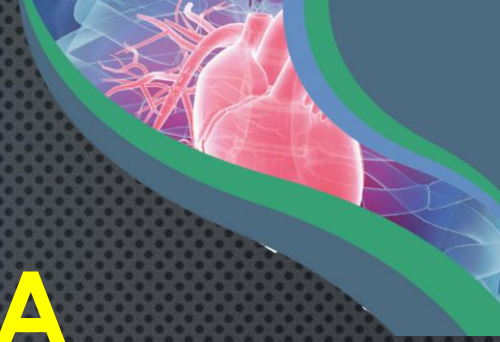


# CORRELAZIONE TRA CARDIOPATIA ISCHEMICA E DISFUNZIONE ERETTILE



**PROF. GIUSEPPE SANGIORGI, MD, FESC, FSCAI**

Professore Associato di Cardiologia

Direttore Emodinamica

Cattedra di Cardiologia

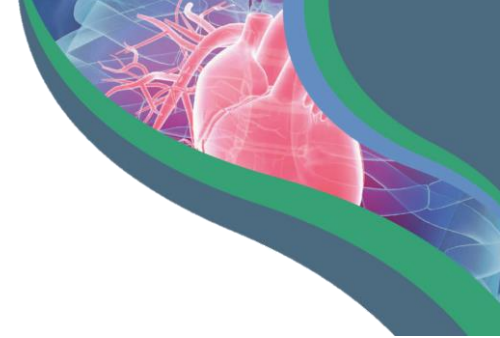
Dipartimento di Biomedicina

Università di Roma Tor Vergata



Hot Topics in Cardiologia 2023 - 13-14 Novembre – Villa Doria D'Angri

# Disclosures:



- Prof. Sangiorgi has received research grants from Concept Medical, Medtronic, Medalliance

# We May Have Fun and Joke On it



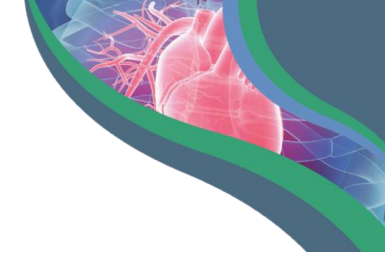
# ...But Remember... Erectile Dysfunction Is a Big Problem !



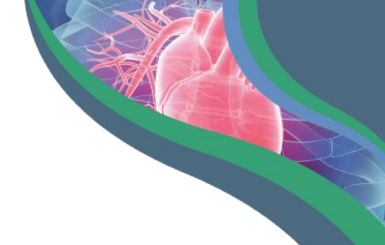
A collage of newspaper advertisements for male impotence treatments. The main ad is titled 'MALE IMPOTENCE' and 'THE SOLUTION'. It includes a photo of a man and text describing the solution. Other smaller ads include 'MALE UPRIGHT ENLARGER', 'MALE IMPOTENCE PERFORMANCE CAPSULES!', and 'Ginger &amp; Impotence FREE REPORT'. The background of the collage is a newspaper page with the title 'NEWS OF THE WORLD'.

ED negatively impacts the quality of life in terms of Self Esteem, Depression Relationship with Partner

# Definition and Prevalence



- Sexual dysfunction (ED) is defined as **the recurrent inability to achieve and maintain an erection satisfactory for sexual intercourse.**
- Successful treatment of ED has a strong impact on quality of life.
- More than 300 million men worldwide have ED, and 52% of men in the United States - 40 to 70 years of age - report some degree of ED.



# Myths Surrounding Erectile Dysfunction



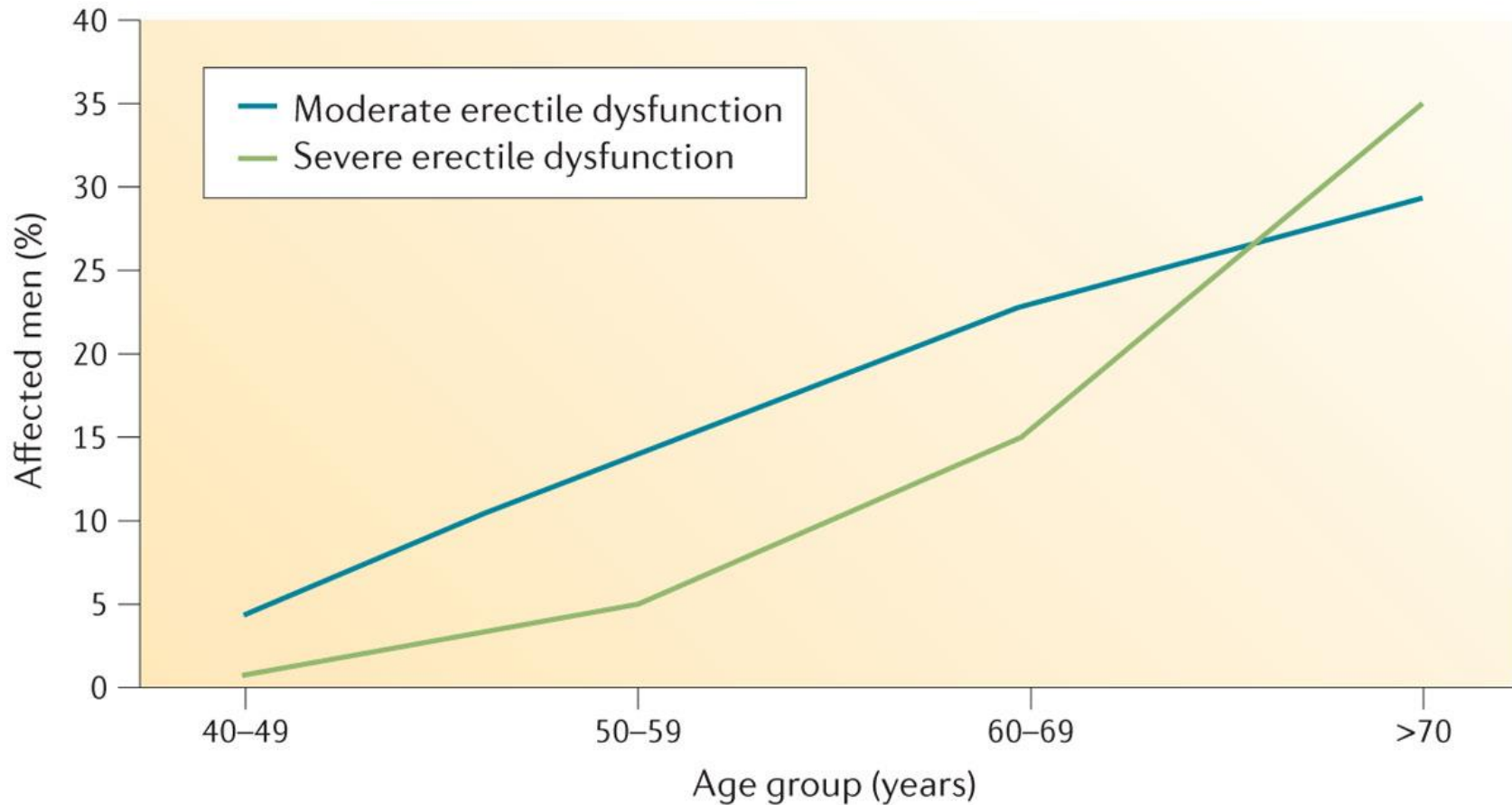
**IT'S TO BE EXPECTED AT MY AGE, ISN'T IT?**

**NOTHING CAN BE DONE**

**DO YOU THINK IT'S ALL IN MY MIND,  
DOCTOR?**

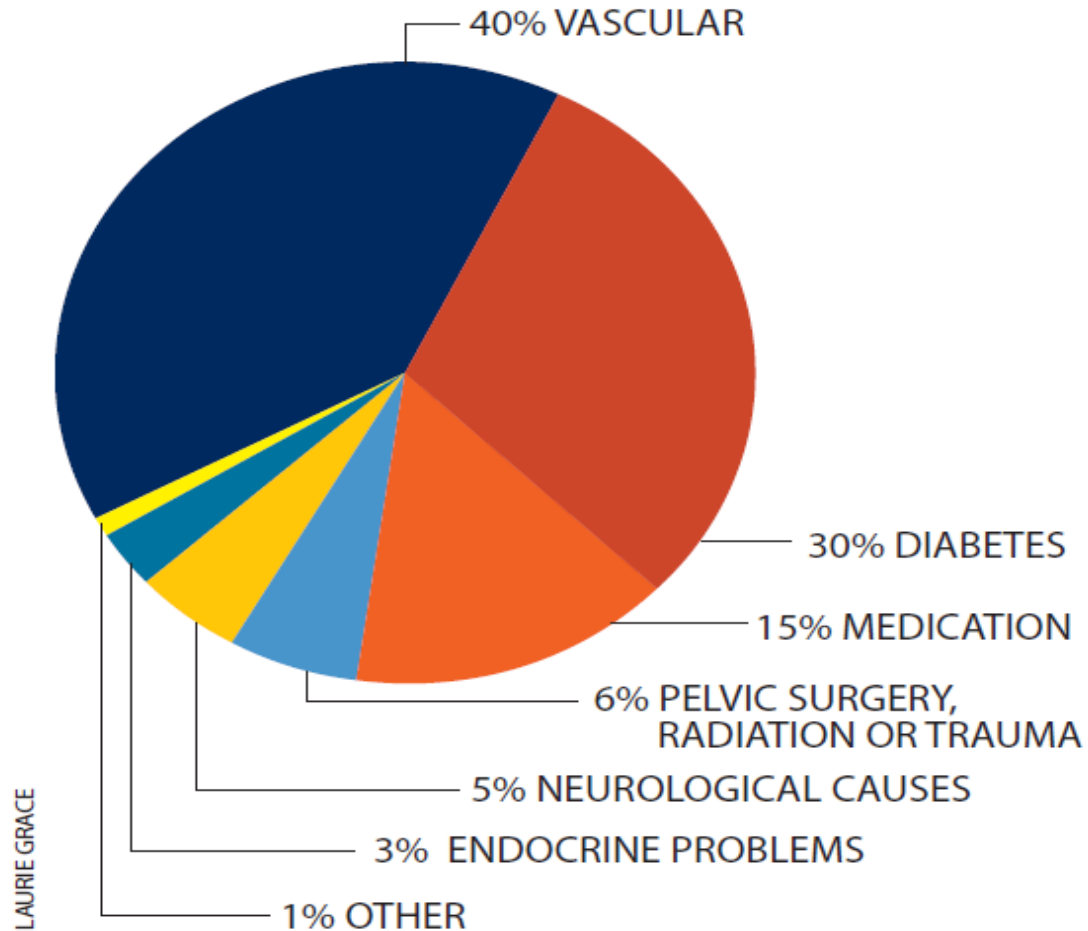
# Certainties Surrounding Erectile Dysfunction

## Increasing prevalence with age



Yafi, F. A. *et al.* (2016) Erectile dysfunction  
*Nat. Rev. Dis. Primers* doi:10.1038/nrdp.2016.3

# Causes of ED



Goldstein et al, Male Sexual Circuitry, Scientific American, Vol 283(2), 70-75



# Link Between ED and CVD

## The relationship of erectile dysfunction and subclinical cardiovascular disease: A systematic review and meta-analysis

Vascular Medicine  
2018, Vol. 23(1) 9–20  
© The Author(s) 2017  
Reprints and permissions:  
sagepub.co.uk/journalsPermissions.nav  
DOI: 10.1177/1358863X17725809  
journals.sagepub.com/home/vmj  


**Chukwuemeka U Osondu<sup>1,2,\*</sup>, Bryan Vo<sup>3,\*</sup>, Ebenezer T Oni<sup>4</sup>,  
Michael J Blaha<sup>5</sup>, Emir Veledar<sup>1,6</sup>, Theodore Feldman<sup>1,3</sup>,  
Arthur S Agatston<sup>1,3</sup>, Khurram Nasir<sup>1,2,3,5,7</sup>  
and Ehimen C Aneni<sup>1,2,8</sup>**

our results suggest that ED may be a marker of subclinical CVD and atherosclerosis, even in patients without an overt diagnosis of peripheral vascular disease. ED may be used to identify patients who may benefit from early screening for vascular dysfunction.

# Link Between ED and CVD

## Risk Factors

Age, DM, HTN

Alcohol, tobacco



Endothelial  
Dysfunction  
+

Atherosclerosis



- Up to 46% of men with CAD have ED and more than 85% with CHF
- 75% of men with CAD have problem achieving erection and 65% maintaining it
- ED predates the onset of symptomatic CVD by ~ 3 years in 67% of cases
- ED increases the risk of CV events by 44%, 62% for MI and 25% for overall mortality

Gazzaruso et al. Circulation 2004;110: 22; Rosen et al. J Urol 1991;145:759

Montorsi et al., European Heart Journal 2006; 27, 2632

Vlachopoulos et al. Circ Card Quality Outcome 2013; 6: 99

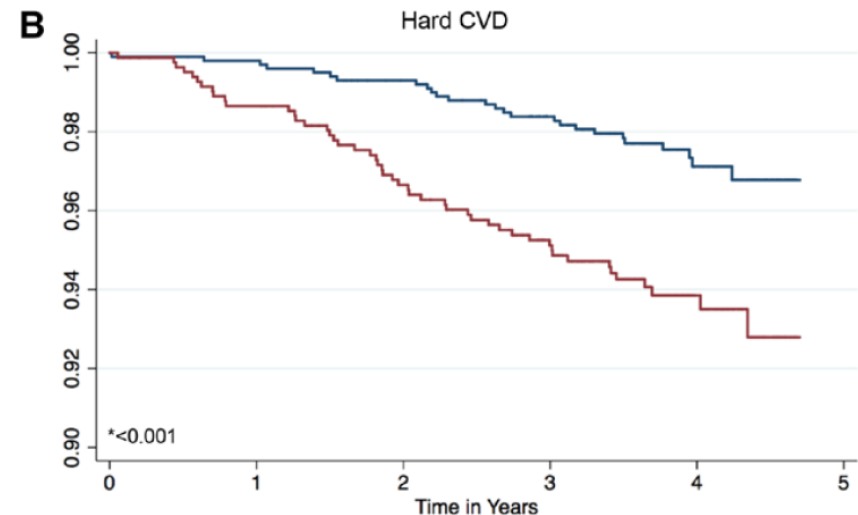
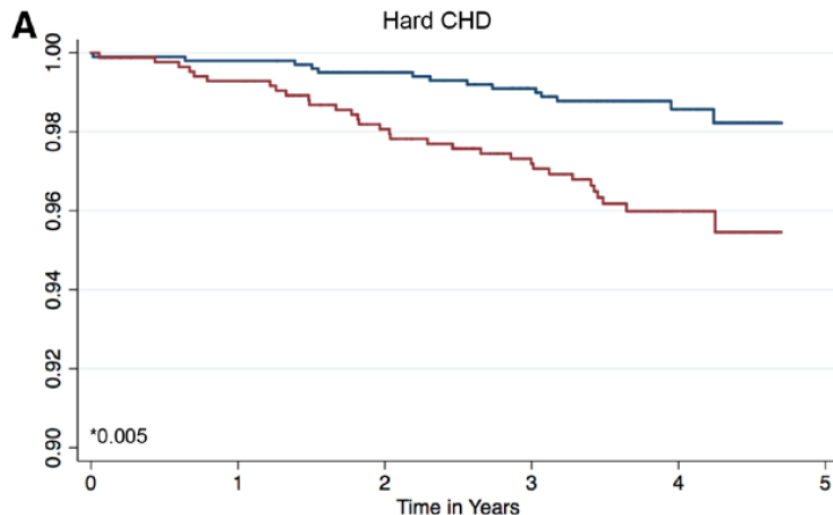
# Link Between ED and CVD

## Circulation

### RESEARCH LETTER

## Erectile Dysfunction as an Independent Predictor of Future Cardiovascular Events

The Multi-Ethnic Study of Atherosclerosis



**C**

	Events, N (%)	Unadjusted HR (95% CI)	Model 1 HR (95% CI) †	Model 2 HR (95% CI) ‡	Model 3 HR (95% CI) §
Hard CHD	40 (2.3%)	2.5 (1.3 – 4.8)	1.7 (0.8 – 3.6)	1.6 (0.8 – 3.4)	1.8 (0.8 – 4.0)
Hard CVD	75 (4.3%)	2.6 (1.6 – 4.1)	1.7 (1.0 – 2.9)	1.8 (1.0 – 3.2)	1.9 (1.1 – 3.4)

# Clinical efficacy of PDE5-inhibitors

- **No or suboptimal response in up to 50% of patients.**
- **Relevante side effects in up to 25% of patients.**

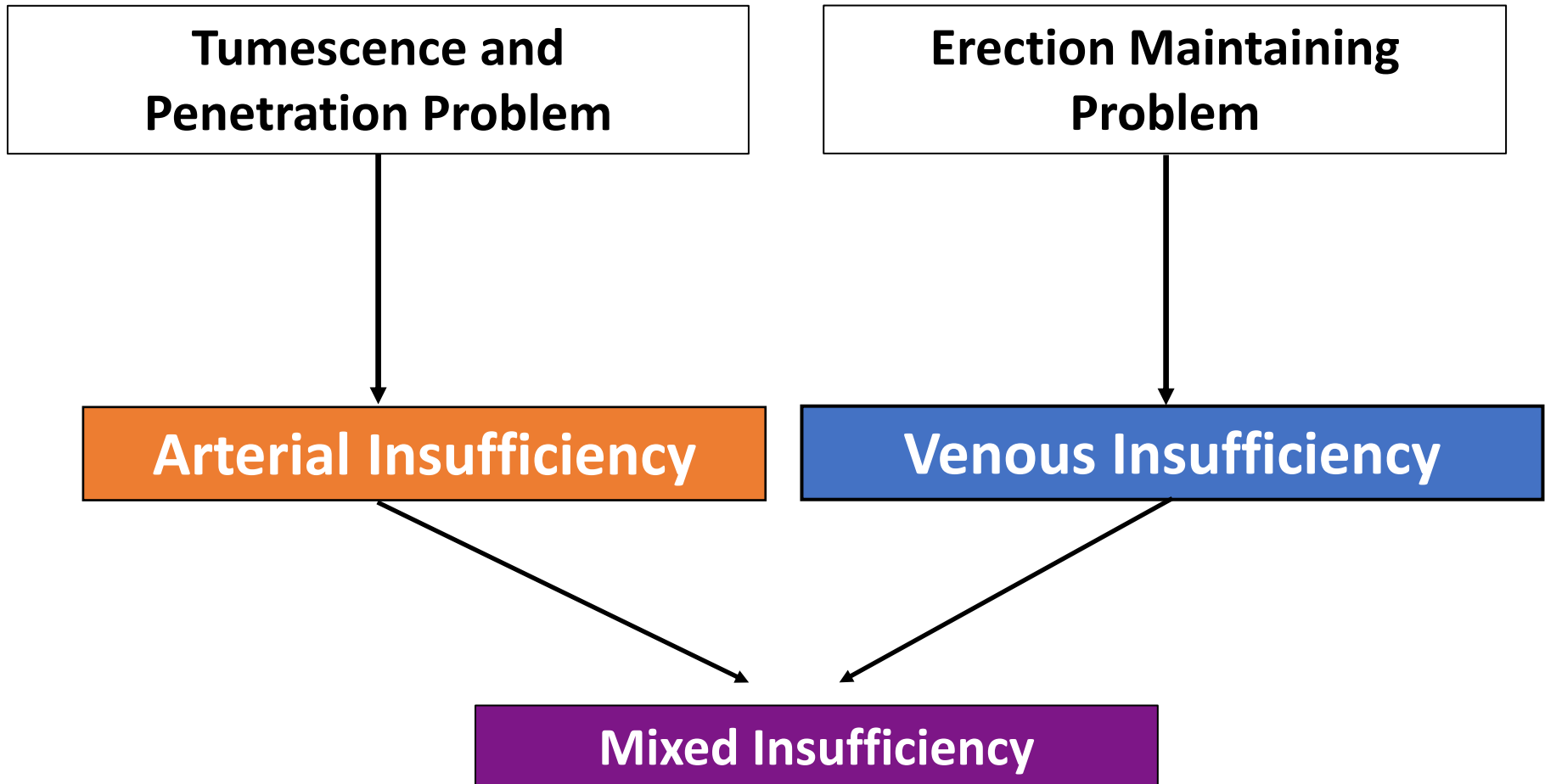


# What do you need for a natural erection?

- **Intact nerves (somebody to start the air flow)**
- **Good blow Flow (working compressor tubing)**
- **Intact/healthy cavernosal tissue (a good tire sort of)**
- **The ability to block the venous output from penis (no air leak in the tire)**



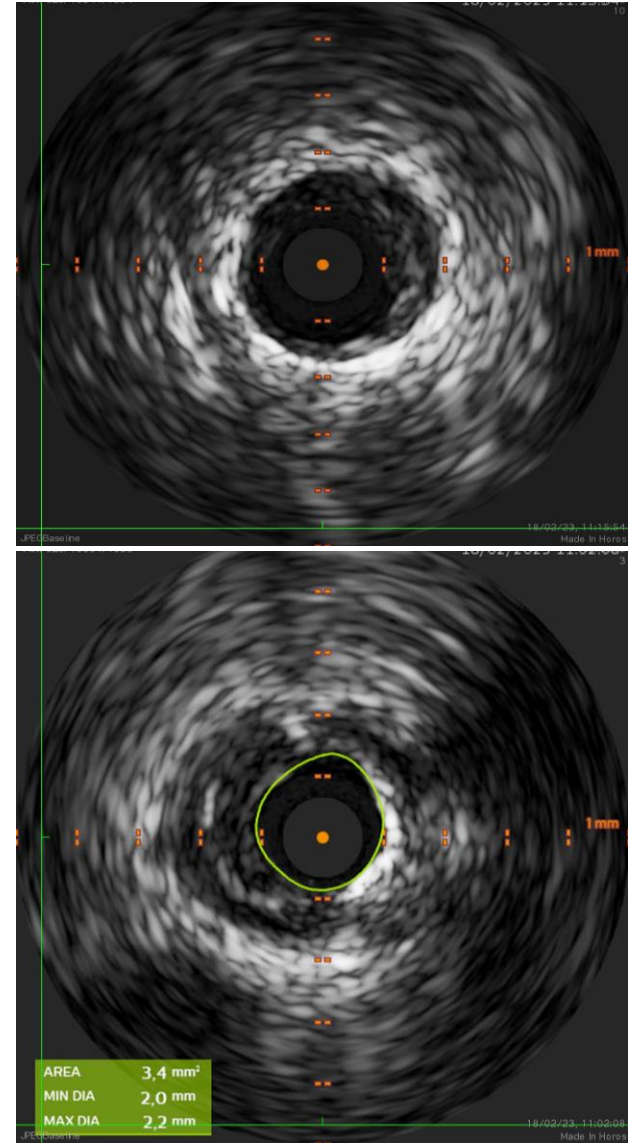
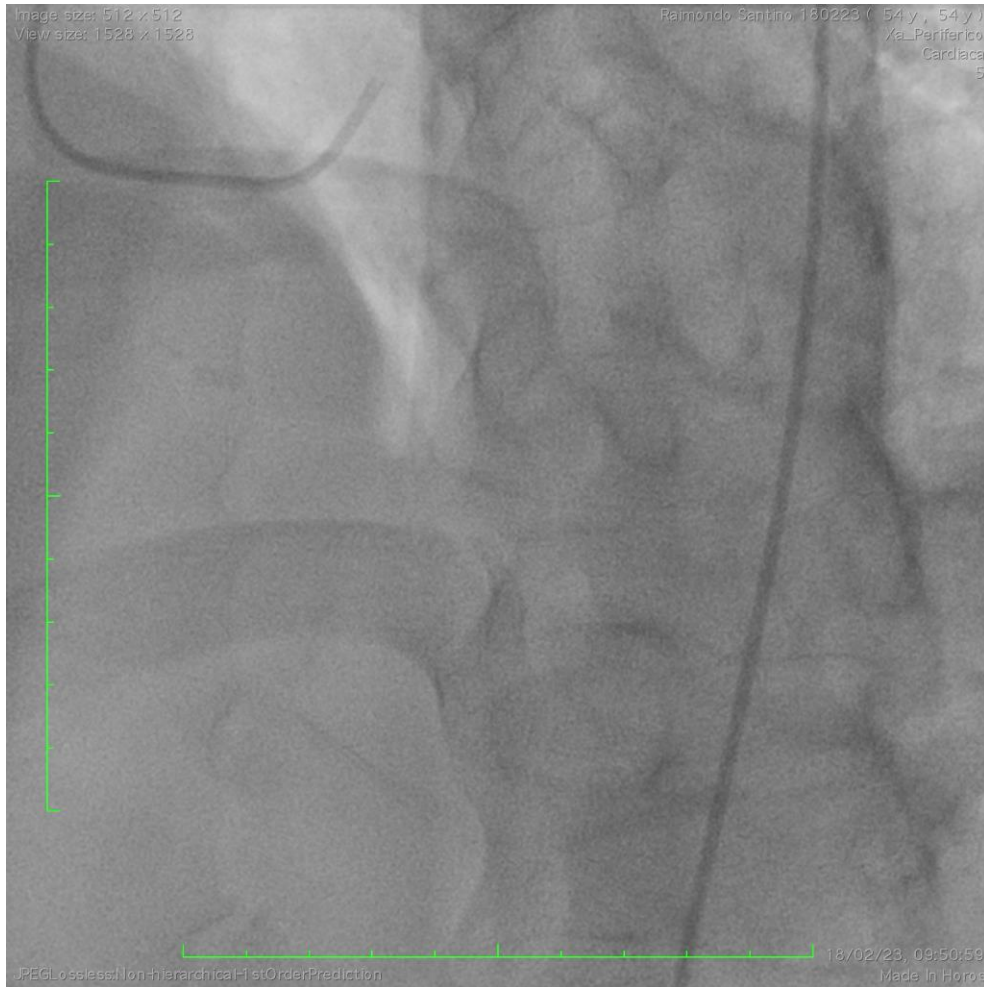
# The Scenarios



# Typical case we see in our clinical practice

- ♂ 56 yo hypertensive, diabetic NID for 15 years, hypercholesterolemia (LDL 129, tot chol 234, HDL 49 mg/dL)
- ♂ No cardiovascular events. Erectile dysfunction since 2018, not responding anymore to PDEF5i from 1 year (Spedra on demand + Cialis 5 mg once daily).
- ♂ Patient attempted 6 LISW and 3 PRP applications with no beneficial effect
- ♂ IEF-5 score = 2 (severe erectile dysfunction)
- ♂ Submitted to selective coronary and pudendal angiography

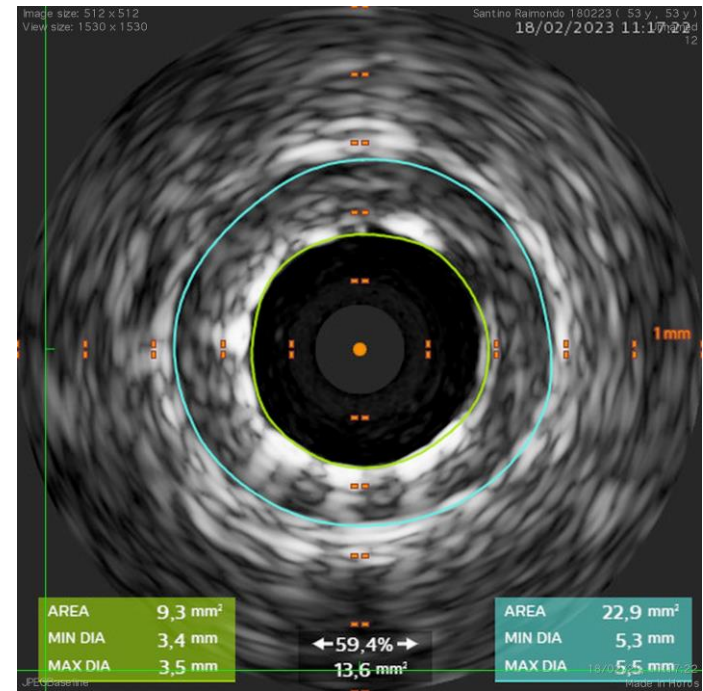
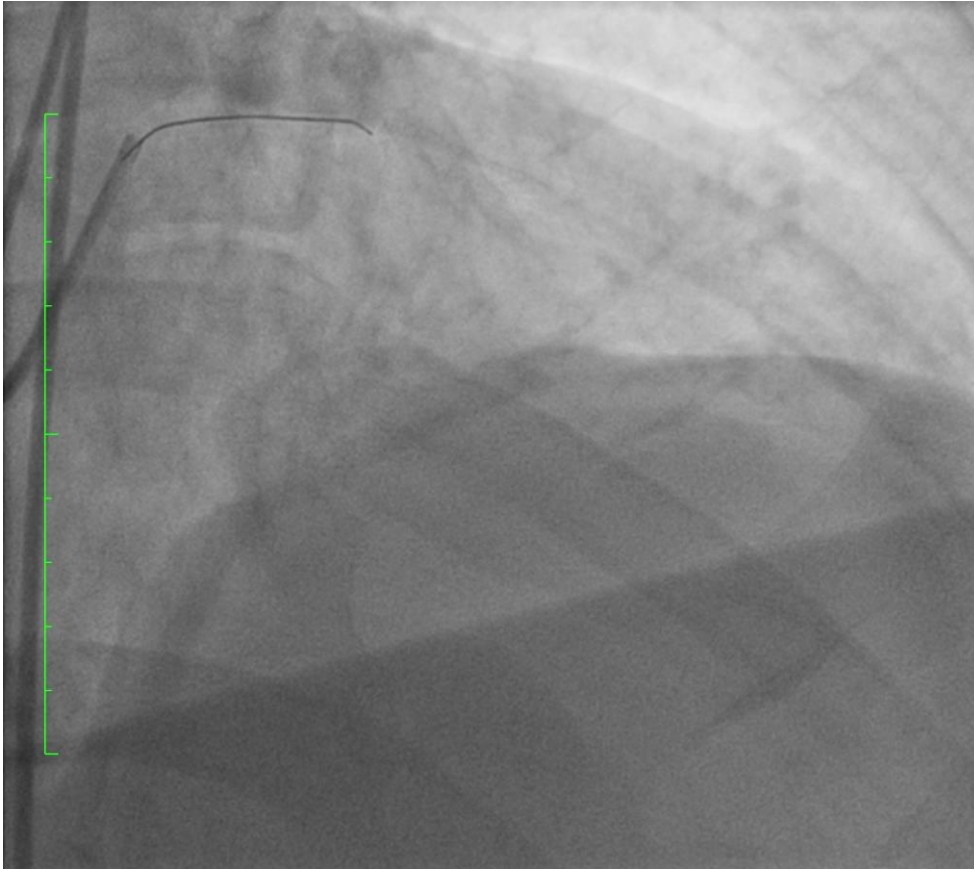
# Basal Angiography and IVUS



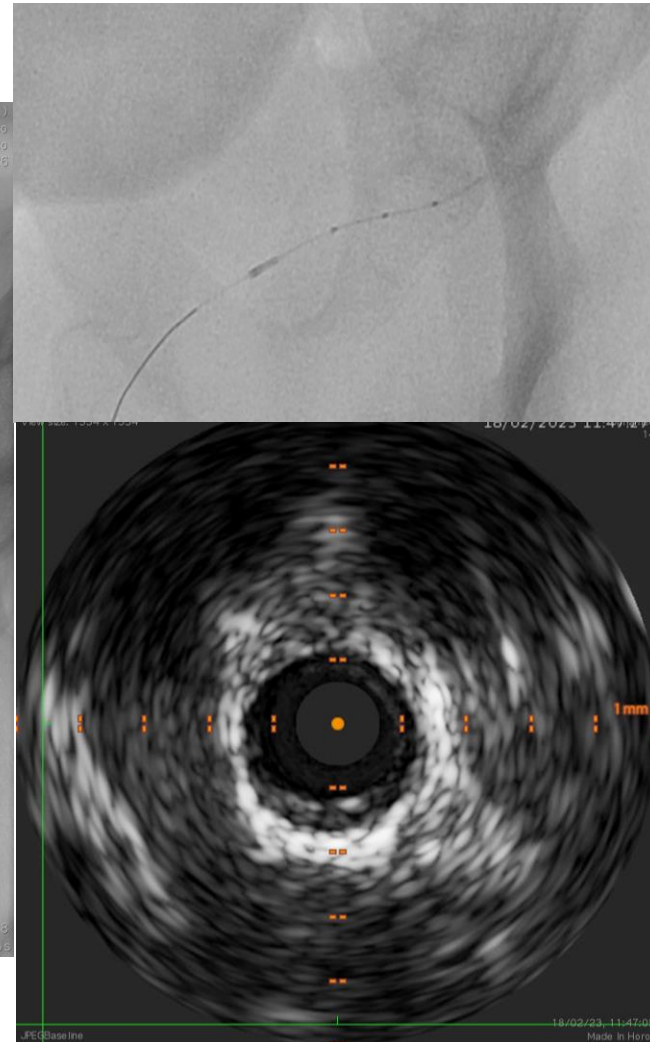
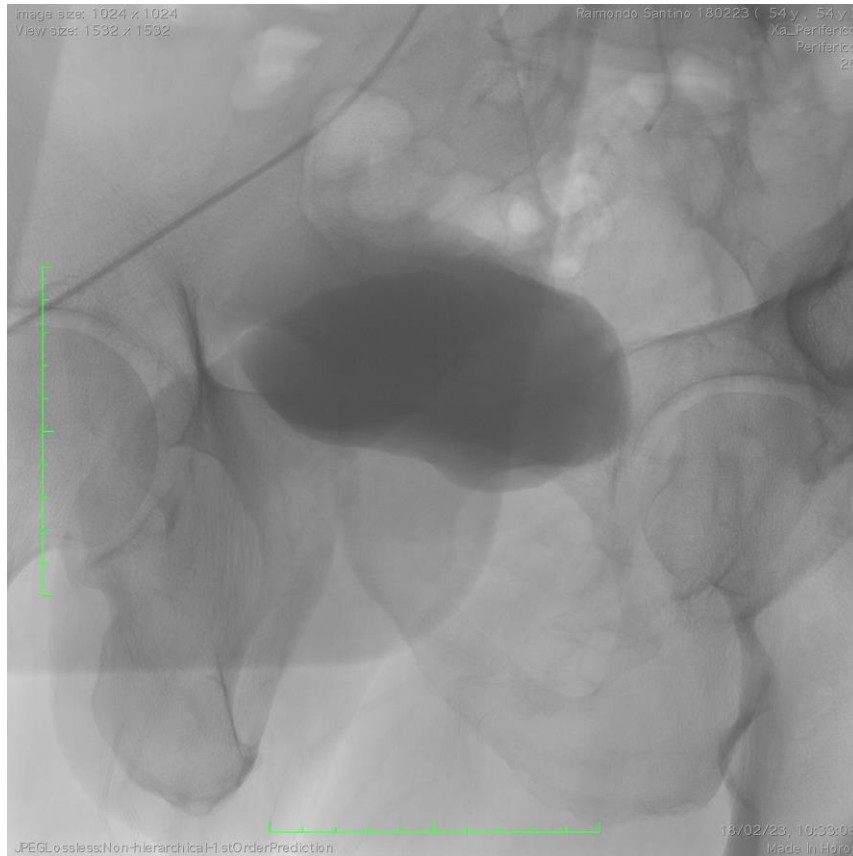


# Final Angiography and IVUS

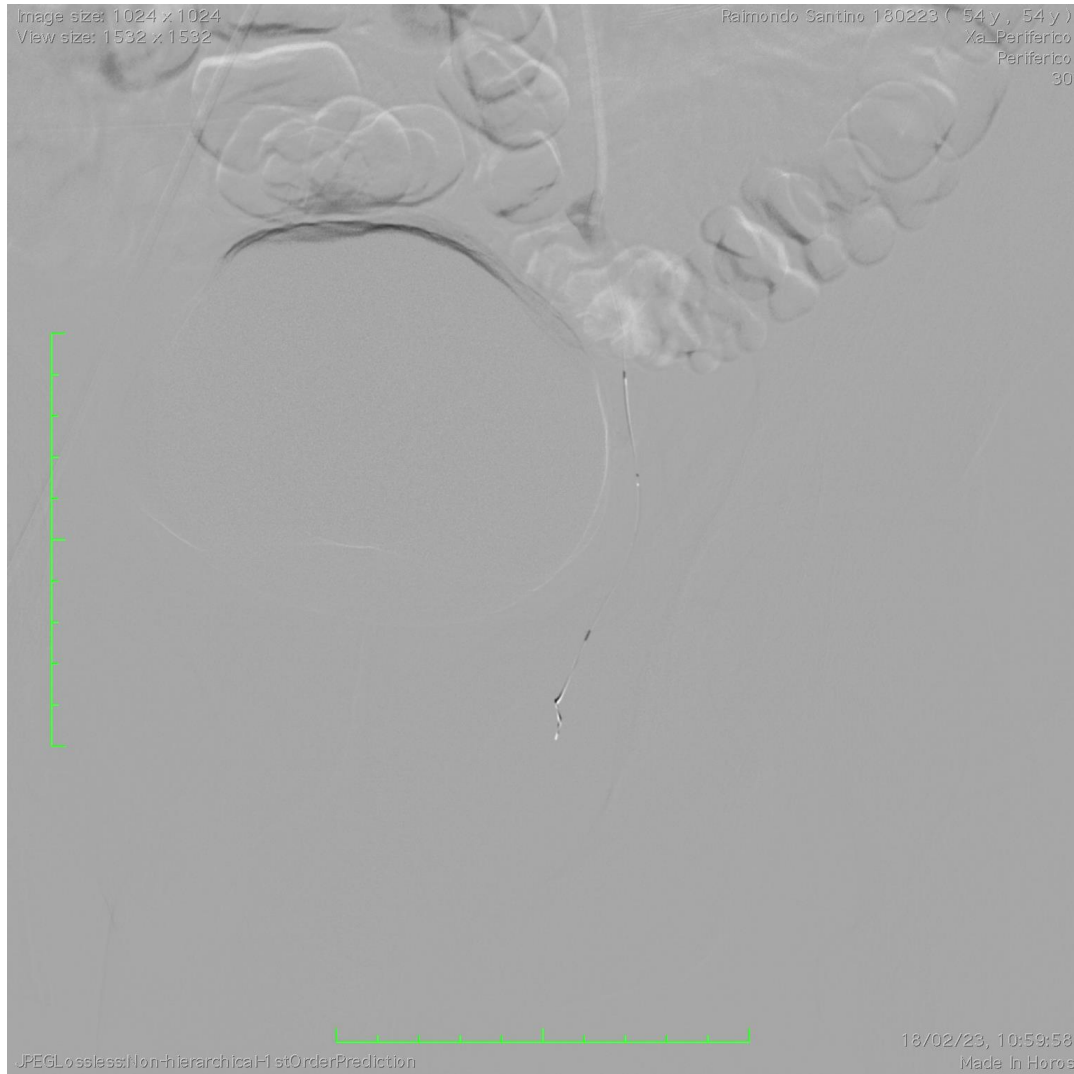
DES 3.5x23 postdilated at 24 atm with NC 3.5x20



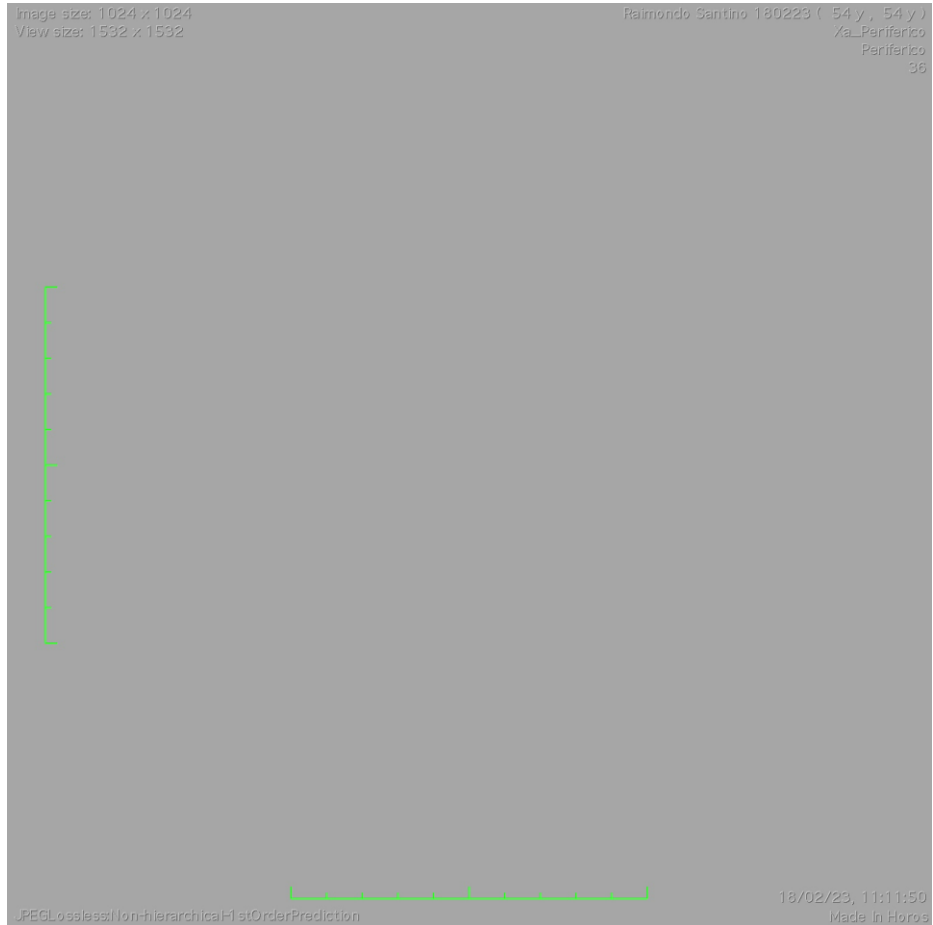
# Left Pudendal Angiography and IVUS



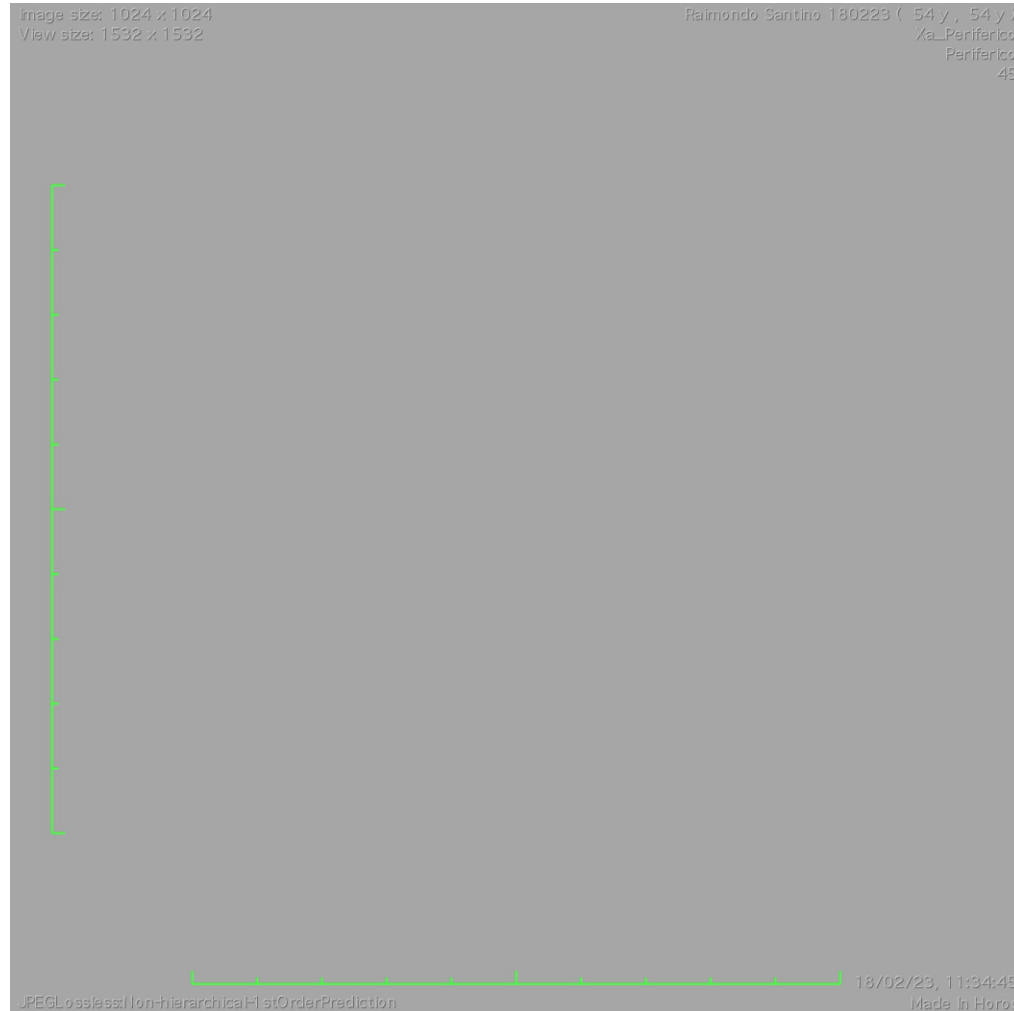
# Left Pudendal Final Result



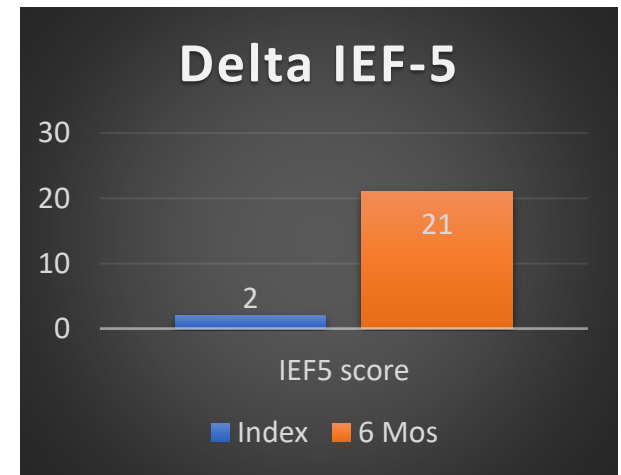
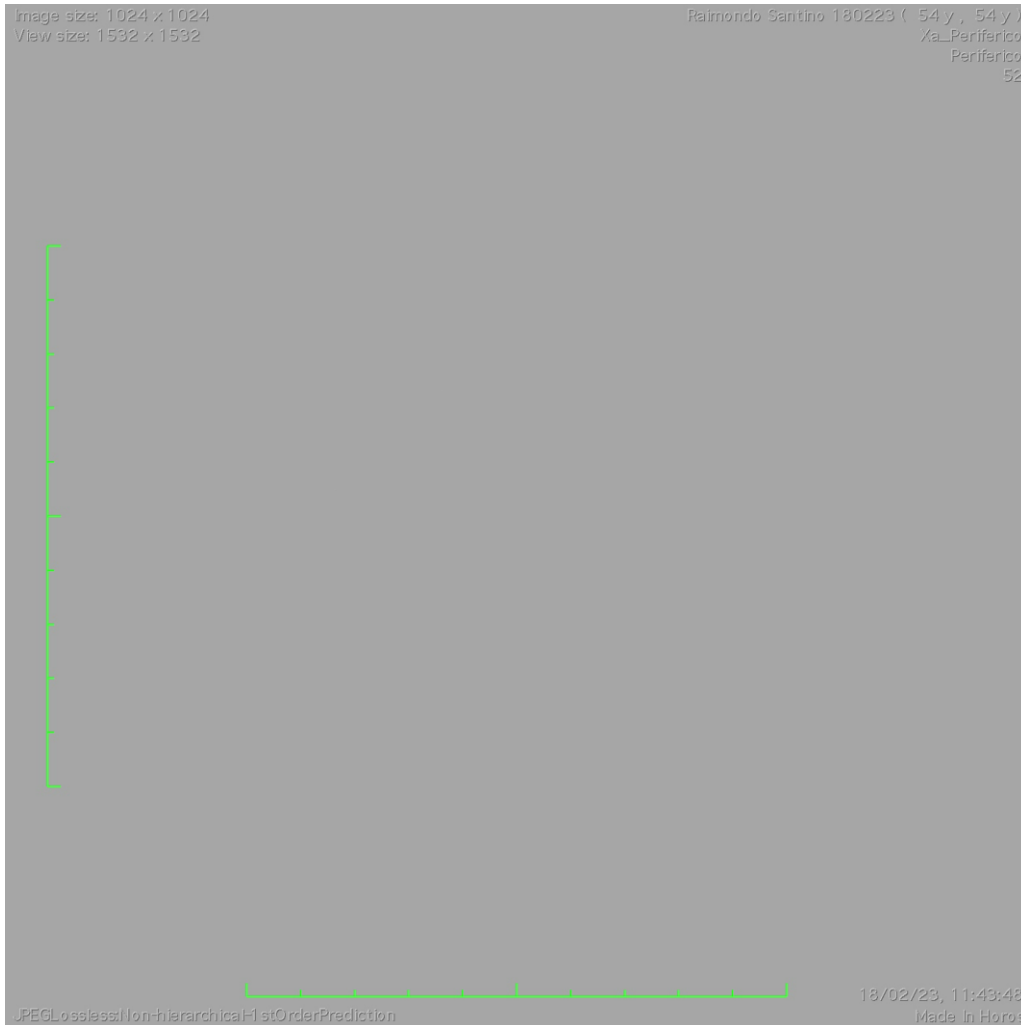
# Right Pudendal Baseline



# Selective Injection for Right Cavernous Body



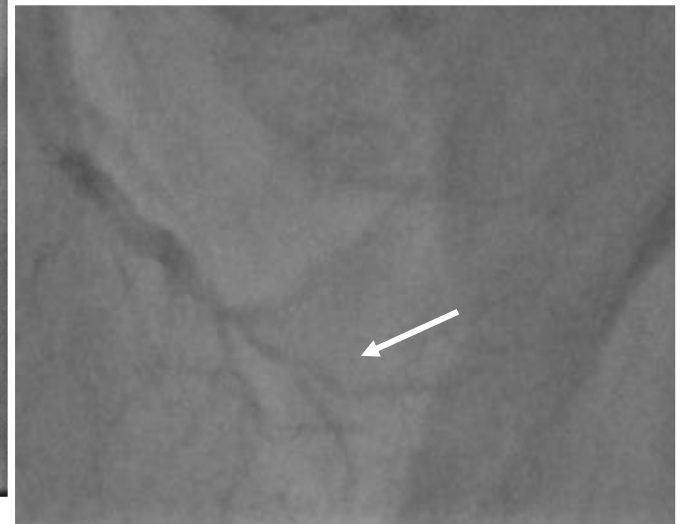
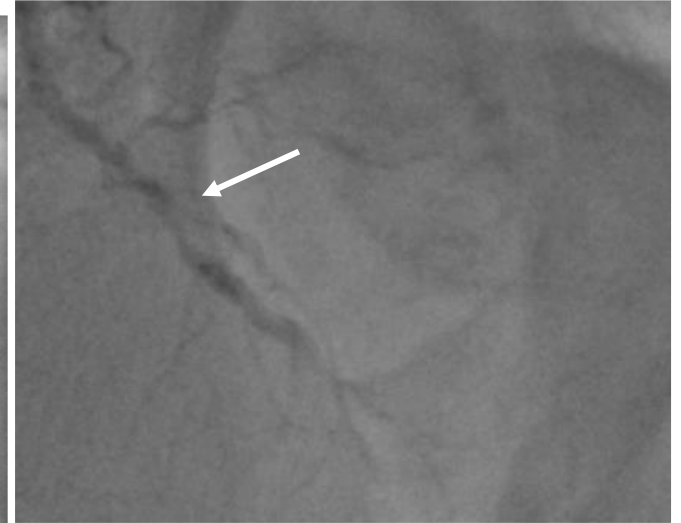
# Final Result



# 2nd Case

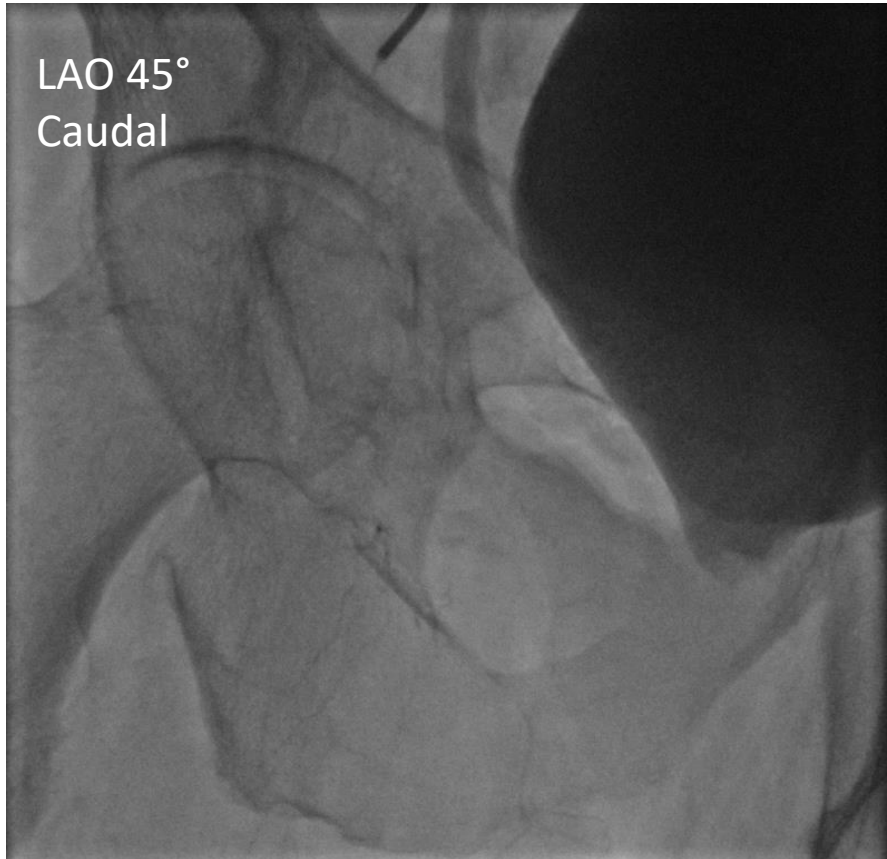
- ♂ 54 yo hypertensive, diabetic NID for 22 years, normocholesterolemic.
- ♂ No cardiovascular events. Coronary angio-CT negative.
- ♂ Erectile dysfunction since 2018, not responding anymore to PDEF5i from 1 year (Spedra on demand + Cialis 5 mg once daily).
- ♂ Patient attempted 6 applications of LiSW with no beneficial effect
- ♂ IEF-5 score = 6 (severe erectile dysfunction)
- ♂ Submitted to selective pudendal angiography

# Basal Angiography

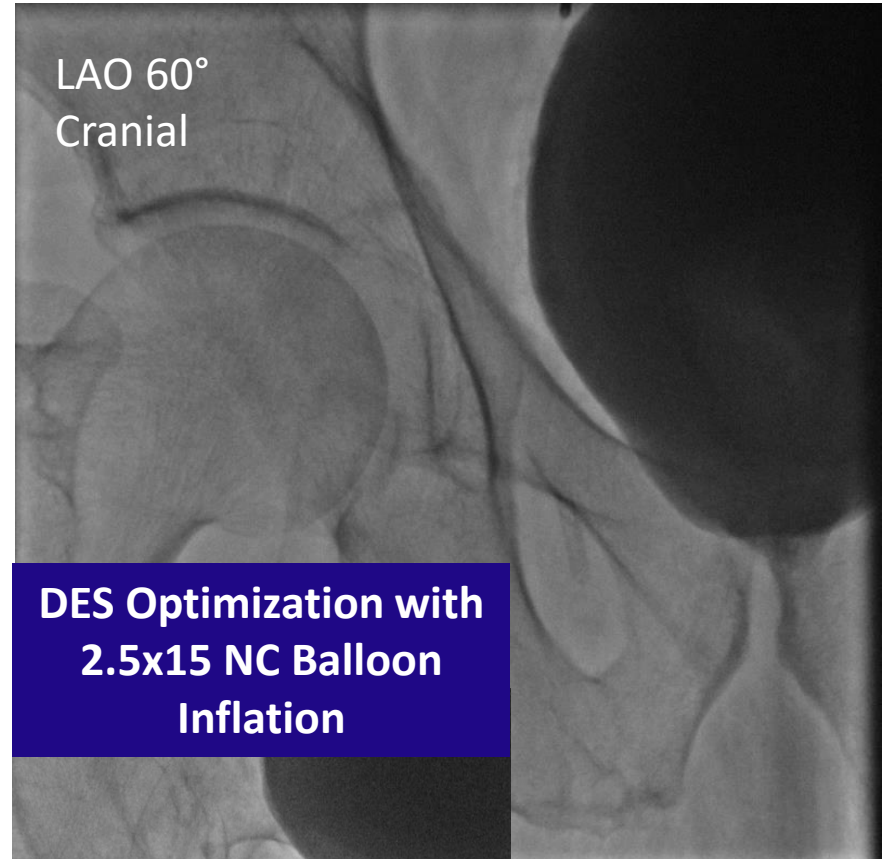




# Pudendal a. Treatment



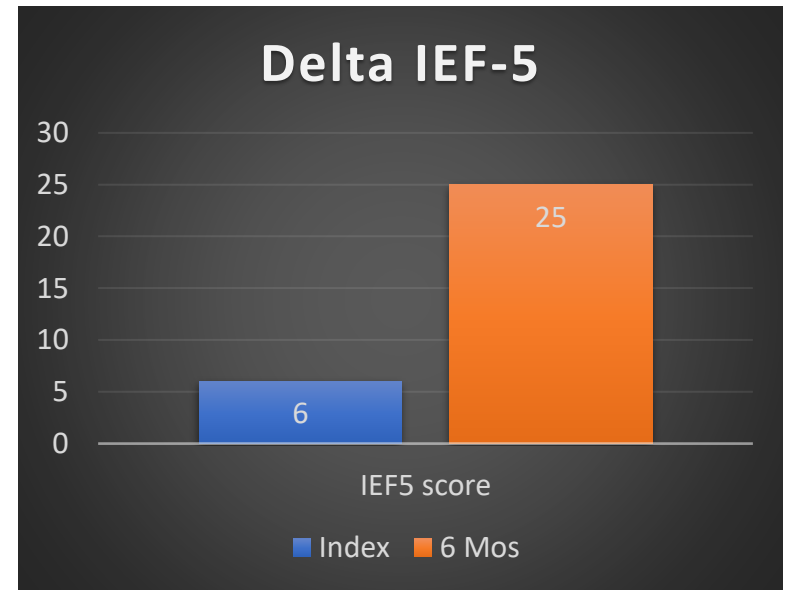
**DES Crutz 2.5x18 mm  
Implantation**



# Final Result



After Magic Touch ED 2.0x20 mm  
inflation for 2 min



# INTERVENTIONAL TREATMENT FOR ERECTILE DYSFUNCTION

Erectile Dysfunction Alternative Treatment



“I’ve performed the procedure several times.”

DEVICE TYPE	TRIAL NAME	SAMPLE SIZE	ANGIOGRAPHY/ANGIOPLAST Y CLINICAL OUTCOMES
DES (Zotarolimus eluting stent), POBA	ZEN Trial <sup>1</sup>	N=383	Stenosis (33.7%, n = 30), Acute gain(41.4%), late loss (34.4%, n = 11 ), penile Doppler (14.4 ± 10.7 to 22.5 ± 23.7 cm /s)
POBA	PERFECT-1 <sup>2</sup>	N=145	Lumen loss (0.32 ± 0.60), Binary restenosis (41%).

1. JH Rogers, Goldstein I, Kandzari DE, et al. Zotarolimus-eluting peripheral stents for the treatment of erectile dysfunction in subjects with suboptimal response to phosphodiesterase-5 inhibitors. *J Am Coll Cardiol* 2012; 60: 2618-27.
2. Wang TD, Lee WJ, Yang SC, et al. Safety and six-month durability of angioplasty for isolated penile artery stenoses in patients with erectile dysfunction: a first-in-man study. *EuroIntervention* 2014; 10: 147-56

# PERFECT-3 Study Design

## Design

- **DESIGN:** Prospective, randomized, open-label, single-center study
- **OBJECTIVE:** To assess the efficacy of treatment with either a **paclitaxel drug-eluting balloon (SeQuent Please®)**, **drug-eluting stents**, or **balloon angioplasty alone** for lesions in the distal internal pudendal artery in patients with erectile dysfunction and obstructive pelvic arterial lesions
- **ENDPOINTS:** **Primary endpoint: Binary in-segment restenosis** (diameter stenosis  $\geq 50\%$ ) by CT or invasive angiography at 8 months; **Secondary endpoints:** Diameter stenosis at 8 months; **clinical success** (change of IIEF-5 from baseline by  $\geq 4$  points or IIEF-5  $\geq 22$  points) at 6 months

79 patients w/ ED (IIEF-5, 5-21) and distal internal pudendal arterial lesions in CTA enrolled between Jan 2013 and Dec 2014 in NTUH

27 patients failed angio criteria

52 patients randomized in a 1:1:1 manner

DEB  
(N=20)

DES  
(N=12)\*

Balloon  
(N=20)

Clinical follow-up at 1, 3, and 6 months

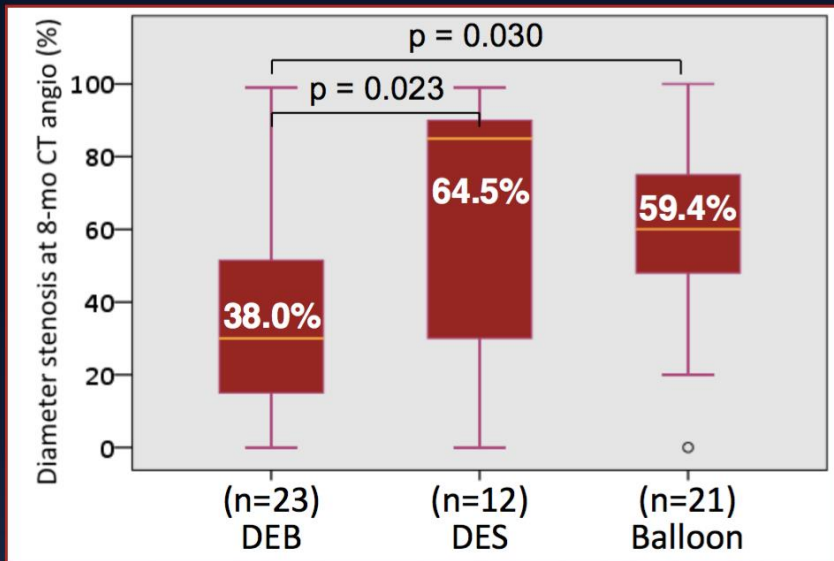
CT angiographic follow-up at 8 months

\*DES group was early terminated due to a high restenosis rate ( $>60\%$ )

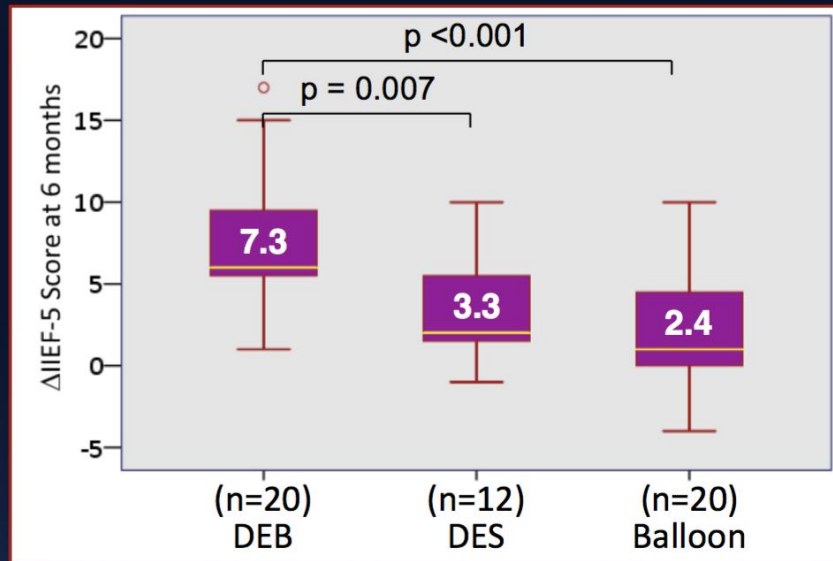
NCT02178761 ([www.clinicaltrials.gov](http://www.clinicaltrials.gov))

# Primary and Secondary Endpoints

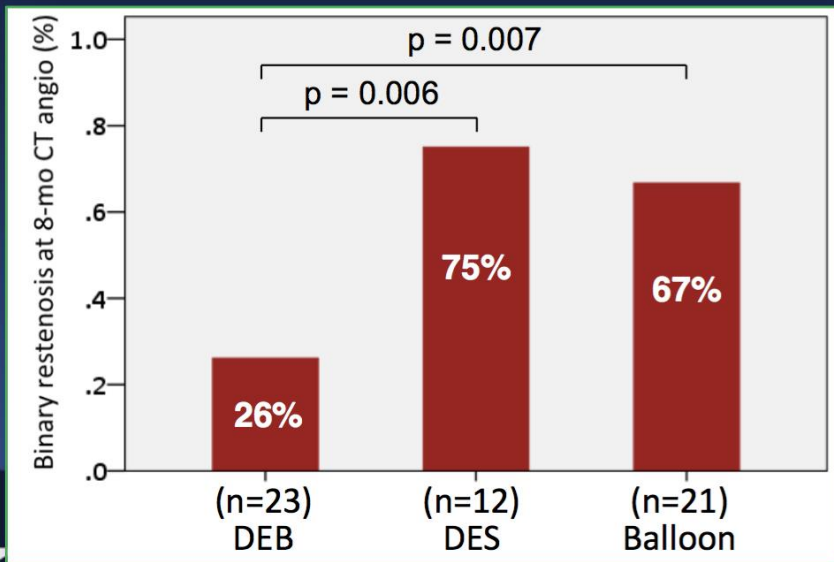
Diameter Stenosis at 8 months



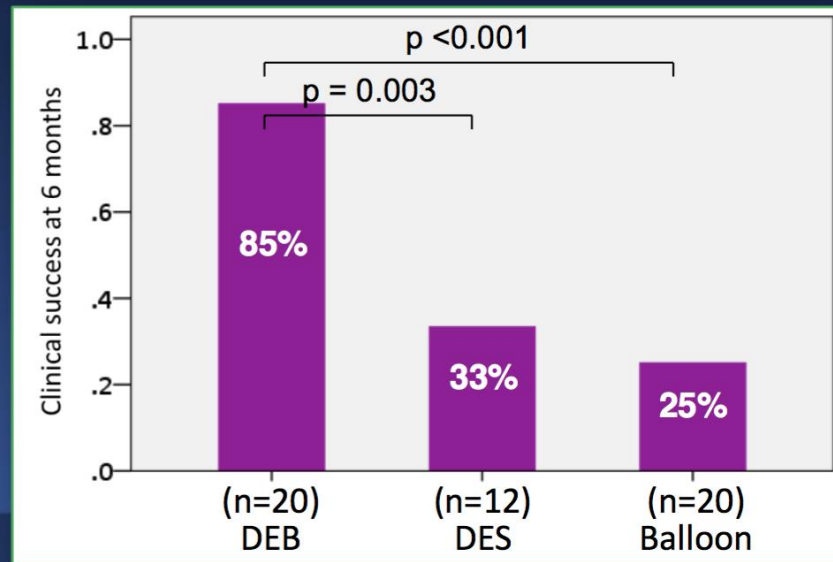
ΔIIEF-5 at 6 months



Binary Restenosis at 8 months



Clinical Success at 6 months\*



\*Clinical success: ΔIIEF-5 ≥4 or IIEF-5 ≥22

## Different Studies Published Related to Percutaneous Revascularization for Erectile Dysfunction

Author	Year	Study Type	Pts #	Stenotic Segment	Follow-up (mos)	Procedural Success (%)	Utilized Device
Castaneda-Zuniga et al. (59)	1982	Clinical Case	2	IIA	18	100	POBA
Van Unnik et al. (60)	1984	Clinical Case	1	EIA	ND	100	POBA
Goldwasser et al. (61)	1985	Clinical Case	1	IIA	ND	100	POBA
Dewar et al. (62)	1985	Prospective, Non-Randomized	30	Ao-IL (70%) IIA (47%)	ND	33	POBA
Angelini et al. (63)	1985	Clinical Case	5	IAA	2-18	80	POBA
Urigo et al. (64)	1994	Prospective, Non-Randomized	23	IAA IPA	ND	65-100	POBA
Rogers et al. (65)	2012	Prospective, Non-Randomized	30	IPA	12	100	DES
Wang et al. (66)	2014	Prospective, Non-Randomized	20	IPA	12	100	POBA
Wang et al. *	2014	Prospective, Non-Randomized	48	CIA, IIA, EIA, IPA, PA, AO	ND	65	POBA
Wang et al.*	2015	RCT	52	IPA	12	100	DES vs.PEB vs.POBA
Wang et al. (121)	2016	RCT	50	IPA	12	100 vs.96	PEB vs.POBA
Sangiorgi et al. (85)	2018	All-Comers Registry	84	IPA	12	100	PEB

RCT: Randomized Clinical Trial; Ao-IL Aorto Iliac artery; CIA Common Iliac Artery; EIA External Iliac Artery; IIA Internal Iliac Artery; AO Obturatory Artery; PA Penile Artery

\*Presented at TCT Meeting, Not Published

# MagicTouch<sup>ED</sup>

SIROLIMUS COATED BALLOON CATHETER

Only Approved SEB  
For ED treatment

Sirolimus Coated  
Balloon Catheter

## Assuring Safety by Delivering Sirolimus



### TECHNOLOGY

An innovative proprietary Nanolute technology providing better bioavailability of SIROLIMUS



### COATING

Unique coating technology leads to 100% balloon surface coating



### DRUG

Sirolimus: A drug with proven safety profile



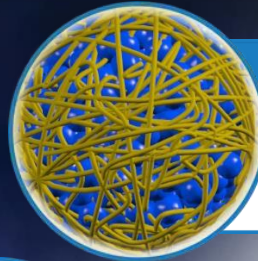
### CARRIER

A biocompatible phospholipid drug carrier improving the adhesion property of Sirolimus



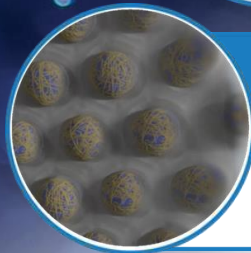
# Sirolimus-Eluting Balloon with Sustained Release

SelutionSLR™  
SUSTAINED LIMUS RELEASE



## Proprietary MicroReservoir Technology

- Creation of MicroReservoirs combining sirolimus & biodegradable polymer
- Sirolimus - a proven safe & effective cytostatic drug
- Offering a wider therapeutic range



## MicroReservoirs: Miniature Drug-Delivery Systems

- Optimal size MicroReservoirs to achieve pharmacokinetic release profile comparable to best in class DES
- Consistent and predictable drug release
- Sustained therapeutic effect for up to 90 days<sup>1</sup>



## Cell Adherent Technology (CAT™)

### Proprietary amphipathic lipid technology which binds MicroReservoirs to the balloon surface

- Contains and protects micro-reservoirs during insertion and inflation
- Enhances drug retention and bioavailability, allowing for a lower drug dose concentration on the balloon surface (1µg/mm<sup>2</sup>)
- Optimizes transfer of MicroReservoirs to the tissue and maximizes the cellular uptake of sirolimus



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ORIGINAL ARTICLE

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# Rationale and design of the sirolimus eluting balloon utilization for treatment of vasculogenic erectile dysfunction: the SUASION Registry

Andrea MATTEUCCI \*, Daniela BENEDETTO, Michela BONANNI,  
Gianluca MASSARO, Debora RUSSO, Giulio RUSSO, Gaetano CHIRICOLO,  
Giuseppe BIONDI-ZOCCAI, Giuseppe SANGIORGI

Division of Cardiology, Policlinico Tor Vergata, University of Rome, Rome, Italy

\*Corresponding author: Andrea Matteucci, Division of Cardiology, Policlinico Tor Vergata, University of Rome, viale Oxford 81, 00133 Rome, Italy. E-mail: [andrea.matteucci2@gmail.com](mailto:andrea.matteucci2@gmail.com)

# First in Man Study of Sirolimus Eluting Balloon for Treatment of Vasculogenic Erectile Dysfunction

Giuseppe Sangiorgi\* MD, Nicolas Diehm^ MD, Francesco Greco° MD,  
Alberto Cereda\* MD, Riccardo Iorio\* MD, Sante Bongo\* MD

From the \*Department of Cardiovascular Disease – Clinica San Gaudenzio – Novara, Italy

^Department of Angiology, Vascular Institute Central - Aarau, Switzerland

°Department of Urology, Humanitas Gavazzeni - Bergamo, Italy

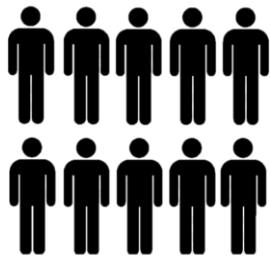
# How was the study executed?

## The SUASION study

Sirolimus Eluting Balloon Utilization for Treatment of Vasculogenic  
Erectile Dysfunction



**Design:** Prospective, post-market, non-randomized, all-comers, multicenter single-arm study



**Target**  
N=100



### **Efficacy End-points**

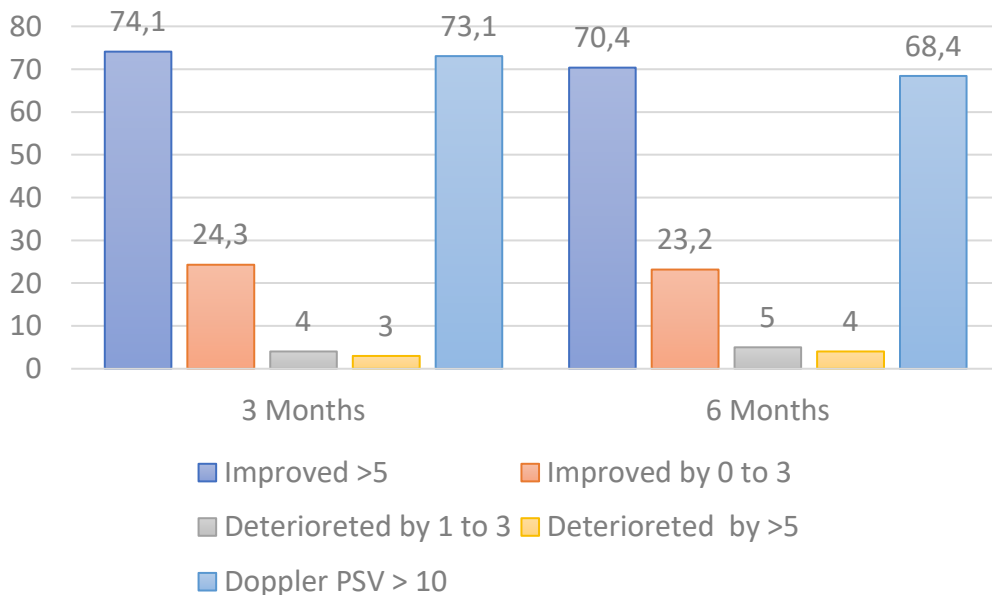
Composite of:

- 1) Delta International Index of IEF-6  $\geq 5$   
(Erectile Function-6 score) at 6 mos FU
- 2) Delta Doppler PSV velocity  $>5\text{cm/s}^{-1}$   
at 6 mos FU

### **Safety End-point**

Freedom from target lesion  
revascularization (TVR) at 8 months FU

57 Patients affected by ED  
Not responding to PDEF-5i



**Treatment Success Reflected by Minimum Clinically Relevant Improvement in the International Index of Erectile Function-6 (IIEF-6) score and Dynamic Doppler PSV between Baseline and 6 months FU**

# Swiss experiences

*Clinical Investigation*

## **Endovascular Therapy for Erectile Dysfunction—Who Benefits Most? Insights From a Single-Center Experience**

JOURNAL OF  
**ENDOVASCULAR**  
THERAPY  
A SAGE Publication  
ISEVS

Journal of Endovascular Therapy  
1–10

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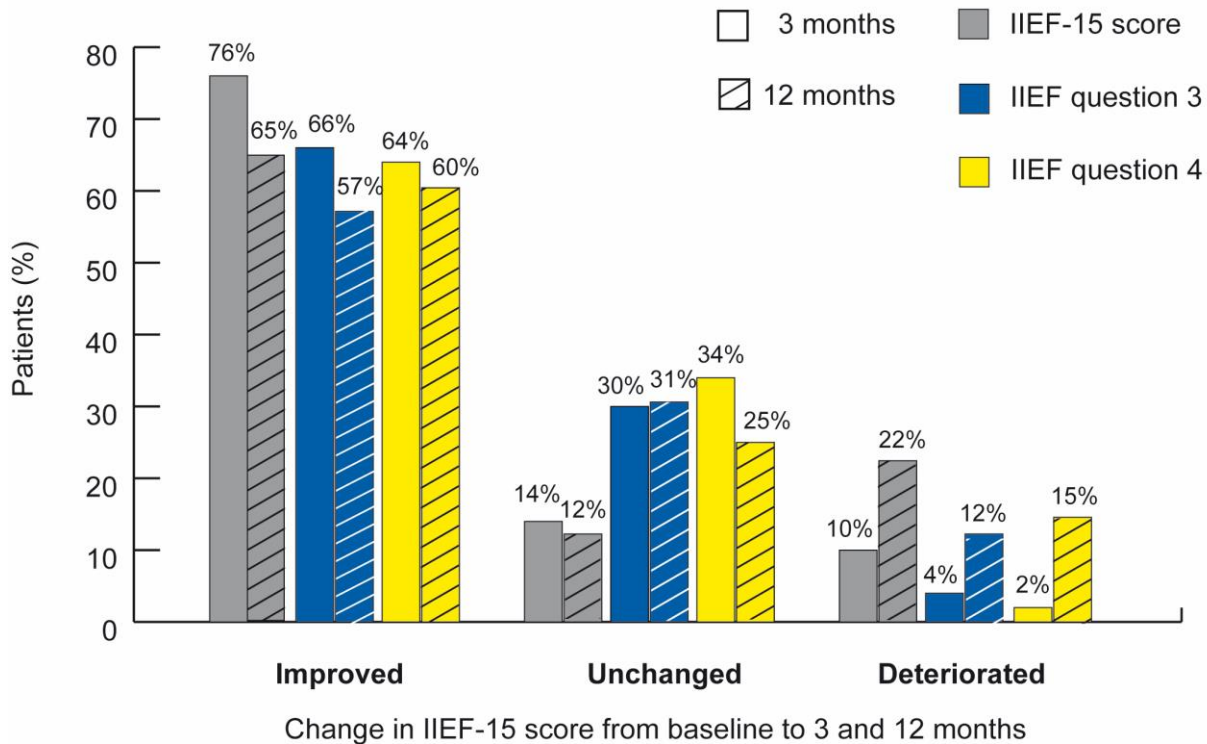
DOI: 10.1177/1526602819829903

[www.jevt.org](http://www.jevt.org)



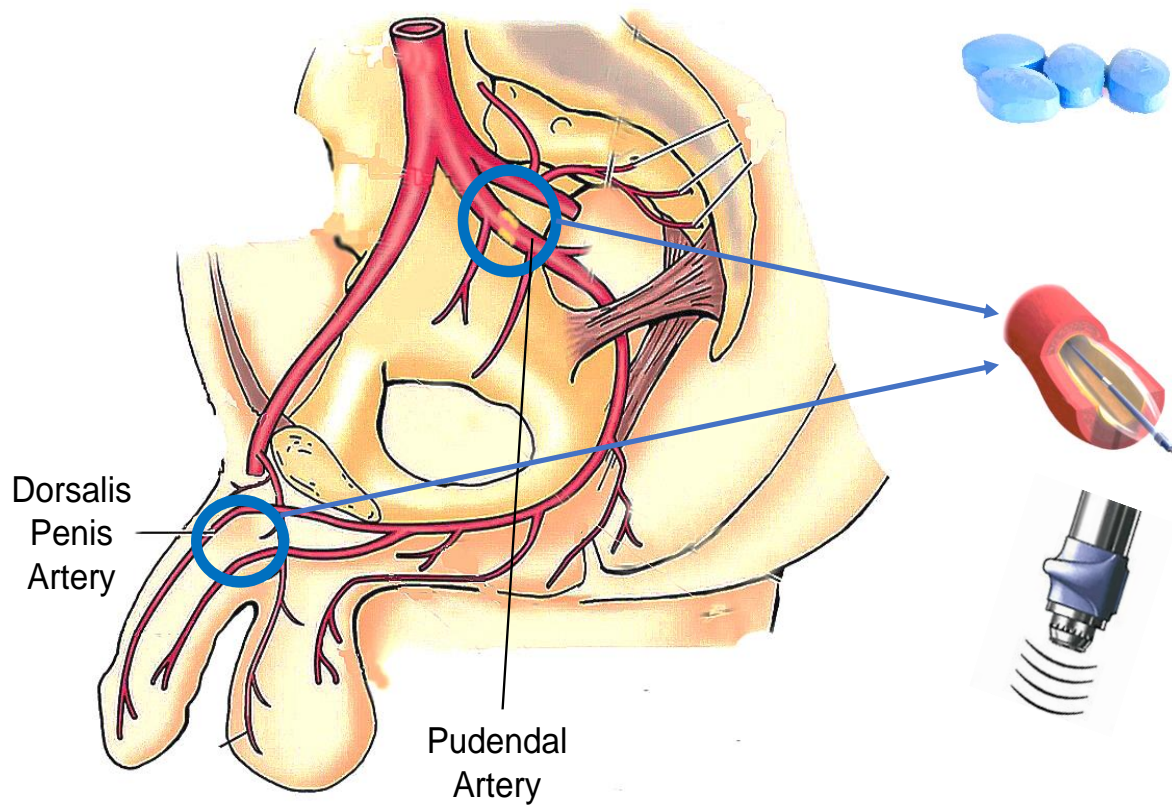
- All-comers quality control investigation.
  - 50 patients with 82 lesions treated with POBA (15.9%), DCB (26.8%), or DES (54.9%); 4/2016 – 10/2017.
  - **Primary safety endpoint** was freedom from (MAE) at 30 days and at 3 months.
  - **Primary feasibility endpoint:** incidence of a minimum clinically relevant improvement of  $\geq 4$  in the IIEF-6 score at 12 months.
  - **Secondary clinical effectiveness endpoint:** mean change of the total IIEF-15 score and IIEF-15 Q3 and 4 at 3 and 12 months.
-

# Clinical Improvement



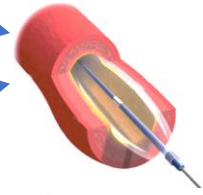
**„Viagra Study Endpoints“**

# Proposed Treatment Algorithm for Vasculogenic ED



- ↑ Vasodilatation
- ↑ Endothelial function
- VSMC preservation
- ↓ Cavernal fibrosis

**1st**  
Line Treatment (Proven)  
- Lifestyle Changes  
- PDE-5i  
**Botox**

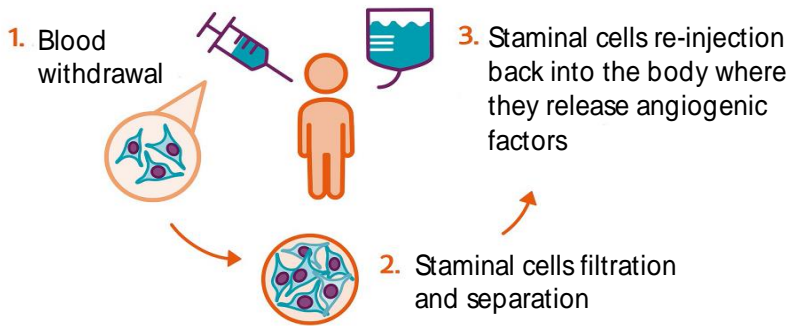
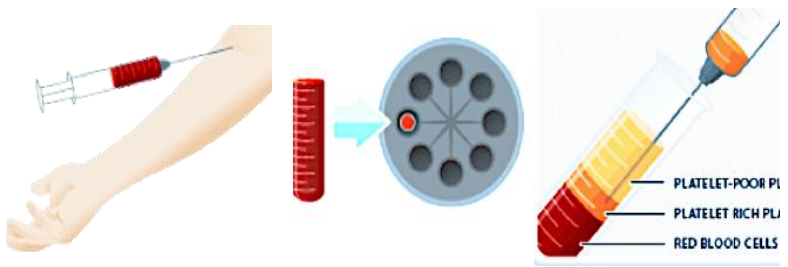


↑ Blood Flow

**2nd**  
Line Treatments (Proven)  
- PTA  
- LiSWT




- ↑ E-nos Stimulation
- ↑ VEGF Release
- ↑ PCNA Production
- ↑ Neovascularization



**3rd**  
Line Treatment (Unproven)  
**PRP Staminal**



## The Italian Society of Andrology and Sexual Medicine (SIAMS), along with ten other Italian Scientific Societies, guidelines on the diagnosis and management of erectile dysfunction

G. Corona<sup>1</sup> · D. Cucinotta<sup>2</sup> · G. Di Lorenzo<sup>3,4</sup> · A. Ferlin<sup>5</sup> · V. A. Giagulli<sup>6,7</sup> · L. Gnessi<sup>8</sup> · A. M. Isidori<sup>9</sup> · M. I. Maiorino<sup>10</sup> · P. Misserendino<sup>11</sup> · A. Murrone<sup>12</sup> · R. Pivonello<sup>13,14</sup> · V. Rochira<sup>15</sup> · G. M. Sangiorgi<sup>16</sup> · G. Stagno<sup>17</sup> · C. Foresta<sup>5</sup> · A. Lenzi<sup>8</sup> · M. Maggi<sup>18</sup> · E. A. Jannini<sup>19</sup> 

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### Abstract

**Purpose** Erectile dysfunction (ED) is one of the most prevalent male sexual dysfunctions. ED has been in the past mistakenly considered a purely psycho-sexological symptom by patients and doctors. However, an ever-growing body of evidence supporting the role of several organic factors in the pathophysiological mechanisms underlying ED has been recognized.

**Methods** The Italian Society of Andrology and Sexual Medicine (SIAMS) commissioned an expert task force involving several other National Societies to provide an updated guideline on the diagnosis and management of ED. Derived recommendations were based on the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system.

**Results** Several evidence-based statements were released providing the necessary up-to-date guidance in the context of ED with organic and psychosexual comorbidities. Many of them were related to incorrect lifestyle habits suggesting how to associate pharmacotherapies and counseling, in a couple-centered approach. Having the oral therapy with phosphodiesterase type 5 inhibitors as the gold standard along with several other medical and surgical therapies, new therapeutic or controversial options were also discussed.

**Conclusions** These are the first guidelines based on a multidisciplinary approach that involves the most important Societies related to the field of sexual medicine. This fruitful discussion allowed for a general agreement on several recommendations and suggestions to be reached, which can support all stakeholders in improving couple sexual satisfaction and overall general health.

**\* Remarks** Emerging evidence provides data supporting a possible role of percutaneous approach with drug eluting balloon and/or drug eluting stent implantation [294, 295].



# Conclusions

- ♂ PTA of pudendal district is technically demanding
  - ♂ Excellent angiographic and clinical results could be obtained with SEB and/or stenting as ITT or bailout strategy
  - ♂ Future studies and **RCTs** will finally prove if percutaneous mechanical revascularization of pudendal district can be adopted as second line therapy for vasculogenic erectile dysfunction
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Giuseppe M. Sangiorgi · Francesco Greco

## Erectile dysfunction from bench to bedside

This book, promoted by the Italian Society of Interventional Cardiology (SICI-GISE), the Italian Society of Urology (SIU) and the Italian Society of Andrology (SIA), with the contribution of several key opinion leaders in the field of cardiovascular disease and erectile dysfunction, has been written with the aim to offer to the Readers a modern multidisciplinary team approach for evaluation and treatment of men affected by erectile dysfunction. The book follows a "bench to bedside" pathway beginning with anatomy and physiology of erection, describing the pathophysiologic basis of erectile dysfunction, then moving to the different diagnostic modalities for patient evaluation and finally describing in deep the pharmacological, mechanical and surgical treatment strategies. The Editors and co-Editors really hope that this effort will be of help to urologists, andrologists and cardiologists to understand that a multidisciplinary approach can open new possibilities to increase our knowledge in the field of erectile dysfunction.

Giuseppe M. Sangiorgi · Francesco Greco

Erectile dysfunction

# Erectile dysfunction

## from bench to bedside

With the collaboration of

Vincenzo Mirone  
Giuseppe Tarantini  
Alessandro Palmieri  
Giuseppe Musumeci  
David Holmes Jr.



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