New Devices and Future Therapies In the Treatment of Abdominal Aortic Aneurysms

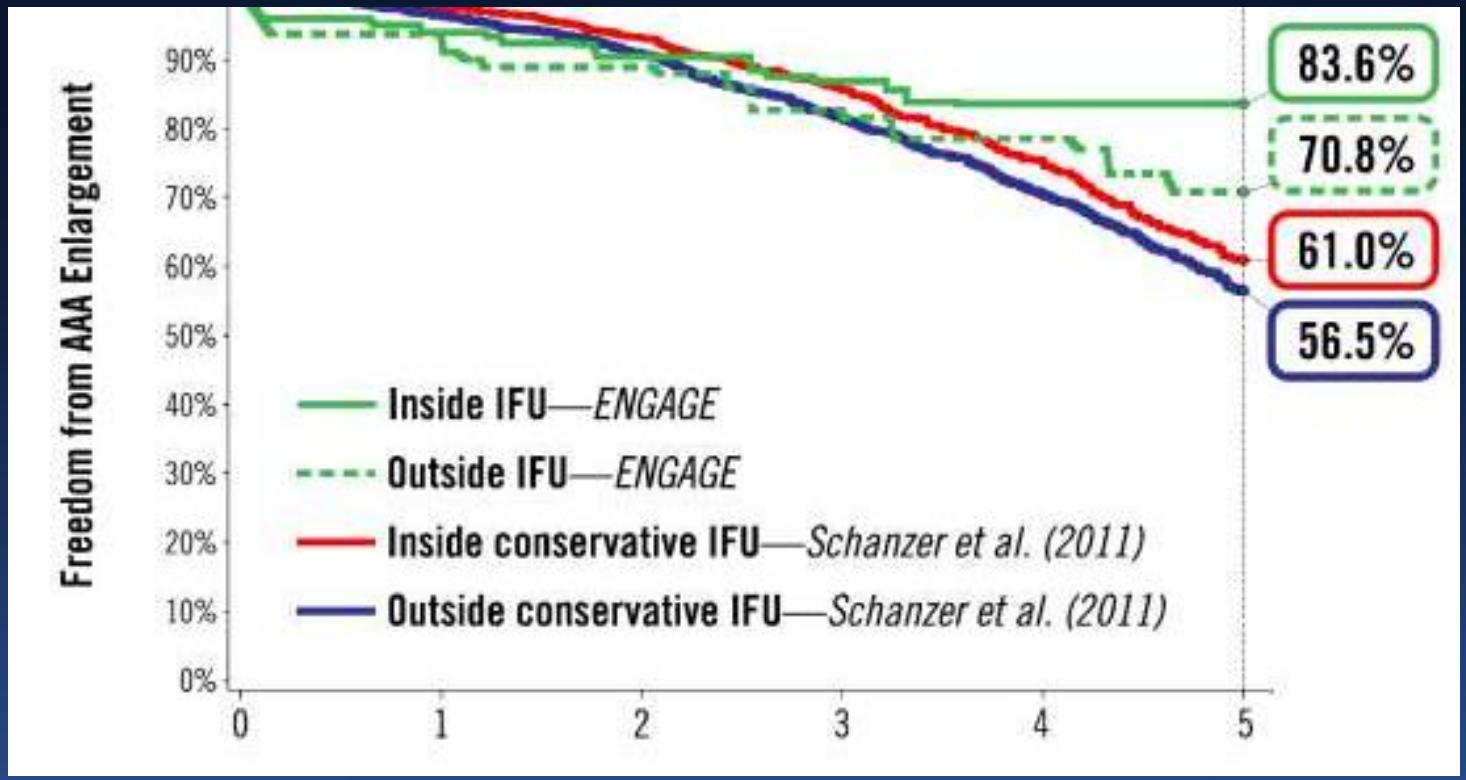
Robert M. Bersin, MD

Disclosure Statement of Financial Interest

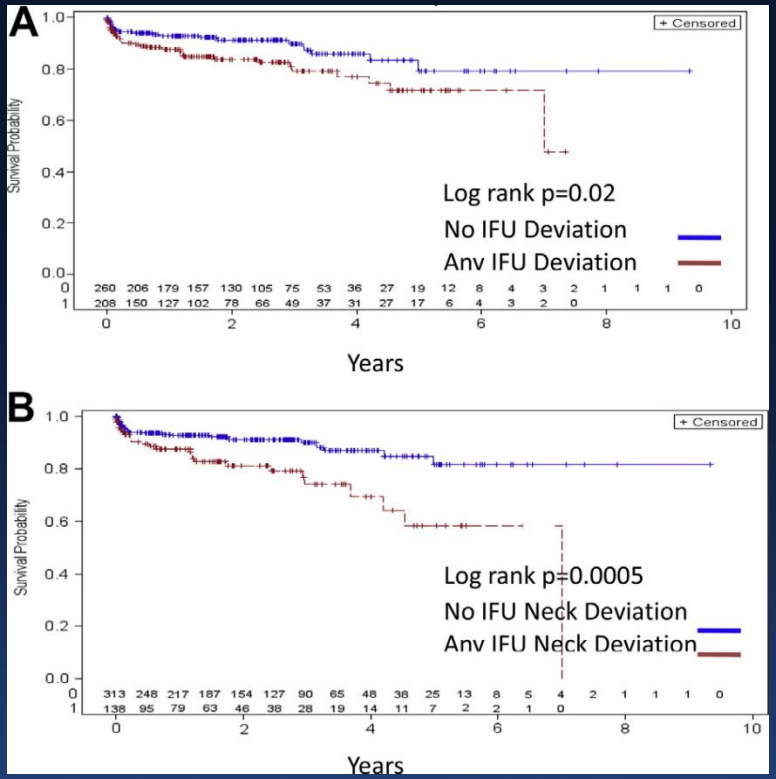
I, Robert M. Bersin, have a financial interest/arrangement or affiliation with the following organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation:

- **Nectero Corporation**

High Rate of Continued Sac Enlargement with Current Generation of Endografts



Survival On vs. Off Label EVAR Use



49% had ≥1 IFU deviation

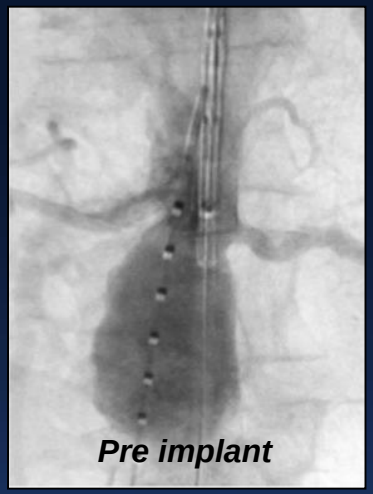
A. With and without any instructions for use (IFU) deviation.
B. With and without neck IFU deviations.

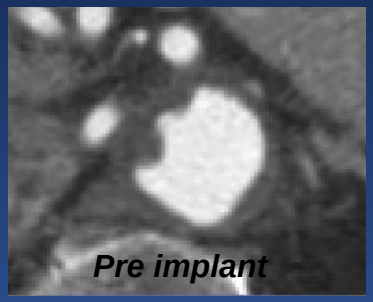
Predictors: Neck length (p = 0.004; OR 1.91) and aneurysm angle (p = 0.006; OR 2.06)

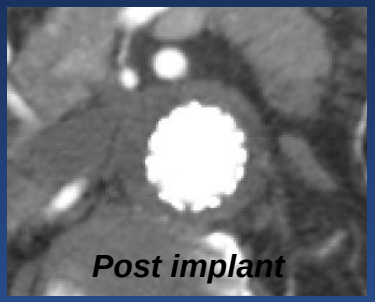
Cain BC et al J Vasc Surg 2016; 64(5): 1533

Ovation Global Pivotal Trial

No Type I Leaks in Patients With Adverse Neck Anatomy







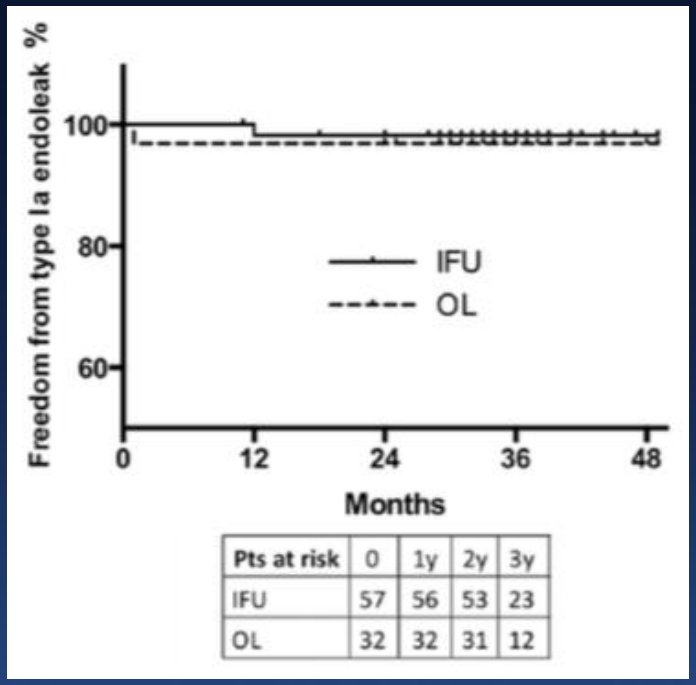
35% of enrolled patients had 1 or more hostile neck feature (56/161)

Mehta M et al *J Vasc Surg* 2014; 59: 65-73

Ovation On- vs Off-Label Use

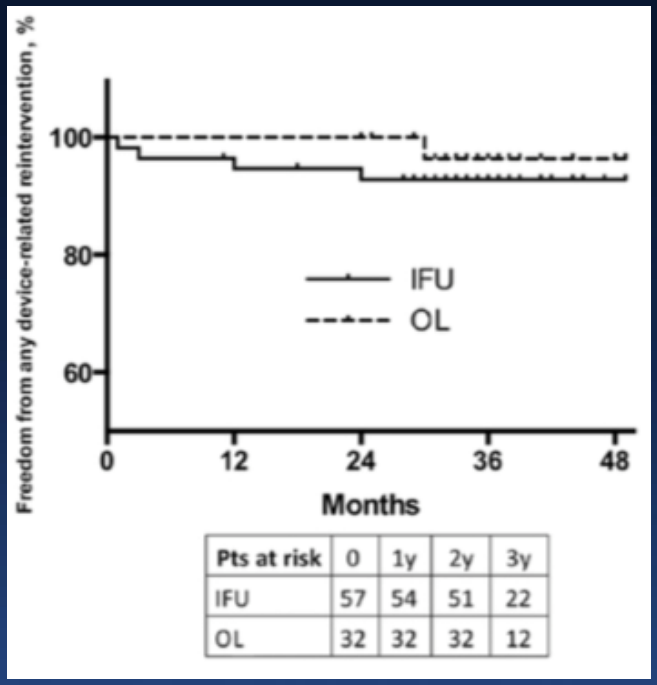
TriVascular Ovation Italian Study (TOIS)

Neck Lengths On-Label ≥7 mm vs. Off-Label <7 mm



Pts at risk	0	1y	2y	3y
IFU	57	56	53	23
OL	32	32	31	12

Type Ia endoleak p = 0.6, NS



Pts at risk	0	1y	2y	3y
IFU	57	54	51	22
OL	32	32	32	12

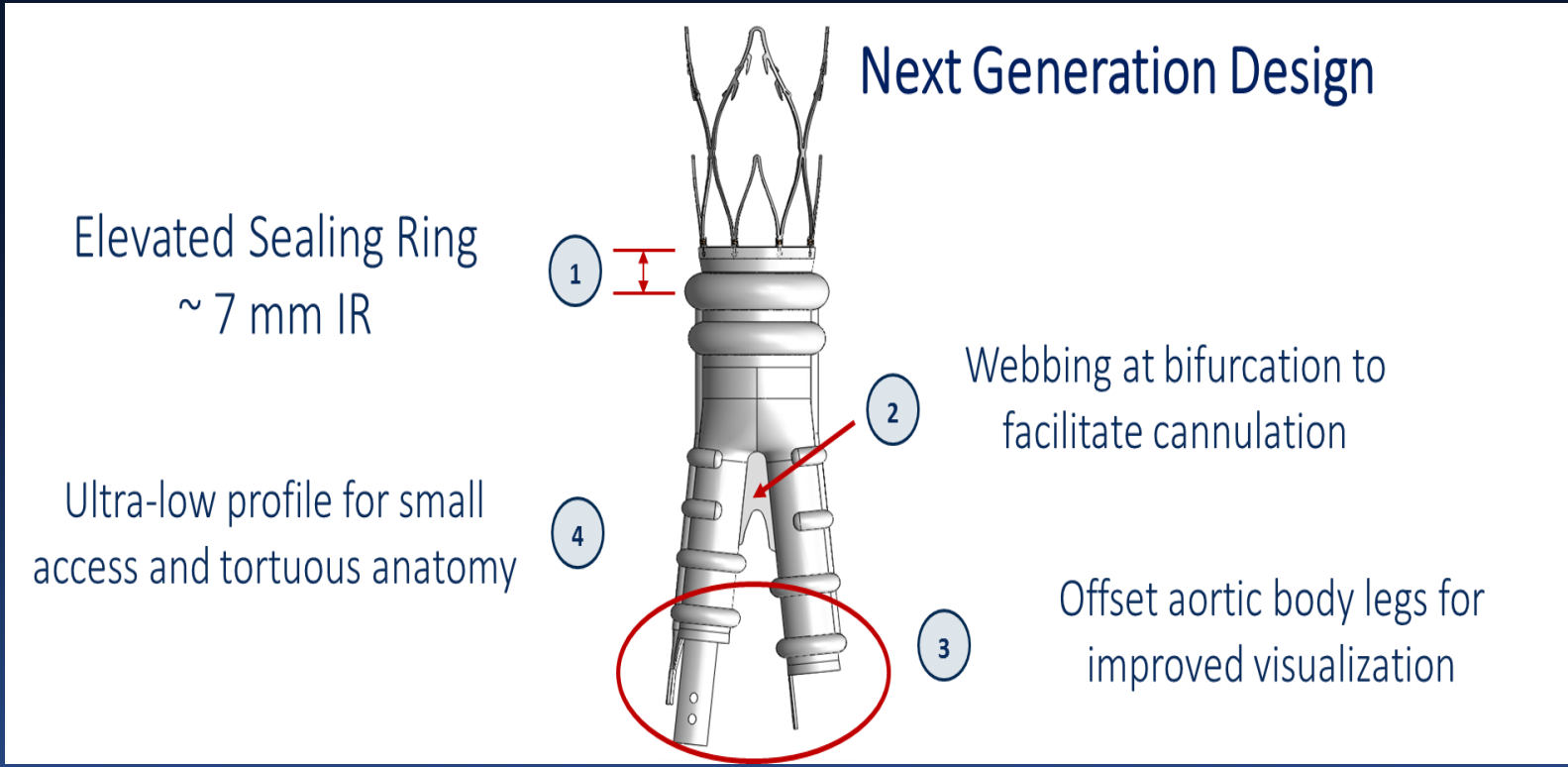
Re-intervention p = 0.4, NS

≥7 mm neck length requirement removed from IFU

de Donato et al *J Endovasc Ther* 2017; 24(2): 191–197

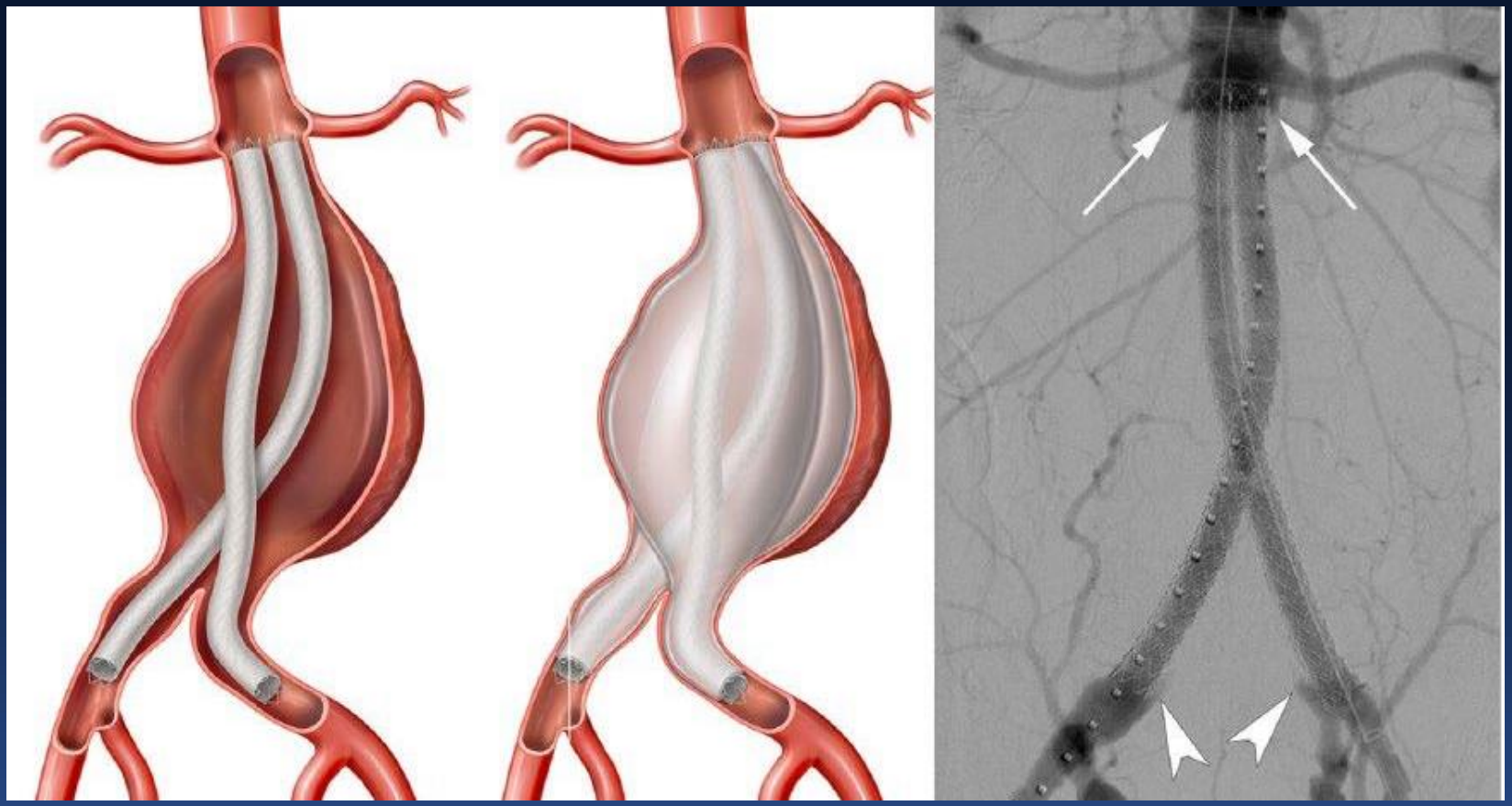
Ovation Alto

First sealing ring is 7mm below fabric collar instead of 13 mm

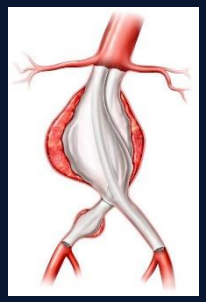


ELEVATE IDE trial enrollment complete

EVAS-Endovascular Aneurysm Sealing



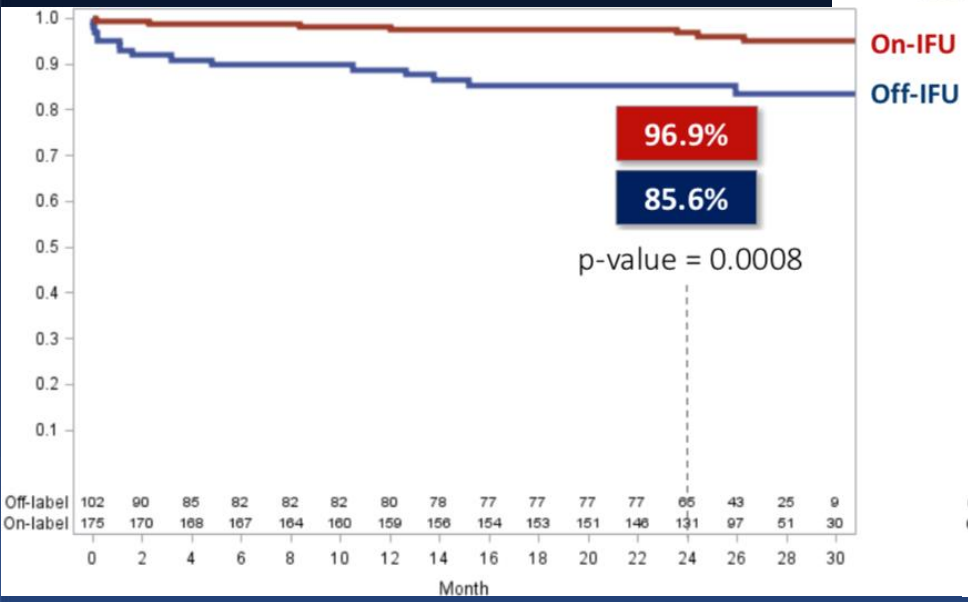
Carpenter JP et al *J Vasc Surg* 2016;63:23-31



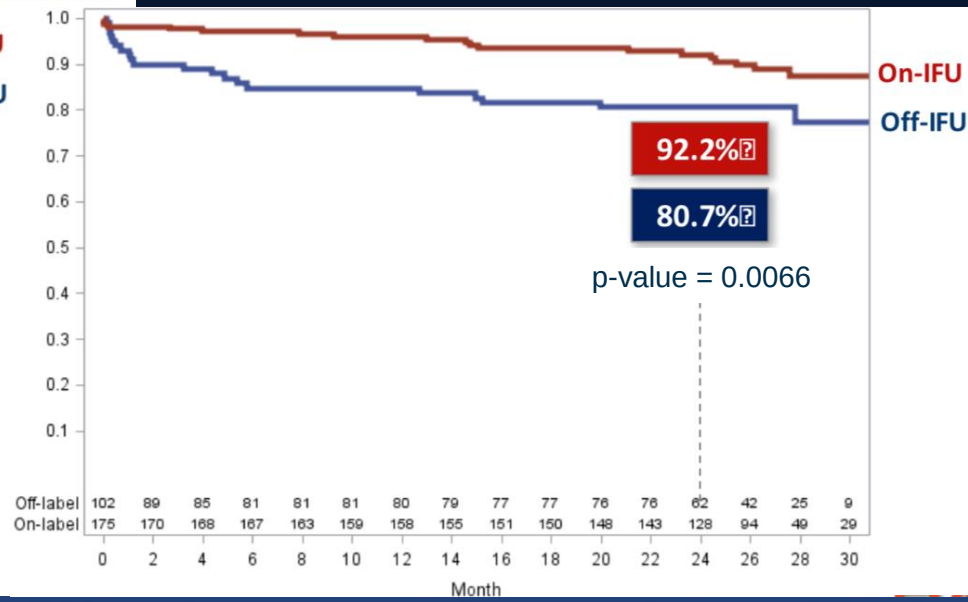
EVAS Forward Global Registry On- vs. Off-Label Outcomes

Freedom from type Ia endoleak

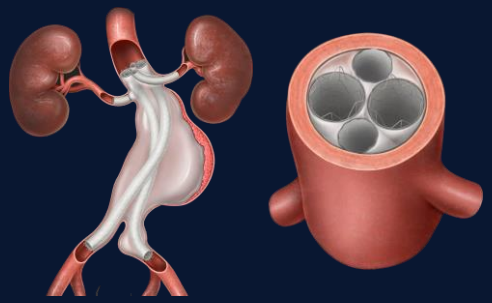
EVAS FORWARD GLOBAL REGISTRY



Freedom from re-intervention



Type Ia endoleak rate 3.1% on-label vs. 14.4% off-label at 2-years
Secondary intervention rate 7.8% on-label vs. 19.3% off-label at 2-years



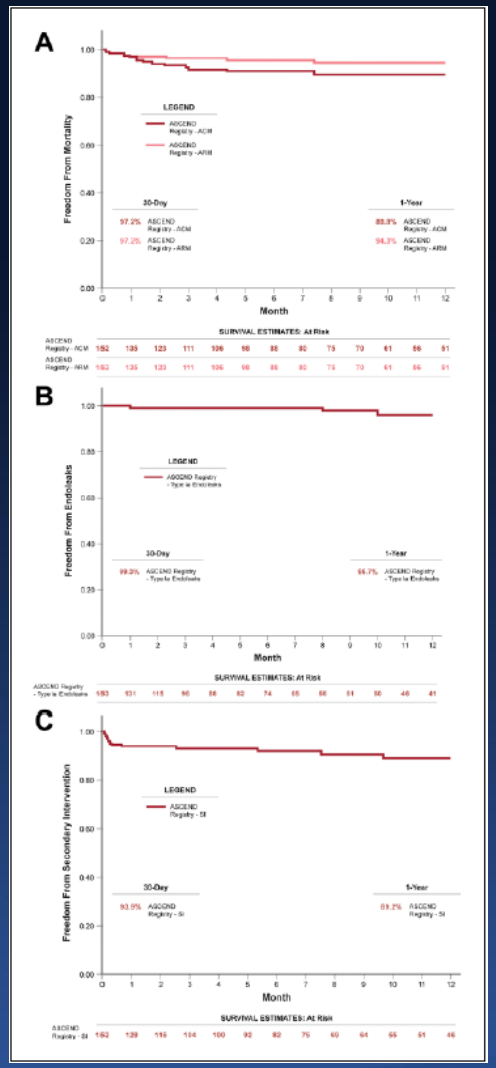
ASCEND

Aneurysm Sealing for Complex AAA: Evaluation of Nellix Durability

Single-arm post-market registry of the Nellix EVAS utilizing chimney grafts

1-year outcomes (N=154)

- Type Ia endoleak 4.3%
- Type II or III endoleak 0.0%
- Re-intervention 10.8%
- Aneurysm-related mortality 5.7%

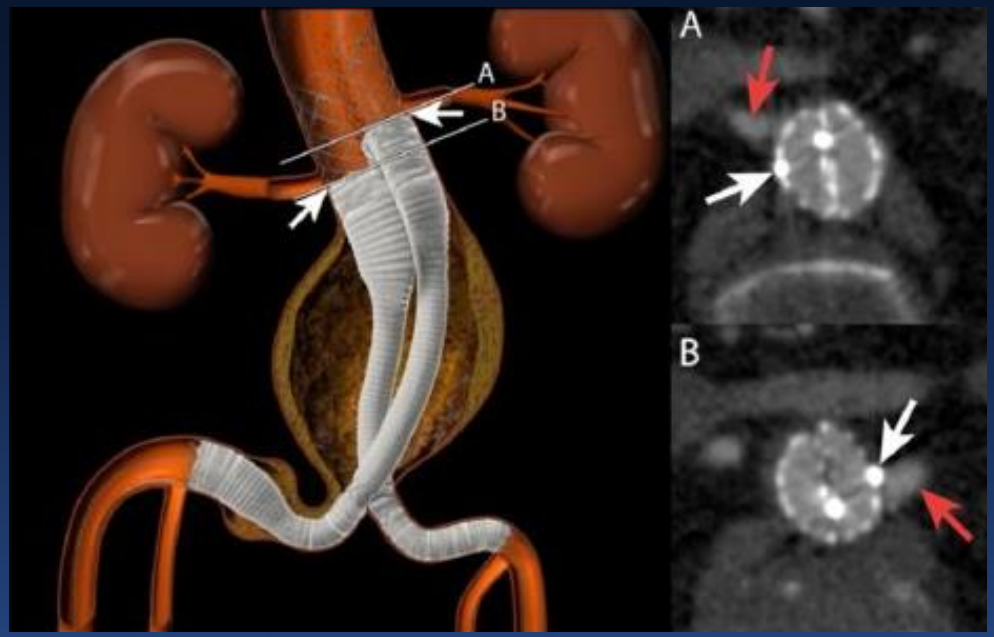


Thompson M et al *J Endovasc Ther* 2017: 24(6): 764–772

Altura Double D Endograft

FIH and ELEVATE Registry 1-Year Results (N=90)

Clinical Success	99.0%
Aneurysm-related mortality	0.0%
Type I endoleak	1.1%
Re-intervention rate	6.7%



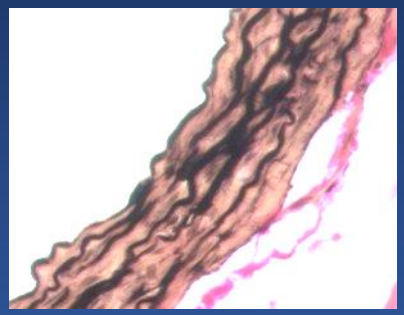
CE Marked 2017
ALTITUDE Global Registry (N=1000) initiated 2018

Kreivins D et al *J Endovasc Ther* 2018; 25(3): 379-386

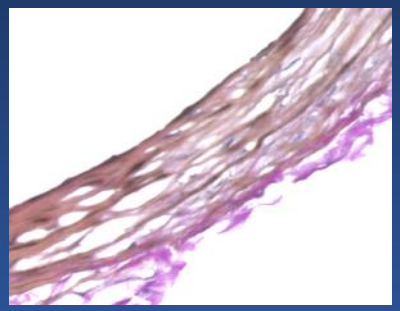
Endovascular Aneurysm Stabilization Therapy

Pathophysiology of Aneurysm Formation

- Atherosclerosis is associated with chronic inflammation of the aortic wall
- With inflammation, vascular smooth muscle cells (VSMCs) and infiltrating macrophages release metalloproteinases, principally MMP-2, MMP-7, MMP-9 and MMP-12 (also known as human macrophage elastase or HME)
- MMP-9 and MMP-12 are the metalloproteinases most responsible for loss of extracellular matrix components, especially elastin in atherosclerotic tissues



Healthy Aortic Tissue



Diseased Aortic Tissue

Pathophysiology of Aneurysm Formation

- **Elevation of tissue elastase levels appears to be a key factor in aneurysm formation**
- **Collagenase levels have not correlated with aneurysm formation**

24 patients with atherosclerosis of the aorta

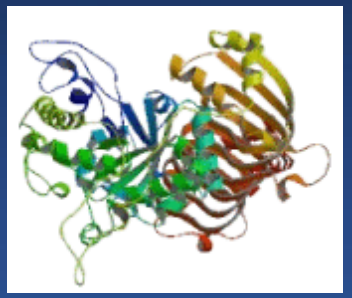
	Aneurysm (8)	Occlusive (16)	P value
Aortic wall elastase (nmol/gr tissue)	8.211 (3.408-14.205)	3.049 (0.000-5.636	0.0030
Aortic wall elastase (nmol/gr protein)	2.303 (0.616-5.171)	0.559 (0.000-1.345)	0.0018

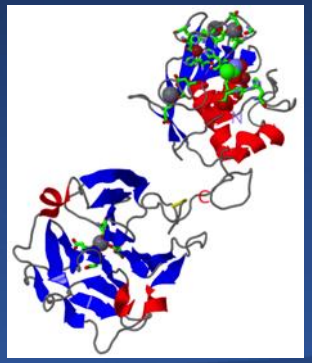
Samy AK et al 1994; *J Vasc Endovasc Surg* 28(5): 311-317

EAST Polymer Binds With Elastin to Prevent Degradation by Elastase

- EAST polymer binds with elastin making it resistant to enzymatic degradation by elastase and other enzymes
- Binding is durable, not easily reversed
- Stabilization of elastin increases tissue strength and resistance to stretch
- Stabilization of tissue elastin results in aneurysm stabilization

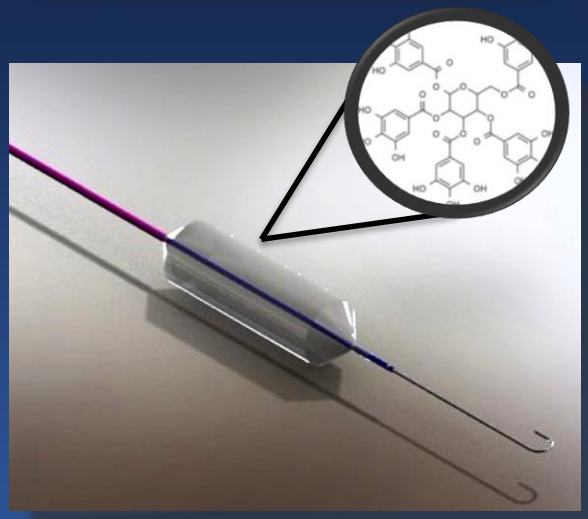
Elastin ***EAST Polymer*** ***Elastase***



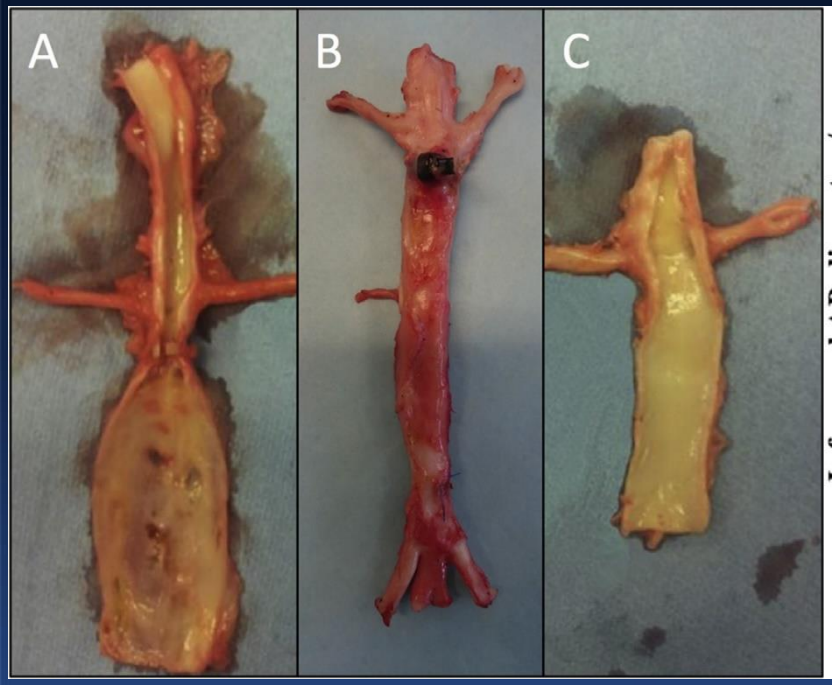


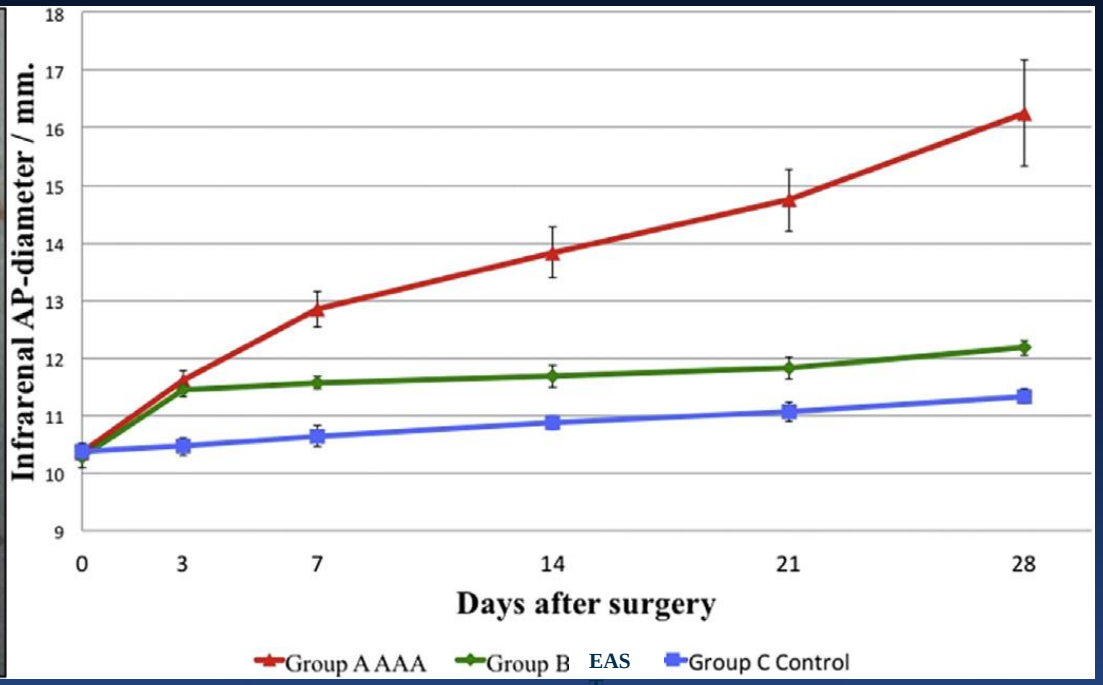
EAST Polymer Delivered Via Aavert™ Coated Balloon

- Ultra-compliant polymer-coated balloon gently conforms to diseased vessel segment
  - Expands to 5+ cm, covers irregular anatomy
  - Pressure is greater than blood but less than 1 atm
  - Balloon dimples at side vessels, demonstrating compliance
- Hydrophobic polymer transfers to tissue in 3 min
- Minimally invasive, 30 minute procedure
  - 10 FR catheter delivery
  - Outpatient procedure



Intraluminal Delivery of EAST Polymer Prevents AAA Formation



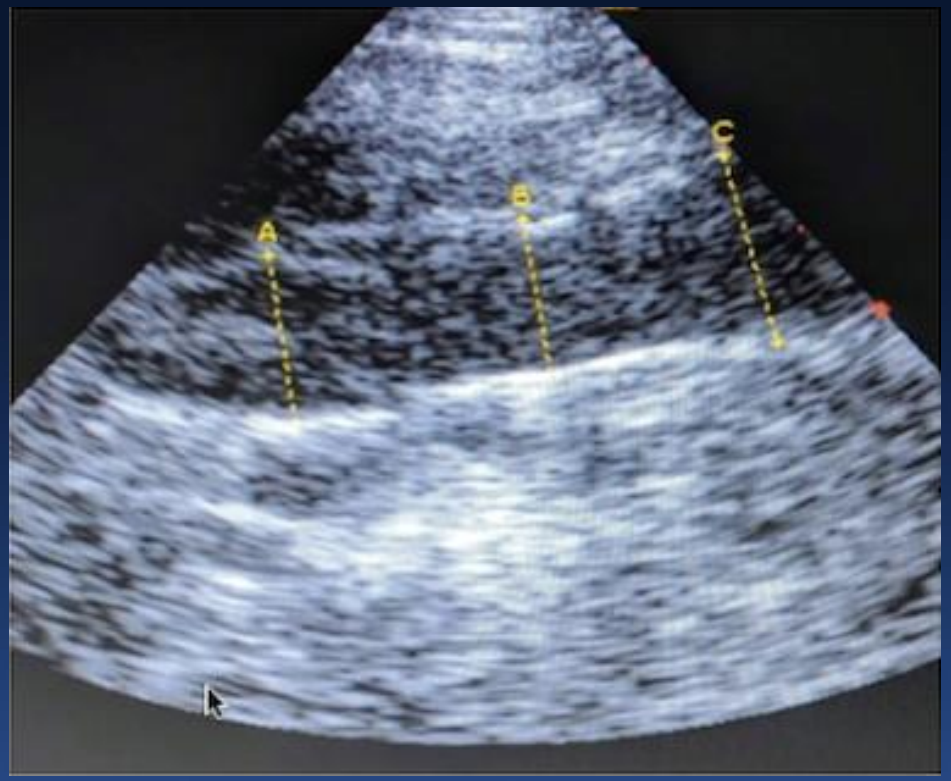


A. Balloon dilation plus elastase
B. Balloon dilation plus elastase plus EAST polymer
C. Control group (sham procedure)

Kloster, B et al *Ann Med and Surg* 2016; 7: 65-70

Intraluminal Delivery of EAST Polymer Promotes AAA Regression

AAA pre-treatment



Regression with EAST polymer

EAST Polymer Increases Human Aortic Tissue Strength

Ex Vivo Study

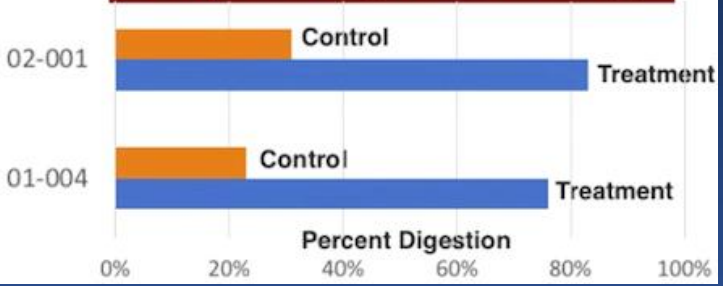
- 4 Male surgical AAA repair patients
- Ages 59-72
- Average sac size 5.7cm
- Each patient served as their own control
- Treatment tissue was submerged in 0.06% EAST solution for 15-20 min.
- Only 2 patients had sufficient tissue for additional enzymatic degradation testing

- **Near 2x modulus improvement**
- **~ 3x Enzymatic protection**

Modulus Testing (kPa)

Patient ID	Control	EAST
02-001	7.2	17.5
01-002	5.9	9.1
01.003	6.4	12.2
01-004	4.1	6.7
Average	**5.9**	**11.4**

Enzymatic Degradation Testing



Conclusions

- Rate of continued sac enlargement remains high with the current generation of endografts
- Off-label use of endografts is associated with more sac enlargement, more secondary interventions and a higher mortality
- Most common cause is adverse neck anatomy
- Next generation devices are focusing on sealing short, angulated necks with polymeric and/or “Double D” designs
- Aneurysm stabilization technologies hold promise to arrest aneurysm growth and obviate the need for repair