Initial results of treatment with Linear Shockwave Therapy (LSWT) by Renova in patients with Erectile Dysfunction

A pilot clinical study

Investigators

- **Dr. Ahmed Hind, MD**

  Consultant to Pr.Catanzaro Milano

  Pr. S. Leoni Reggio Emilia, Italy

  Head of Urology and Andrology Center Red Crescent Hospital (RCH), Ramallah Palestine
- **Dr. Omar Saleh, MD**

  RCH, Ramallah Palestine
- **Dr. Yousef Abu Asbeh, MD**

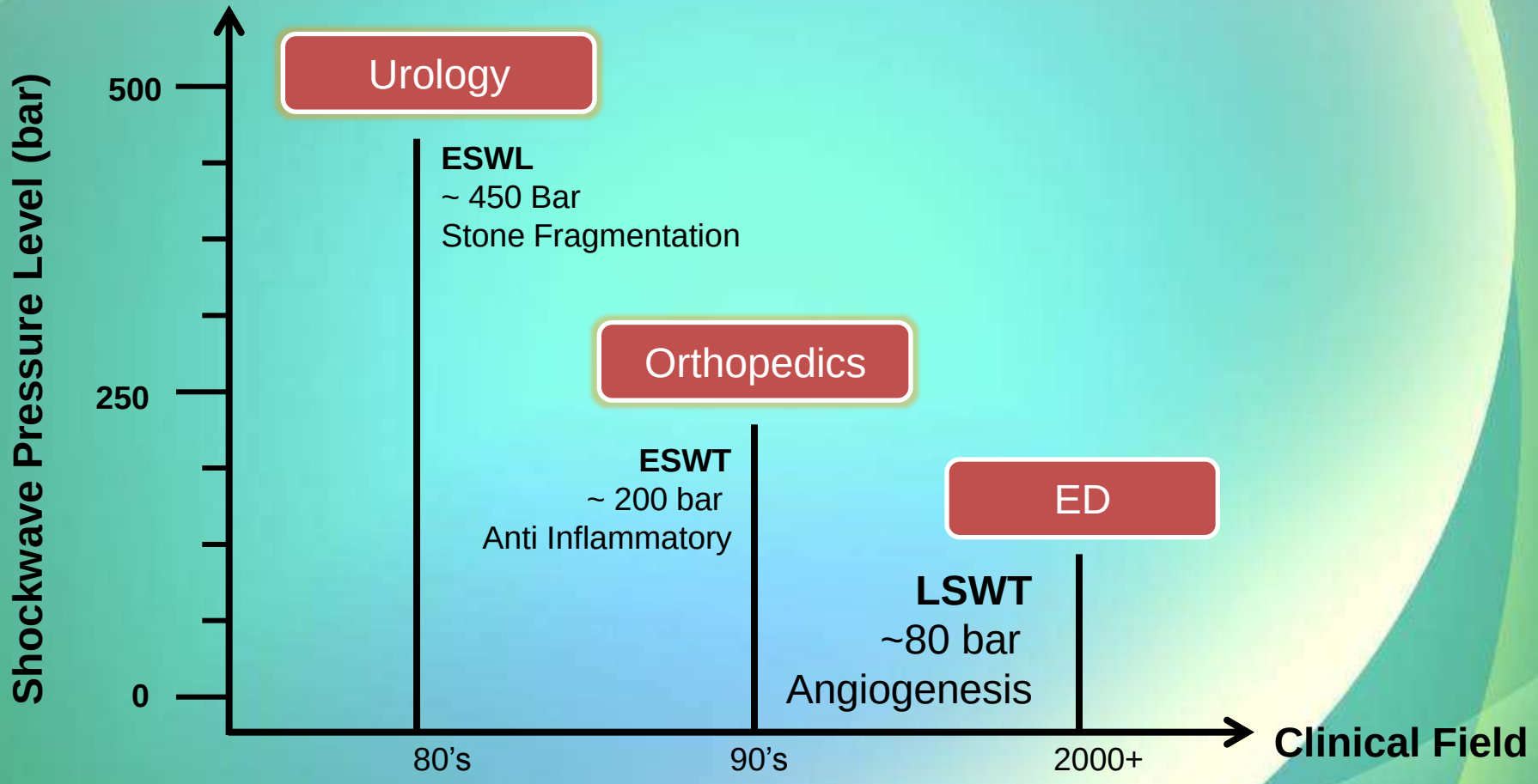
  RCH, Ramallah Palestine

Introduction

Low intensity shockwave therapy to the penis and crura may help men with the following conditions:

- Mild to moderate erectile dysfunction (ED)
- Both responders and non-responders to conventional phosphodiesterase type 5 inhibitor (PDE-5) treatment

Shockwave Therapy Applications



How Low Energy Shockwaves Induce Angiogenesis

Shear stress

↓

Intracellular & extracellular responses

↓

Stimulates endothelial Nitric Oxide Synthase (Enos)

↓

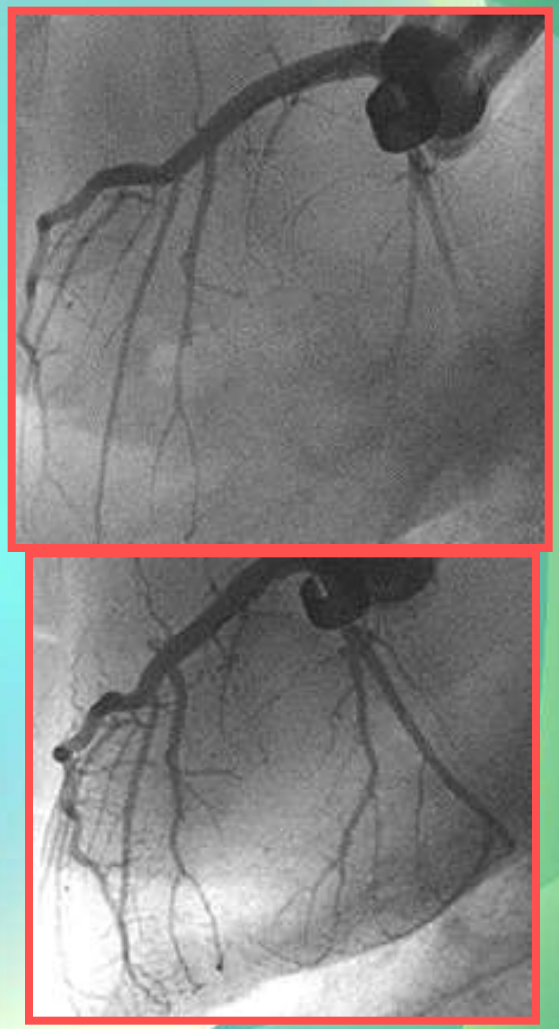
Release of Vascular Endothealial Growth Factors (VEGF)

↓

Proliferating Cell Nuclear Antigen (PCNA) production

↓

Neovascularization



Shockwaves Effect on Angiogenesis

Clinical Background

- Extracorporeal Cardiac Shockwave Therapy markedly ameliorate ischemia - induced myocardial dysfunction in pigs in Vivo[1].
- These results suggest that extracorporeal cardiac SW therapy is an effective and noninvasive therapeutic strategy for ischemic heart disease[2].

[1]Nishida T, Shimokawa H et al. Department of Cardiovascular Surgery, Cardiovascular Medicine, Kyushu University, Fukuoka, Japan

[2]Circulation. 2004;110:30553061

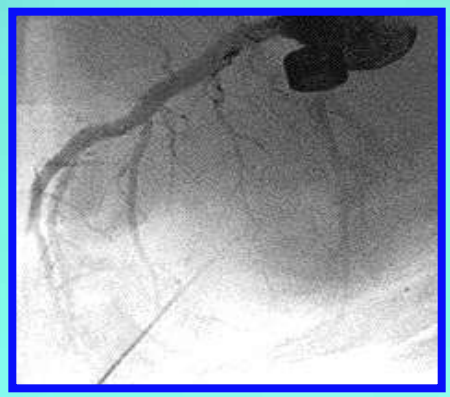
Enhancement of Coronary Collaterals

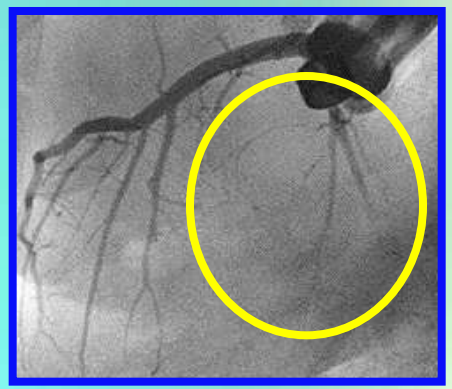
Clinical Background

Control Group

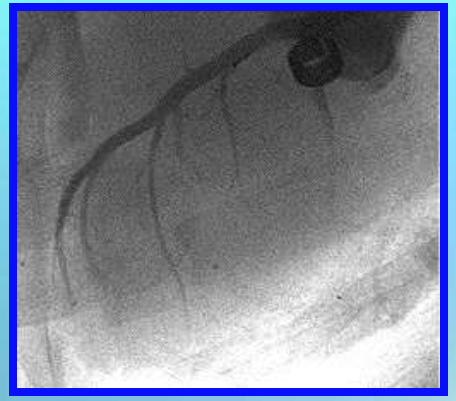
SW Group

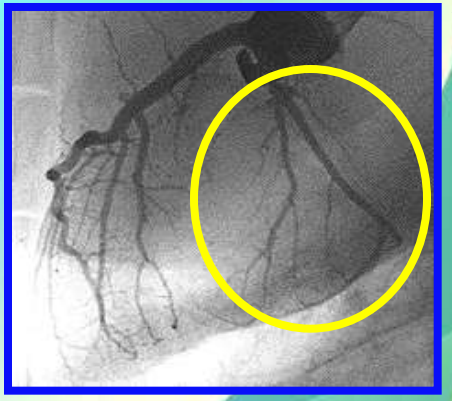
4 weeks post AC implantation





4 weeks post treatment





EUROPEAN UROLOGY 58 (2010) 243–248

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Sexual Medicine

Editorial by Konstantinos Hatzimouratidis on pp. 249–250 of this issue

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

Neuro-Urology Unit, Rambam Healthcare Campus and the Technion, Haifa, Israel

Article info

Article history:
Accepted April 7, 2010
Published online ahead of print on April 16, 2010

Keywords:
Extracorporeal shock wave
Low intensity
Erectile dysfunction
Penis

Abstract

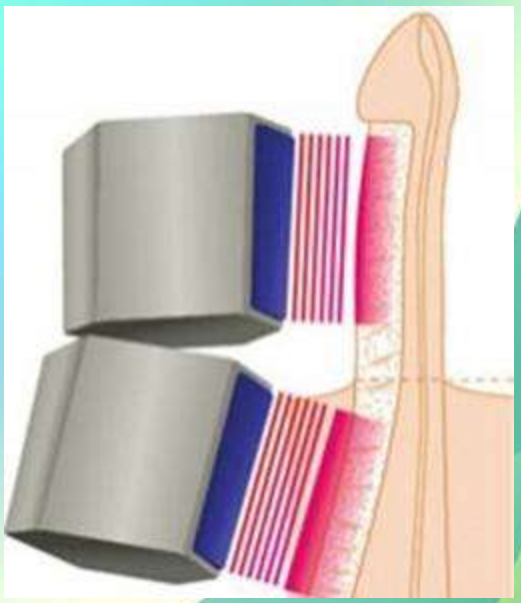
Background: Low-intensity extracorporeal shockwave therapy (LI-ESWT) is currently under investigation regarding its ability to promote neovascularization in different organs.
Objective: To evaluate the effect of LI-ESWT on men with erectile dysfunction (ED) who have previously responded to oral phosphodiesterase type 5 inhibitors (PDE5-I).
Design, setting, and participants: We screened 20 men with vasculogenic ED who had International Index of Erectile Function ED (IIEF-ED) domain scores between 5–19 (average: 13.5) and abnormal nocturnal penile tumescence (NPT) parameters. Shockwave therapy comprised two treatment sessions per week for 3 wk, which were repeated after a 3-wk no-treatment interval.
Intervention: LI-ESWT was applied to the penile shaft and crura at five different sites.
Measurements: Assessment of erectile function was performed at screening and at 1 mo after the end of the two treatment sessions using validated sexual function questionnaires, NPT parameters, and penile and systemic endothelial function testing.

Study Rationale

- Low Intensity Shockwaves (LISW) are known to produce revascularization and have been used for the past decade in the treatment of Cardiac Chronic Ischemia by various systems.
- LISW utilize very low energy - 0.09 mJ/mm2 - equivalent to 10% of the energy used by conventional kidney stone lithotripters in the treatment of urinary tract stones.

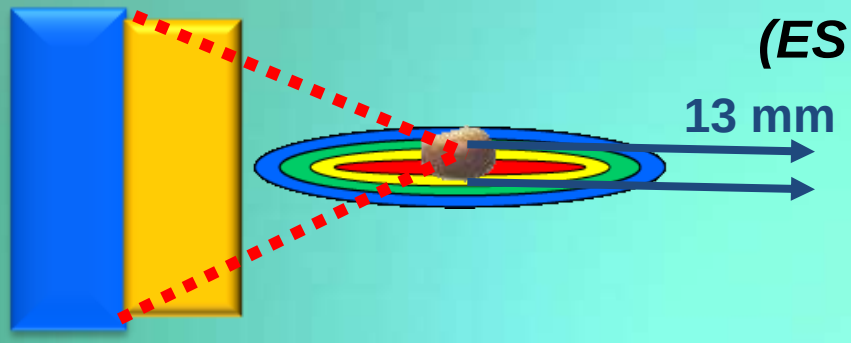
RENOVA Pilot study

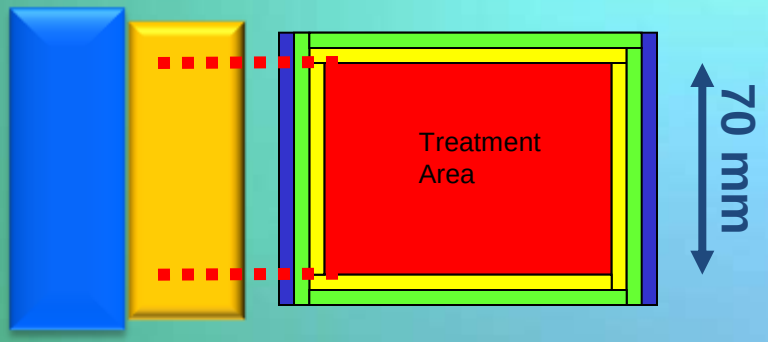
The present study uses a dedicated device (Renova) that utilizes Line Focused Shockwaves, differing from previous models in that it achieves substantially superior organ coverage.



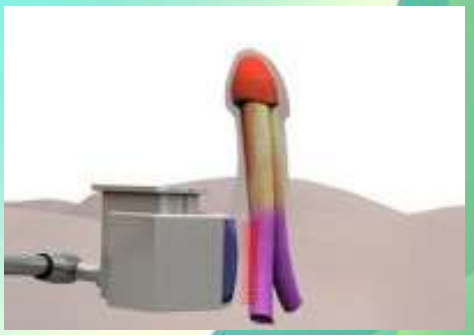
Focal Zone ESWL vs. ED

Traditional SW Therapy (ESWL/orthopedics)





LSWT (ED application)



Renova Clinical Application

1

Two applications to the crura:

- left crus
- right crus

2

Two applications to the shaft:

- left corpus cavernosum
- right corpus cavernosum

Study Objectives

- **Primary Efficacy Objective** :

  To evaluate the change in the **IIEF- EF** from baseline to 1, 3 and 6 months post treatment. IIEF is widely accepted as the best method to verify ED progress.

- **Secondary Efficacy Objective**:

  To study the clinical efficacy of Renova in terms of improvement in sexual activity at 1, 3 and 6 months post treatment, according to the following assessment tools:

- Sexual Encounter Profile (SEP- Questions 2 and 3)
- Global Assessment Question (GAQ)

Success Criteria

An increase of IIEF-EF score from baseline to the 1st follow up according to the severity of the symptoms by the *minimal clinically important differences in the erectile function domain of the International Index of Erectile Function scale*.

IIEF-EF Baseline Score	Success Factor
6-10	improvement of 7 points or more
11-16	improvement of 5 points or more
17-25	improvement of 2 points or more

Study Population

- Number of patients: 20
- Patients with mild to severe ED symptoms
- Both PDE5-i responders and non-responders

Design

- This is a pilot clinical study assessing the safety and efficacy of treatments performed by Renova on vasculogenic ED patients.
- Non-responders to PDE5-I will be accepted after challenged with maximum dose of PDE5-I. In case they respond, they will be classified as responders .
- All patients undergo a 3 weeks flush out from PDE5-I before starting treatment.
- After the treatment ends, patients resume PDE5-I consuming.

Treatments

- **4 weekly** treatment sessions
- **4** treatment **areas** (left/right corpus cavernosum, left/right crus)
- **900 shocks** at each area
- **3600 shocks** per session
- Energy Density: **0.09 mJ/mm2**
- Frequency: **5 Hz**
- Session time: **15 minutes**

Follow-up

Follow-up is composed of:

- Questionnaires
- Adverse events report

Timing:

- **1 month** post treatment
- **3 months** post treatment
- **6 months** post treatment

Eligibility

- **Ages Eligible for Study:** 20 to 80 Years
- **Genders Eligible for Study:** Male (Heterosexual)

Inclusion Criteria

1. Good general health
2. ED for at least 6 months
3. International Index of Erectile Function -EF (IIEF-EF) of 7-24 while on PDE5-I
4. Positive response to PDE5-I (able to penetrate on demand=Responders)
5. Negative response to PDE5-I (unable to penetrate on demand even with maximum PDE5-I dosage = Non-responders)
6. Stable heterosexual relationship for more than 3 months

Exclusion Criteria

1. Hormonal, neurological or psychological pathology
2. Past radical prostatectomy or extensive pelvic surgery
3. Recovering from cancer during last 5 years
4. Any unstable medical, psychiatric, spinal cord injury and penile anatomical abnormalities
5. Clinically significant chronic hematological disease
6. Anti-androgens, oral or injectable androgens
7. Radiotherapy in pelvic region

Potential Adverse events

In all known studies where LISW was used for treatment of ED, there have been no reported adverse events.

Initial Results

IIEF-EF
Baseline evaluation data

	Patient Initials	Age (yrs)	IIEF-EF: Q1	IIEF-EF: Q2	IIEF-EF: Q3	IIEF-EF: Q4	IIEF-EF: Q5	IIEF-EF: Q6	IIEF-EF: Total Score
1	MIM	66	2	1	2	1	2	1	9
2	HIS	73	2	2	1	1	1	1	8
3	NMM	72	2	1	1	1	1	2	8
4	JHS	51	3	3	2	2	3	4	17
5	MNS	53	3	2	2	2	3	2	14
6	OIS	53	3	3	3	3	4	3	19
7	MMK	60	2	2	2	2	2	1	11
8	AAD	61	1	1	1	1	1	1	6
9	IHA	51	4	3	3	3	3	3	19
10	AH	38	4	3	3	3	3	3	19
11	SA	33	2	2	2	2	1	3	12
12	AMH	60	3	3	3	3	2	3	17
Average		56	2.58	2.17	2.08	2.00	2.17	2.25	13.25

IIEF-EF

1 Month Follow up data

	Patient Initials	IIEF- EF: Q1	IIEF- EF: Q2	IIEF- EF: Q3	IIEF- EF: Q4	IIEF- EF: Q5	IIEF- EF: Q6	IIEF-EF: Total Score
1	M I M	3	2	3	3	4	3	18
2	HIS	2	2	1	1	1	1	8
3	N M M	2	2	1	1	1	2	8
4	J H S	4	4	4	4	4	4	24
5	M N S	4	4	4	4	5	4	25
6	O I S	4	4	4	4	5	4	25
7	M M K	4	4	4	4	4	4	24
8	A A D	3	3	3	3	4	3	19
9	I H A	5	5	5	4	5	4	28
10	A H	5	5	5	5	4	4	28
11	S A	4	4	3	3	2	4	20
12	A M H	4	4	4	4	4	4	24
Average		3.67	3.58	3.42	3.33	3.58	3.42	20.92

Improvement in IIEF–EF (%)

		Baseline Evaluation	1 Month Follow-up	
	Patient Initials	IIEF-EF: Total Score	IIEF-EF: Total Score	% improvement
1	M I M	9	18	100.00
2	HIS	8	8	0.00
3	N M M	8	8	0.00
4	J H S	17	24	41.18
5	M N S	14	25	78.57
6	O I S	19	25	31.58
7	M M K	11	24	118.18
8	A A D	6	19	216.67
9	I H A	19	28	47.37
10	A H	19	28	47.37
11	S A	12	20	66.67
12	A M H	17	24	41.18
Average		13.25	20.92	57.86

Improvement in IIEF–EF

Success determination

		Baseline	1 Month follow up		
	Patient Initials	IIEF-EF: Total Score	IIEF-EF: Total Score	IIEF Difference	Success
1	M I M	9	18	9	Success
2	HIS	8	8	0	Failure
3	N M M	8	8	0	Failure
4	J H S	17	24	7	Success
5	M N S	14	25	11	Success
6	O I S	19	25	6	Success
7	M M K	11	24	13	Success
8	A A D	6	19	13	Success
9	I H A	19	28	9	Success
10	A H	19	28	9	Success
11	S A	12	20	8	Success
12	A M H	17	24	7	Success
Average		13.25	20.92	7.67	84 %

Results for Sexual Encounter Profile Questionnaire

- **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……**

SEP Results

Baseline

SEP: Q2	SEP: Q3
NO	NO
NO	NO
NO	NO
YES	YES
YES	NO
YES	YES
NO	NO
NO	NO
YES	NO
YES	YES
NO	NO
YES	YES

1 month follow up

SEP: Q2	SEP: Q3
YES	YES
NO	NO
NO	NO
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES

Results for Global Assessment Questions (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……**

GAQ Results
1 month follow up

GAQ- Q1	GAQ- Q2
YES	YES
NO	NO
NO	NO
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES
YES	YES

Results of 1 and 3 months follow up

	Patients Initials	Response to PDE5-I	Baseline IIEF-EF Score	month 1 IIEF-EF Score	3 months IIEF-EF Score	Results Comparison	DELTA	Success
1	M I M	YES	9	18	18	Same	9	Yes
2	HIS	NO	9	8	8	Same	1-	No
3	N M M	NO	8	8	8	Same	0	No
4	J H S	YES	17	24	24	Same	6	Yes
5	M N S	YES	14	25	30	Improvement	16	Yes
6	O I S	YES	19	25	25	Same	6	Yes
7	M M K	YES	11	24	24	Same	13	Yes
8	A A D	NO	6	19	19	Same	13	Yes
9	I H A	YES	19	28	28	Same	7	Yes
10	A H	YES	19	28	28	Same	7	Yes
11	S A I	YES	12	20	20	Same	8	Yes
12	A M H	YES	17	24	24	Same	7	Yes

Results of 1 and 3 months follow up
Comparison

- Results are essentially the same.
- Successful results are seen at 1 month post treatment.
- Success is maintained at least 3 months post treatment. Therefore, there is no evident placebo effect.

Summary

- Initial results at 1 and 3 months show great progress in erectile function.
- *Average IIEF-EF increased from 13.25 to 20.92 (57.86 % improvement).*
- *84 % Success according to success criteria*
- All mild to moderate cases have succeeded.
- One severe case has improved while 2 severe cases failed.
- SEP and GAQ results have improved.
- No pain and no complications were reported.

Conclusions

- The initial results of 1 and 3 months follow up are very encouraging and indicate success.
- This may be due to perfect organ coverage and direct application to the Crura using a **Linear Focused Shockwave Therapy** device.
- Additional studies with more patients are needed in order to confirm these results.