

Glue for the Treatment of Varicose Veins



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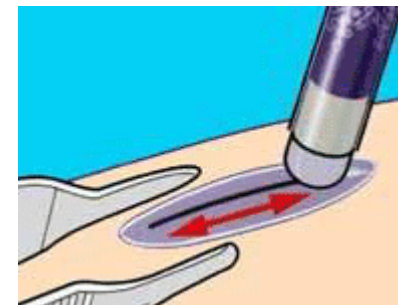
CAN IMPROVEMENTS BE MADE TO THERMAL ABLATION?

- Eliminate need for tumescent anesthesia
- Eliminate need for compression stockings
- Significantly reduce post-procedure pain and bruising

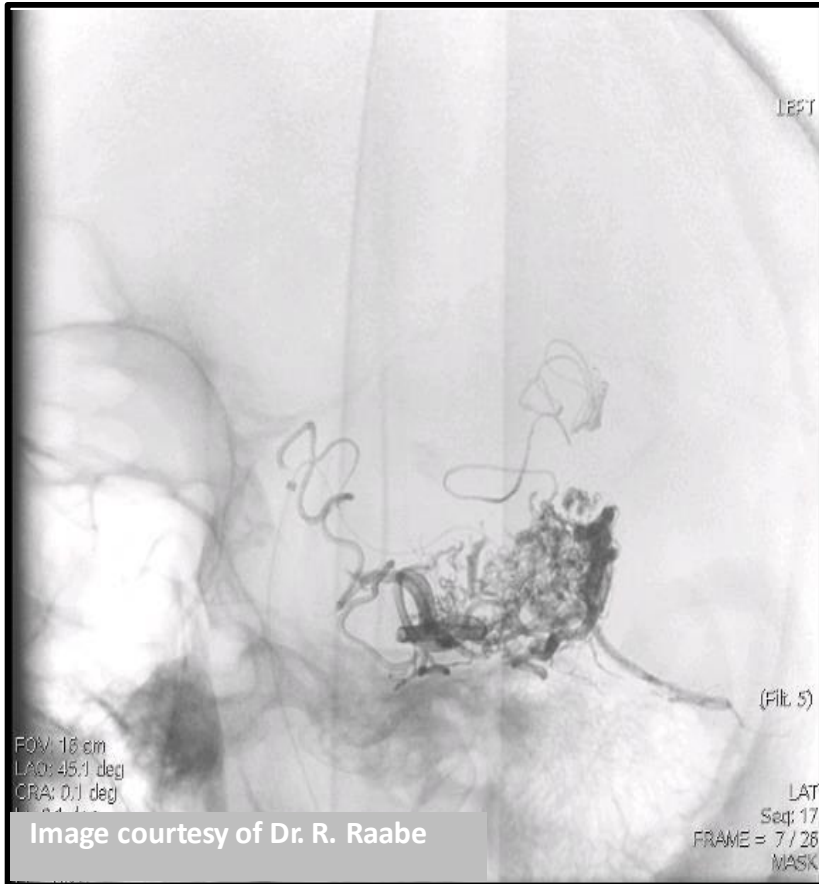


Rod Raabe, MD

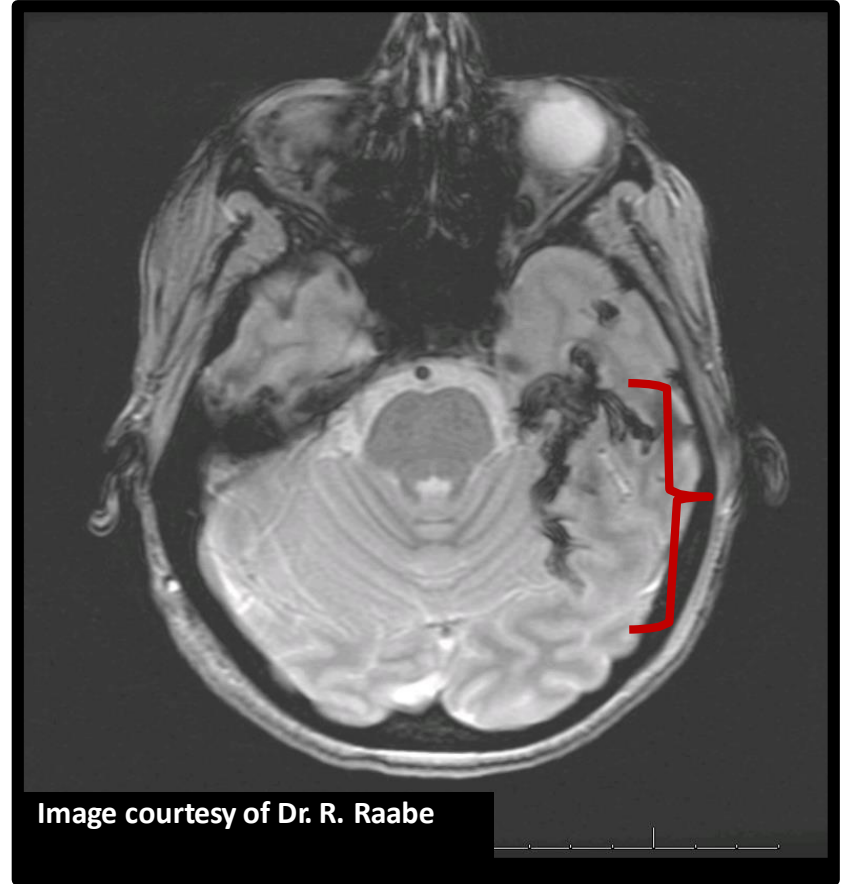




CYANOACRYLATE USE: OCCLUSION

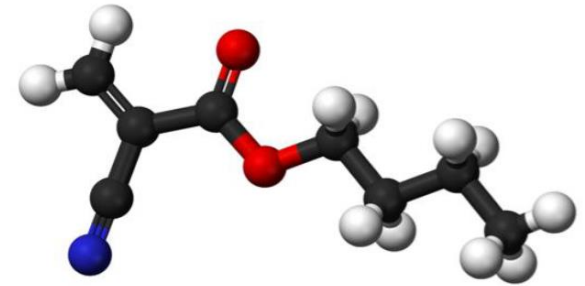


Adhesive cast in AVM delivered via micro catheter



Adhesive cast in AVM delivered via micro catheter

ADHESIVES IN MEDICINE¹



	Date	Use
Cyanoacrylate Adhesives₂	1950s	Wound adhesives
Histoacryl Blue™ *	1980s	Skin incisions
Dermabond™ *	1998	Skin incisions/lacerations
Ethicon OMNEX™ *	1998	Surgical adhesives
Trufill™ *	2000	Liquid Embolic System, AVM embolization
Indermil™ *	2002	Skin incisions/lacerations

¹Not a complete list. 2. Pollak J, White R. The use of cyanoacrylate adhesives in peripheral embolization. J Vasc Interv Radiol 2001; 12:907-913 p.908

CYANOACRYLATE USE: OCCLUSION

- Vascular closing agent for
 - Cerebral Arteriovenous malformations (AVM)
 - Pelvic congestion syndrome and Varicoceles
 - Gastric varices
 - Aortic aneurysms

CYANOACRYLATE POLYMERIZATION STRUCTURE

Proprietary Formulation



Microscopic view of the polymerized adhesive



Proprietary formulation of advanced medical cyanoacrylate-based adhesive designed to coapt and close the vein

FIBROTIC CELLULAR GROWTH ACROSS THE LUMEN RESULTING IN PERMANENT OCCLUSION. FOREIGN BODY REACTION

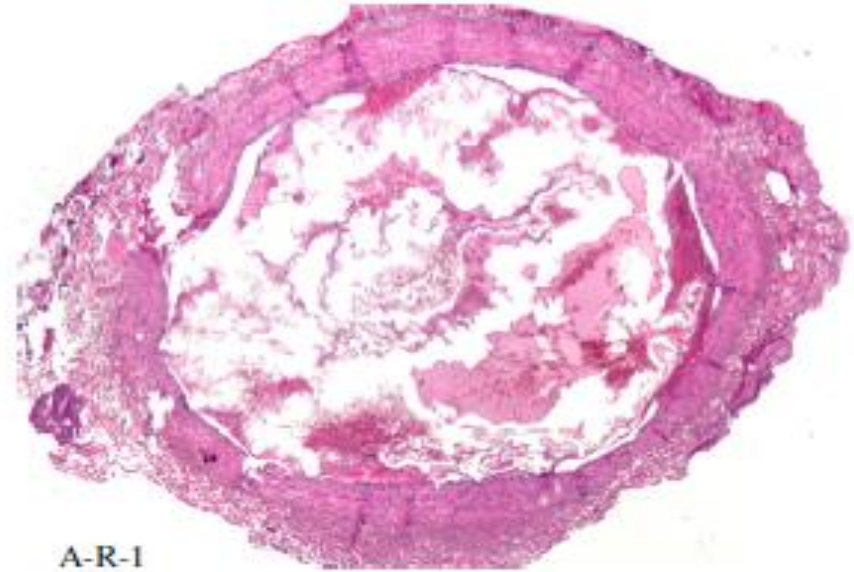
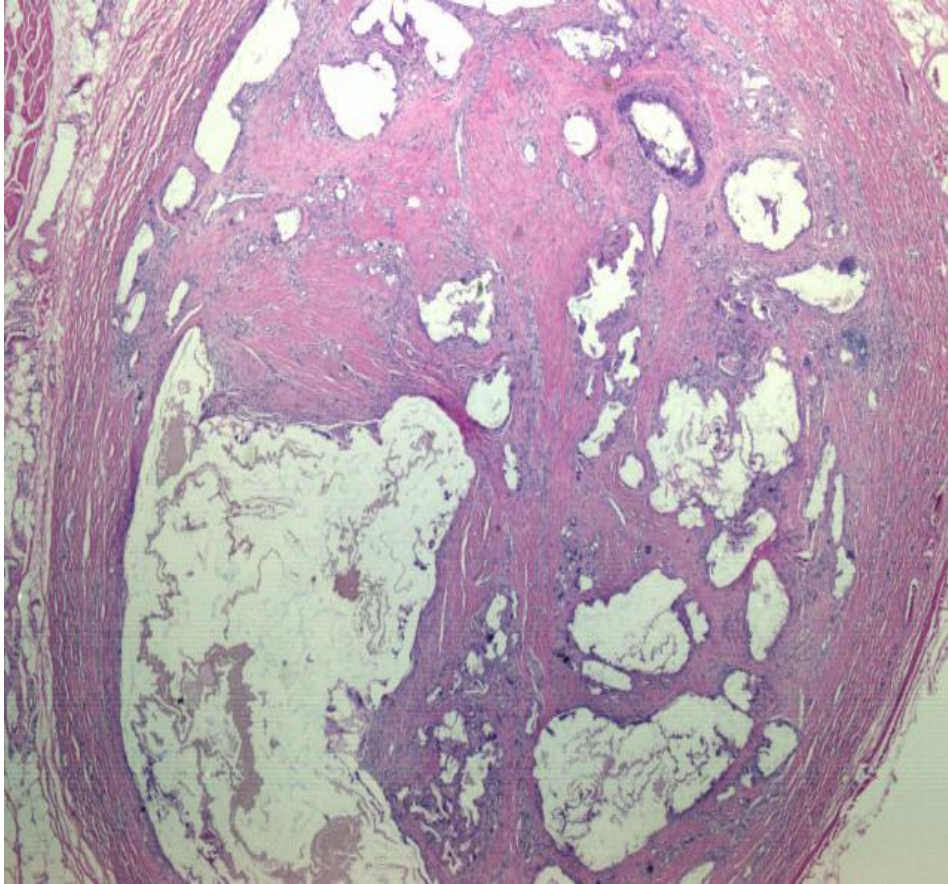
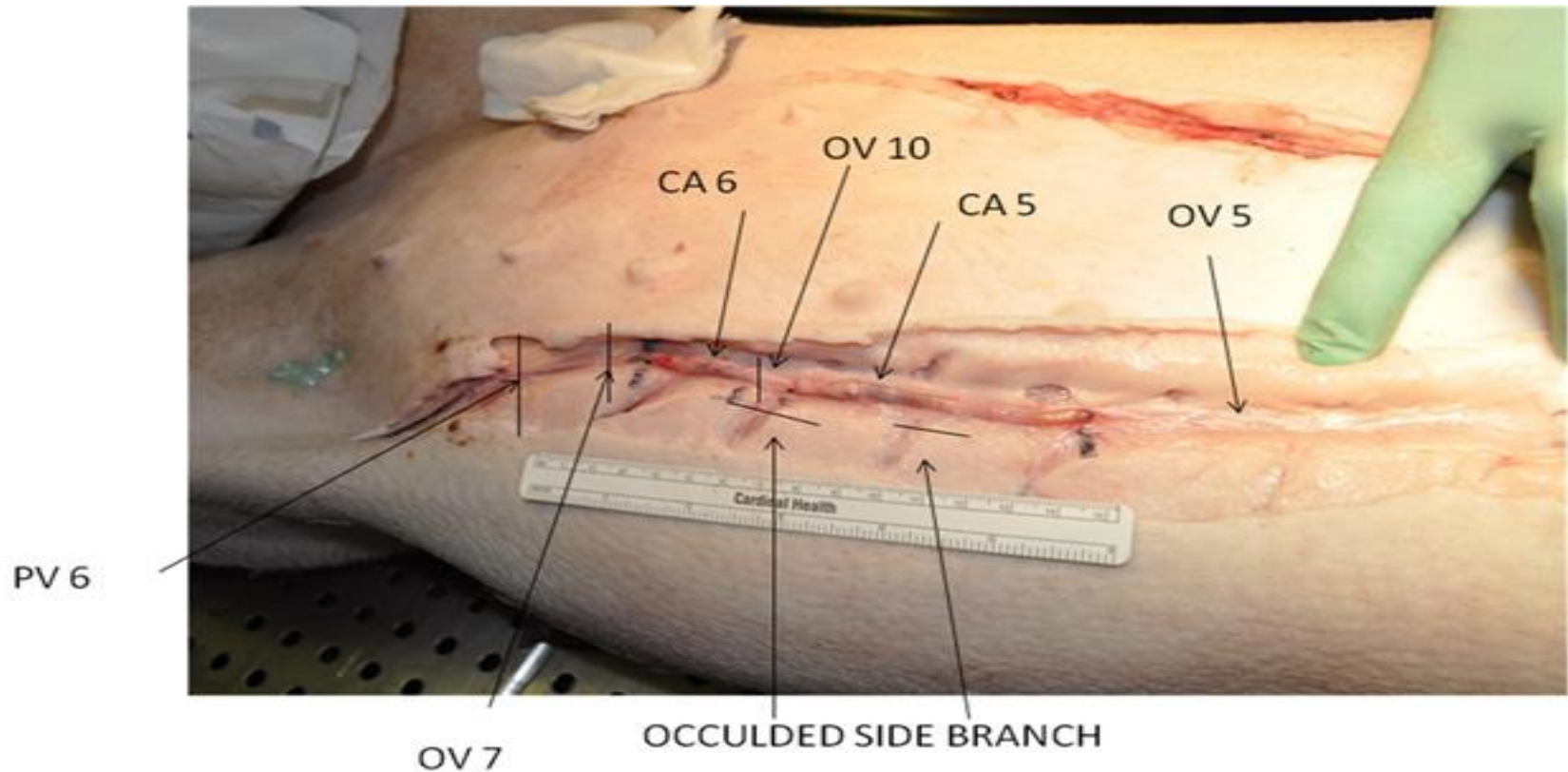


Image courtesy of Dr. R. Raabe

INITIAL ANIMAL EXPERIMENT COMPLETED

6-25-09



Positive Study Objective: Complete Vein Closure in all tests 3/3

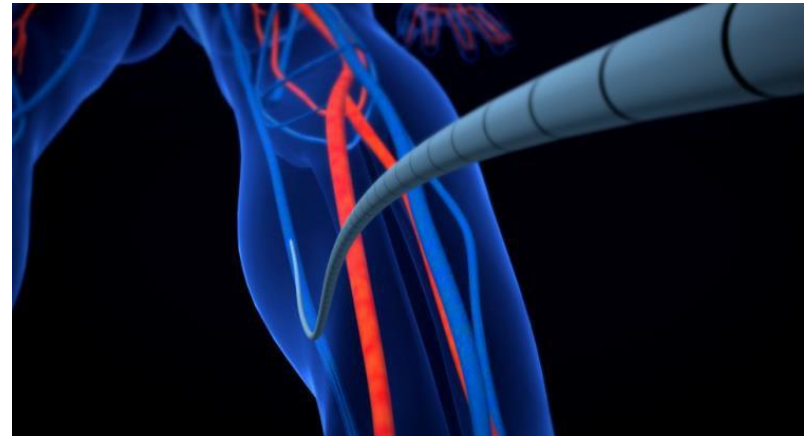
Venoseal (Cyanoacrylate Glue)



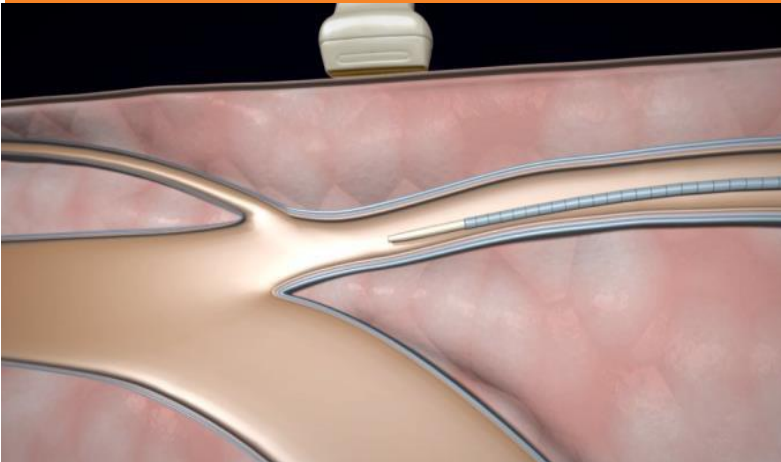
VENASEAL™ CLOSURE SYSTEM: *PROCEDURE*



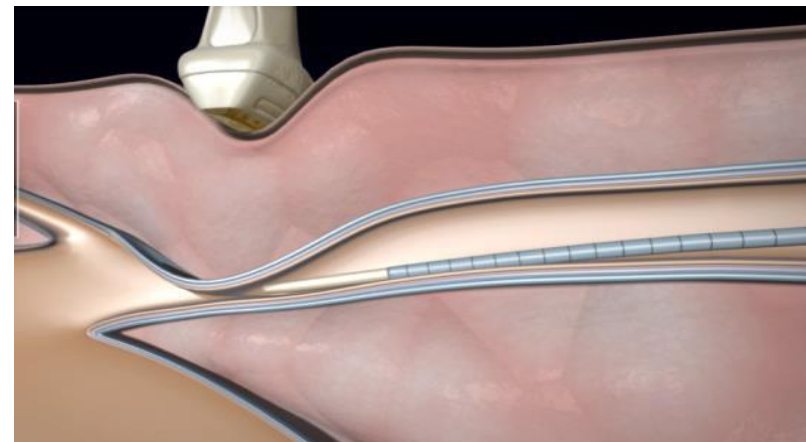
VenaSeal™ Closure System



Access GSV using catheter technique

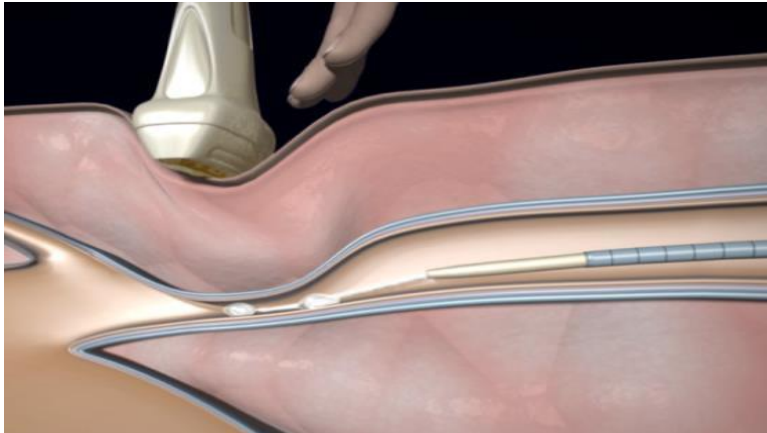


Position catheter 5 cm from SFJ

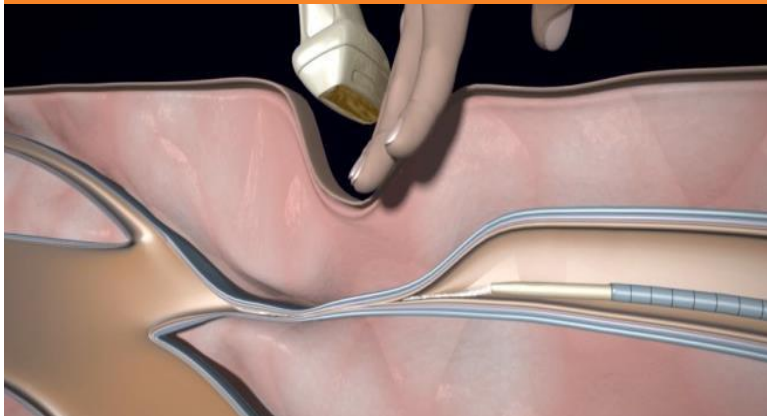


Compress cephalad to catheter

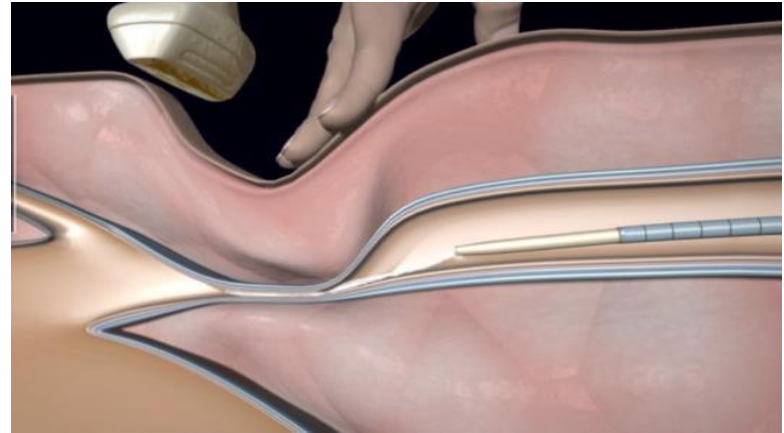
VENASEAL™ CLOSURE SYSTEM: *PROCEDURE*



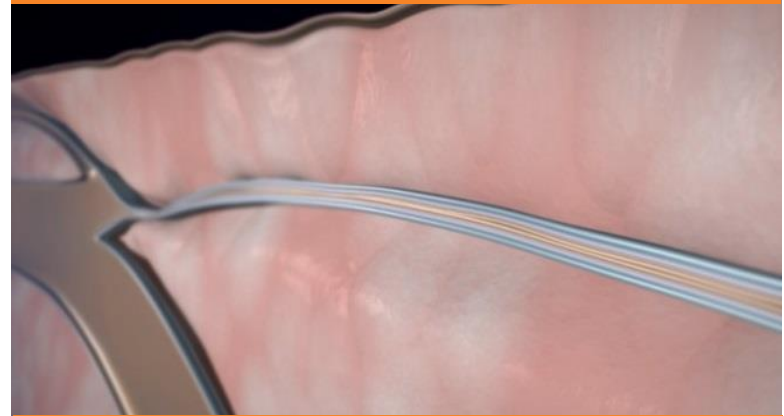
Inject 0.10 cc adhesive into the vein, pull back 1 cm, inject 0.10 cc pull back 3 cm



Inject 0.10 cc, pull back 3 cm, compress for 30 seconds



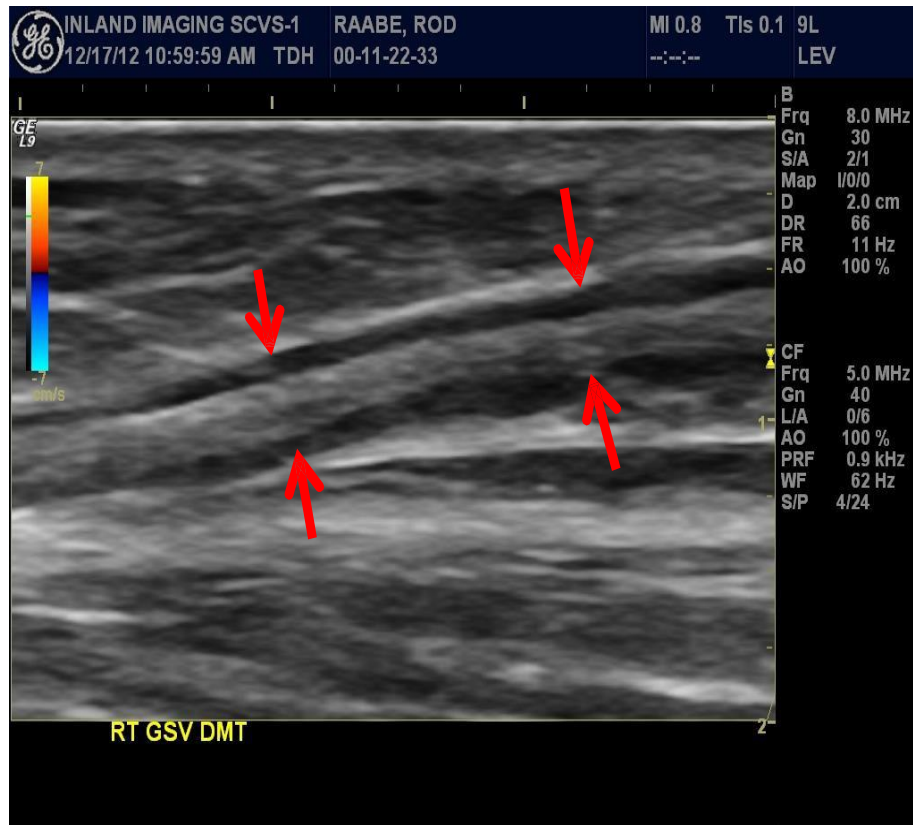
Compress 3 minutes



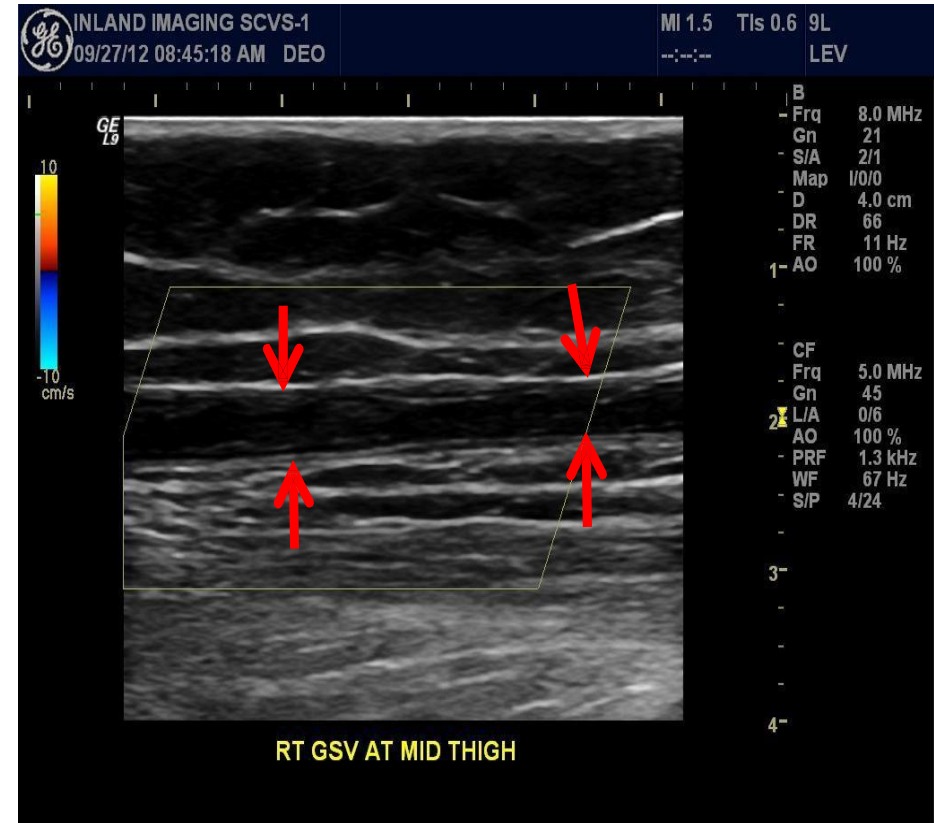
Repeat process throughout vein

ULTRASOUND IMAGES 8 WEEKS POST TREATMENT

VenaSeal™ Procedure Closure



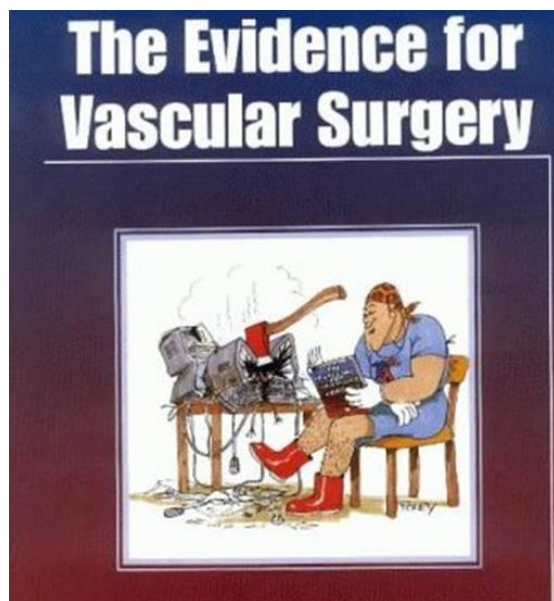
RFA Procedure Closure



Images courtesy of Dr. R. Raabe



Let's Look at the Evidence



Clinical Studies with the VenaSeal™ System

Feasibility Study

- 38 Patients, enrollment completed Aug. 2011
- 1 day, 1, 3, 6, 12, 24 and 36 month follow-ups
- Primary endpoint: Safety: rate of serious adverse events, Efficacy: vein closure during follow-up

eSCOPE

(European multicenter study)

- 70 patients, enrollment completed Sept. 2012
- 2 day, 1, 3, 6, 12, 24 and 36 month follow-ups
- Primary endpoint: closure w/o use of sedation, tumescent anesthesia or compression stockings

VeClose

(U.S. pivotal trial)

- 242 patients, enrollment completed Sept. 2013
- 3 day, 1, 3, 6, 12, 24 and 36 month follow-ups
- Primary endpoint: non-inferior to RFA in GSV closure
- Secondary endpoint: superiority in reduction of post procedural pain and bruising

VeClose (*U.S. pivotal trial*)

Primary Endpoint

- Duplex ultrasound determined **closure** of the GSV, non-inferiority of VenaSeal™ closure system to ClosureFast™ (RFA)

Secondary Endpoints

- Intraoperative **pain**, rated on a 0-10 numeric rating scale
- **Ecchymosis** at day 3, rated on a 0-5 ordinal scale
- **Adverse events** at 1 month

Follow-up occurred at

- Day 3, and
- 1, 6 and 12 months post-procedure

No adjunctive therapy before 3 months

Morrison N, et al. Randomized trial comparing cyanoacrylate embolization and radiofrequency ablation for incompetent great saphenous veins (VeClose). Journal of vascular surgery 2015.

Morrison N. Use Of Cyanoacrylate Adhesive For Treatment Of Incompetent Great Saphenous Veins: 12-month Results of the VeClose Trial. European Venous Forum. 2015

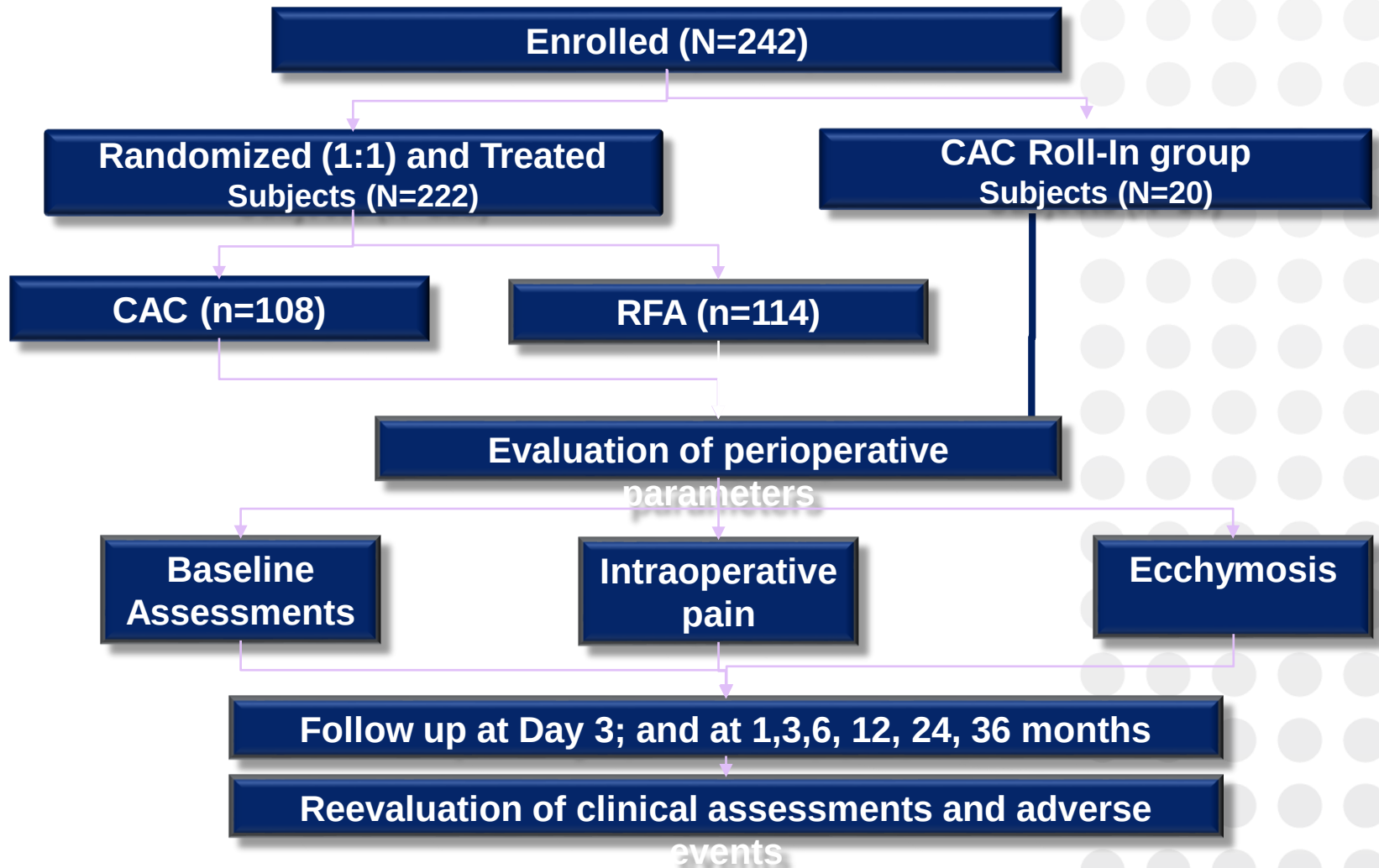
24 Month Results (VeClose)

• **VenaSeal Saphenon Closure System**

VS.

Radiofrequency Ablation

Study Design



Demographics and Baseline Characteristics

Baseline Characteristics	CAC (N=108)	RFA (N=114)	P-value
Age (years)	49.0	50.5	0.34
Body Mass Index	27.0	27.0	0.95
Mean GSV diameter (mm)			
Proximal	6.3	6.6	0.15
Mid-thigh	4.9	5.1	0.28
Mean Treatment Length (cm)	32.8 (108)	35.1 (114)	0.17
Mean VCSS	5.5 ± 2.6	5.6 ± 2.6	0.99
Mean AVVQ	18.9 ± 9.0	19.4 ± 9.9	0.72
Mean EQ-5D TTO	0.935 ± 0.113	0.918 ± 0.116	0.29

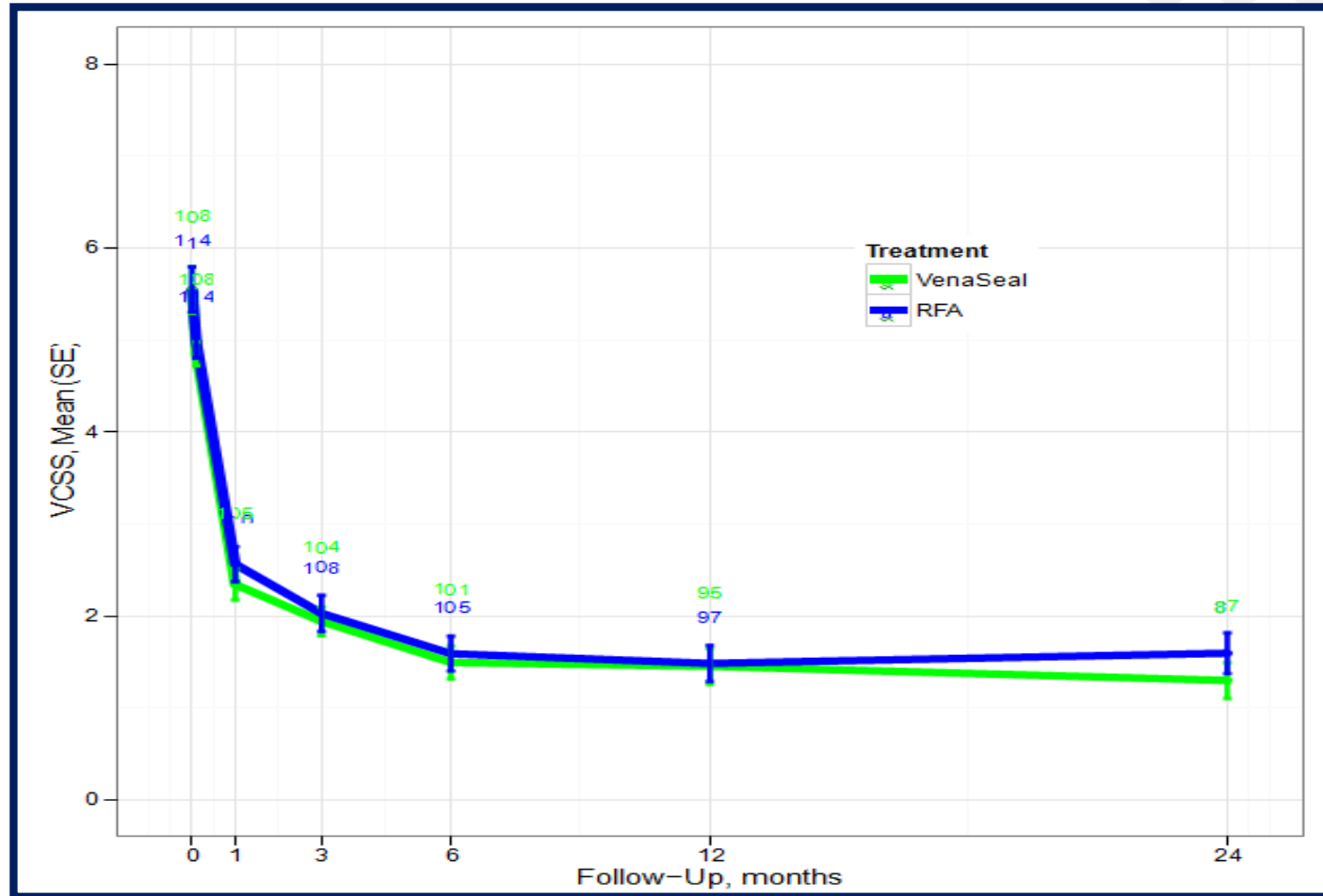
Primary Endpoint – Complete Closure

Timepoint	Closure Rate CAC	Closure Rate RFA
Day 3	100% (108)	99.1% (114)
Month 1	100% (105)	87.3% (110)
Month 3	99% (104)	95.4% (108)
Month 6	99% (101)	96.2% (105)
Month 12	96.8% (95)	95.9% (97)
Month 24	94.3% (87)	94% (84)

94.3% closure rates, demonstrating continued non-inferiority to RFA (P=0.0075) thru 24 months

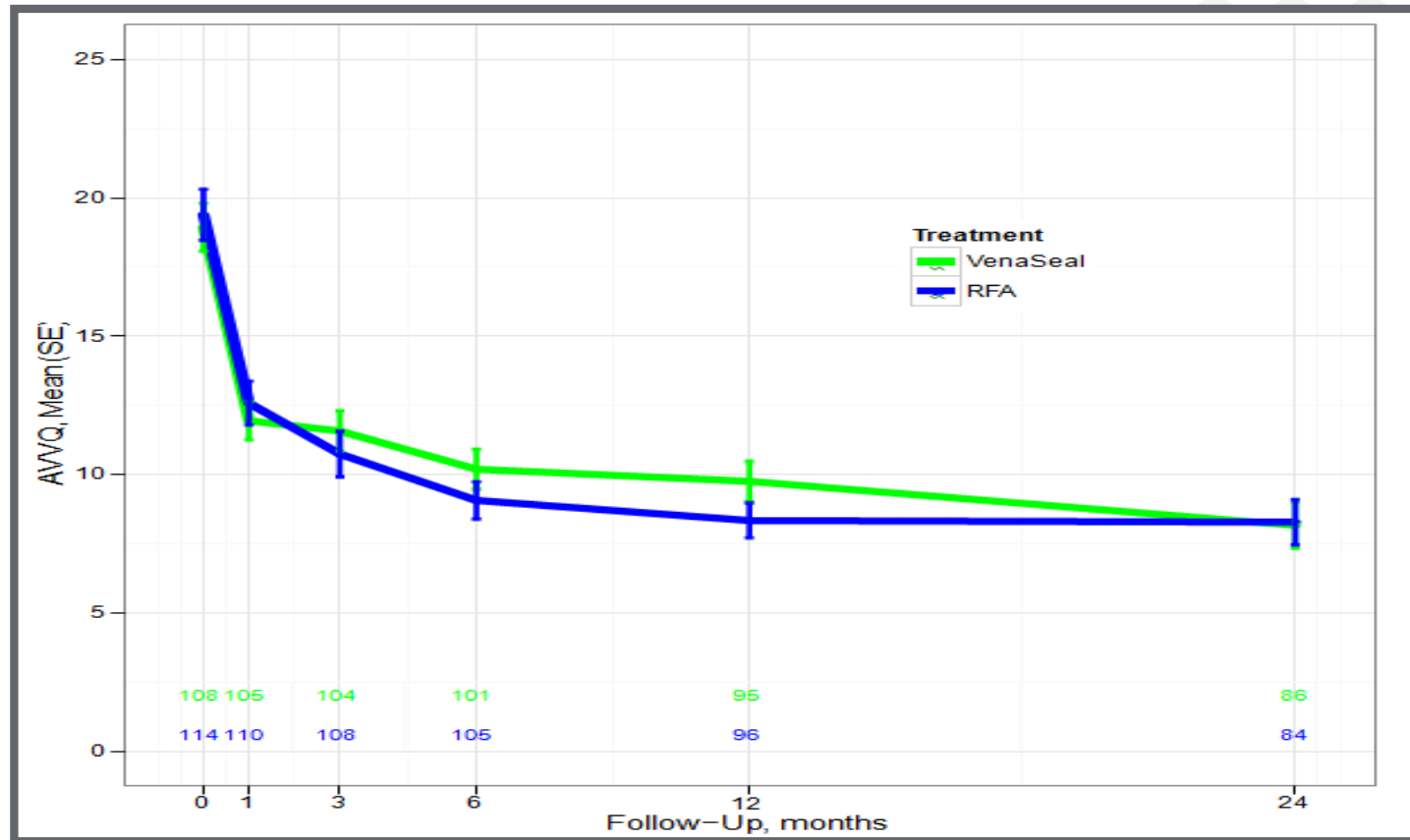
24 Month - Venous Clinical Severity Score (VCSS)

VCSS demonstrated statistically significant improvement out to Month 6 and sustained through 12M and 24M time points.



24 Month - Aberdeen Varicose Vein Questionnaire

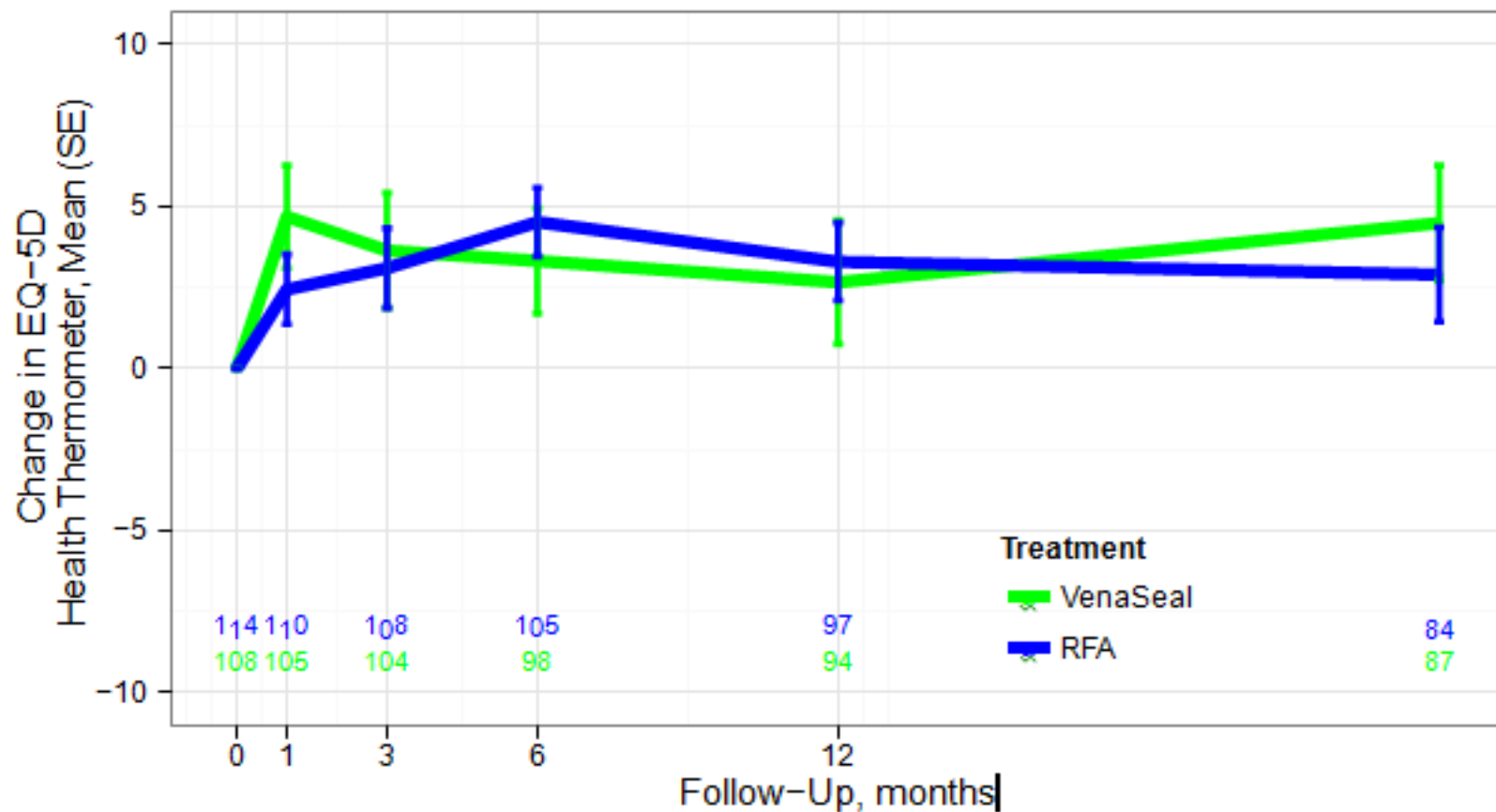
Subjects experienced statistically significant improvement over time, $p < 0.0001$, but there was no difference between treatment groups



AVVQ: a 13-question survey addressing physical symptoms, pain, ankle edema, ulcers, compression therapy use, and limitations on daily activities are examined, as well as the cosmetic effect of varicose veins and social issues.

24 Month - EQ5D Results

- EQ-5D was improved significantly from baseline at all time periods across all subjects.
- There was no difference in improvement of EQ-5D between randomization groups.

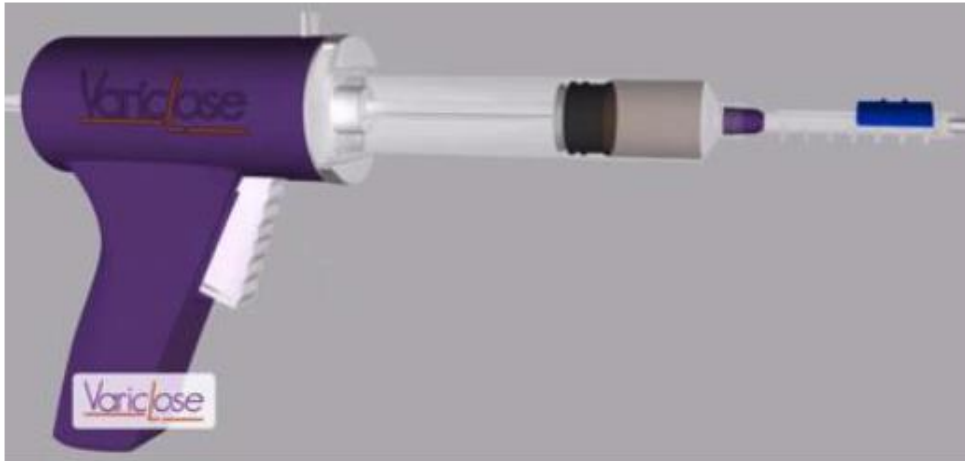


The EQ-5D includes single item measures of: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each item is coded using 3-levels (1 = no problems; 2 = some problems; 3 = severe problems).

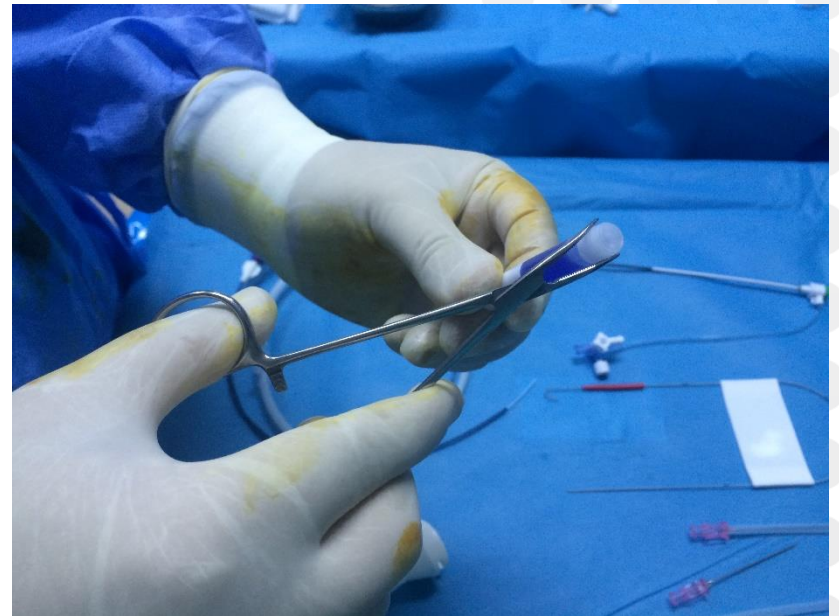
Summary 24 months

- **94.3% closure rates=non-inferiority results to RFA**
 - **(p=0.0075) at 24 months**
- **VCSS, AVVQ and EQ5D significant improvement**
 - **No difference between Rx Groups at 24 months**
- **Adverse events were extremely low in**
 - **The time period of 12-24 months across both treatment options**

Biolas – Variclose Cyanoacrylate Adhesive (Turkey)







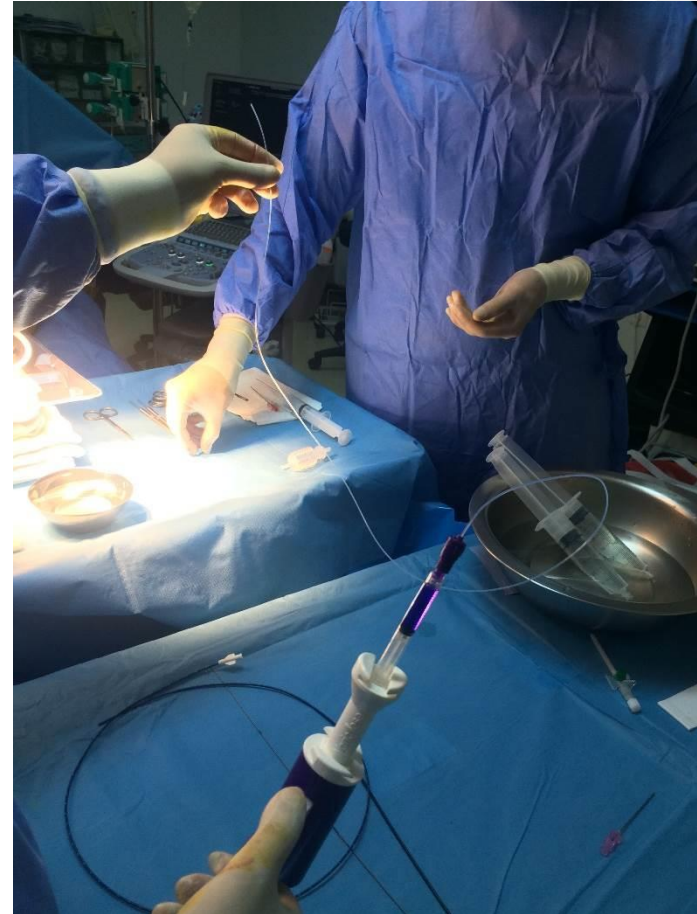
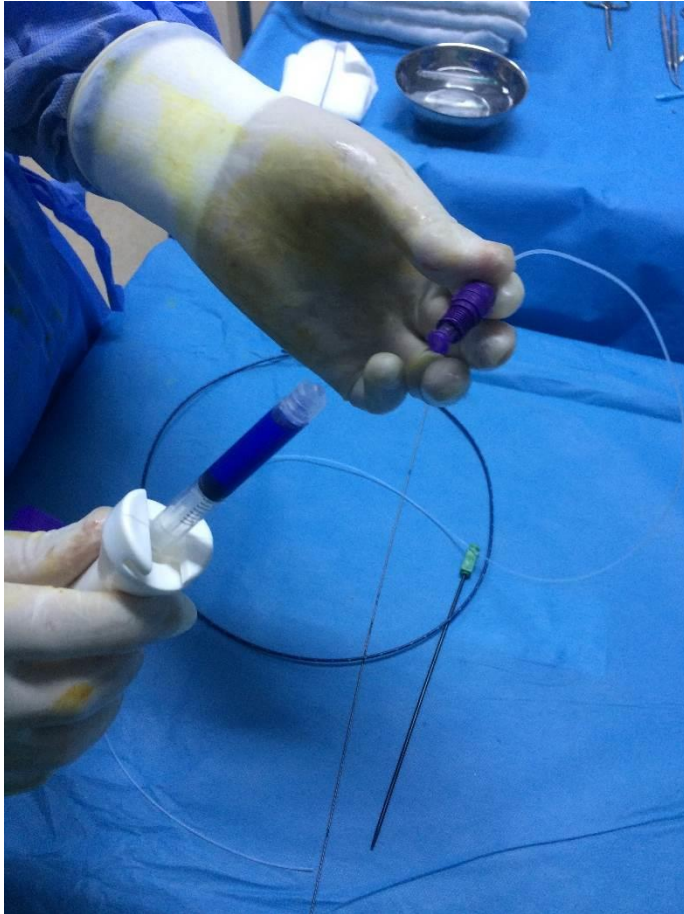




Long J wire in and US appearance



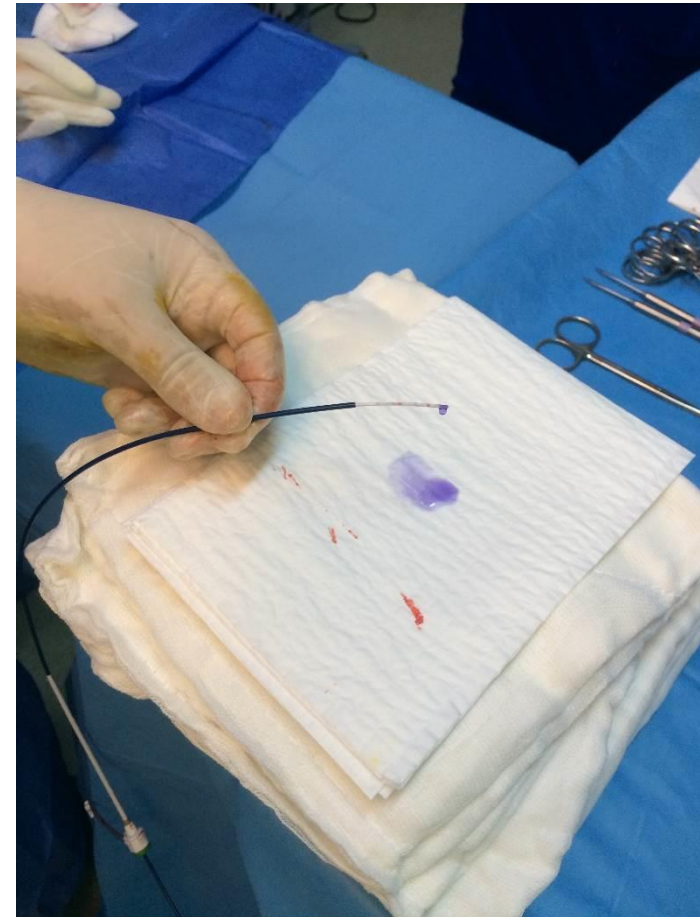
Priming of the catheter



Insertion and Connection

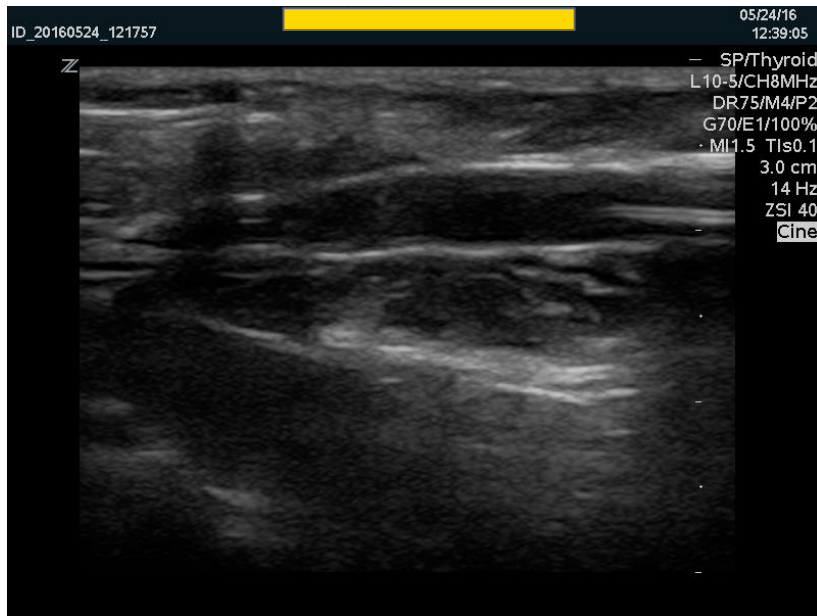


Pullback





Pulling back the catheter 3 cm to the SFJ



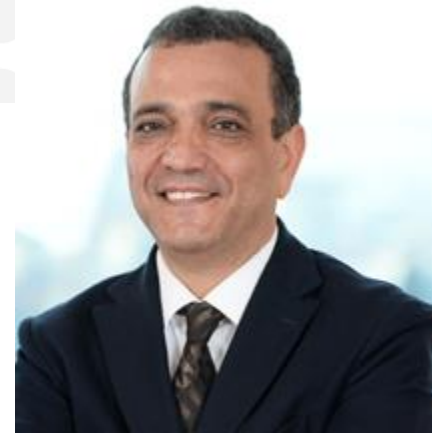
2nd Generation CAA

- Automatic pull back
- Automatic dispenser

A prospective comparison of a new cyanoacrylate glue and laser ablation for the treatment of venous insufficiency

Ahmet Kürşat Bozkurt¹ and Muhammet Fatih Yılmaz²

The authors concluded that there was essentially clinical equipoise.



2016





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