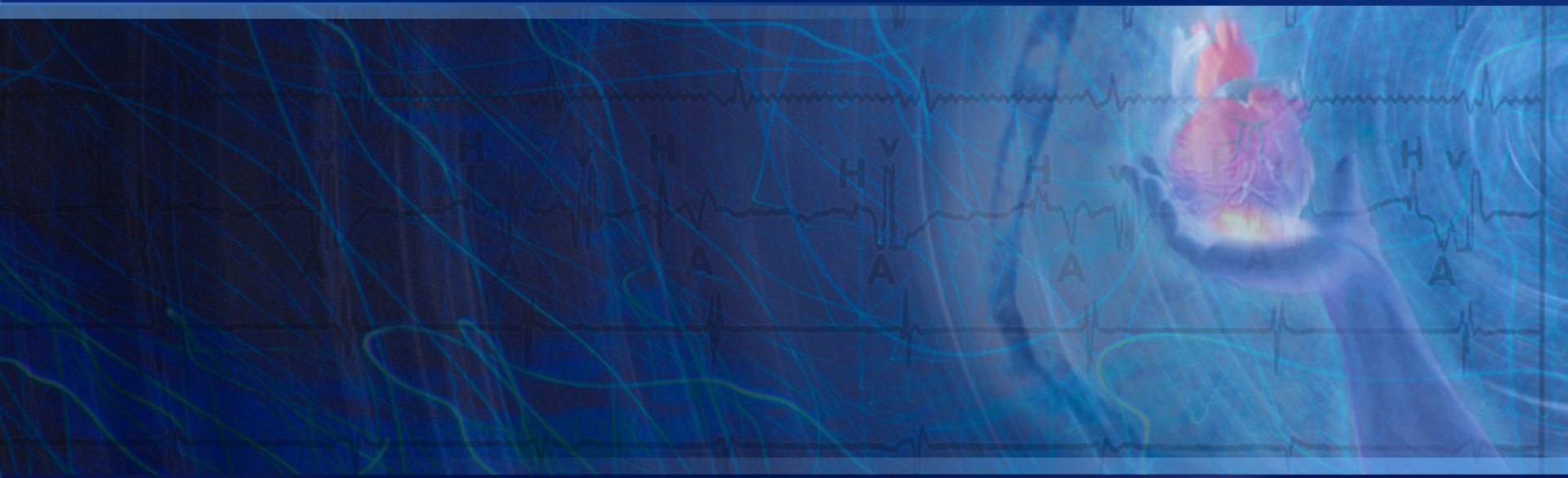
LAA and Stroke Prevention



Samuel J. Asirvatham, MD
Professor of Medicine, Professor of Pediatrics
Program Director Cardiac Electrophysiology;
Vice Chair – Innovations Mayo Clinic

Turin, October 26, 2012

Disclosure

I receive royalties for work licensed through Mayo Clinic to a privately held company for contributions related to the use of nerve signal modulation to treat central, autonomic, and peripheral nervous system disorders, including pain. Mayo Clinic receives royalties and owns equity in this company. The company does not currently license or manufacture any drug or device in the medical field.

Co-patent holder for technique to minimize coagulum formation during radiofrequency ablation

Products or techniques related to the above disclosures are not being discussed in this presentation.

Pertains to inventions/startup companies that include Nevro, Aegis, and the Phoenix Corp.

Honoraria/Speakers:	**Consulting:**
Abiomed	**Sanofi**
Biotronik	**Stereotaxis**
Blackwell Futura	
Boston Scientific	
Medtronic	
Sanofi-aventis	
Spectranetics	
St. Jude	

Appendage Ligation and AF Ablation

- Do they work?
- Additional risk
- Additional Benefit
- Approach dependence
- Electrophysiology
- Additional procedures

AF and Stroke

- Risk of stroke 5 times greater in patients with AF than those without[1]
- When AF occurs in association with stroke
  - Higher mortality
  - Greater disability
  - Lower discharge rate home
  - 15% risk of stroke recurrence within 1 year, if untreated

[1]Wolf PA et al. Stroke 1991;22:983-8.
[2]Lip GYH, Edwards SJ. Thromb Res 2006;118:321-33.

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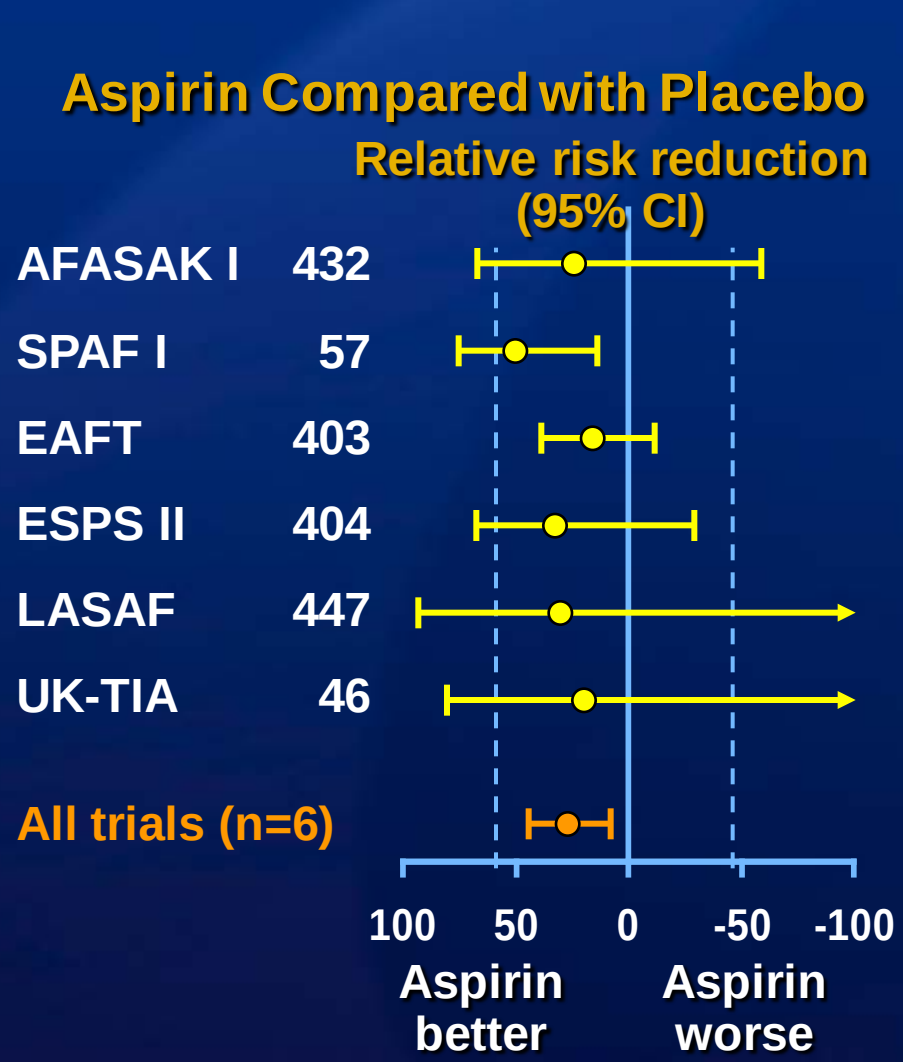
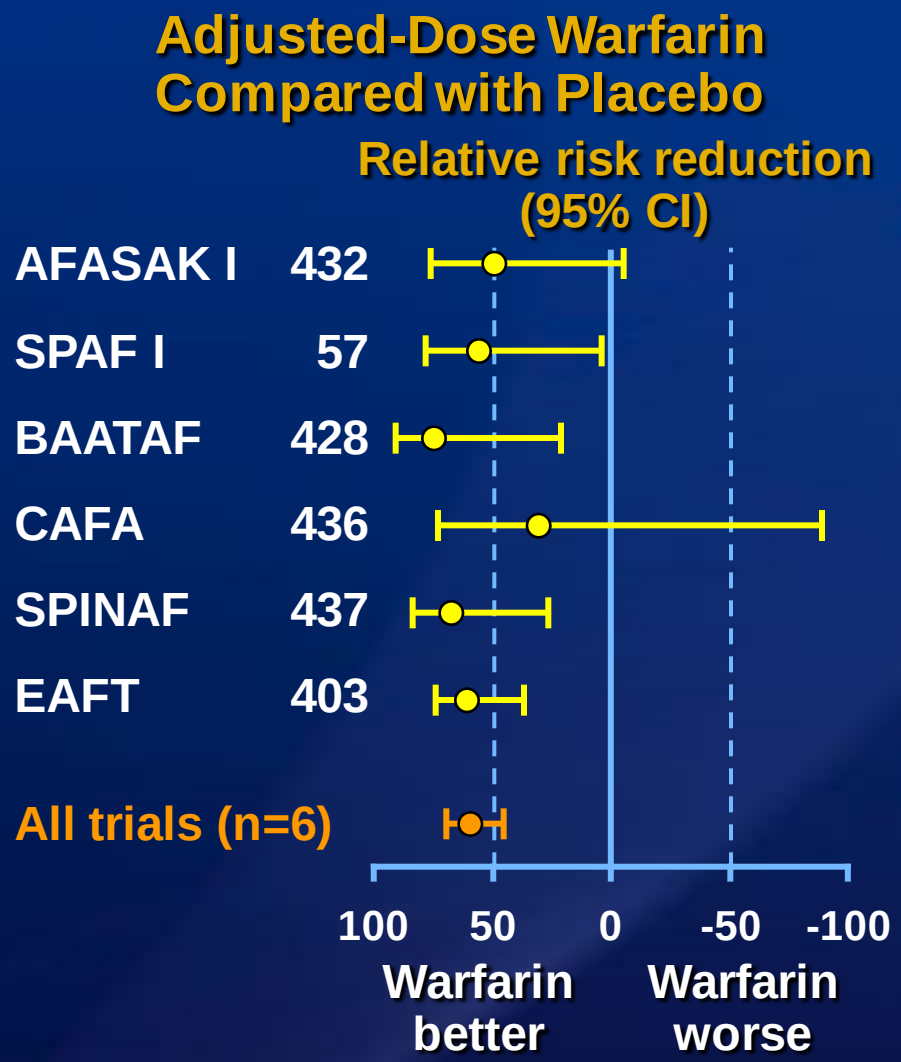
Stroke Prevention in Non-Rheumatic AF





Nondisabling > disabling
More effective with HTN/DM

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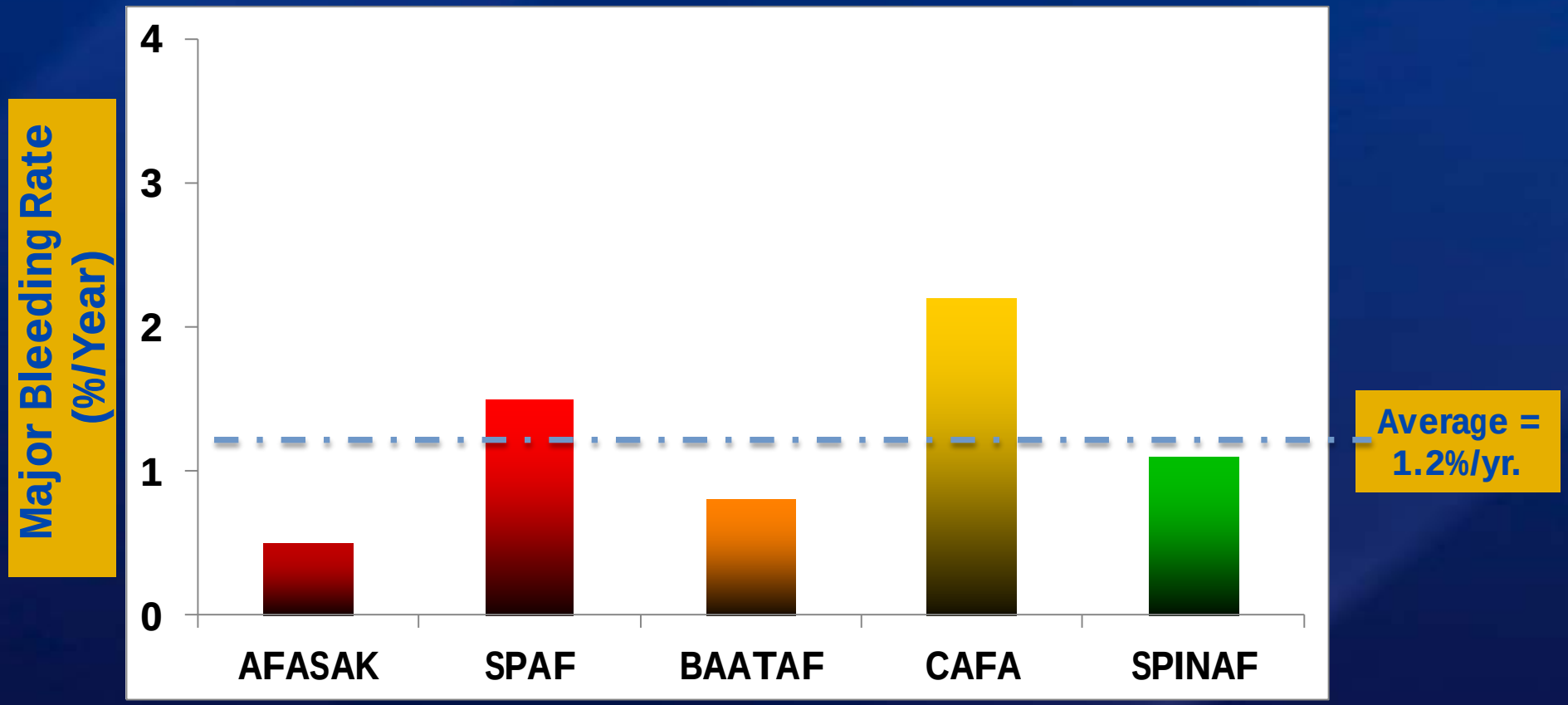
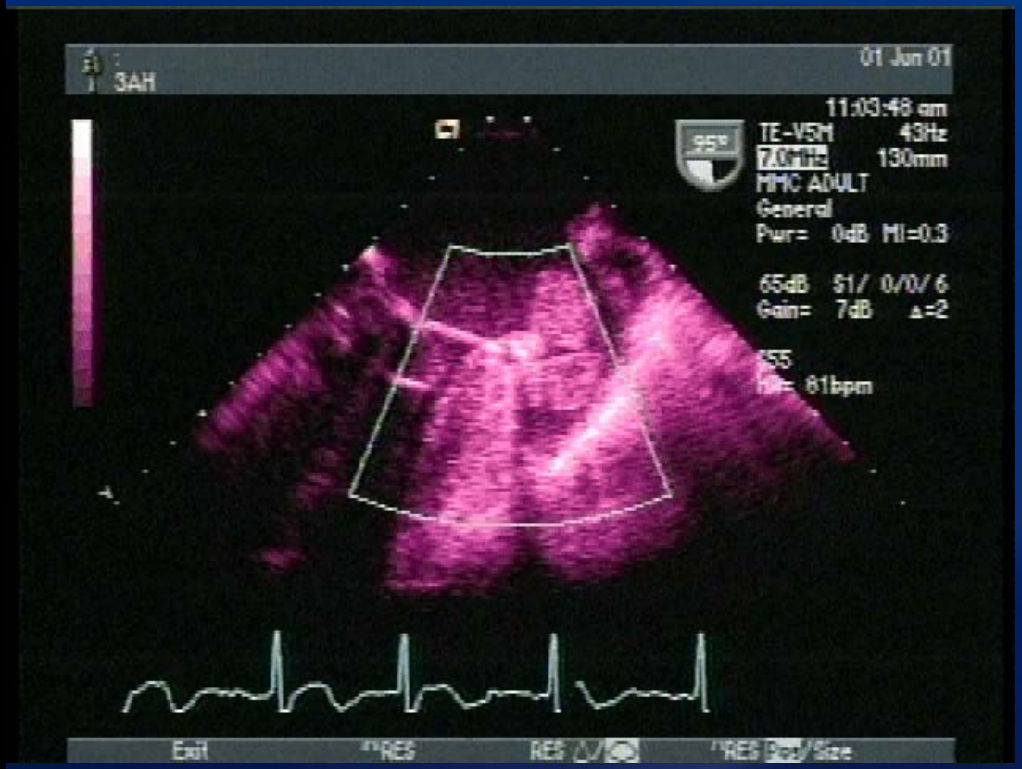
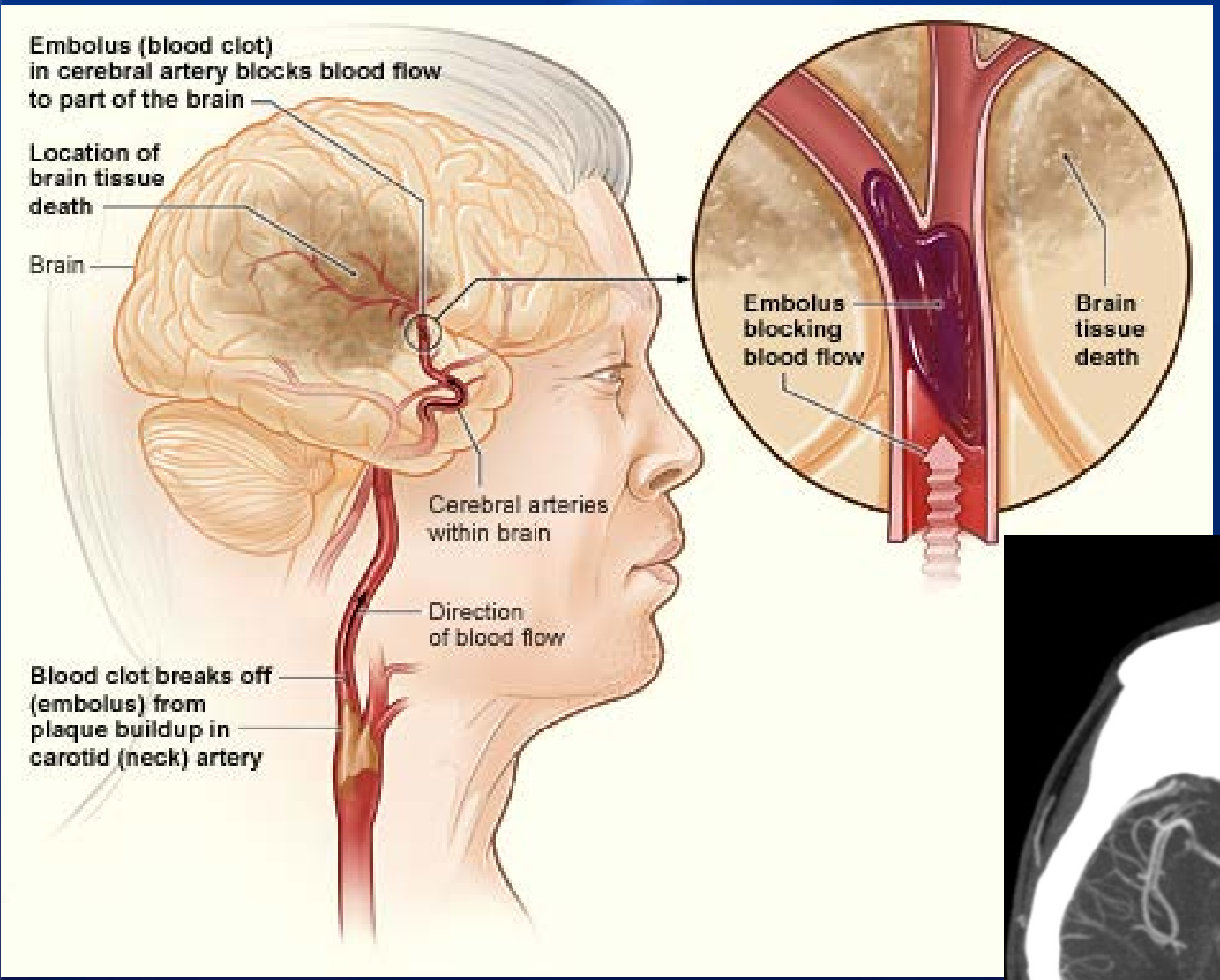
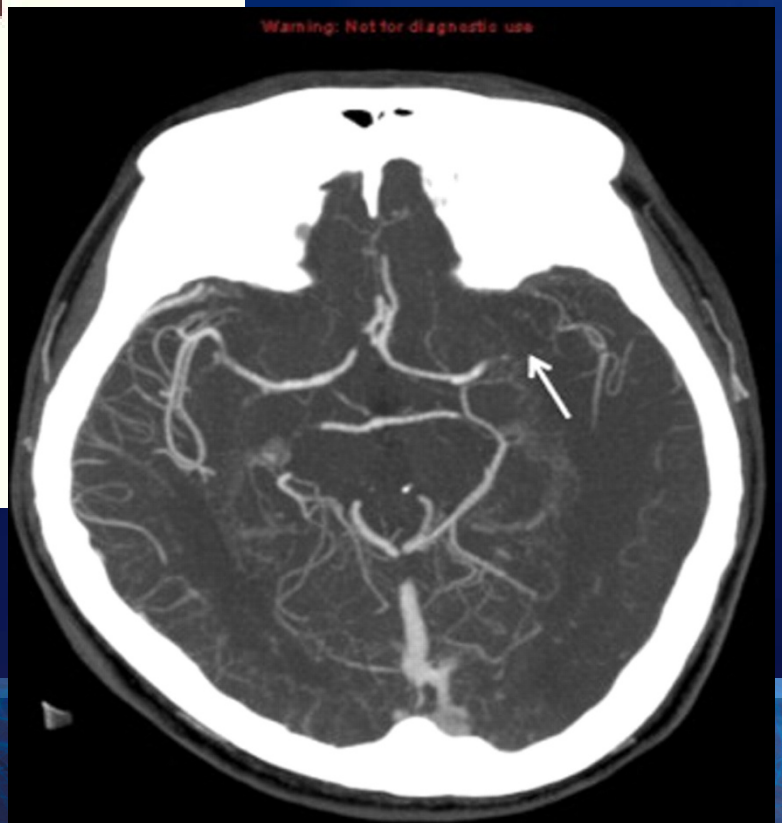
Annual Rates of Major Hemorrhage During Anticoagulation



Fuster V et al.J Am Coll Cardiol 2011;57:e101-e198.

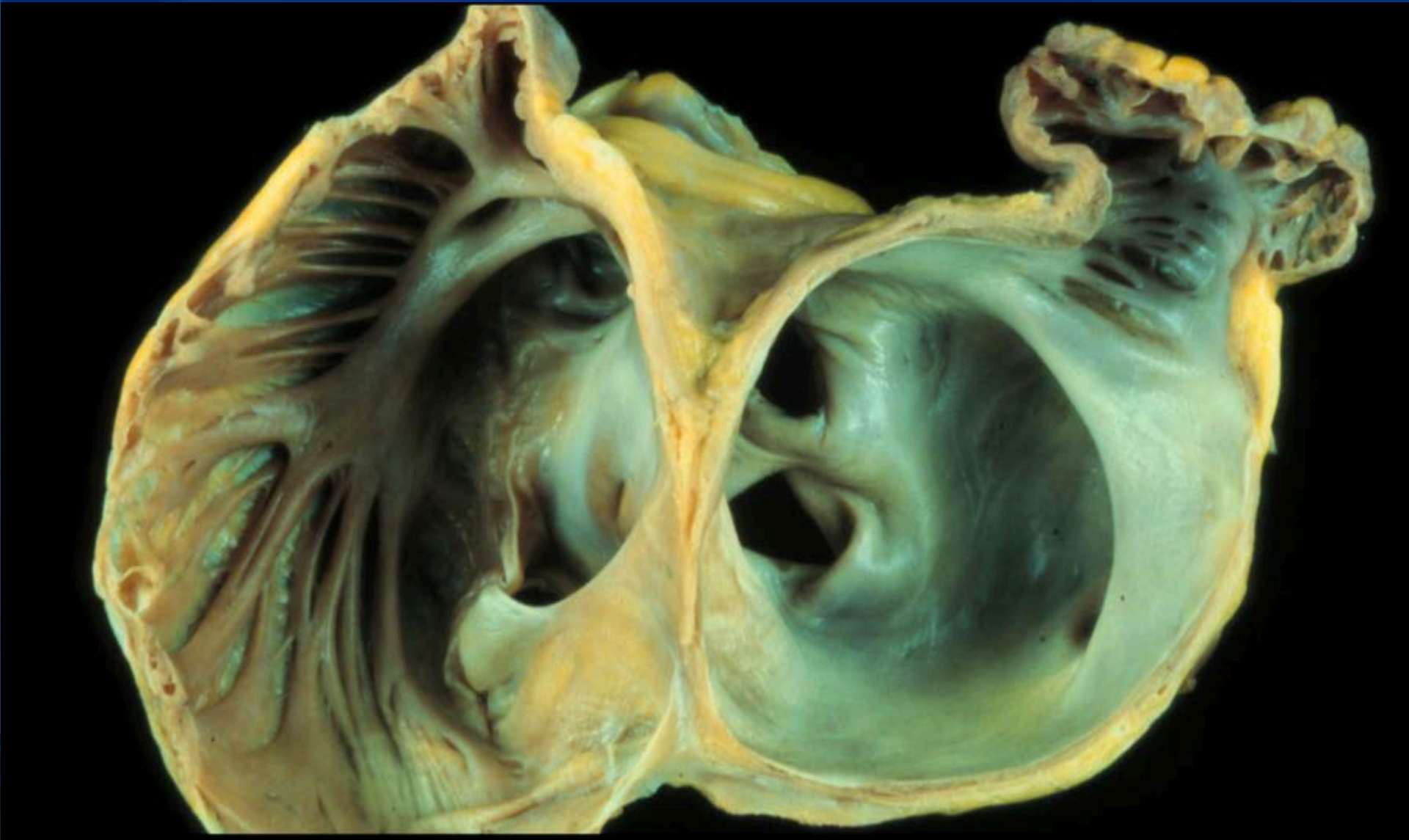




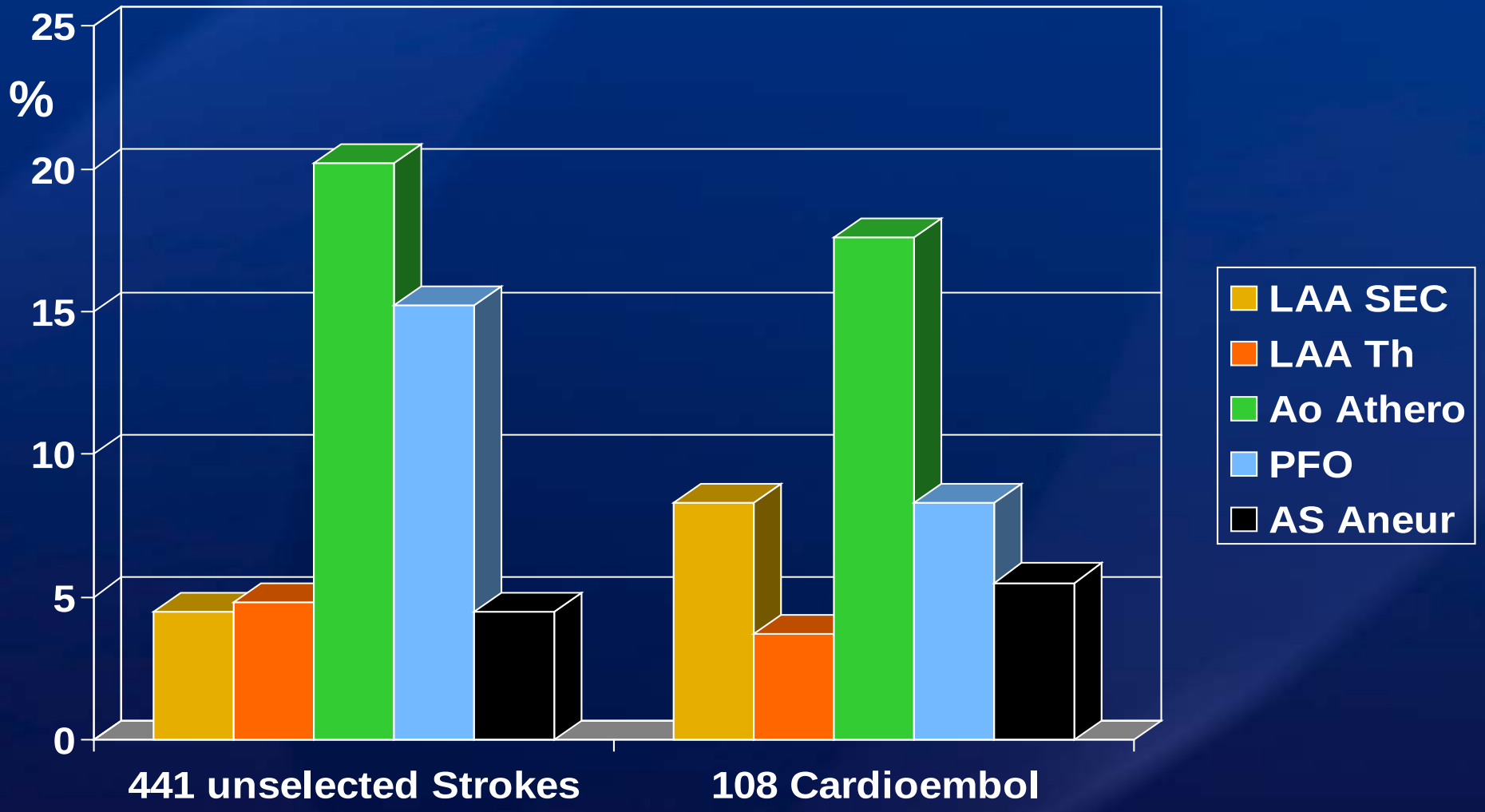


White CJ et al J Am Coll Cardiol 2011;58:101-16.

Since the AF risk factors also cause atherosclerosis, how important is the LAA for stroke in AF?



Stroke: TEE findings for source of Embolism



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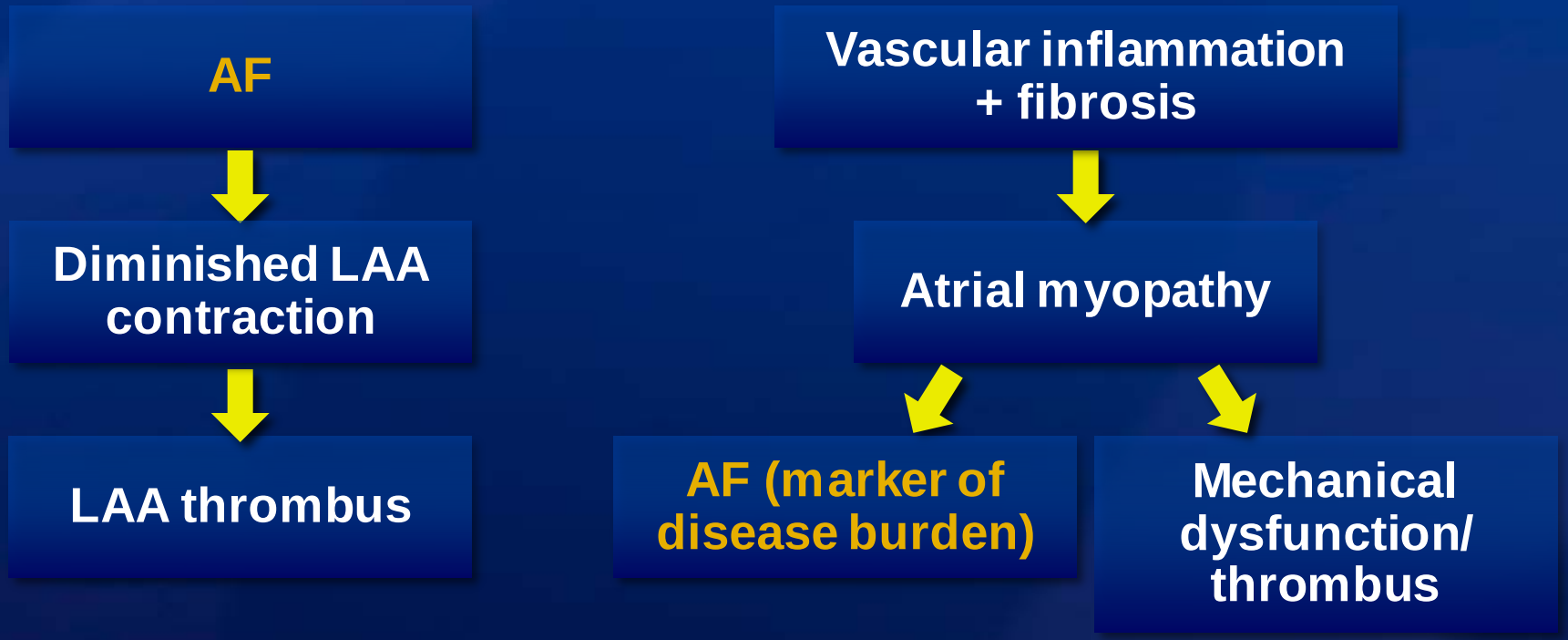
Strandberg et al
JNNP 2002;73:29

Sorescu et al
Am J Med Sci 2003;326:31

Association Between AF and Stroke

Mechanism



Implications

- AF precedes CVA
- Control of AF may prevent CVA
- LAA closure prevents CVA
- AF burden predicts risk
- No temporal association between AF and stroke
- Role of LAA depends on which tissue affected

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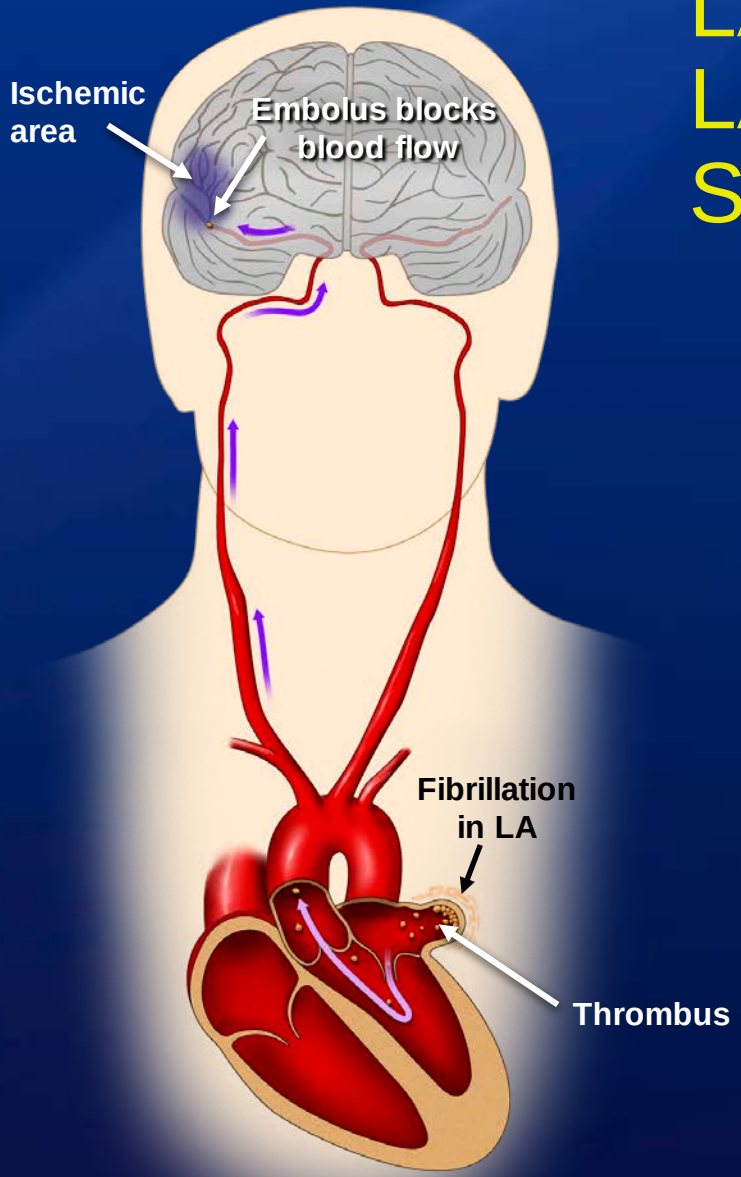
LAA-Dependent and LAA-Independent Stroke in AF

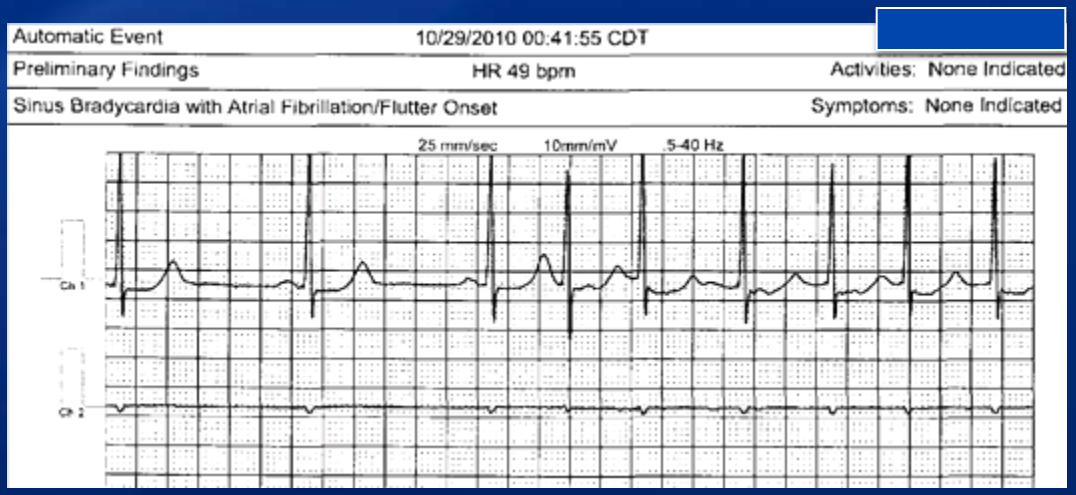


LAA independent-arch, carotid, intracerebral → **Aspirin sensitive**

LAA dependent → **Warfarin/ anticoagulant sensitive**

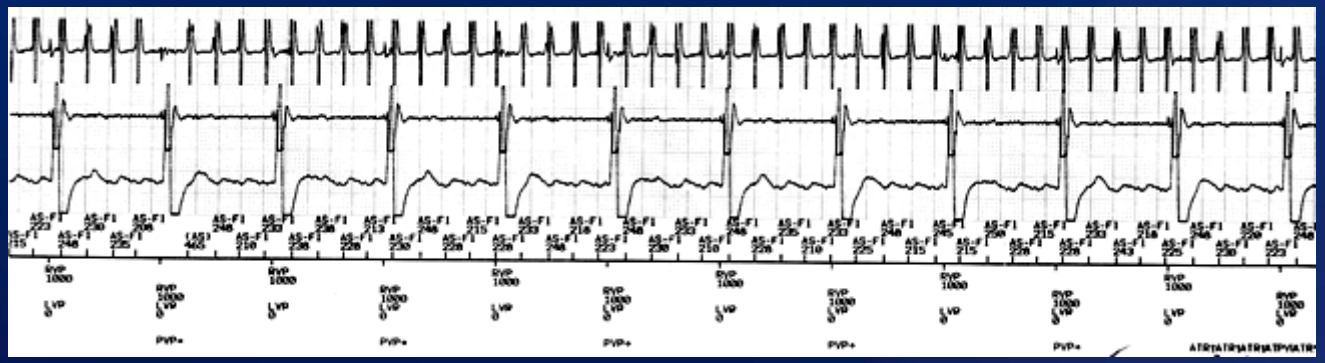
Figure 3

A.



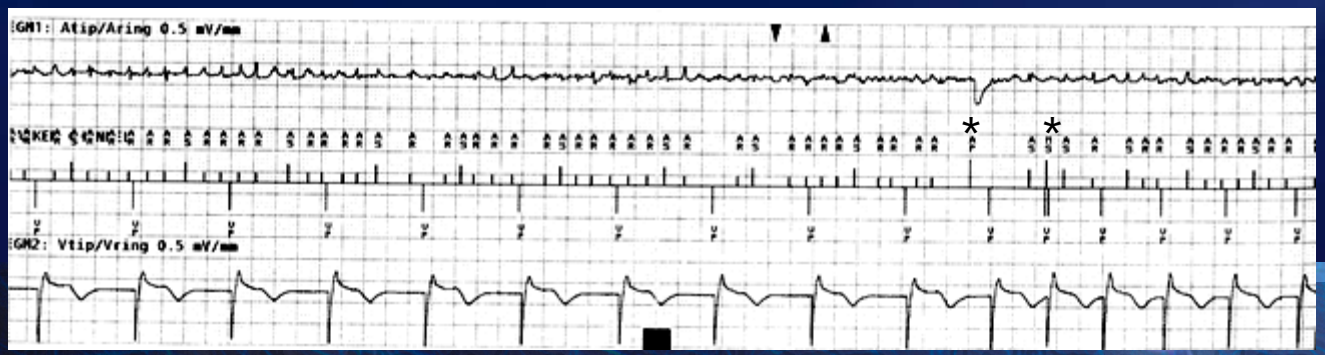
Duration: 7 sec

B.



Atrial rate: 270 bpm

C.



Atrial rate: 350 bpm

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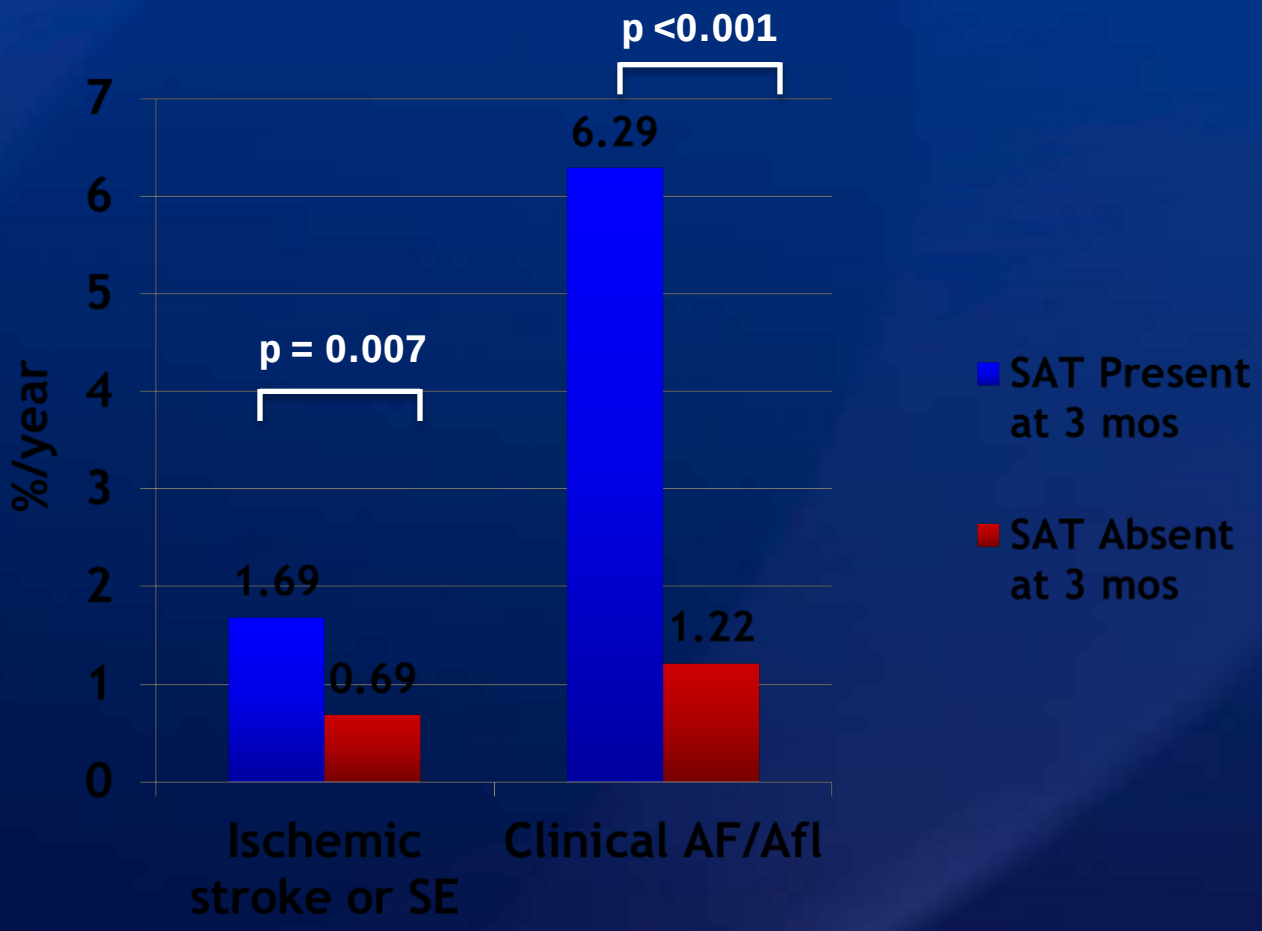
ASSERT: Subclinical AF and Stroke

- Subclinical atrial tachyarrythmias (SAT) detected in 10.1% at 3 mos
- SATs independently associated with 2.5-fold increased risk of ischemic stroke/SE after adjustment (p=0.008)
- Risk independent of other risk factors for stroke and of presence of clinical AF



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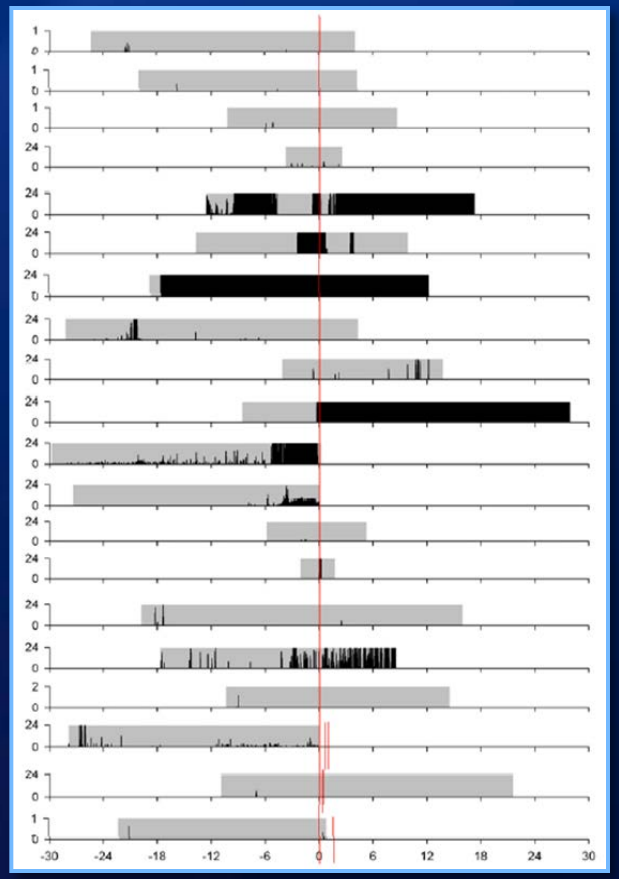
Healey JS et al. N Eng J Med 2012;366:120-9.

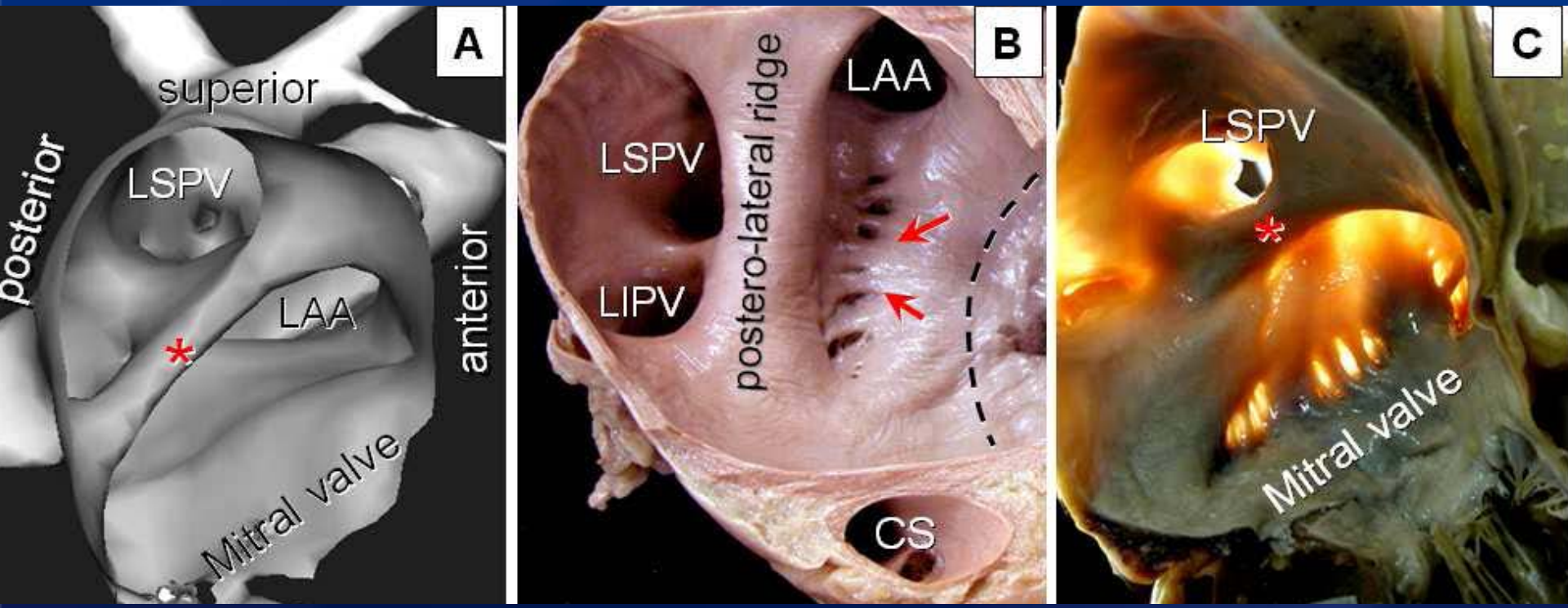
Temporal Relationship Between AF and Stroke



Patient #	$CHADS_2$ score	Baseline Antithrombotic therapy
1	2	Therapy
2	3	ASA
3	6	None
4	5	ASA
5	1	OAC
6	4	ASA
7	2	ASA
8	1	OAC/ASA
9	1	OAC
10	3	ASA
11	4	OAC/ASA
12	5	ASA
13	2	None
14	2	None
15	3	ASA
16	3	None
17	3	OAC/ASA
18	4	OAC/ASA
19	2	ASA
20	2	None

The majority of CVE/SE did not occur proximate to AT/AF episodes

Proud et al: HRJ 2011; 8:1416-1423



What have we learned from TEE ?

- We do not see often a clot
- When we see a clot it is in the LAA
- LAA has a strange shape prone to clots
- LAA low velocity predisposes to clots

What do we do about it?

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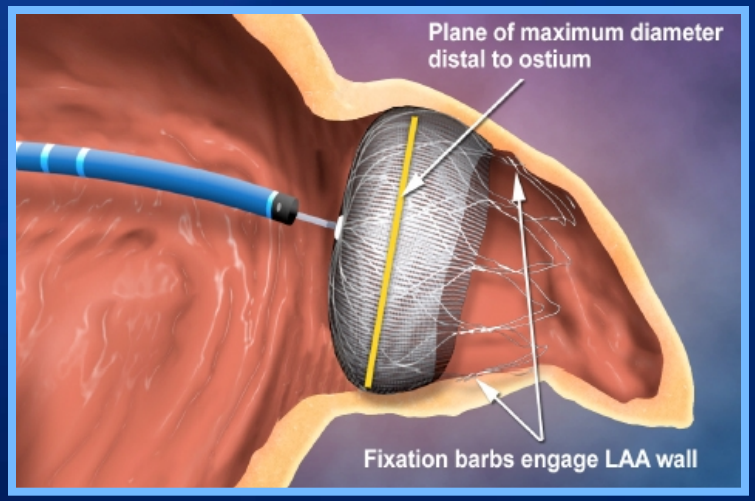
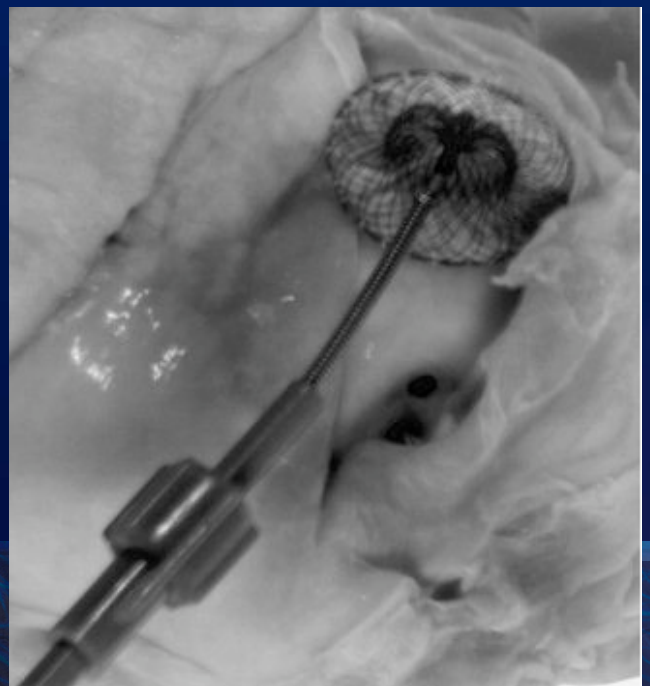
LAA Occlusion Devices





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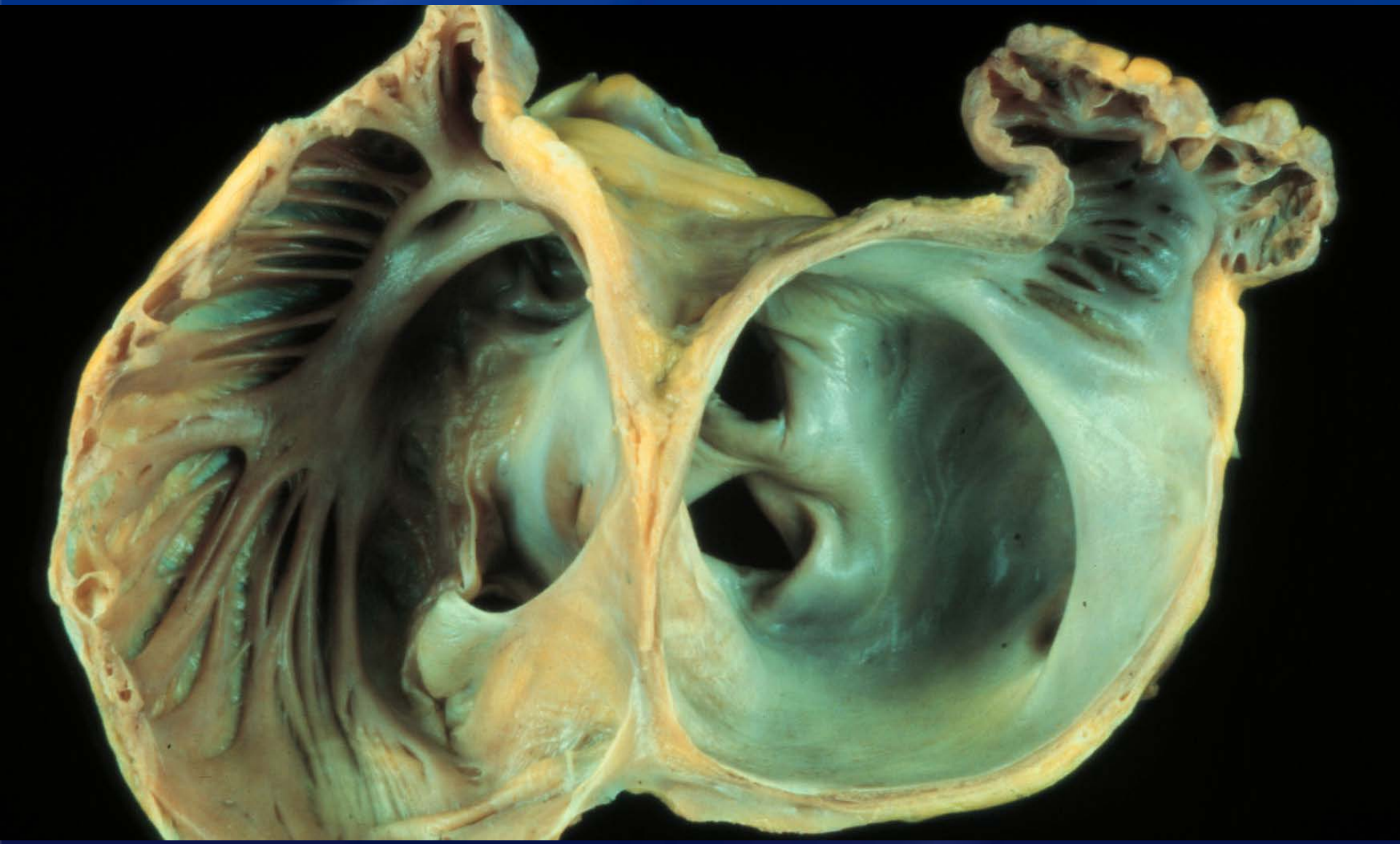
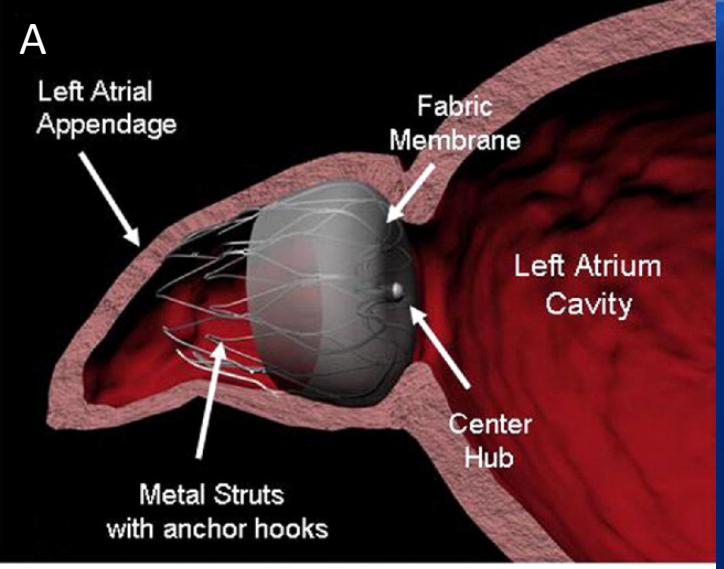
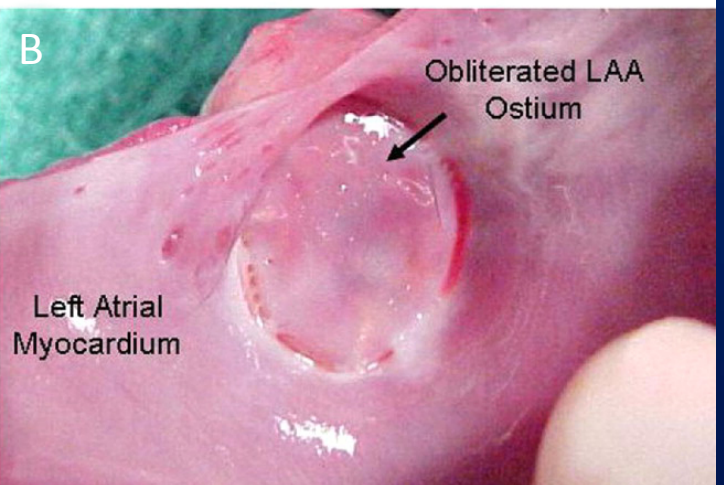
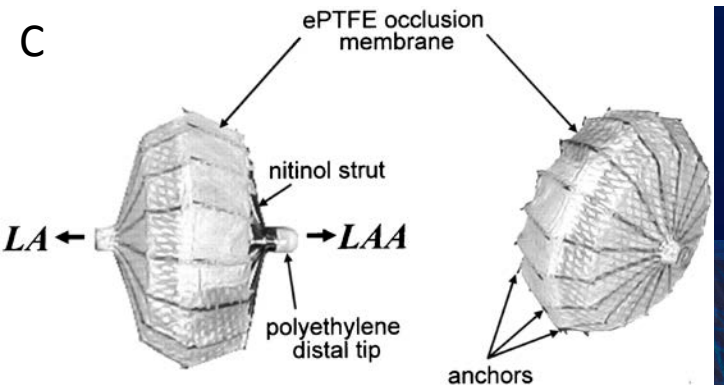
Catheter and Cardiovascular Interventions, Oct 2003

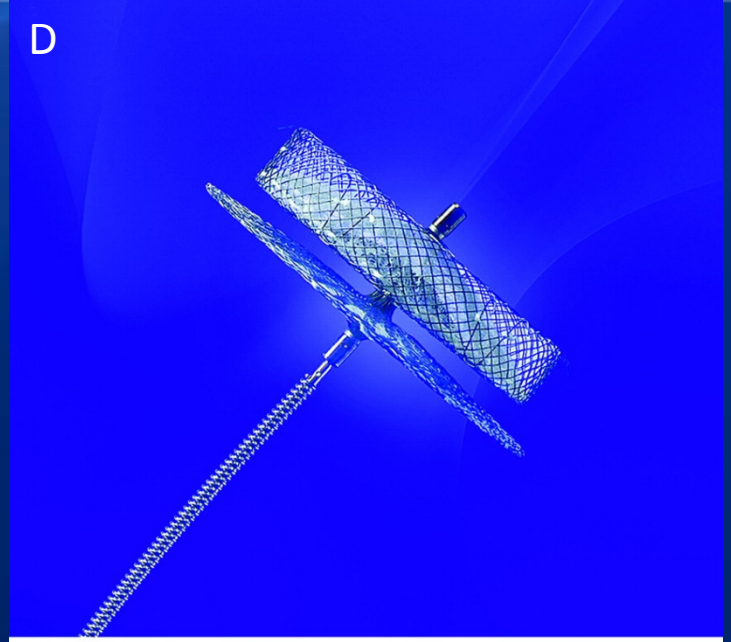
**DR Holmes JR. ACC March 2009

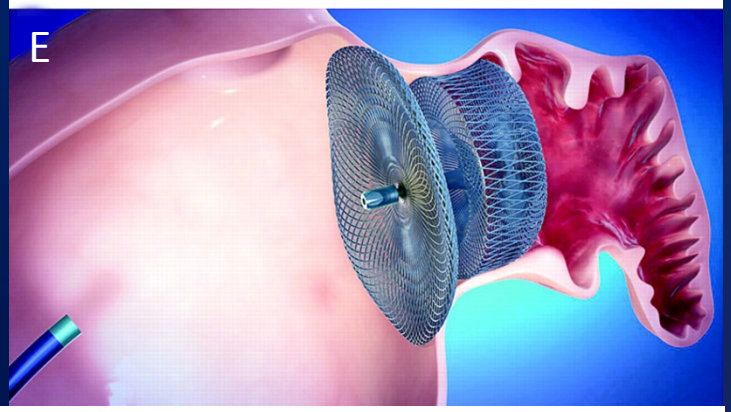








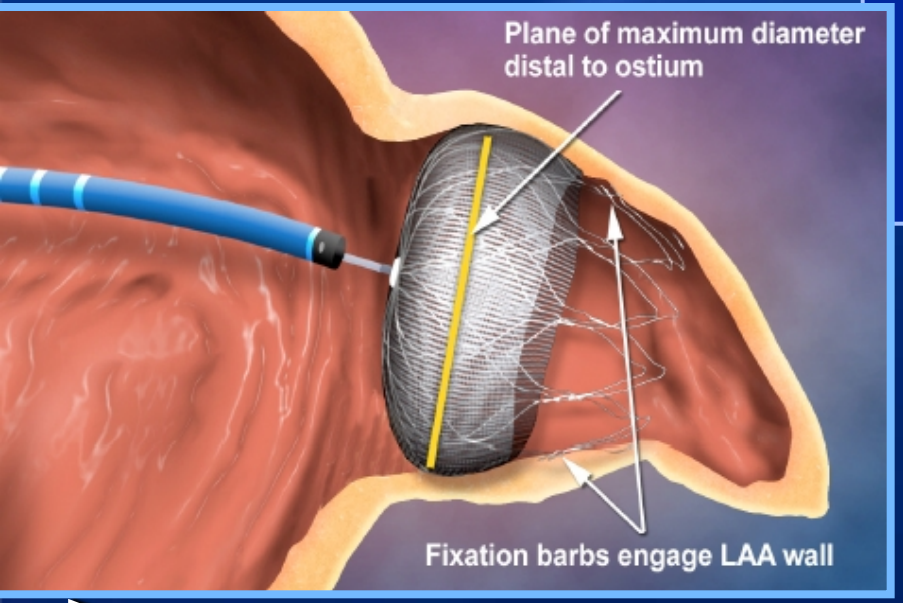




Device Therapy Targeting the Appendage

- Endovascular appendage occlusion
  - WATCHMAN Device
  - Other approaches
- Surgical appendage ligation
- Surgical appendage removal
- Minimally invasive bronchoscopic approaches
- Percutaneous subxiphoid approaches
- Pericardial appendage obliteration

Evidence that Warfarin Prevent stroke via LAA dependent mechanisms



Intent-to-Treat
All Stroke

Randomization allocation
(2 device:1 control)

Key Implication: Confirms Role of LAA in CVA

Holmes et all Lancet 2009

PROTECT AF Clinical Trial Design

Prospective, randomized study of WATCHMAN LAA Device vs. Long-term Warfarin Therapy

2:1 allocation ratio device to control

800 Patients enrolled from Feb 2005 to Jun 2008

- **Device Group (463)**
- **Control Group (244)**
- **Roll-in Group (93)**

59 Enrolling Centers (U.S. & Europe)

Follow-up Requirements

- **TEE follow-up at 45 days, 6 months and 1 year**
- **Clinical follow-up biannually up to 5 years**
- **Regular INR monitoring while taking warfarin**

Enrollment continues in Continued Access Registry

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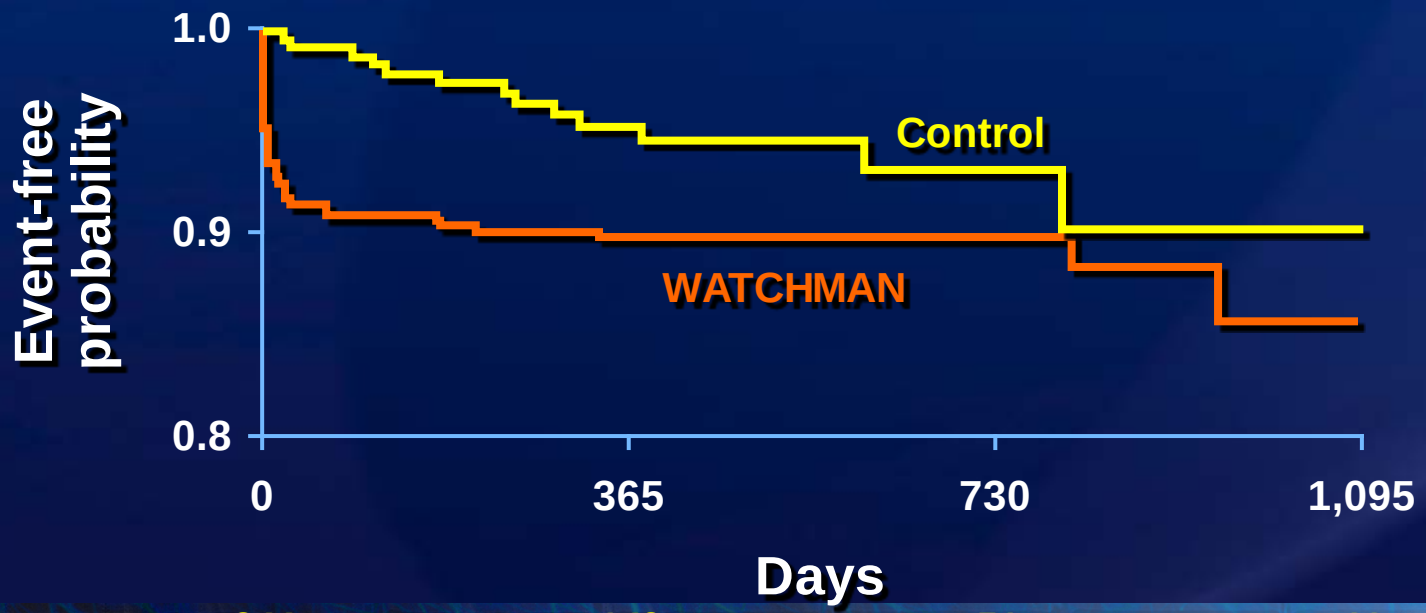
Intent-to-Treat
Primary Safety Results

Randomization allocation (2 device : 1 control)

Cohort	Device Events (no.)	Device Total pt-yr	Device Rate (95% CI)	Control Events (no.)	Control Total pt-yr	Control Rate (95% CI)	Rel. Risk (95% CI)
900 pt-yr	48	554.2	8.7 (6.4, 11.3)	13	312.0	4.2 (2.2, 6.7)	2.08 (1.18, 4.13)



**DR Holmes JR. ACC March 2009

3001664-1

Intent-to-Treat
Primary Safety Results

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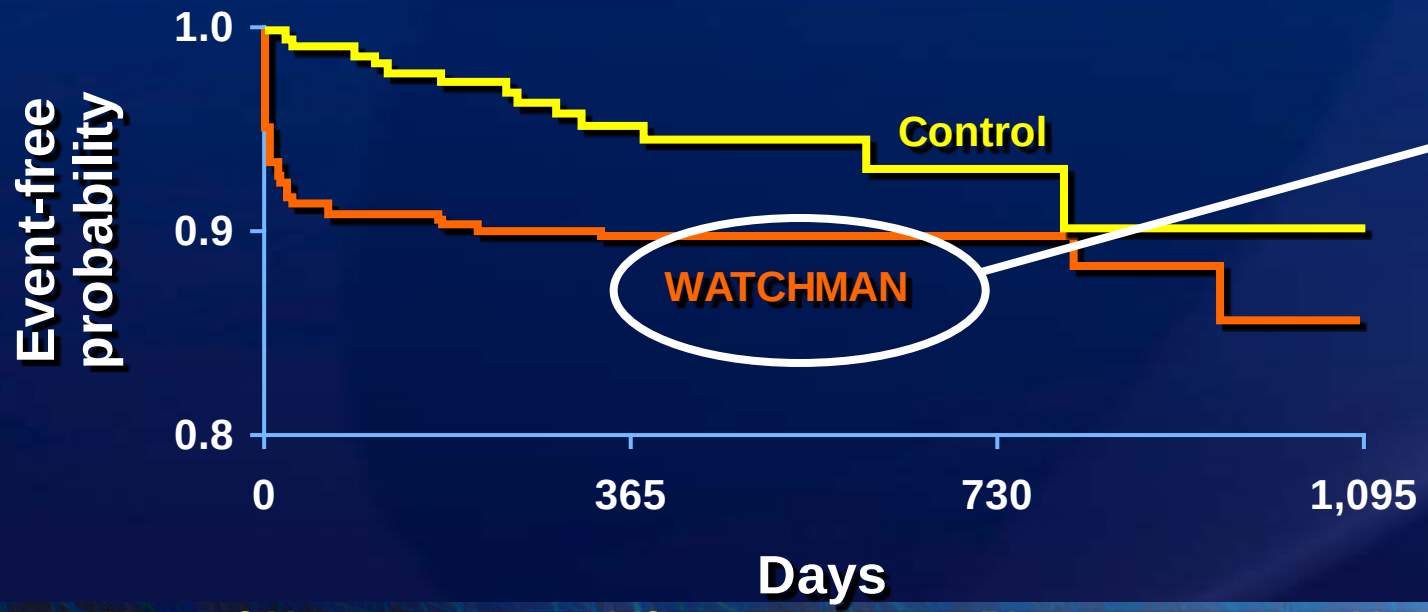


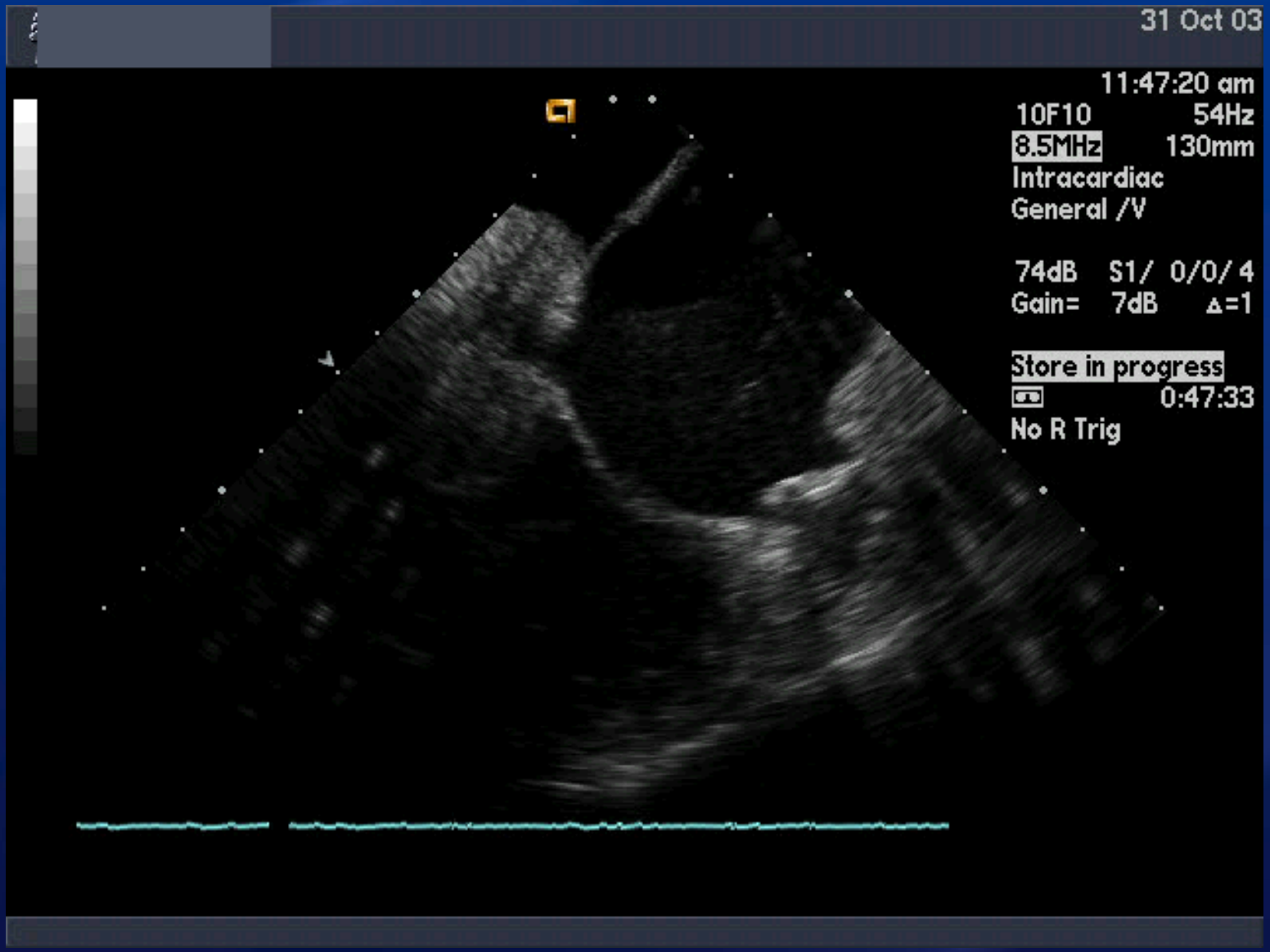
- Effusion
- Bleeding

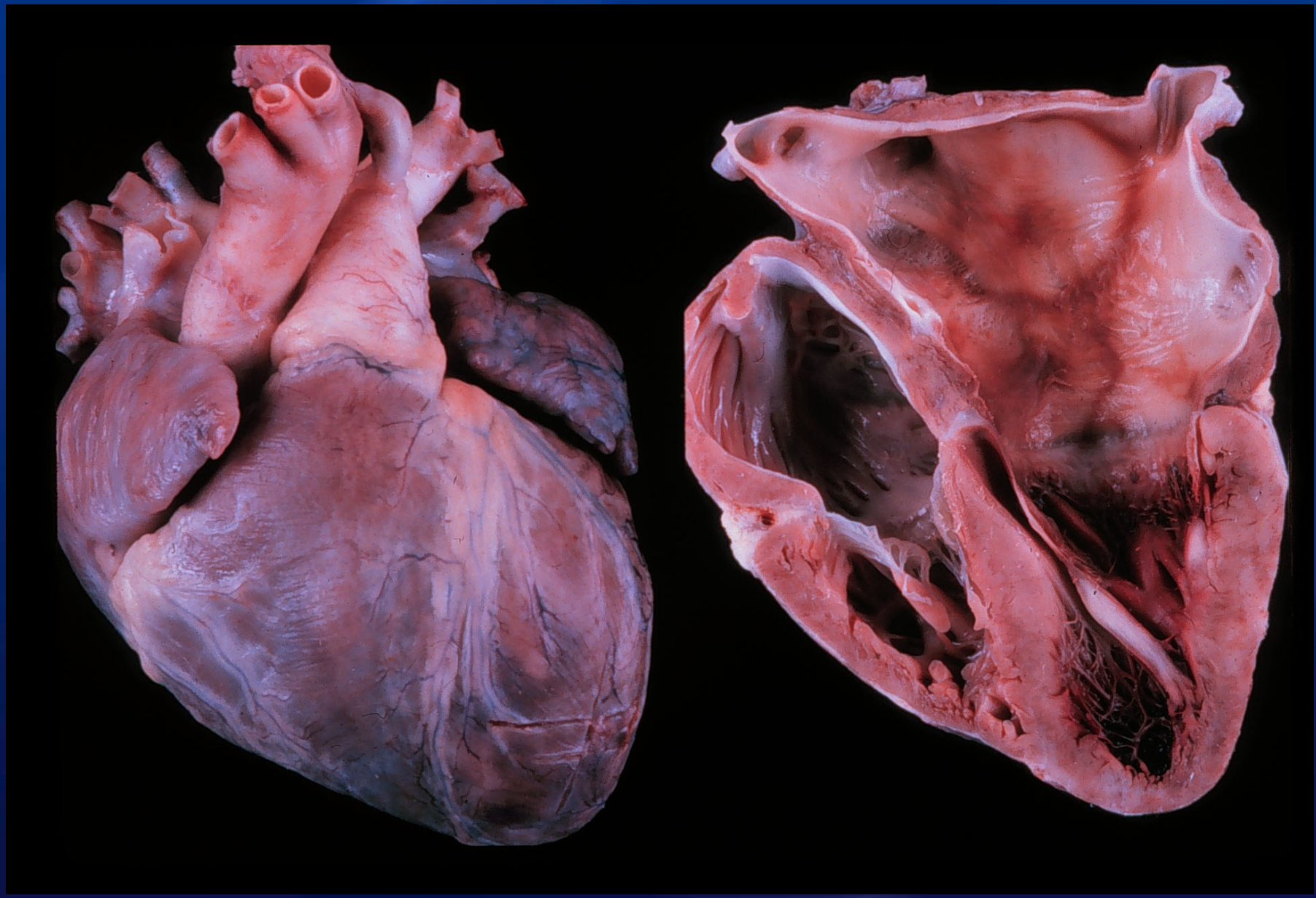
"Double Jeopardy" Since must be On coumadin

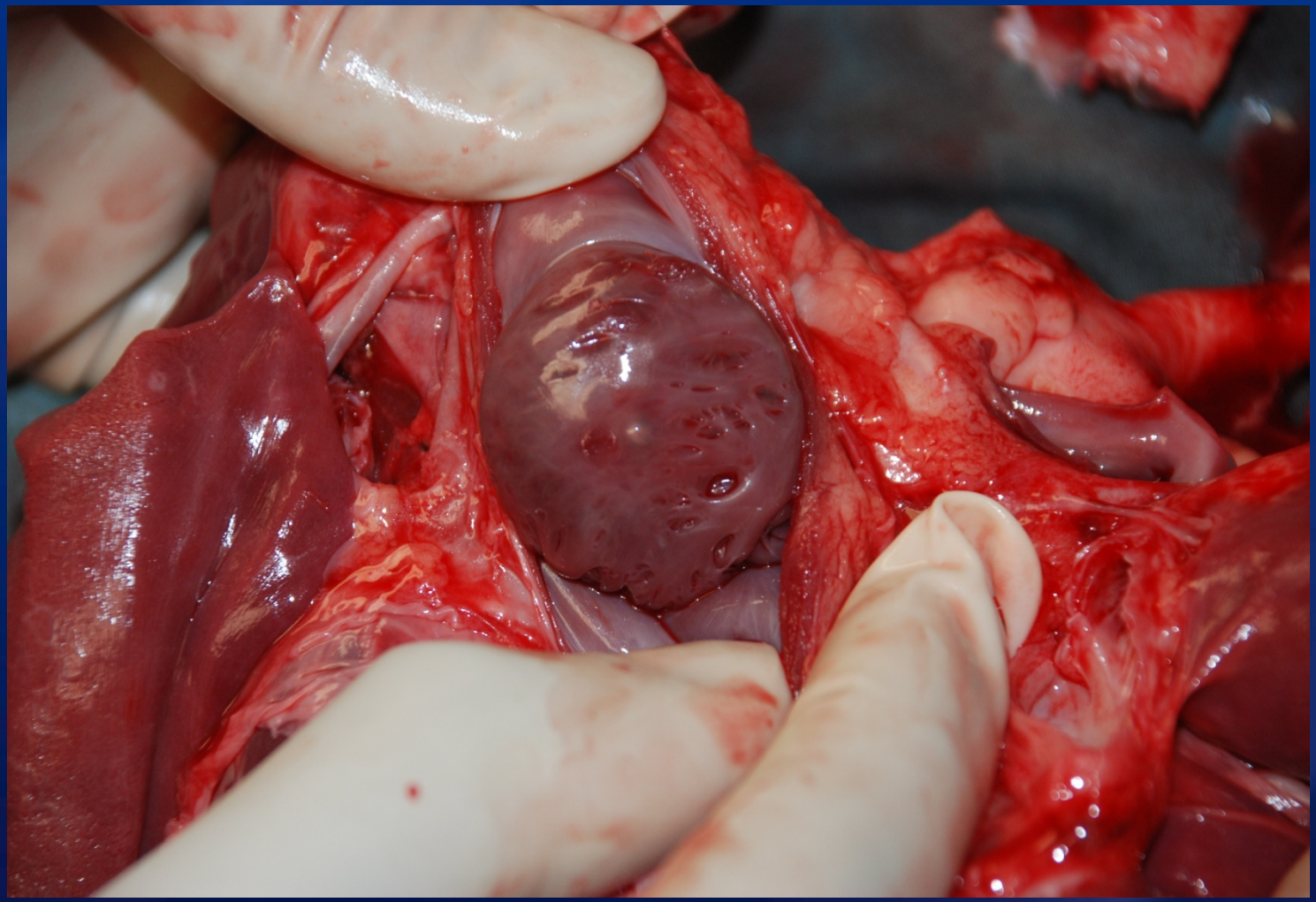
**DR Holmes JR. ACC March 2009

Basic Procedure Steps

- Access the left atrium via a transseptal approach
- Locate the LAA via fluoroscopy, (TEE) and/or (ICE)
  - Determine size, shape of LAA
  - Select appropriate sized device
- Deliver filter in LAA (distal to LAA ostium)
- Assess device post deployment (confirm: position, size and stability)
- Release the device



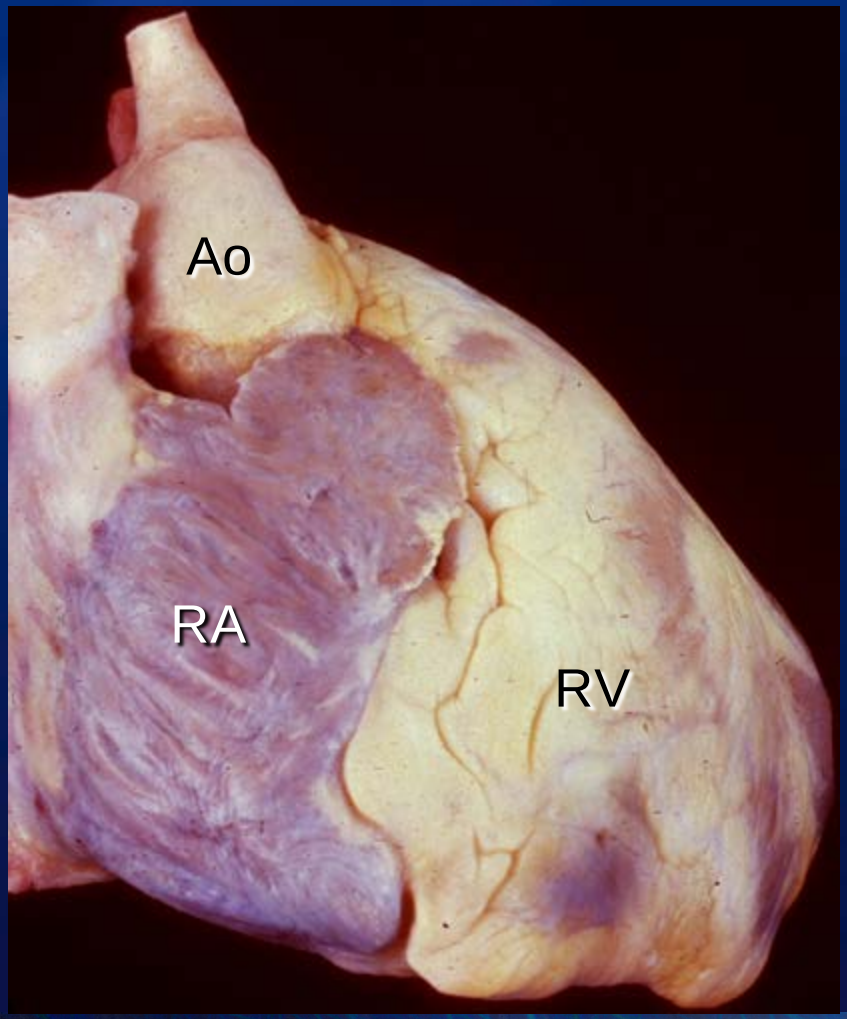


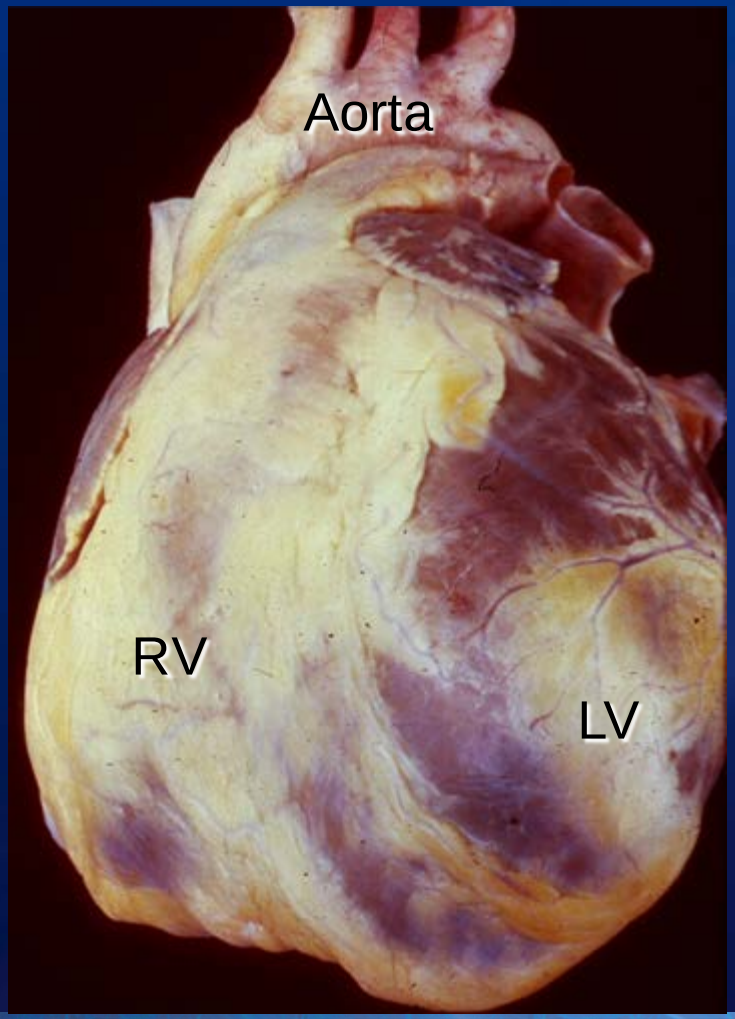


Ideal Approach

- No need for anticoagulation
- No need to enter the left atrium
- Simple to deploy
- Rapid recovery
- No need for post operative bed rest

Normal Heart
External Topography

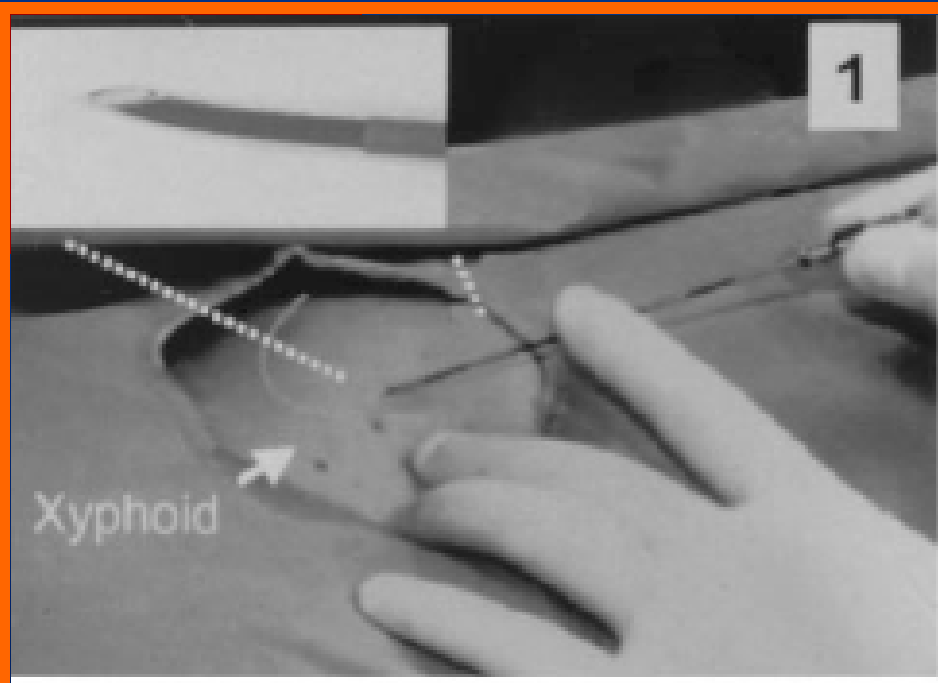




R Ant Oblique

L Ant Oblique

Epicardial Approach



- Epicardial approach shown to be feasible for VT ablation in patients with CAD.
  - Complication seen in 4/53 patients in form of RV perforation and tamponade.

Eduardo Sosa, JACC 2000

- Also effective for other arrhythmias **(VT with & without SHD, WPW, RVOT VT, AT)** especially when endocardial ablation unsuccessful.
  - No complications seen.

Schweikert et al. Circulation. 2003;108:1329-1335.

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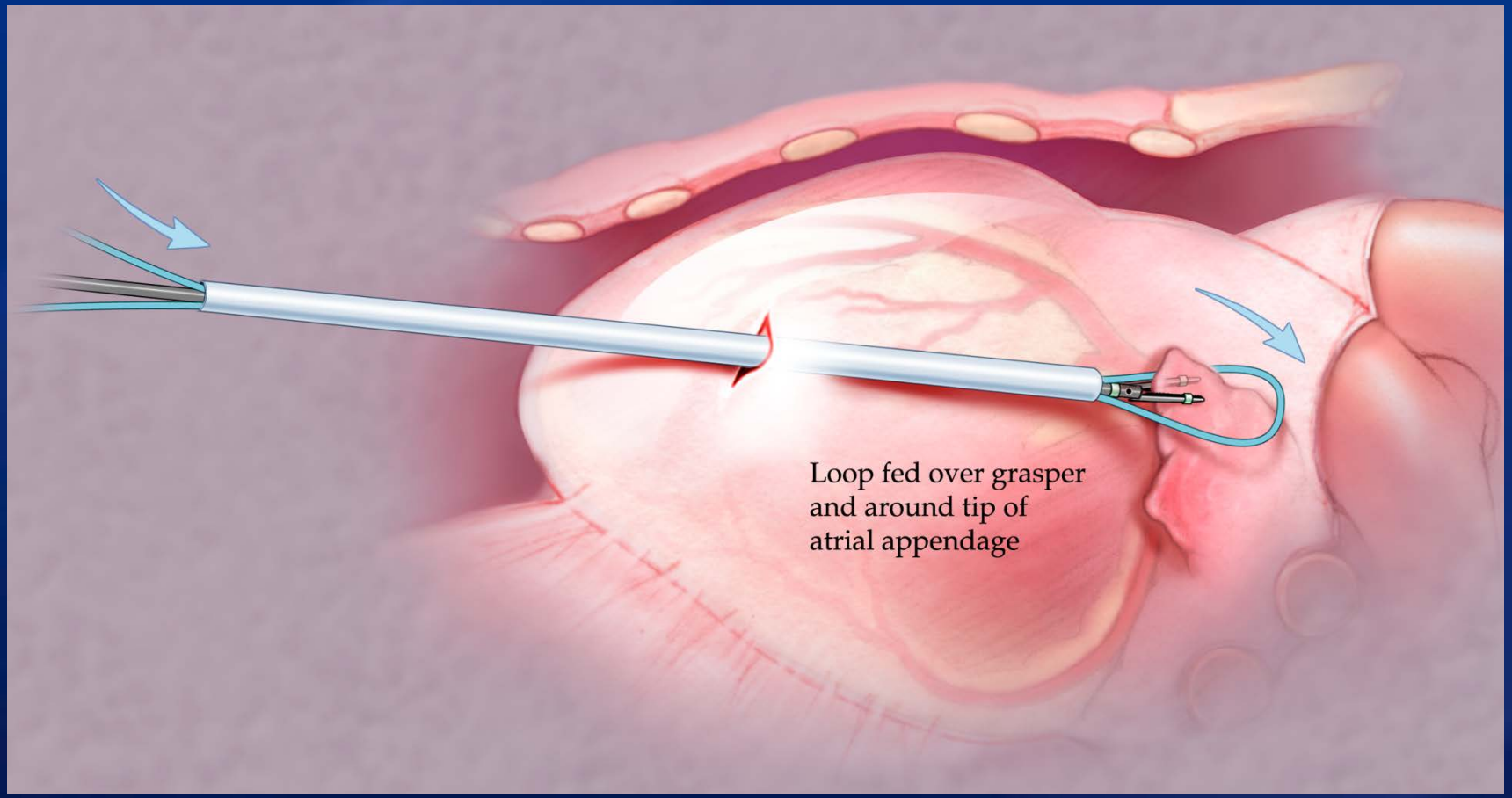
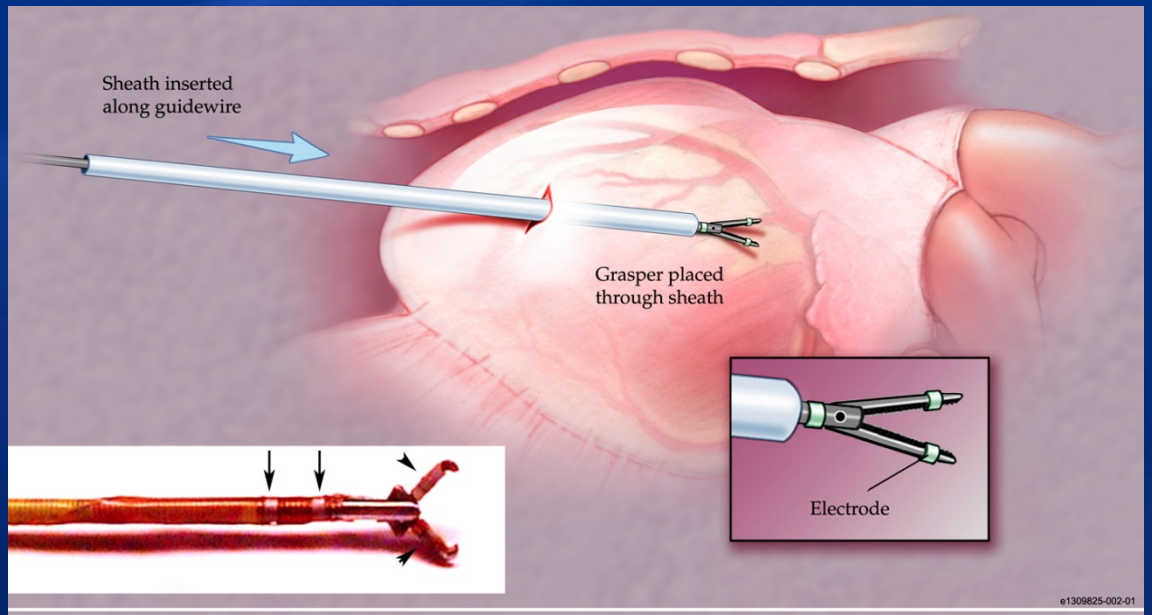
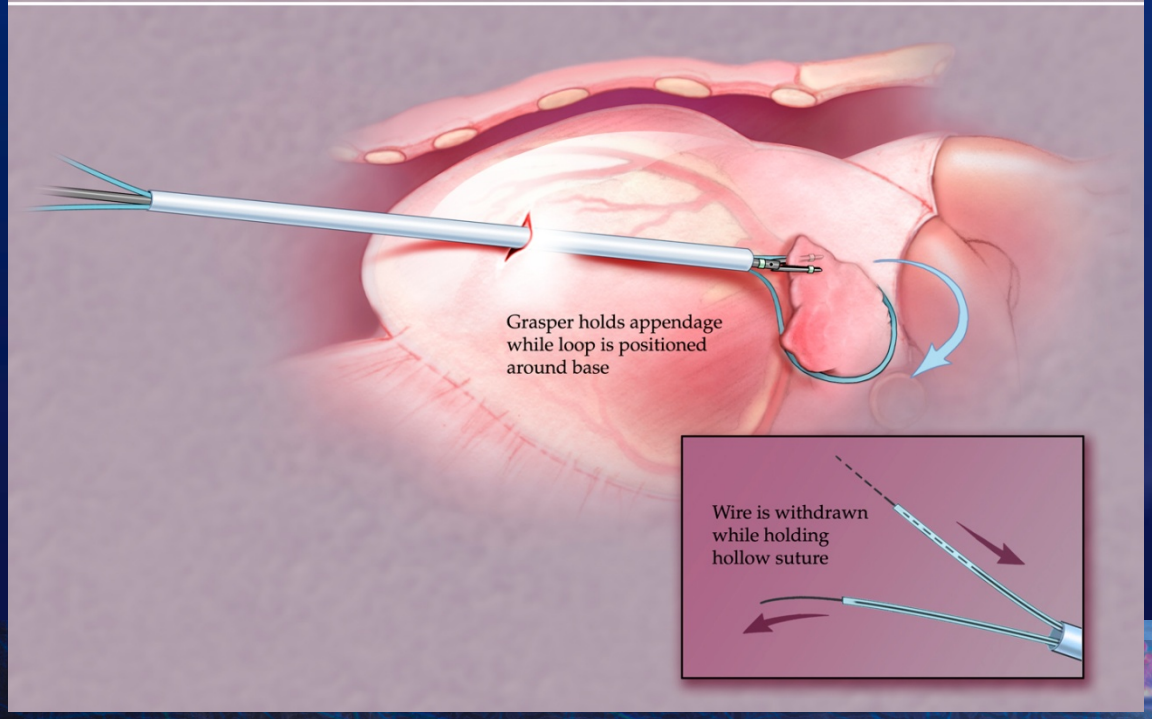
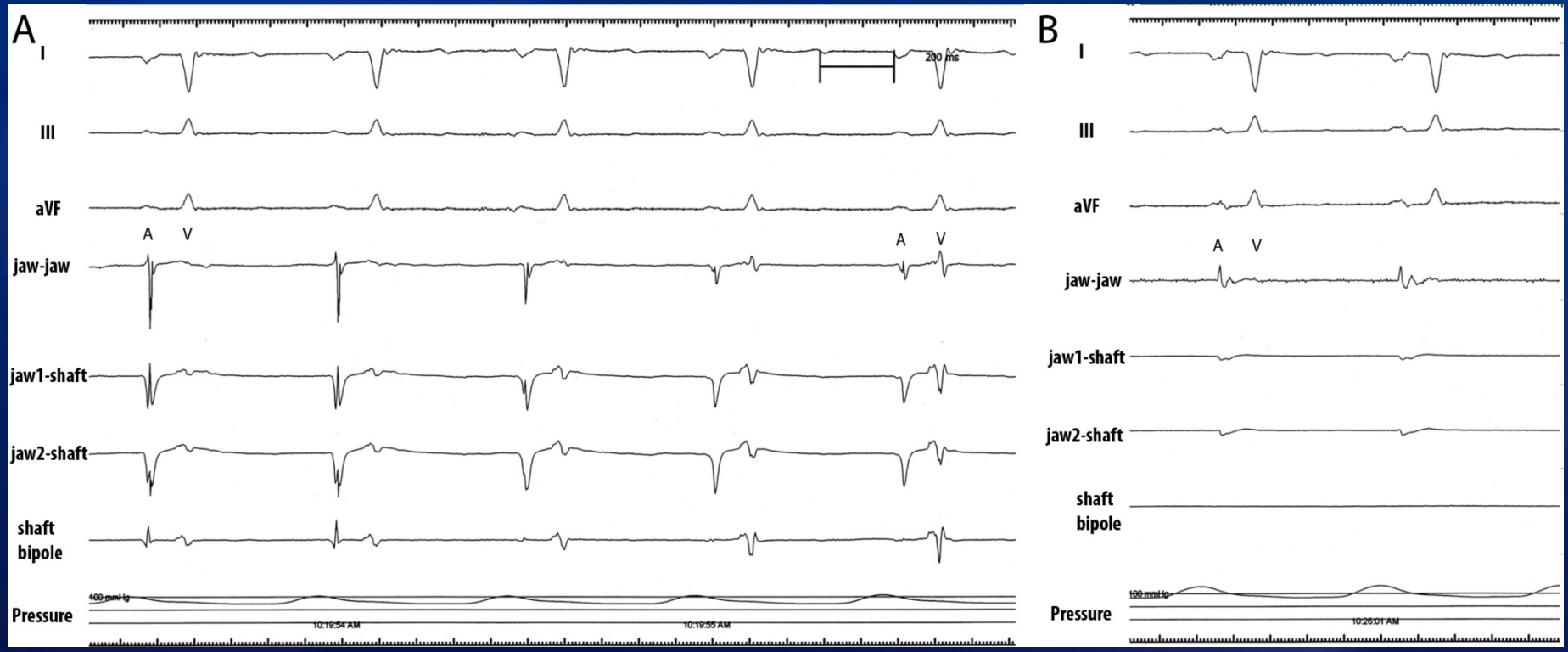


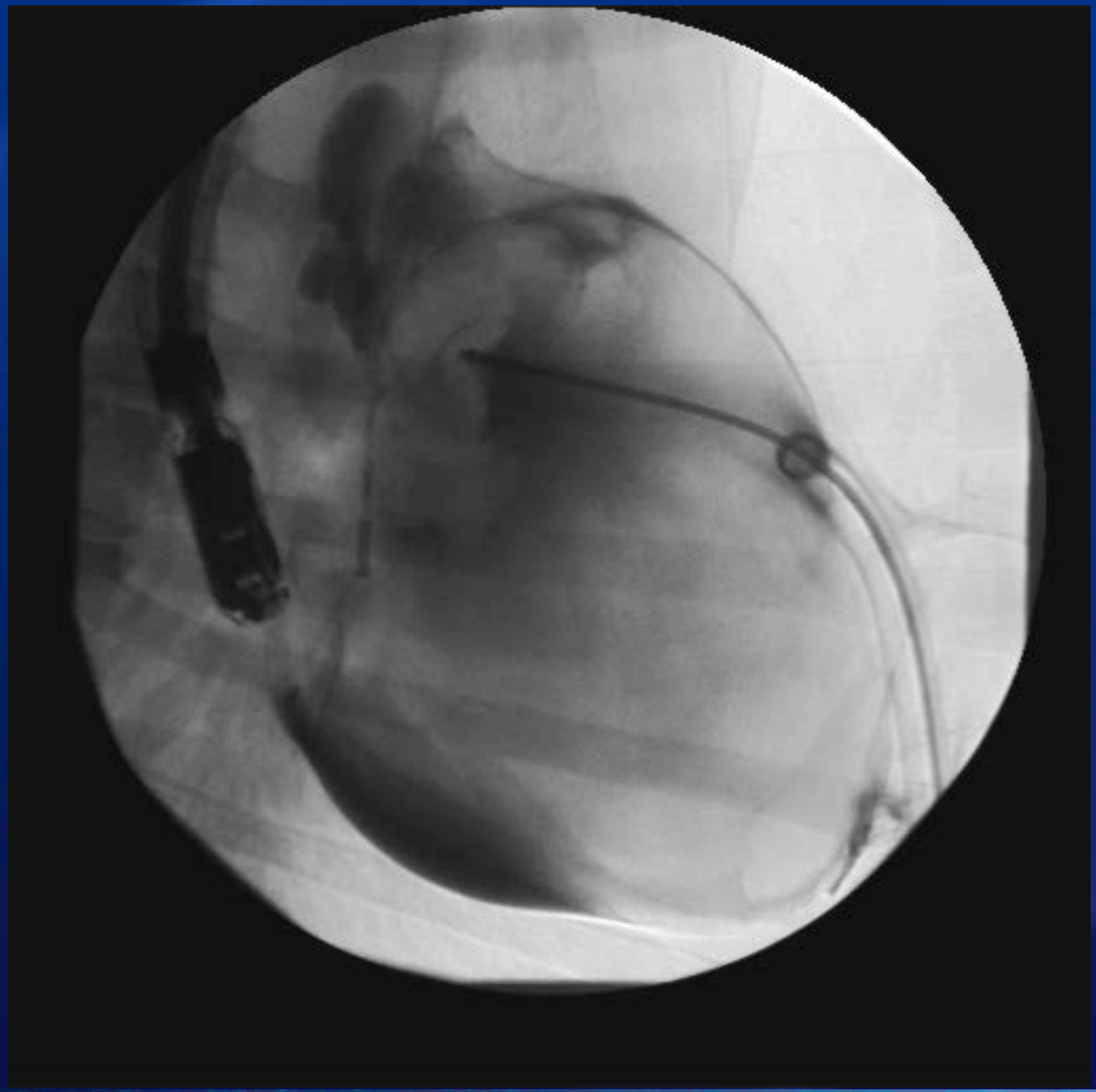
Asirvatham SJ: Innovation Focus: the Patient with Arrhythmia. Journal of Cardiovascular Translational Research 2008; 1:258-272.



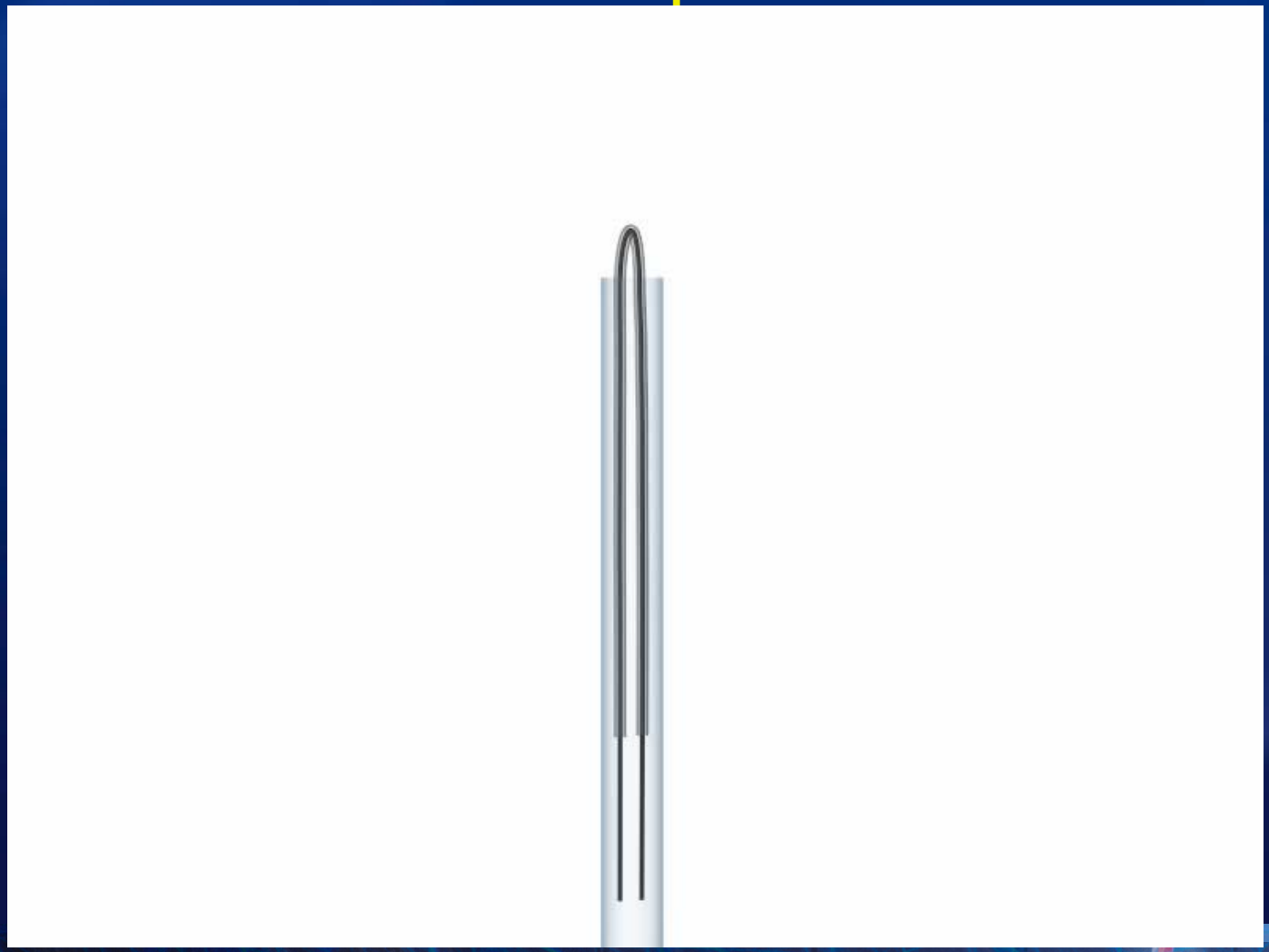


Electrical Navigation to Move Within the Closed Pericardial Space

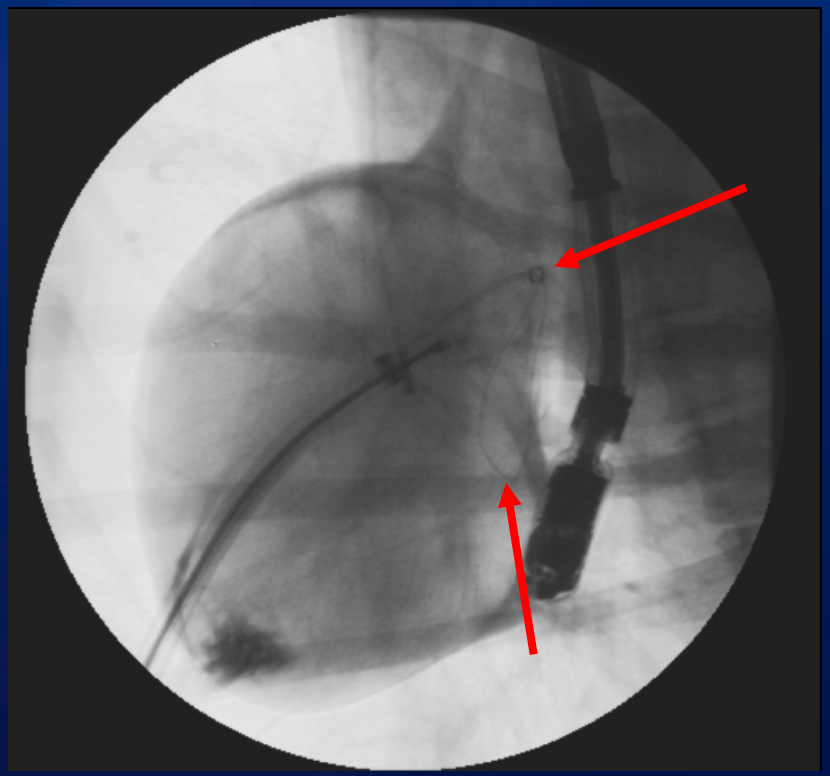


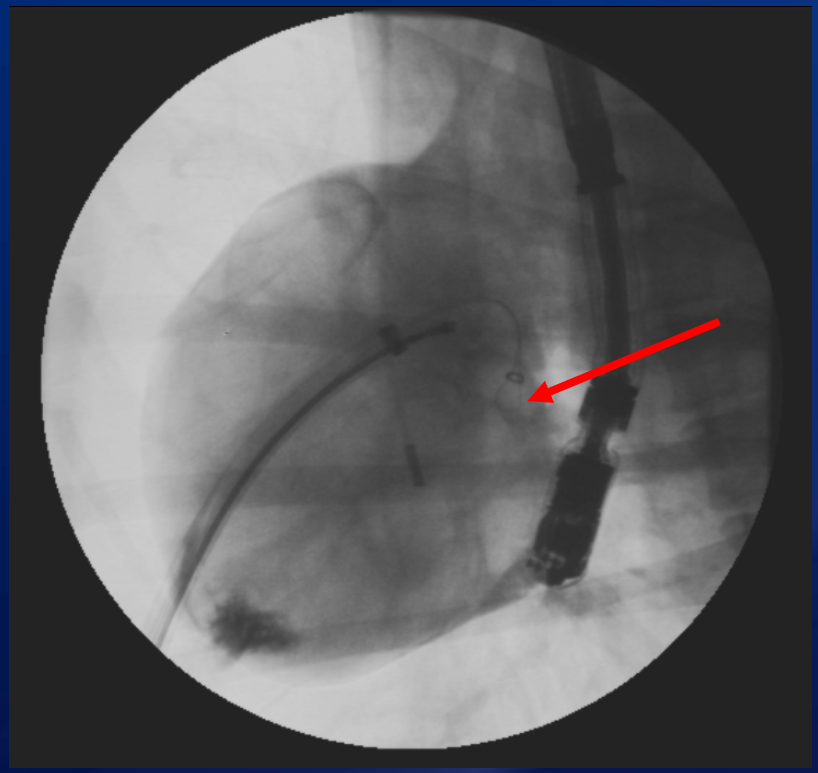


Hollow Suture Concept

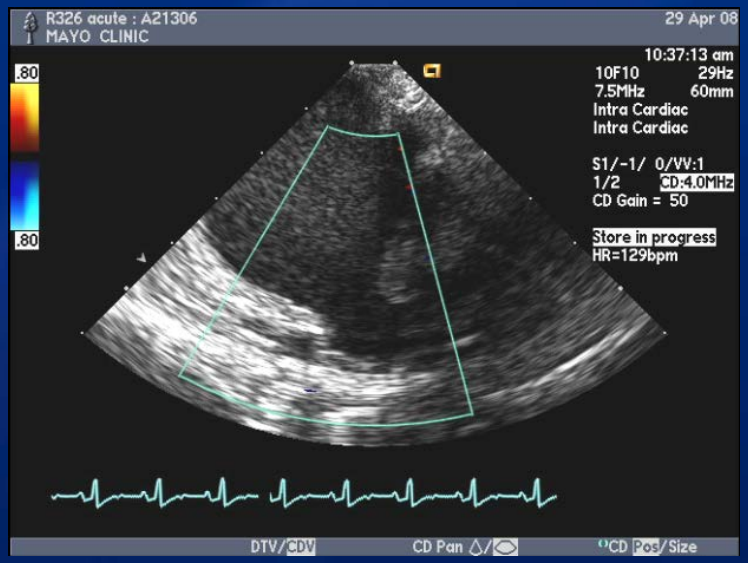


Closing Hollow Suture Around LAA

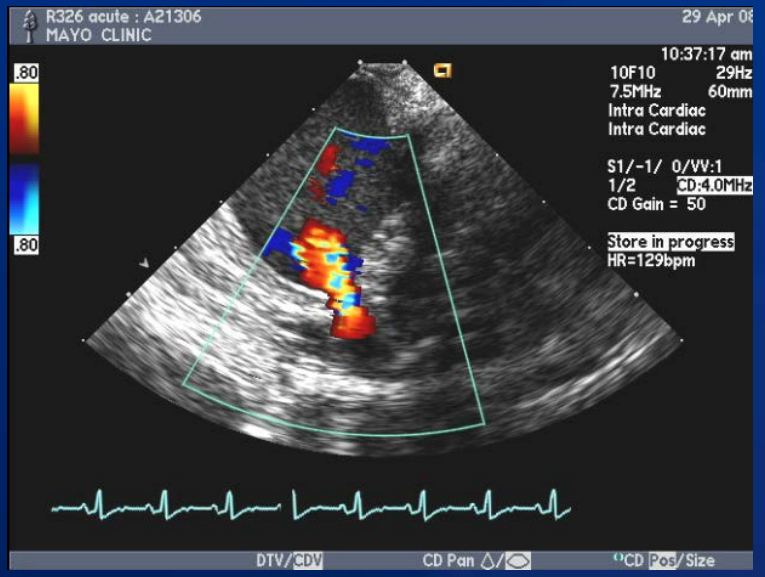




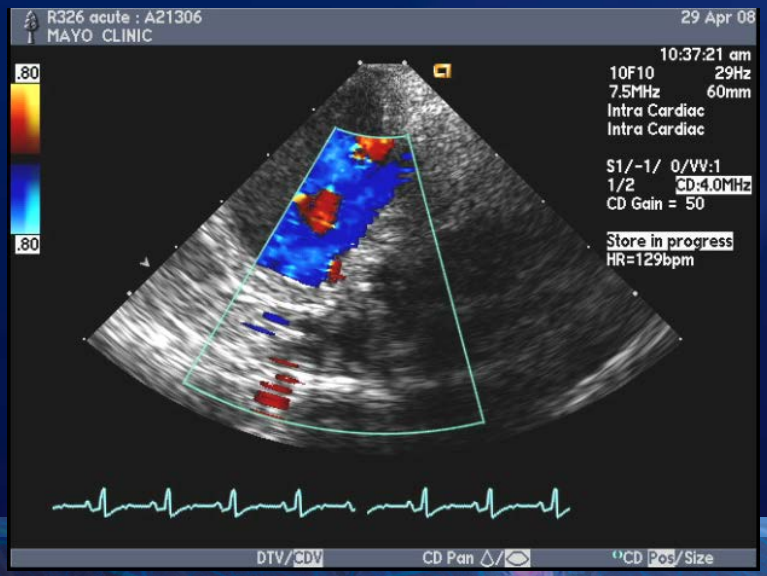
No Occlusion



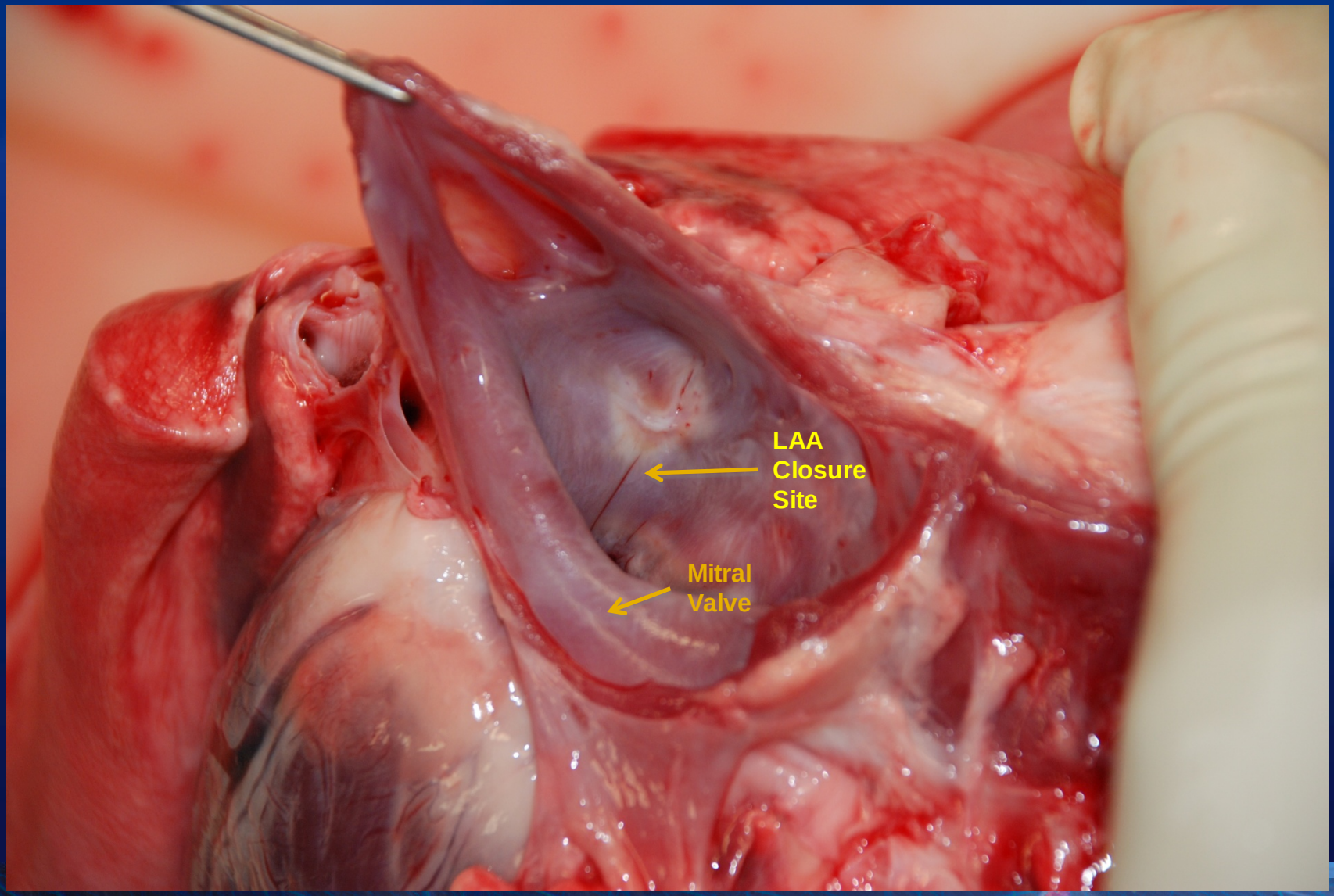
High Jet Flow During Occlusion



No Flow Across Ostium – Complete Occlusion



Chronic LAA ligation

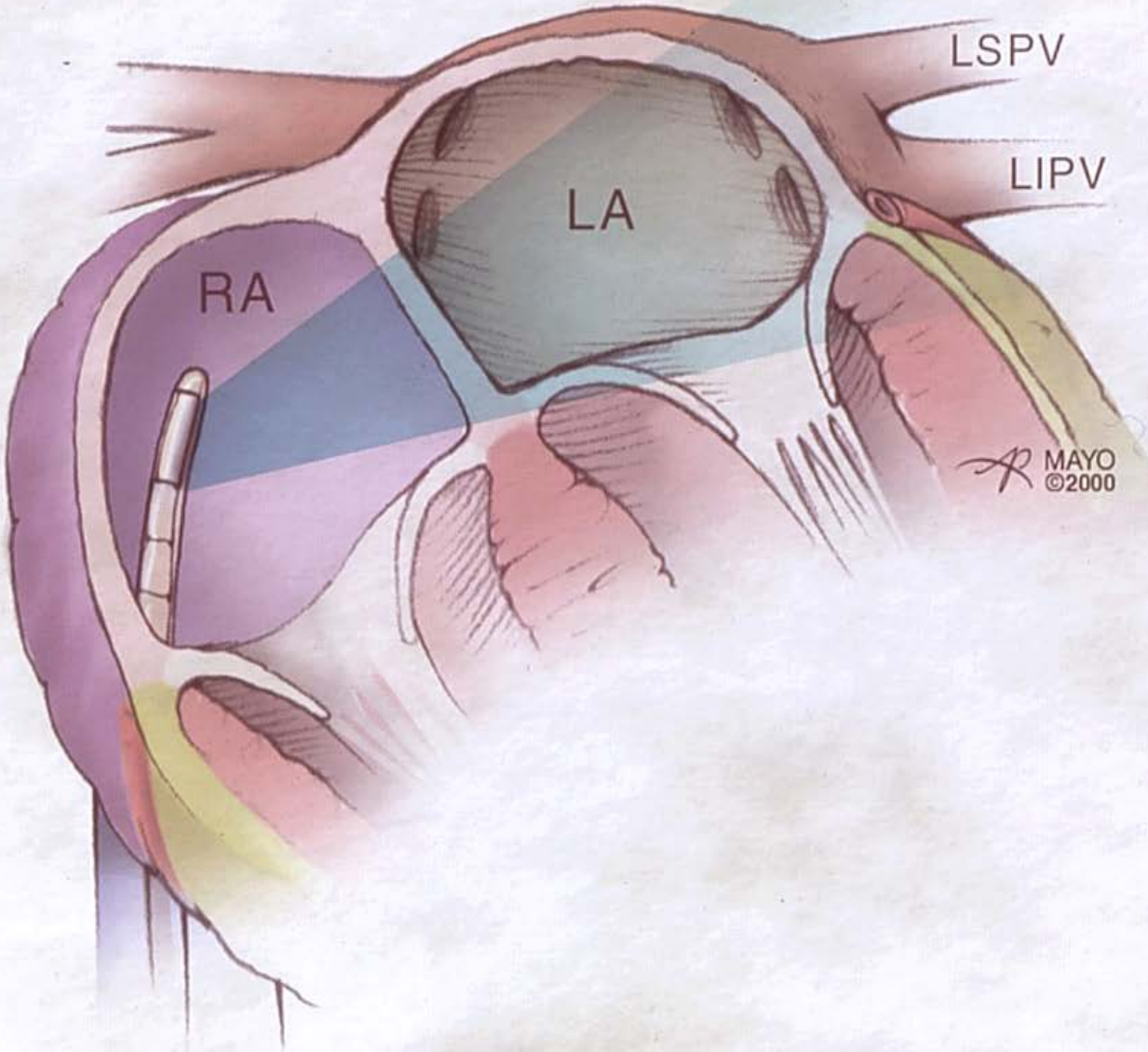


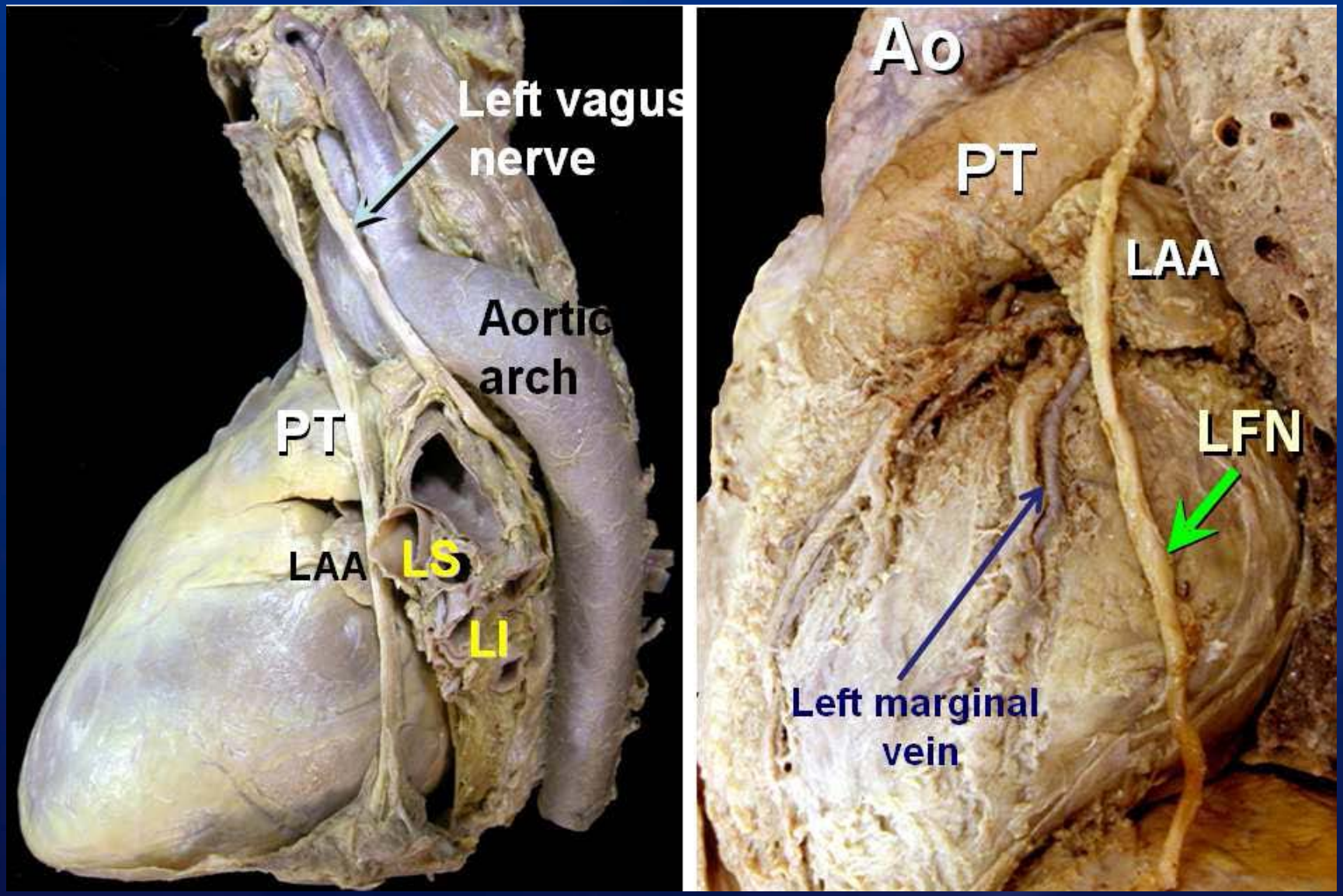
MAYO CLINIC

Utility of ICE With LAA Closure Device Deployment

- Transseptal access facilitation
- Identification of left atrial appendage ostium
- Exclusion of left atrial or left atrial appendage thrombus
- Identification of unusual left atrial appendage morphology
- Easy discernment from ostium of left-sided pulmonary vein
- Accurate sizing of ostium of the appendage
- Identification of accurate positioning at the mouth of the LAA
- Identification of blood flow around inappropriately-sized device and assessment of stability

MAYO CLINIC



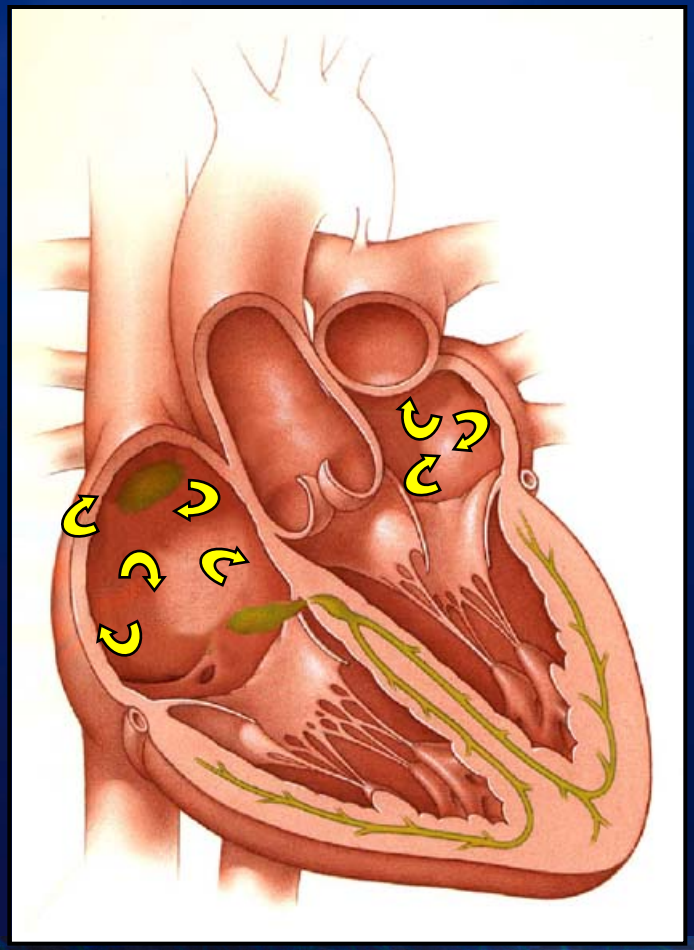


Appendage Ligation and AF Ablation

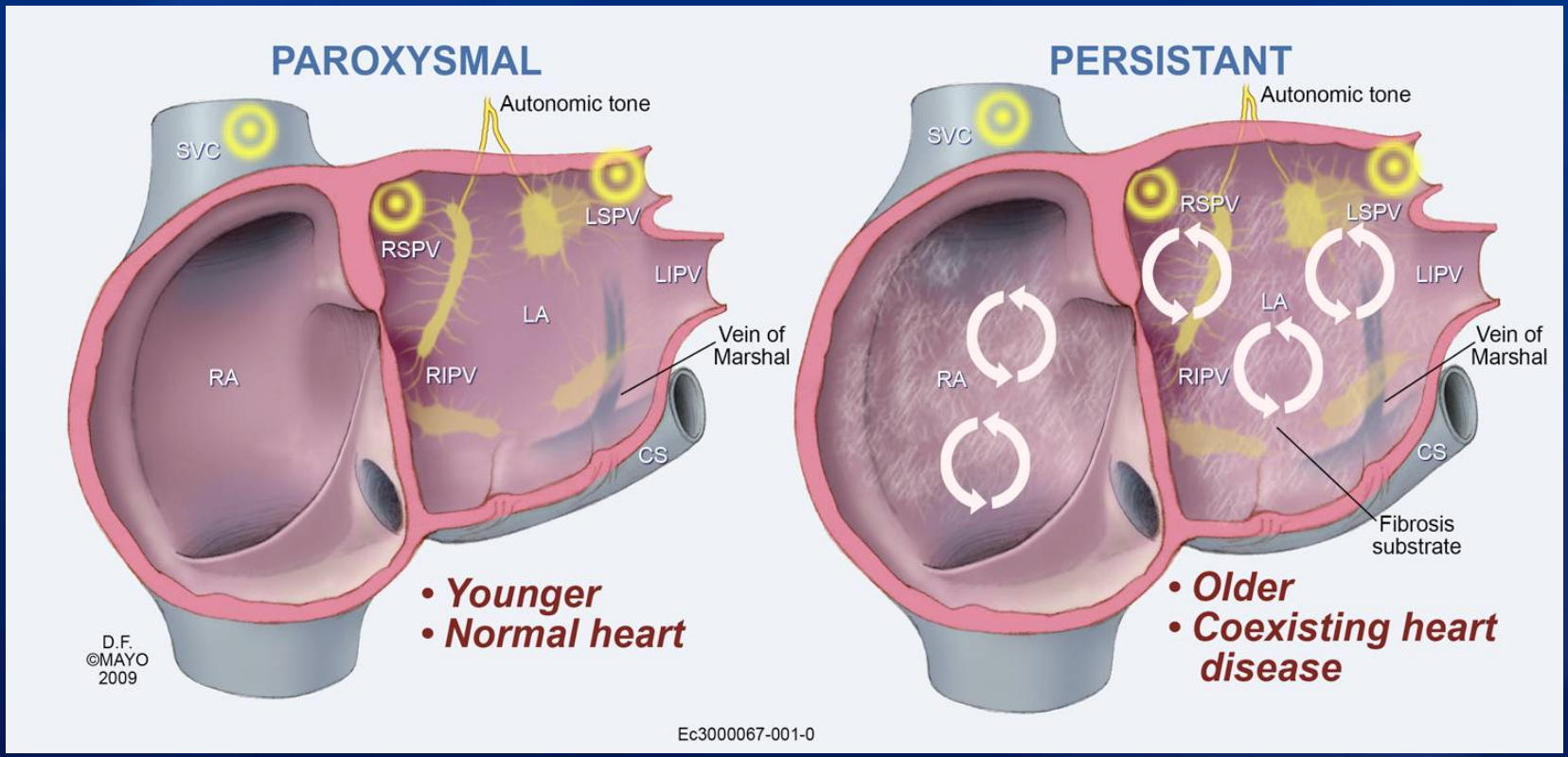
- Do they work?
- Additional risk
- Additional Benefit
- Approach dependence
- Electrophysiology
- Additional procedures

AF and Thrombo-embolism

Atrial fibrillation

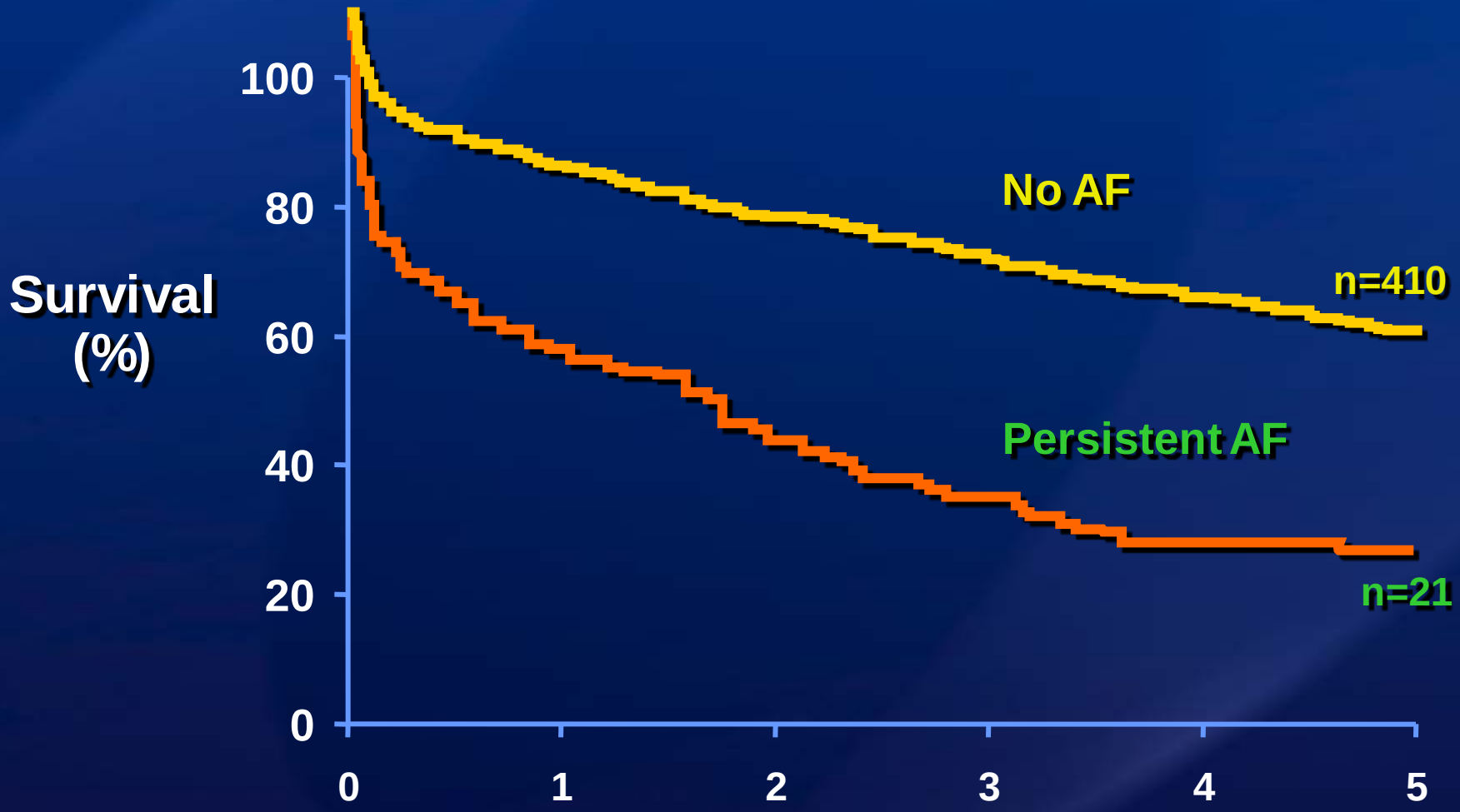


- Atria quiver
- Blood clots form in atrial appendage
- Common cause of throbmoembolism



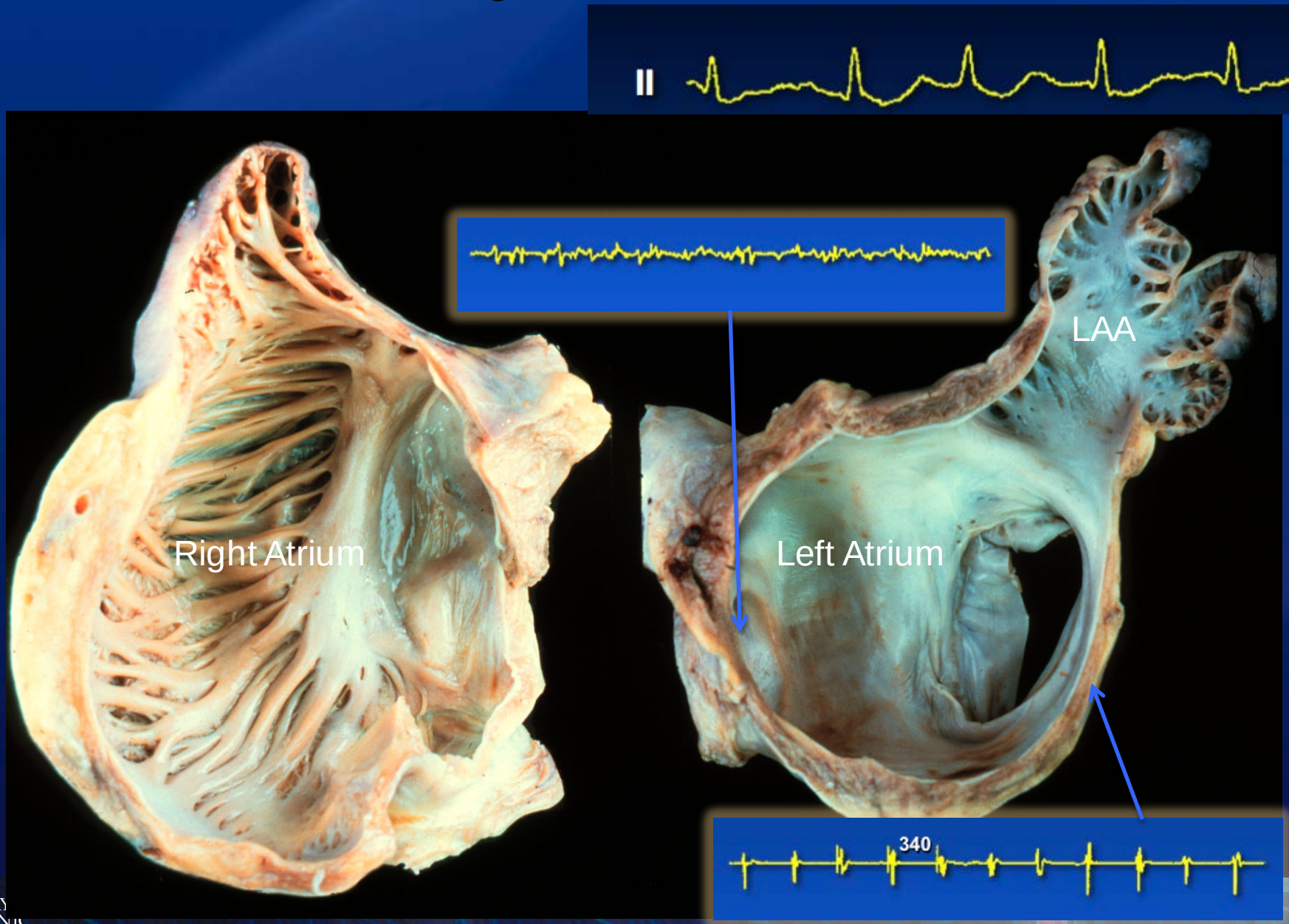
Survival After Stroke

AF Effect



Petty GW et al: Neurology 1998; 50:208-216

Atrial Fibrillation is Heterogeneous



Modified from:Seet, Friedman, Rabinstein Circ 2011

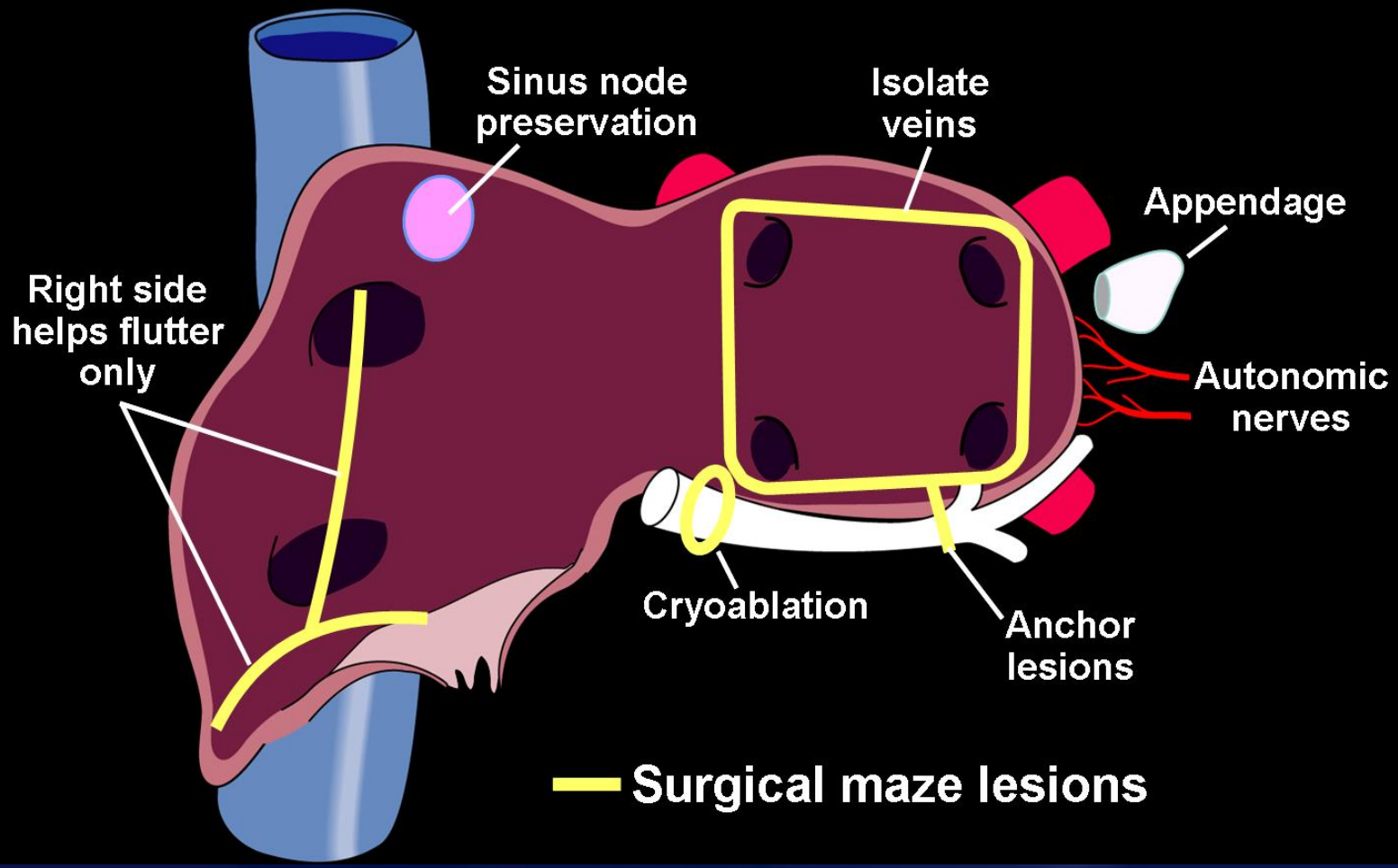
Reporting Results of AF Surgery

Event	Depiction
Freedom from permanent AF	Time-related event depiction Time zero = 6 months after date of surgery
Freedom from surgical failure	Time-related event depiction Time zero = 6 months after date of surgery
Prevalence of AF	Prevalence vs time Time zero = date of surgery
Freedom from stroke	Time-related event depiction Time zero = date of surgery
Freedom from pacemaker	Time-related event depection Time zero = date of surgery

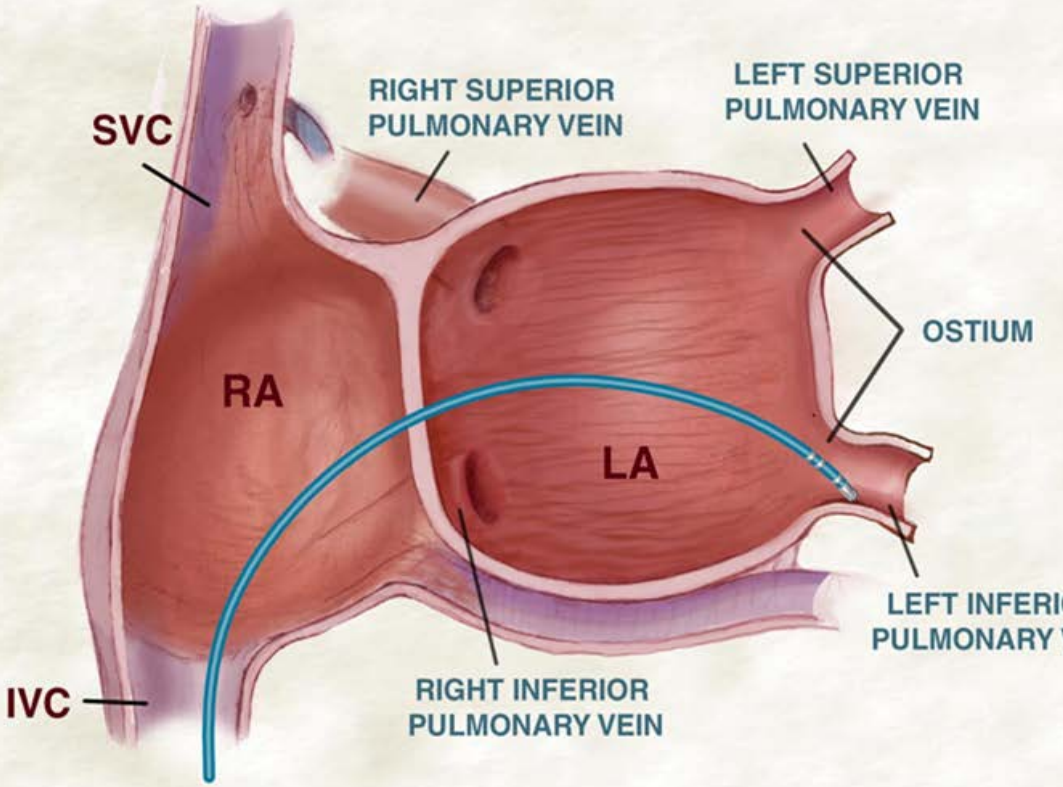
Gillinov: Surg Atrial Fib, 2002

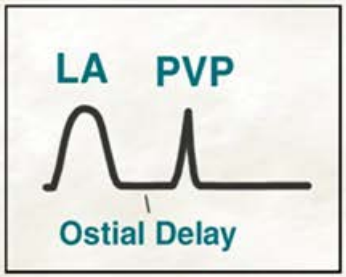
Atrial Fibrillation

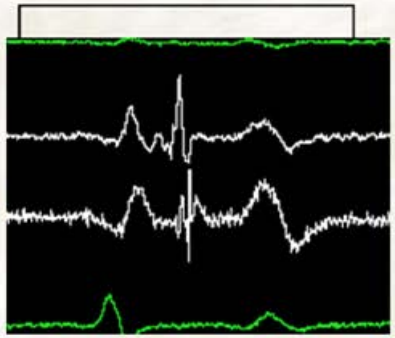
Lessons from the OR



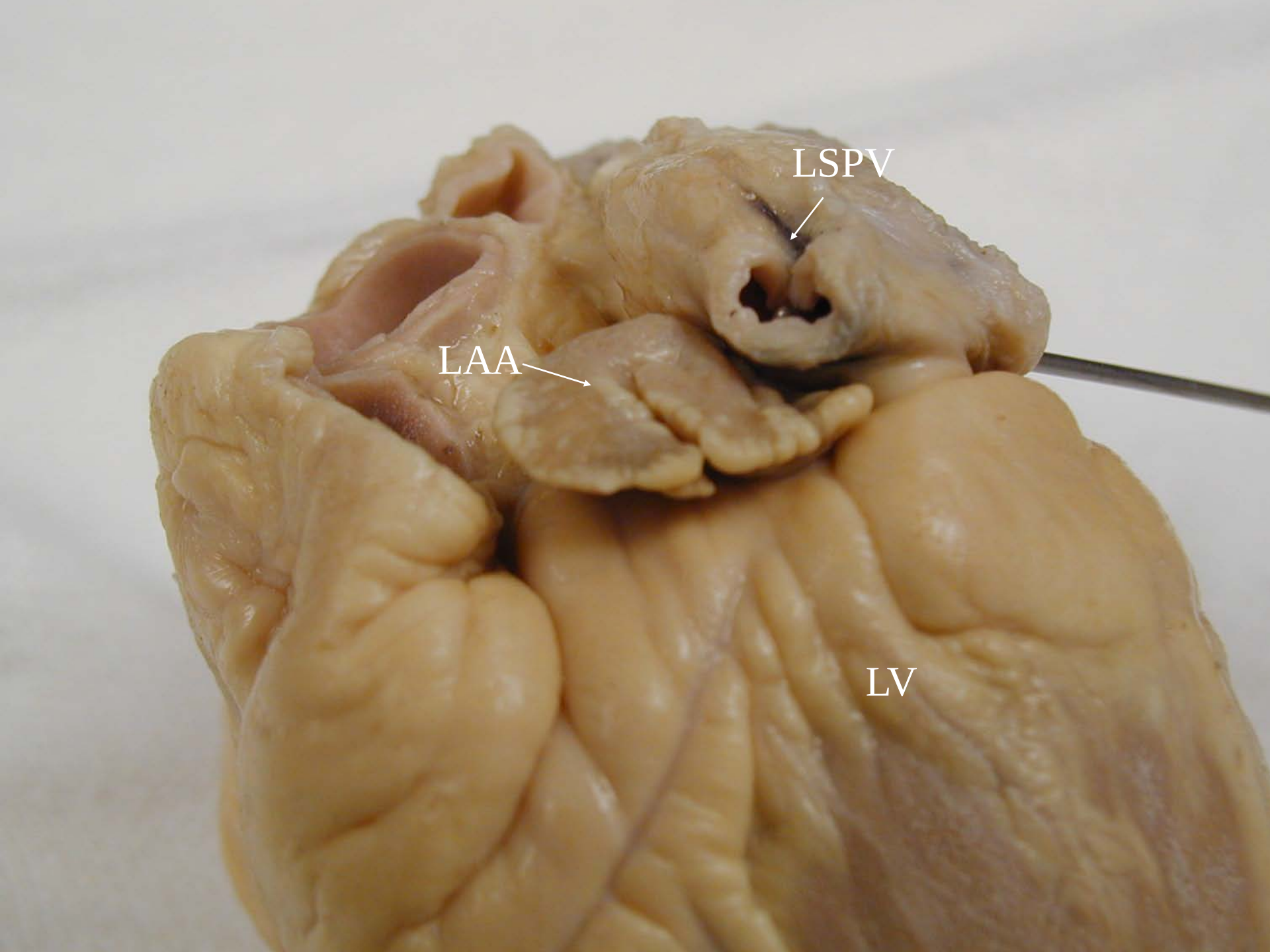
THE PULMONARY VEIN POTENTIAL



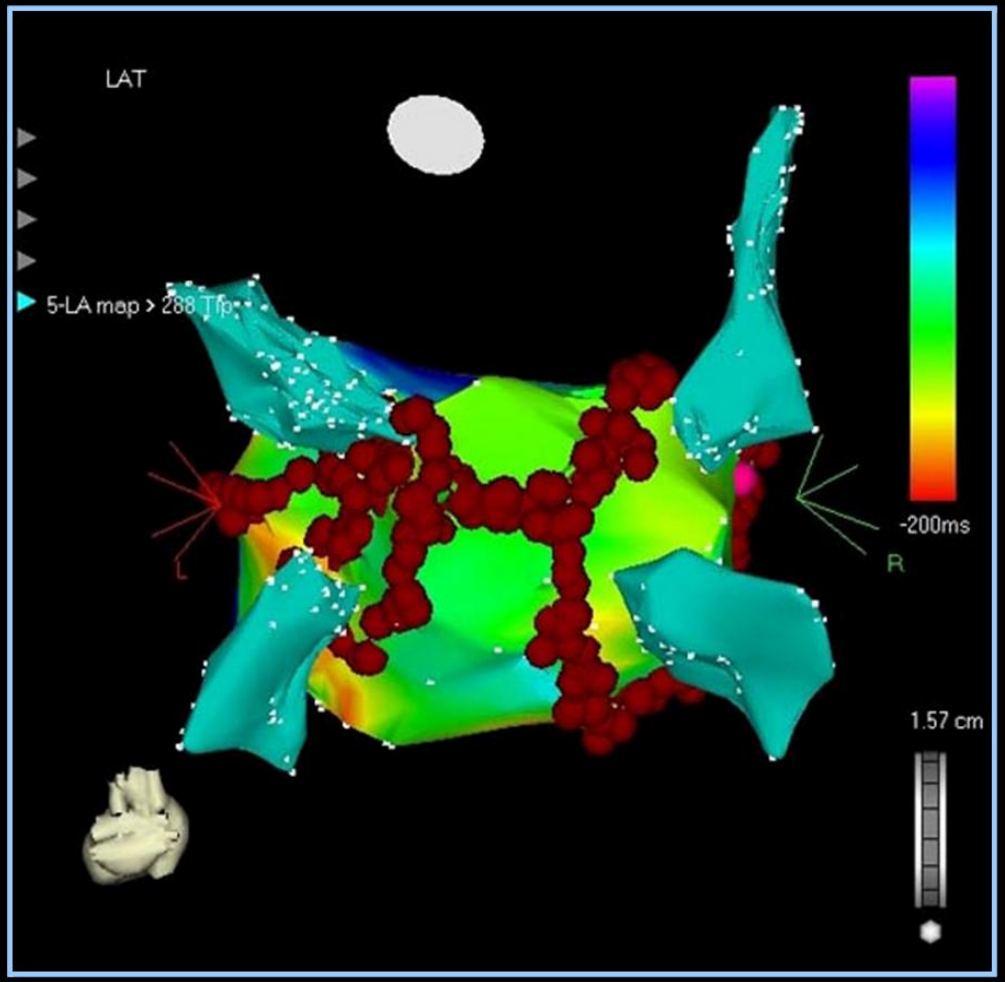


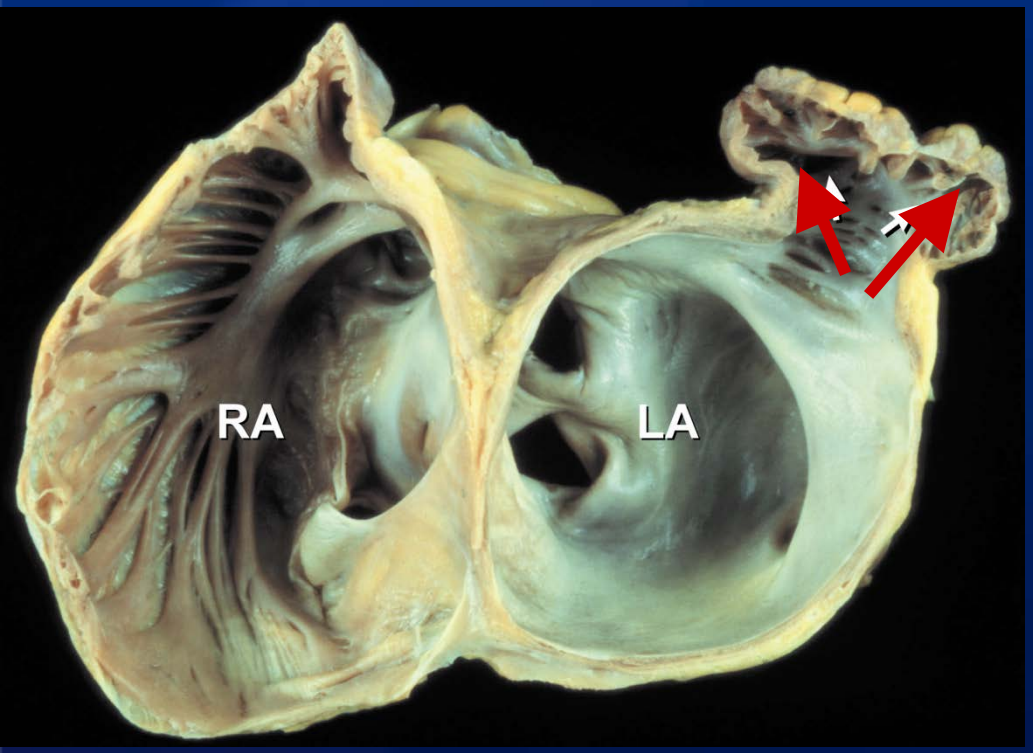


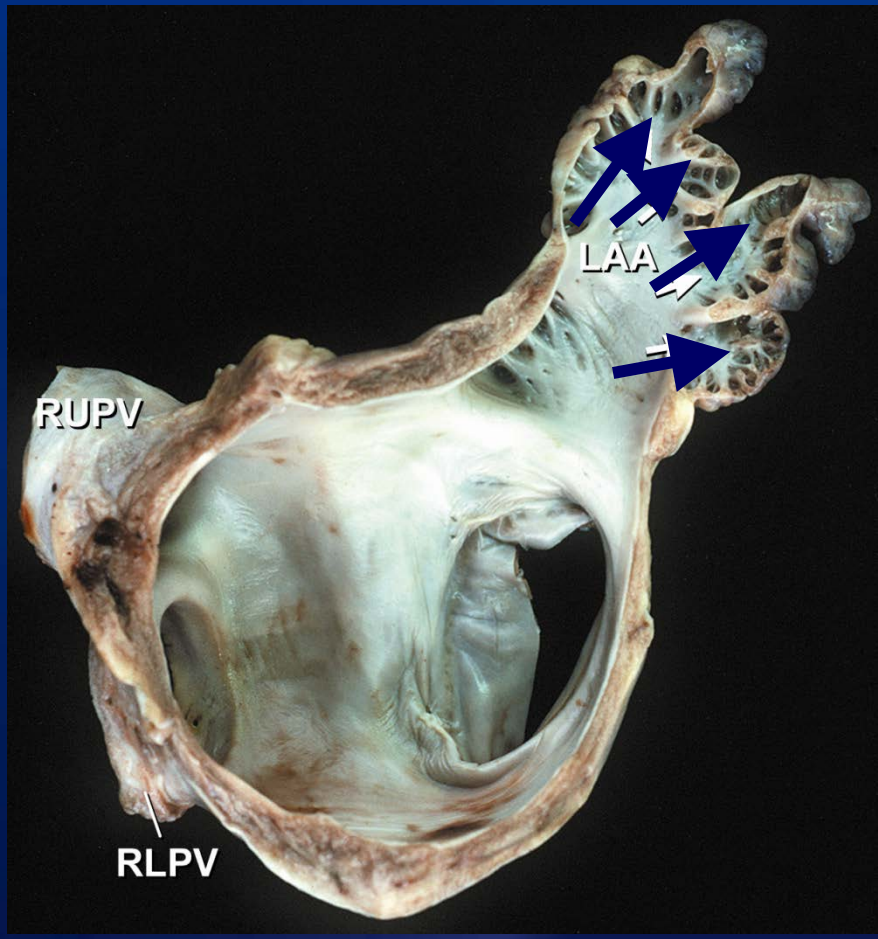
Asirvatham S: Pulmonary vein-related maneuvers: Part I. Heart Rhythm 2007; 4:538-544


LSPV
LAA
LV

Wide Area Circumferential Ablation: More than Trigger Elimination







Appendage Ligation and AF Ablation

- Do they work?
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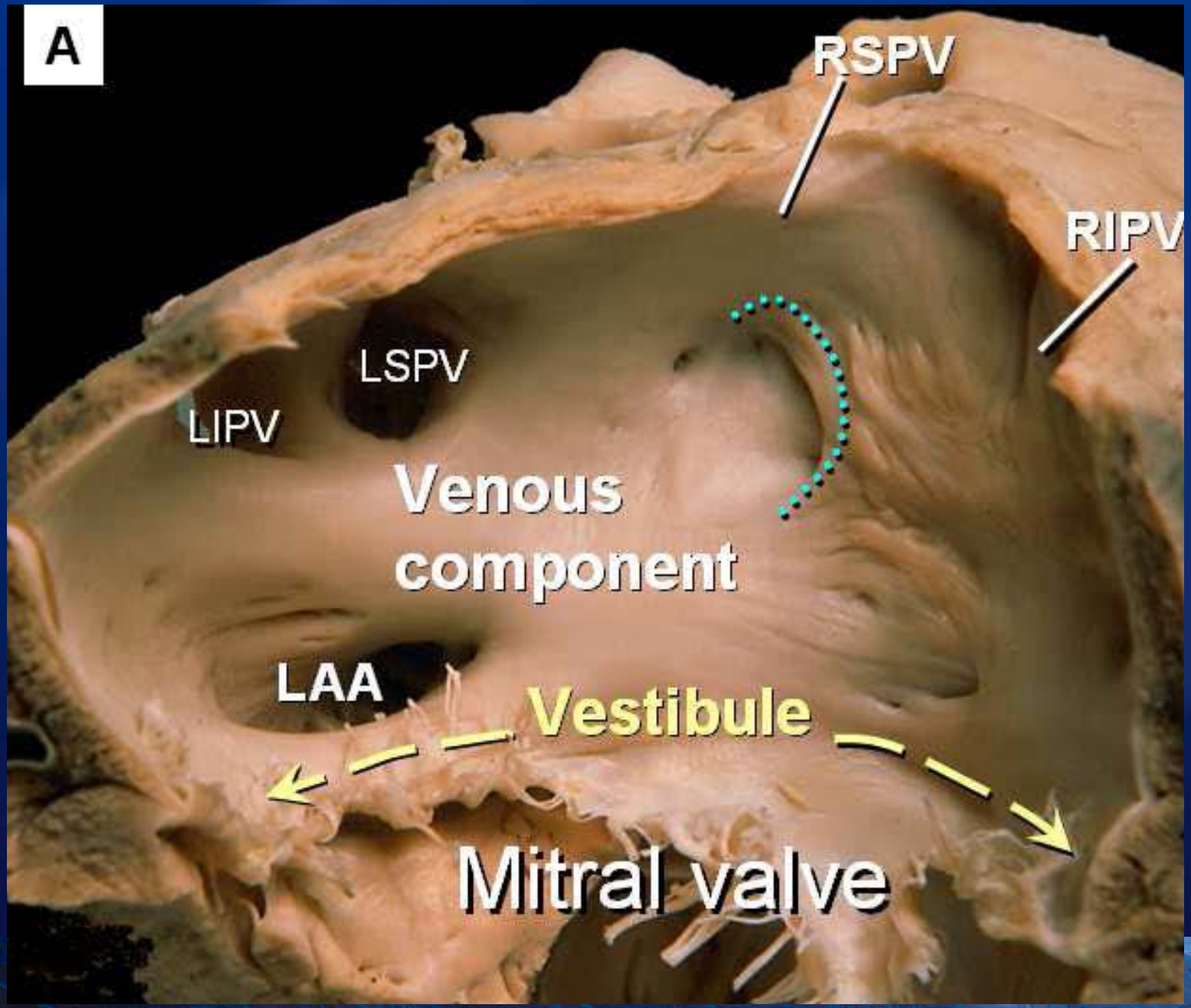
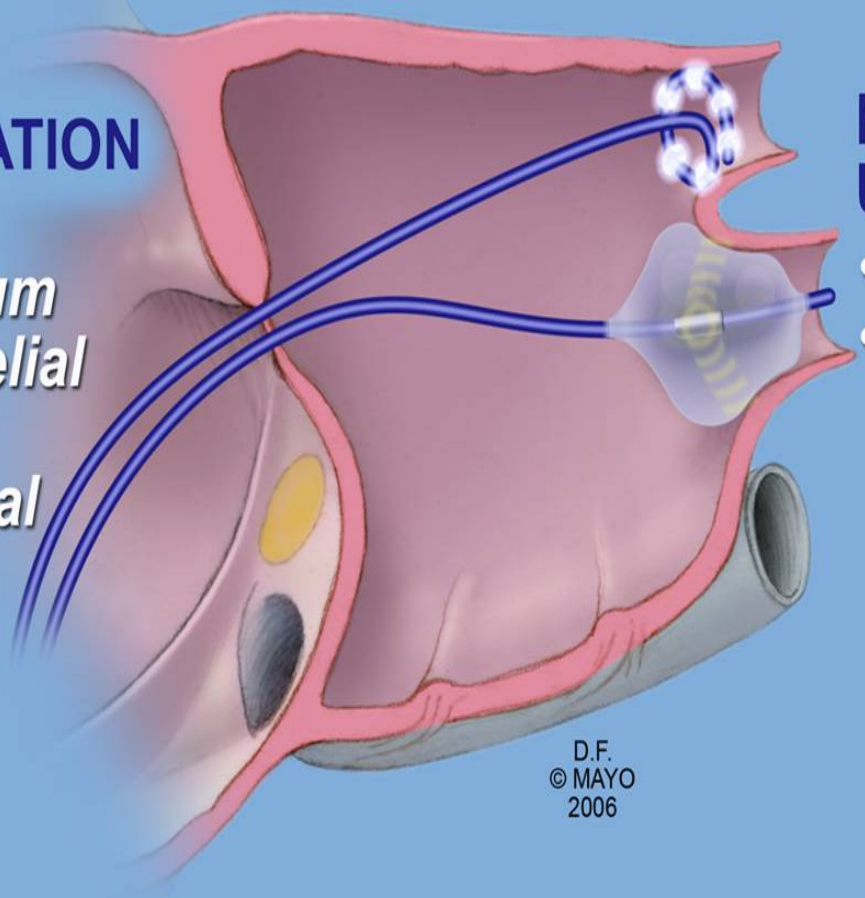


MAYO CLINIC

CRYOABLATION

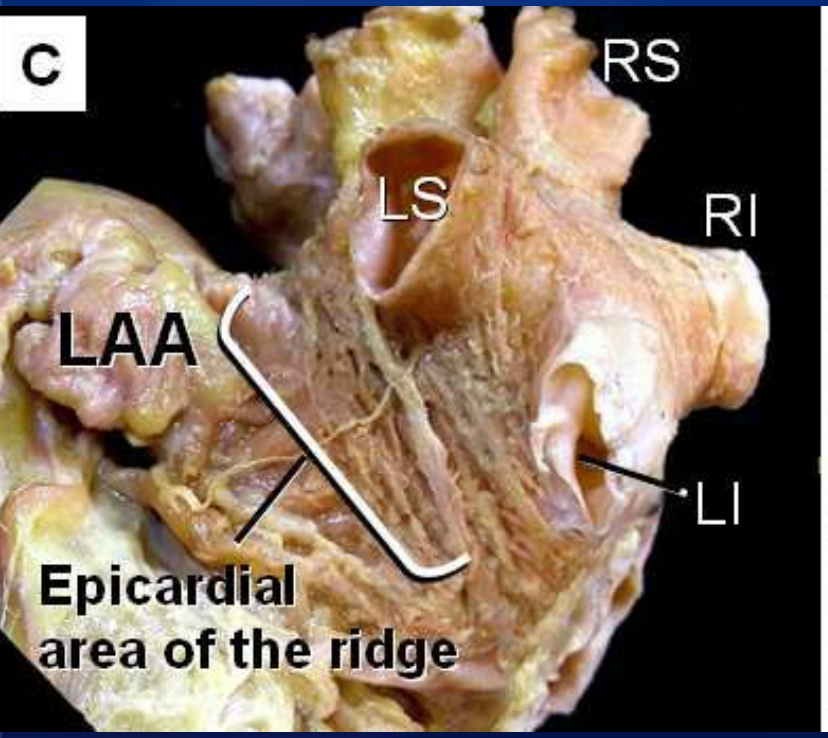
- Stability
- ↓Coagulum
- ↓Endothelial damage
- ↓Collateral injury

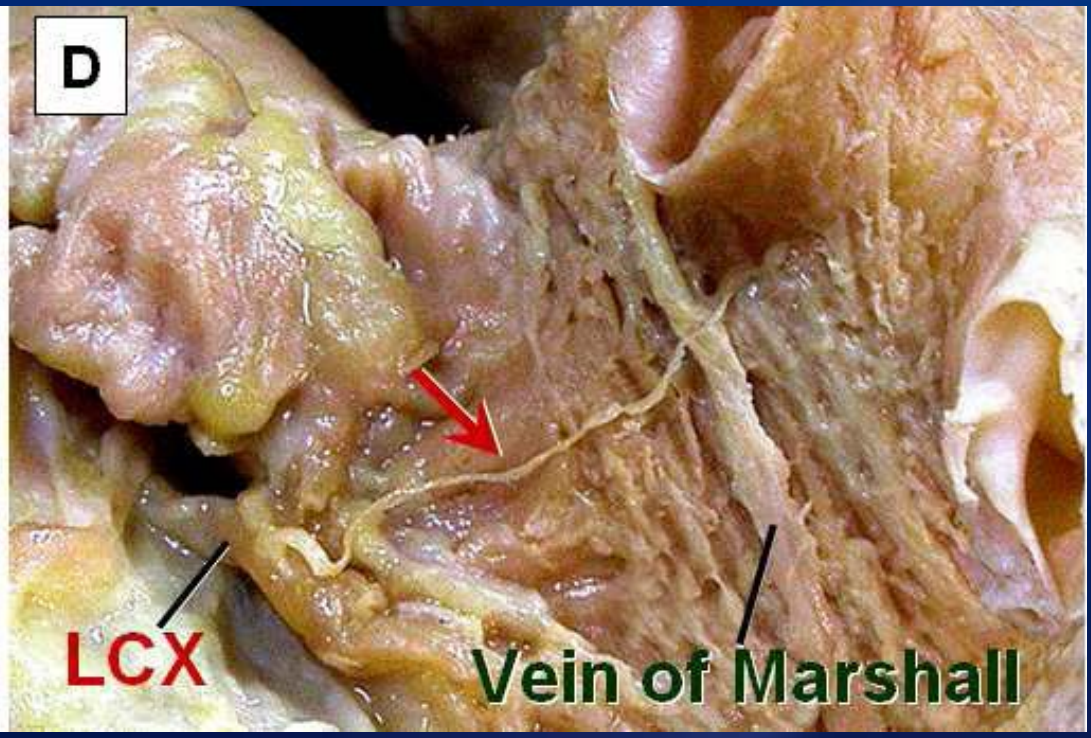


FOCUSED ULTRASOUND

- ? Periosteal
- ?↓Endothelial injury

Ec1249379-001-0





MAYO CLINIC

Appendage Ligation and AF Ablation

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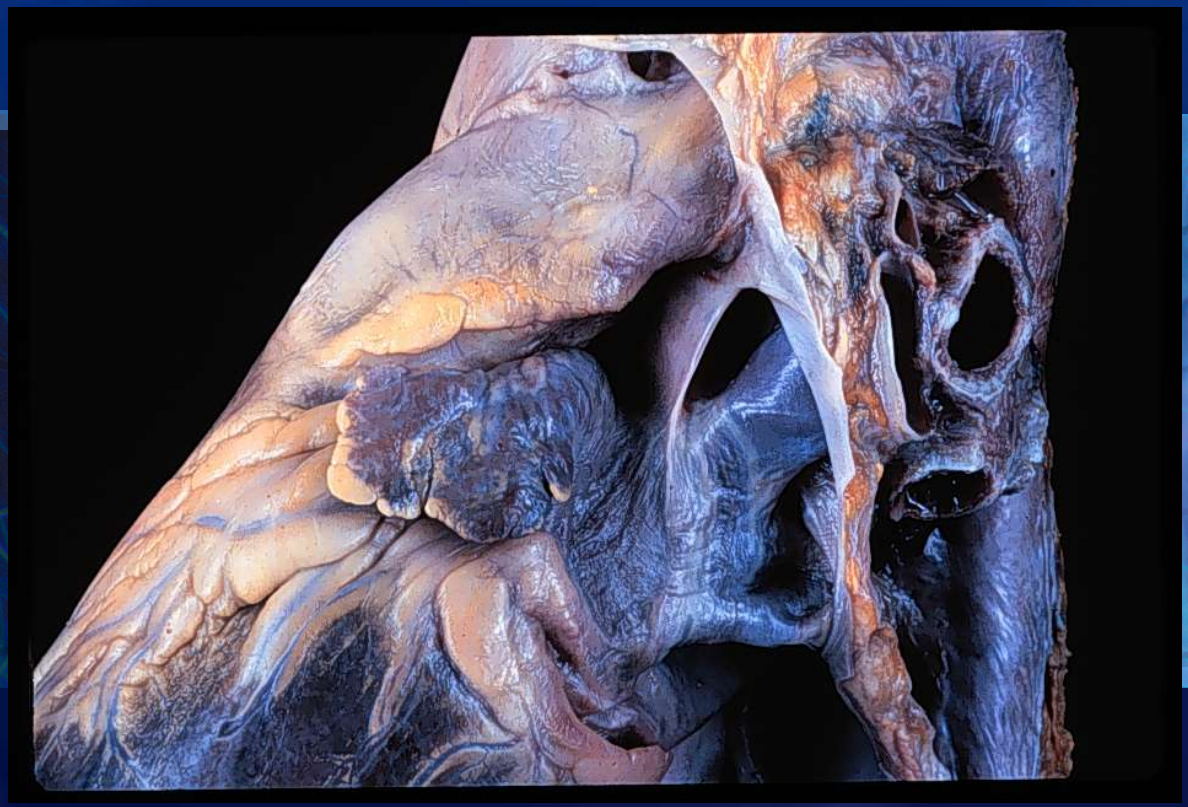
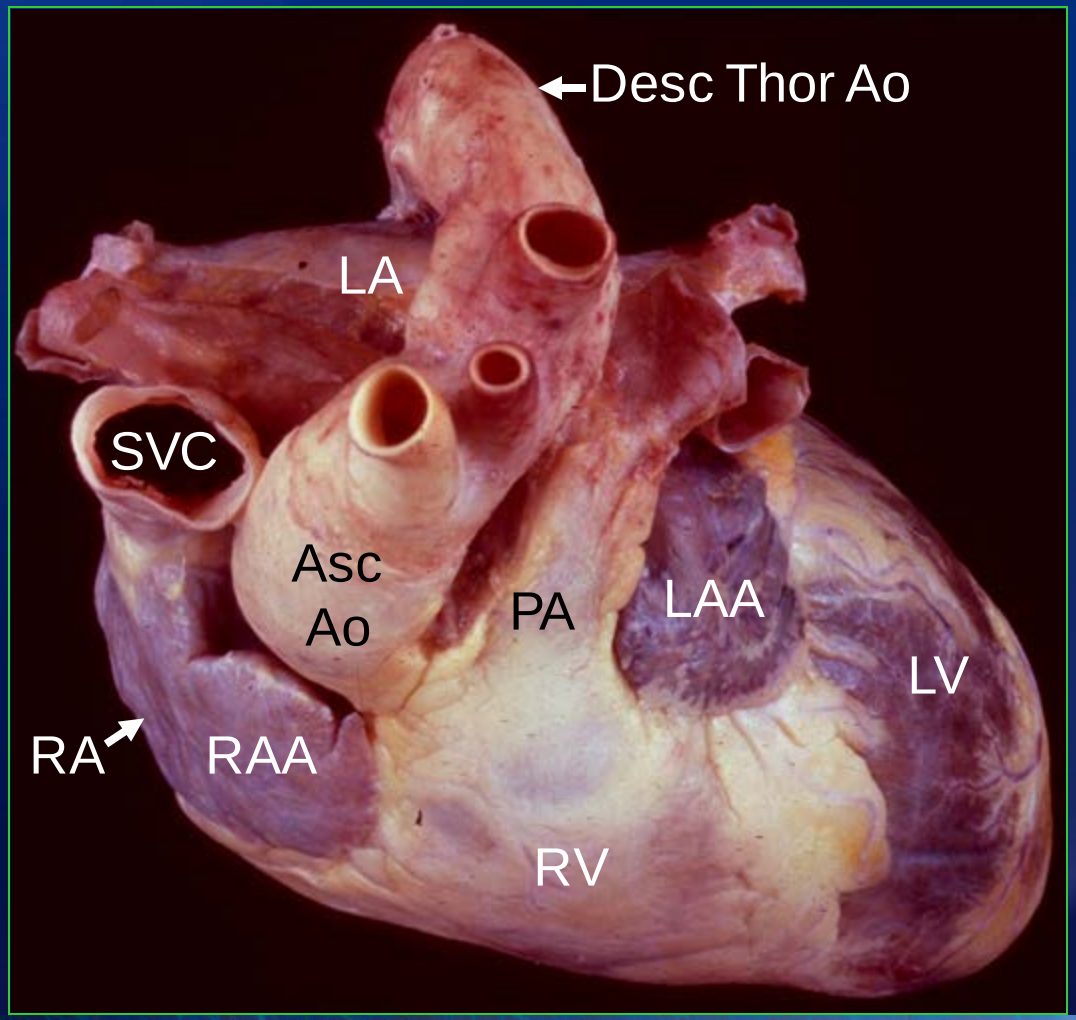
MAYO CLINIC



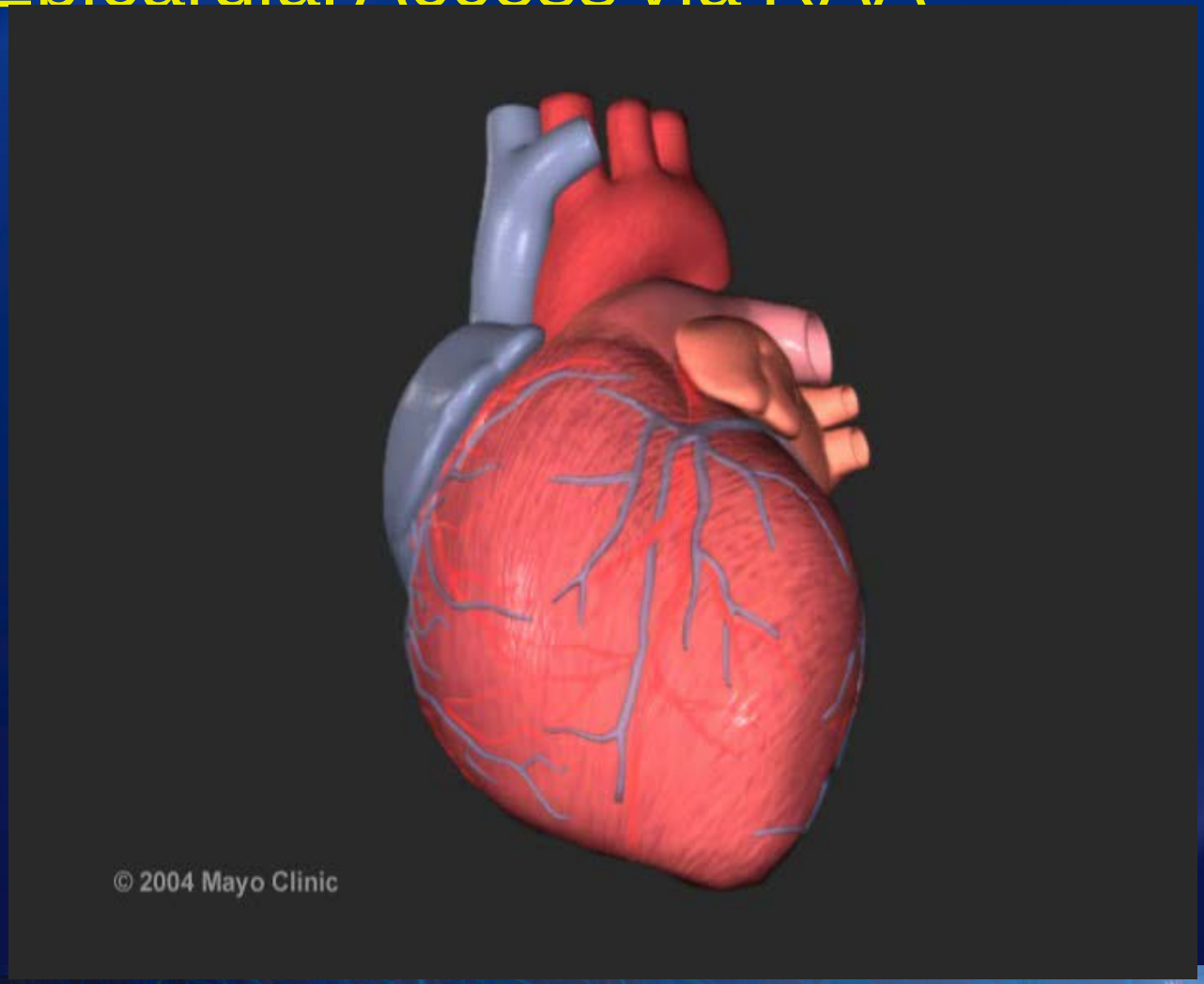
External Cardiac Anatomy

Cardiac Chambers

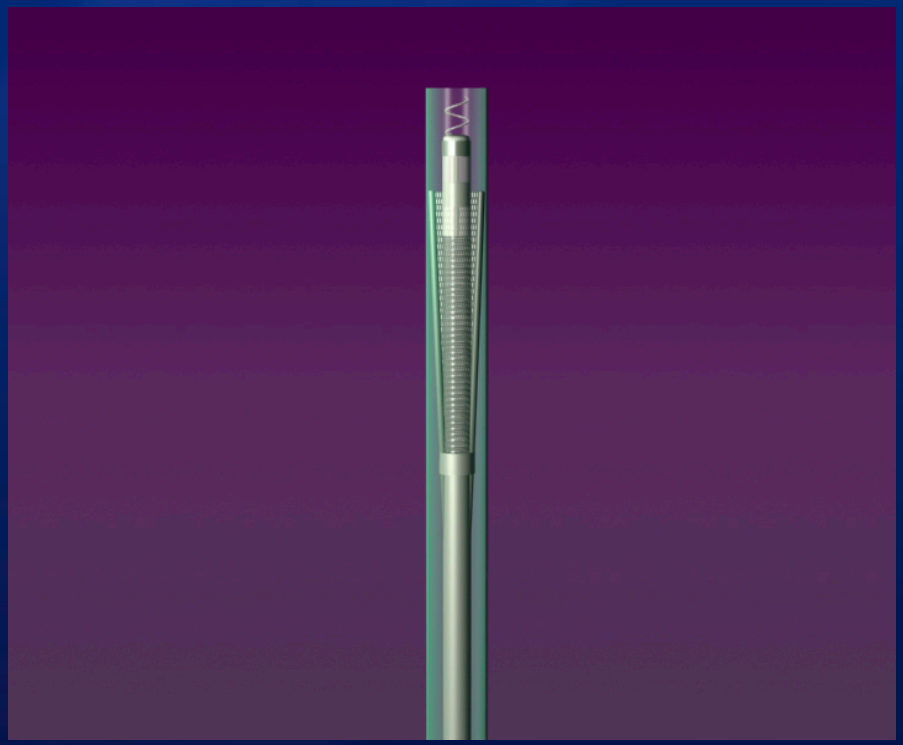


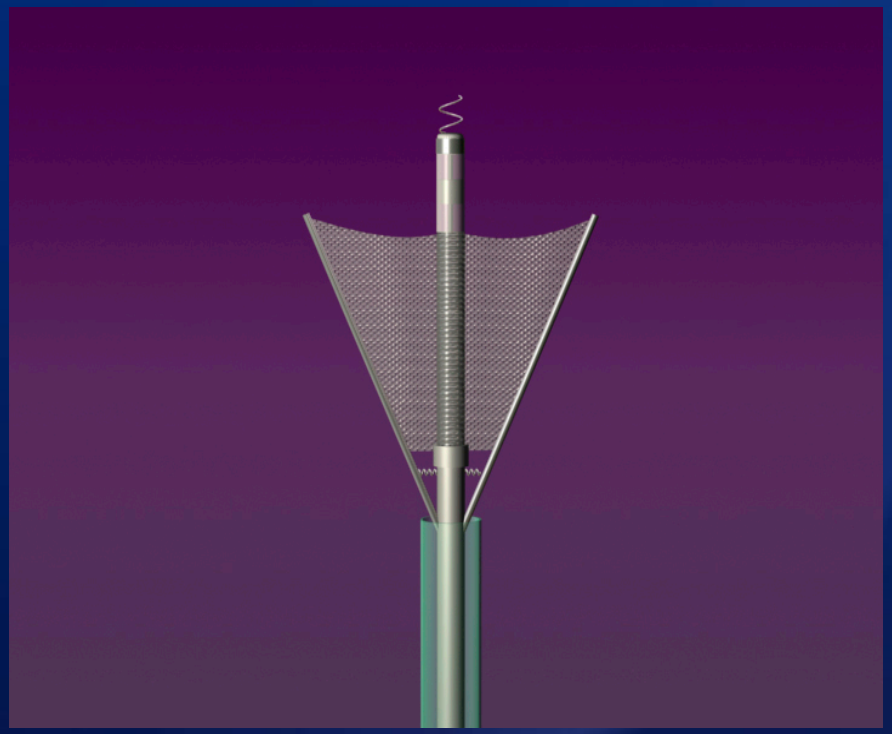
Superior View

Epicardial Access via RAA



One lead to pace LV and defibrillate





Deflection/flexibility could be added to distal screw/tip to facilitate LV placement

Clips for thoracotomy

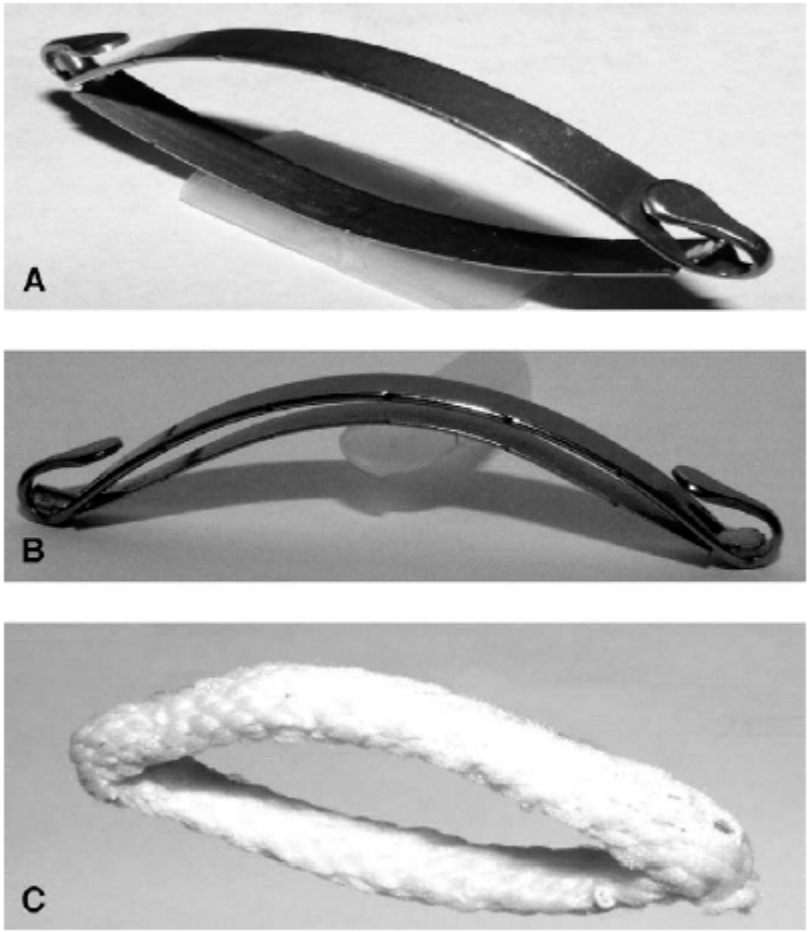
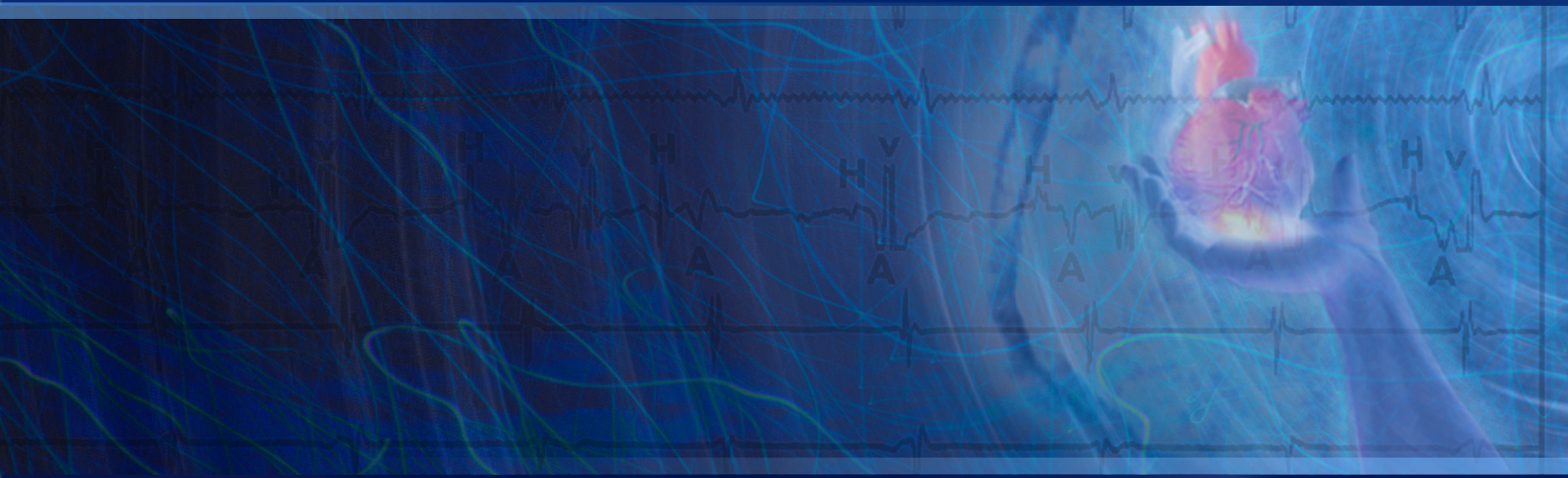


Figure 1. The atrial exclusion device (AED) consists of 2 stainless

LAA and Stroke Prevention



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Program Director Cardiac Electrophysiology;
Vice Chair – Innovations Mayo Clinic

Turin, October 26, 2012