

IPOGONADISMO,  
PATOLOGIA PROSTATICA  
E DISFUNZIONI SESSUALI:  
Endocrinologo ed Urologo a confronto

28 SETTEMBRE 2018

MILANO

Starhotel Echo  
Viale Andrea Doria 4

# Onde urto e trattamento della disfunzione erettile post trattamento del carcinoma prostatico

STATE OF THE ART



# BACKGROUND\_

## Prostate Cancer\_Epidemiology

### Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries

Prostate cancer is the **second most frequent Cancer** and **the fifth leading cause of cancer death in men.**

An estimated 1.3 million cases were diagnosed worldwide with prostate cancer in 2018, accounting for **7,2% of the cancers diagnosed** in both sexes.

#### Prostate Cancer

### Global Incidence and Mortality for Prostate Cancer: Analysis of Temporal Patterns and Trends in 36 Countries

Table 2 – Group categories for trends in prostate cancer incidence and mortality in the most recent 10 years

	Incidence	Mortality	Countries <sup>a</sup>
Group A	↑	↑	Bulgaria, Philippines, Singapore
Group B	↑	↓	Brazil, Czech Republic, France, Ireland, Israel, Italy, Japan, Netherlands, Poland, Spain, Switzerland, UK
Group C	↑	Stable	China, Croatia, Estonia, Latvia, Lithuania, Portugal, Slovakia, Slovenia
Group D	Stable	↓	Australia, Austria, Colombia, Canada, Denmark, New Zealand, Norway
Group E	Stable	Stable	Costa Rica, Iceland, Malta
Group F	↓	↓	Finland, Sweden, USA

<sup>a</sup> All countries had a very high human development index (HDI; >0.796) except for Bulgaria, Brazil, Colombia, and Costa Rica (high HDI, 0.710–0.796) and Philippines (medium HDI, 0.534–0.710).

Global Cancer Statistics 2018

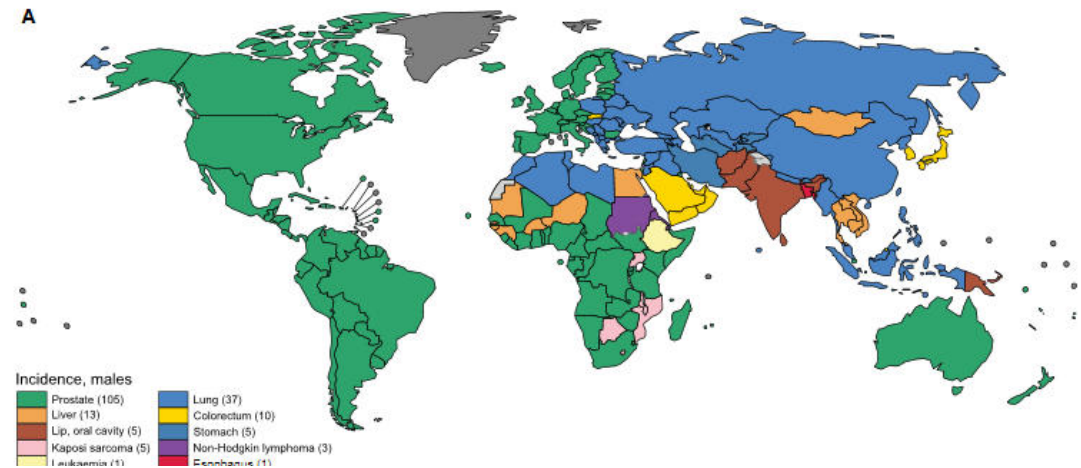
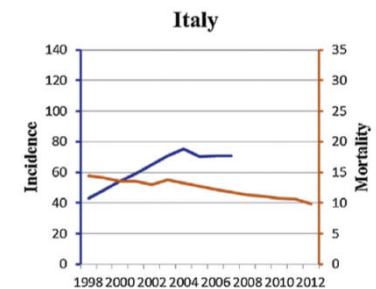


FIGURE 5. Global Maps Presenting the Most Common Type of Cancer Incidence in 2018 in Each Country Among (A) Men and (B) Women. The numbers of countries represented in each ranking group are included in the legend. Source: GLOBOCAN 2018.

EUROPEAN UROLOGY 70 (2016) 862–874

#### Group B:

- increasing incidence
- decreasing mortality



# BACKGROUND\_

## Prostate Cancer\_Treatment strategies

© European Association of Urology 2017

### Radical Prostatectomy

#### 6.2.10 Guidelines for radical prostatectomy

Recommendations	LE	GR
Offer both radical prostatectomy (RP) and RT in patients with low- and intermediate-risk disease and a life expectancy > 10 years.	1b	A
Offer AS as an alternative to surgery or RT in patients with low-risk disease and a life expectancy of > 10 years.	1b	A
Offer nerve-sparing surgery in patients with a low risk of extracapsular disease (refer to Partin tables/nomograms).	2b	B
Offer RP in patients with high-risk localised PCa and a life expectancy of > 10 years only as part of multi-modal therapy.	2a	A
Offer RP in selected patients with locally advanced (cT3a) disease and a life expectancy > 10 years only as part of multi-modal therapy.	2b	B
Offer RP in highly selected patients with locally advanced disease (cT3b-T4 N0 or any T N1) only as part of multi-modal therapy.	3	C
Do not offer neoadjuvant hormonal therapy before RP.	1a	A
Do not offer adjuvant hormonal therapy after RP for pN0 disease.	1a	A

Nerve-Sparing Surgery is **clearly contraindicated** when:

- HR of extracapsular disease
- Gleason Score > 7 on biopsy
- Doubt residual tumor

There is **emerging data** to suggest some benefits of the robotic approach over the laparoscopic and open approaches, in terms of perioperative, recovery and short-term functional outcomes; however, there is uncertainty over oncological outcomes, longer-term functional and QoL outcomes.

(Urol Int 2016;96:373–378, DOI: 10.1159/000435861)

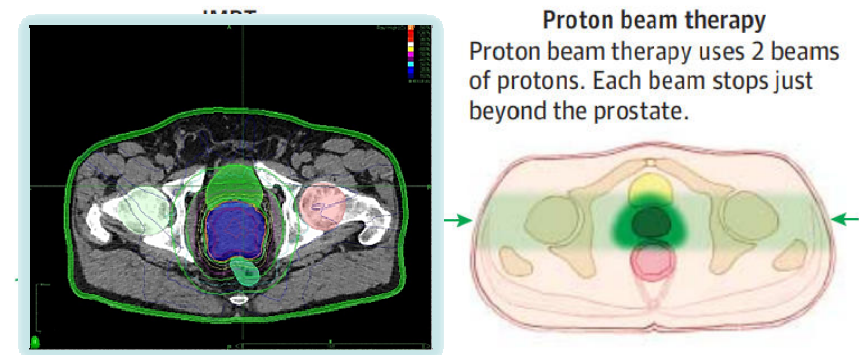
# BACKGROUND\_

## Prostate Cancer\_Treatment strategies

### Definitive Radiotherapy

Intensity-modulated radiotherapy (**IMRT**), with or without image-guided radiotherapy (IGRT), is the accepted **best standard** for **EBRT**

Recommendations	LE	GR
Offer external beam radiation therapy (EBRT) to all risk groups of non-metastatic PCa	1b	A
In low-risk PCa, use a total dose of 74 to 78 Gy.	1a	A
In patients with low-risk PCa, and selected intermediate-risk PCa, without a previous transurethral resection of the prostate (TURP) and with a good International Prostate Symptom Score and a prostate volume < 50 mL, offer low-dose rate (LDR) brachytherapy.	2a	A
In patients with intermediate-risk PCa use a total dose of 76-78 Gy, in combination with short-term ADT (four to six months).	1b	A
In patients with high-risk localised PCa and locally advanced cN0 PCa, use EBRT to a dose of 76-78 Gy, or combined EBRT with brachytherapy boost (either high-dose rate [HDR] or LDR). Radiotherapy should be given in combination with long-term androgen deprivation therapy (two to three years).	1a EBRT	A
	1b brachytherapy	
Offer intensity-modulated radiotherapy (IMRT) for definitive treatment of PCa by EBRT.	2a	A
Moderate hypofractionation (HFX) with IMRT including image-guided radiation therapy (IGRT) to the prostate only can be offered to carefully selected patients with localised disease (as discussed in the text).	1a	A
Moderate HFX should adhere to radiotherapy-protocols from trials with equivalent outcome and toxicity, i.e. 60 Gy/20 fractions in four weeks or 70 Gy/28 fractions in six weeks.	1a	A
In patients with cN+ or pN+ PCa offer pelvic external irradiation in combination with immediate long-term ADT.	2b	B
In patients with pT3, N0M0 PCa and an undetectable prostate-specific antigen (PSA) following radical prostatectomy, discuss adjuvant EBRT because it improves at least biochemical-free survival.	1a	A
Inform patients with an undetectable PSA following RP about salvage irradiation as an alternative to adjuvant irradiation when PSA increases (see Section 6.9.5.1).	1b	A



# BACKGROUND\_



## Prostate Cancer\_Treatment strategies

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### Hormonal therapy

Androgen deprivation can be achieved by either suppressing the secretion of testicular androgens or inhibiting the action of circulating androgens at the level of their receptor.

These two methods can be combined to achieve what is known as complete (or maximal or total) androgen blockade.

- Bilateral orchiectomy → castration level (serum Testosterone < 1 nmol/L)
- LHRH agonists → «flare-up» phenomenon
- LHRH antagonists → rapid decrease of LH, FSH & Testosterone
- Anti-androgens → blockage of AR
- New compounds → for castrate-resistant pts only

# BACKGROUND

## Impact of treatments on Erectile Function

ORIGINAL CONTRIBUTION

### PREDICTING ERECTILE FUNCTION AFTER PROSTATE CANCER

JAMA, September 21, 2011—Vol 306, No. 11  
Corrected on September 20, 2011

Among the 1201 men registered for follow-up, 777 (86%) completed the 24-month interval and are the focus of this study.

Their primary treatment included either prostatectomy (n=524), external beam radiotherapy (n=241), or brachytherapy (n=262).

#### Results at 2 year follow-up

37% of all patients and 48% of those with functional erections prior to treatment reported functional erections.

**Table 1.** Multivariable Logistic Regression Models Predicting Functional Erections Suitable for Intercourse at 2 Years After Treatment, According to Planned Primary Prostate Cancer Treatment in the PROSTQA Cohort<sup>a</sup>

Parameter, Variable	Parameter Estimate (SE)	OR (95% CI)	Wald $\chi^2$ P Value	Bootstrap Parameter Estimate (SE)
Intercept	-2.96 (1.38)			-3.00 (1.42)
Pretreatment sexual HRQOL score (per 10 points)	0.45 (0.07)	1.6 (1.4-1.8)	<.001	0.45 (0.07)
Age (per 10 y)	-0.56 (0.16)	0.6 (0.4-0.8)	<.001	-0.58 (0.16)
Neoadjuvant hormone therapy	1.18 (0.38)	3.6 (1.3-10.1)	.01	1.39 (0.57)
PSA $\leq$ 10 ng/mL	0.85 (0.36)	2.3 (1.2-4.7)	.02	0.88 (0.37)
External radiotherapy				
Intercept	-5.22 (0.76)			-5.37 (0.79)
Pretreatment sexual HRQOL score (per 10 points)	0.54 (0.08)	1.7 (1.4-2.0)	<.001	0.55 (0.09)
No neoadjuvant hormone therapy	1.18 (0.38)	3.3 (1.5-7.0)	.003	1.24 (0.41)
PSA <4 ng/mL	1.17 (0.47)	3.2 (1.3-8.0)	.01	1.24 (0.48)
Brachytherapy				
Intercept	-3.13 (2.21)			-3.40 (2.34)
Pretreatment sexual HRQOL score (per 10 points)	0.72 (0.11)	2.1 (1.7-2.5)	<.001	0.75 (0.11)
Age (per 10 y)	-0.63 (0.28)	0.5 (0.3-0.9)	.03	-0.64 (0.30)
African American race/ethnicity	1.18 (0.38)	3.1 (0.9-10.0)	.06	1.18 (0.64)
BMI <sup>b</sup>				
<25	2.22 (0.86)	9.2 (1.7-50.0)	.01	2.30 (0.94)
25-34.9	1.40 (0.77)	4.0 (0.9-18.4)	.07	1.45 (0.85)
$\geq$ 35	0	1 [Reference]		

# BACKGROUND\_

## Impact of treatments on Erectile Function

Prostate cancer survivorship: a review of erectile dysfunction and penile rehabilitation after prostate cancer therapy

THE MEDICAL JOURNAL OF AUSTRALIA

MJA

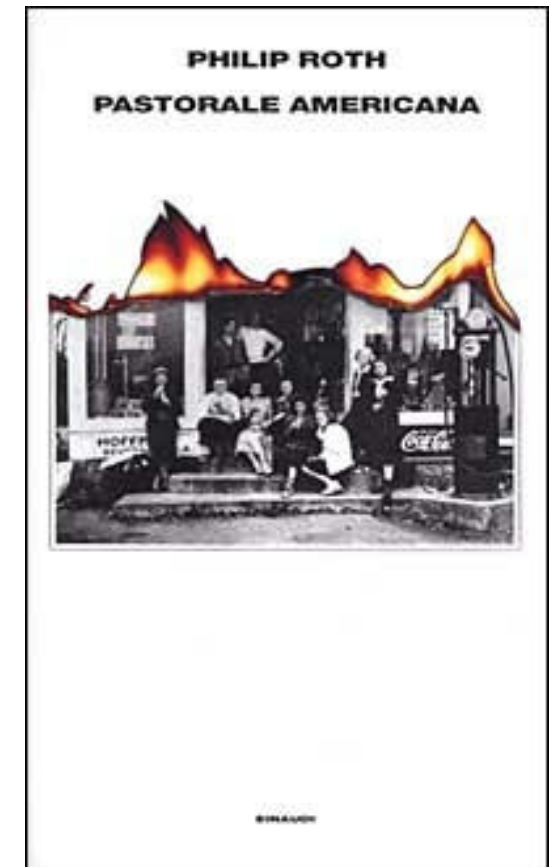
MJA 200 (10) · 2 June 2014

- ❖ The **true incidence of ED** after prostate cancer therapy **is unknown**
- ❖ ED rate after RP of around 60–70%
- ❖ ED induced by radiation therapy continues to develop for up to about 3 years, and that the actual rates of ED between RP and radiation groups are similar
- ❖ brachytherapy may confer better preservation of erectile function scores compared with external beam radiotherapy
- ❖ hormone therapy alone or in combination with external beam therapy significantly increases the risk of ED

# BACKGROUND\_

## Impact of treatments on Erectile Function

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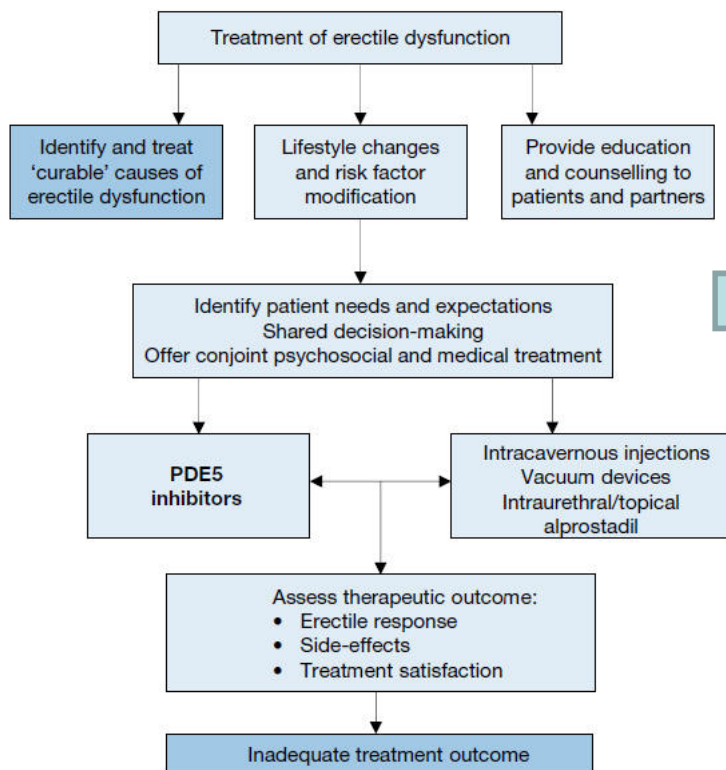
# BACKGROUND

## Guidelines for DE management

## EAU Guidelines on Erectile Dysfunction

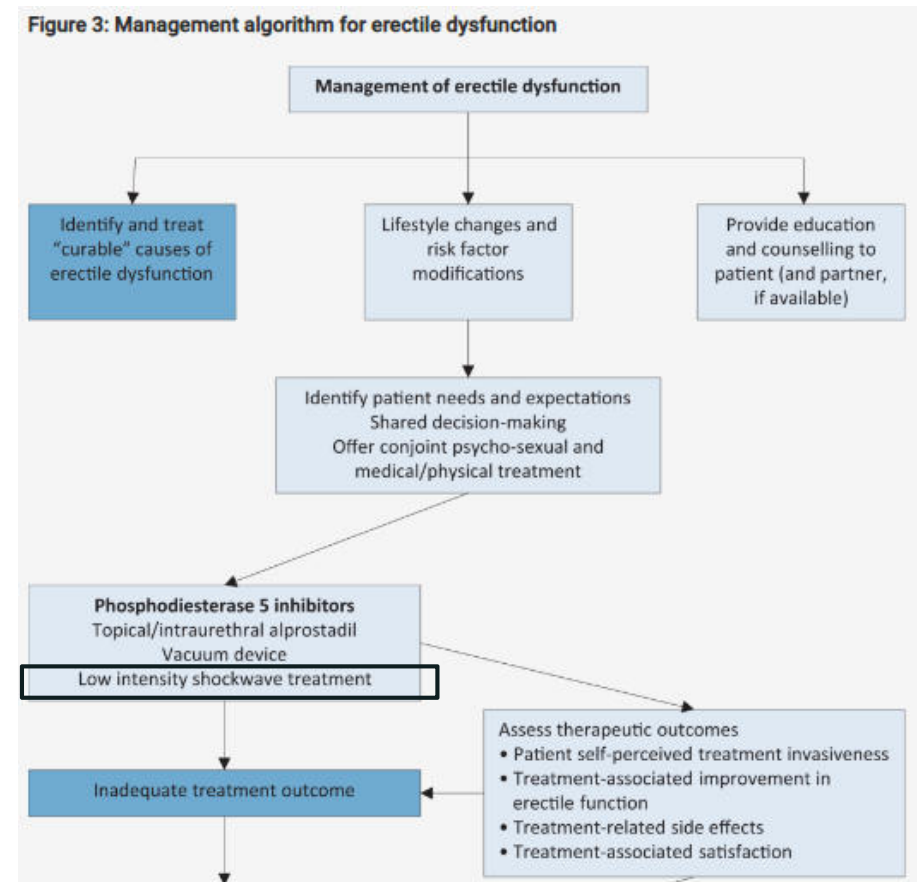
### 2016 Update

Figure 3: Treatment algorithm for erectile dysfunction

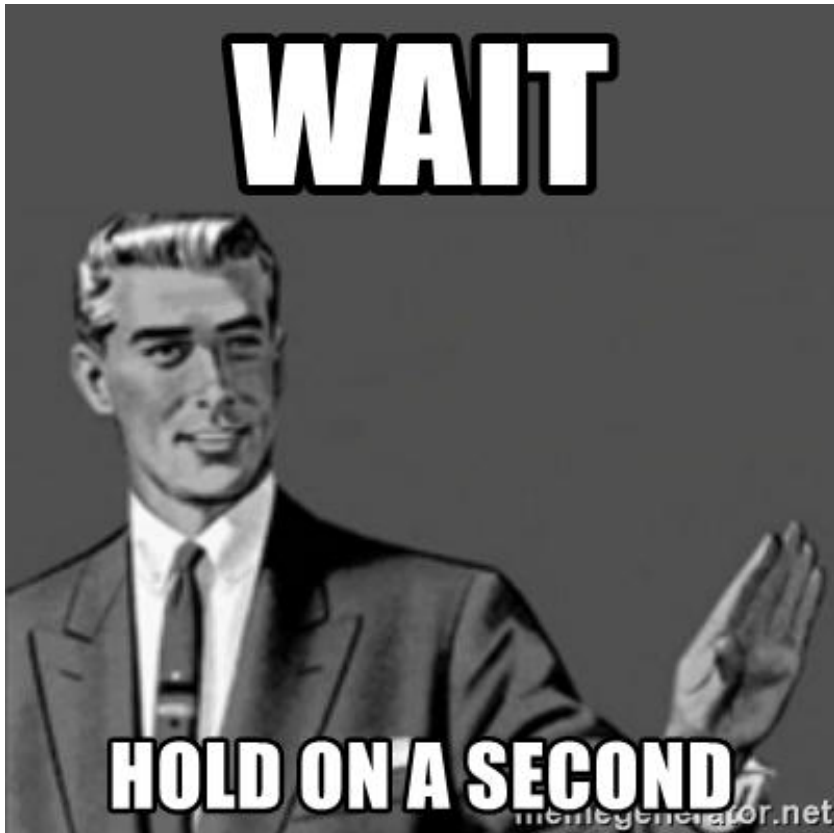


### 2018 Update (online version)

Figure 3: Management algorithm for erectile dysfunction



# BACKGROUND\_



Wait a second...

Low Intensity Shockwave  
Treatment ???

# BACKGROUND\_

## HISTORY OF SHOCKWAVES IN MEDICINE

### **Our Experience on the Association of a New Physical and Medical Therapy in Patients Suffering from Induratio penis plastica**

European  
Urology

V. Mirone C. Imbimbo A. Palmieri F. Fusco

1950 1971 1980 1983 1985 1988-90 1999 2010

### **Can Low-Intensity Extracorporeal Shockwave Therapy Improve Erectile Function? A 6-Month Follow-up Pilot Study in Patients with Organic Erectile Dysfunction**

*Yoram Vardi\*, Boaz Appel, Giris Jacob, Omar Massarwi, Ilan Gruenwald*

**OK but...**

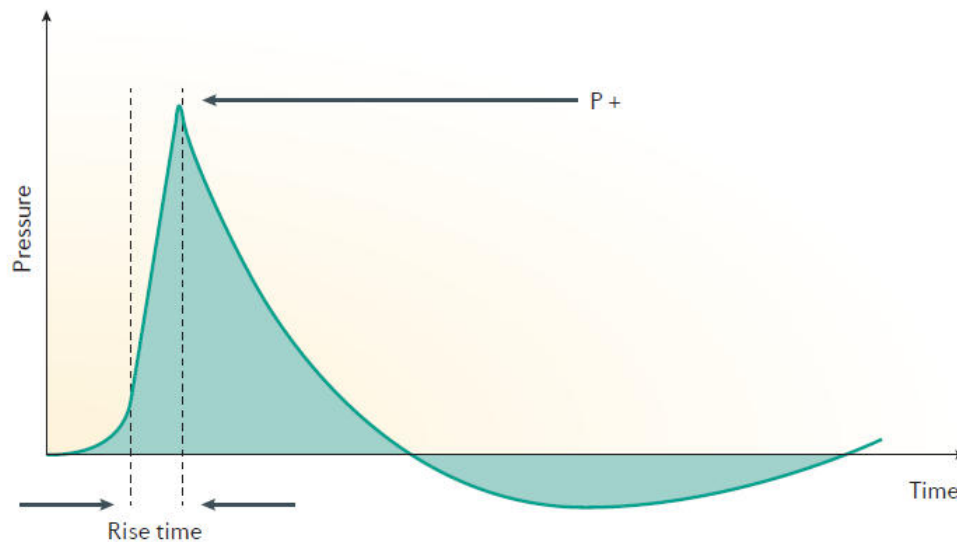
**How does  
LI-SWT  
work ?**

# BACKGROUND\_Mechanisms of action

Low-intensity shockwave therapy for erectile dysfunction: is the evidence strong enough?

nature  
REVIEWS UROLOGY

## Shockwaves and their effects on tissues



### Two main mechanisms:

1. direct **mechanical stress** associated with the high-amplitude shockwave itself
1. associated with the growth and violent collapse of so-called **cavitation bubbles** in fluid.

Figure 1 | **Schematic depiction of a shockwave as used in the treatment of erectile dysfunction.** A shockwave is a longitudinal acoustic wave consisting of a short pulse of about 5  $\mu$ s duration that is characterized by a near instantaneous jump to a peak positive acoustic pressure, which is referred to as a 'shock', followed by a longer-lasting period of negative pressure. The amplitude of the negative pressure is always much less than that of the peak positive pressure, and no abrupt transition is observed in the negative phase of the waveform. Depending on the energy flux density used and the source of the shockwave, variations are seen in the shape and amplitude of the shockwave.

# BACKGROUND\_Mechanisms of action

Low-intensity shockwave therapy for erectile dysfunction: is the evidence strong enough?



## NEOANGIOGENESIS

shear stress affects small vessels causing micro-trauma and endothelial damage

both these factors result in neoangiogenesis

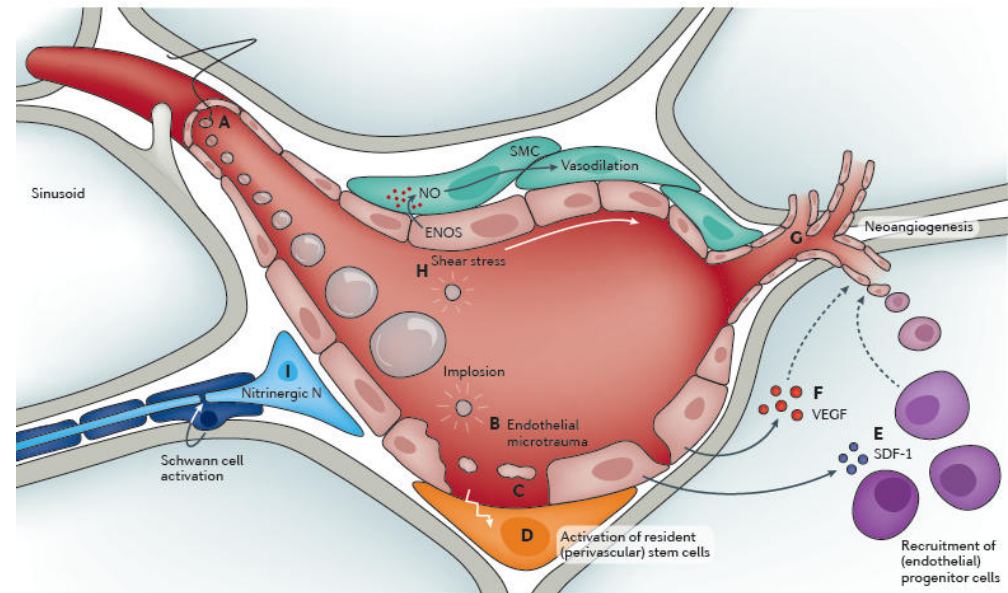


Figure 2 | Putative mechanisms of action of shockwave therapy for ED. Shockwaves form microbubbles (A) in the vasculature and tissue that collapse (B) and cause disruption of the endothelium (C). Endothelial disruption might activate resident stem cells (D) and result in chemokine production with attraction of (endothelial) progenitor cells (E) and release of VEGF (F); these factors combine to initiate neoangiogenesis (G). In addition, microbubble collapse induces shear stress and might stimulate endothelial NO production (H). Furthermore, shockwave therapy might also enhance Schwann-cell-mediated nitric-oxide-nerve repair after injury (I).

# BACKGROUND\_Mechanisms of action

Low-intensity shockwave therapy for erectile dysfunction: is the evidence strong enough?

nature  
REVIEWS UROLOGY

## ACTIVATION OF RESIDENT STEM CELLS & RECRUITMENT OF CIRCULATING PROGENITOR ENDOTHELIAL CELLS

Shockwaves enhance neovascularization by:

- Upregulation of angiogenetic factors (VEGF, SDF-1)
- Attraction of cells important for new blood vessels formation

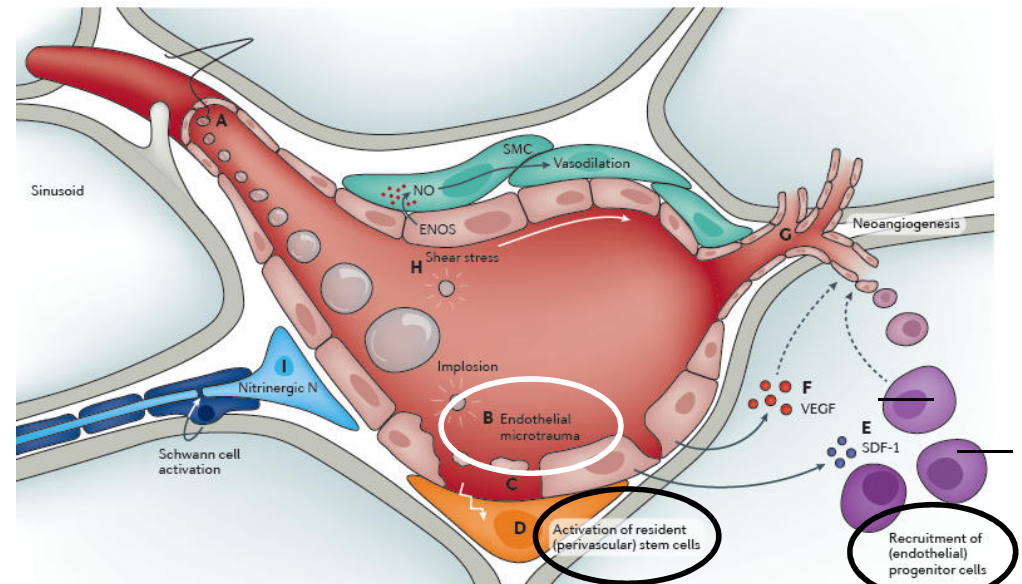


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# BACKGROUND\_Mechanisms of action

Low-intensity shockwave therapy for erectile dysfunction: is the evidence strong enough?

## MODULATION OF VASODILATATION

Shockwaves induce immediate vasodilatation and this effect could involve NO or other molecules

Shockwaves stimulate neuronal nOS (nitric oxide synthase) in a dose-dependent fashion

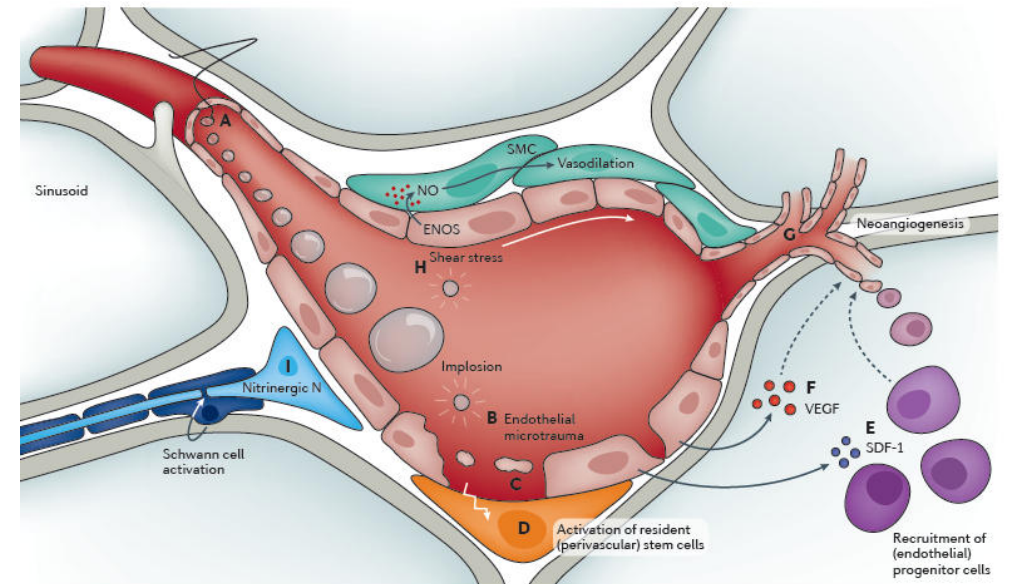


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# BACKGROUND\_Mechanisms of action

Low-intensity shockwave therapy for erectile dysfunction: is the evidence strong enough?



## NERVE REGENERATION

Shockwaves could act supporting Schwann cells proliferation after peripheral nerve injury

(few studies)

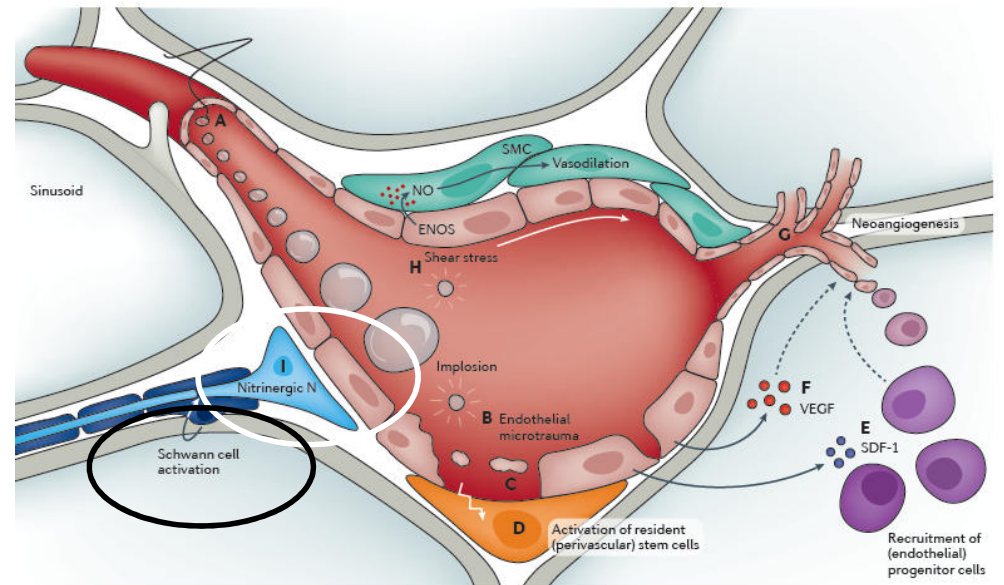


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.....rehabilitation post NSRP.....?

# BACKGROUND Animal studies

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

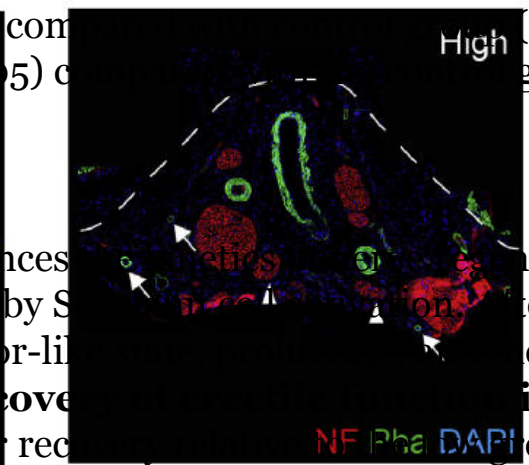
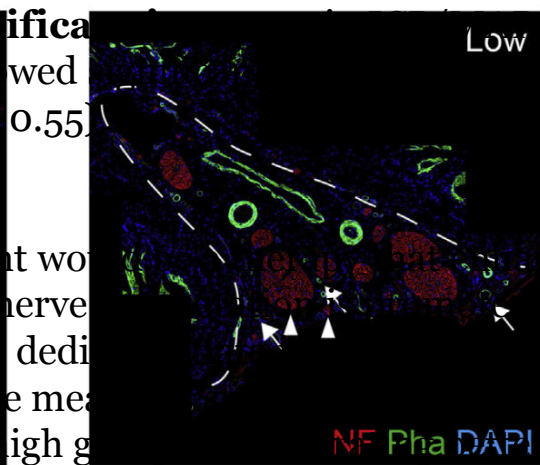
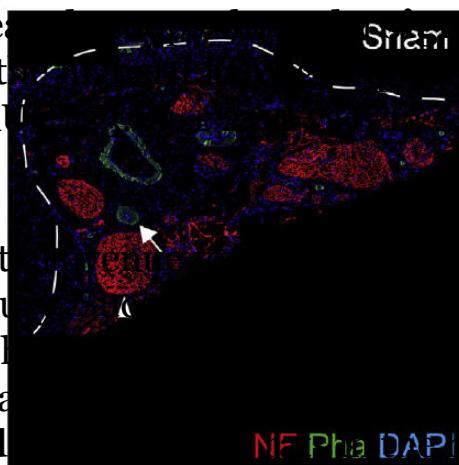
THE JOURNAL OF  
SEXUAL MEDICINE

J Sex Med 2016;13:22–32

In the current study, we developed a new **ED rat model of pelvic neurovascular injury (PVNI)** by bilateral cavernous nerve injury and internal pudendal bundle injury, and **tested the effect of LESW treatment at different energy levels**. We hypothesized that LESW might improve function, angiogenesis, and innervations by activating local Schwann cells and increasing progenitor cell recruitment.

Both treated  
Rats in the  
larger A

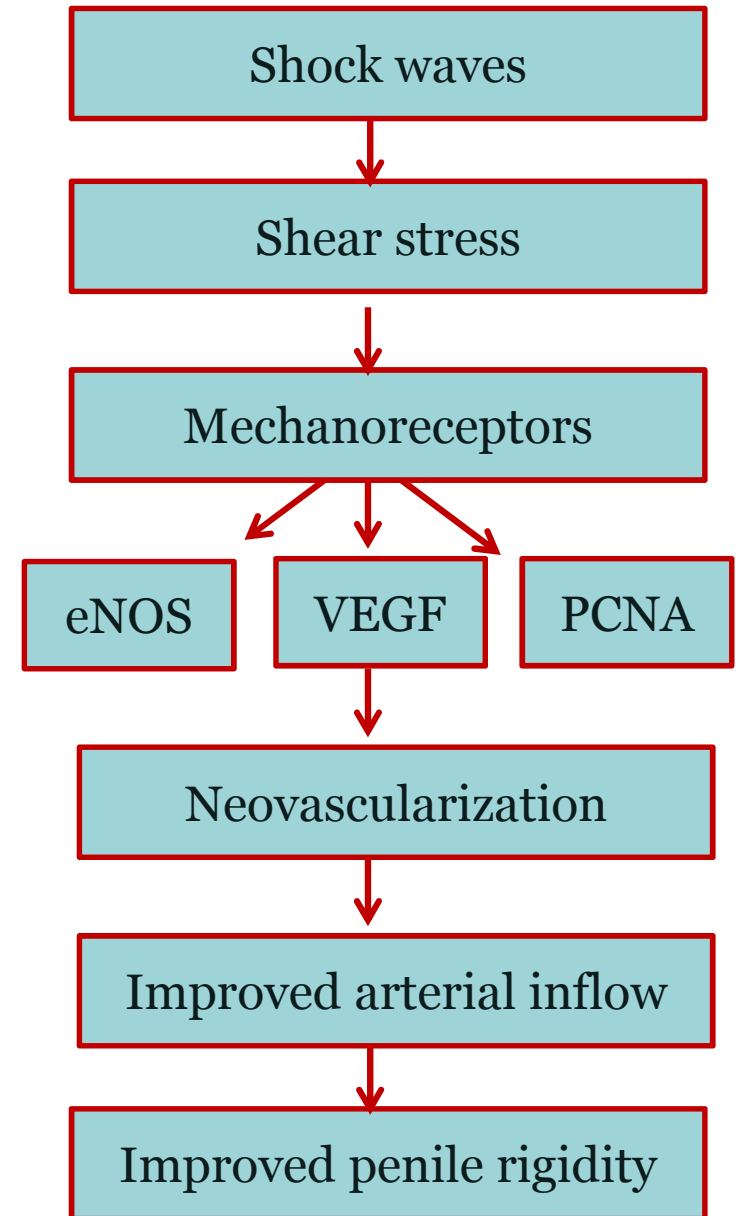
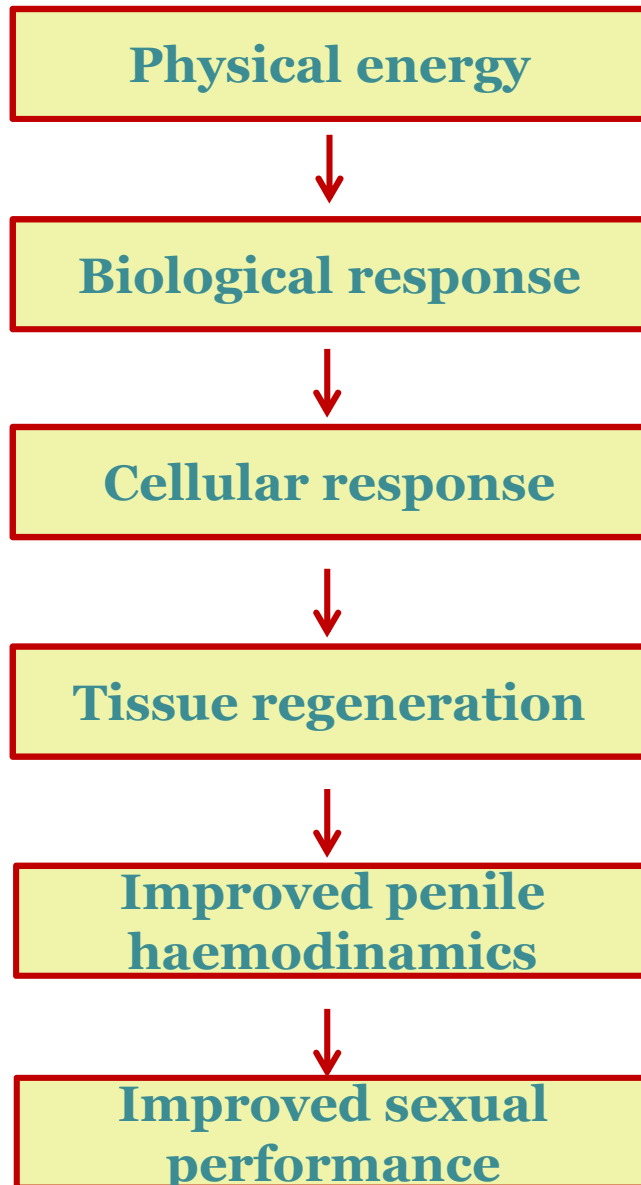
A potent  
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Significant  
Low  
High

group with  
p < .05).  
generation  
injury, it  
in both  
group.

**Li-ESWT: physical energy initiates a cascade of biologic responses, potentially leading to reversal of vasculogenic ED**



September 17 th, 2018

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[Low-Intensity Shockwave Therapy for Erectile Dysfunction: A Randomized Clinical Trial](#)

1. [Comparing 2 Treatment Protocols and the Impact of Repeating Treatment.](#)

Kalyvianakis D, Memmos E, Mykoniatis I, Kapoteli P, Memmos D, Hatzichristou D.

J Sex Med. 2018 Mar;15(3):334-345. doi: 10.1016/j.jsxm.2018.01.003. Epub 2018 Feb 1.

PMID: 29396020

[Similar articles](#)

[Extracorporeal shockwave therapy in the treatment of erectile dysfunction: a prospective,](#)

2. [randomized, double-blinded, placebo controlled study.](#)

Yee CH, Chan ES, Hou SS, Ng CF.

Int J Urol. 2014 Oct;21(10):1041-5. doi: 10.1111/iju.12506. Epub 2014 Jun 17.

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[Effect of Low-Energy Linear Shockwave Therapy on Erectile Dysfunction-A Double-Blinded,](#)

3. [Sham-Controlled, Randomized Clinical Trial.](#)

Fojecki GL, Tiessen S, Osther PJ.

J Sex Med. 2017 Jan;14(1):106-112. doi: 10.1016/j.jsxm.2016.11.307. Epub 2016 Dec 6.

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[Can low-intensity extracorporeal shockwave therapy improve erectile dysfunction? A prospective,](#)

4. [randomized, double-blind, placebo-controlled study.](#)

Olsen AB, Persiani M, Boie S, Hanna M, Lund L.

Scand J Urol. 2015;49(4):329-33. doi: 10.3109/21681805.2014.984326. Epub 2014 Dec 3.

PMID: 25470423

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shockwave therapy AND erectile dysfunction (59) PubMed

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# Low-intensity shockwaves (LiS) for ED: 7 years of clinical improvement

2010



## First paper: innovative treatment

Can Low-Intensity Extracorporeal Shockwave Therapy Improve Erectile Function? A 6-Month Follow-up Pilot Study in Patients with Organic Erectile Dysfunction

Yoram Vardi\*, Boaz Appel, Giris Jacob, Omar Massarwi, Ilan Gruenwald

2012



## Li-ESWT better than placebo!

Does Low Intensity Extracorporeal Shock Wave Therapy Have a Physiological Effect on Erectile Function? Short-Term Results of a Randomized, Double-Blind, Sham Controlled Study

Yoram Vardi\*,† Boaz Appel, Amichai Kilchevsky and Ilan Gruenwald

2016



## Li-ESWT improves PDE5i effect in non responders!

Penile Low Intensity Shock Wave Treatment is Able to Shift PDE5i Nonresponders to Responders: A Double-Blind, Sham Controlled Study

Noam D. Kitrey\*,† Ilan Gruenwald,\* Boaz Appel,‡ Arik Shechter,\* Omar Massarwa\* and Yoram Vardi‡

2017



## Li-ESWT improves penile hemodynamics!

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



# «The market»

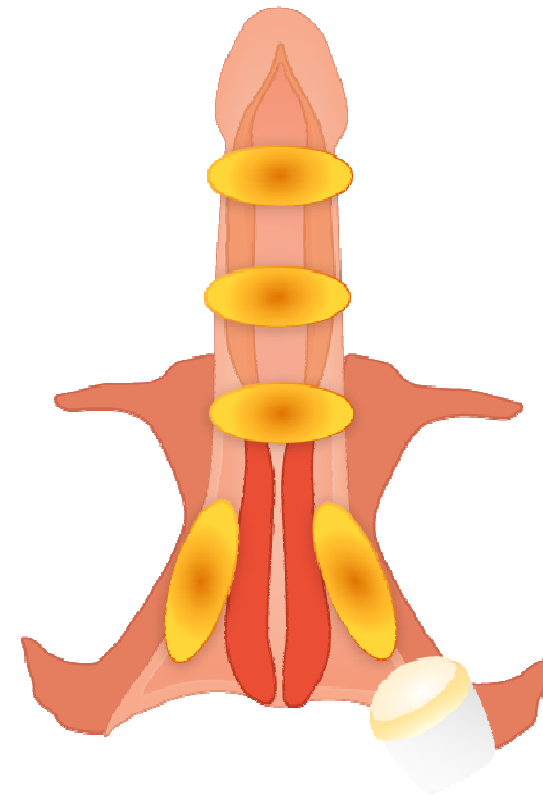
	Karl Storz	Dornier	MTS	Medispec	Direx	Richard Wolf
Machine	Duolith SD1	Aries	Urogold 100	ED 1000	Renova	Piezowave2
Technology	Electro-magnetic	Electro-magnetic	Electro-hydraulic	Electro-hydraulic	Electro-magnetic	Piezoelectric
Focal zone	Narrow focus	Wide focus	Wide focus (OP155)	Wide focus	Wide focus	Linear focus 46x20x4 mm
Energy penetration depth	0-125 mm	0-70 mm	0-80 mm	0-140 mm	0-40 mm	0-172 mm
Maximum energy flux density	1.25 mJ/mm <sup>2</sup>	0.31 mJ/mm <sup>2</sup>	0.19 mJ/mm <sup>2</sup> (OP155)	0.09 mJ/mm <sup>2</sup>	0.09 mJ/mm <sup>2</sup>	0.82 mJ/mm <sup>2</sup>
Frequency	1-8 Hz	0.5-20 Hz	0.5-8 Hz	2-2.6 Hz	5 Hz	1-8 Hz
Applicator Lifespan	Warranty 1 M	Warranty 2 M	100-200 K (estimated)	Stops at 180 K	1 M (estimated)	Warranty 5 M
Adjustable buttons on applicator	Yes	Yes	No	Yes (operating & reload)	No	Yes
Applicator weight	770g	500g	850g	1 Kg	N.A. (on holder)	0.55-1.58

# Conduct of treatment for ED with urogold100

**Spark Wave therapy is applied on penile shaft and corpus**

The following regions are treated:

- Distal, mid and proximal penis shaft (Corpora Cavernosa)
- Left and right-hand crus of penis shaft



# Randomized control trials (652 pz/211 placebo)

<b>Name</b>	<b>year</b>	<b>Pts n°</b>	<b>Type of machine</b>	<b>Target population</b>	<b>% success / time of assessment</b>	<b>Journal</b>
Vardi	2012	60	ED 1000 (Medispec)	Responders	58 % , 3m	J urol
Yee	2014	58	ED 1000 (Medispec)	Mixed	Significant only in severe, 1 m	Int J urol
Olsen	2014	105	Duolit (Storz)	Responders	57 % , 1m	Scan J urol
Sirini	2015	77	ED 1000 (Medispec)	Responders	78 % , 12 m	Can, J Urol (sponsored)
Kitrey	2016	55	ED 1000 (Medispec)	Non-responders	54 % , 3 m	J urol
Motil	2016	125	Pyezowave (wolf)	\	77,1 %	Adv Sex Med (sponsored)
Kalyvianakis	2017	46	ED 1000 (Medispec)	Responders	56 % , 6m	J sex Med
Fojecki	2017	126	Pyezowave (wolf)	Mixed	No effect 1 m	J Sex Med



# Low-intensity Extracorporeal Shock Wave Therapy for Erectile Dysfunction: A Systematic Review and Meta-analysis

Libo Man and Guizhong Li

UROLOGY ■■ (■■), 2017

101 Records identified through database searching

52 records hits, titles and abstracts reviewed by LGZ, MLB for inclusion

18 studies about the LI-ESWT and ED were included.

9 RCT studies were included. The details were checked for meta-analysis

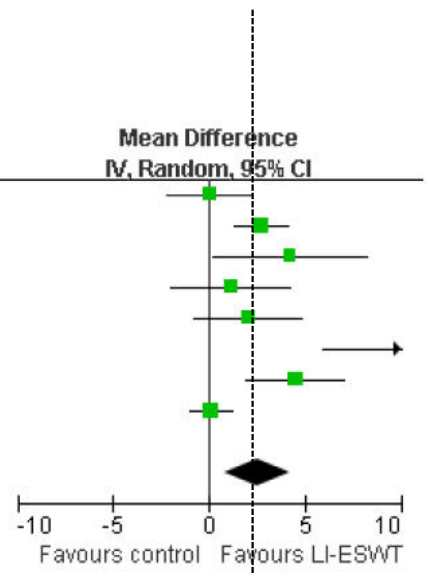
49 records excluded:  
 14 not related papers  
 18 review articles  
 4 animal studies  
 3 papers came from the same medical center  
 3 non-English papers  
 2 meeting highlights  
 4 editorial and comments  
 1 guideline

9 of full-text articles excluded for their cohort design

Study or Subgroup	LI-ESWT			Control			Weight	Mean Difference IV, Random, 95% CI	Year
	Mean	SD	Total	Mean	SD	Total			
Poulakis 2006	12	4.5	53	12	3.7	15	14.1%	0.00 [-2.23, 2.23]	2006
Zimmermann 2009	20	2.4	30	17.3	3.1	30	16.4%	2.70 [1.30, 4.10]	2009
Chitale 2010	19.9	4.8	16	15.7	7.5	20	9.1%	4.20 [0.16, 8.24]	2010
Vardi 2012	12.6	6.5	40	11.5	5.5	20	11.4%	1.10 [-2.04, 4.24]	2012
Yee 2014	17.8	4.8	30	15.8	6.1	28	12.3%	2.00 [-0.84, 4.84]	2014
Srini 2015	22	10.1	60	10.6	10.1	17	6.4%	11.40 [5.96, 16.84]	2015
Kitrey 2016	13	6.7	37	8.5	3	18	13.1%	4.50 [1.93, 7.07]	2016
Fojecky 2017	13.1	3	58	13	3	60	17.2%	0.10 [-0.98, 1.18]	2017

**Total (95% CI)** 324 208 100.0%  
 Test for heterogeneity:  $\text{Chi}^2 = 30.83, \text{df} = 7 (P < 0.0001), I^2 = 77.3\%$   
 Test for overall effect:  $Z = 2.91 (P = 0.004)$

**2.54 [-0.83, 4.25]**  
 ( $\Delta$  IIEF)



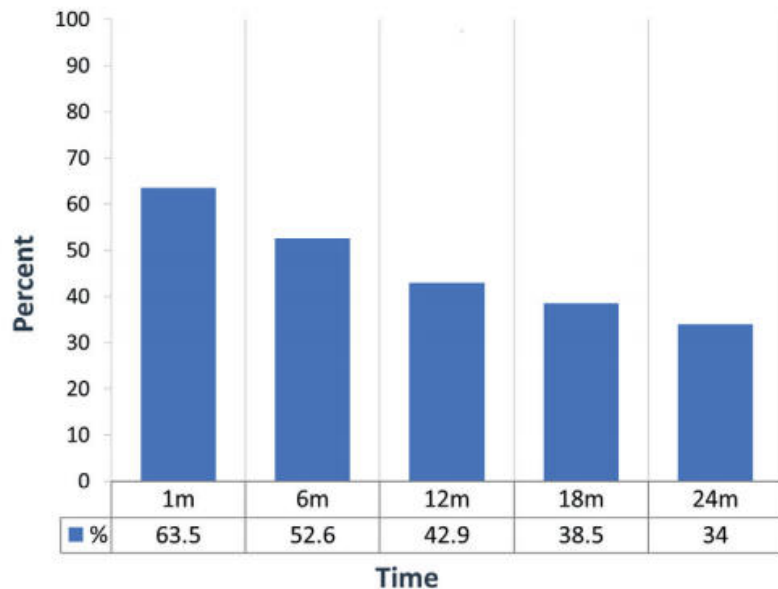
# Low Intensity Shock Wave Treatment for Erectile Dysfunction—How Long Does the Effect Last?

0022-5347/18/2001-0167/0  
THE JOURNAL OF UROLOGY®  
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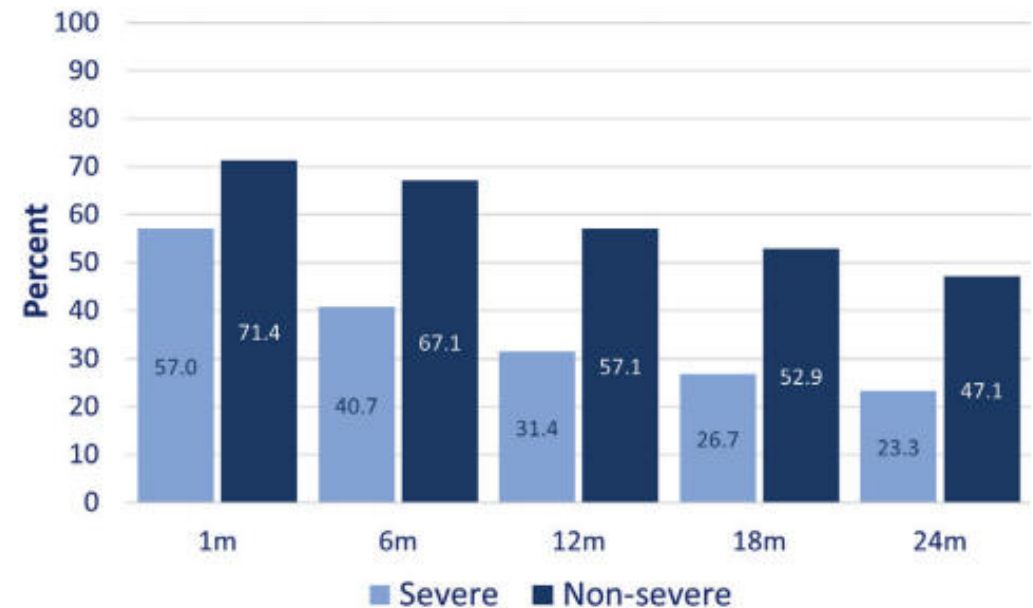
Noam D. Kitrey,\* Yoram Vardi, Boaz Appel,† Arik Shechter, Omar Massarwi, Yasmin Abu-Ghanem and Ilan Gruenwald

## Improvement: achievement of IIEF – Minimally Clinical Important Difference

- severe ED > 7
- moderate ED > 5
- mild ED > 2



**Figure 1.** Percent of patients in whom improvement was maintained with time. *m*, months.



**Figure 2.** Maintenance of success with time according to ED severity. *m*, months.

# SAFETY OF LI-ESWT

## Low-Intensity Shockwave Therapy for Erectile Dysfunction

Paul J. Rizk, BS,<sup>1</sup> Jordan R. Krieger, BS,<sup>1</sup> Taylor P. Kohn, MPhil,<sup>1</sup> and Alexander W. Pastuszak, MD, PhD<sup>2,3</sup>

- None of the studies included in this review reported adverse effects for Li-ESWT, except:  
1 patient an allergic reaction to the gel used during treatment.

**→ Li-ESWT is safe.**

- Assuming that micro-trauma is induced during Li-ESWT, no current data are available examining whether men undergoing Li-ESWT have an increased predisposition to Peyronie's disease or any other long-term complication.
- Long-term follow-up as part of RCTs is needed to fully assess risks of therapy.

# LI-ESWT IN MEN WITH POST-PROSTATECTOMY ED

SCANDINAVIAN JOURNAL OF UROLOGY, 2015  
<http://dx.doi.org/10.3109/21681805.2015.1100675>



## RESEARCH ARTICLE

### Low-intensity extracorporeal shockwave therapy in the treatment of postprostatectomy erectile dysfunction: a pilot study

Anders Frey, Jens Sønksen and Mikkel Fode

#### LIMITS OF THIS STUDY

- Population: 16 men, RALP-NS, post-operative ED.
- lack of treatment control group
- lack of control for PDE5i use
- Baseline assessment: median IIEF-5 score 9.5 and median time since surgery was 24 months.
- small number of patients

**Limited generalization of results**

Treatment protocol: 2 Li-ESWT treatments per week, for a total of 6 weeks, 3,000 shocks delivered

#### CRITICAL ANALYSIS OF RESULTS

- **most men** in this study, despite the improvements in score, were **unable to maintain erections sufficient for**
- the fact that IIEF increased and then decreased suggest **reversible effect of Li-ESWT on ED.**<sup>10\*</sup>

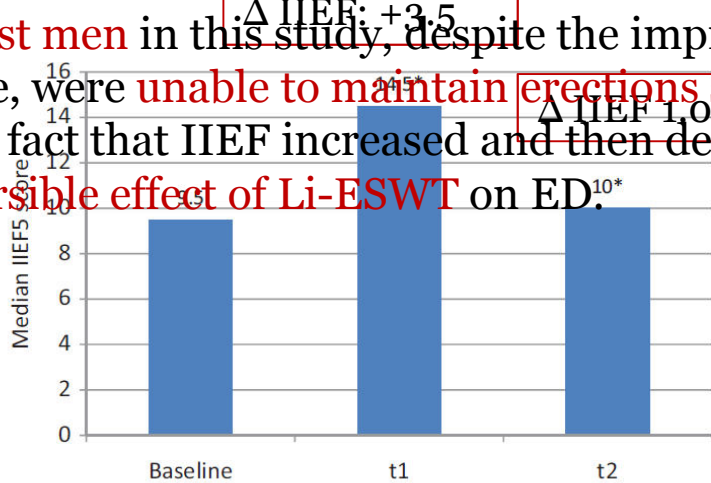


Figure 1. Median changes in International Index of Erectile Function-5 (IIEF5) scores. \* $p < 0.05$ .

Table 1. Changes in erectile function (ED) categories.

Patient no.	ED category (baseline)	ED category (t1)	ED category (t2)
1	Severe	Severe	Severe
2	Severe	Severe	Severe
3	Severe	Mild to moderate	NA
4	Moderate	Mild to moderate	Moderate
5	Moderate	Moderate	Mild to moderate
6	Mild	Mild	Mild
7	Mild	No ED	No ED
8	Severe	Severe	Severe
9	Severe	Moderate	Moderate
10	Moderate	Moderate	Moderate
11	Moderate	Moderate	Severe
12	Moderate	Mild to moderate	No ED
13	Mild to moderate	Mild	Mild
14	Mild	Mild	Mild
15	Mild	Mild	Mild
16	Moderate	Mild to moderate	Moderate

NA = not applicable.

ED or a

# LI-ESWT IN MEN WITH POST-PROSTATECTOMY ED

**The Effects of Focal Therapy for Prostate Cancer on Sexual Function: A Combined Analysis of Three Prospective Trials**



European Association of Urology

*Tet Yap<sup>a,\*</sup>, Hashim U. Ahmed<sup>a,b</sup>, Richard G. Hindley<sup>c</sup>, Stephanie Guillaumier<sup>a,b</sup>, Neil McCartan<sup>a,b</sup>, Louise Dickinson<sup>a,b</sup>, Mark Emberton<sup>a,b</sup>, Suks Minhas<sup>a</sup>*

EUROPEAN UROLOGY 69 (2016) 844–851

**118 men** who were reported in the **3 TRIALS** of focal therapy \*

Eligibility : men with low, intermediate, and high-risk disease (PSA 15 ng/ml, Gleason 4 + 3, stage T2NoMo), aged 45–80 yr with a life expectancy of 10 yr or more, a prostate volume of 40 ml or maximum anterior-posterior length of 40 mm.

Men were carefully characterised using a combination of (mp-MRI) and concordant biopsy (transperineal template-prostate-mapping [TPM] or transrectal biopsies)

\*

- Ahmed HU, Dickinson L, Charman S, et al. Focal ablation targeted to the index lesion in multifocal localised prostate cancer: A prospective development study. *Eur Urol* 2015;68:927–36.

- Ahmed HU, Freeman A, Kirkham A, et al. Focal therapy for localised prostate cancer: a phase I/II trial. *J Urol* 2011;185: 1246–54.

- Ahmed HU, Hindley RG, Dickinson L, et al. Focal therapy for localised unifocal and multifocal prostate cancer: a prospective development study. *Lancet Oncol* 2012;13:622–32.

# LI-ESWT IN MEN WITH POST-PROSTATECTOMY ED

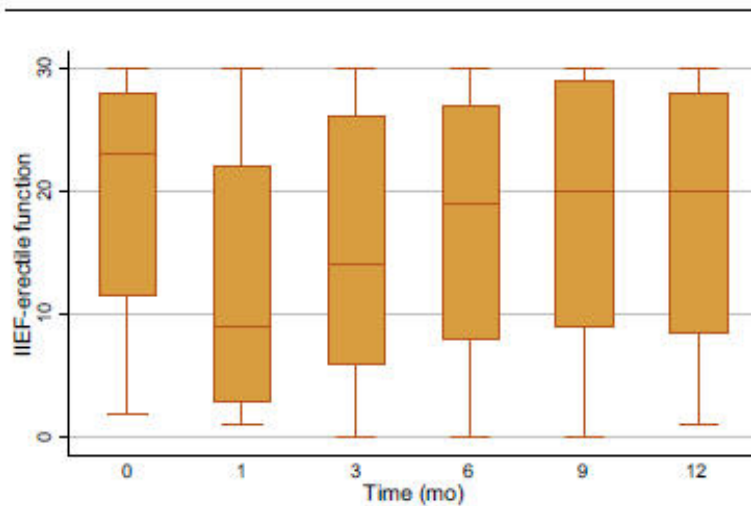
## The Effects of Focal Therapy for Prostate Cancer on Sexual Function: A Combined Analysis of Three Prospective Trials



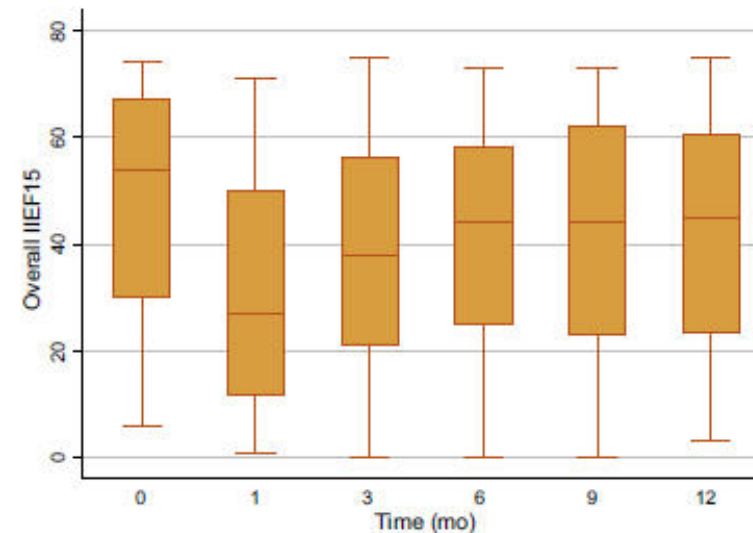
European Association of Urology

Tet Yap<sup>a,\*</sup>, Hashim U. Ahmed<sup>a,b</sup>, Richard G. Hindley<sup>c</sup>, Stephanie Guillaumier<sup>a,b</sup>, Neil McCartan<sup>a,b</sup>, Louise Dickinson<sup>a,b</sup>, Mark Emberton<sup>a,b</sup>, Suks Minhas<sup>a</sup>

EUROPEAN UROLOGY 69 (2016) 844–851



**Fig. 1 – Distribution and median International Index of Erectile Function-erectile function from baseline to 12 mo. Median level is represented by the line within the box, margins of the box represent the interquartile range, and the whiskers represent the extremes of distribution. The box plots show a gradual recovery of median International Index of Erectile Function-erectile function to baseline levels at 9 mo and 12 mo posttreatment. IIEF = International Index of Erectile Function.**



**Fig. 2 – Distribution of median International Index of Erectile Function-total from baseline (score = 58) to 12 mo. Median level is represented by the line within the box, margins of the box represent the interquartile range, and the whiskers represent the extremes of distribution. The box plots show a gradual recovery of median International Index of Erectile Function-total to baseline levels at 9 mo and 12 mo posttreatment. IIEF = International Index of Erectile Function.**

# LI-ESWT IN MEN WITH POST-PROSTATECTOMY ED

Table 2 – International Index of Erectile Function (IIEF)-erectile and total IIEF between the three groups at baseline, 1 mo, 3 mo, 6 mo, and 12 mo post-focal therapy, along with IIEF questionnaire completion rates at each time-point

Median value (IQR)	Baseline	1 mo	3 mo	6 mo	9 mo	12 mo
IIEF-erectile (FOCAL)	24 (15–29)	6 (3–20)	12 (7–25)	19 (12–26)	23 (11–29)	21 (11–27)
IIEF-erectile (HEMI)	23 (20–25)	11 (8–22)	22 (7–27)	26 (14–28)	28 (21–29)	25 (14–29)
IIEF-erectile (LESION CONTROL)	22 (10–29)	11 (4–22)	15 (6–26)	16 (5–26)	18 (5–28)	16 (6–27)
IIEF-erectile (IQR) (ALL)	23 (11–28)	9 (3–22)	15 (6–26)	19 (8–27)	20 (9–29)	20 (9–28)
<i>p</i> value (difference between groups, Kruskal-Wallis)	0.34	0.14	0.61	0.06	0.06	0.10
<i>p</i> value (difference from baseline)	–	0.004*	0.009*	0.06	0.59	0.30
IIEF-total (FOCAL)	58 (32–67)	18 (11–47)	33 (21–55)	47 (27–58)	50 (28–64)	55 (30–63)
IIEF-total (HEMI)	63 (59–70)	32 (21–51)	52 (25–62)	57 (40–64)	62 (49–67)	55 (36–65)
IIEF-total (LESION CONTROL)	54 (30–65)	33 (17–53)	39 (21–56)	42 (24–59)	43 (19–61)	42 (21–59)
IIEF-total (IQR) (ALL)	58 (32–67)	28 (13–50)	39 (21–58)	47 (26–61)	51(26–64)	47 (28–62)
<i>p</i> value (difference between groups, Kruskal-Wallis)	0.26	0.06	0.56	0.85	0.06	0.18
<i>p</i> value (difference from baseline)	–	0.005*	0.009*	0.08	0.57	0.30
IIEF completion rate (all groups)	98%	97%	97%	96%	96%	95%

IIEF = International Index of Erectile Function; IQR = interquartile range.  
 \* Significant difference; significance level:  $p > 0.05$ .

When IIEF-erectile and total scores were compared between the three groups, there was **no significant difference** at baseline, 1 mo, 3 mo, 6 mo, 9 mo, and 12 mo postfocal therapy.

# CONCLUSIONS

**LI-ESWT and ED in patients treated for prostate cancer:**



**WE HAVE MANY  
QUESTIONS...**

**...BUT ONLY FEW  
ANSWERS**

come a new rehabilitation  
*ED.*





*“That’s all Folks!”*