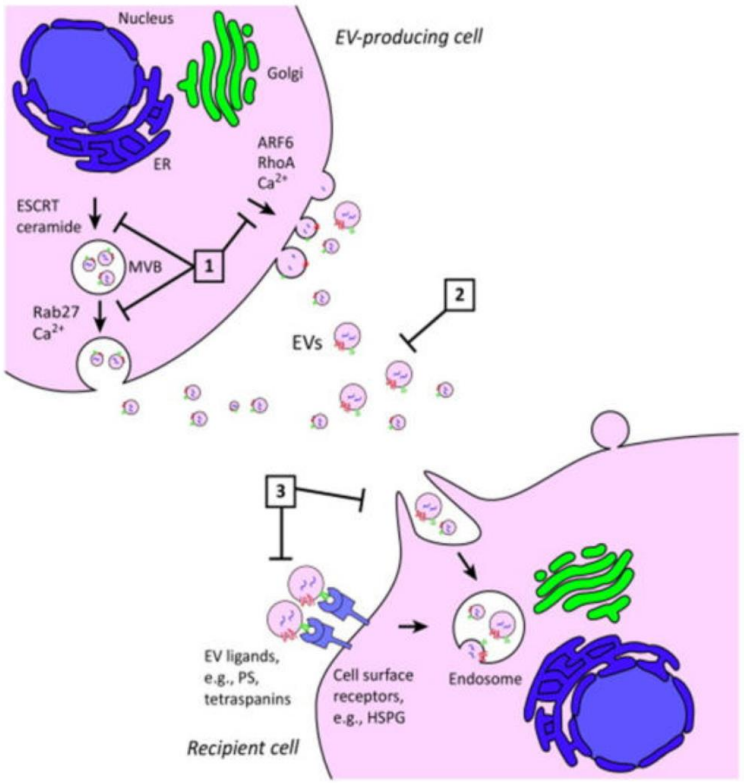
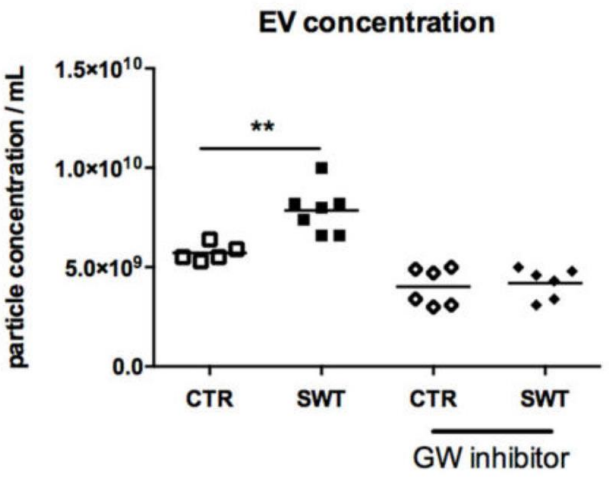
Shockwave therapy induces numerous physiologic responses

Inhibition of exosome release



Vader et al., Trends in Mol Med 2014



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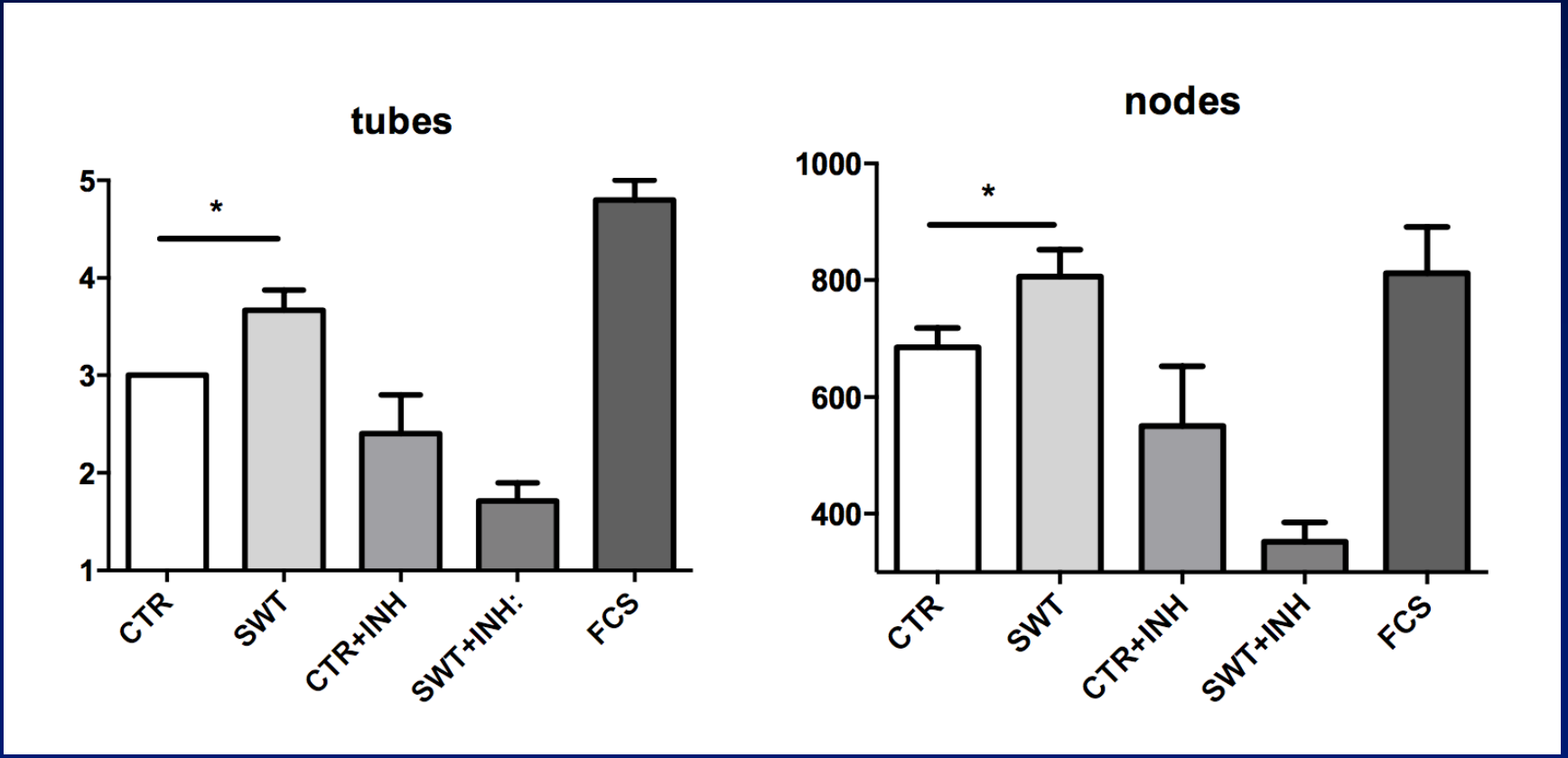
Shockwave therapy induces numerous physiologic responses

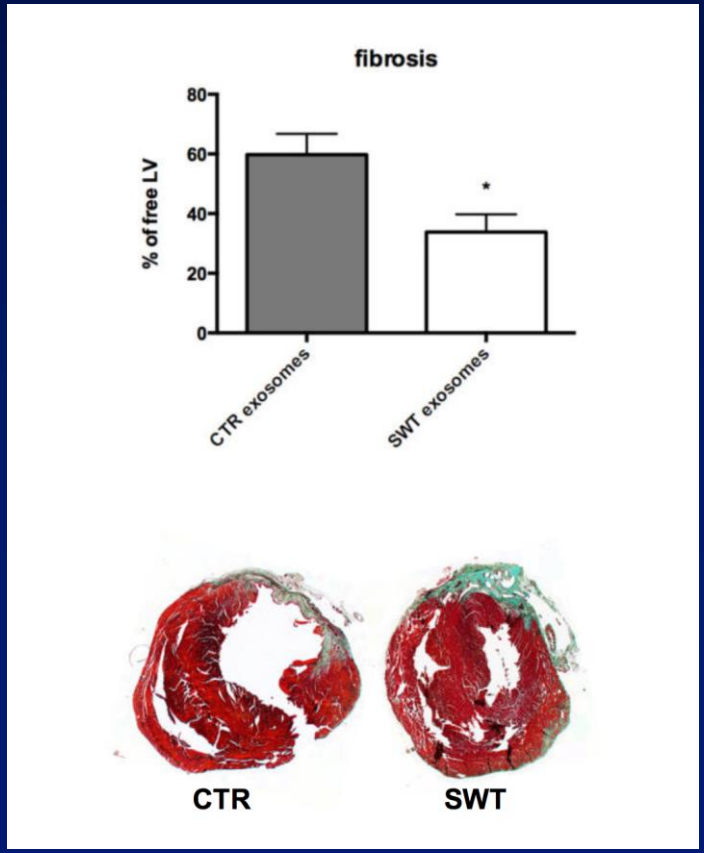
angiogenic effect of the SWT abolished upon exosome release inhibition



Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy induces numerous physiologic responses

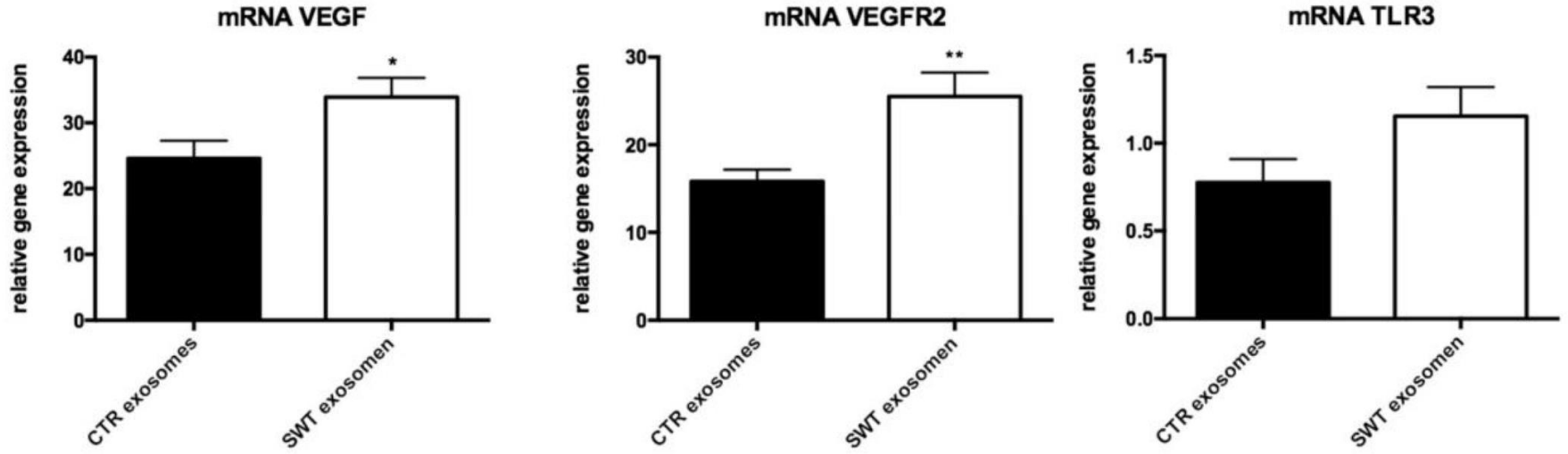
released exosomes prohibit fibrosis after myocardial infarction



Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy induces numerous physiologic responses

released exosomes induce angiogenesis after myocardial infarction

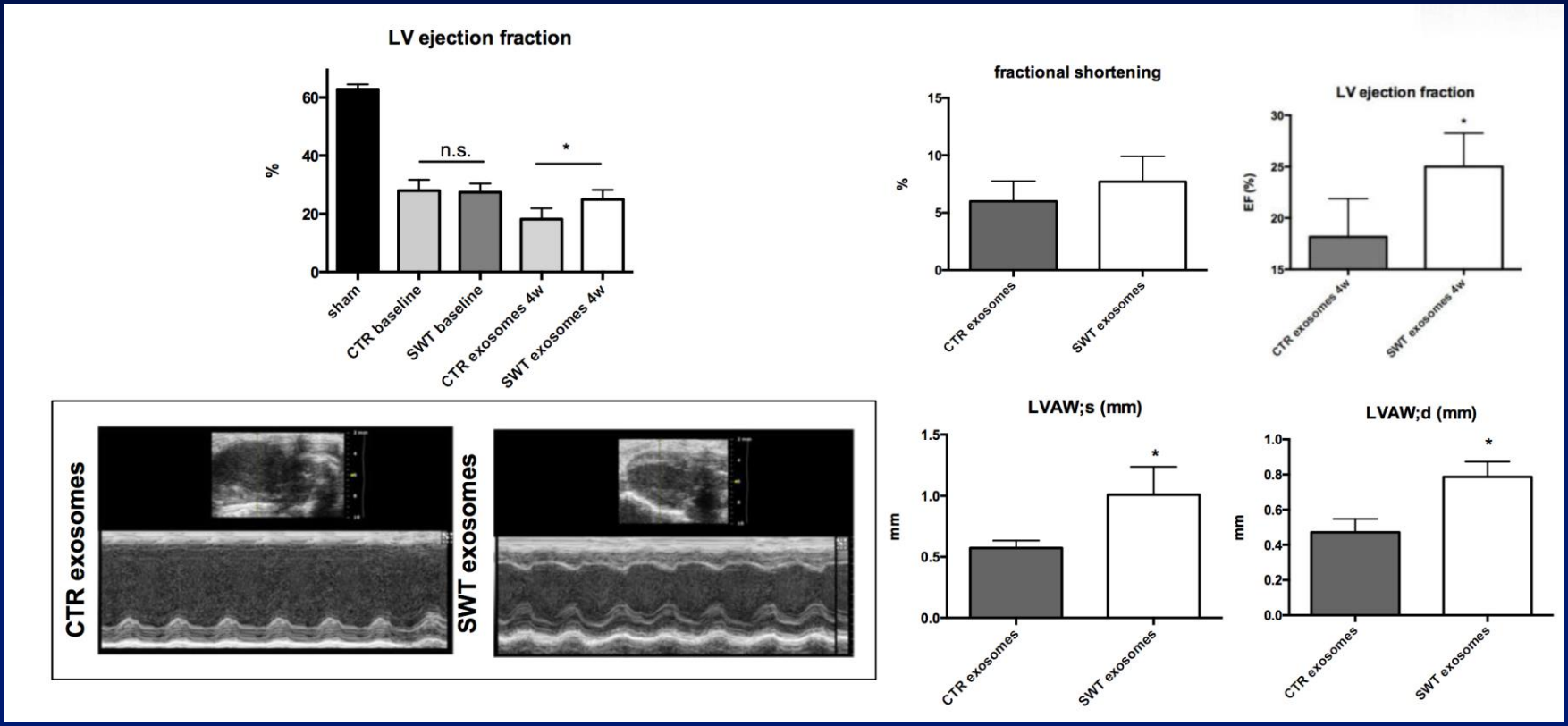


4 weeks after injection

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy induces numerous physiologic responses

released exosomes preserves cardiac function after myocardial infarction



Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Clinical principles of shockwave therapy in medicine

What is the difference between genuine shockwaves and "imitation shockwaves"

How does shockwave therapy activate stem cells

Animal data

Clinical data for ED

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy has been studied in numerous ED patients and demonstrates safety and efficacy

Management (Diagnosis and Treatment) of Erectile Dysfunction

Diagnosis of Erectile Dysfunction

- Sex Therapy Assessment
- Pelvic Floor Physical Therapy and Musculoskeletal Assessment
- History (Erection Hardness Scale) and Physical Examination (Tunical plaques, Stretched Flaccid Length)
- Endocrine Assessment
- Neurologic Assessment
- Assessment During Pharmacologic Smooth Muscle Relaxation (Erect State):
  1. Photography, Length/Girth/Goniometry
  2. Tunica albuginea thickness
  3. Cavernosal artery diameter, atherosclerosis
  4. Erectile tissue homogeneity/fibrosis (expandability)
  5. Cavernosal Artery Peak Systolic Velocity
  6. End Diastolic Velocity/Corporal Veno-occlusive Function
  7. Dynamic Infusion Cavernosometry
  8. Selective Internal Pudendal Arteriograph
  9. Rigiscan Nocturnal or In-office Penile Erection Monitoring
- CT – angiography with contrast

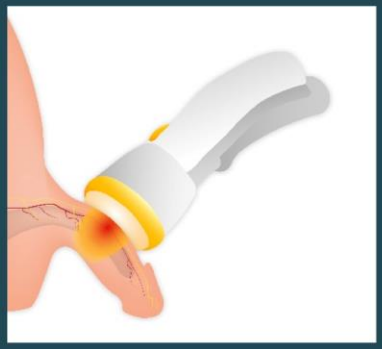
Treatment of Erectile Dysfunction

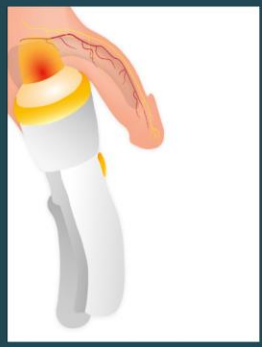
Symptomatic Treatments

- Oral Pills
- Vacuum Erection Devices
- Mechanical Constriction Devices
- Urethral Pellets
- Penile Self-injection
- Penile Prosthesis

Disease Modification Strategies

- Sex Therapy
- Physical Therapy
- Endocrine Therapy
- Neurologic Therapy
- Penile Revascularization
- Drug-Eluting Stents (IPA)
- Regenerative Stem Cell
- Platelet Rich Plasma
- Low Intensity Shockwave Therapy





The difference

	Reverse pathology	Symptom Relief	Side effects Complications	Invasiveness
Intracavernosal Injections ICI		✓	✓	
Phosphodiesterase Type 5 inhibitors PDE5i		✓	✓	
Penile prosthesis PP		✓	✓	✓
Low-intensity Extracorporeal shockwave therapy LIESWT	✓			

Shockwave therapy may one day be considered a safe and effective disease modification strategy

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy has been studied in numerous ED patients and demonstrates safety and efficacy

Technical characteristics

results of meta-analysis

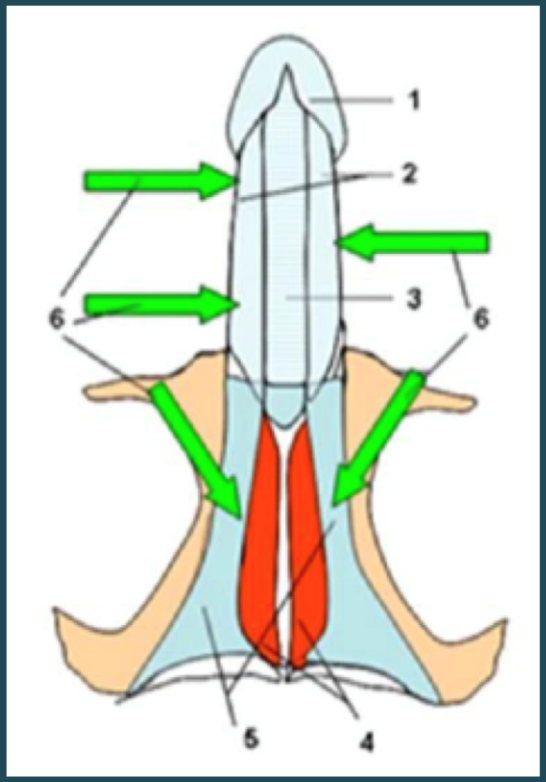
- The studies using **higher energy flux density** (EFD; >0.2 mJ/mm^2) resulted in significantly increased IIEF (mean difference [MD]: 2.86; 95% confidence interval [CI], 1.54–4.19; $p < 0.0001$)
- The improvement of IIEF was better for the group **with EFD 0.09 mJ/mm^2 compared with EFD 0.1–0.2 mJ/mm^2**, although it did not reach statistical significance.
- The studies delivering **more shock waves per treatment (5000 vs 1500) resulted in an increased IIEF** (MD: 2.86; 95% CI, 1.54–4.19; $p < 0.0001$).
- The studies **with total course of treatment <6 wk revealed significant IIEF increase** (MD: 2.11; 95% CI, 0.98–3.25; $p = 0.0003$) versus studies with longer courses of treatment (9 wk).

Lu Z, et al: Eur Urol. 2017;71(2):223-233

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Low-Intensity Shock Wave Therapy for Treatment of Vasculogenic Erectile Dysfunction: Phase 1 results of the Dornier Aries in American patients

- open-label single arm pilot study, 23 patients (IIEF-ED) scores 11-25
- 1 month PDE5i wash out - weekly sessions of Li-ESWT (5000 shocks/session - energy flux density 0.051-0.062 mJ/mm^2 – total 6 sessions
- questionnaires administered - screening, baseline, 1-mo and 3-mo FU
- no oral PDE5i 's
- minimally clinically important difference (MCID) achieved in 5 of 7 patients with mild ED (71%), and 7 of 16 patients with moderate ED (44%)
- 70% of subjects - treatment improved ability to have sexual intercourse



Pilot clinical trial in the US

San Diego Sexual Medicine

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy has been studied in numerous ED patients and demonstrates safety and efficacy

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ERECTILE FUNCTION

Low-Intensity Shockwave Therapy Improves Hemodynamic Parameters in Patients With Vasculogenic Erectile Dysfunction: A Triplex Ultrasonography-Based Sham-Controlled Trial

Dimitrios Kalyvianakis, MD, FECSM, and Dimitrios Hatzichristou, MD, PhD, FECSM

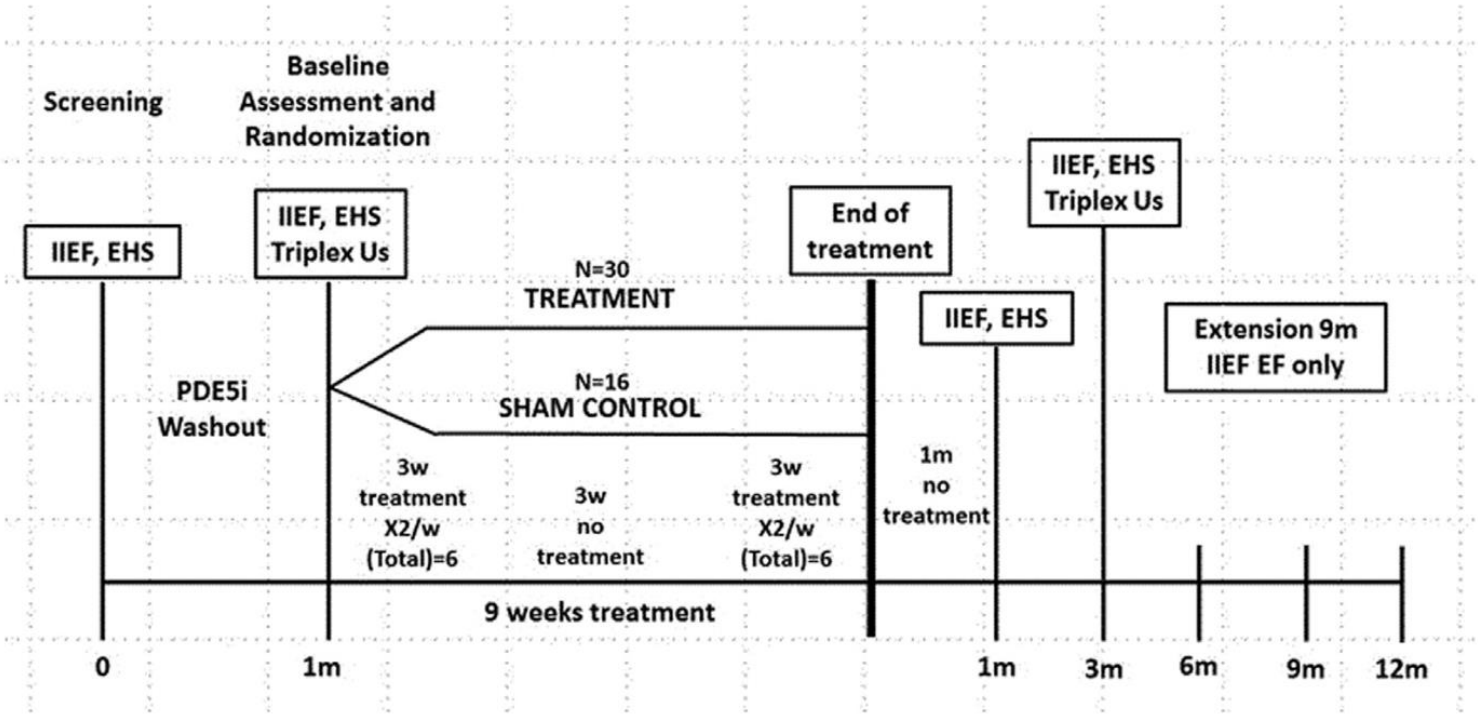

Figure 1. Study flowchart. EHS = Erection Hardness Scale; IIEF = International Index of Erectile Function; IIEF-EF = International Index of Erectile Function erectile function domain; m = months; PDE5i = phosphodiesterase type 5 inhibitor; Us = ultrasonography.

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Table 1. Baseline characteristics of study population at randomization (no phosphodiesterase type 5 inhibitor use)

	Sham	Treatment	*P* value
Men, n	16	30	
Age (y), median (range)	55.1 (38–72)	53.0 (31–72)	.52†
ED (y), median (range)	5.5 (1–15)	5.5 (1–20)	.99†
Concomitant condition, %			
Cardiovascular risk factors*	56.3	50	.69§
Diabetes mellitus	37.5	26.7	.45§
IIEF-EF domain score, mean ± SD	14.6 ± 3.4	13.8 ± 3.6	.47‡
EHSG score, mean ± SD	2.75 ± 0.45	2.95 ± 0.41	.70‡
PSV (cm/s), mean ± SD	30.7 ± 3.55	31.1 ± 3.23	.70‡
EDV (cm/s), mean ± SD	5.95 ± 1.87	5.86 ± 1.65	.86‡
RI, mean ± SD	0.81 ± 0.07	0.80 ± 0.05	.53‡

ED = erectile dysfunction; EDV = end-diastolic velocity; EHSG = Erection Hardness Grading Scale; IIEF-EF = International Index of Erectile Function erectile function domain; PSV = peak systolic velocity; RI = resistance index.

*Including at least one of the following: hypertension, metabolic syndrome, obesity, smoking, and hypercholesterolemia.

†By median test.

‡By Student t-test.

§By χ^2 test

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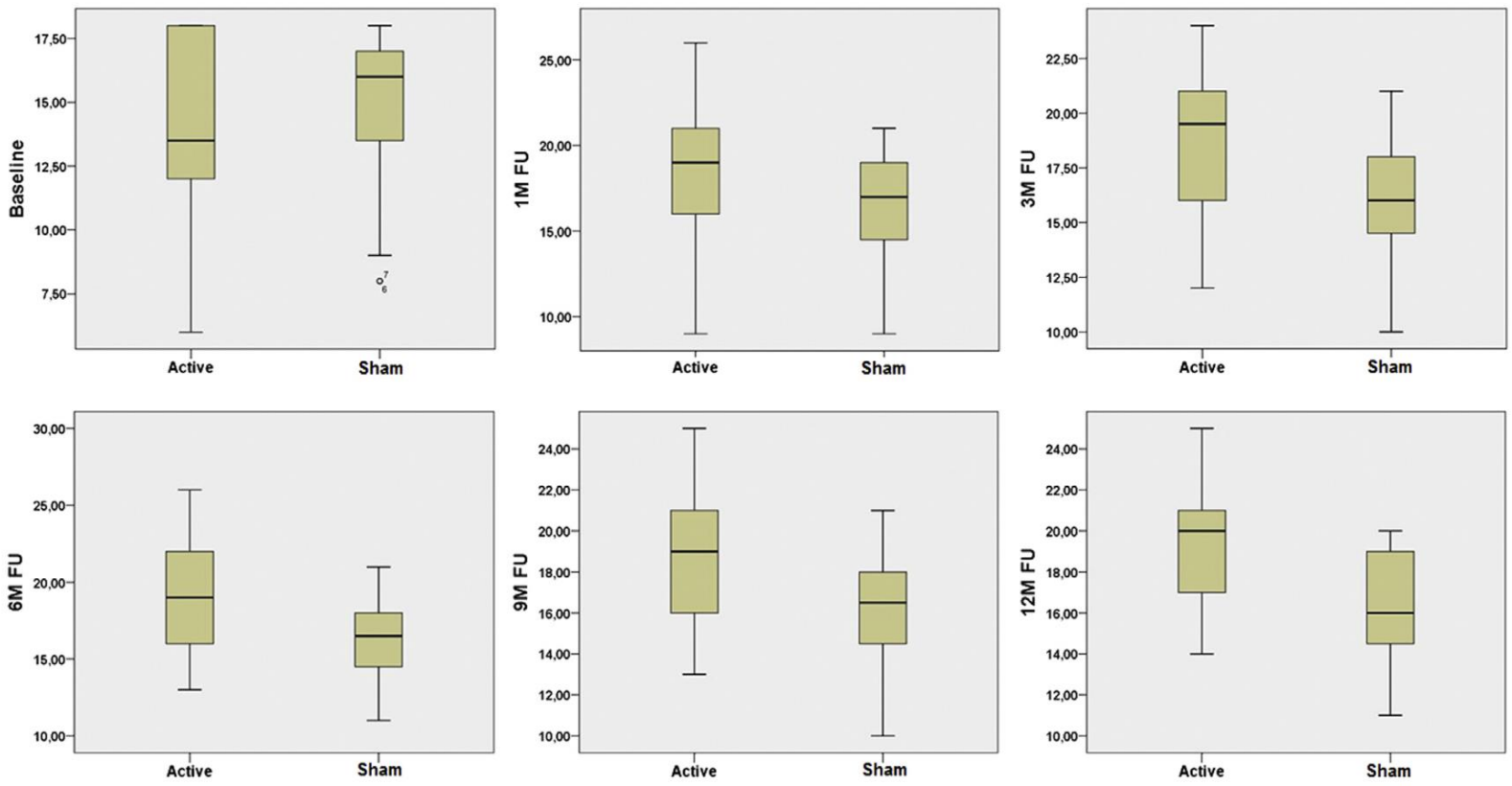

Figure 2. Twelve-month FU of International Index of Erectile Function erectile function score. All analyses were done using Student t-test. FU = follow-up; M = month. Figure 2 is available online at www.jsm.jsexmed.org.

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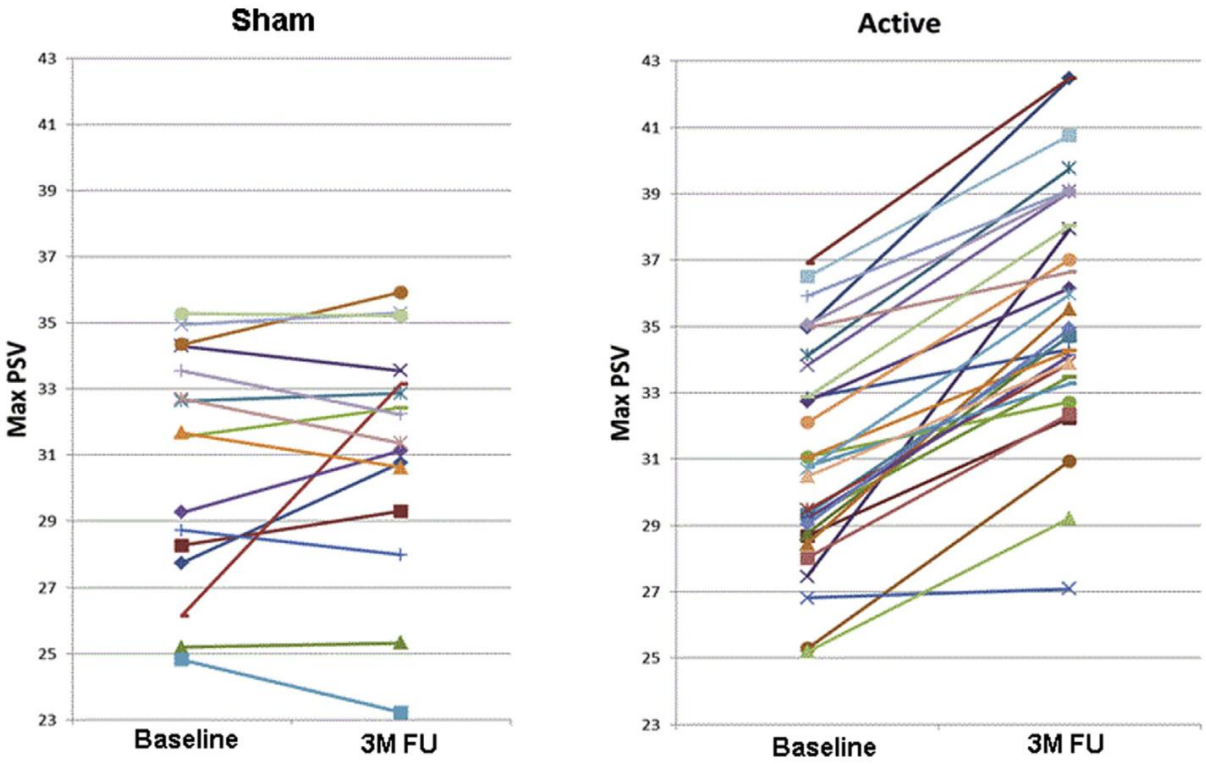

Figure 4. Individual plots of maximum PSV at baseline and at 3 months after low-intensity shockwave therapy. All but one patient showed an increase in PSV in the active group. 3M FU = 3-month follow-up; Max PSV = maximum peak systolic velocity. Figure 4 is available online at www.jsm.jsexmed.org.

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy has been studied in numerous ED patients and demonstrates safety and efficacy

Penile low intensity shock wave therapy for PDE5i non-responders suffering from vasculogenic Erectile Dysfunction since 2 to 10 years: A prospective, randomized, placebo-controlled study (2016)

Andrology Department, Fundació Puigvert / Universidad Autònoma de Barcelona, Barcelona, Spain

Curbelo, J. R. Sánchez, Álvaro Vives, Eduard Ruiz Castañé, Osvaldo Rajmil Marquenson, María Fernanda Peraza Gogoy, Daniel Moreno Mendoza, José Ignacio Vinay Barriga

Background: Several animal and human studies have evaluated the role of low-intensity extracorporeal shockwave therapy (LIST) in the management of multiple disorders such as chronic wounds, peripheral neuropathy and cardiac ischemic disease. LIST was reported to trigger a chain of events that releases angiogenic factors, recruits endothelial progenitor cells, induces neovascularization and enhances blood flow in treated areas. Recently, some studies with contradictory results have assessed the efficacy and safety of this therapy on patients suffering erectile dysfunction.

Aim: Investigate the effects of penile LIST on erectile function in long-term patients suffering from erectile dysfunction since 2-10 years and are refractory to phosphodiesterase type 5 inhibitors (PDE5i).

Methods: Prospective, randomized, simple-blind, sham-controlled study. In total 58 patients with vasculogenic erectile dysfunction refractory to PDE5i were randomized into two groups. 30 were treated with electrohydraulic low intensity shock waves (1 session/week for 6 weeks; 1,500 pulses of 0.10 mJ/mm^2 at 5 Hz, urogold100® MTS) and 28 were treated with a sham probe. Eleven patients withdrew from the study and were lost to follow-up. All patients were evaluated at baseline and 1 month after the end of treatment using validated erectile dysfunction questionnaires like the International Index of Erectile Function (IIEF-5) and the Sexual Encounter Profile (SEP). Demographic and clinical characteristics were recorded. Data analysis investigated specifically the long-term patients suffering from ED since 2-10 years, which were in total forty-one patients; 22 in the verum group, 19 in the sham group.

Results: 22 active-treated patients and 19 sham-treated patients, suffering from ED since 2-10 years were analyzed. There was no significant difference between the two groups in baseline characteristics. Baseline five-item version of the IIEF-5 mean scores, in the active and sham groups, were 10.0 ± 4 and 9.9 ± 4.6, respectively (p= 0.94). At baseline, 14% of patients in the active group (3 of 22) and 10.5% of patients in the placebo group (2 of 19) had a positive answer to the SEP 3 question (p= 0.8). One month after treatment IIEF-5 scores mean changes from baseline, in the active and placebo group, were 2.2 ± 4.9 and 0.25 ± 4.4, respectively (p= 0.2). SEP 3 positive responders increased by 33% in the active group (7 of 22) and even decreased in the placebo group to 5% (1 of 19) (p=0.03) after LIST.

Conclusion: In this prospective study, 1 month of moderate LIST treatment led to partial recovery of erectile function at one-month follow up, as the amount of positive SEP3 responders significantly increased 4 times and the average IIEF-5 score improved 8 times in the active group compared to the sham control group which, showed no placebo-effect. More studies with larger sample size and longer follow-up, comparing different lithotripters and shock wave protocols, are imperative to define alternative protocols and the role of LIST in erectile dysfunction for long term ED patients.

Baseline characteristics and statistical outcome of patients with 2-10 years ED

	Active group	Sham group	p-value (unpaired, two-tailed student`s t-test)
No. patients	22	19	
Median age (years, mean ± SD)	62.7 ± 6.5	58.8 ± 7.9	0.1
ED duration (years, mean ± SD)	4.6 ± 2.9	5.5 ± 2.6	0.29
Patients with cardiovascular risk factors (%)	19 (86%)	14 (74%)	0.32
Median IIEF-ED score baseline (mean ± SD)	10 ± 4.0	9.9 ± 4.6	0.94
Median IIEF-ED score after treatment (mean ± SD)	12.2 ± 6.1	10.2 ± 4.7	0.25
Median IIEF-ED score difference (after treatment - baseline) (mean ± SD)	2.2 ± 4.9	0.26 ± 4.4	0.2
Positive SEP-3 (%) baseline	3 (14%)	2 (10.5%)	0.8
Positive SEP-3 (%) after treatment	7 (32%)	1 (5%)	0.03
Positive SEP-3 (%) difference (after treatment - baseline)	4 (18%)	-1 (0%)	0.94

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Summary outcome of patients with 2-10 years ED:

1. **SEP-3:** Number of patients who turned from negative into positive SEP-3 response upon 1 month of LIST treatment:
- Sham group: 0, (n = 19)
- Active group: 4, (n = 21)
- → **SEP-3 increase of 400% vs. control**
  4-times more positive upon LIST compared to the control group.

2. **IIEF-ED:** Average improvement of the IIEF score upon 1 month of LIST:
- Sham group: 0.26
- Active group: 2.2
- → **IIEF-ED score increase of 829% vs. control**
  8.3-times better score in average compared to the control group.

Summary outcome of all patients that were analyzed:

1. **SEP-3:** Number of patients who turned from negative into positive SEP-3 response upon 1 month of LIST treatment:
- Sham group: 1, (n = 20)
- Active group: 5, (n = 27)
- → **SEP-3 increase of 500% vs. control**
  5-times more positive upon LIST compared to the control group.

2. **IIEF-ED:** Average improvement of the IIEF score upon 1 month of LIST:
- Sham group: 0.5
- Active group: 1.6
- → **IIEF-ED score increase of 319% vs. control**
  3.2-times better score in average compared to the control group.

Summary outcome of patients with cardiovascular risk factors (ischemic heart disease/hypertension/dislipemia) but NO diabetes mellitus:

1. **SEP-3:** Number of patients who turned from negative into positive SEP-3 response upon 1 month of LIST treatment:
- Sham group: 1, (n = 12)
- Active group: 5, (n = 16)
- → **SEP-3 increase of 500% vs. control**
  5-times more positive upon LIST compared to the control group.

2. **IIEF-ED:** Average improvement of the IIEF score upon 1 month of LIST:
- Sham group: -0.7
- Active group: 1.8
- → **IIEF-ED score increase of 180% vs. control**
  1.8-times better score in average compared to the control group.

Summary outcome of patients WITH diabetes mellitus AND cardiovascular risk factors (ischemic heart disease/hypertension/dislipemia):

Penile low intensity shock wave therapy for PDE5i non-responders suffering from vasculogenic Erectile Dysfunction since 2 to 10 years: A prospective, randomized, placebo-controlled study (2016)

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1. **SEP-3:** Number of patients who turned from negative into positive SEP-3 response upon 1 month of LIST treatment:
- Sham group: 0, (n = 8)
- Active group: 0, (n = 11)
- → **no difference between treatment and control**
2. **IIEF-ED:** Average improvement of the IIEF score upon 1 month of LIST:
- Sham group: 2.3
- Active group: 1.3
- → **SEP3 decrease of 43.3% vs. control**
  Patients suffering from diabetes mellitus did not respond to LIST treatment in this study.

ED: Erectile Dysfunction

IIEF-ED: International Index of Erectile Dysfunction – erectile function domain

LIST: Low-Intensity Extracorporeal Shockwave Therapy

SD: Standard Deviation

SEP: Sexual Encounter Profile question 3: *Did your erection last long enough for you to have successful intercourse?*

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy has been studied in numerous ED patients and demonstrates safety and efficacy

Effectiveness of shock wave therapy: implementation of a soft wide focus applicator in patients with erectile dysfunction (2016)

AUTHORS(*): Joseph P. Saffon, Juan M. Martínez, Carolina Sandoval, Hector A. Corridor.

INTRODUCTION

Low-intensity extracorporeal shock wave therapy (LI-ESWT) is of great clinical interest for the treatment of erectile dysfunction (ED), chronic pelvic pain (CPP) and Peyronie's disease. Extensive research in animal and human studies showed that the beneficial effect of LI-ESWT is due to its angiogenic properties. It is thought to stimulate neovascularization by inducing the expression of regeneration- and growth-related factors, like for example eNOS, VEGF and PCNA although the precise underlying mechanisms are not entirely clear yet. Thereby LI-ESWT can increase penile blood flow and endothelial function and represents a new, sustainable therapeutic strategy to restore erectile function, independent of, or supporting the conventional palliative medication. [1][2][3]

OBJECTIVE

Progress report on LI-ESWT in the treatment of vascular ED using a SWFA (soft wide focused applicator) handpiece for a cohort of 20 patients in a clinical center in Bogota, Columbia.

METHODS

Clinical records of patients treated at the medical centre were reviewed during the first half of 2016, with diagnosis of vascular ED and underwent a protocol of LI-ESWT once a week for 5 weeks, energy flux density 0.15mJ and 3000 pulses per session, with the MTS urogold100® and applicator OP155. Outcome measurements: Erection Hardness Score (EHS), International Index of Erectile Function, 5-item version (IIEF-5).

RESULTS

20 patients with a mean age of 53.1 ±12.1 years were included. At admission, 70% of patients had mild / moderate (n = 14), 20% (n = 4) moderate and 10% (n = 2) severe ED according to the IIEF-5 scale. After five sessions 25% (n = 5), and after one month follow-up even 45% (n = 9) of patients showed a clinical important difference (defined as an increase of ≥ 4 points) in the IIEF score with an average increase of 5 points (18 ±4.4, p= 0.001). Assessing the EHS, 55.5% of patients at baseline (mean EHS: 3 ±0.6) had an erection insufficient to penetrate, this proportion decreased significantly to 28% after therapy (mean EHS: 4 ±0.7, p = 0.05), a beneficial effect that was still persisting after one moth follow-up (mean EHS: 4 ±0.7, p = 0.04).

CONCLUSIONS

The preliminary results of LI-ESWT in the treatment of ED with the MTS urogold100® and applicator OP155 are promising and indicate a clinically significant improvement in both, the IIEF and EHS by this technology. Studies with a larger group of patients, a longer follow-up and a comparative shock wave protocol setup are necessary to further assess the statistical, clinical significance and efficacy of this improvement in erectile function upon LI-ESWT.

Effectiveness of shock wave therapy: implementation of a soft wide focus applicator in patients with erectile dysfunction

José Pablo **SAFFON** 1, *Juan Manuel* **MARTÍNEZ** 1, *Carolina* **SANDOVAL** 2, *Héctor A.* **CORREDOR** 3 1MD, Clinical Sexology, Universidad Javeriana , Bogota, Colombia; 2 Epidemiologist, Universidad El Bosque, Bogota, Colombia; 3MD, Specialist in Urology, Universidad Nacional de Colombia, Bogota, Colombia.

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OBJECTIVE

Report progress on LI-ESWT in the treatment of vascular ED using a SWFA (soft wide focused applicator) handpiece for a cohort of patients in a clinical center in Bogota, Colombia.

METHODS

Clinical records of patients treated in a Boston Medical Group centre in Bogota were reviewed during the first half of 2016, with diagnosis of vascular ED. Patients underwent a protocol of LI-ESWT once a week for 5 weeks, energy flux density 0.15mJ and 3000 pulses per session, with the MTS urogold100® and applicator OP155. Outcome measurements: Erection Hardness Score (EHS), International Index of Erectile Function, 5-item version (IIEF-5).

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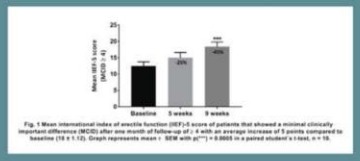
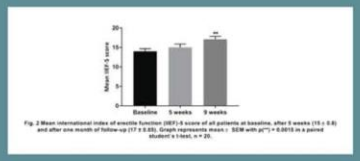
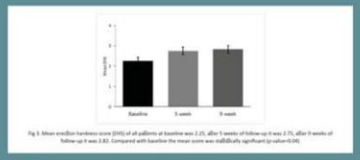






Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy has been studied in numerous ED patients and demonstrates safety and efficacy

Case Series of Weekly Low Intensity Shock Wave Therapy for Erectile Dysfunction

All Cleveland Clinic, Department of Urology, Glickman Urological and Kidney Institute
Daniel A Shoskes MD, Nic Tadros MD, Brandon Mooney PA

Background & Aim: Low Intensity Shock Wave (LiSW) has emerged as a therapy for vasculogenic erectile dysfunction (ED). Mechanism may be related to angiogenesis, release of growth factors and/or recruitment of stem cells. Several sham controlled studies have shown improvement in peak arterial velocity and efficacy in the 60-65% range depending on the definition. The initial protocol of twice weekly treatments for 3 weeks with a rest period and repeat has remained the standard, although this can be very inconvenient for patients. We wished to study the efficacy and safety of LiSW using a modified protocol of 4 weekly treatments.

Methods: Men were enrolled in this IRB approved study provided they had a diagnosis of ED for at least 6 months and were able to return for weekly treatments. Low Intensity Shockwave was delivered with the Urogold 100 machine (Tissue Regeneration Technologies, Woodstock, GA) using the soft wide focused applicator probe (figure 1). There were 6 treatment sites: one at each crus of the penis and 2 on the shaft bilaterally with about 500 shocks each for a total of 3000 shocks. Energy flux was 0.13 mJ/mm^2 and frequency was 4 Hz yielding a biologic energy density of 1560. ED severity was measured with the Sexual Health Inventory for Men (SHIM) score at baseline and 1 month following the 4 weekly treatments. Pre and post SHIM values were compared with the paired t test with significance set at $p<0.05$.

Results: Eight men enrolled with a mean age of 56.8 years (range 26-70) and median duration of 36 months (range 12-120). Five had previously tried PDE5 inhibitor (PDE5i) oral medications without adequate success. One patient stopped after 3 treatments but was included for an intent to treat analysis. The treatments were painless and there were no side effects. Overall, SHIM score improved from 11.0±3.6 to 17.2±5.2 ($p=0.01$). SHIM was unchanged in 2 patients (25%), mildly improved in 1 patient but not sufficiently for intercourse and significantly improved with erection sufficient for intercourse in 5 patients (62.5%) (figure 2). Two of these 5 men required a PDE5i for optimal erections however both had failed PDE5i in the past.

Discussion: Low Intensity Shockwave Lithotripsy with the Urogold 100 using a once a week protocol produced a similar success rate to previously published twice weekly protocols. One of the treatment failures had psychogenic ED suggesting that inclusion criteria should focus on men with an arteriogenic etiology. Whether this once weekly therapy remains durable will await longer term follow up. Since in the United States this device is not approved by the FDA and patients will need to pay cash for therapy, a protocol that minimizes time away from work and out of pocket expense is highly desirable.

Conclusion: Once weekly low intensity shock wave lithotripsy improved erections sufficient for intercourse in 62.5% of our patients without side effects.

Cleveland Clinic

Case Series of Weekly Low Intensity Shock Wave Therapy for Erectile Dysfunction

Daniel A Shoskes MD, Nic Tadros MD, Brandon Mooney PA
All Cleveland Clinic, Department of Urology, Glickman Urological and Kidney Institute

Introduction

Low Intensity Shock Wave (LiSW) has emerged as a therapy for vasculogenic erectile dysfunction (ED). Mechanism may be related to angiogenesis, release of growth factors and/or recruitment of stem cells.

Several sham controlled studies have shown improvement in peak arterial velocity and efficacy in the 60-65% range depending on the definition.

The initial protocol of twice weekly treatments for 3 weeks with a rest period and repeat has remained the standard, although this can be very inconvenient for patients. We wished to study the efficacy and safety of LiSW using a modified protocol of 4 weekly treatments.

Methods

Men were enrolled in this IRB approved study provided they had a diagnosis of ED for at least 6 months and were able to return for weekly treatments. Low Intensity Shockwave was delivered with the Urogold 100 machine (Tissue Regeneration Technologies, Woodstock, GA) using the soft wide focused applicator probe (**figure 1**). There were 6 treatment sites: one at each crus of the penis and 2 on the shaft bilaterally with about 500 shocks each for a total of 3000 shocks. Energy flux was 0.13 mJ/mm^2 and frequency was 4 Hz yielding a biologic energy density of 1560.

ED severity was measured with the Sexual Health Inventory for Men (SHIM) score at baseline and 1 month following the 4 weekly treatments. Pre and post SHIM values were compared with the paired t test with significance set at $p<0.05$.

Results

Eight men enrolled with a mean age of 56.8 years (range 26-70) and median duration of 36 months (range 12-120). Five had previously tried PDE5 inhibitor (PDE5i) oral medications without adequate success. One patient stopped after 3 treatments but was included for an intent to treat analysis. The treatments were painless and there were no side effects.

Overall, SHIM score improved from 11.0±3.6 to 17.2±5.2 ($p=0.01$). SHIM was unchanged in 2 patients (25%), mildly improved in 1 patient but not sufficiently for intercourse and significantly improved with erection sufficient for intercourse in 5 patients (62.5%) (**figure 2**). Two of these 5 men required a PDE5i for optimal erections however both had failed PDE5i in the past.

Figure 1: Urogold 100 device used in this study

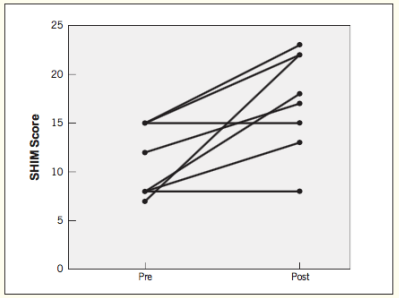


Figure 2: Change in SHIM score in individual patients before and after therapy

Discussion

Low Intensity Shockwave Lithotripsy with the Urogold 100 using a once a week protocol produced a similar success rate to previously published twice weekly protocols. One of the treatment failures had psychogenic ED suggesting that inclusion criteria should focus on men with an arteriogenic etiology.

Whether this once weekly therapy remains durable will await longer term follow up. Since in the United States this device is not approved by the FDA and patients will need to pay cash for therapy, a protocol that minimizes time away from work and out of pocket expense is highly desirable.

Conclusion

Once weekly low intensity shock wave lithotripsy improved erections sufficient for intercourse in 62.5% of our patients without side effects

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy has been studied in numerous ED patients and demonstrates safety and efficacy

Efficacy of extracorporeal shock wave therapy (ESWT) for males chronic pelvic pain syndrome: A phase III, randomized, double blind controlled with placebo study

S. Ramon Rona (PhD, MD) [1], R. A. Lorente Garin (PhD, MD), O. Bielsa Garli (PhD, MD), L. M. Romero Vargas (MD)

[1] Hospital Quiron Barcelona Physical Medicine and Rehabilitation Department, Barcelona, Spain

Introduction: Chronic Prostatitis/ Chronic Pelvic Pain Syndrome (CP/CPPS) according to NIH is genitourinary pain or discomfort lasting 3 or more months with undetectable uropathogenic bacteria.

Material & Methods: Randomized, double blind, placebo controlled study has been conducted in 40 male patients who have had CPPS. Patients were randomly assigned to receive extracorporeal shock wave therapy (ESWT) or placebo. The study was conducted together by both Urology and Rehabilitation services. The primary outcome was to assess the efficacy of extracorporeal shock wave therapy for treatment of males CPPS.

Results: 38 patients were evaluated. ESWT group improved their pain relief statistically significantly compared to placebo group (11 +/- 3.15 vs 6.31 +/- 2.55, $p < 0.05$). Also improved voiding quality as measured by IPSS score (11 +/- 2 vs 7.21 +/- 1.5, $p < 0.05$) and NIH-CPSI urinary symptoms (5 +/- 1.5 vs. 3.42 +/- 1.5, $p < 0.05$). These results were maintained until 12 week. No AEs.

Discussion: At 4 and 12 weeks, patients who received ESWT experienced improvement in pain relief, quality of life, and voiding symptoms. In the literature the patients experienced the maximum relief of their symptomatology after 4 weeks of treatment, according to our results patients have achieved an improvement even better at 12 weeks. The results obtained are similar to those reported in the bibliography. Several studies in orthopedics, urology and cardiology have shown very low rate of AEs derived from ESWT.

Conclusion: It has been demonstrated ESWT is an effective and safe treatment for CPPS. Due to high prevalence of CPPS and none specific treatment, ESWT should be considered an effective and safe treatment alternative.

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Shockwave therapy has been studied in numerous ED patients and demonstrates safety and efficacy

Case series of low intensity shock wave therapy for men with chronic prostatitis/chronic pelvic pain syndrome

Shoskes, D[1]; Mooney, B[1]

1: Cleveland Clinic, United States

Objectives: Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CPPS) is a heterogeneous syndrome. Low Intensity Shock Wave (LiSW) has emerged as a potential therapy and several sham controlled studies have shown efficacy. We wished to study the efficacy and safety of LiSW in CPPS patients with clinical phenotyping to better understand who may best respond.

Methods: Men were enrolled provided they had a diagnosis of CPPS for at least 6 months. Concurrent stable medications were not stopped. LiSW was delivered with the Urogold 100 machine (Tissue Regeneration Technologies, Woodstock, GA) at 0.14 mJ/mm^2. There were 4 treatment sites, 2 on each side of the perineum at 500 shocks each for a total of 2000 shocks. Symptom severity was measured with the National Institute of Health Chronic Prostatitis Symptom Index (CPSI) at baseline and 1 month following the 4 weekly treatments. Patients also self reported a General Response Assessment (GRA) ranging from 1 (significantly improved) to 5 (significantly worse). Patients were clinically phenotyped by the validated UPOINT system (www.upointmd.com). Pre and post CPSI values were compared with the paired t test with significance set at $p<0.05$.

Results: 14 men enrolled with a mean age of 45.1 years (range 22-67) and median duration of 36 months (range 9-240). Men had a mean of 2.6 positive UPOINT domains (range 1-5) and all but 2 had pelvic floor tenderness (domain T). Total CPSI improved from 27.7 +/- 5.4 to 19.4 +/- 7.5 ($p=0.003$). While the pain and quality of life scores improved significantly, there was no change in the urinary subscore. 9 patients (64.3%) had a >6 point drop in CPSI. By GRA, 7 patients said they were significantly improved, 2 were somewhat improved and 5 were unchanged. There were no significant differences in responders to non-responders for phenotype or symptom duration although responders had a higher starting pain score (14.0 vs 9.4, $p=0.005$) and both patients without pelvic floor spasm failed to improve.

Discussion: LiSW with the Urogold 100 using a once a week protocol improved symptoms of CP/CPPS in the majority of patients without side effects. Of note, all responders had pelvic floor spasm, and shock wave therapy is well established in the treatment of pain from neuromuscular trigger points.

Disclosure:

Work supported by industry: no. The presenter or any of the authors act as a consultant, employee (part time or full time) or shareholder of an industry.

Case Series of Low Intensity Shock Wave Therapy for Men with Chronic Prostatitis/Chronic Pelvic Pain Syndrome

Daniel A Shoskes • Brandon Mooney

Cleveland Clinic

Glickman Urologic and Kidney Institute,
Department of Urology

Introduction

- Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CPPS) is a heterogeneous syndrome that is often challenging to treat.
- Low Intensity Shock Wave (LiSW) has emerged as a potential therapy and several sham controlled studies have shown efficacy.
- We wished to study the efficacy and safety of LiSW in CPPS patients with clinical phenotyping to better understand who may best respond.

Methods

- Men were enrolled in this IRB approved study provided they had a diagnosis of CPPS for at least 6 months and were able to return for weekly treatments. Those on multi-modal therapy continued other therapies as long as the dose was stable.
- LiSW was delivered with the Urogold 100 machine (Tissue Regeneration Technologies, Woodstock, GA) using the standard probe. **Figure 1**
- There were 4 treatment sites, 2 on each side of the perineum at 500 shocks each for a total of 2000 shocks.
- Symptom severity was measured with the National Institute of Health Chronic Prostatitis Symptom Index (CPSI) at baseline and 1 month following the last treatment. Patients also self reported a General Response Assessment (GRA) ranging from 1 (significantly improved) to 5 (significantly worse).
- Patients were clinically phenotyped by the UPOINT system (www.upointmd.com).
- Pre and post values were compared with the paired t test with significance set at $p<0.05$.

Results

- 14 men enrolled with a mean age of 45.1 years (range 22-67) and median duration of 36 months (range 9-240).
- Men had a mean of 2.6 positive UPOINT domains (range 1-5) and all but 2 had pelvic floor tenderness (domain "T").
- Total CPSI improved from 27.7 ± 5.4 to 19.4 ± 7.5 ($p=0.003$).
- While the pain and quality of life scores improved significantly, there was no change in the urinary subscore. **Figure 2**
- 9 patients (64.3%) had a >6 point drop in CPSI. **Figure 3**
- By GRA, 7 patients said they were significantly improved, 2 was somewhat improved and 5 were unchanged. There were no significant differences in responders to non-responders for phenotype or symptom duration although responders had a higher starting pain score (14.0 vs 9.4, $p=0.005$) and both patients without pelvic floor spasm failed to improve.

Figures

Figure 1: Device used in this study

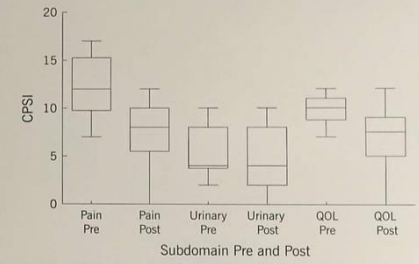


Figure 2: Box plot of mean CPSI (total and subscores) before and after therapy

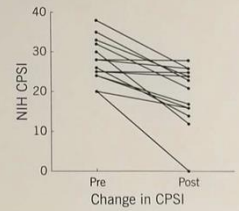


Figure 3: Change in total CPSI after therapy by individual patient

Conclusion

Once weekly low intensity shock wave lithotripsy improved the symptoms of CP/CPPS in the majority of patients without side effects. This treatment may be most effective in those with pelvic floor spasm and less effective for men with mostly urinary symptoms.

Low Intensity Shock Wave Therapy: Regenerative Therapy for Erectile Dysfunction

Clinical principles of shockwave therapy in medicine

What is the difference between genuine shockwaves and "imitation shockwaves"

How does shockwave therapy activate stem cells

Animal data

SDSM Shockwave Therapy Protocols

SDSM Shockwave Therapy Protocols

Erectile Dysfunction – Penile Shockwave Therapy

LUTS/PE– Perineal Shockwave Therapy

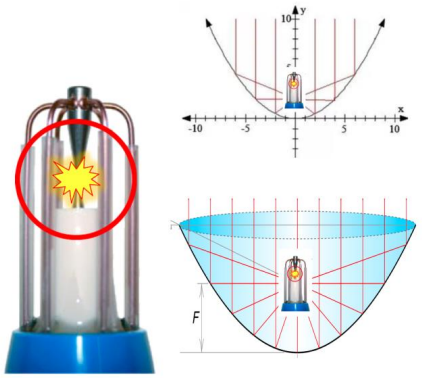
Peyronie's Disease– PD Shockwave Therapy

Radiculopathy of Sacral Spinal Nerve Root – Lumbosacral Shockwave Therapy

Vestibulodynia – Vestibular Shockwsve Therapy

Urogold 100 MTS – Electrohydraulic Shockwaves

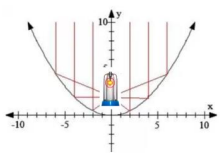
Electrohydraulic Shockwaves

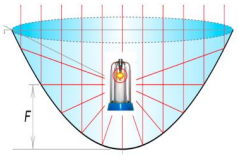


- Underwater spark gap discharge creates a spherical shockwave
- Shockwave is reflected by parabola - unfocused

Urogold 100 MTS – Electrohydraulic Shockwaves

Electrohydraulic Shockwaves

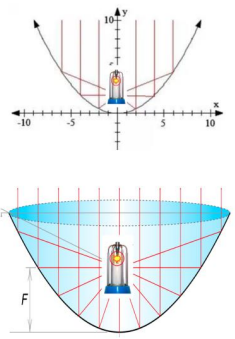




- **Underwater spark gap discharge creates a spherical shockwave**
- **Shockwave is reflected by parabola - unfocused**

Urogold 100 MTS – Electrohydraulic Shockwaves

Electrohydraulic Shockwaves



- **Underwater spark gap discharge creates a spherical shockwave**
- **Shockwave is reflected by parabola - unfocused**

Urogold 100 MTS – Electrohydraulic Shockwaves

A SINGLE-BLIND, SHAM-CONTROLLED, RANDOMIZED, PROSPECTIVE STUDY CHARACTERIZING ERECTILE TISSUE ULTRASOUND CHANGES RESULTING FROM LOW INTENSITY PENILE SHOCKWAVE TREATMENT WITH UROGOLD 100TM

Applicator OP 155; 4 HZ; Membrane level 1

Rx 1 = 5000 shocks

Rx 2, 3 = 3000 shocks

3 weeks no Rx

Rx 4 = 5000 shocks

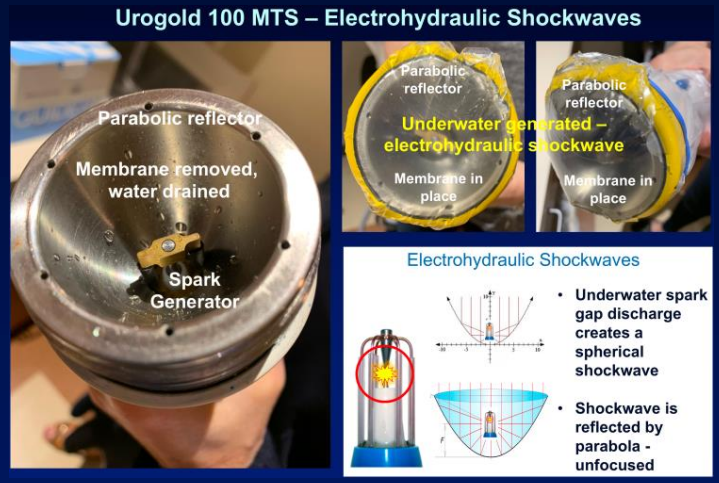
Rx 5, 6 = 3000 shocks

Rx 1 and Rx 4

	ENERGY SETTING	NUMBER OF SHOCKS
Right hilum	0.10 - 12 mJ/mm2	500
Left hilum	0.10 - 12 mJ/mm2	500
Right penile shaft	0.10 - 12 mJ/mm2	1000
Left penile shaft	0.10 - 12 mJ/mm2	1000
Right crus	0.10 - 12 mJ/mm2	1000
Left crus	0.10 - 12 mJ/mm2	1000
	TOTAL SHOCKS	5000

Rx 2, 3 and Rx 5, 6

Right hilum	0.10 - 12 mJ/mm2	300
Left hilum	0.10 - 12 mJ/mm2	300
Right penile shaft	0.10 - 12 mJ/mm2	600
Left penile shaft	0.10 - 12 mJ/mm2	600
Right crus	0.10 - 12 mJ/mm2	600
Left crus	0.10 - 12 mJ/mm2	600
	TOTAL SHOCKS	3000



Urogold 100 MTS – Electrohydraulic Shockwaves

TRT Protocol for ED

Applicator OP 155; 4 HZ; Membrane level 1

Rx 1 = 5000 shocks

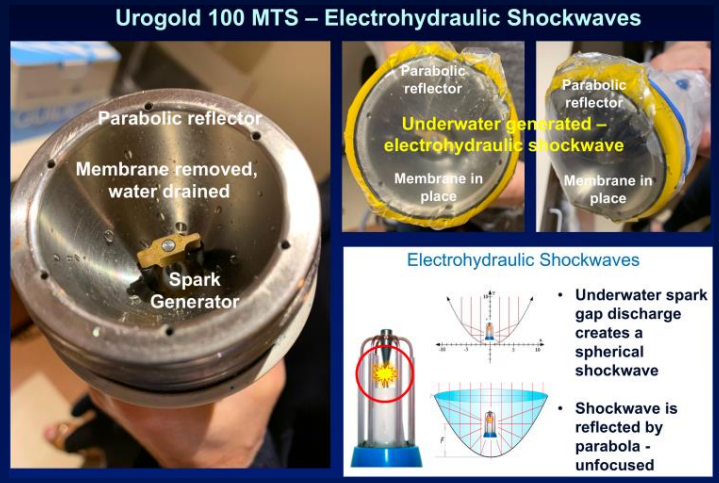
Rx 2, 3, 4, 5, 6 = 2500 shocks

Rx 1

	ENERGY SETTING	NUMBER OF SHOCKS
Right hilum	0.10 - 12 mJ/mm2	500
Left hilum	0.10 - 12 mJ/mm2	500
Right penile shaft	0.10 - 12 mJ/mm2	1000
Left penile shaft	0.10 - 12 mJ/mm2	1000
Right crus	0.10 - 12 mJ/mm2	1000
Left crus	0.10 - 12 mJ/mm2	1000
	TOTAL SHOCKS	5000

Rx 2, 3, 4, 5, 6

Right hilum	0.10 - 12 mJ/mm2	250
Left hilum	0.10 - 12 mJ/mm2	250
Right penile shaft	0.10 - 12 mJ/mm2	500
Left penile shaft	0.10 - 12 mJ/mm2	500
Right crus	0.10 - 12 mJ/mm2	500
Left crus	0.10 - 12 mJ/mm2	500
	TOTAL SHOCKS	2500



Urogold 100 MTS – Electrohydraulic Shockwaves

ED - SDSM Protocol for Penile Shockwave Therapy

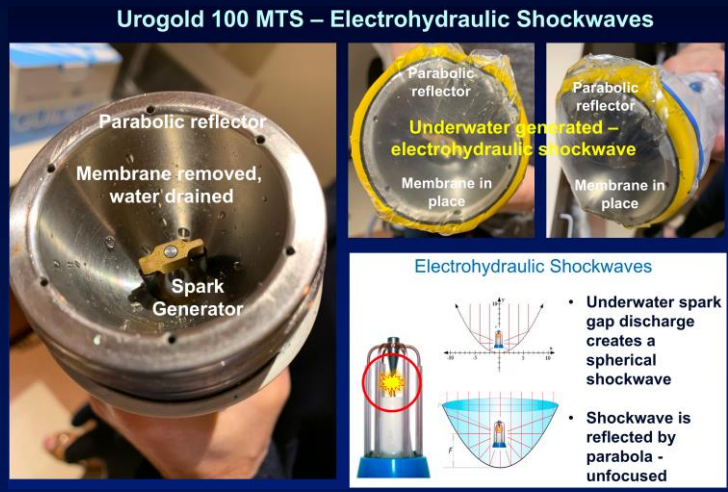
Applicator OP 155; 3HZ; Membrane level 1

Cycle 1: Rx's #1, #2, #3, #4, #5, #6 over the most convenient time period for the patient. May take a few weeks to a few months

GRAYSCALE/DUPLEX DOPPLER in 8 wks following 6th Rx

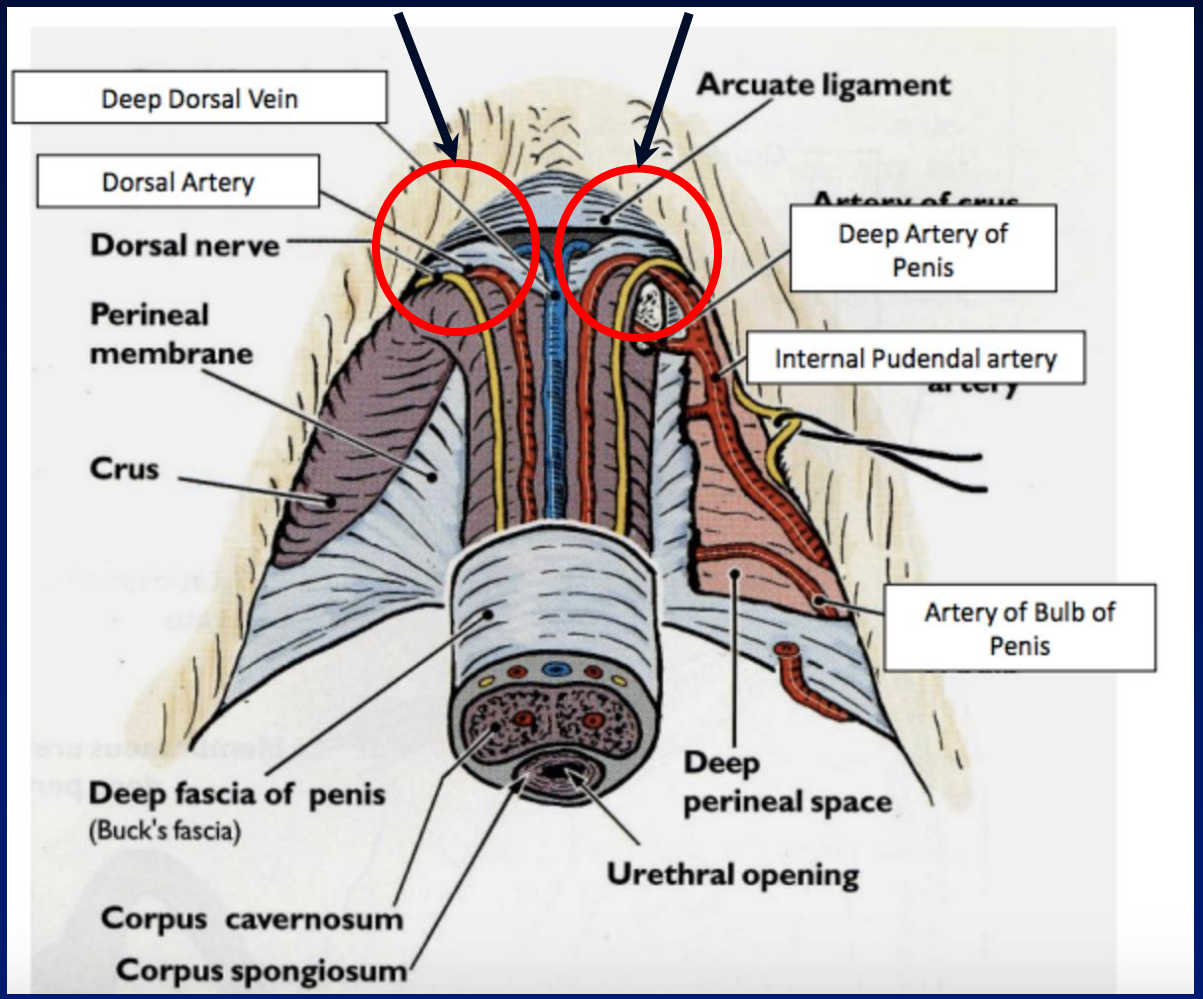
Shocks – 3500 total

R hilum:	**350 shocks @ 0.10 – 0.13 mJ/mm²**
L hilum:	**350 shocks @ 0.10 – 0.13 mJ/mm²**
R shaft:	**700 shocks @ 0.10 – 0.13 mJ/mm²**
L shaft:	**700 shocks @ 0.10 – 0.13 mJ/mm²**
R crus:	**700 shocks @ 0.11 – 0.13 mJ/mm²**
L crus:	**700 shocks @ 0.11 – 0.13 mJ/mm²**



Urogold 100 MTS – Electrohydraulic Shockwaves

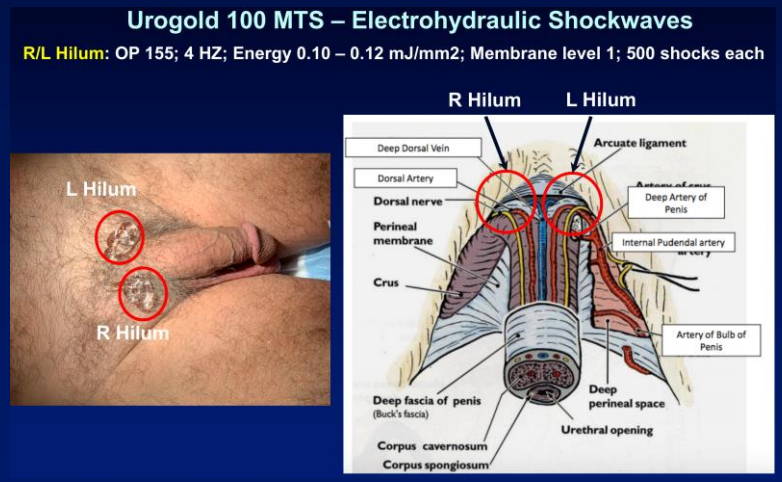
R/L Hilum: OP 155; 3 HZ; Energy 0.10 – 0.13 mJ/mm2; Membrane level 1



Urogold 100 MTS – Electrohydraulic Shockwaves

R/L Hilum: OP 155; 3 HZ; Energy 0.10 – 0.13 mJ/mm2; Membrane level 1

R Hilum



L Hilum

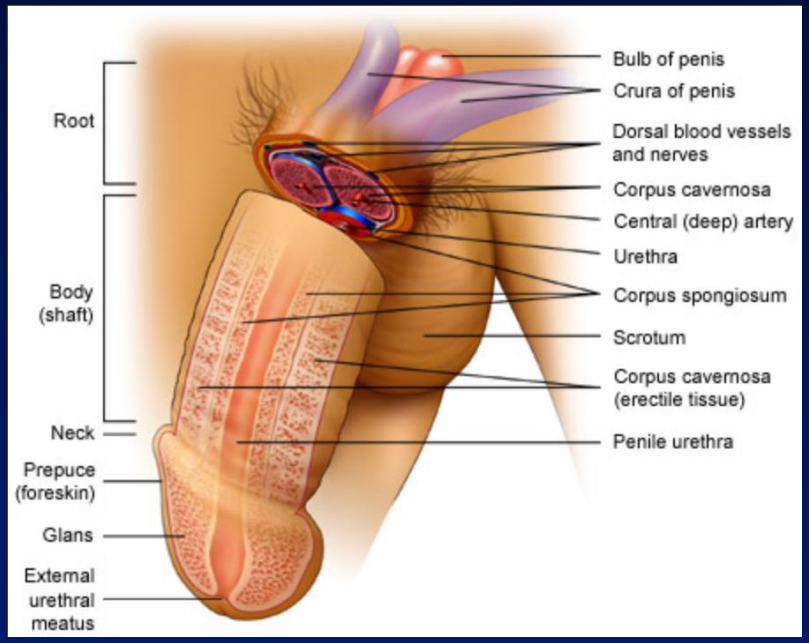
Gently stretch penile shaft at glans (gauze as needed)

Urogold 100 MTS – Electrohydraulic Shockwaves

R/L Shaft: OP 155; 3 HZ; Energy 0.10 – 0.13 mJ/mm2; Membrane level 1

R Shaft

L Shaft



Gently stretch penile shaft at glans (gauze as needed)

Urogold 100 MTS – Electrohydraulic Shockwaves

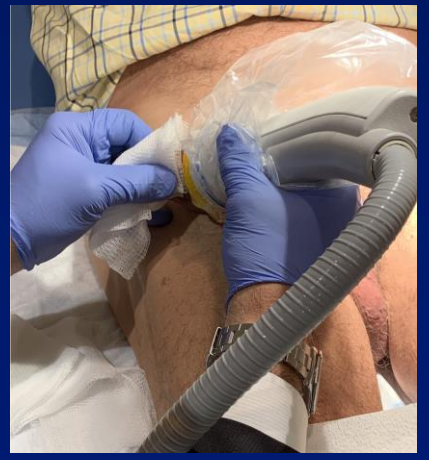
R/L Shaft: OP 155; 3 HZ; Energy 0.10 – 0.13 mJ/mm2; Membrane level 1

R Proximal Shaft

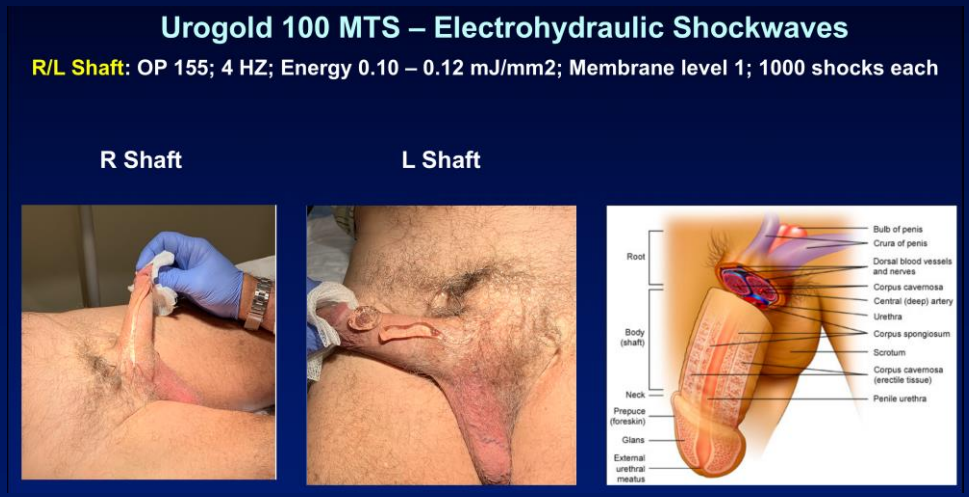
L Proximal Shaft

R Distal Shaft

L Distal Shaft

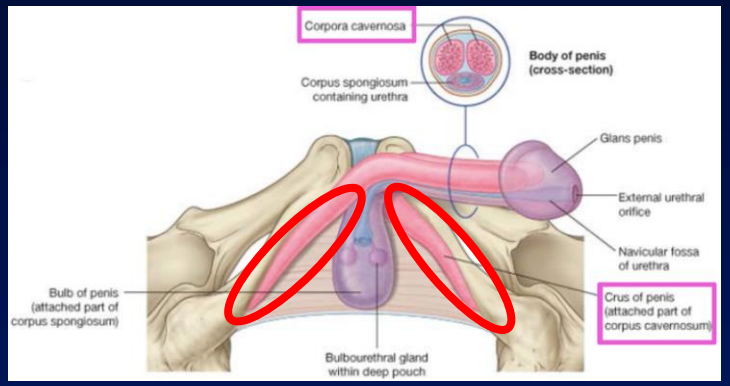


Gently stretch penile shaft at glans (gauze as needed)

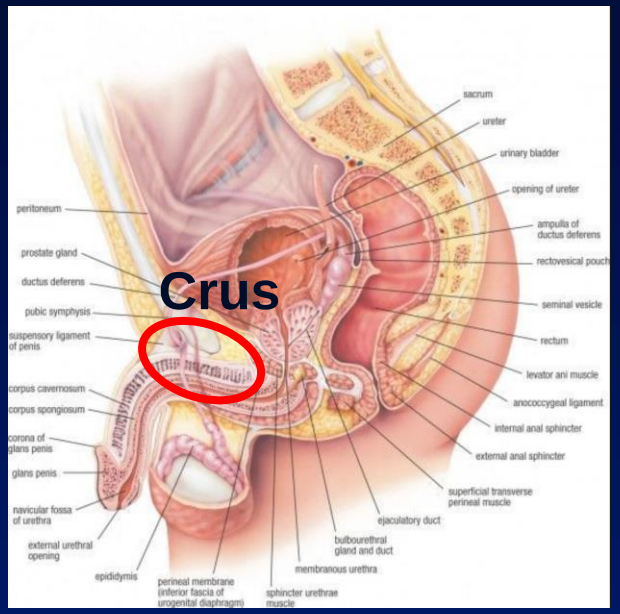


Urogold 100 MTS – Electrohydraulic Shockwaves

R/L Crus: OP 155; 3 HZ; Energy 0.10-0.13 mJ/mm2; Membrane level 1



R Crus L Crus

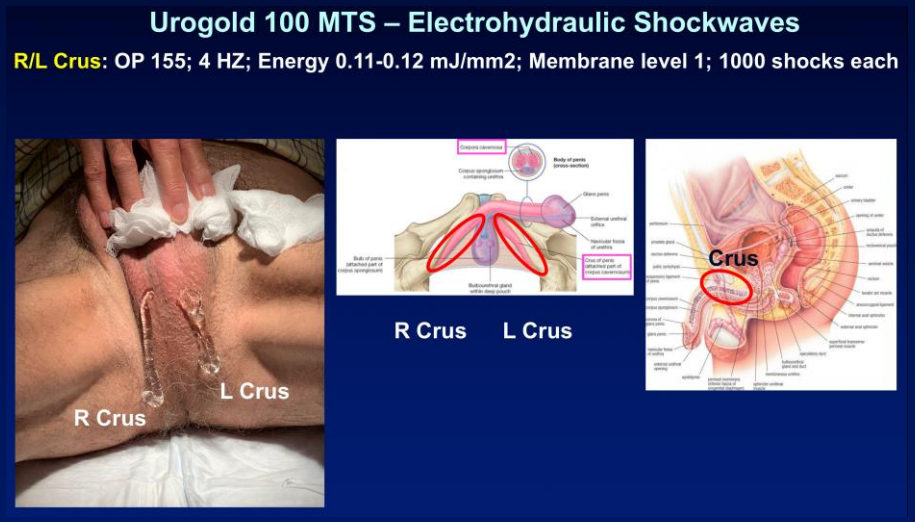


Frog leg position, Patient gently elevates his scrotum (gauze as needed)

Urogold 100 MTS – Electrohydraulic Shockwaves

R/L Crus: OP 155; 3 HZ; Energy 0.10 – 0.13 mJ/mm2; Membrane level 1

R Crus



L Crus

Frog leg position, Patient gently elevates his scrotum (gauze as needed)

SDSM Shockwave Therapy Protocols

Erectile Dysfunction – Penile Shockwave Therapy

LUTS/PE– Perineal Shockwave Therapy

Peyronie's Disease– PD Shockwave Therapy

Radiculopathy of Sacral Spinal Nerve Root – Lumbosacral Shockwave Therapy

Vestibulodynia – Vestibular Shockwsve Therapy

Urogold 100 MTS – Electrohydraulic Shockwaves

LUTS/PE SDSM Protocol for Perineal Shockwave Therapy

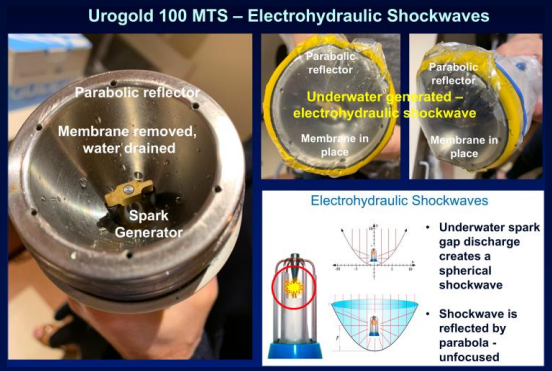
Applicator OP 155; 3HZ;
Membrane level 1

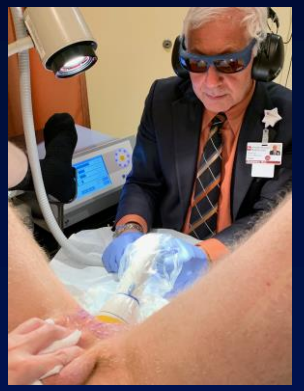
Cycle 1: Rx's #1, #2, #3, #4, #5, #6 over the most convenient time period for the patient. May take a few weeks to a few months

Urinary flow rate, PSA, AUA symptom score, nocturia

Shocks – 1400 total

Proximal perineum: 700 shocks @ 0.10 – 0.13 mJ/mm^2
Distal perineum: 700 shocks @ 0.10 – 0.13 mJ/mm^2





SDSM Shockwave Therapy Protocols

Erectile Dysfunction – Penile Shockwave Therapy

LUTS/PE– Perineal Shockwave Therapy

Peyronie's Disease– PD Shockwave Therapy

Radiculopathy of Sacral Spinal Nerve Root – Lumbosacral Shockwave Therapy

Vestibulodynia – Vestibular Shockwsve Therapy

Urogold 100 MTS – Electrohydraulic Shockwaves

PD - SDSM Protocol for PD Shockwave Therapy

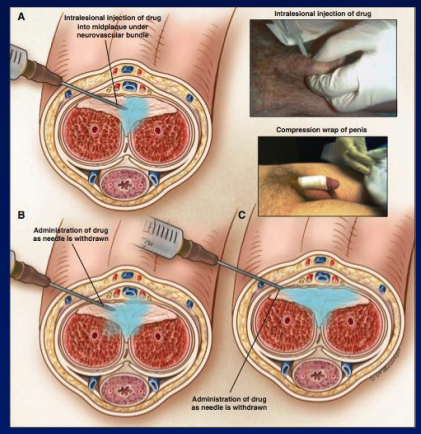
Applicator OE 035 or OP155; 3 HZ; Membrane level 1

Rx's #1, #2, #3, #4, #5, #6

Peyronie's plaque pre-treated with intralesional agent (interferon/Xiaflex)

Penis is modeled/hyperstretched overlying 30 ml syringe barrel – opposite to direction of bend – patient holds the syringe barrel – provider grasps the glans with gauze

Peyronie's plaque stretched: 2100 shocks @ 0.10 – 0.13 mJ/mm²



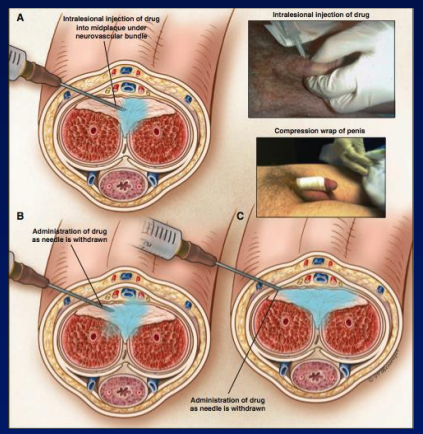
Urogold 100 MTS – Electrohydraulic Shockwaves

SDSM Protocol for PD

Applicator OE 035 or OP155; 3 HZ; Membrane level 1; 0.10 - 0.13 mJ/mm2); 2100 shocks total

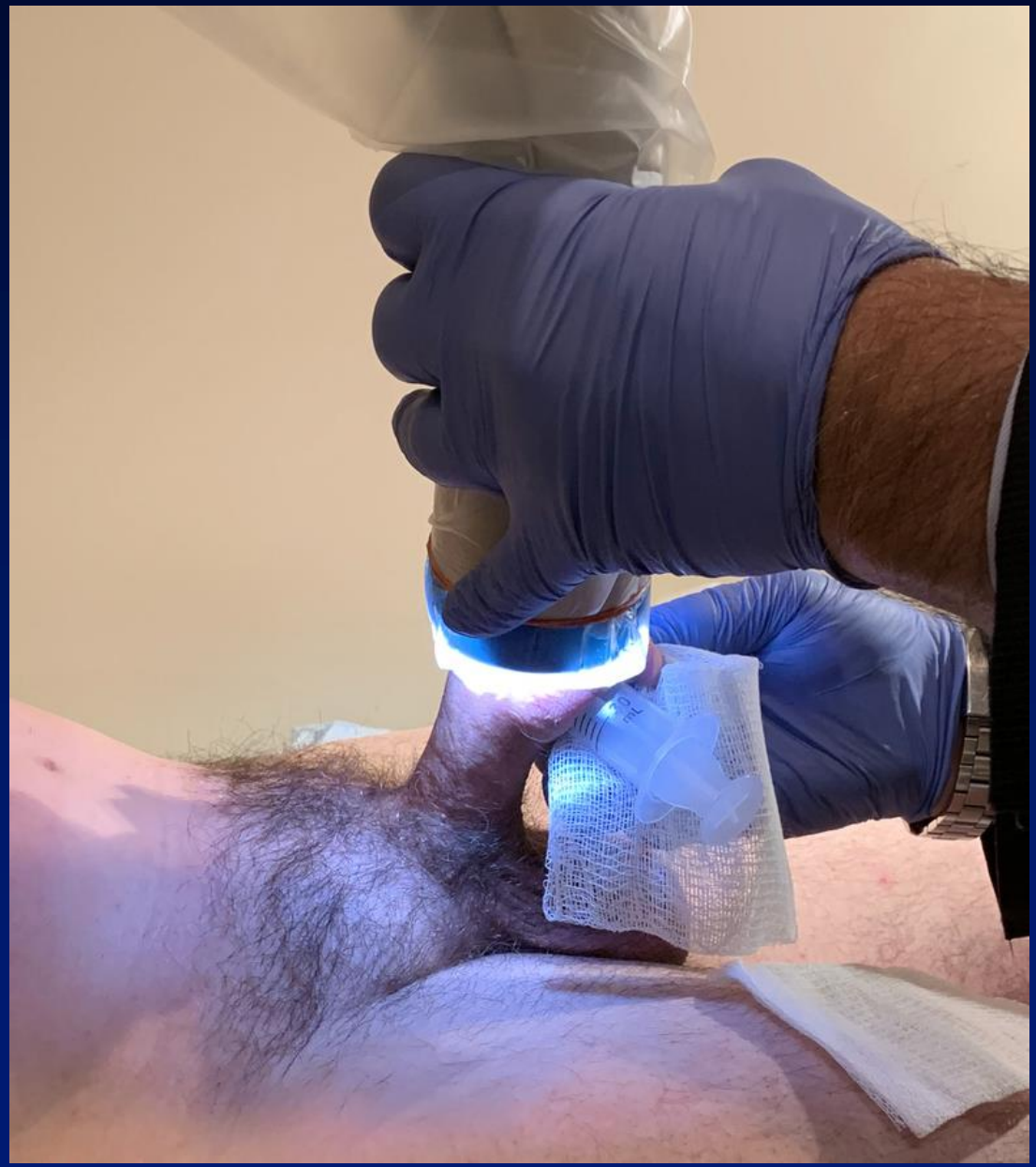
1. Intracavernosal bimix/trimix to obtain penile erection and measure angle/distance from peak curvature to corona (cms) - using a goniometer/ruler; locate with marking pen
2. Intralesional injection of interferon or Xiaflex (0.25 ml of the agent) at location marked previously - (upper right photo and middle photo)
3. Perform penile modeling in opposite direction to angle of penile curvature - (if angle is dorsal modeling is ventral) (lower right photo)
5. Use 30 ml syringe barrel - held by patient as shown in lower left photo, provider stretches penis over barrel (lower right and left photo)
6. Use 2100 shocks to Peyronie's plaque while modeling (lower left photo)

Need to compare effect on penile curvature from intralesional injection alone versus effect on penile curvature from intralesional injection in combination with modeling with penile plaque shockwave therapy.



Urogold 100 MTS – Electrohydraulic Shockwaves

Plaque: OE 035 or OP 155; 3 HZ; Energy 0.10-0.13 mJ/mm2; Membrane level 1; 2100 shocks



Urogold 100 MTS – Electrohydraulic Shockwaves

Plaque: OE 035 or OP 155; 4 HZ; Energy 0.10 – 0.13 mJ/mm2; Membrane level 1; 2100 shocks

SDSM Shockwave Therapy Protocols

Erectile Dysfunction – Penile Shockwave Therapy

LUTS/PE– Perineal Shockwave Therapy

Peyronie's Disease – PD Shockwave Therapy

Radiculopathy of Sacral Spinal Nerve Root – Lumbosacral Shockwave Therapy

Vestibulodynia – Vestibular Shockwsve Therapy

Urogold 100 MTS – Electrohydraulic Shockwaves

Radiculopathy of Sacral Spinal Nerve Root - SDSM Protocol for Lumbosacral Shockwave Therapy

Applicator OP 155; 3 HZ; Membrane level 1

Neuro-Genital testing, MRI and Spine surgeon consultation.
Not considered a candidate for, not interested in, spine surgery

Cycle 1: Rx's #1, #2, #3, #4, #5, #6 over the most convenient time period for the patient. May take a few weeks to a few months

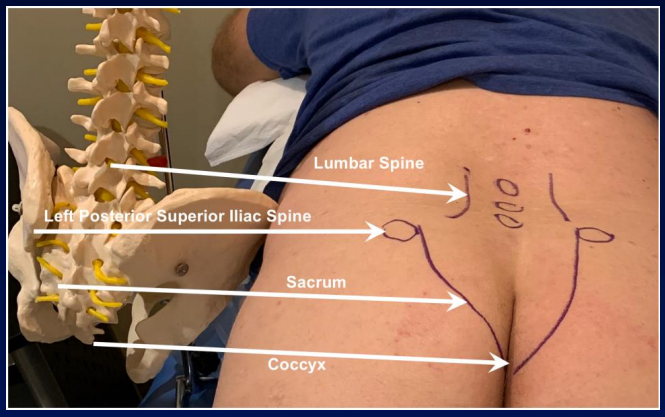
Shocks – 2100 – 2800 total shocks/treatment. Try to elicit discomfort in a region, often bilateral, hover probe over area, discomfort will typically diminish over time, increase energy level, repeat process

Coccyx and right and left sacrum: 700 shocks @ 0.07 – 0.14 mJ/mm^2

Left lumbar region: 700 shocks @ 0.07 – 0.14 mJ/mm^2

Right lumbar region: 700 shocks @ 0.07 – 0.14 mJ/mm^2

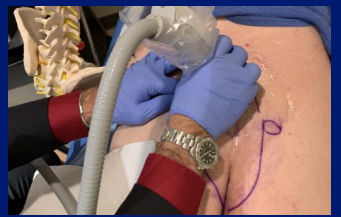
Repeat Neuro-Genital testing



Coccyx and right and left sacrum

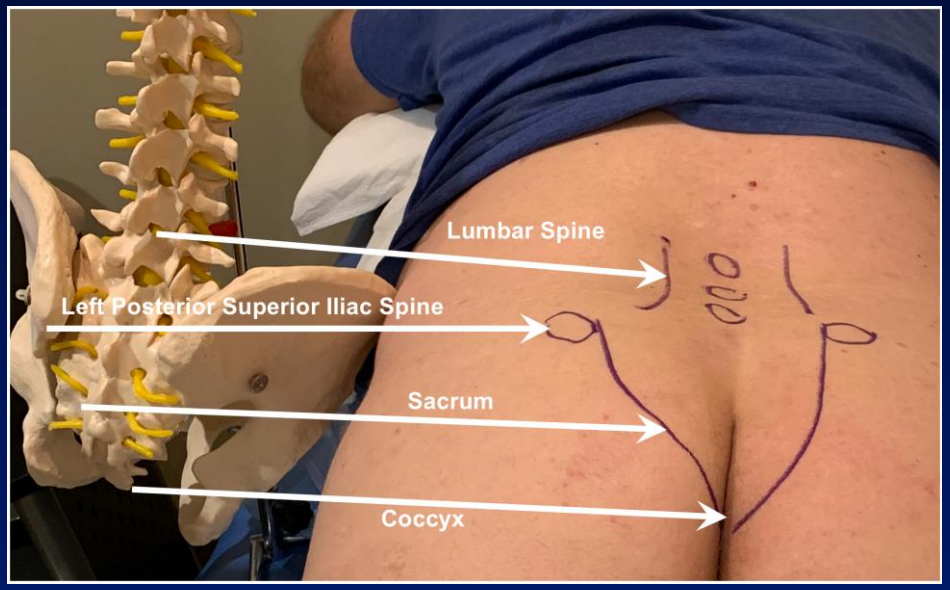
Left lumbar region

Right lumbar region

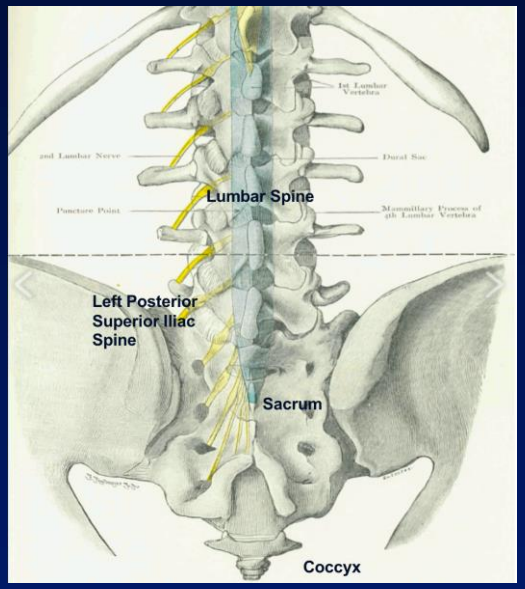


Urogold 100 MTS – Electrohydraulic Shockwaves

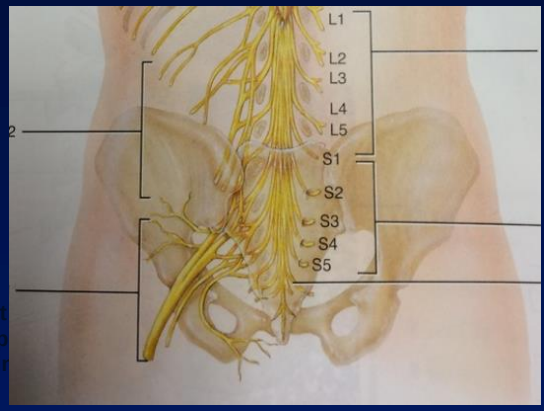
Lumbosacral Spine Pathology : OP 155; 3 HZ; Energy 0.07 – 0.14 mJ/mm2; Membrane level 1; 700 shocks each for: i) Coccyx and right and left sacrum, ii) Left lumbar region, iii) Right lumbar region



Coccyx and right and left sacrum



Left lumbar region



Right lumbar region

SDSM Shockwave Therapy Protocols

Erectile Dysfunction – Penile Shockwave Therapy

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Vestibulodynia – Vestibular Shockwave Therapy

Urogold 100 MTS – Electrohydraulic Shockwaves

SDSM Protocol for Female Genital Arousal Disorder or Genital Dysesthesia (including Interstitial Cystitis)

Applicator OP 155; 3 HZ; Membrane level 1

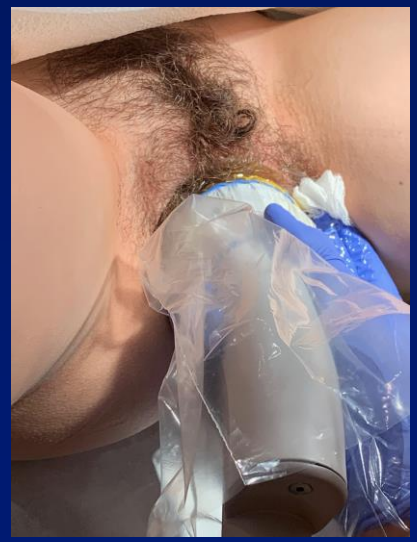
Cycle 1: Rx's #1, #2, #3, #4, #5, #6 over the most convenient time period for the patient. May take a few weeks to a few months

Shocks – 2100 total shocks/treatment

Right vestibule - 700 shocks @ 0.07 -0.13 mJ/mm^2

Left Vestibule - 700 shocks @ 0.07 -0.13 mJ/mm^2

Posterior Fourchette - 700 shocks @ 0.07 -0.13 mJ/mm^2

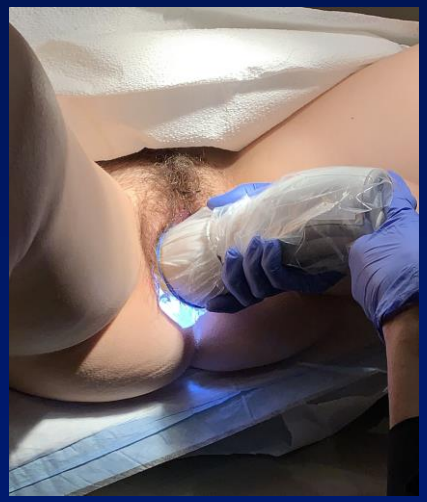


Urogold 100 MTS – Electrohydraulic Shockwaves

SDSM Protocol for Female Genital Arousal Disorder or Genital Dysesthesia (including Interstitial Cystitis)

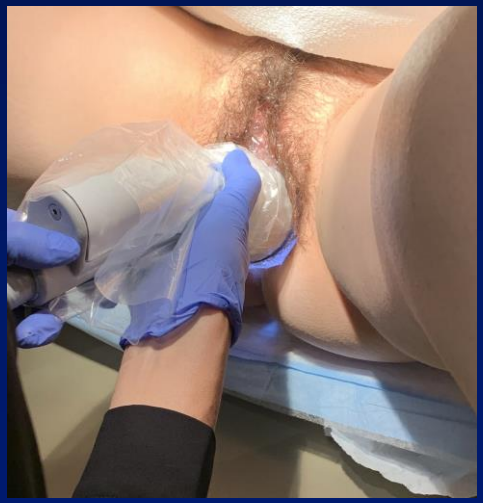
Applicator OP 155; 3 HZ; Membrane level 1; Shocks – 2100 total

Right/Left Vestibule, Posterior Fourchette - 700 shocks @ 0.07-0.13 mJ/mm^2



Right Vestibule

Left Vestibule



Posterior Fourchette

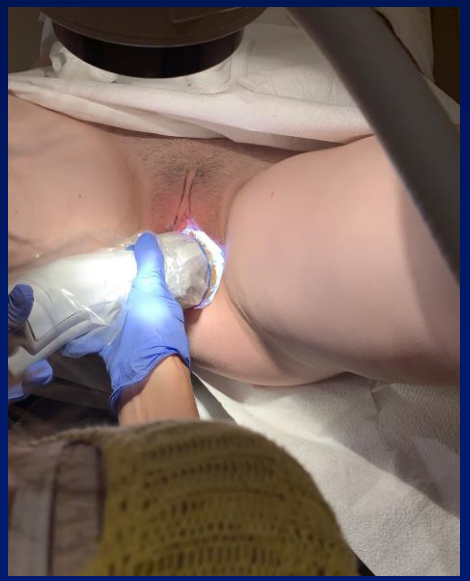
Urogold 100 MTS – Electrohydraulic Shockwaves

SDSM Protocol for Female Genital Arousal Disorder or Genital Dysesthesia (including Interstitial Cystitis)

Applicator OP 155; 3 HZ; Membrane level 1; Shocks – 2100 total

Right/Left Vestibule, Posterior Fourchette - 700 shocks @ 0.07-0.13 mJ/mm^2

Right Vestibule



Left Vestibule

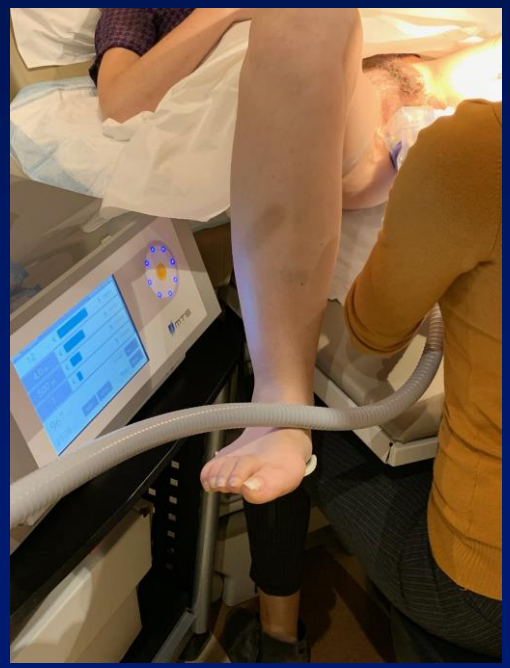
Posterior Fourchette

Urogold 100 MTS – Electrohydraulic Shockwaves

SDSM Protocol for Female Genital Arousal Disorder or Genital Dysesthesia (including Interstitial Cystitis)

Applicator OP 155; 3 HZ; Membrane level 1; Shocks – 2100 total

Right/Left Vestibule, Posterior Fourchette - 700 shocks @ 0.07-0.13 mJ/mm^2



Right Vestibule

Left Vestibule

Posterior Fourchette

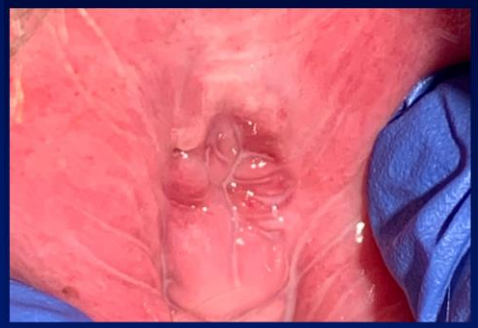
Urogold 100 MTS – Electrohydraulic Shockwaves

SDSM Protocol for Female Genital Arousal Disorder or Genital Dysesthesia (including Interstitial Cystitis)

Applicator OP 155; 3 HZ; Membrane level 1; Shocks – 2100 total

Vestibule - 1000 shocks @ 0.10-0.13 mJ/mm^2

Urethral Meatus Prior to Shockwave Treatment June 12, 2019



Urethral Meatus Prior to Second Shockwave Treatment June 26, 2019

Urogold 100 MTS – Electrohydraulic Shockwaves

SDSM Protocol for ED: Applicator OP 155; 4 HZ; Membrane level 1
Shocks 5000; 500 R/L Hilum; 1000 R/L Shaft; 1000 R/L Crus
Shocks 3000; 500 R/L Hilum; 500 R/L Shaft; 500 R/L Crus