

LE ONDE D'URTO NEL DEFICIT ERETTILE DELL'AGING MALE

Genova, 30 settembre 2014



VILLA MONTALLEGRO

Prevenzione e trattamento
del deficit erettile con
onde d'urto

Antonio Casarico e Paolo Puppo
Villa Montallegro
Genova

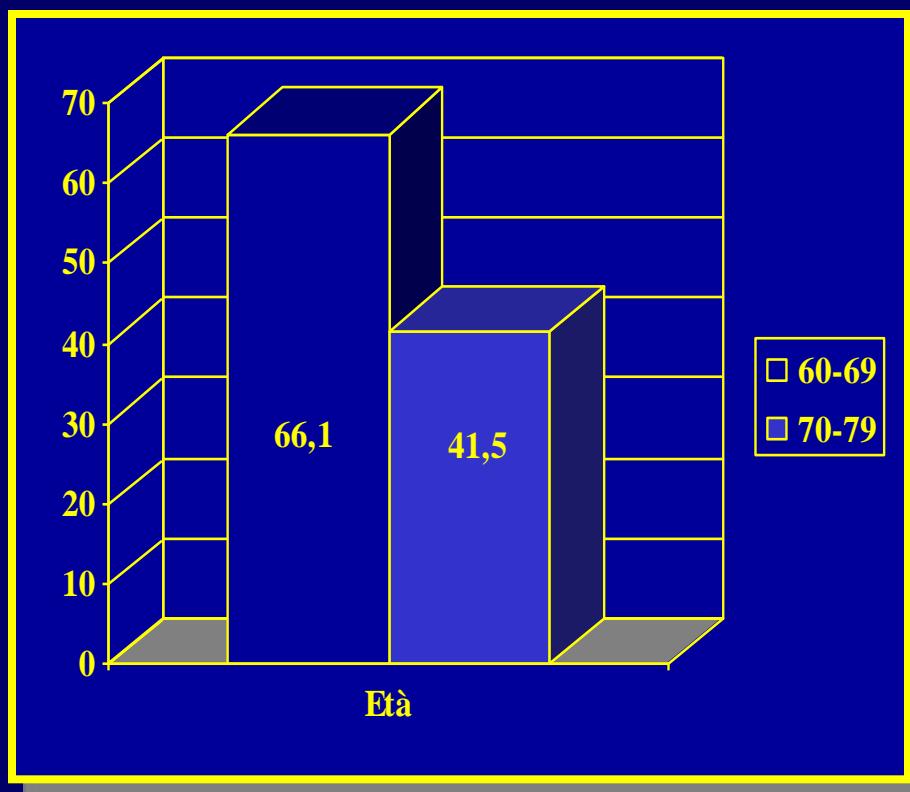
Età ed attività sessuale

La maggioranza dei maschi rimane sessualmente attivo anche dopo i 70 anni

Cologne Male Survey:
attività sex settimanale

Braun M, Int J Impot Res, 2000

Rosen R, Eur Urol, 2003



Età ed attività sessuale

Cologne Male Survey

- La sessualità rimane una componente fondamentale della Qol
- Aumenta con l'età la percentuale di soggetti insoddisfatti della propria vita sessuale (31,3 - 44 %)

L'interesse a mantenere la funzione sessuale
non diminuisce con l'età

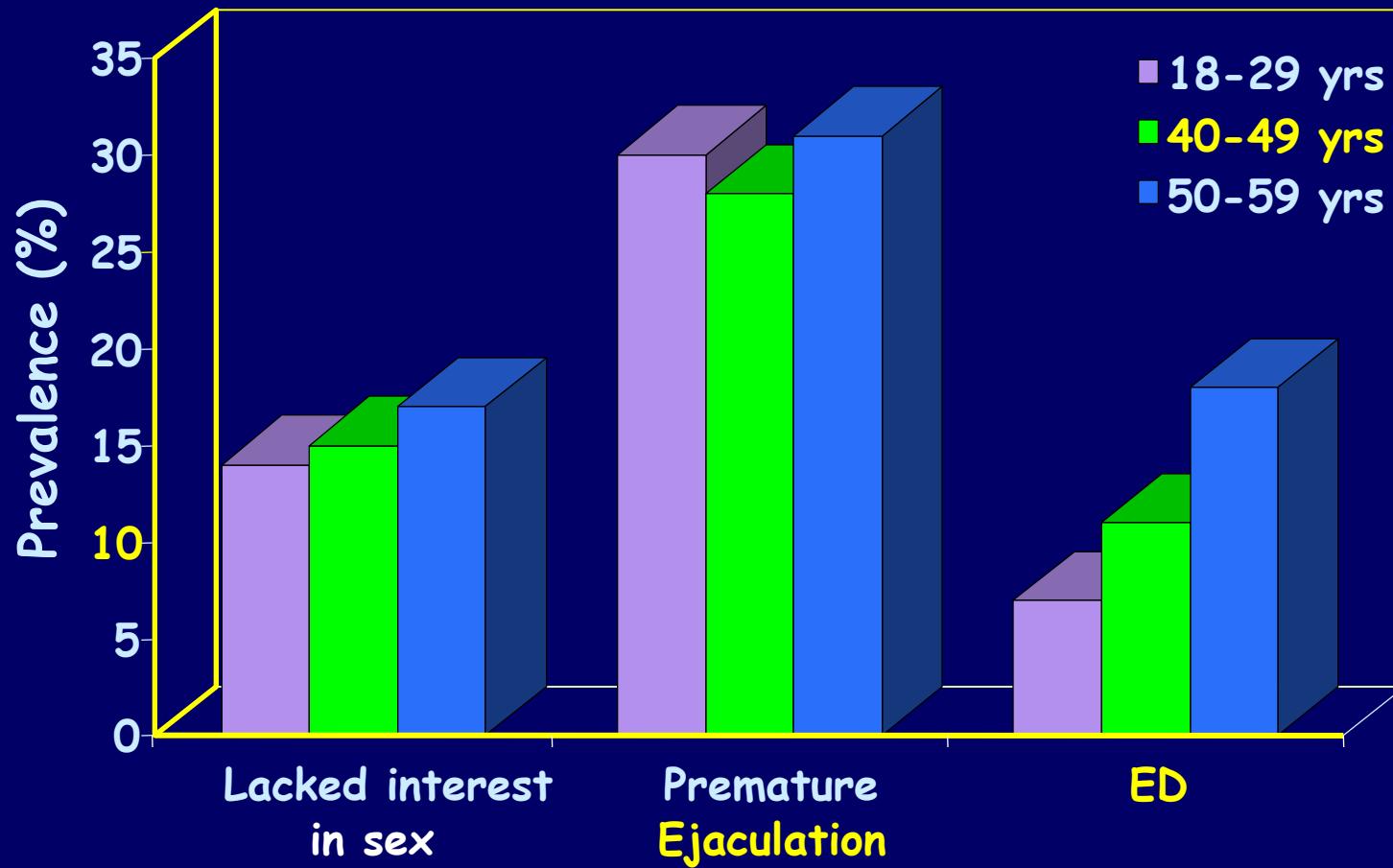
Braun M, Int J Impot Res, 2000

Rosen R, Eur Urol, 2003

*"... NON E' LA QUANTITA' DEI
VOSTRI RAPPORTI SESSUALI
QUELLO CHE CONTA , MA LA
QUALITA'...
PERO' SE LA QUANTITA' E' MENO
DI UNA VOLTA OGNI SEI MESI ,
IO UN' OCCHIATINA ME LA FAREI
DARE"*

WOODY ALLEN
(*in AMORE E GUERRA*)

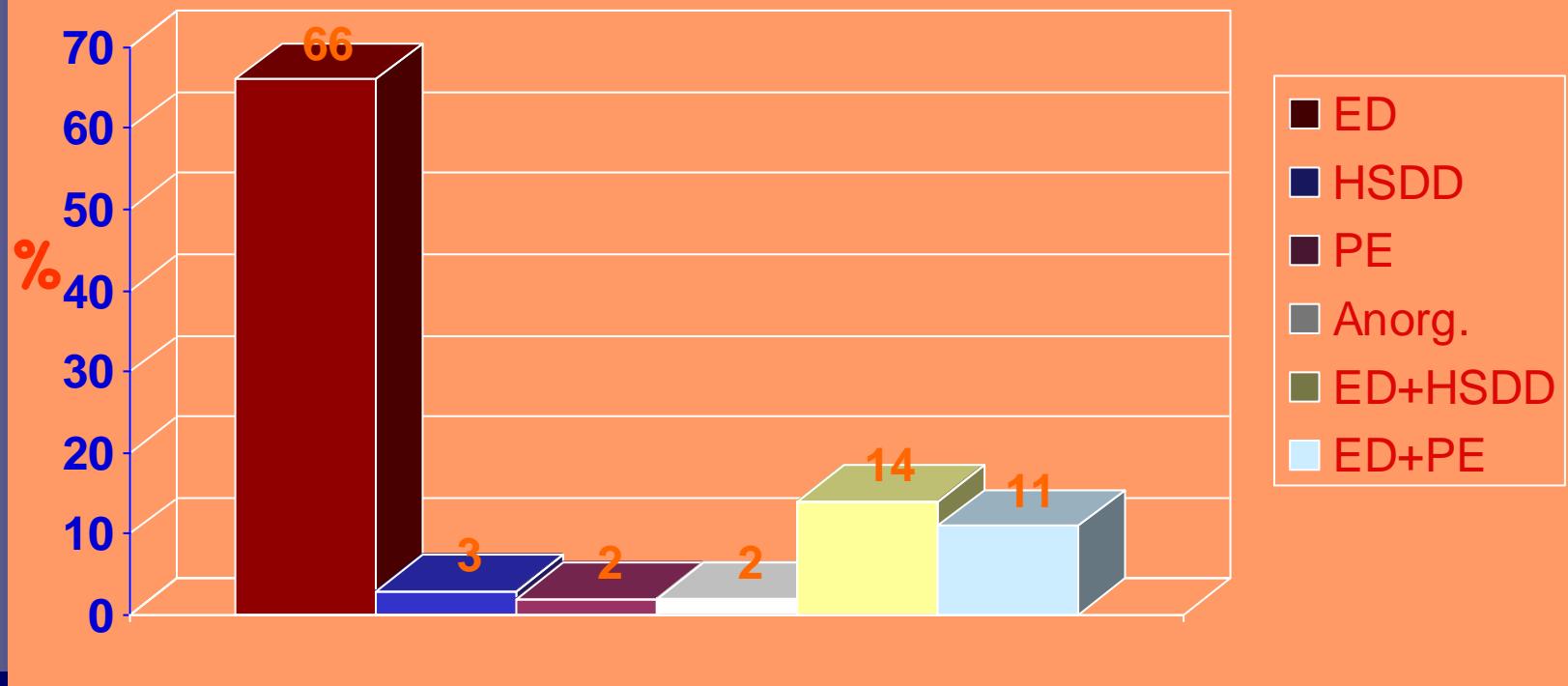
Prevalenza delle Disfunzioni Sessuali Maschili



Laumann EO, et al. JAMA. 1999;281:537-544.

Disfunzioni Sessuali nell'Anziano

n = 270 men > 60 y.o.



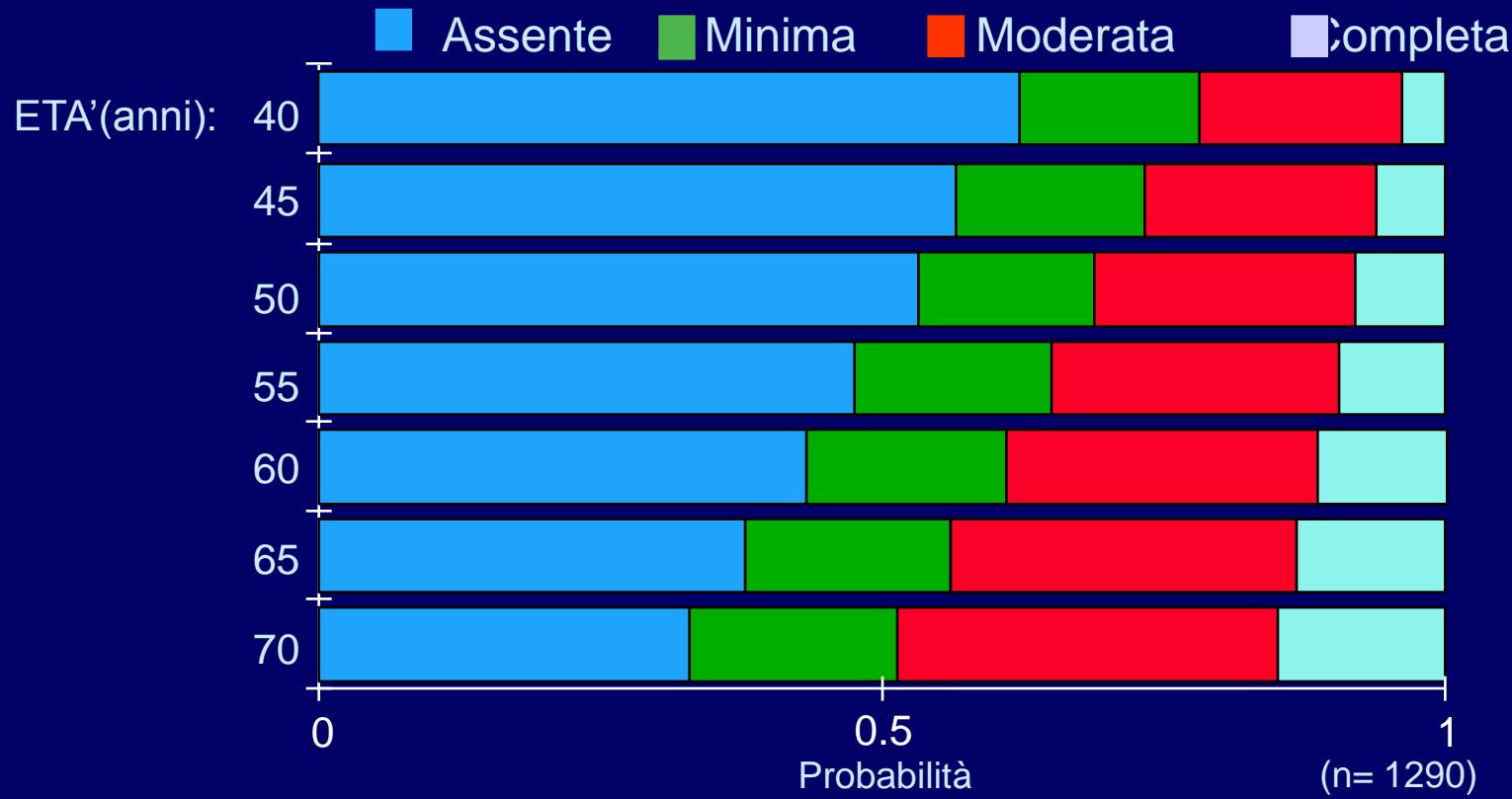
Schiavi, R.C. Aging and Male Sexuality. Cambridge University Press 1999.

MMAS (Massachusetts Male Ageing Study)

Feldman HA, J Urol, 1994

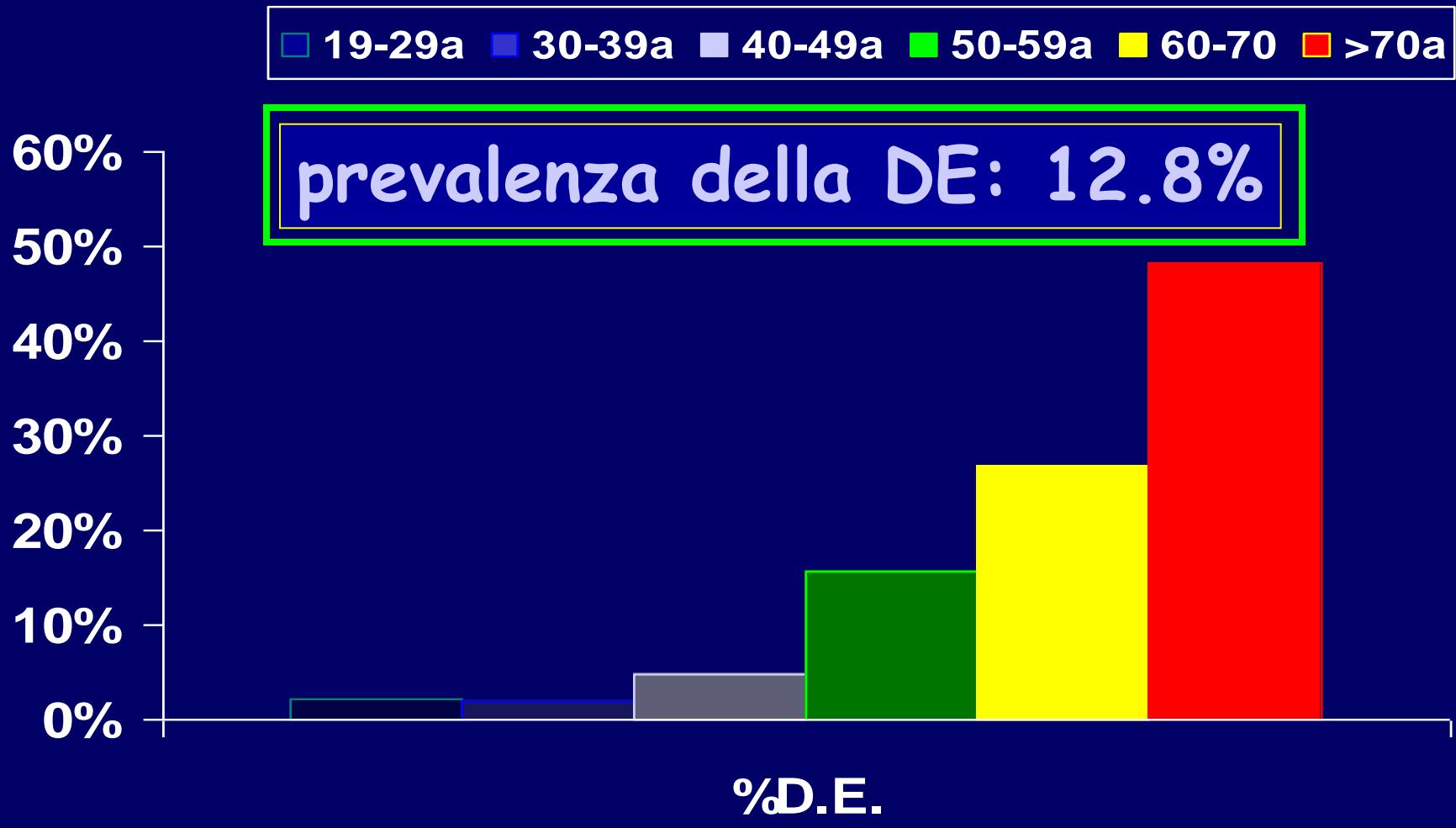
Epidemiologia

Età e Probabilità di disfunzione erettile



Frequenza della DE in Italia

SIA, SIU, SIMMG, Istituto Mario Negri



**Apoptosi
muscolo liscio**

**Stress
ossidativo**

**Disfunzione
endoteliale**

**SINDROME
DISMETABOLICA**

Benign prostatic
hyperplasia

DE

OAB

Ipopgonadismo

Nefrolitiasi

Obesity

Hypertension

Dyslipidemia

Prostate cancer

Atherosclerotic
disease

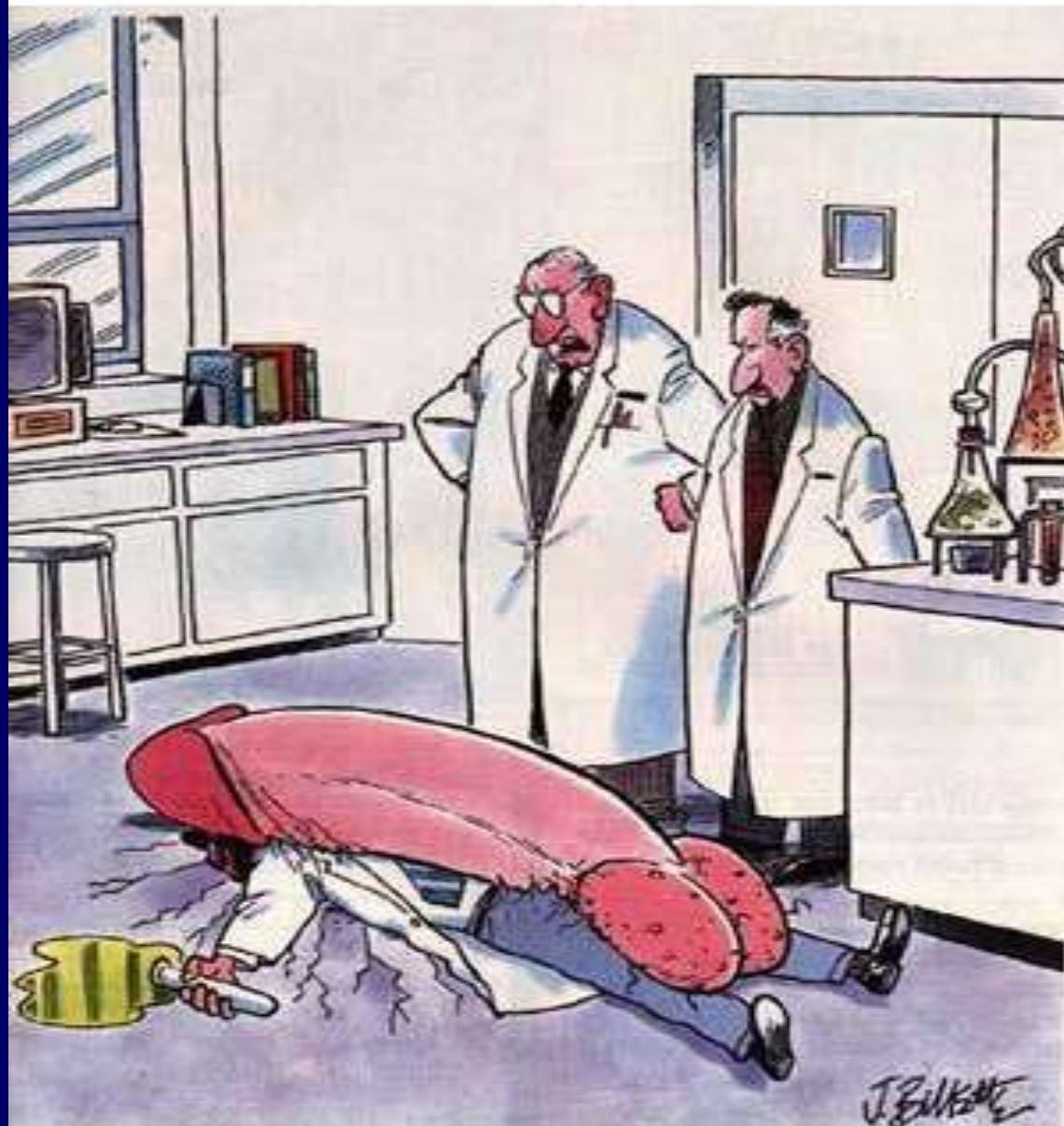
Type 2
diabetes

DISFUNZIONE ERETTILE

le terapie non chirurgiche

- ❖ Modificazione stili di vita
- ❖ Coinvolgimento della partner
- ❖ Terapie psicosessuologiche
- ❖ Terapia ormonale
- ❖ Farmaci orali (Sildenafil, Tadalafil, Vardenafil, Avanafil)
- ❖ Vacuum device
- ❖ Farmaci iniettabili (intracavernosi)

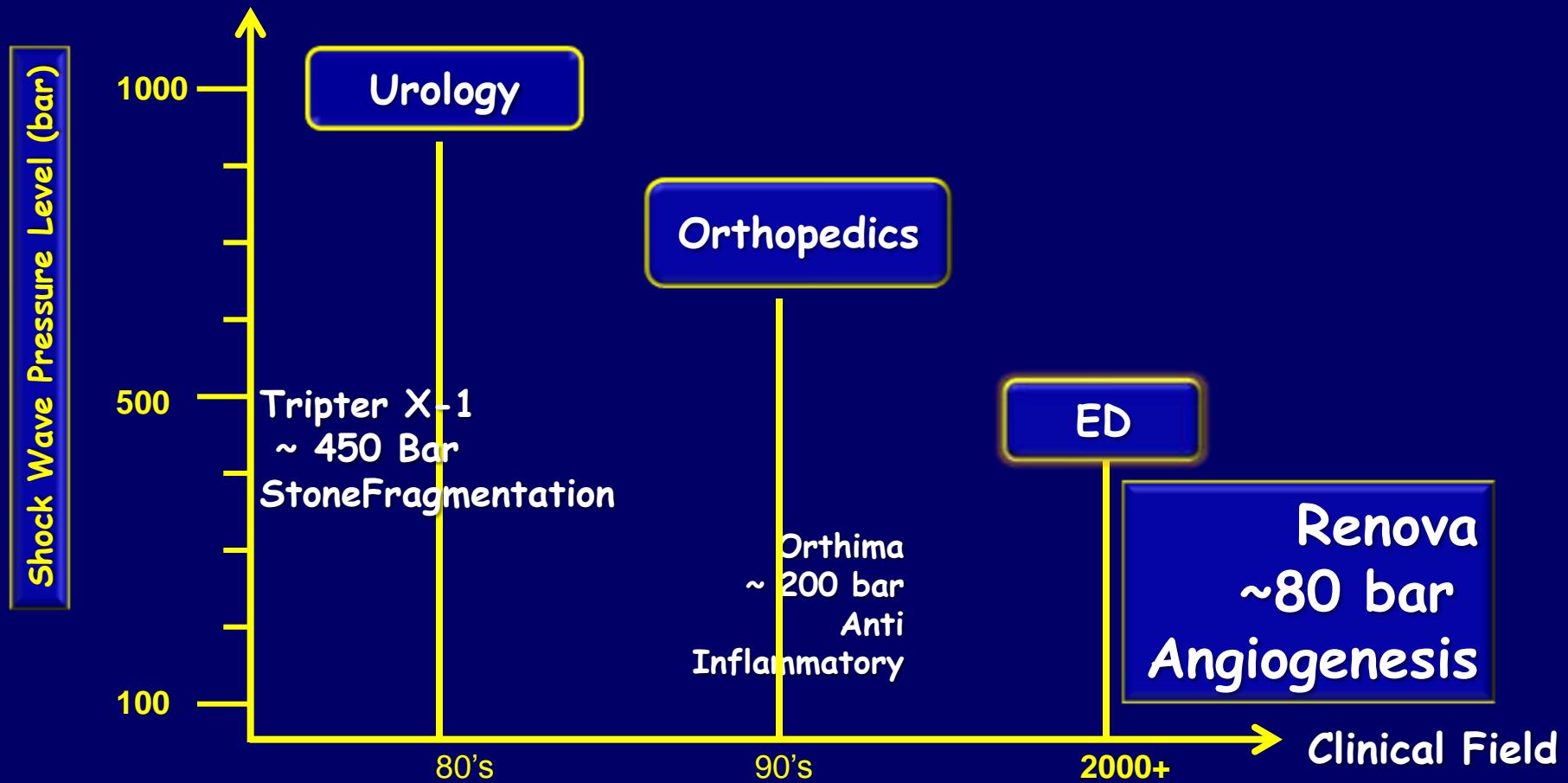
non modificano le alterazioni del meccanismo erettivo, devono essere assunte a richiesta ed il loro effetto è limitato nel tempo. Sono una **terapia sintomatica** e comportano, a volte, effetti collaterali e, conseguentemente, una scarsa aderenza alla terapia..



"Ok, This Viagra works
now we need to calculate the dosage"

La Rivoluzione delle Onde d'Urto

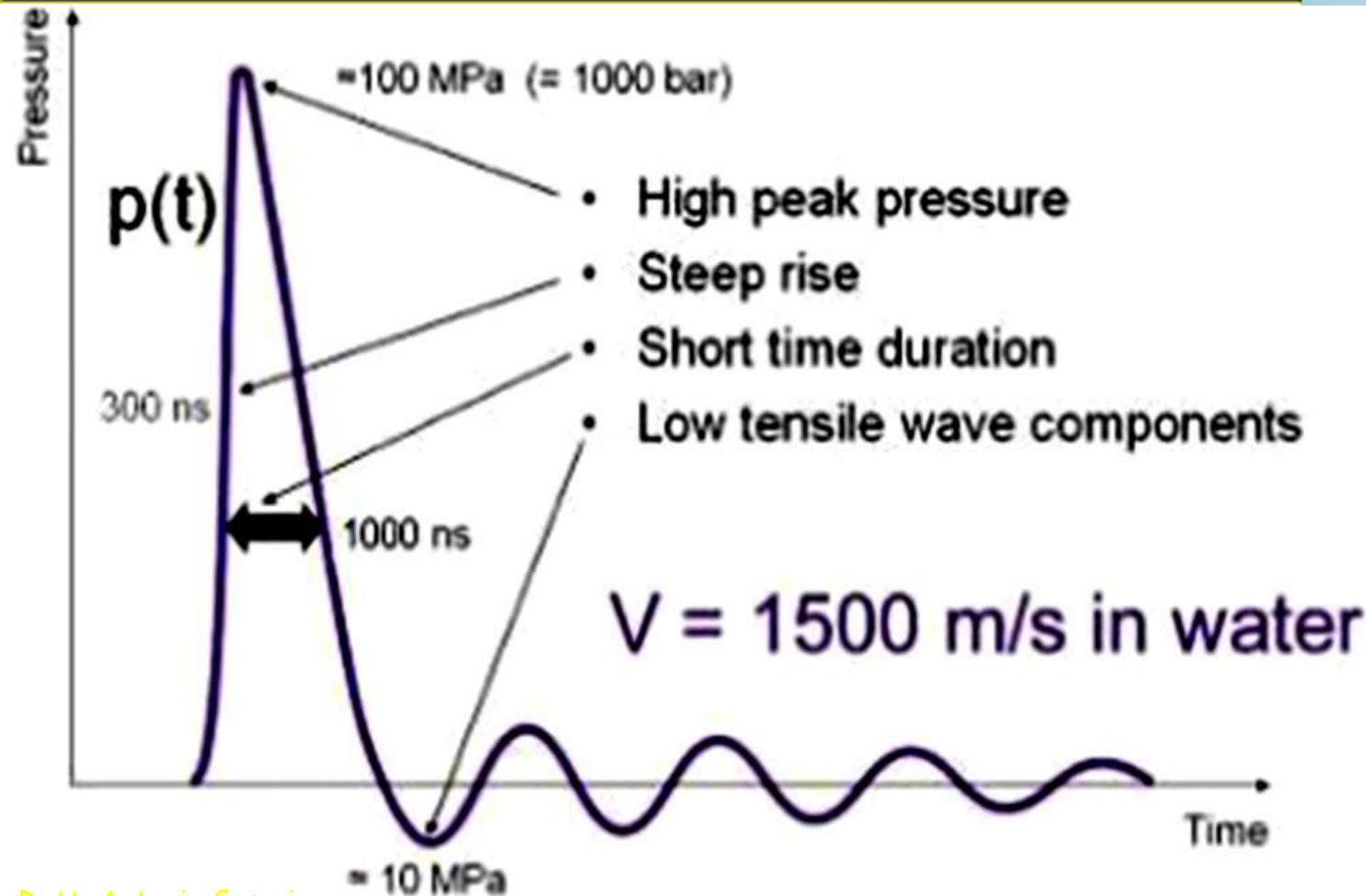
Shockwave Therapy Applications



SHOCKWAVES

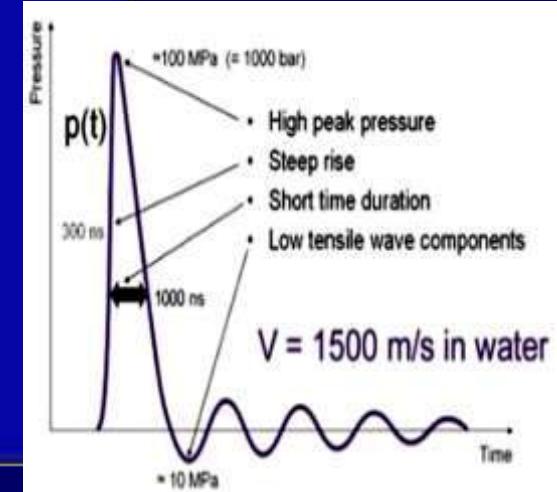
Carry energy - able to propagate through a medium.

- sequence of single sonic pulses
- fast pressure rise (<10 nanoseconds)
- high-pressure peak (100 MPa),
- short lifecycle (10 microseconds)

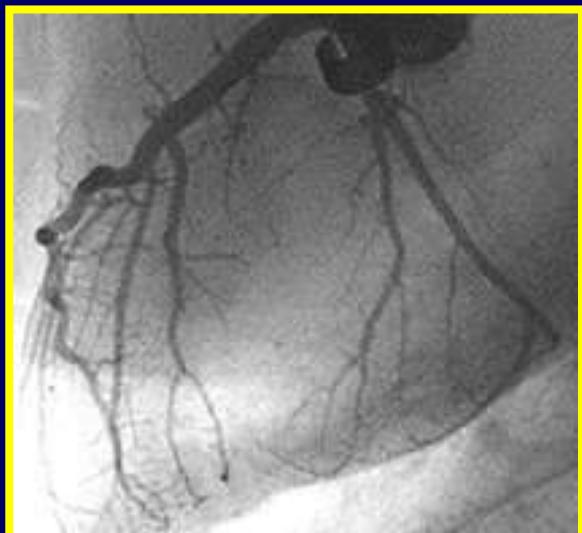
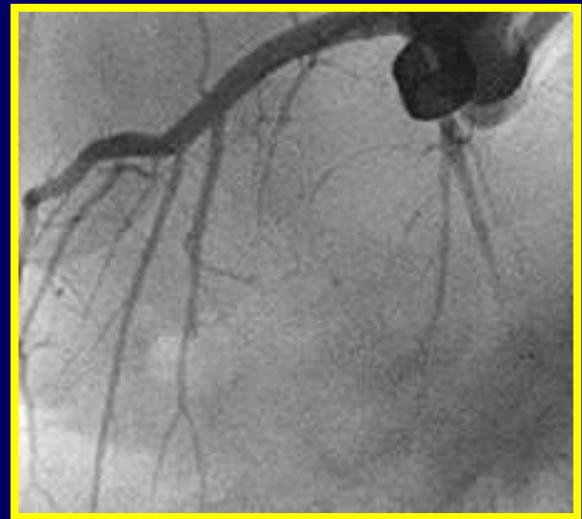
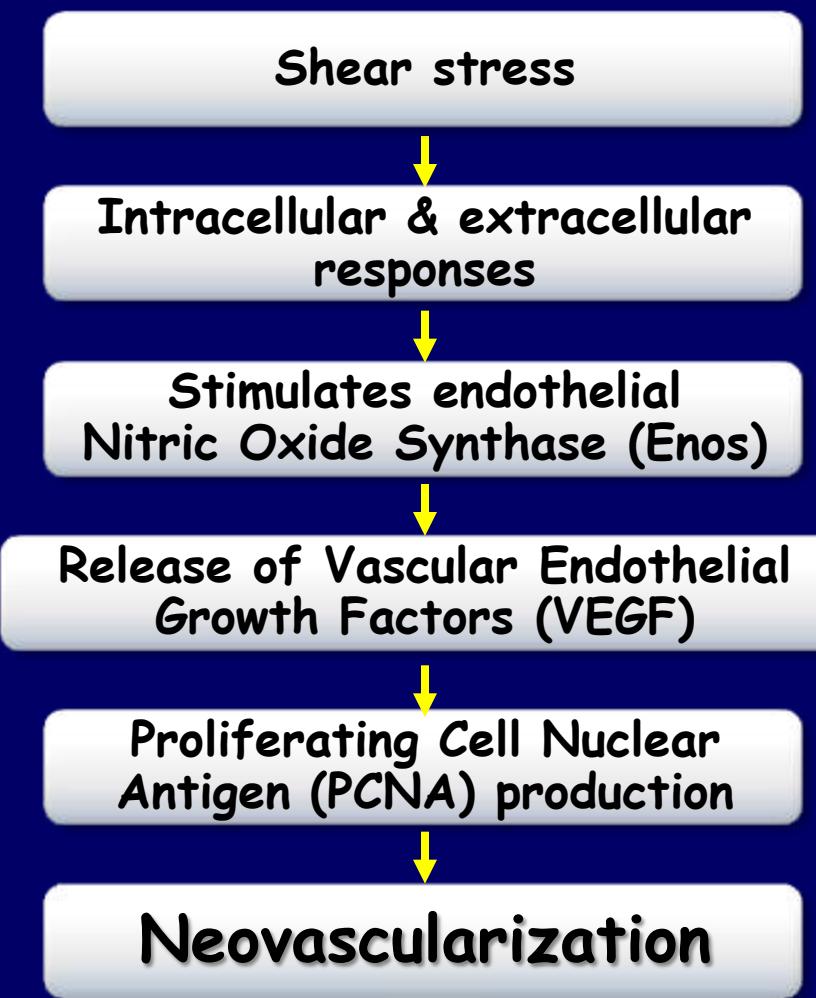


SHOCKWAVES

- ✓ tissue is first compressed due to the positive pressure
- ✓ then expands due to the tensile properties of the tissue
- phenomenon: CAVITATION (resembled a micrometer-sized violent collapse of bubbles)
- SW induces a SHEAR STRESS on endothelial cell membranes



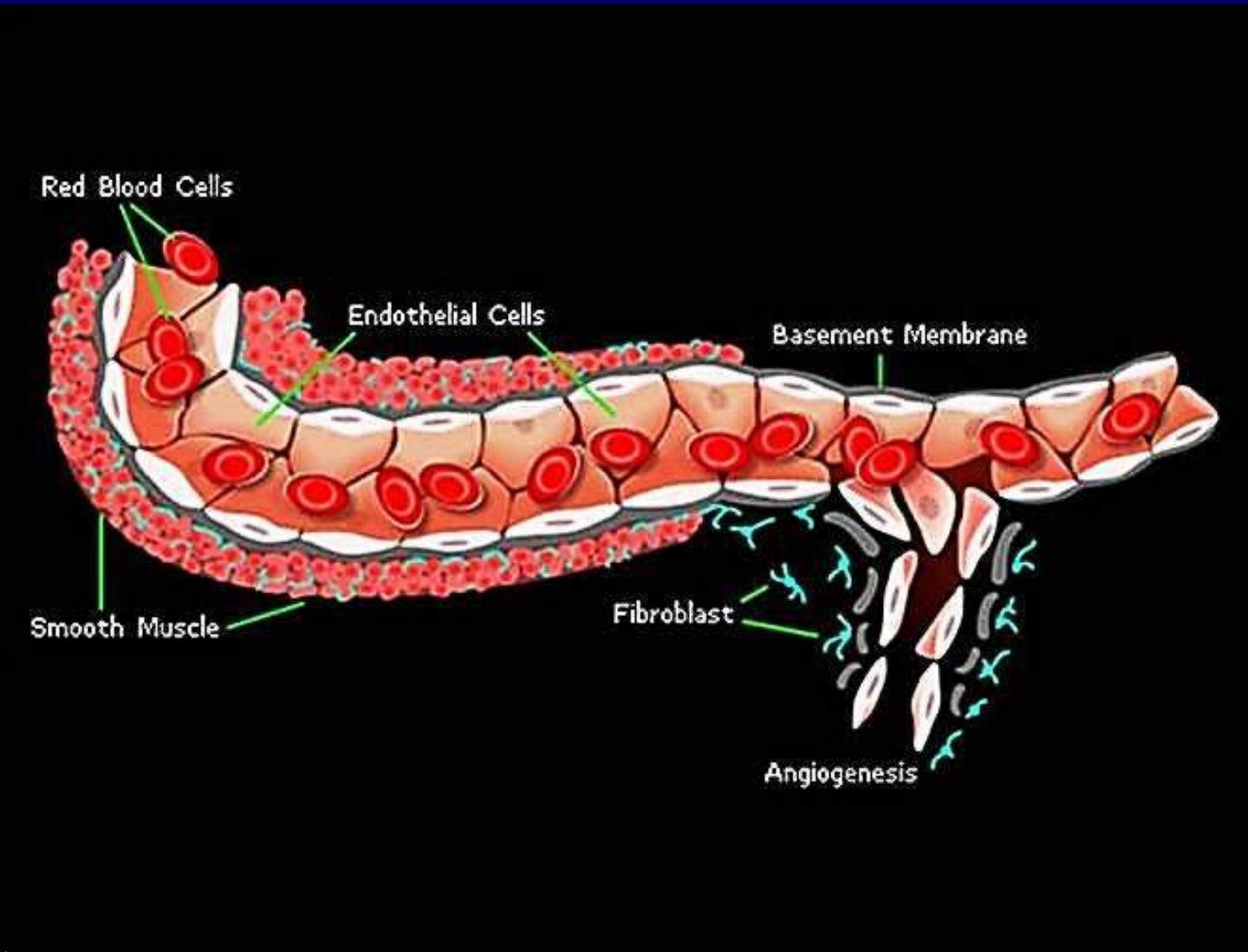
Low Energy Shock Waves Induce Angiogenesis



Angiogenesis

- process of sprouting new blood vessels from pre-existing vessels.
- major cells involved in this process are the endothelial cells, which line the blood vessels and constitute capillaries.

Angiogenesis



Clinical Background

Extracorporeal Cardiac Shock Wave Therapy
Markedly Ameliorate Ischemia - Induced

Nishida
Cardiova

"Y.
55-3061

ANIMAL STUDIES

Extracorporeal cardiac SW therapy is an effective and noninvasive therapeutic strategy for ischemic heart disease.

Clinical History - Enhancement of Coronary Collaterals

Control Group

SW Group

4 weeks
AC impla

4 weeks
treatment

HUMAN STUDIES



**Double-blind and placebo-controlled study
of the effectiveness and safety of
extracorporeal cardiac shock wave
therapy for severe angina pectoris.
Kikuchi Y et al. Circ J. 2010 Mar;74(3):589-91.**

LI-ESWT

- ❖ Improved LV ejection fraction and strokevolume
- ❖ Significantly ameliorated severity of the chest pain after a 6-minute walk.

Initial clinical experience with extracorporeal shock wave therapy in treatment of ischemic heart failure.

Vasyuk YA et al. Congest Heart Fail. 2010 Sep-Oct;16(5):226-30.

A modified regimen of extracorporeal cardiac shock wave therapy for treatment of coronary artery disease.

Wang YCardiovasc Ultrasound. 2012 Aug 17;10:35.

Randomized and double-blind controlled clinical trial of extracorporeal cardiac shock wave therapy for coronary heart disease.

Yang P et al. Heart Vessels. 2013 May;28(3):284-91.

LI-ESWT ameliorated the severity of angina pectoris and ischemic heart failure

Clinical History

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

Vardi Y, Appel B, Jacob G, Massrwi O, Gruenwald I Eur Urol 58: 243-248, 2010

Conclusions:

first study that assessed the **efficacy of LI-ESWT for ED.... tolerable and effective**, suggesting a physiologic impact on Cavernosal hemodynamics. potential to **improve erectile function** and to contribute to **penile rehabilitation without pharmacotherapy**.short-term results are **promising**

Clinical History

Low-intensity extracorporeal shock wave therapy- a novel effective treatment for erectile dysfunction in severe ED patients who respond poorly to PDE5 inhibitor therapy.

Gruenwald I, Appel B, Vardi Y. J Sex Med 9: 259-264, 2012

CONCLUSIONS:

LI-ESWTpotential to treat a subgroup of severe ED patients. ...need to be reconfirmed by multicenter sham control studies in a larger group of ED patients.

Clinical History

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.

Vardi Y, Appel B, Kilchevsky A, Gruenwald I J. Urol. May;187(5):1769-75, 2012

Conclusions:

first randomized, double-blind, sham controlled study shows positive short-term clinical and physiological effect on the erectile function of men who respond to oral phosphodiesterase type 5 inhibitor therapy...feasibility and tolerability potential rehabilitative characteristics

Low-Intensity Extracorporeal Shock Wave Therapy in Vascular Disease and Erectile Dysfunction: Theory and Outcomes

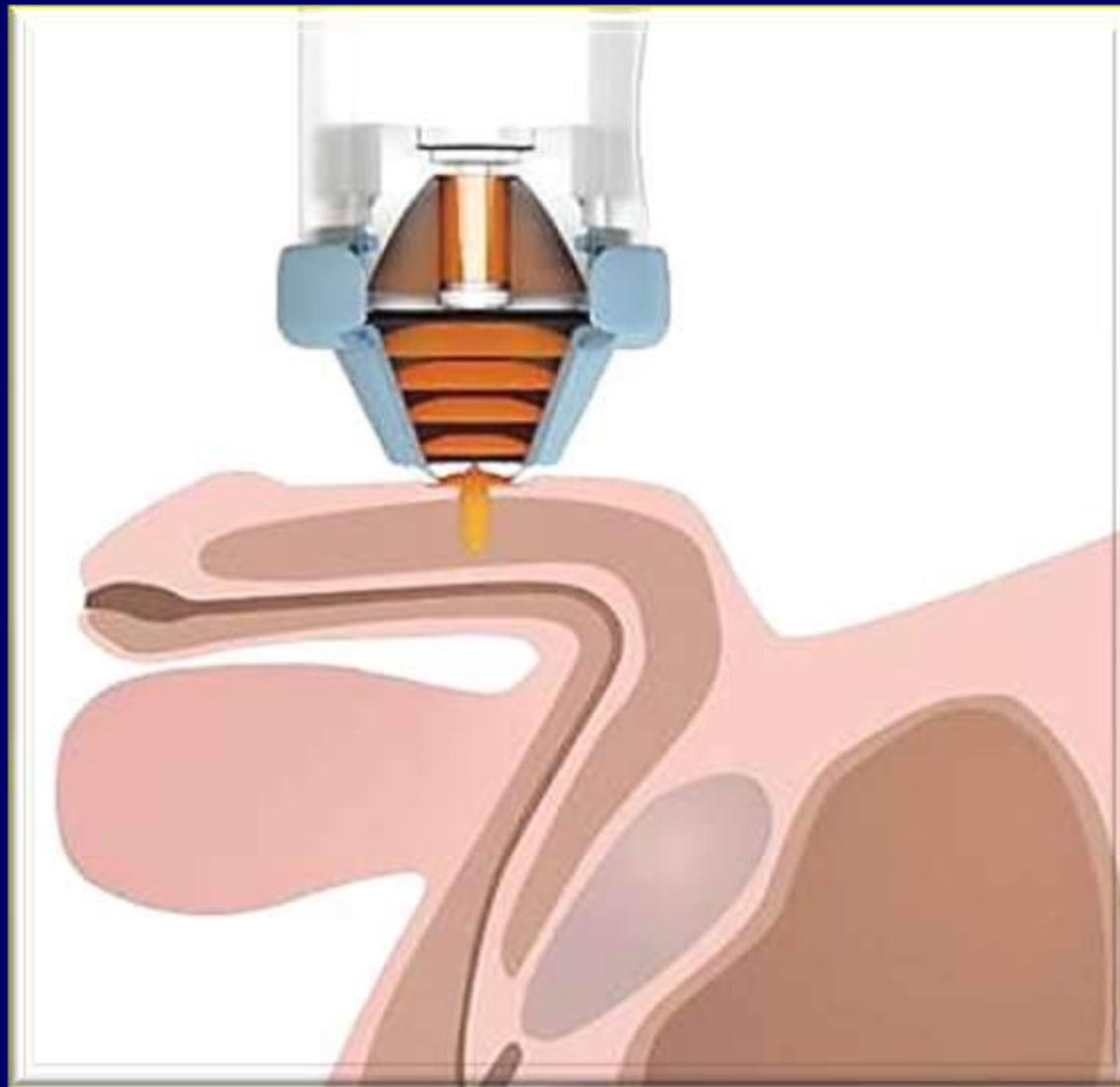
Ilan Gruenwald, MD,^{*†} Noam D. Kitrey, MD,^{*†} Boaz Appel, MD,^{*†} and Yoram Vardi, MD^{*†}

Sex Med Rev 2013;1:83–90.

Results. From the results of numerous preclinical and animal studies that have been done to date, sufficient evidence shows that the underlying mechanism of action of LI-ESWT is probably neovascularization. Therefore, local application of LI-ESWT to the corpora cavernosa may potentially act in the same mechanism and increase corporal blood flow. We found that the application of LI-ESWT to patients who responded to oral therapy (PDE5i) eliminated their dependence on PDE5i and they were able to successfully achieve erections and vaginal penetration (60-75%). Furthermore, PDE5i non-responders became responders and capable of vaginal penetration (72%). Additionally, LI-ESWT resulted in long-term improvement of the erectile mechanism.

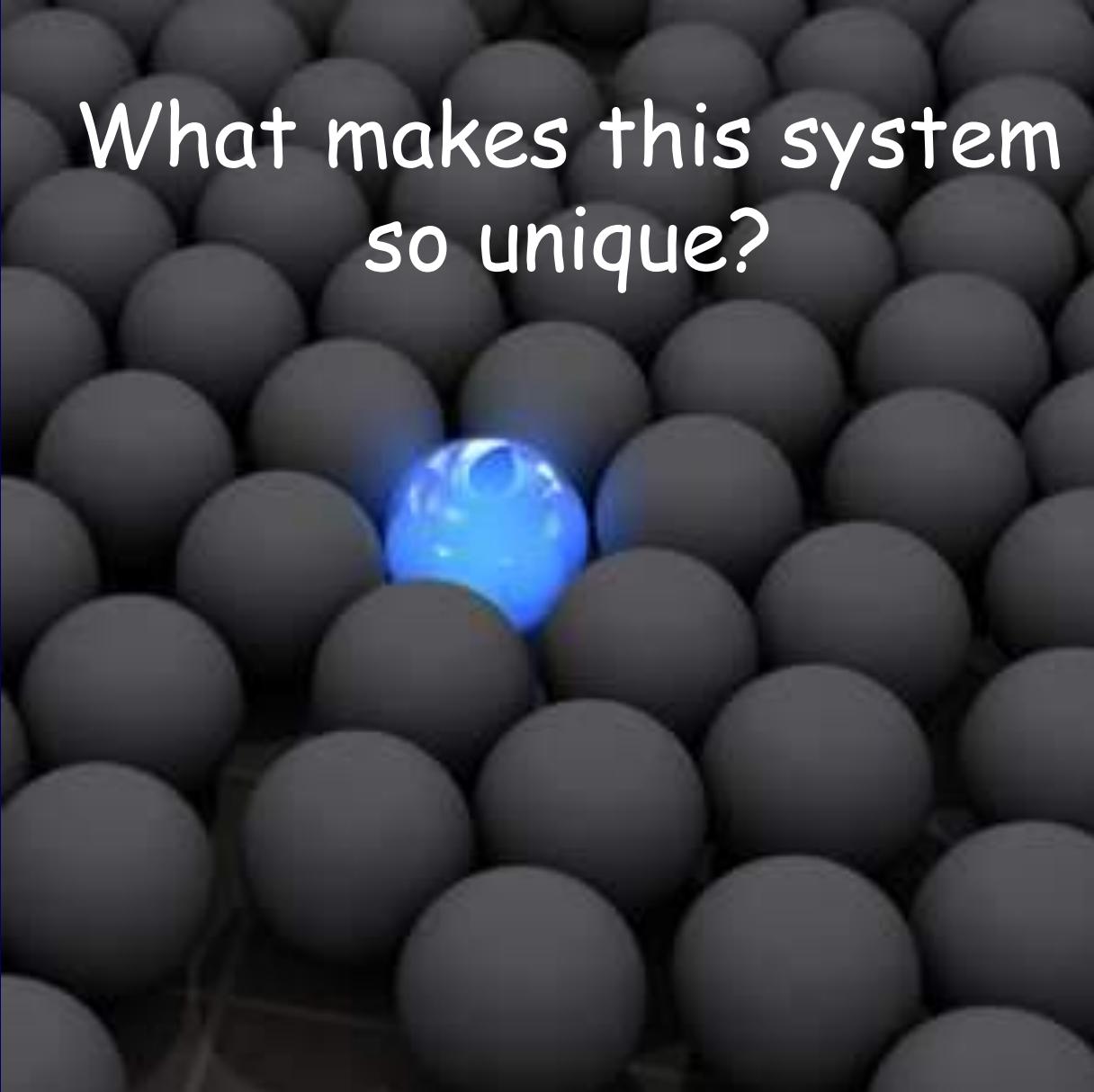
Conclusions. LI-ESWT has the potential to improve and permanently restore erectile function by reinstating the penile blood flow. Although these results on LI-ESWT are promising, further multi- centered studies with longer follow-up are needed to confirm these findings. Gruenwald I, Kitrey ND, Appel B, and Vardi Y. Stem low-intensity extracorporeal shock wave therapy in vascular disease and erectile dysfunction: Theory and outcomes. *Sex Med Rev* 2013;1:83–90.

The first “lithotripsy type” technology focalized at one point



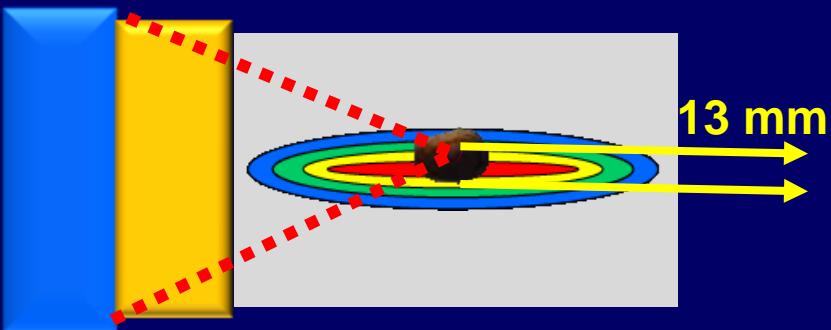
RENOVA - Low Intensity Shock Wave





What makes this system
so unique?

Focal Zone ESWL vs. ED



Tripter Compact X-1
Stone Fragmentation



Electrohydraulic Technology

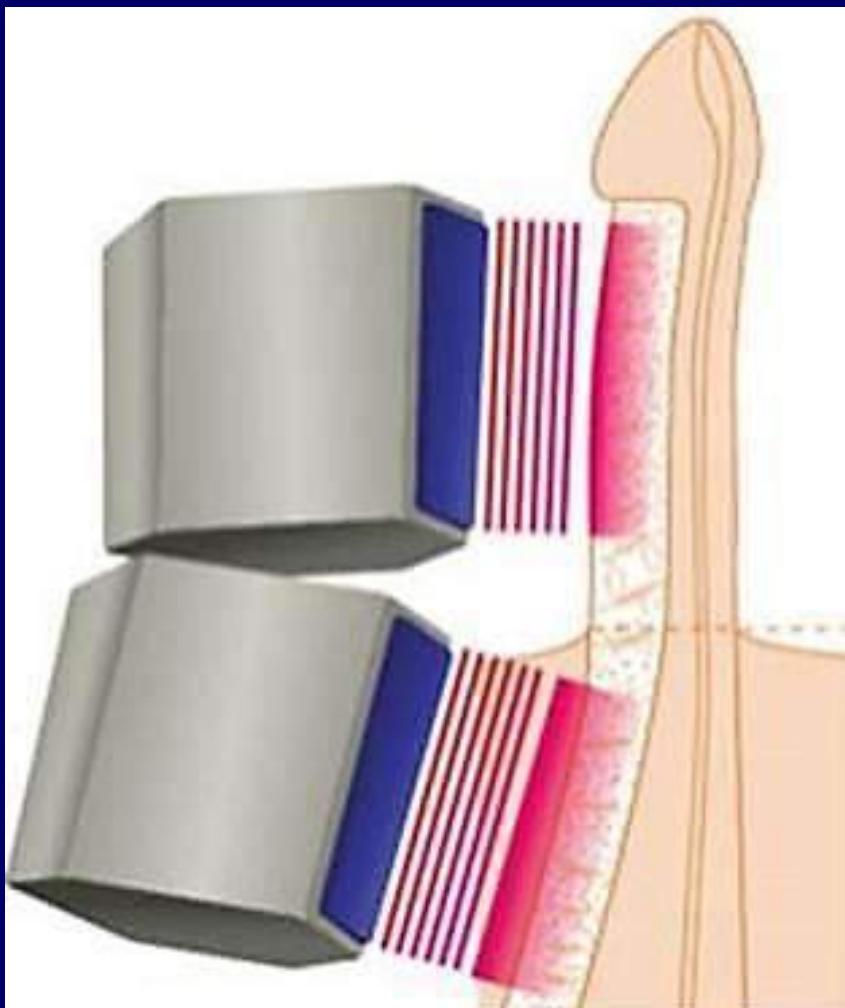


Renova
LSWT ED Therapy



Electromagnetic Technology

Second Generation: Line Focused Shockwave Therapy



Renova is the first SW
therapy device developed
especially for ED
treatment

Low Intensity Linear Focused Shockwave Therapy: a New Treatment to Improve the Quality of Life of Vascular Erectile Dysfunction Patients



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ASSOCIAZIONE UROLOGI ITALIANI

XXI

05

04

giugno

06

Antonio Casarico e Paolo Puppo

Villa Montallegro
Genova

Safety and Efficacy Associated with Treating ED Patients with Low Intensity Shockwaves by Renova

A prospective pilot study

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Inclusion Criteria

- ✓ ED (Non-hormonal, neurological or psychological) for at least 6 months.
- ✓ (IIEF- 6) between 7 to 24 (= Mild to Moderate) WHILE ON PDE5i
- ✓ Responder to PDE5i (able to penetrate on demand)
- ✓ Non-responders to PDE5i (unable to penetrate on demand even with maximum dosage)

Exclusion Criteria

- ✓ Psychogenic ED
- ✓ Neurological pathology
- ✓ Past RP / Radiotherapy in pelvic region
- ✓ Recovering from cancer (last 5 years)
- ✓ Any unstable medical, psychiatric, spinal cord injury and penile anatomical abnorm
- ✓ Clinically significant chronic hematological disease
- ✓ Anti-androgens, androgens

Safety and Efficacy Associated with Treating ED Patients with Low Intensity Shockwaves by Renova

A prospective pilot study

LSWT is applied to the entire penile shaft and crus (intensity of 0.09 mJ/mm²)

Treatment parameters:

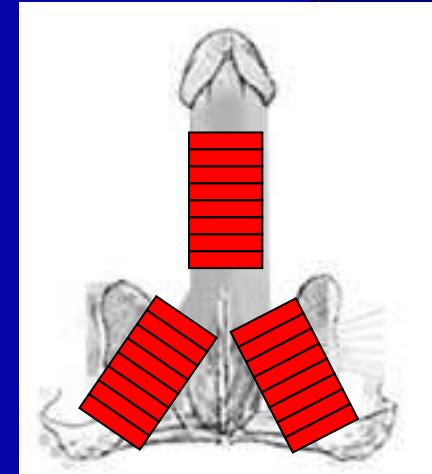
Treatment Frequency: 120 shocks/min

Number of shockwaves:

1600 at right and left crus

900 at right and left corpus cavernosum

Number of treatment sessions: 4



Safety and Efficacy Associated with Treating ED Patients with Low Intensity Shockwaves by Renova

A prospective pilot study

Primary Efficacy Objective:

- change in the IIEF- EF

Secondary Efficacy Objective:

- improvement in sexual activity according to
 - SEP- Sexual Encounter Profile: Questions 2 and 3
 - GAQ- Global Assessment Questions: 1 and 2
 - EHS- Erection Hardness Score

Safety objective:

- Evaluation of adverse effects

Study Population:

- 25 Vasculogenic ED patients with mild to moderate ED both PDE5-I responders and non-responders (after challenged with the maximum dose of PDE5-I)

Safety and Efficacy Associated with Treating ED Patients with Low Intensity Shockwaves by Renova

A prospective pilot study

IIEF-EF Baseline Score

Success Factor

7-16

improvement of 5 points or more

17-25

improvement of 2 points or more

EHS- Erection Hardness Score

How would you rate the hardness of your erection?

0: Penis does not enlarge

1: Penis is larger but not hard

2: Penis is hard but not hard enough for penetration

3: Penis is hard enough for penetration but not completely hard

4: Penis is completely hard and fully rigid

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Sexual Encounter Profile (SEP- Questions 2 and 3)

SEP-Q2: Over the past 4 weeks, were you able to insert your penis into your partner's vagina?

Yes.....

No.....

SEP-Q3: Over the past 4 weeks, did your erection last long enough for you to have successful intercourse?

Yes.....

No.....

Global Assessment Question (GAQ)

GAQ-Q1: Over the past 4 weeks, has the treatment you have been taking improved your erectile function?

Yes.....

No.....

GAQ-Q2: If yes, has the treatment improved your ability to engage in sexual activity over the past 4 weeks?

Yes.....

No.....

Safety and Efficacy Associated with Treating ED Patients with Low Intensity Shockwaves by Renova A prospective pilot study

25 pts enrolled - 24 ASSESSED (finished full treatment)

24 pts FOLLOW-UP 6 MONTHS

Mean age $62,58 \pm 8,32$ (45-74)

Mean ED duration $4,84 \pm 4,46$ (1-20) years

Smokers	52%
Diabetes	26%
Dyslipidemia	58%
CV disease	37%
Hypertension	47%

PDE5i RESPONDERS

18 = 75%

PDE5i NON-RESPONDERS

6 = 25%

Safety and Efficacy Associated with Treating ED Patients with Low Intensity Shockwaves by Renova
A prospective pilot study

Overall Success

Success to ALL
Primary and
Secondary Efficacy
Objectives

- ❖ IIEF

IIEF6= 11-16 / +5

IIEF6= 17-25 / +2

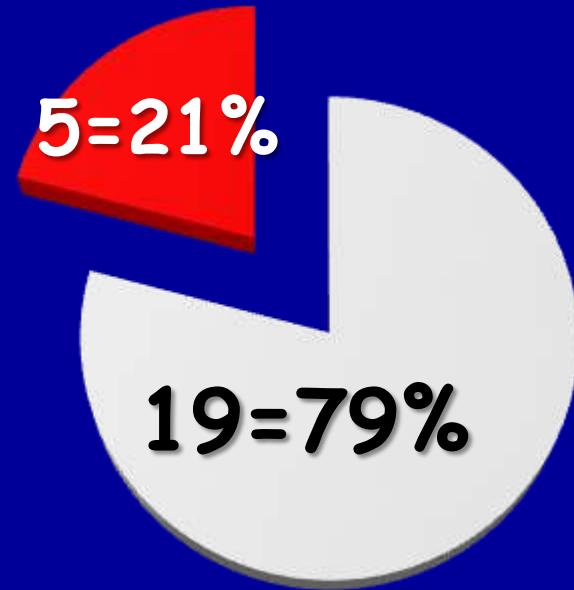
- ❖ SEP 2-3

- ❖ GAQ 1-2

- ❖ EHS

OVERALL SUCCESS

- SUCCESS
- FAILURE

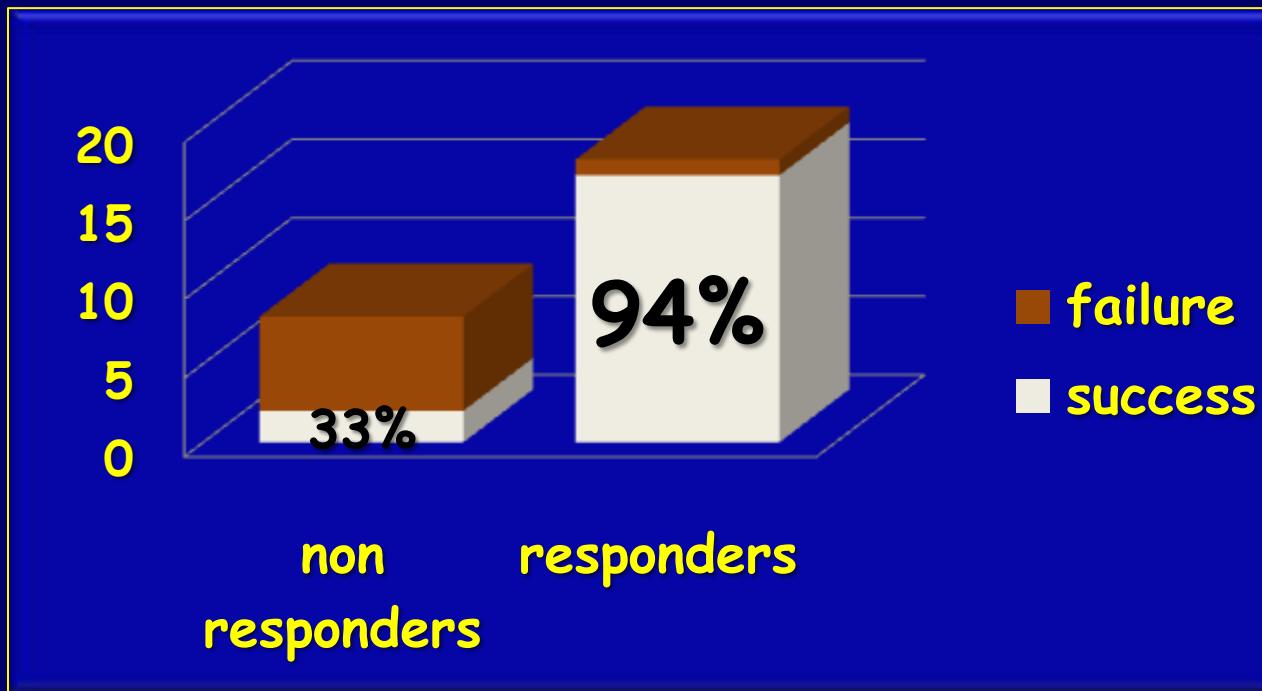


Safety and Efficacy Associated with Treating ED Patients with Low Intensity Shockwaves by Renova
A prospective pilot study

Overall Success

Success to ALL Primary and Secondary Efficacy Objectives

- ❖ NON RESPONDERS $2/6 = 33\%$
- ❖ RESPONDERS $17/18 = 94\%$



IIEF6 INCREASE

ALL pts - n 24
+113

mean +4,7

SUCCESS pts - n 19

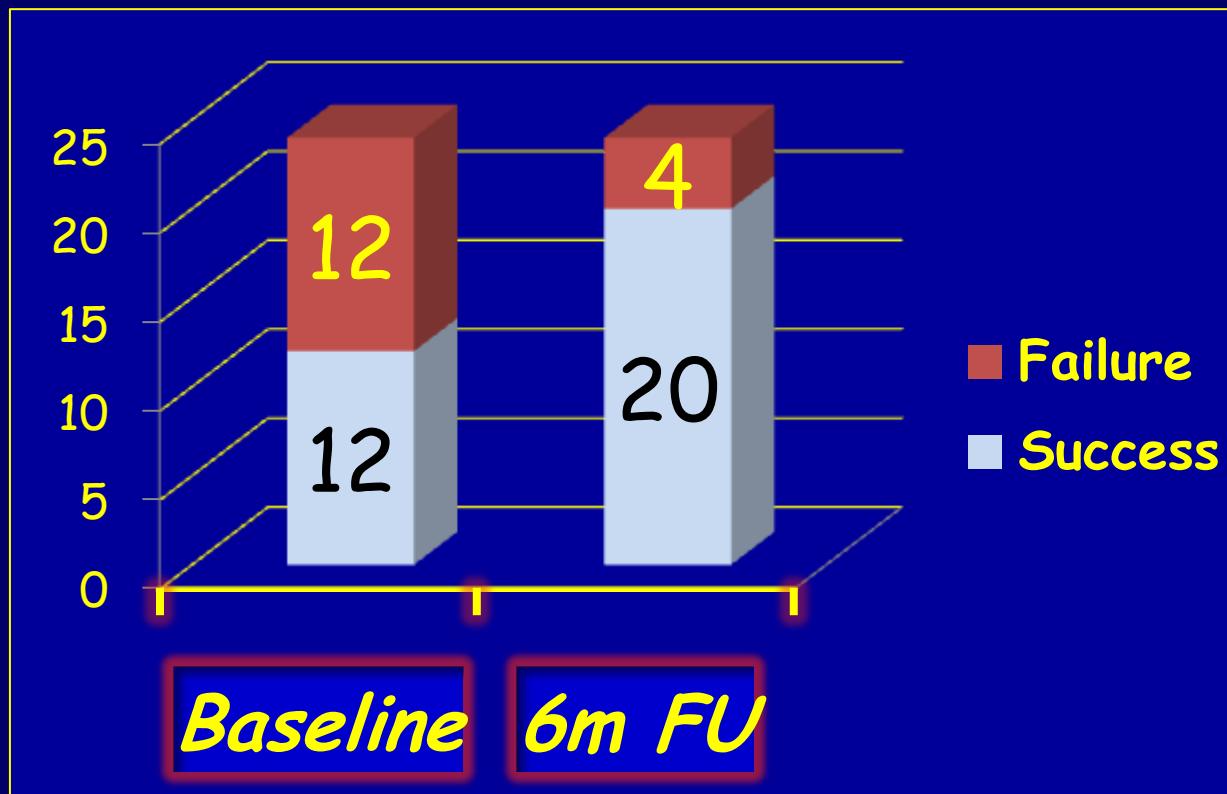
+ 118

mean +6,2

SEP - SUCCESS

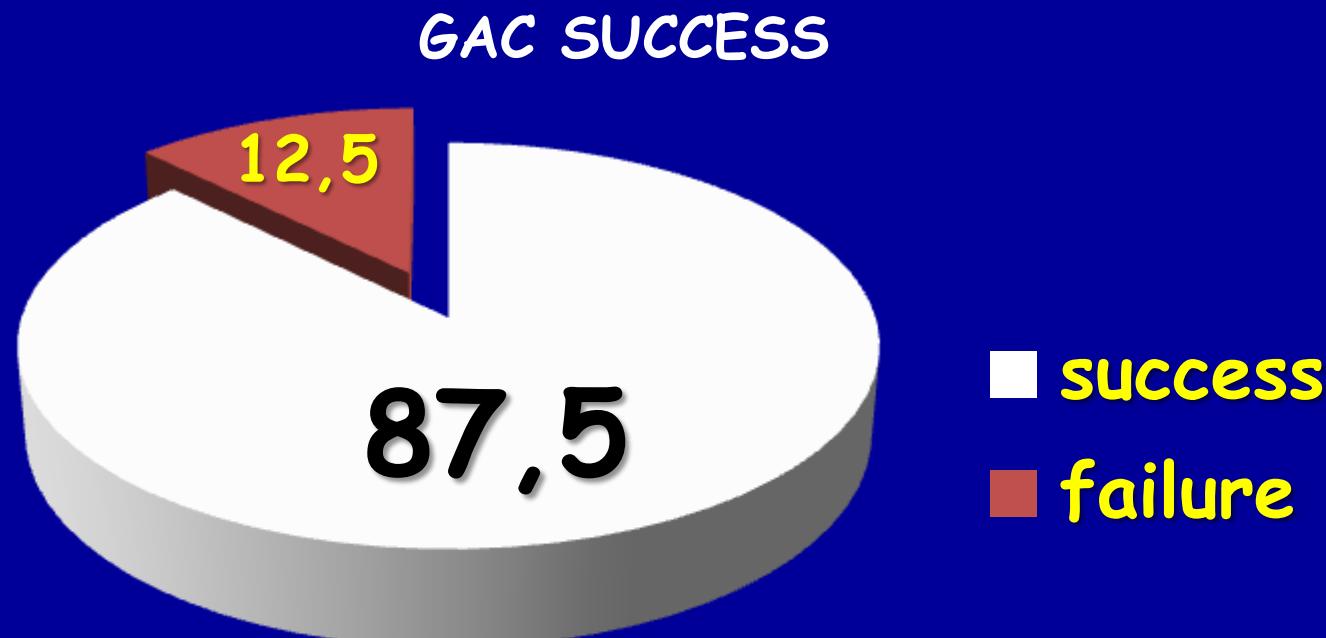
(yes to SEP 2 and 3)

20/24 : 83,3%



GAQ - SUCCESS (yes to GAC 1 and 2)

21/24 : 87,5%



**Safety and Efficacy Associated with Treating ED Patients with
Low Intensity Shockwaves by Renova
A prospective pilot study**

EHS INCREASE TO 3 / 4

6 months follow-up
EHS 3 / 4 = 19 pts

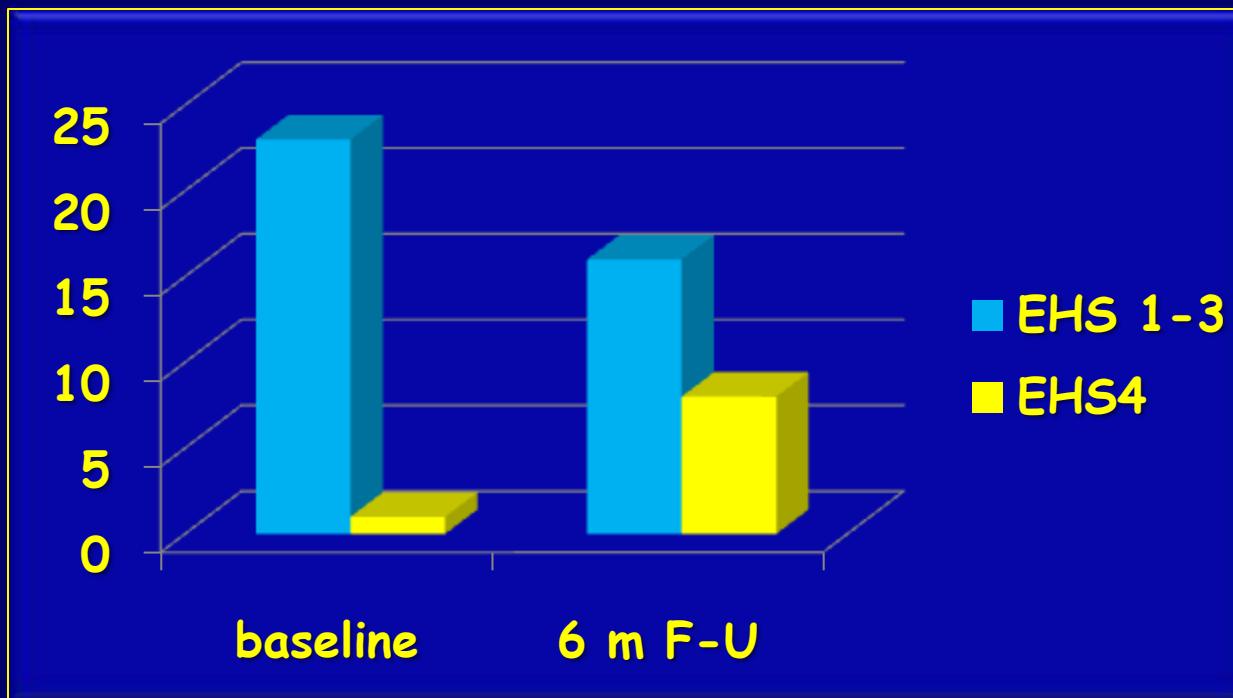
EHS INCREASE + 14

MEAN EHS INCREASE 0,73

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EHS 4

✓ BASELINE = 1 pt
✓ 6 MONTHS F-U = 8 pts

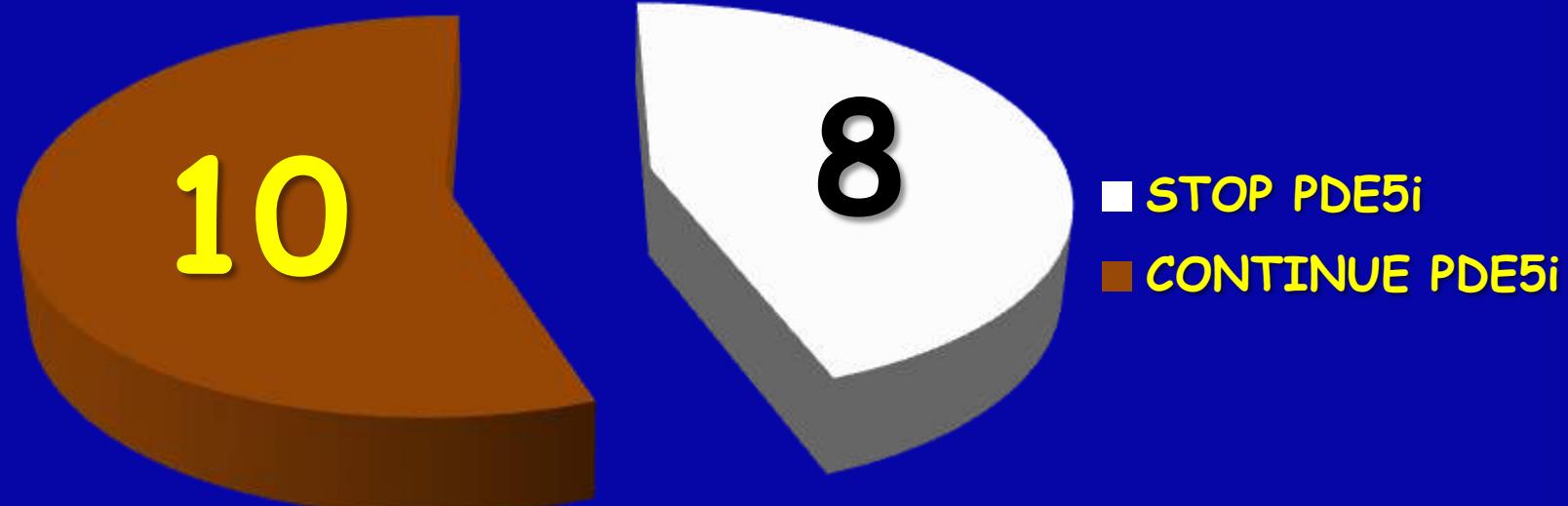


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STOP PDE5i

PDE5i responders = 18

STOPPED PDE5i = 8 (44,4%)





Società Italiana di Andrologia

Presidente SIA
Giorgio Franco

XXX CONGRESSO NAZIONALE SIA

28 - 31 MAGGIO 2014

Grand Hotel Pianeta Maratea - Maratea (PZ)

MARATEA



L'ANDROLOGIA DI CONFINE

La SIA incontra la Società e le Società

Presidente del Congresso
Angelo Vito

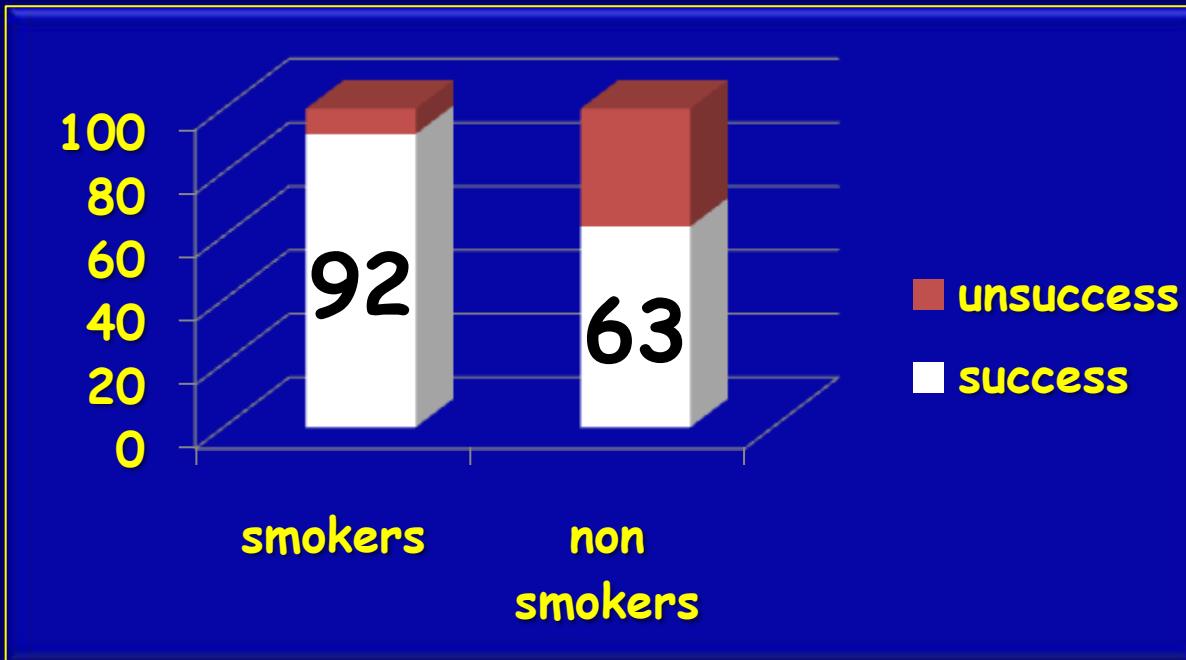
The Effect of Low Intensity Shockwave Therapy on the Erectile Function of Smokers and Non-smokers - Initial Report with a Dedicated System

Antonio Casarico e Paolo Puppo
Villa Montallegro
Genova

Safety and Efficacy Associated with Treating ED Patients with Low Intensity Shockwaves by Renova
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SUCCESS (ALL Objectives)

- **SMOKERS** $12/13 = 92\%$
- **NON SMOKERS** $7/11 = 63\%$



LISWT - INDICAZIONI

DE CON COMPONENTE VASCOLARE

(età, sovrappeso, sedentarietà, fumo, dislipidemia, ipertensione, diabete, malattie cardiovascolari, ictus, ipogonadismo, ipertrofia della prostata)

PREVENZIONE: segni iniziali di DE (difficoltà/lentezza ad ottenere e/o mantenere l'erezione, erezione meno rigida): *per evitare il peggioramento o la necessità di assumere farmaci*

TERAPIA: DE responsiva ai farmaci orali (Viagra, Cialis, Levitra, Spedra): *per migliorare la funzione erettile e non dover utilizzare più i farmaci*

TERAPIA: non si possono assumere farmaci orali a causa degli effetti collaterali o per controindicazioni

TERAPIA: DE non responsiva ai farmaci orali e/o ai farmaci per iniezione intracavernosa: per migliorare la funzione erettile e rispondere ai farmaci

RIABILITAZIONE: dopo interventi di chirurgia pelvica (prostatectomia radicale, cistectomia radicale, interventi demolitivi al sigma-retto) per evitare i danni vascolari possibili nella fase postoperatoria

An aerial photograph of the city of Genoa, Italy, showcasing its dense urban sprawl along the coast. The city is nestled between the Ligurian Sea to the west and the Ligurian Apennines to the east. In the foreground, the large port of Genoa is visible, with numerous ships and industrial structures. A prominent bridge spans a deep blue inlet. The city's architecture is a mix of modern skyscrapers and traditional buildings. The surrounding landscape features rolling green hills under a clear blue sky.

GRAZIE PER L'ATTENZIONE