Analysis of threshold stenosis by multiplanar venogram and IVUS for predicting clinical improvement after iliofemoral vein stenting

Results from the VIDIO study

Multicenter, Prospective Study of Iliofemoral Vein Interventions

Paul J. Gagne, MD, FACS, RVT
Global Principal Investigator on behalf of VIDIO Investigators

The American Venous Forum 29th Annual Meeting

VIDIO
VENOGRAM vs. IVUS FOR DIAGNOSING ILIAC VEIN OBSTRUCTION

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Disclosures

- Consultant and Global Principal investigator:
  Philips

- I have the following potential conflicts of interest to report:
  - Receipt of grants/research support
  - Participation in a company sponsored speakers‘ bureau

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Study Administration	
Core Lab Imaging “Over-reads” and Biostatistics	Syntactx (Led by Kenneth Ouriel, MD) Contract Research Organization, New York, NY
Study Sponsor	Philips San Diego, CA

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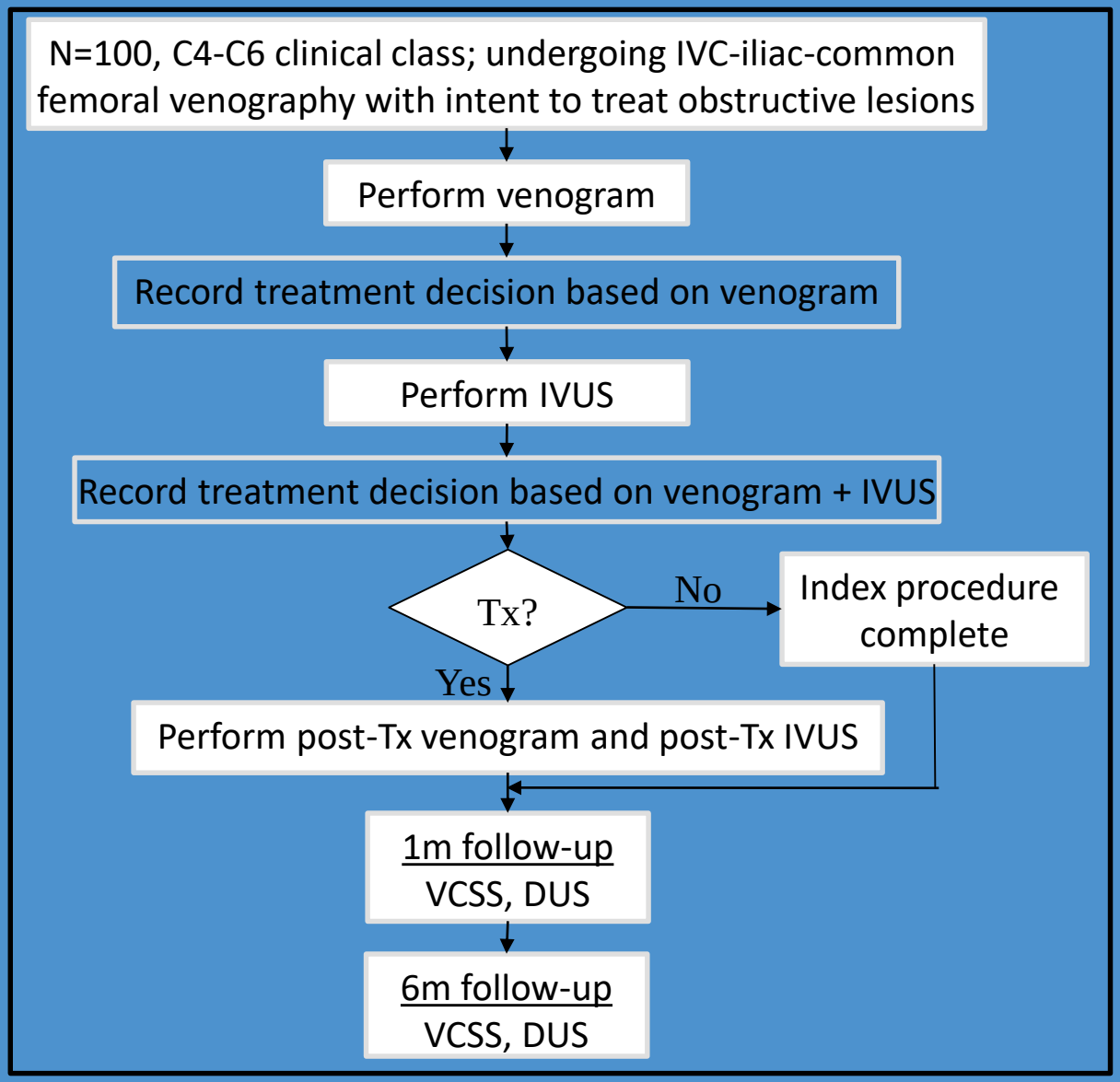
Study Design



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- **Prospective, multi-center, single-arm**
- **14 Sites:**
  - **US (n = 11)**
  - **Europe (n = 3)**
- **100 patients:**
  - **CEAP 4-5, n=50;**
  - **CEAP 6, n=50**
- **Follow-up visits:**
  - **1 month and**
  - **6 months**

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Study Objectives
Primary Objectives

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VENOGRAM vs. IVUS FOR DIAGNOSING ILIAC VEIN OBSTRUCTION

As previously reported:

1. Prospectively compare multiplanar venography vs.Intravascular Ultrasound (IVUS) for diagnosing treatable iliac/common femoral vein obstruction (ICFVO)

2. Prospectively compare clinical decision making regarding treatment based on multiplanar venography vs. IVUS

Today's Discussion:

3. Assess the presence and significance of associations between venography and IVUS findings and symptom resolution.

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Study Design

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- **Venogram Standardized: (CIV, EIV, CFV)**
  - **Catheter (6Fr sheath) at cranial Femoral V**
  - **20cc half-strength contrast (Opacify Veins)**
  - **Hand injection**
  - **AP, 30^0 RAO and 30^0 LAO views**
- **"Significant Stenosis":**

  <u>Venogram</u>: 50% Diameter reduction

  <u>IVUS</u>: 50% CSA reduction

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Conclusions (AVF 2016)

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- **Primary Endpoint: (CEAP4-6 pts.)**

IVUS vs. Multiplanar Venogram

- IVUS more sensitive for identifying significant ICFVO
- IVUS more accurate for degree of stenosis by CSA or diameter
- IVUS best guide for Stent Intervention

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When to Stent?

- What is the Threshold Degree stenosis which when Stented results in Clinical Improvement in CEAP 4-6 patients?

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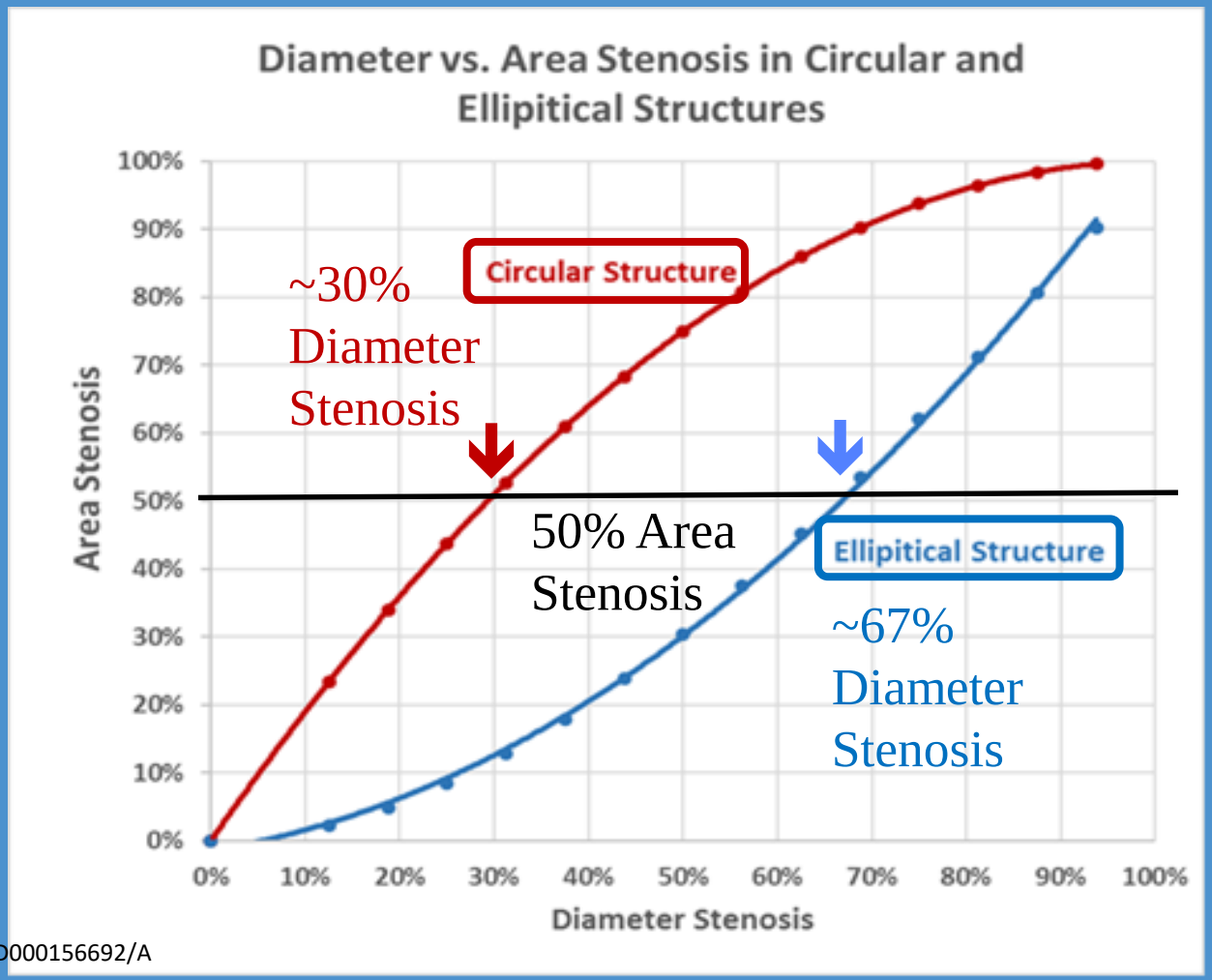
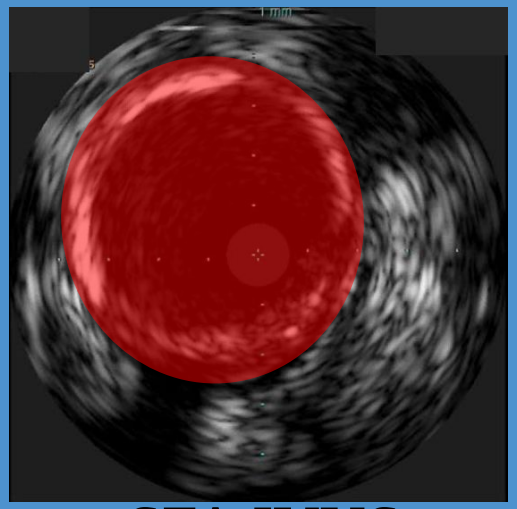
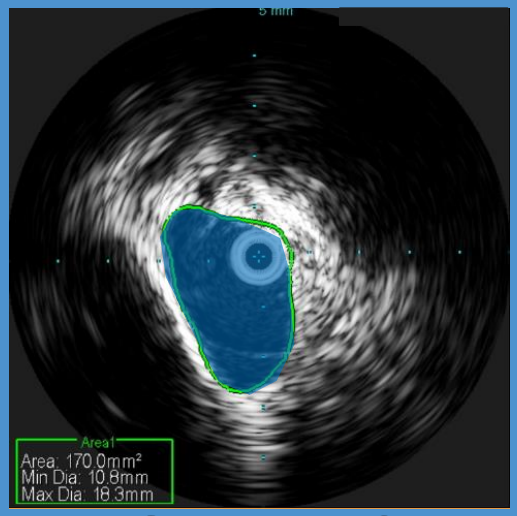
Diameter vs. Area Stenosis Veins vs. Arteries





SFA IVUS



CIV IVUS

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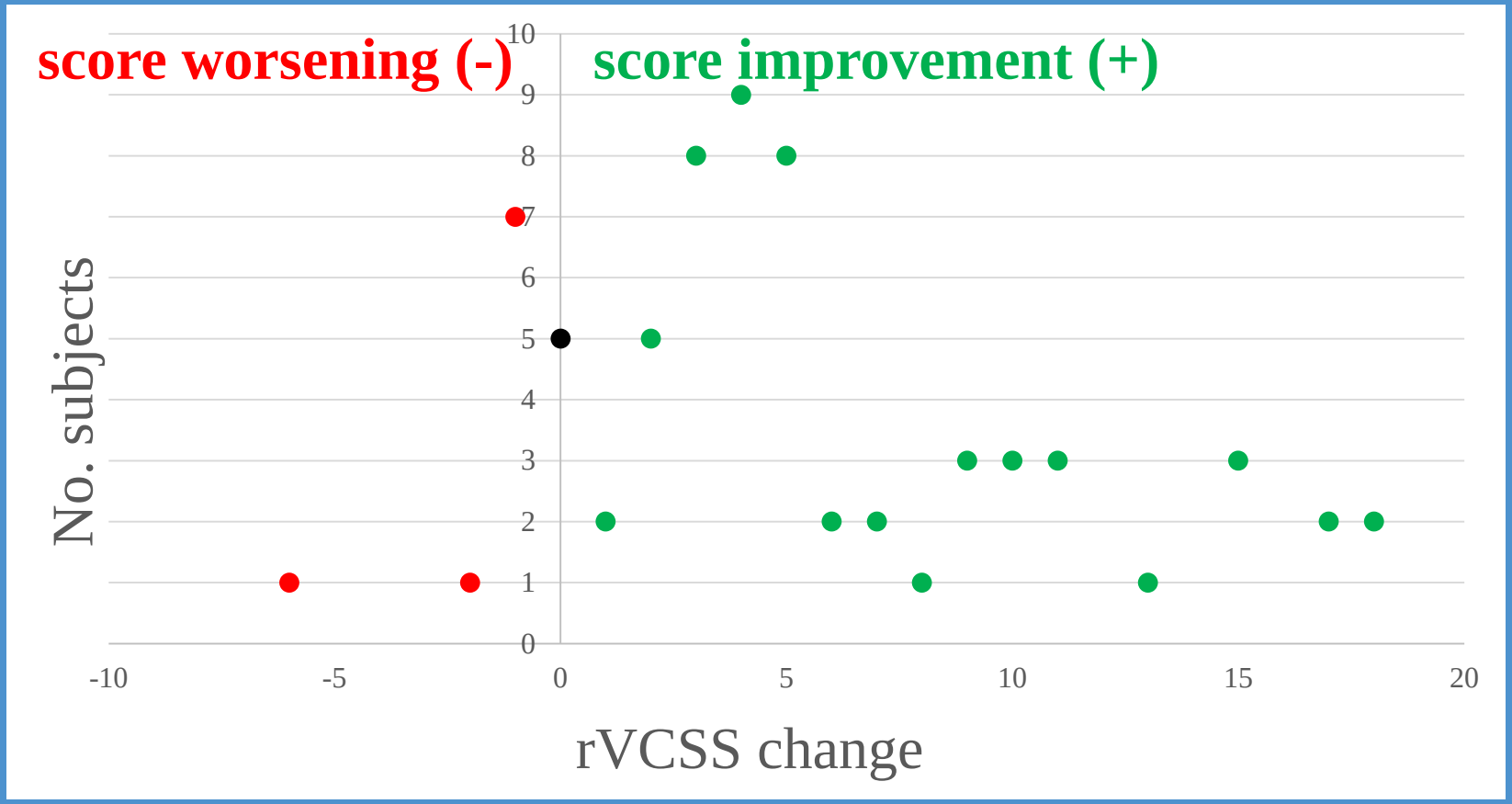
6-month Follow-up Change in revised Venous Clinical Severity Score (rVCSS) after Stenting



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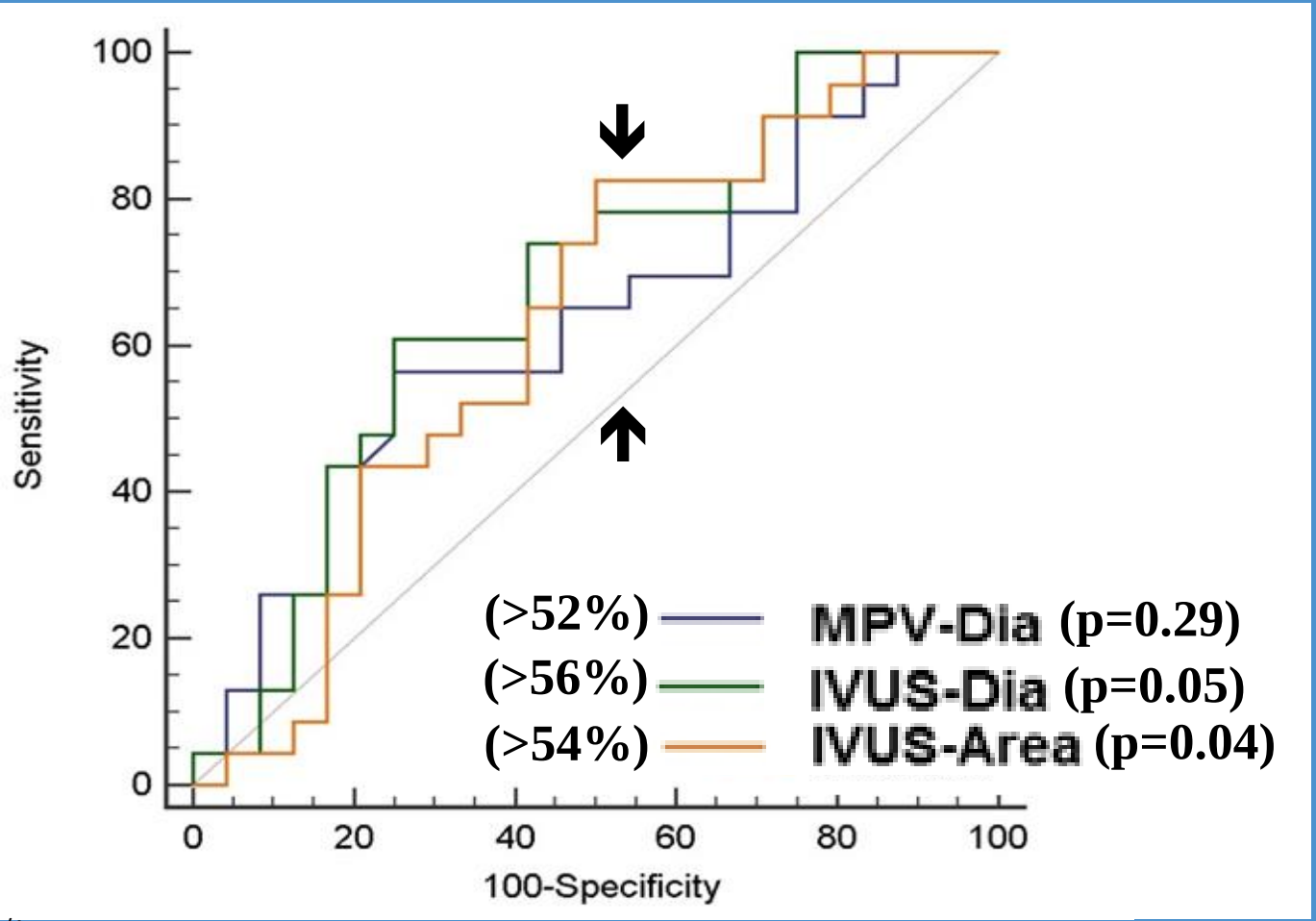
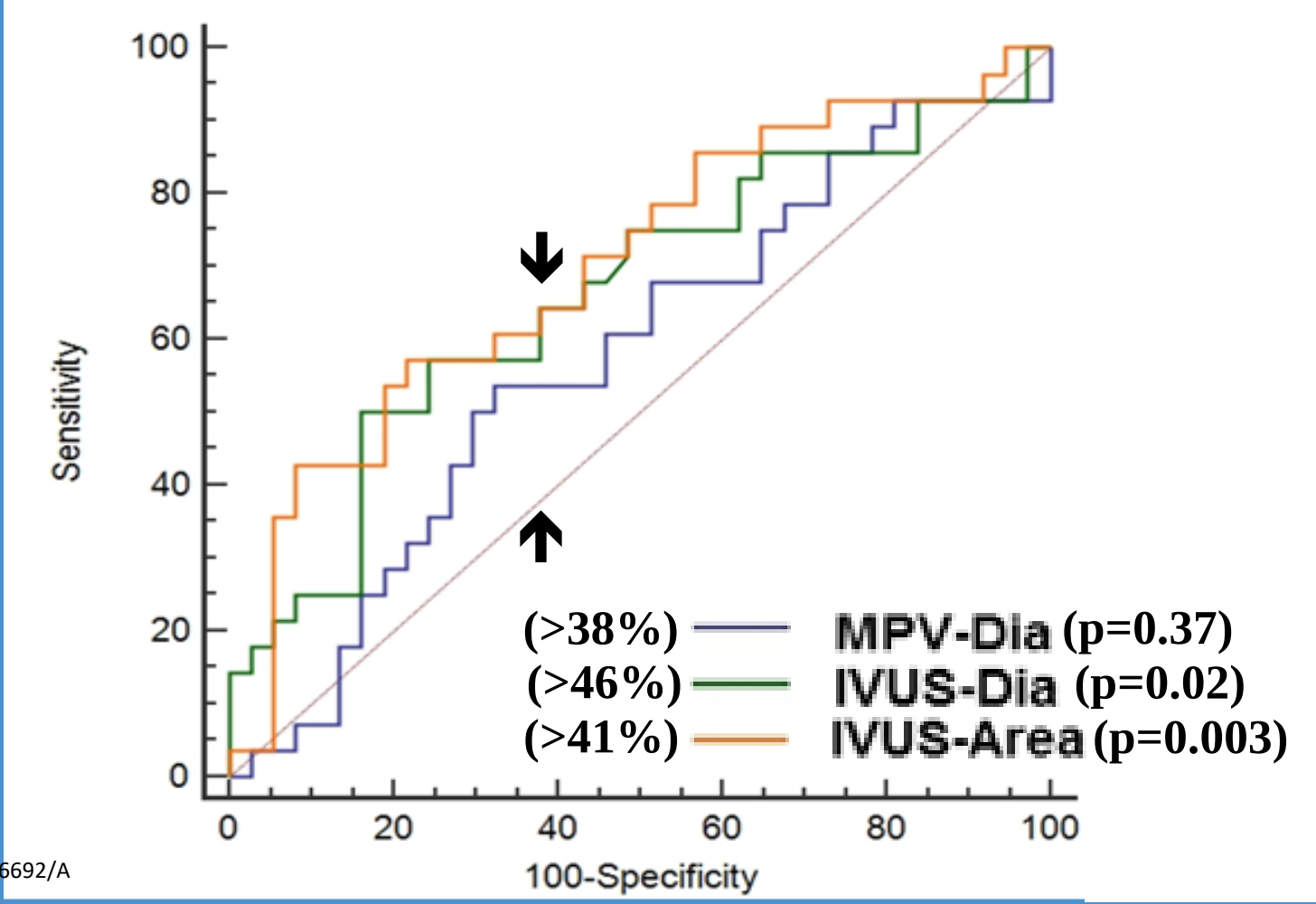
Receiver Operating Curve (ROC) Baseline Stenosis vs. rVCSS @ 6 mos



Receiver Operating Curve (ROC)
Post-Stent Stenosis Reduction vs. rVCSS



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Pre and post-procedural anatomic measurements of stenosis

- Table II: stented population (n=68)

Assessment	*Baseline*	*Post-procedural*
Degree stenosis		
MPV-Dia	46 ± 21%	13 ± 15%
IVUS-Dia	59 ± 15%	25 ± 19%
IVUS-Area	59 ± 17%	28 ± 24%
No. >50% DS		
MPV-Dia	32	
IVUS-Dia[a]	47	
IVUS-Area[a]	49	

[a]1 patient did not undergo IVUS imaging.

Demographics

- 68/100 limbs stented
- 37 males / 31 females
- Mean age 62 ±12 years (Range, 30 – 85 years)
- 48 (71%) non-thrombotic

  20 (29%) post-thrombotic
- CEAP Clinical Class
  - C6 n=36
  - C5 n=8
  - C4A n=22
  - C4B n=2

Demographics

rVCSS assessment at baseline, 30 days, and 6 months, stented population (n = 68)

	Baseline	30 days	P value	Baseline	6 months	P value
rVCSS	14.4 ± 4.6 15 (6, 27)	10.9 ± 5.3 10 (1, 26)	<.001	14.4 ± 4.6 15 (6, 27)	9.2 ± 5.5 8.5 (0, 24)	<.001

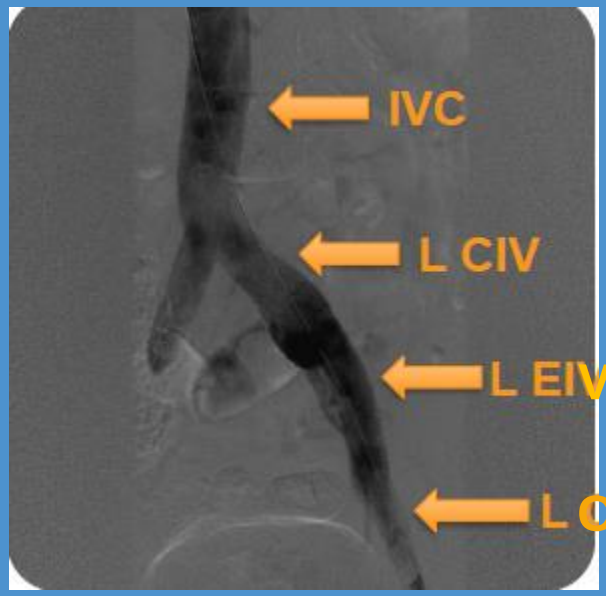
- rVCSS scores are presented as both mean ± standard deviation and median (range).
- A lower score connotes improved health.

Non-Thrombotic vs. Post-Thrombotic Veins

NonThrombotic Outflow Obstruction

Vein Compression

Vein: Normal, Compliant, Large Caliber

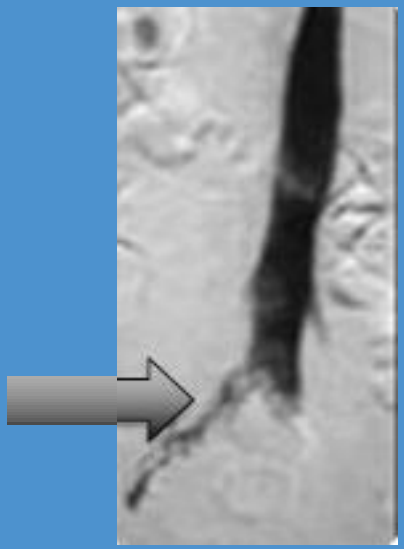


Venous Stenosis In Post Thrombotic Syndrome

Acute DVT recanalizes; Chronic stenosis in venous outflow tract remains

Vein: Small, Sclerotic, Dense Scar

Chronic CIV Stenosis

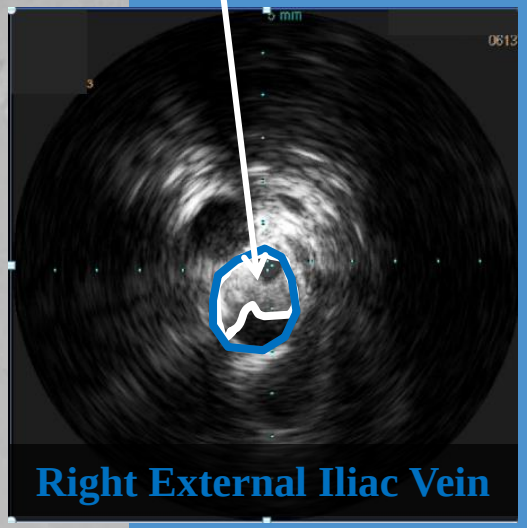


Chronic EIV Stenosis

VIDIO Non-Thrombotic vs. Post-Thrombotic Vein

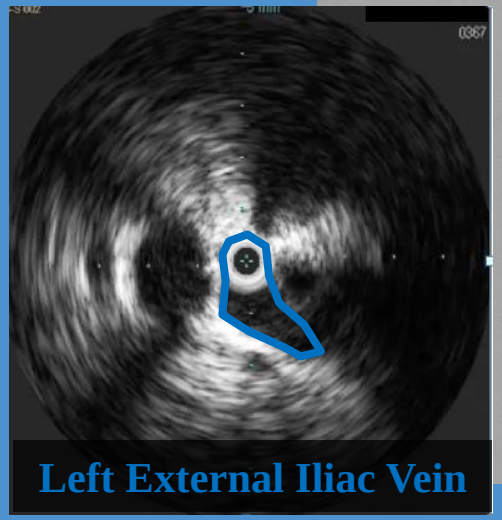
Post-Thrombotic

Chronic thrombus/ scar tissue



Non-Thrombotic

Compression between Lumbo-sacral spine and Left external iliac artery



PTS CASE IMAGES PROVIDED BY Grzegorz Oszkinis, MD and Lukas Dzieciuchowicz, MD

NIVL CASE IMAGES PROVIDED BY Winsor Ting, MD

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Non-thrombotic Subset (N=48)

- Of the 68 stented subjects, 48 were classified with non-thrombotic stenosis.
- Non-thrombotic lesions considered significantly more:
  - Stenotic (*P* = .03)
  - Eccentric (*P* = .005)

Non-thrombotic Subset (N=48)

- IVUS baseline diameter measurements of stenosis:
  - Significant and better predictor of future improvement in clinical symptoms (*P* = .03) than area stenosis.
  - Estimated a higher threshold of baseline stenosis to justify stenting (>61%, Youden Index 0.36).
- With measurements of Post-intervention stenotic change:
  - All three modalities were determined to be significant predictors of later clinical improvement.
    - MPV, *P* = .05
    - IVUS-diameter and IVUS-area, *P* = .001

Conclusions

- >50% MPV Diameter stenosis best predicts clinical improvement.
- Intervention for 50% MPV Diameter stenosis poor correlation w/ rVCSS improvement.
- Baseline stenosis measurements obtained with IVUS were demonstrated to be significant predictors of 6-month patient improvement in rVCSS.
  - IVUS Diameter, *P* = .05
  - IVUS Area, *P* = .04
  - Venographic baseline measurements were a less reliable predictor of improved rVCSS at 6 months. (*P* = .29)

Conclusions

- >50% IVUS Area & Diameter stenosis Significantly predicts Clinical Improvement after Stent (rVCSS improved >4)
- Nonthrombotic IVUS Diameter >61% best predicts Clinical improvement after Stent
- Stenosis Reduction (i.e. Lumen Gain) may be better predictor of clinical improvement
- **Further prospective studies needed to identify best thresholds for stenting CEAP 4-6 with Iliofemoral vein thrombosis**

Thanks for Your Attention

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Is Venography Alone Adequate to Evaluate the Deep Veins?

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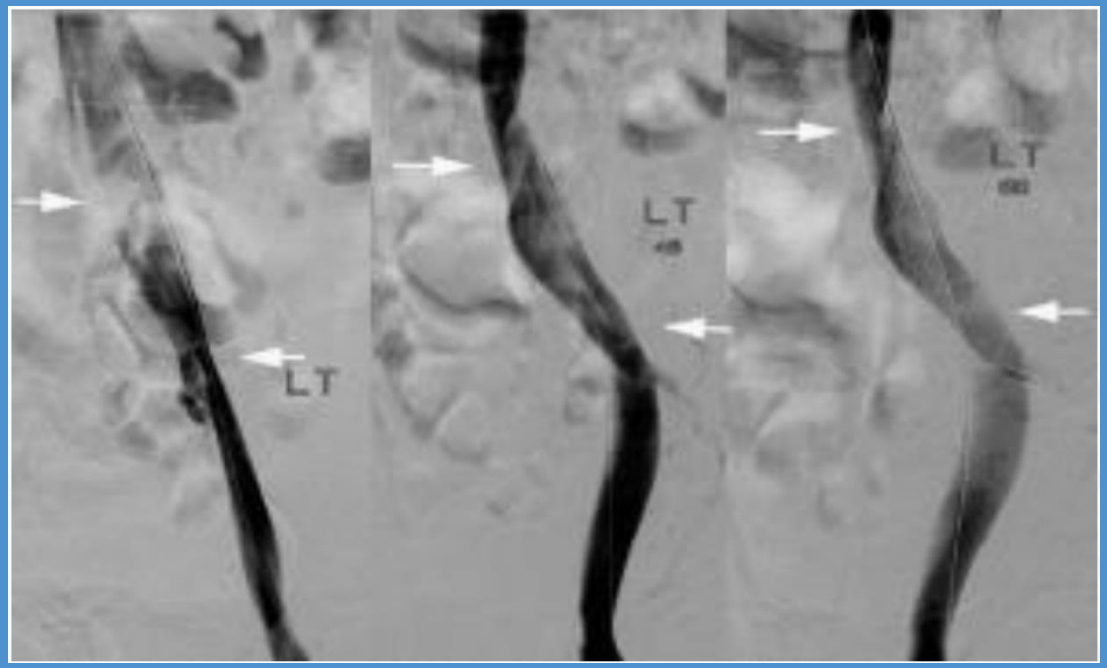
VENOGRAM vs. IVUS FOR DIAGNOSING ILIAC VEIN OBSTRUCTION

"We develop strategies to compensate for the shortcomings of venography and convince ourselves it's adequate."
– Peter Neglén, MD, Ph.D.

- Venogram **poor diagnostic sensitivity**[1]
- 34% of pts. w/ chronic venous symptoms had iliac vein obstruction and normal venogram[2]
- **Collaterals**, 43% of limbs that were stented[3]



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3. 3. Raju S, Darcey, Neglén P. Unexpected major role for venous stenting in deep reflux disease. J Vasc Surg 2010;51:401-9.

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Baseline Clinical Characteristics

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Characteristic	N = 100
Gender (female:male)	43:56
Index leg (left:right)	63:37
Age (mean ± SD, range)	62 ± 12 (30 – 85)
Race (Caucasian)	86 %
BMI (kg/m^2)	33.6 ± 7.5
CEAP	N
0-3	0 (by protocol)
4a	33
4b	2
5	15
6	50

Baseline Imaging:
Venogram and IVUS (Site-Reported)

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Venogram and IVUS Findings	Veins Segment*	Percent of Lesions
Total Segments Assessed	**300**	**100.0%**
Lesion on IVUS but not Venogram	63	21.0%
Lesion on Venogram but not IVUS	5	1.7%
Lesion on both Venogram and IVUS	62	20.7%
No appreciable stenosis, Venogram or IVUS	170	56.7%

**Common Iliac, External Iliac, and Common Femoral veins*

IVUS more sensitive for ICFVO Stenosis vs. Venogram

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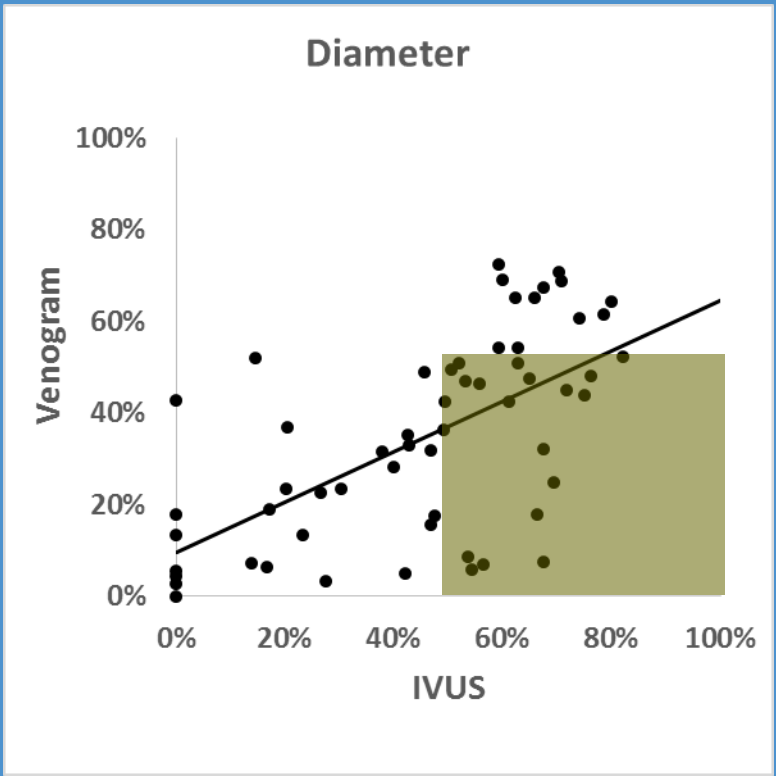
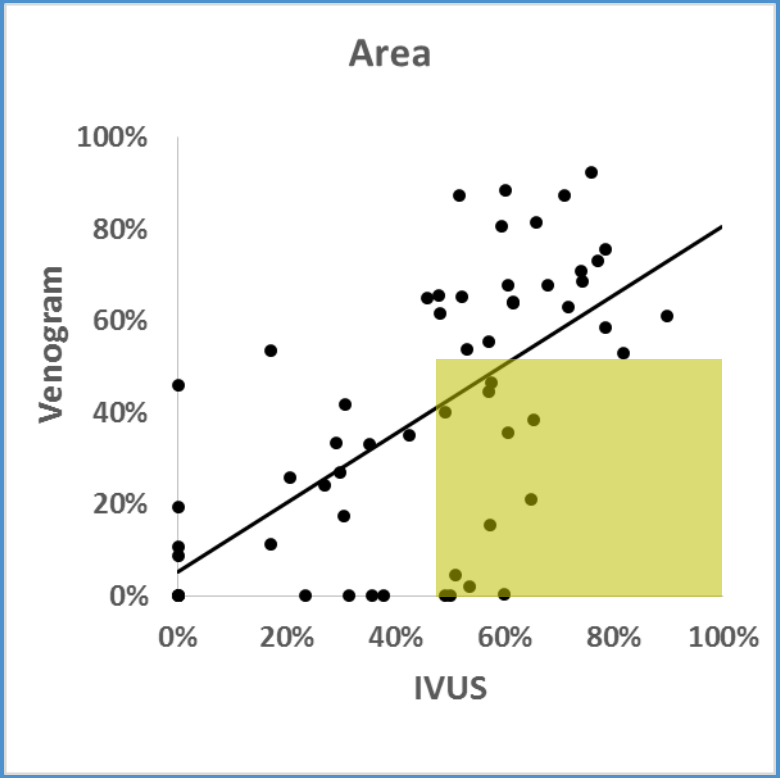
IVUS vs. Venogram:
Diameter (Core Laboratory)



- Multiplanar Venography underestimates the degree of diameter stenosis compared to IVUS.
- Venogram missed 26% of >50% diameter-reduction lesions
- IVUS determined stenoses, in general, were 10.9% more severe (mean) than by Venogram (P < .001)

IVUS vs. Venogram:
Area (Core Laboratory)



- Surprisingly, multiplanar venography correlate with assessment of area reduction / stenosis by IVUS
- 17.7% of significant CSA lesions (defined by >50% area reduction) were missed even with 3 view venograms

Shortcoming of 2-D Imaging

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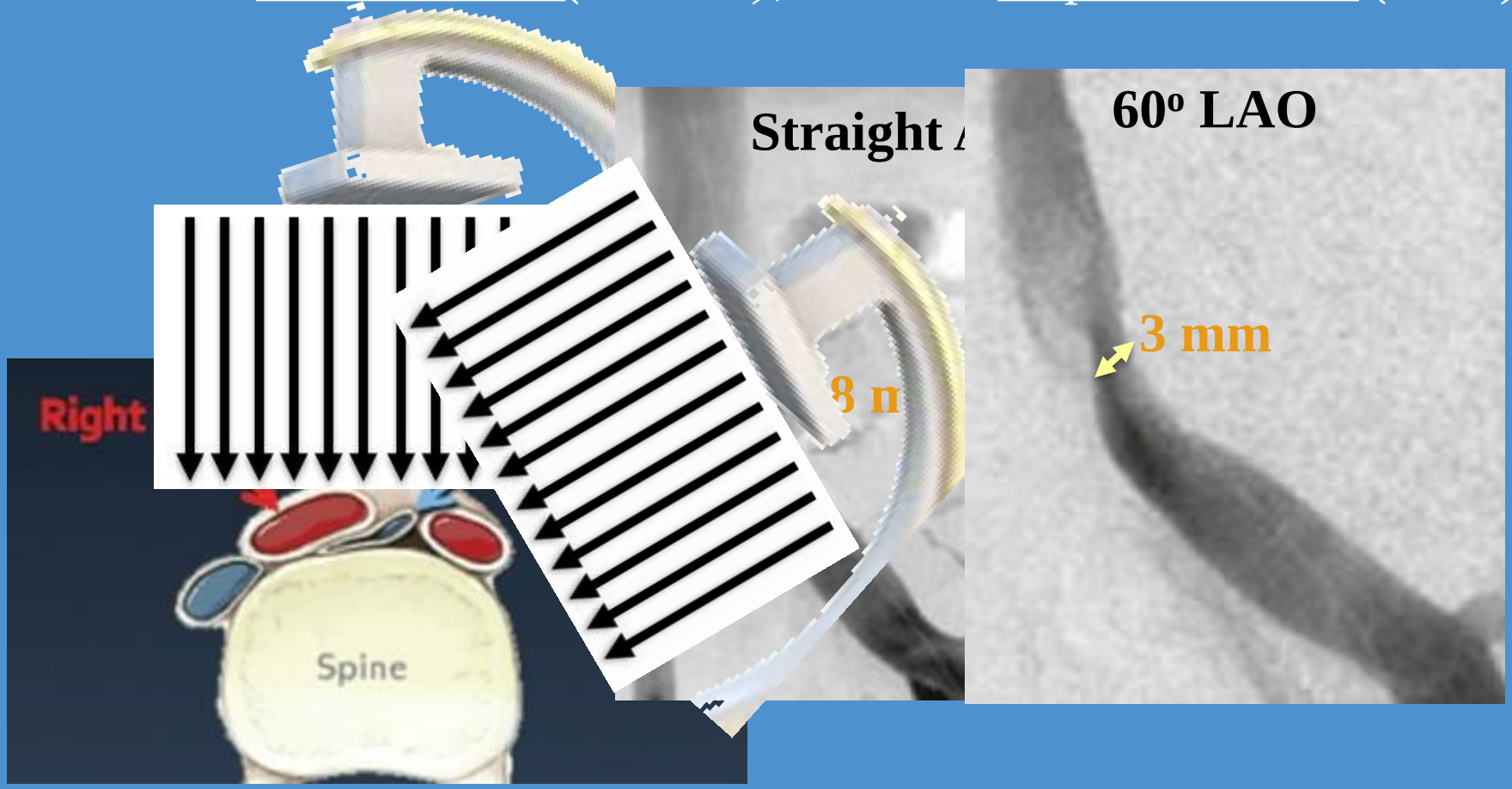
VENOGRAM vs. IVUS FOR DIAGNOSING ILIAC VEIN OBSTRUCTION

Great for *round vessels (arteries)*; Poor for *elliptical vessels (veins)*



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Procedure Decision Making

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Site Investigator:

- Venogram vs. IVUS -> Stent?
- 60/100 (60%) pts., Decision To Stent Changed due to IVUS
- n=50 pts., Stent Number, Increased (0->1 stent or 1->2 stents) due to IVUS
- **Without IVUS, undertreat ICFVO!**

Patient Quality of Life: SF-36

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VENOGRAM vs. IVUS FOR DIAGNOSING ILIAC VEIN OBSTRUCTION

Time Point	Physical Function	Physical Health	Emotional Limitations	Energy / Fatigue	Emotional Well-Being	Social Function	Pain	General Health
Baseline								
Stented	51 ±27	48 ±27	72 ±28	52 ±22	72 ±18	68 ±25	48 ±22	56 ±19
Non-Stented	59 ±28	59 ±27	75 ±28	59 ±22	78 ±17	75 ±23	59 ±25	62 ±16
P Value, Stent vs. No stent	.605	.761	.482	.845	.446	.301	.456	.545
Change: Baseline to 1 month								
Stented	8 ±23	11 ±30	2 ±25	7 ±25	5 ±19	7 ±22	10 ±25	7 ±15
P Value, Stented Subjects	**.006**	**.003**	.505	**.026**	**.024**	**.015**	**.002**	**<.001**
Non-Stented	0 ±22	5 ±23	6 ±25	1 ±17	-2 ±15	8 ±21	3 ±18	6 ±12
P Value, No Stent	.947	.246	.197	.826	.476	.053	.478	**.021**
Change: Baseline to 6 months								
Stented	9 ±19	14 ±30	7 ±31	9 ±21	5 ±15	10 ±22	12 ±25	9 ±17
P Value, Stented Subjects	**<.001**	**.001**	.093	**.001**	**.005**	**.001**	**<.001**	**<.001**
Non-Stented	-1 ±14	7 ±23	8 ±34	3 ±15	0 ±16	12 ±27	2 ±23	6 ±15
P Value, No Stent	.684	.105	.201	.264	.927	**.027**	.587	**.035**

- **QoL improvement was greater in stented patients than non-stented patients.**
- **Improvement in Stented Patients persisted and was statistically greater at 6 months**

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Ulcer Size:
Stented vs. Non-stented Subjects

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Time Point	Mean in Stented Subjects (N = 36)	Mean in Non-Stented Subjects (N=14)
Subjects	36 (72%)	14 (28%)
Baseline	34.6 cm^2	20.5 cm^2
1 month	26.0 cm^2	12.2 cm^2
6 months	27.5 cm^2	18.4 cm^2
Baseline vs. 1 month	**P = .002**	**P = .021**
Baseline vs. 6 months	**P = .017**	P = .055
1 Month vs. 6 months	P = .855	P = .202

Wilcoxon Signed Ranks Test

Ulcer Size: Non Stented > Stented @ 6 mos.
Compared to Baseline size
Ulcer Recurring at 6 mos.?

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Conclusions

- Secondary Endpoints (CEAP4-6 pts.)
  - QOL / SF-36 markedly improve when stent ICFVO
  - Relation between ICFVO, Stenting & Ulcer healing unclear!
- More Work to be Done!!!!
- IVUS: Gold Standard for diagnosing & directing treatment of ICFVO; the basis for future trial and research imaging

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Sample Case

Multiplanar Venography

VIDIO Case

VENOGRAM vs. IVUS FOR DIAGNOSING ILIAC VEIN OBSTRUCTION

Demographics

84 y/o male patient

BMI = 25.8

History

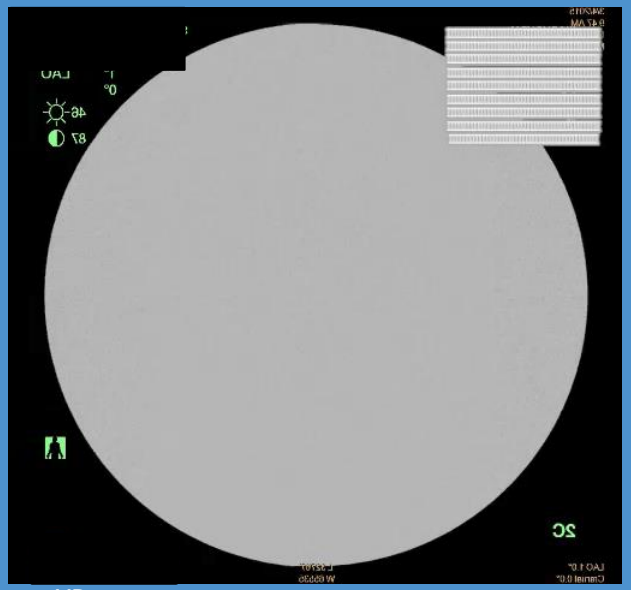
Non- Contributory

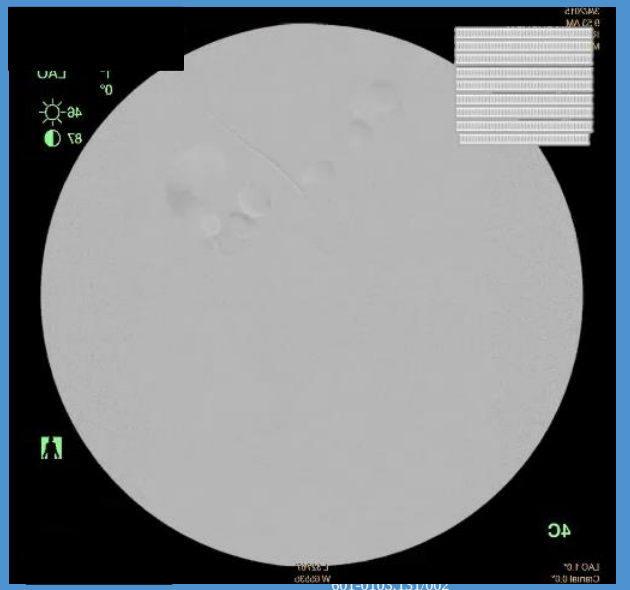
Physical Exam

Study Leg: Left

CEAP C6: 10 x 14 mm Ulcer, present for > 12mos

Diagnostic Venography: AP Views





Case details, images, and footage courtesy of Paul Gagne, MD.

Multiplanar Venography

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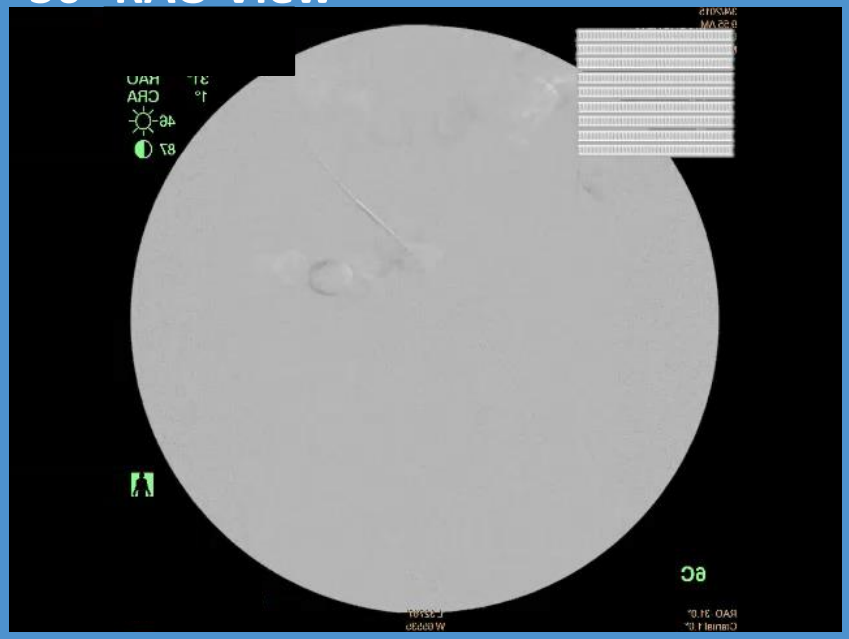
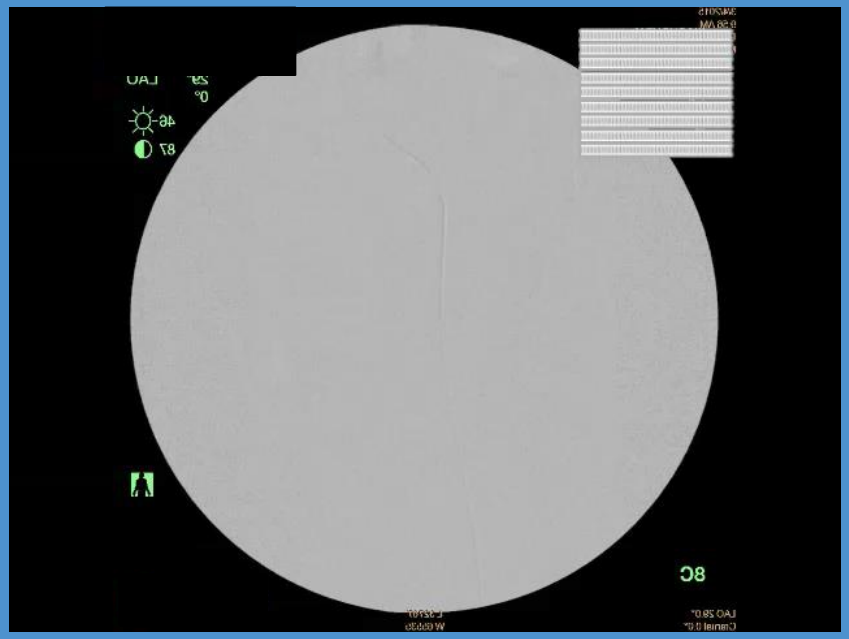
30º RAO View



30º LAO View



Case details, images, and footage courtesy of Paul Gagne, MD.

Intravascular Ultrasound

VIDIO Case

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Diagnosis:

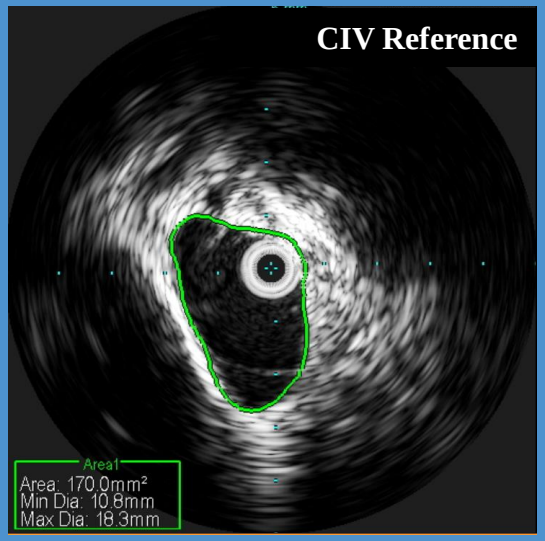
Non-Thrombotic Iliac Vein Lesions (NIVL) x2

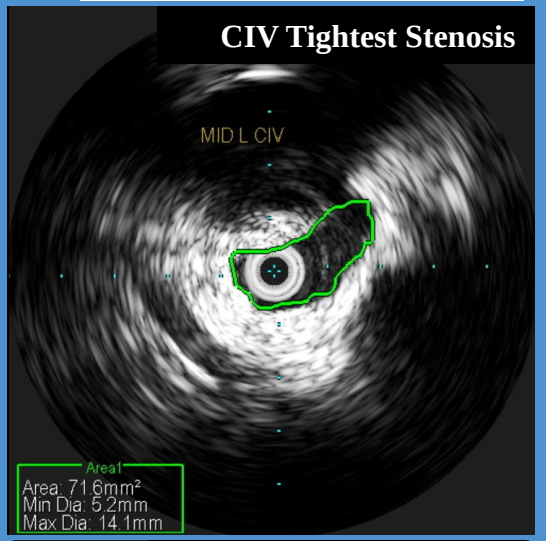
Common Iliac Vein

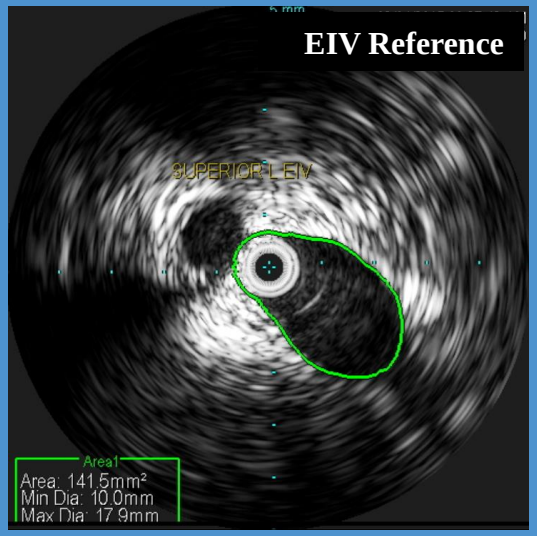
- 58% Cross-Sectional Area Reduction
- Tightest Stenosed Area of 72mm²

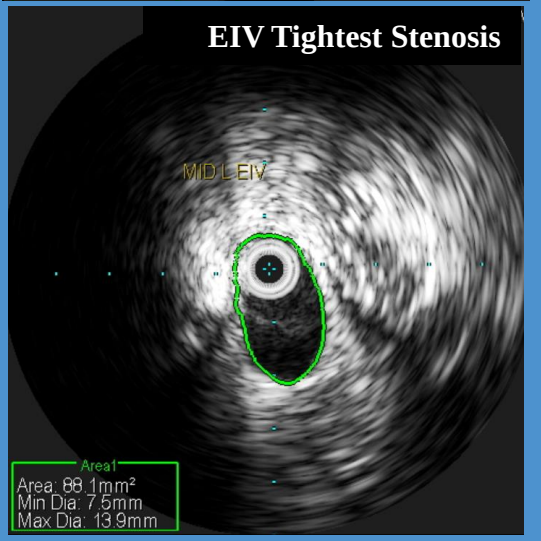
External Iliac Vein

- 38% Cross-Sectional Area Reduction
- Tightest Stenosed Area of 88mm²









601-0103.131/002

Venous Clinical Severity Score (rVCSS): *By Ulcer and By Stent*

VIDIO
VENOGRAM vs. IVUS FOR DIAGNOSING ILIAC VEIN OBSTRUCTION

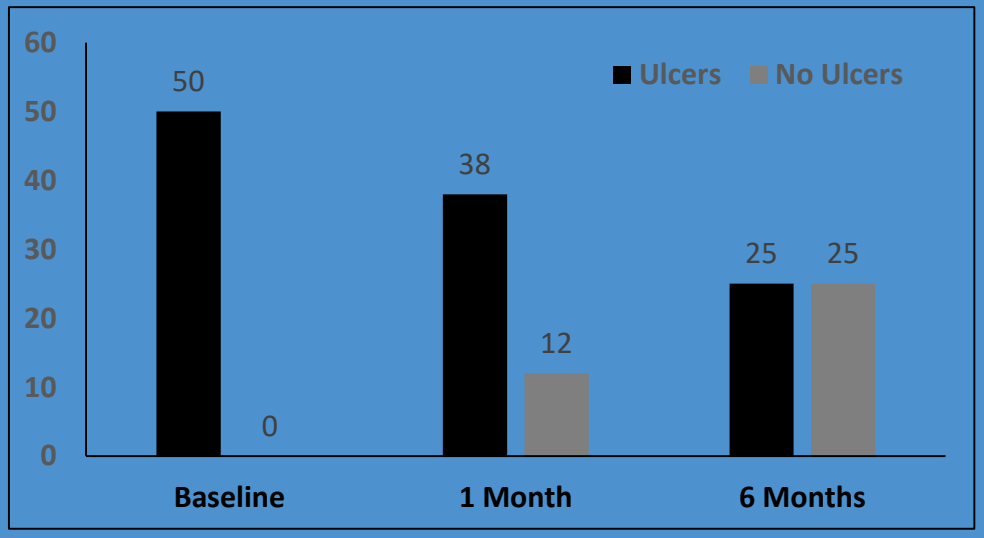
Time Point	No Ulcer (N = 50)		Ulcer (N = 50)	
	Stent (32)	No Stent (18)	Stent (36)	No Stent(14)
Baseline	11.0 ± 2.8	11.5 ± 2.5	17.4± 3.6	19.7 ± 4.0
1 month	7.1 ± 2.7	8.2 ± 4.6	13.6 ± 5.7	13.2 ± 8.4
6 months	7.3 ± 3.4	7.4 ± 4.4	10.9 ± 6.4	11.5 ± 5.5
Baseline vs. 1 month	**P < .001**	**P = .008**	**P < .001**	**P = .008**
Baseline vs. 6 months	**P < .001**	**P = .004**	**P < .001**	**P < .001**
1 Month vs. 6 months	P = .757	P = .336	**P = .001**	P = .537

No Ulcer / Ulcer No Stent: Pt. VCSS improve by 1 mos.
Ulcer Stent: Pt. w/ continuous improvement 1->6 mos.

Ulcer Size (N=50 at Baseline)

VIDIO
VENOGRAM vs. IVUS FOR DIAGNOSING ILIAC VEIN OBSTRUCTION

Time Point	Mean
Baseline	30.7 cm^2
1 month	22.6 cm^2
6 months	24.9 cm^2
Baseline vs. 1 month	**P < .001**
Baseline vs. 6 months	**P = .003**
1 Month vs. 6 months	P = .649



- Median size of the ulcers decreased from 30.7 cm^2 at baselined to 22.6 cm^2 at 1 mos.
- The decrease in ulcer size was statistically significant.
- 24% of ulcers healed at 1 mos.
- 50% were healed at 6 mos.

The Vascular Experts
Southern Connecticut Vascular Center