



LEFT ATRIAL APPENDAGE OCCLUDERS, AN ELECTROPHYSIOLOGISTS PERSPECTIVE

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Treating the Left Atrial Appendage: Can We Do It? Should We Do It?

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I will be discussing devices not yet approved by FDA.

Disclosure:

Nothing relevant to disclosure

Overview of next 20 minutes

- Understand the modest data that implicates the left atrial appendage with stroke risk.
- Learn about how different LAA shapes may impact stroke risk.
- Discover the advantages and drawbacks associated with current LAA closure technologies.
- Tips from our experience with Lariat device.

AF/Stroke Epidemiology

- Each year, nearly 800,000 strokes in the U.S.
- 1 out of 19 deaths in the U.S. is due to a stroke
 - One new stroke every 40 seconds. One new stroke-related death every 4 minutes.
- Over 3 million Americans have AF
- AF quintuples the risk of ischemic stroke
- Strokes associated with AF are more lethal and disabling

Do people care about the LAA?

Growing interest in LAA ligation, largely driven by three developments:

1. Schuessler and Boineau developing the maze procedure (the first reliable operation for AF)
2. Advent of TEE, to document LAA thrombus and closure success
3. Development and marketing of percutaneous occlusion devices

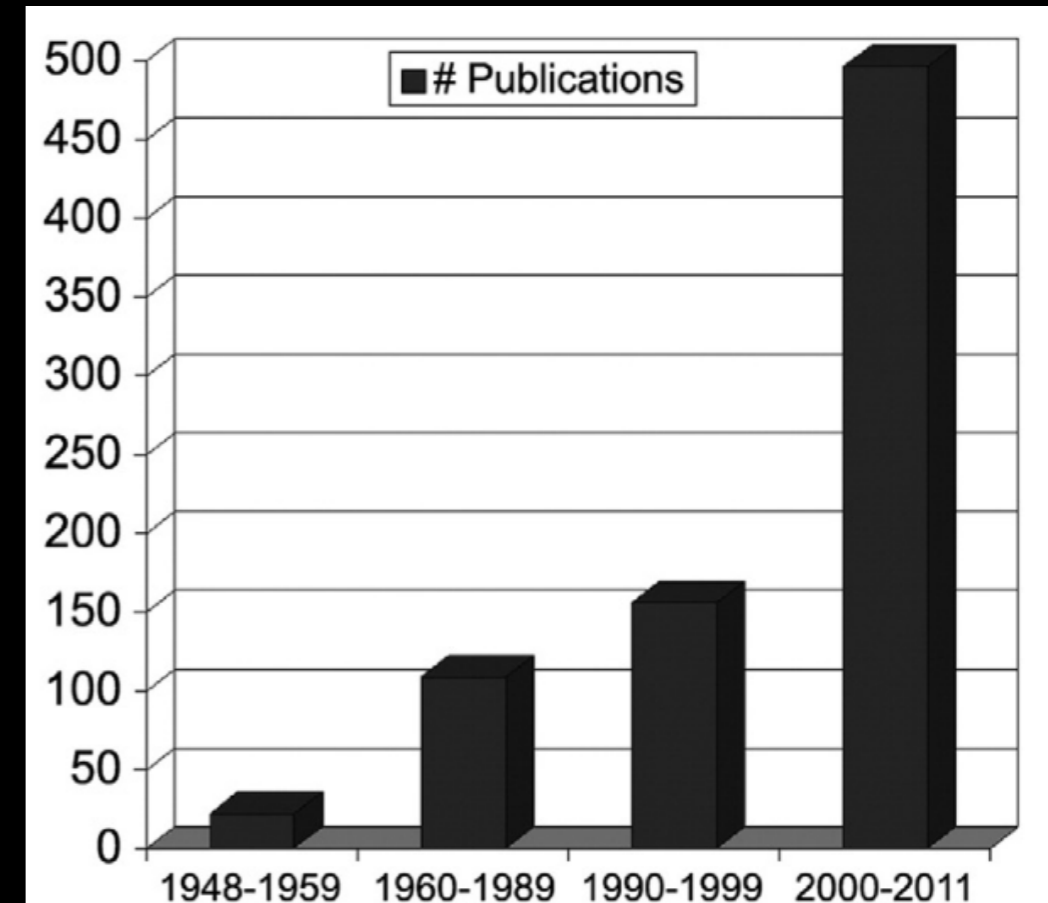
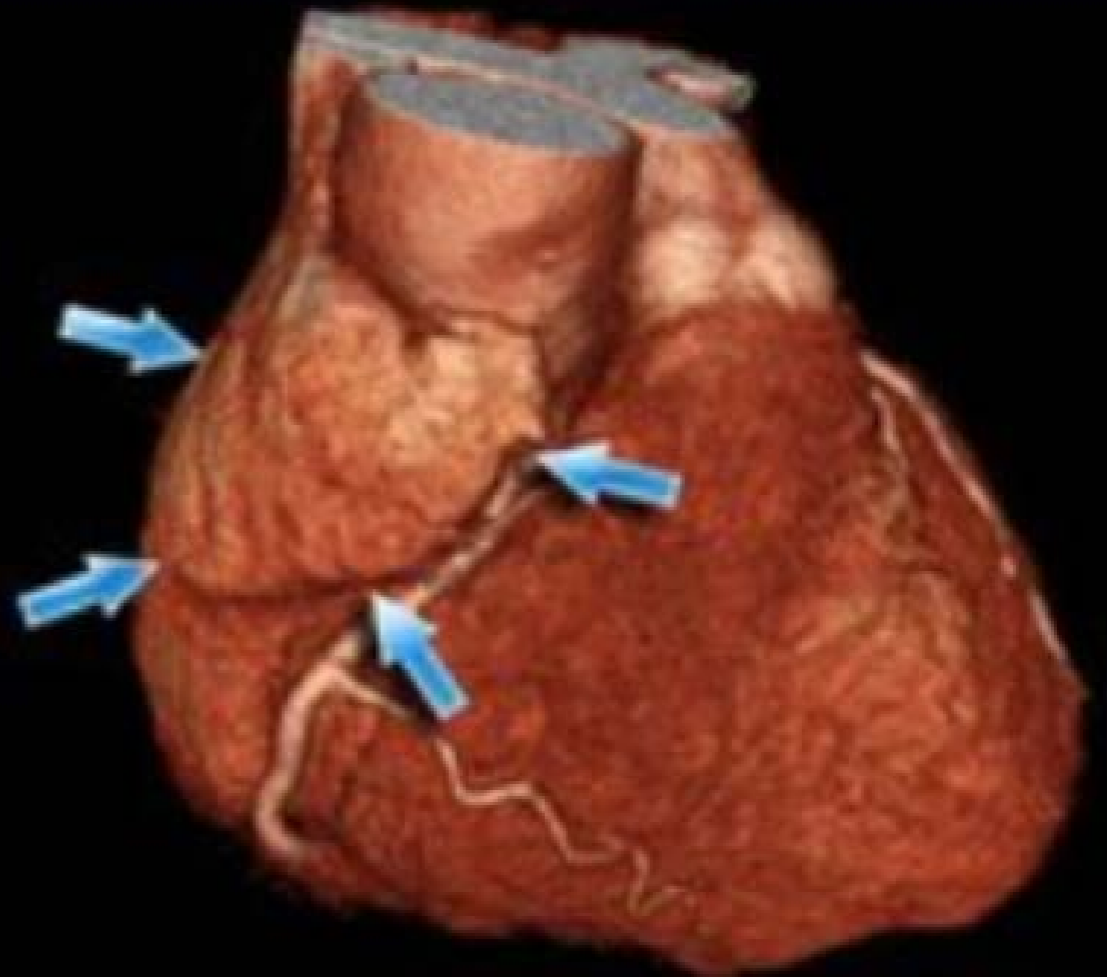


Fig 1. Number of left atrial appendage publications in various periods from 1948 to 2011.

What is the LAA and why do we fear it?

- 2-4 cm long tubular structure
- Often uses a narrow junction
- Forms sharp angles
- In contrast, the RAA is broad based and triangular, forms a wide junction to the RA, gradually angles upward.



What is the LAA and why do we fear it?

- Review of operative/autopsy/TEE studies identified the LAA as the source for 90% of left atrial thrombi in nonvalvular AF.
- LAA thrombus present in 64% of patients with rheumatic MV disease and systemic embolism.
- The LAA has been described in the literature as "our most lethal human attachment."

Blackshear JL. Ann Thorac Surg 1996

Belcher JR. Br Med J 1955.

Johnson WJ. Eur J Cardiothorac Surg 2000

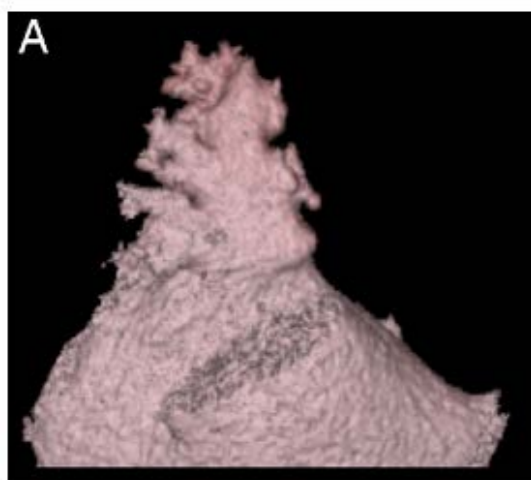
What exactly does the LAA do?

- Endocrine organ: LAA contains stretch receptors that mediate thirst
 - 40 fold higher concentration of ANP in LAA than other areas in the heart
 - Water retention with bilateral atrial appendectomies
- Regulates the LA pressure-volume relationship
- Trigger for recurrent AF (up to 27% of redo AF ablation)

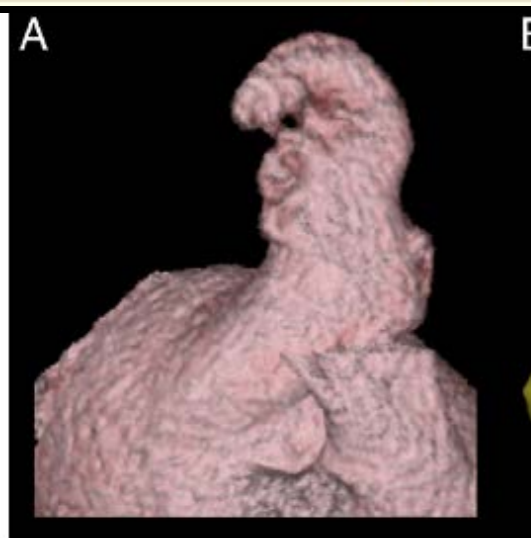
Does the Left Atrial Appendage Morphology Correlate With the Risk of Stroke in Patients With Atrial Fibrillation?

Results From a Multicenter Study

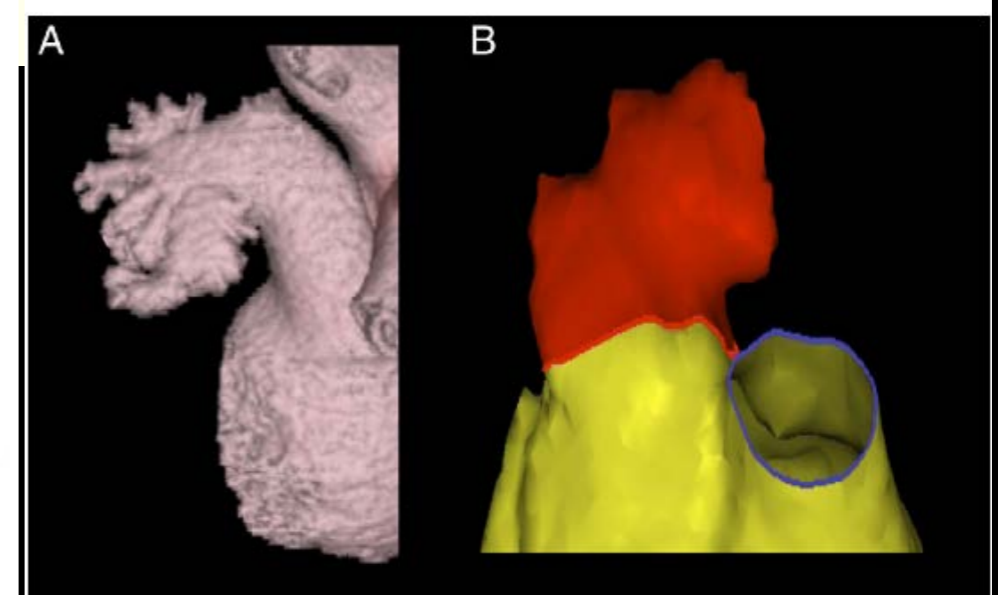
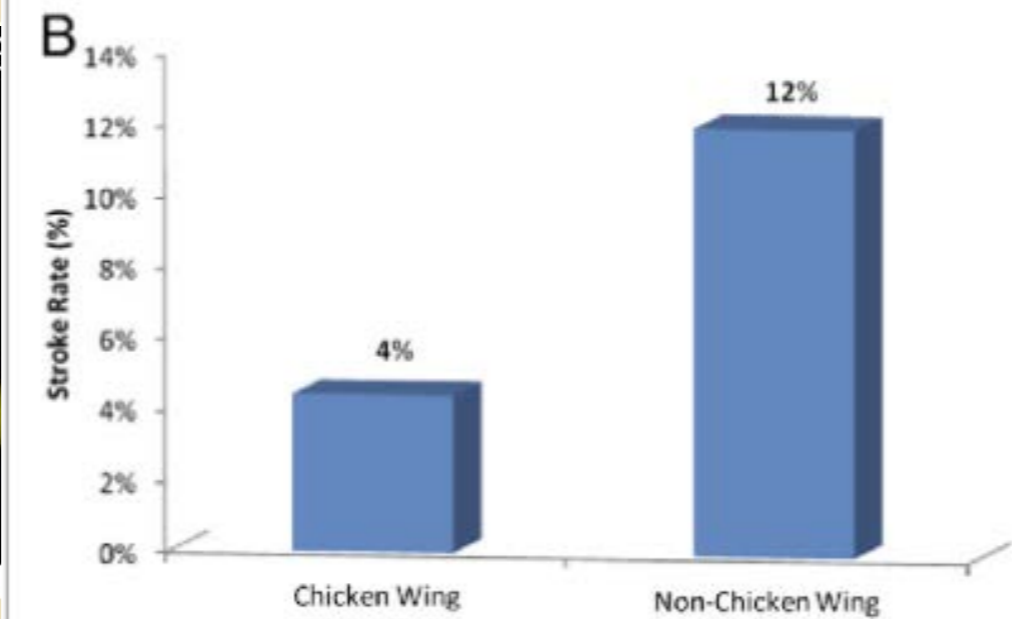
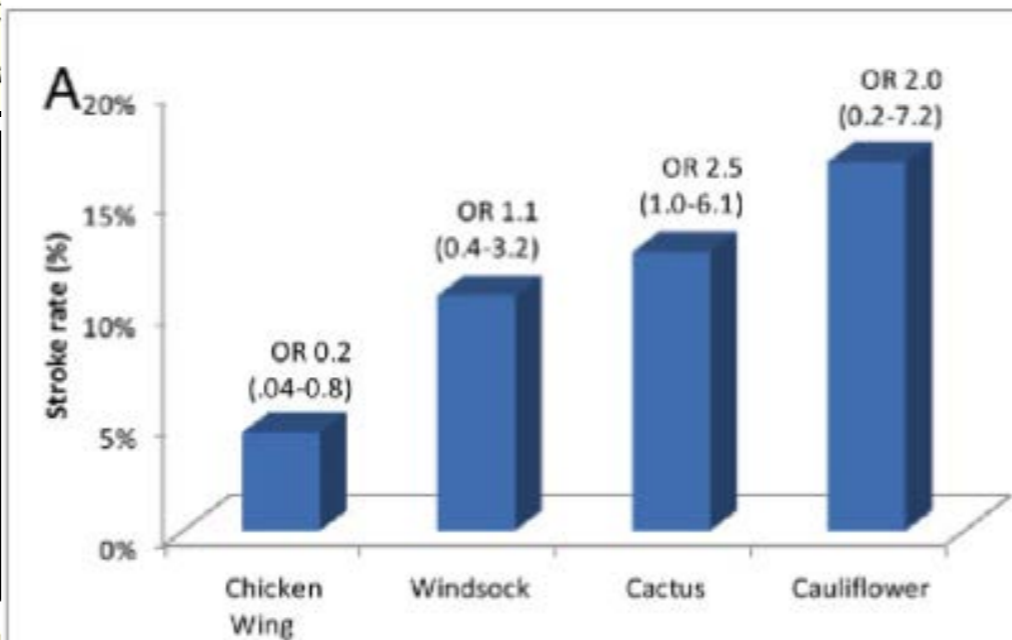
Luigi Di Biase, MD, PhD,*†‡ Pasquale Santangeli, MD,*‡ Matteo Anselmino, MD, PhD,§ Prasant Mohanty, MBBS, MPH,* Ilaria Salvetti, MD,§ Sebastiano Gili, MD,§ Rodney Horton, MD,* Javier E. Sanchez, MD,* Rong Bai, MD,* Sanghamitra Mohanty, MD,* Agnes Pump, MD,* Mauricio Cereceda Brantes, MD,* G. Joseph Gallinghouse, MD,* J. David Burkhardt, MD,* Federico Cesarani, MD,|| Marco Di Biase, MD, PhD,*
 Austin, Texas; and Foggia, Turin



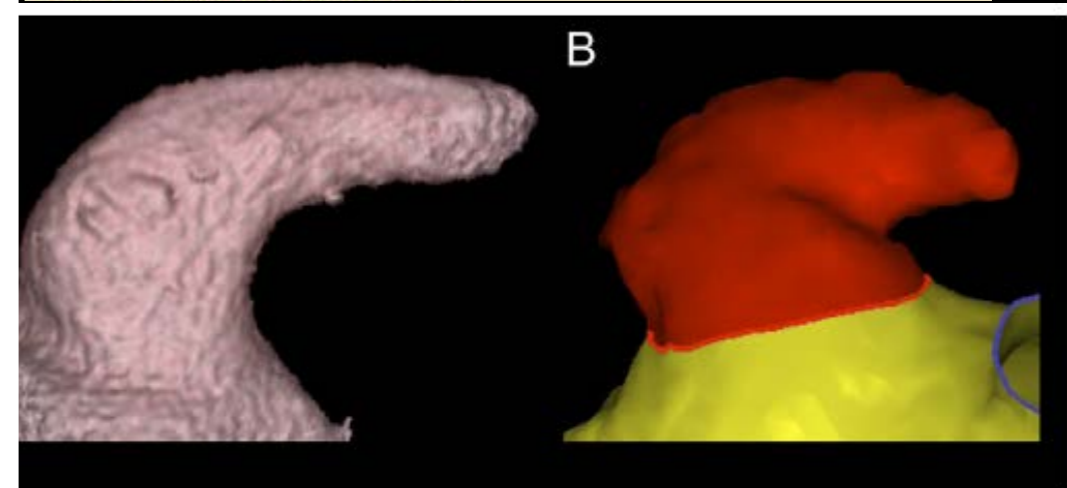
Scans of a Cactus LAA Morphology



Scans of a Windsock LAA Morphology



Scans of a Cauliflower LAA Morphology



Scans of a Chicken Wing LAA Morphology

Does LAA closure actually work?

Table 1. Comparison of Surgical Left Atrial Appendage Closure Techniques

First Author, Year	Country	No. Studied	Method of Closure	Closure Success Rate, ^a %	Effect of LAA Closure on Stroke Prevention
Johnson, 2000 [25]	USA	437	Excision	100	Positive
Katz, 2000 [30]	USA	50	Endocardial suture	64	None
Garcia-Fernandez, 2003 [31]	Spain	205	Endocardial suture	90	Positive
Bando, 2003 [38]	Japan	812	Endocardial suture	Not measured	Negative
Blackshear, 2003 [45]	USA	15	Thoracoscopic epicardial pursestring	93 ^b	Positive
Pennec, 2003 [40]	France	30	Endocardial	70–80	Negative
			Excision	100	Positive
Schneider, 2005 [41]	Germany	6	Endocardial suture	17	Negative
Healey, 2005 [28]	Canada	77	Epicardial suture	45	Positive
			Stapler	72	
Kanderian, 2008 [29]	USA	137	Excision	73 (20% stapler)	Positive trend
			Suture exclusion	23	
			Stapler	0	
Bakhtiary, 2008 [33]	Germany	259	Clamp and epicardial suture	100 ^b	Positive

^a As assessed by transesophageal echocardiography.

^b Remnant size not measured.

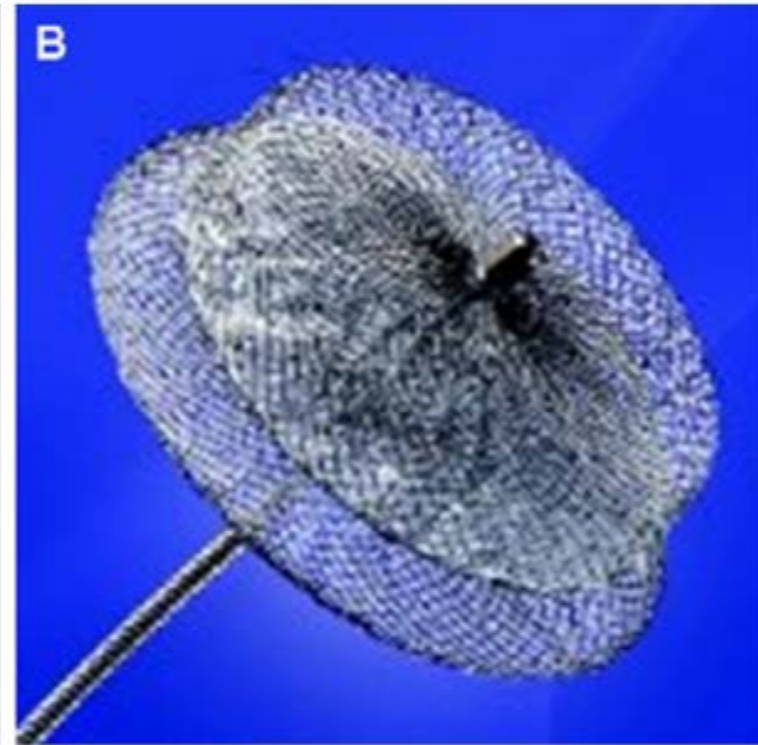
LAA = left atrial appendage.

Transcatheter Closure Devices

PLAATO



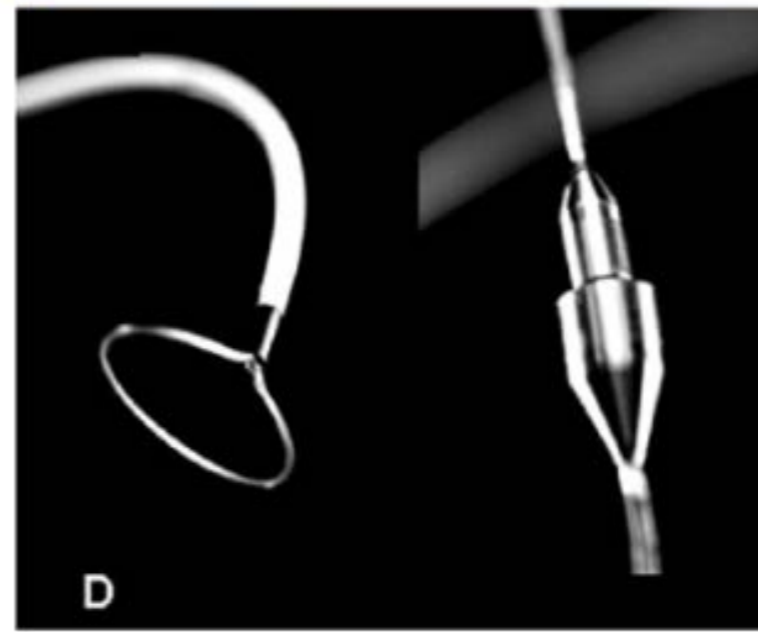
Amplatzer
Cardiac Plug



Watchman

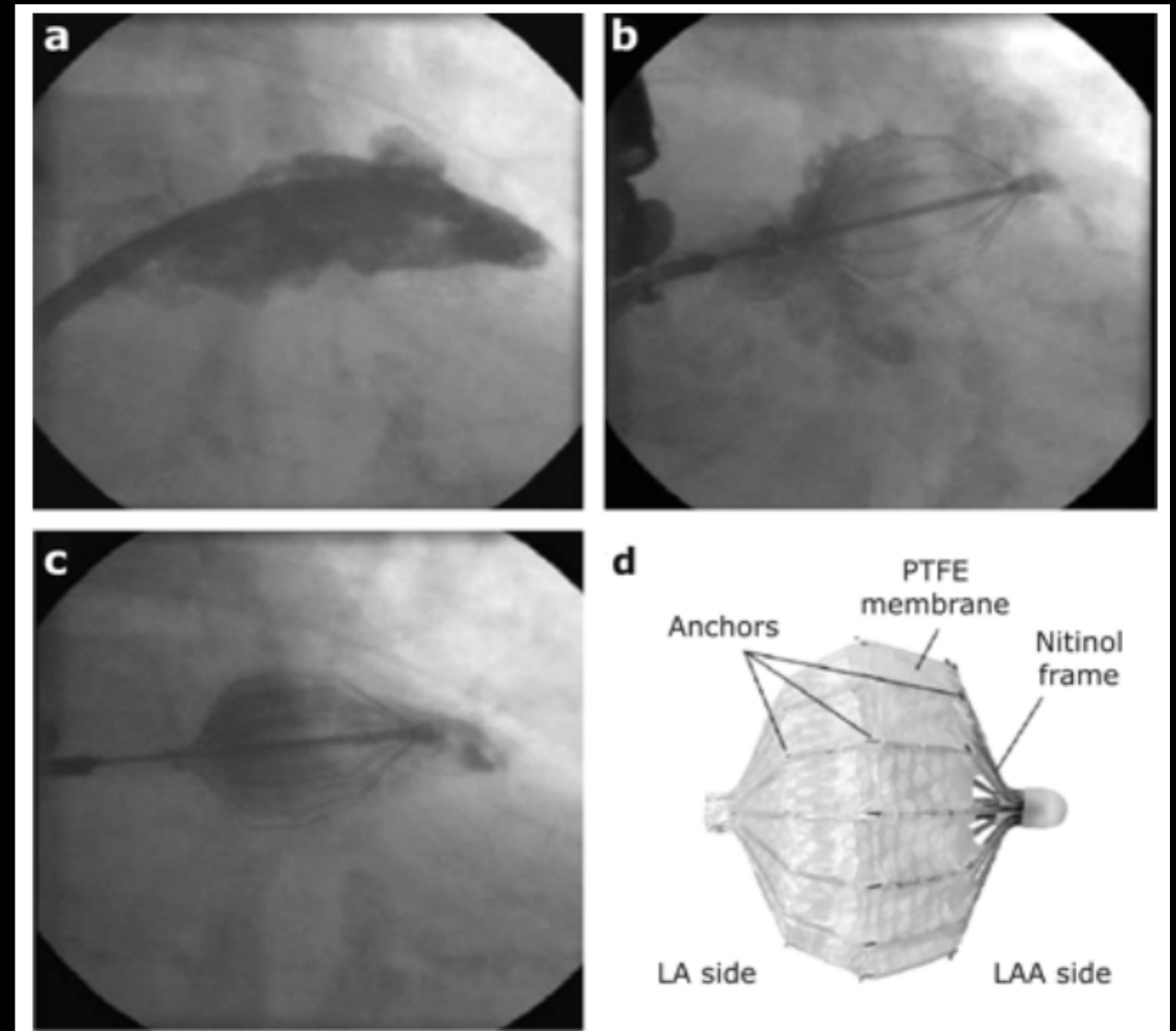


Lariat



PLAATO system (eV3)

- Self-expandable nitinol cage with a PTFE membrane.
- First dog implant a1998.
First human implant 2001.
- Largely positive results: compared 2.2% stroke rate to historical cohort (6.3% assumed rate) led to a 65% RRR in stroke.



PLAATO system (eV3)

Table 4: Large, non-randomized studies on percutaneous LAA occlusion

Study	Device	Patients and follow-up	Procedure related complications	Major results
Ostermayer, 2009 (16)	PLAATO	111 patients (113 procedures) Mean follow-up: 9.8 months	9 SAE's: Cardiac tamponade (2) Pleural effusion (1) Dyspnea requiring intubation (1) Pericardial effusion (2) Left-sided hemothorax (1) Deep vein thrombosis (1) Brachial plexus palsy (1)	Implantation success: 95.6% CHADS ₂ predicted stroke rate: 6.3% per year, observed stroke rate: 2.2% per year.
Block, 2009 (32)	PLAATO	64 patients (65 procedures) 5 yrs follow-up	1 cardiac tamponade requiring surgery	Implantation success: 93.85% CHADS ₂ predicted stroke rate: 6.6% per year, observed stroke rate: 3.8% per year.
Bayard, 2010 (18)	PLAATO	180 patients 129 documented patients months	8 procedure related MAE's: Cardiac tamponade (6) Patient death (2)	Implantation success: 85% CHADS ₂ predicted stroke rate: 6.6% per year, observed stroke rate: 2.3% per year.

PLAATO no longer available
(too many adverse events)

Device Intended Use

The AMPLATZER™ Cardiac Plug (ACP) is a percutaneous transcatheter device intended to prevent thrombus embolization from the left atrial appendage (LAA) in subjects who have nonvalvular atrial fibrillation.



AMPLATZER™ Cardiac Plug
© AGA Medical Corporation

CAUTION – Investigational device. Limited by Federal (or United States) law to investigational use.

Amplatzer Cardiac Plug (AGA/St. Jude Medical)

Amplatzer Cardiac Plug (AGA/St. Jude Medical)

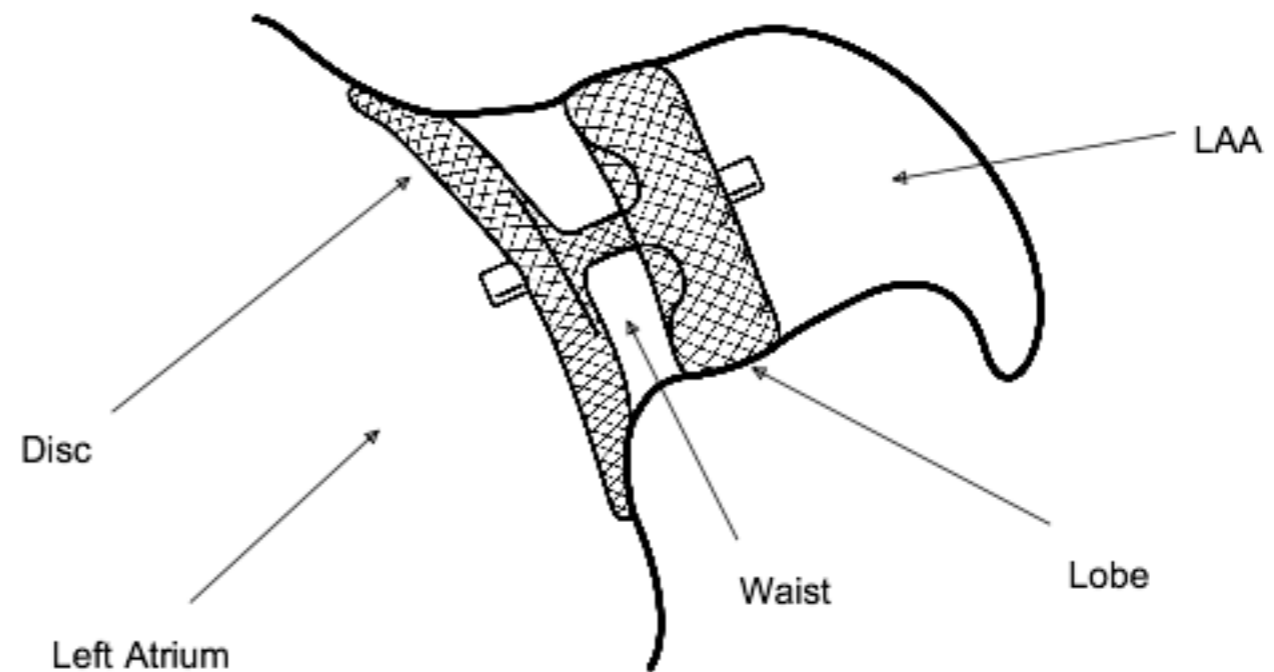
Self-expanding
nitinol mesh

Distal lobe with
retaining hooks
(anchor)

Proximal disk
(cover, not
permeable)

Device Description

The ACP device is delivered transseptally via delivery sheath into the left atrium (LA) and to the LAA



Amplatzer Cardiac Plug (AGA/St. Jude Medical)

- Amplatzer septal occluder has been used for 15+ years, extensive success in PFO/ASD closure
- Amplatzer cardiac plug (ACP) was specifically designed for LAA occlusion.
- Initial experience in EU: 143 pts; 96% successful implant; 7% SAE rate (5 tamponade, 2 embolization, 3 strokes).
- No warfarin. 1 month clopidogrel, 6 month ASA
- CE Mark 2008. 1,200+ procedures performed worldwide. Currently in phase 1 trial in US.



Watchman

(Atritech/Boston Scientific)

Caution: In the United States, WATCHMAN is an investigational device limited by Federal law and investigational use only. Not for sale in the US.

Watchman Components



9 months post implant

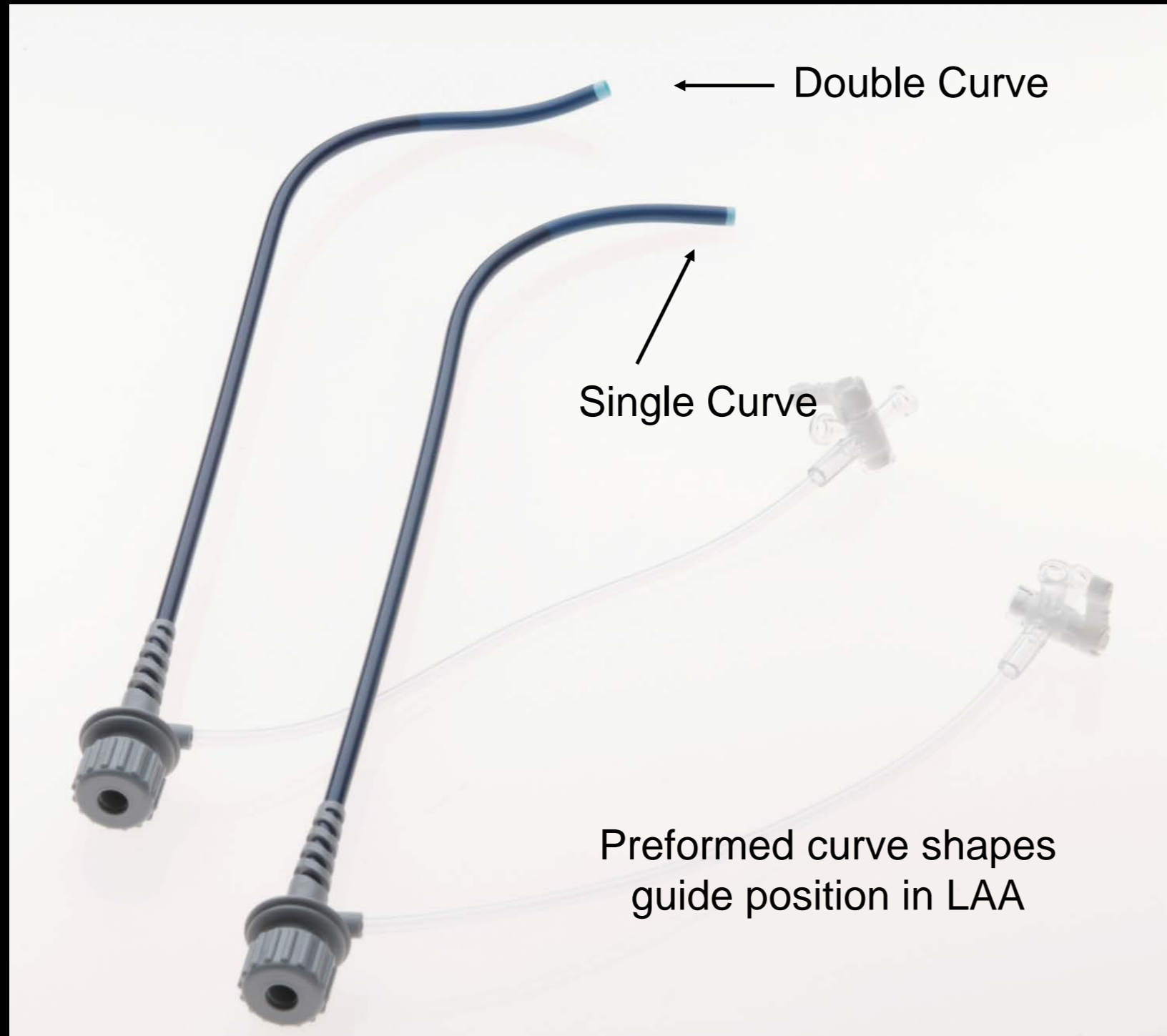
Frame: Nitinol structure

- Available sizes:
 - 21, 24, 27, 30, 33 mm (diameter)
 - 10 Fixation barbs around device perimeter engage LAA tissue
 - Contour shape accommodates most LAA anatomy

Fabric Cap: (PET) Fabric Polyethyl terephthalate

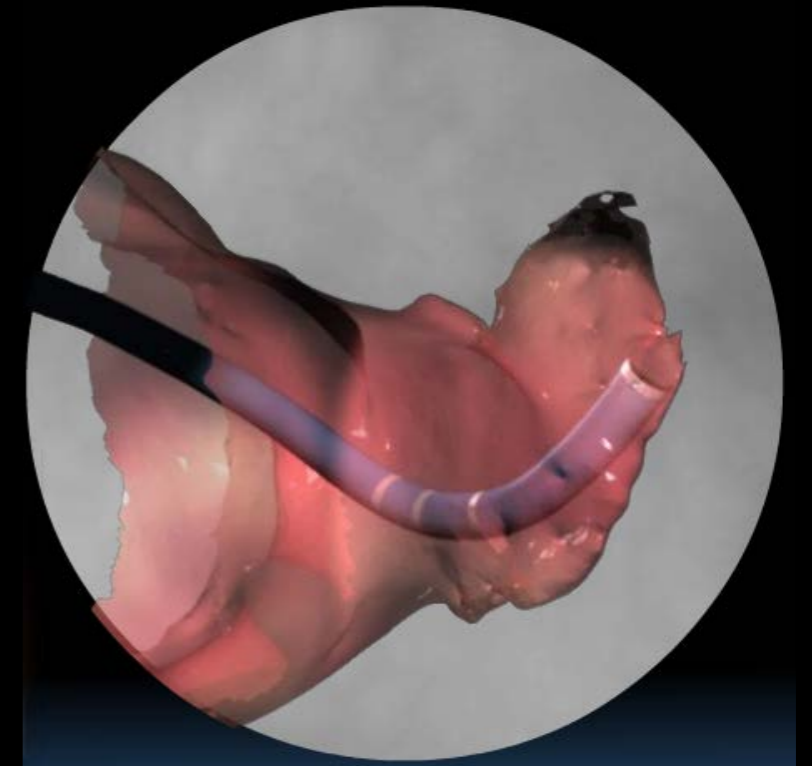
- Prevents harmful emboli from exiting during the healing process
- 160 micron filter

Watchman Delivery System



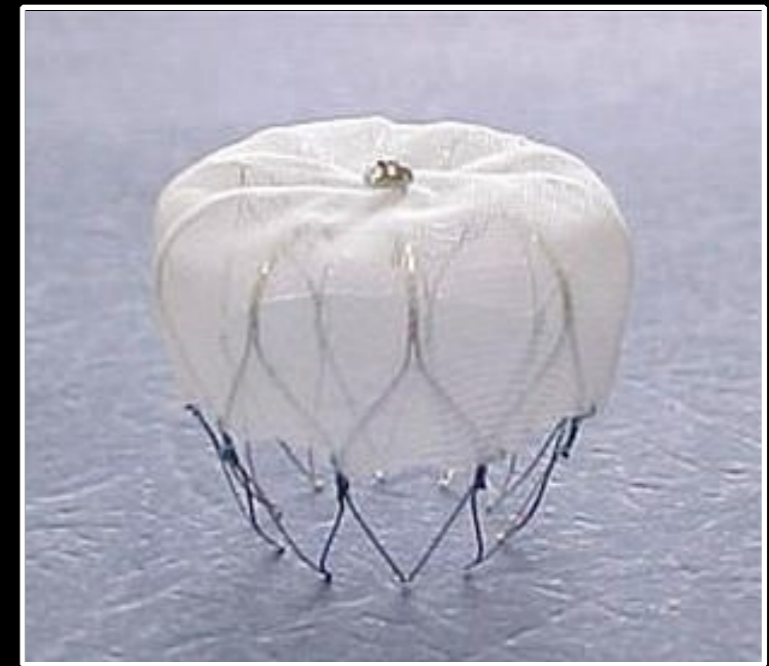
Transseptal Access System

- Double or Single Curve styles
- 14F OD (4.7 mm), 12F ID
- 75 cm working length



➤ Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial

David R Holmes, Vivek Y Reddy, Zoltan G Turi, Shephal K Doshi, Horst Sievert, Maurice Buchbinder, Christopher M Mullin, Peter Sick, for the PROTECT AF Investigators*



Lancet 2009; 374: 534-42

707 subjects
Occluder was noninferior to warfarin, but higher adverse event rate.

	Intervention (n=463)	Control (n=244)
Serious pericardial effusion*	22 (4.8%)	0
Major bleeding†	16 (3.5%)	10 (4.1%)
Procedure-related ischaemic stroke	5 (1.1%)	0
Device embolisation	3 (0.6%)	0
Haemorrhagic stroke‡	1 (0.2%)	6 (2.5%)
Other§	2 (0.4%)	0

*Defined as the need for percutaneous or surgical drainage. †Major bleeding is defined as a bleeding event that required at least 2 units of packed red blood cells or surgery to correct. ‡Of the seven haemorrhagic strokes, six resulted in death (intervention group, n=1; control group, n=5). §An oesophageal tear and a procedure-related arrhythmia.

Table 3: Adverse events

	PROTECT AF ^{1,2}	CAP ²	ASAP ^{3,4}	PREVAIL
Control	Patients able to take warfarin		Warfarin contraindicated patients	Patients able to take warfarin
Primary Endpoint	All stroke, systemic embolism and cardiovascular death	All stroke, systemic embolism and cardiovascular death	All stroke, systemic embolism, and cardiovascular death	All stroke, systemic embolism and cardiovascular death
Mean age /CHADS	72 years/2.2	74years/2.4	72 years/2.8	74 years/2.6
Total Enrolled Subjects	707 randomized ¹ , 93 pts rolled in ²	460	150	461
Total Patients Implanted	542 ²	437	142	303
Implantation Success	89.5% ²	95.0%	94.7%	95.1%
Warfarin discontinuation at 45 days	86.6%	94.9%	No warfarin used	Pending full results
Stroke	Rate ratio 0.71 (0.35–1.64) [Hemorrhagic Stroke: 0.09 (0.00–0.45)]	Reduction in procedure related stroke vs PROTECT AF (<i>P</i> =0.04)	Decreased rate of stroke by 77% vs. expected rate per CHADS ₂ Score	Pending full results
Bleeding	HR 1.69 (1.01–3.19)	Reduction in pericardial effusions vs PROTECT AF (<i>P</i> =0.02)	Pericardial effusion with tamponade=2.0% Major bleeding=2.7%	Pending full results

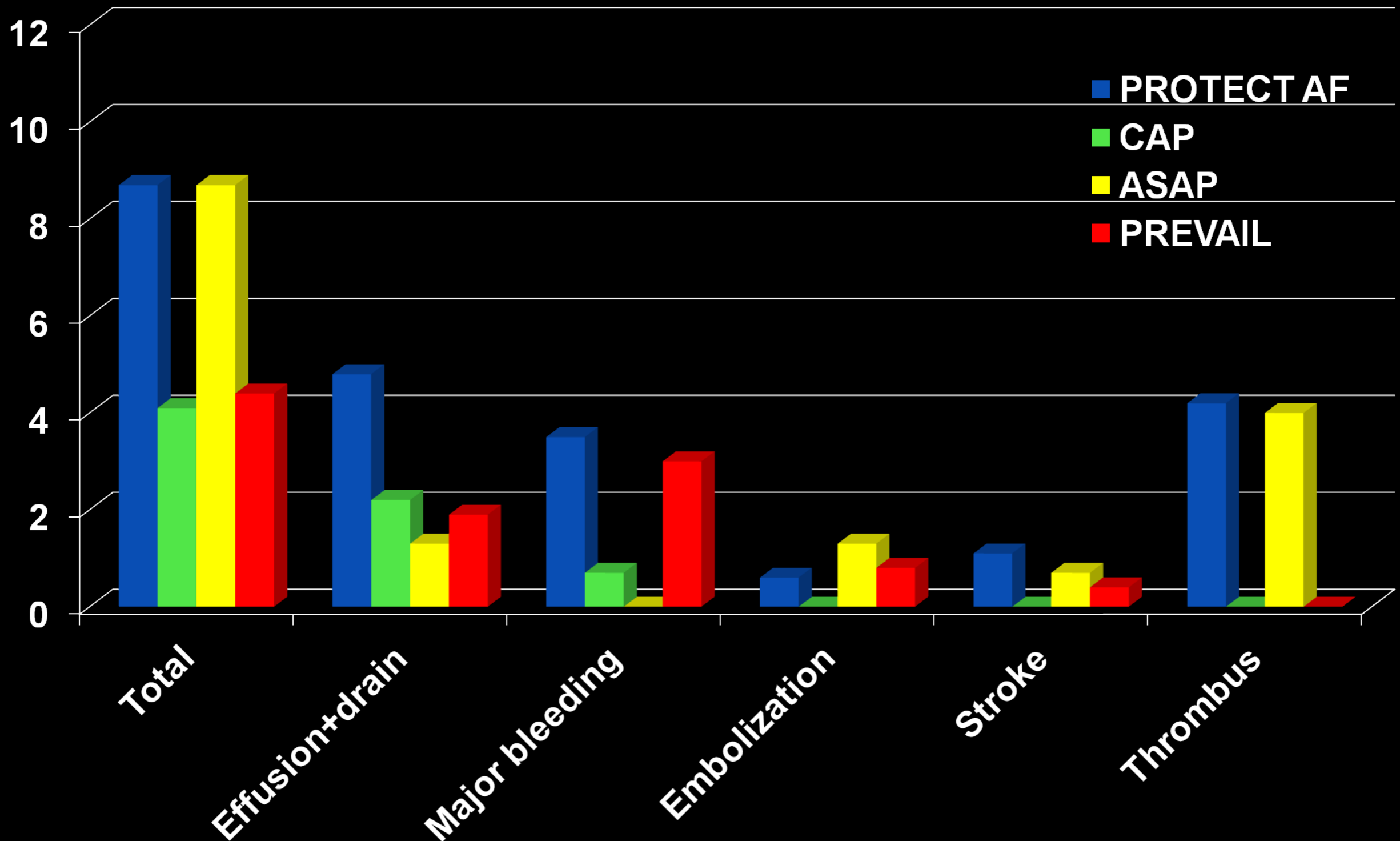
1. Holmes DR, Lancet 2009
2. Reddy VY, Circulation 2011
3. Sievert H, TCT 2011
4. Reddy VY, JACC 2013

Watchman

(Atritech/Boston Scientific)

- FDA denied approval in 2010 based on PROTECT-AF.
- CE Mark in 2005. It is approved in 50 countries.
- To date, over 5000 Watchmans (Watchmen?) implanted.
- PREVAIL study (using a "gentler" device) finished enrolling in July 2012. 6 month follow up at ACC 2013.

Safety Events Related to Implant

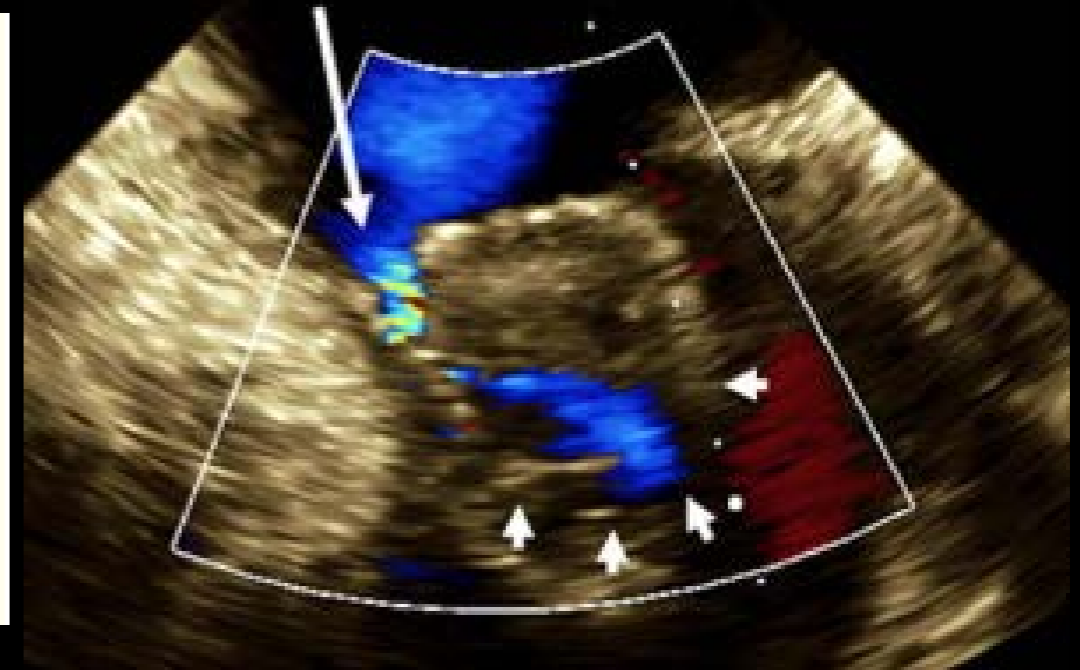


The Clinical Impact of Incomplete Left Atrial Appendage Closure With the Watchman Device in Patients With Atrial Fibrillation

A PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) Substudy

Juan F. Viles-Gonzalez, MD,* Saibal Kar, MD,† Pamela Douglas, MD,‡ Srinivas Dukkipati, MD,* Ted Feldman, MD,§ Rodney Horton, MD,|| David Holmes, MD,¶ Vivek Y. Reddy, MD*

New York, New York; Los Angeles, California; Durham, North Carolina; Evanston, Illinois; Austin, Texas; and Rochester, Minnesota

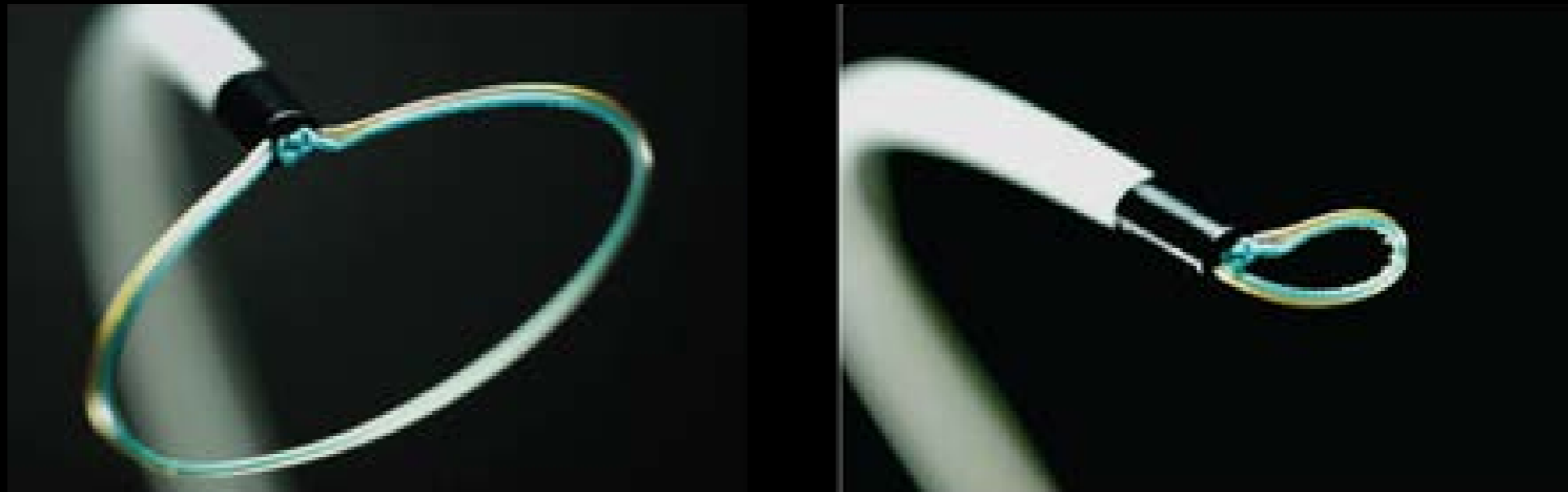


In this study, "closure" was defined as "< 5mm jet"
1/3 of patients had residual flow.
Stroke risk increases with greater residual flow.

Impact of residual peridevice flow on the primary thromboembolic end point in PROTECT-AF, hazard ratio (HR, 95% CI)

End point	HR (95% CI)
Minor peridevice vs no peridevice flow	0.85 (0.11-6.40)
Moderate peridevice vs no peridevice flow	0.83 (0.33-2.09)
Major peridevice vs no peridevice flow	0.48 (0.11-2.09)
Any peridevice flow and continued warfarin (vs no peridevice flow and discontinued warfarin)	0.63 (0.14-2.71)

Lariat LAA Excluder (SentreHEART)



Combination of epicardial and endocardial access

Magnet-tipped guidewires

40-mm pretied radioopaque suture loop to ligate the LAA
from the epicardial surface

Lariat LAA Excluder (SentreHEART)

- FDA Approved in 2009 to "facilitate soft tissue approximation"
- To date, over 2000 patients with LAA ligation
- Requires particular LAA anatomy, chest wall, no prior cardiac surgery

Tips from our experience with Lariat

- Choose appropriate patients and don't minimize the potential risk
- Aim true: epicardial angle is important
- Use up-to-date imaging: atria (and appendages) can dilate over time
- Pericarditis: expect to manage pain afterward
- Anticipate fluid retention, faster AF, mild hypotension

Summary Slide: My Two Cents

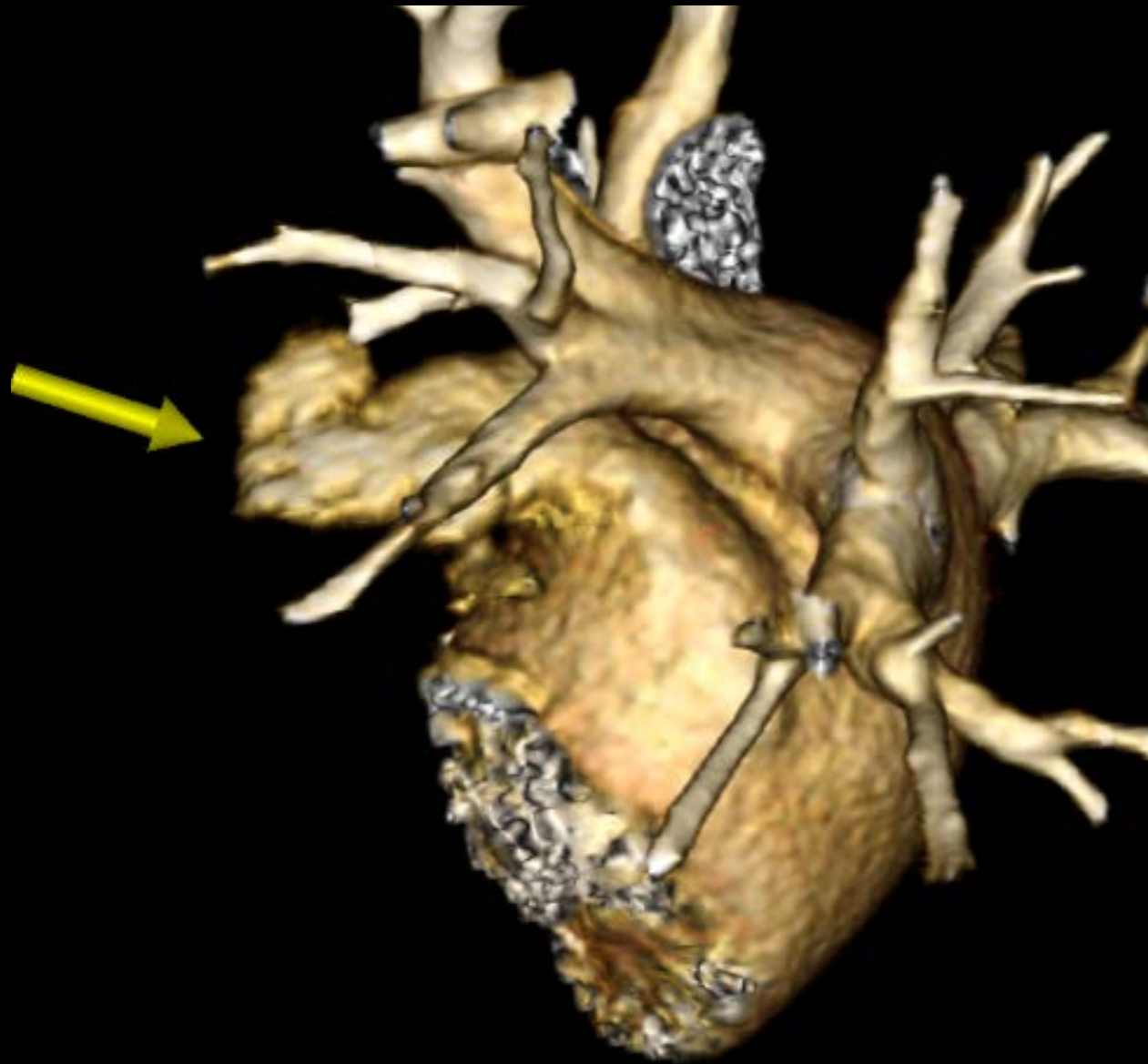
- I wish we had more data.
- Is LAA closure worth doing? I think so, especially for patients at high risks for stroke.
- When safety profile improves, I suspect we'll be offering this to an expanding population.
- Having options for LAA closure allows a personalized approach based on favorable anatomy or previous cardiac surgery

Heart & Vascular Center



NATIONAL LEADERS IN MEDICINE

Lariat LAA Excluder (SentreHEART)



Before



3 Months After

Lariat LAA Excluder (SentreHEART)

