


# Left Atrial Appendage Closure

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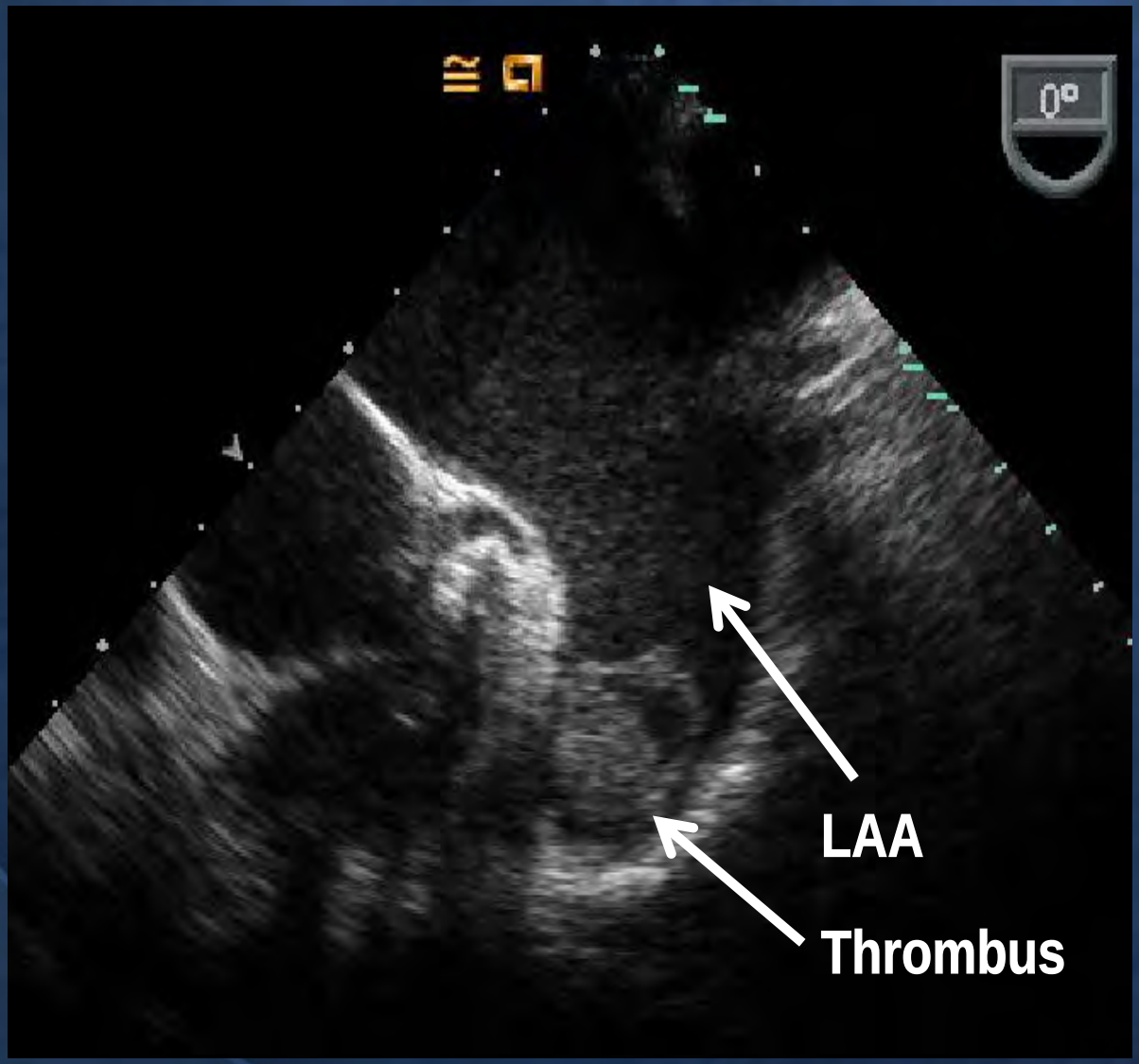
I have no financial relationships to disclose relevant to this presentation.

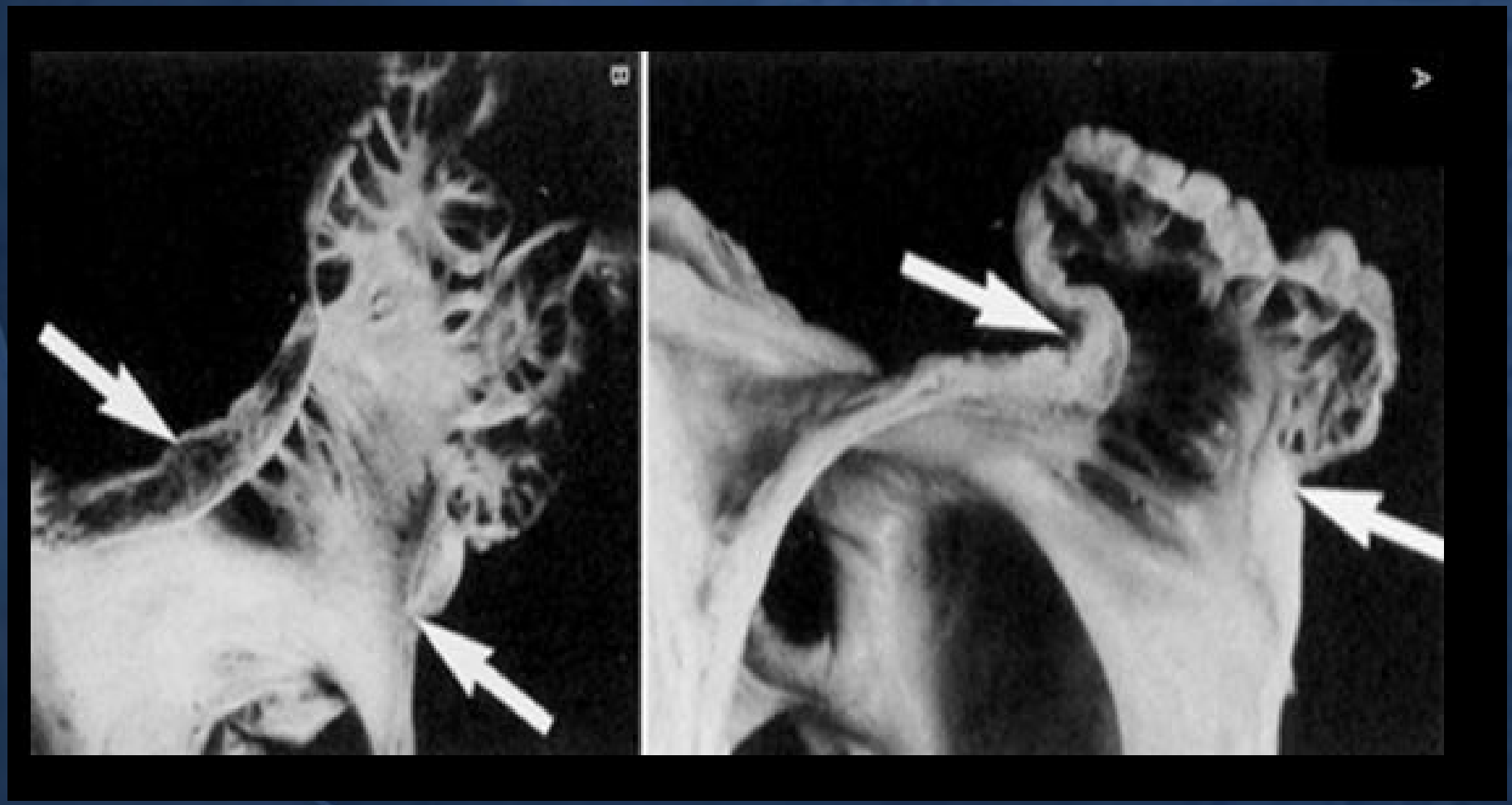
# ASE 2010 CASE
# 77 Female

- Hypertension, diabetes, AF x 12 years, on warfarin
- GI blood loss -> colon cancer, successful resection
- Ongoing blood loss with transfusions, dilated vessels, AVM
- $CHADS_2 = 3$ : stroke risk 6% / yr

# LAA most frequent source of embolus

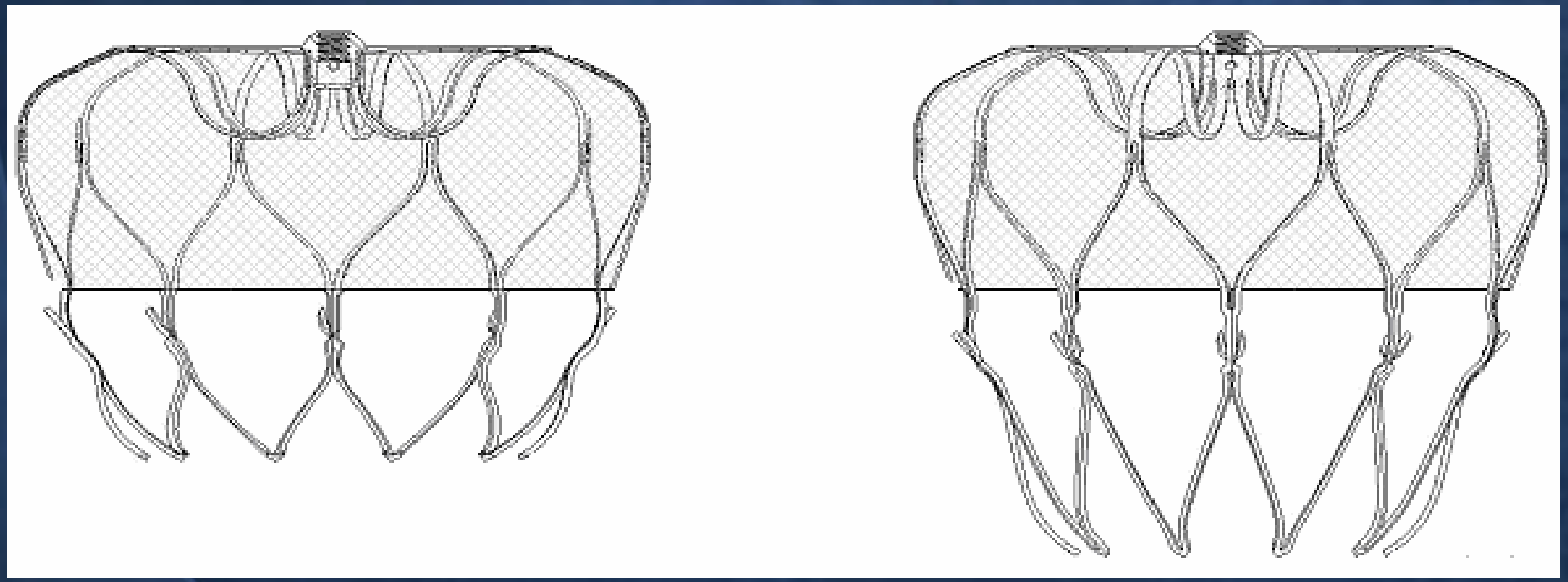


# Evaluating Baseline LAA anatomy – considerations, size, lobe complexity

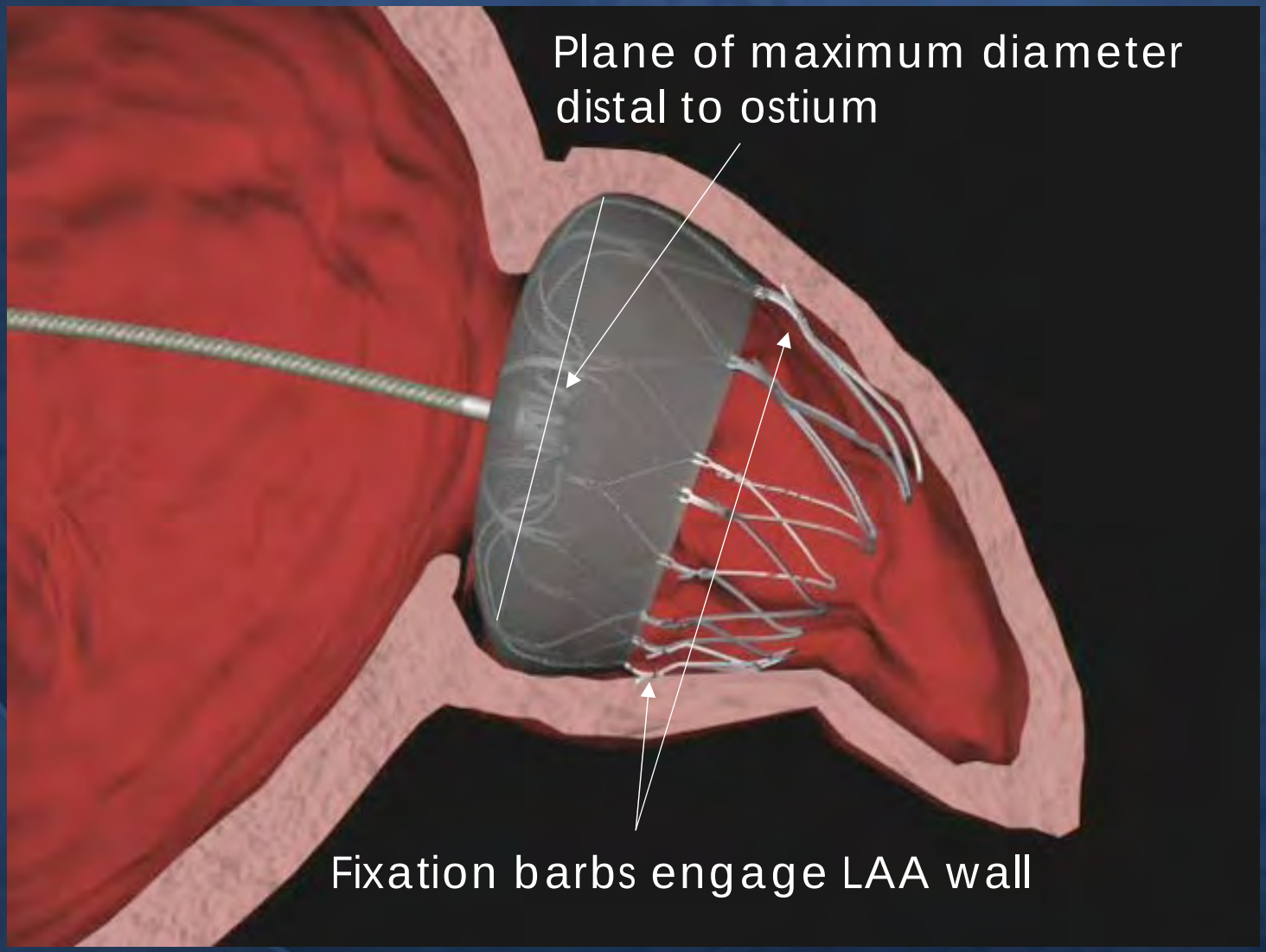


# Left Atrial Appendage – Post Mortem LAA Casts

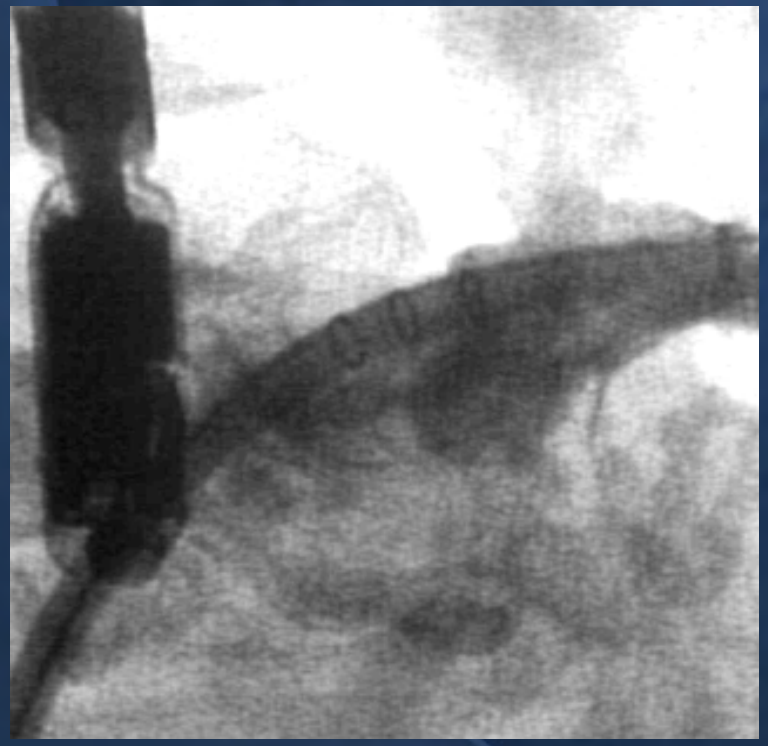
# WATCHMAN device

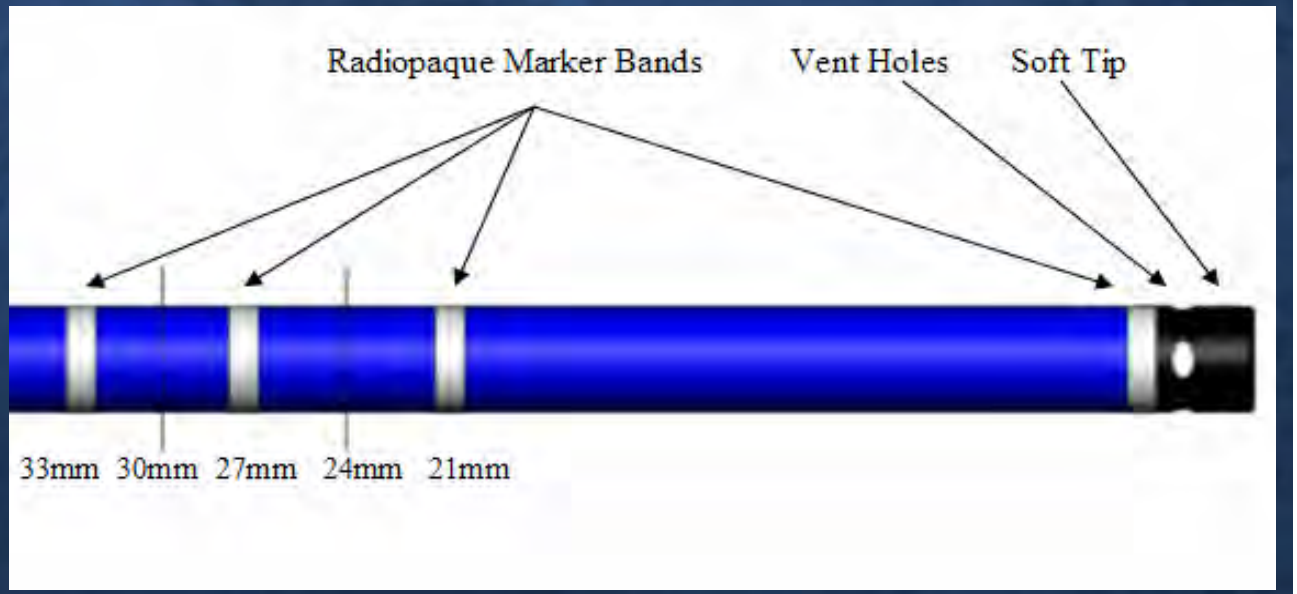


# Ideal position



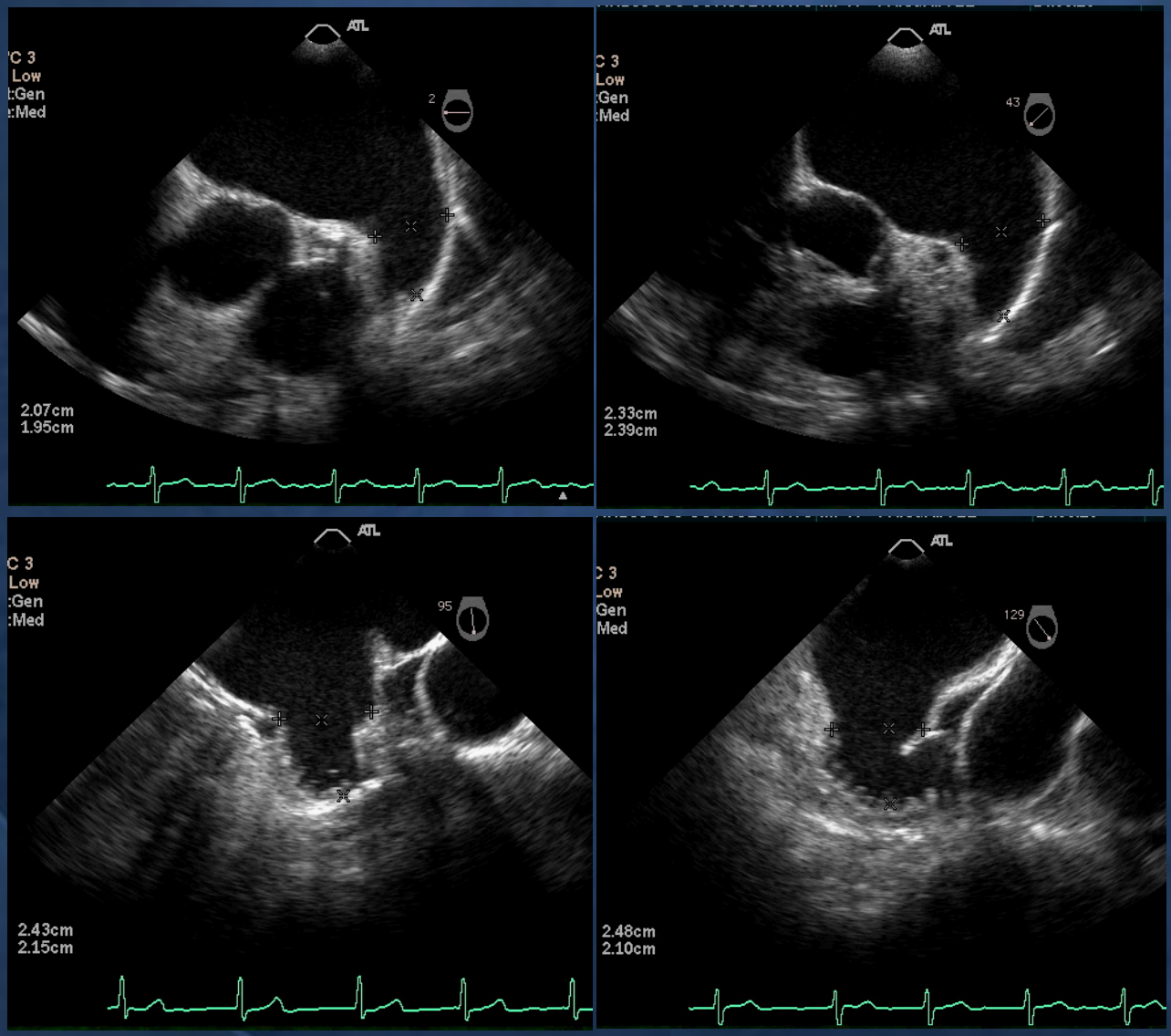
# WATCHMAN® LAA Access Sheath



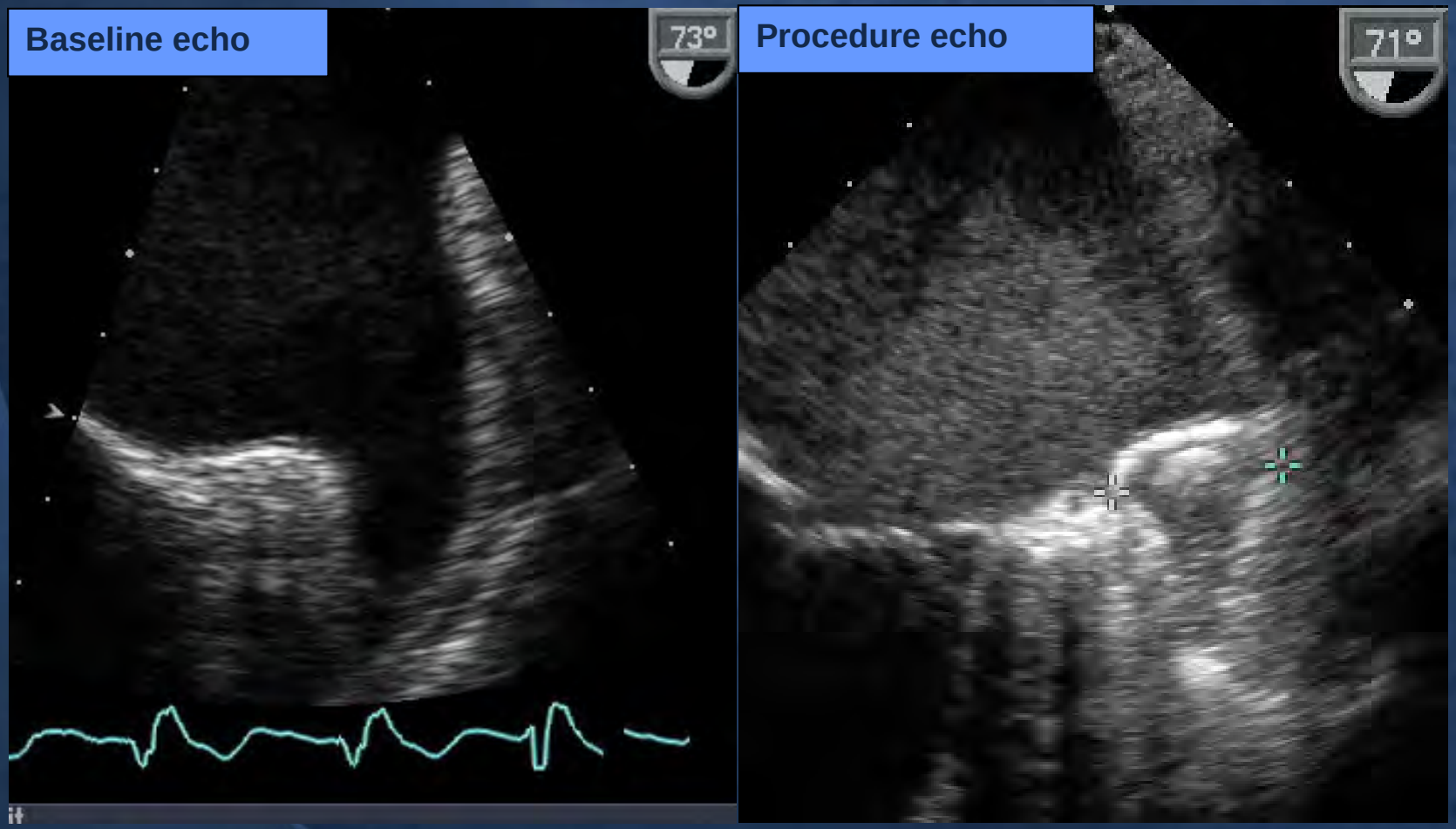


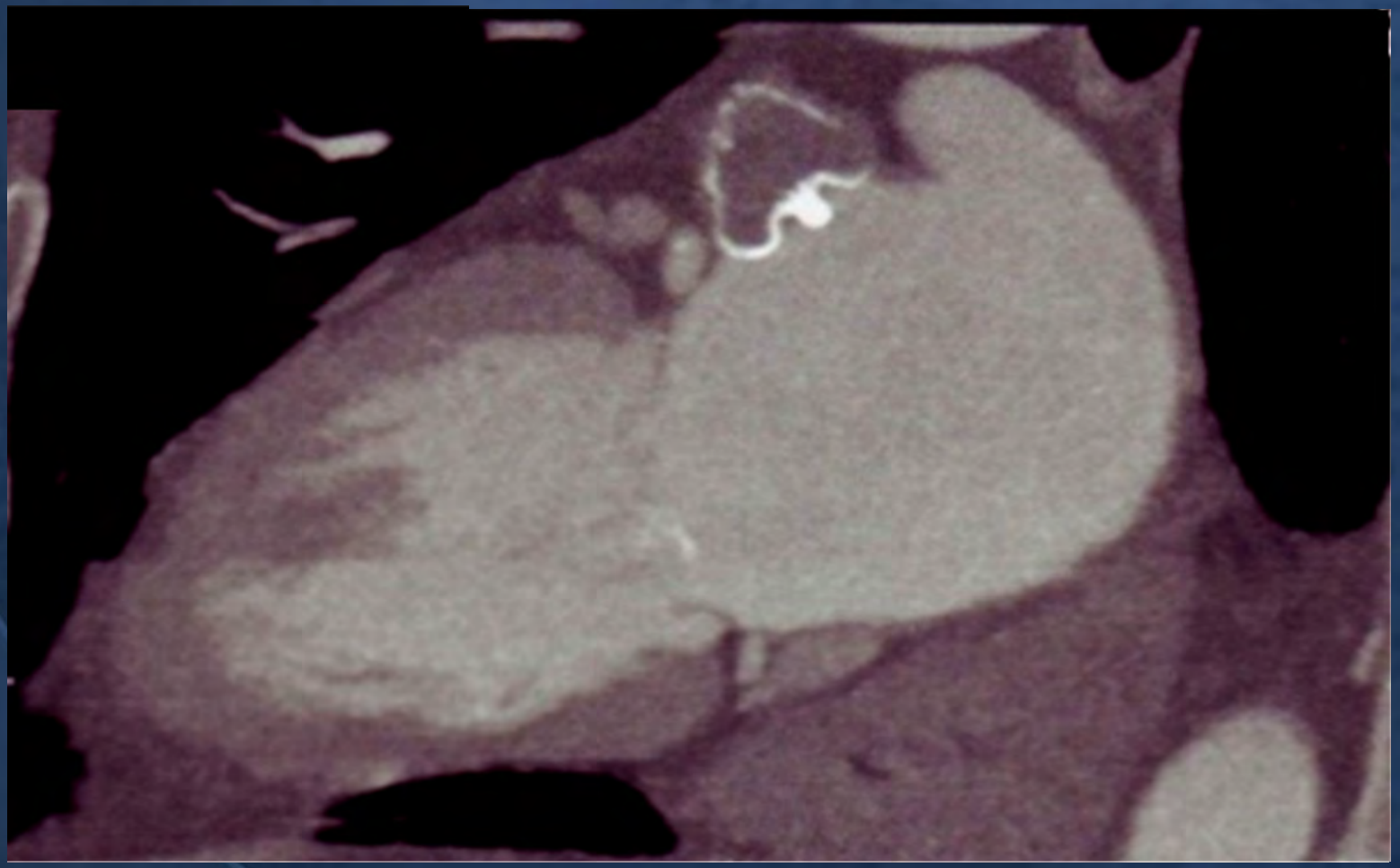
# Considerations for engaging the LAA

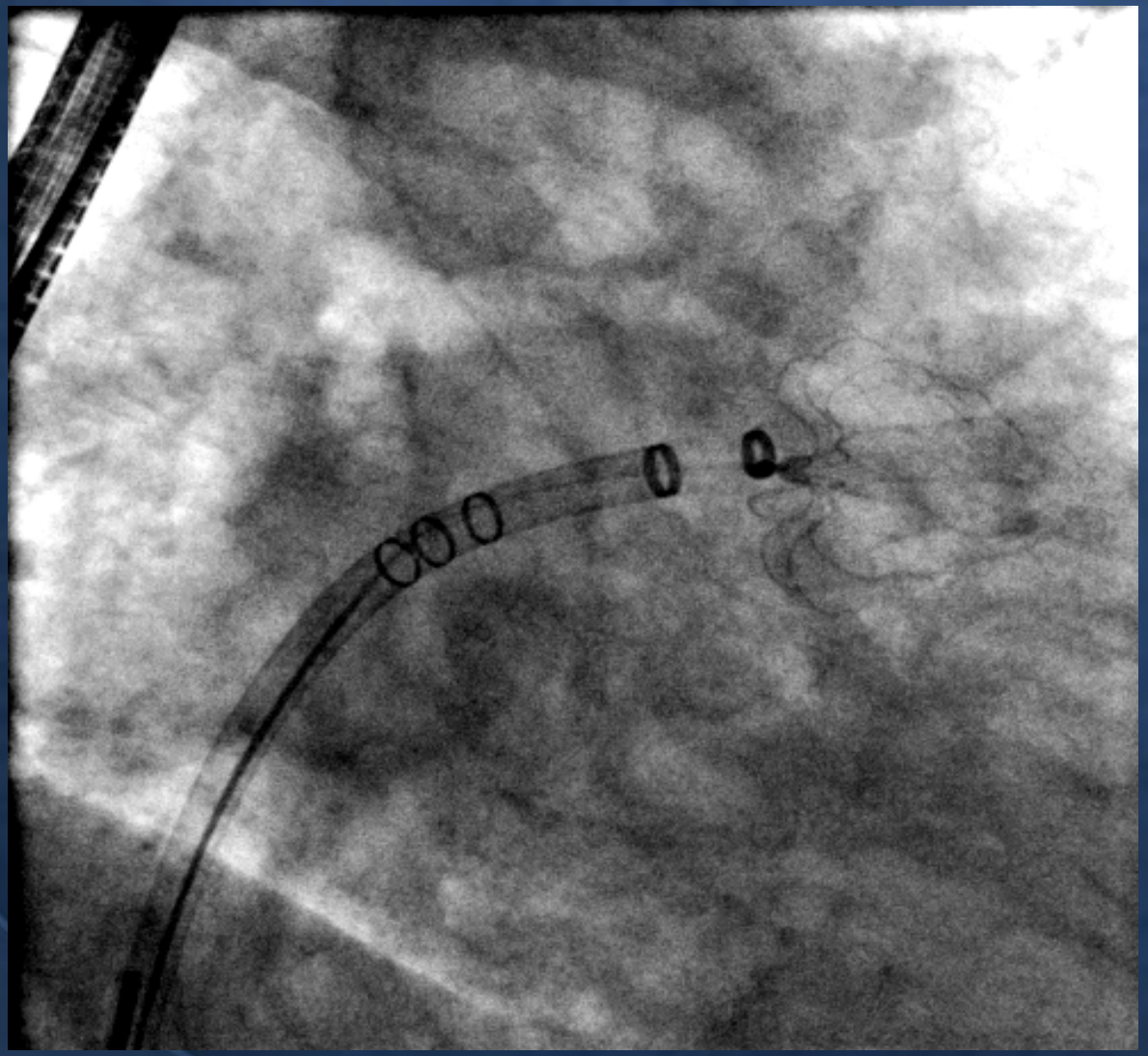

# Anatomic Assessment



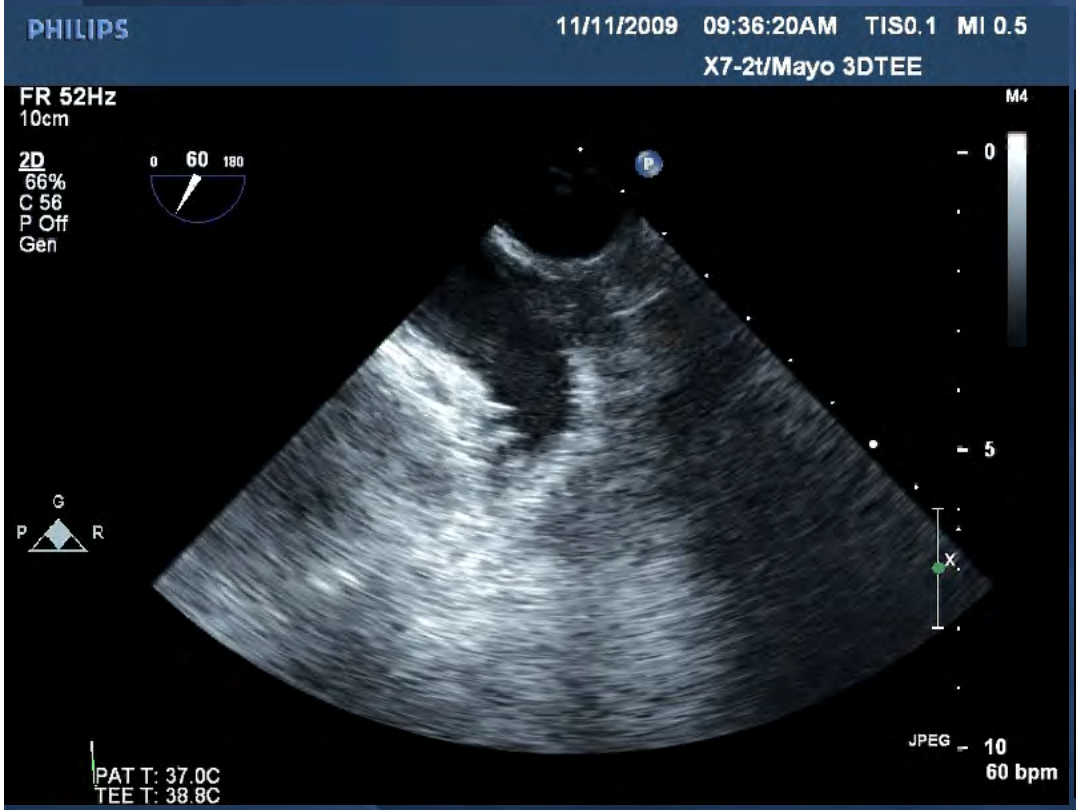
# Device in place

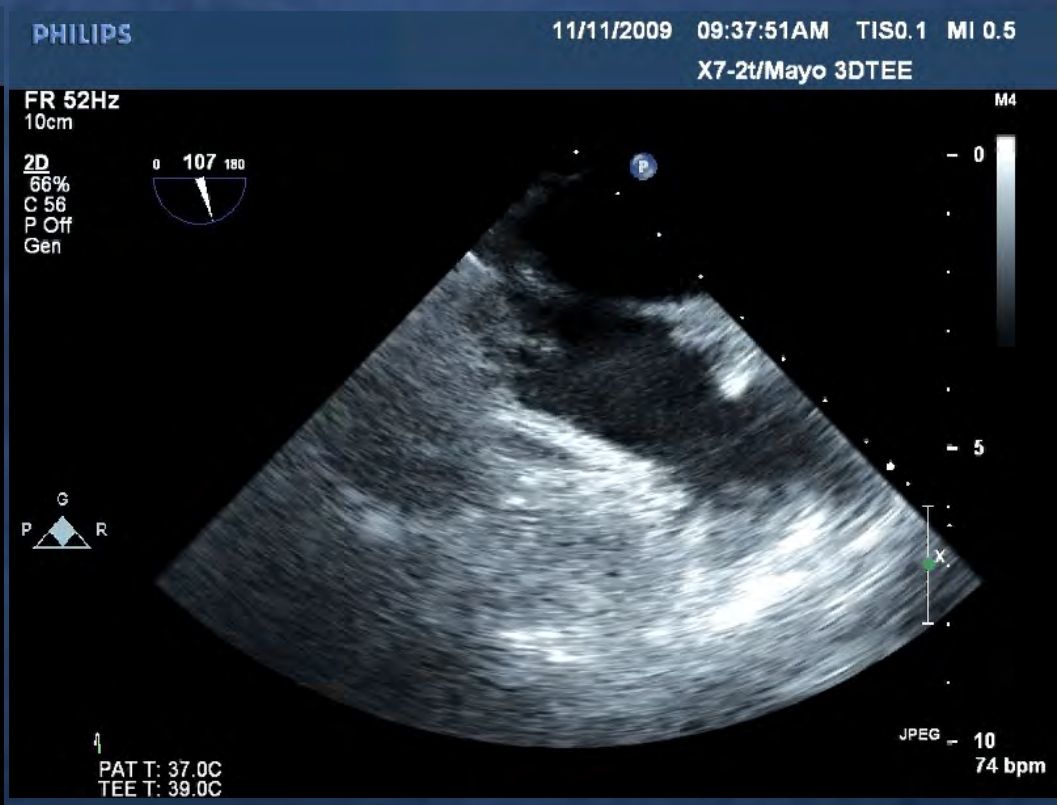






# Procedural TEE



# Procedural TEE

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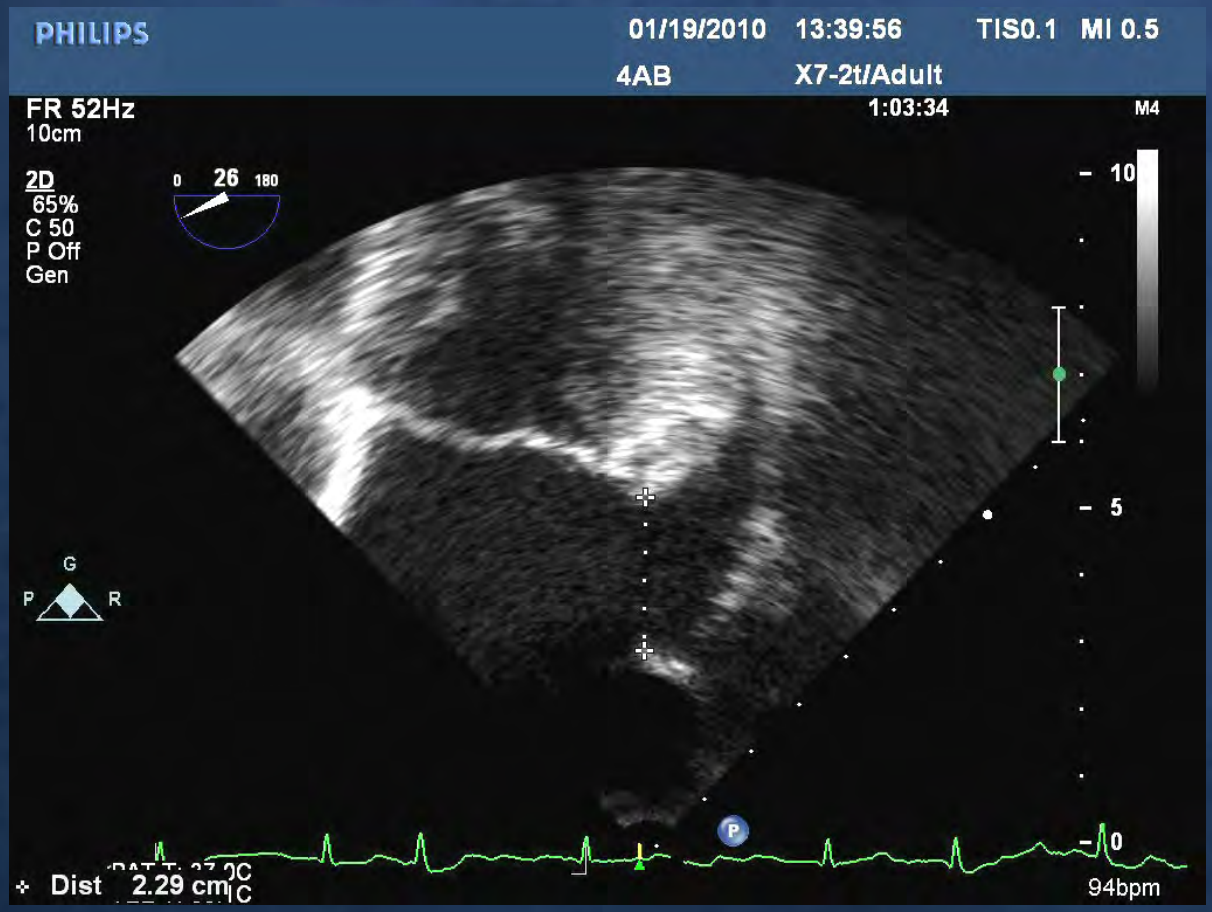
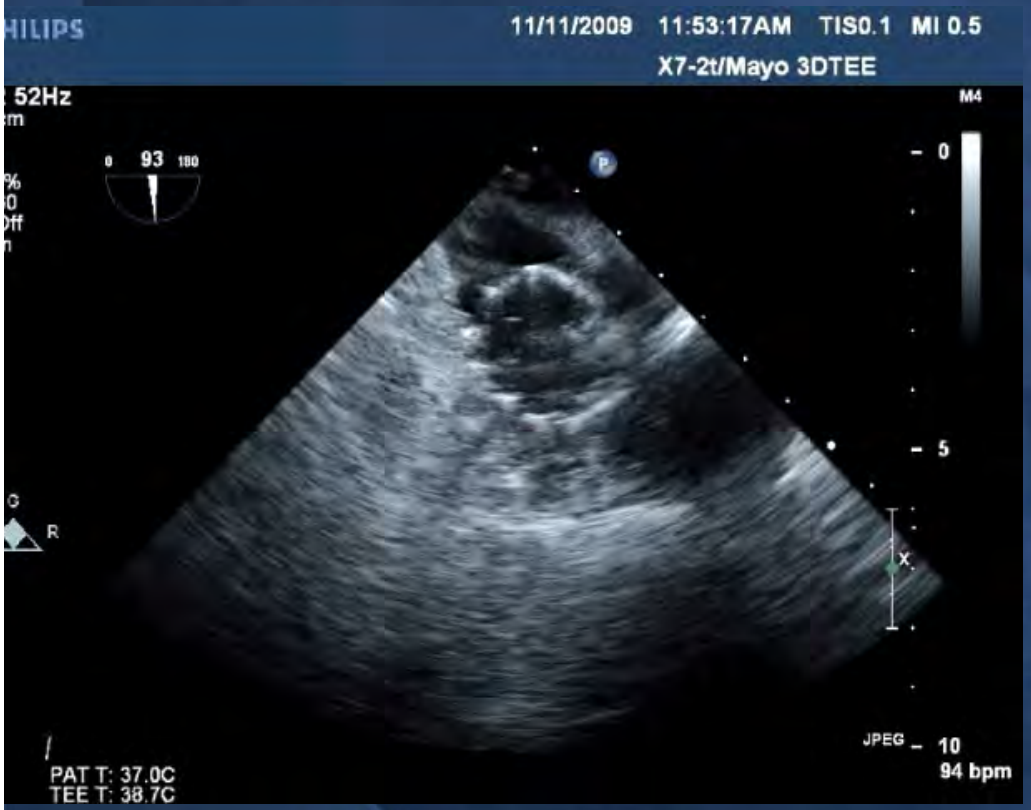
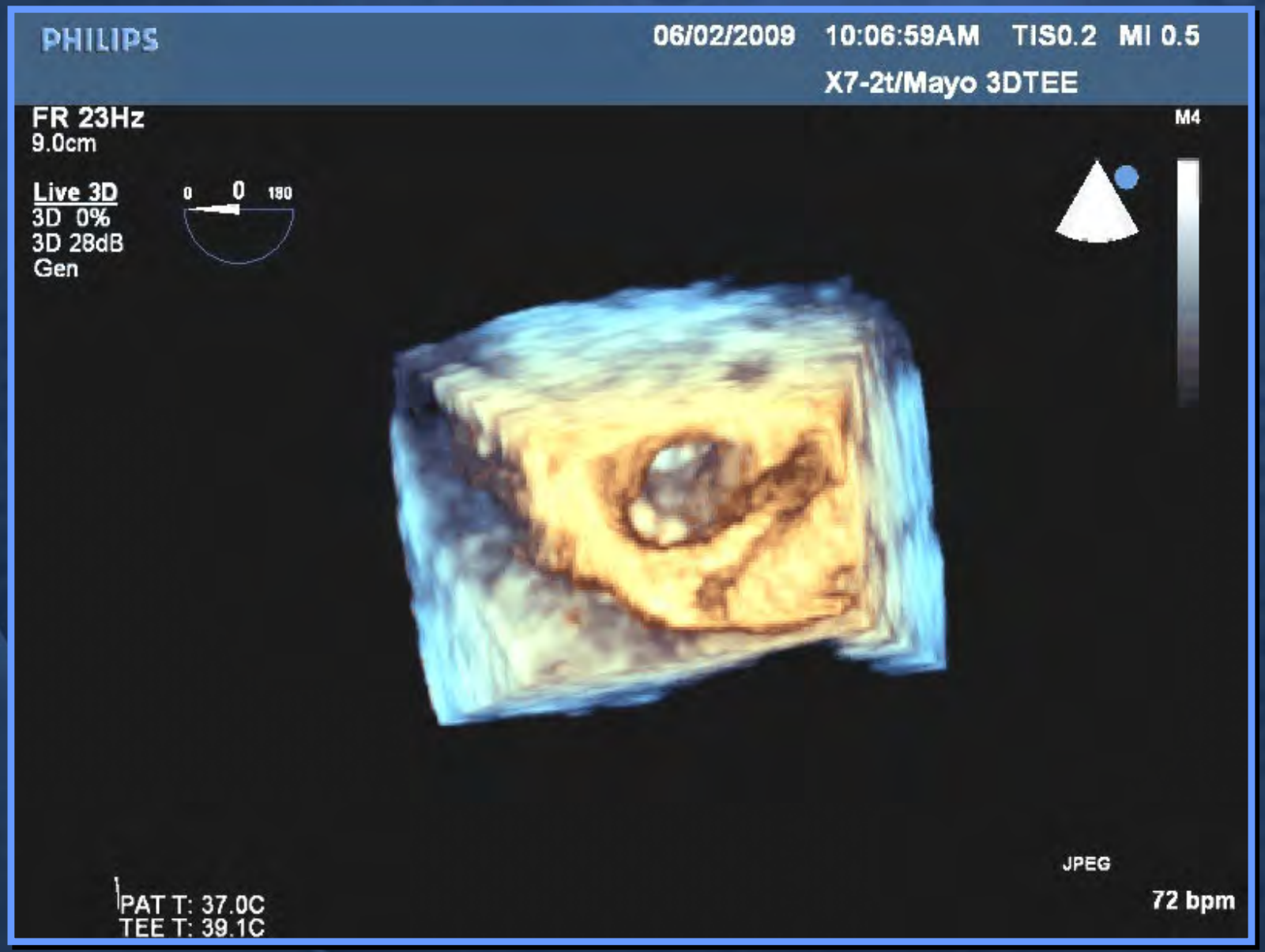


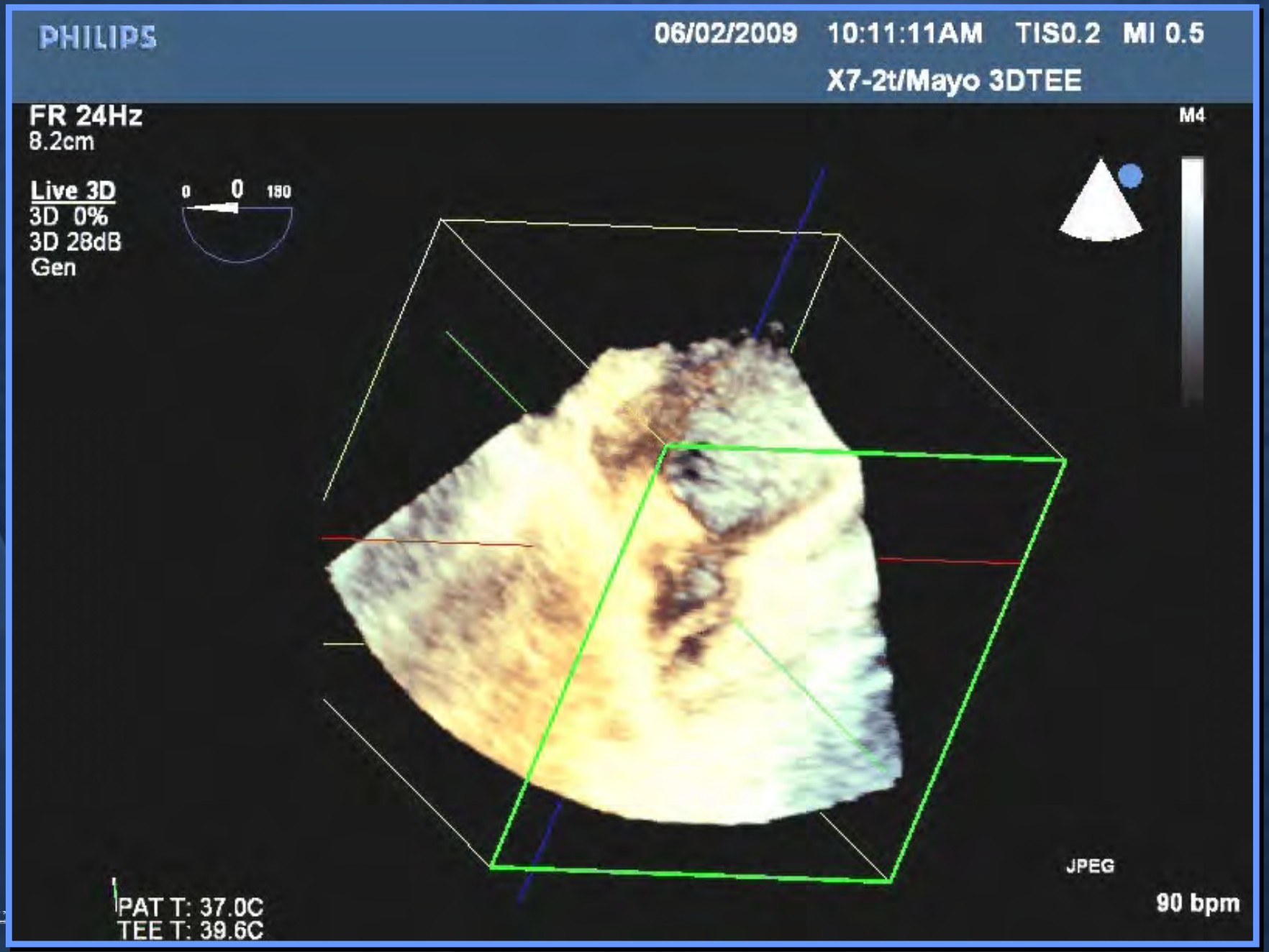
# Procedural TEE




# Watchman LAA Closure



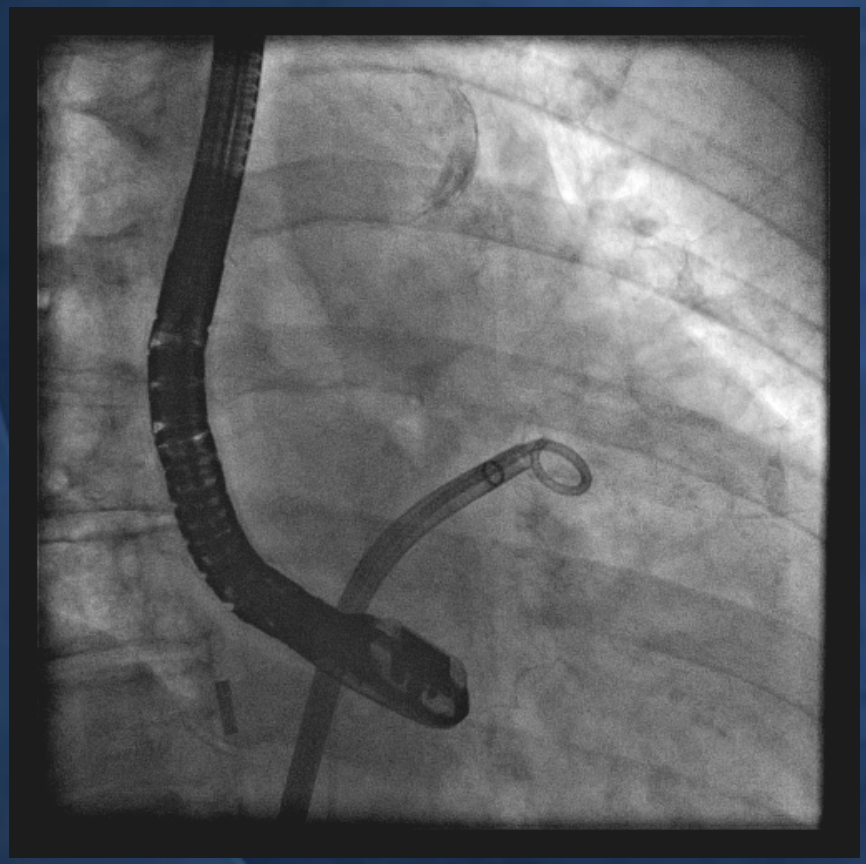
# Watchman LAA Closure

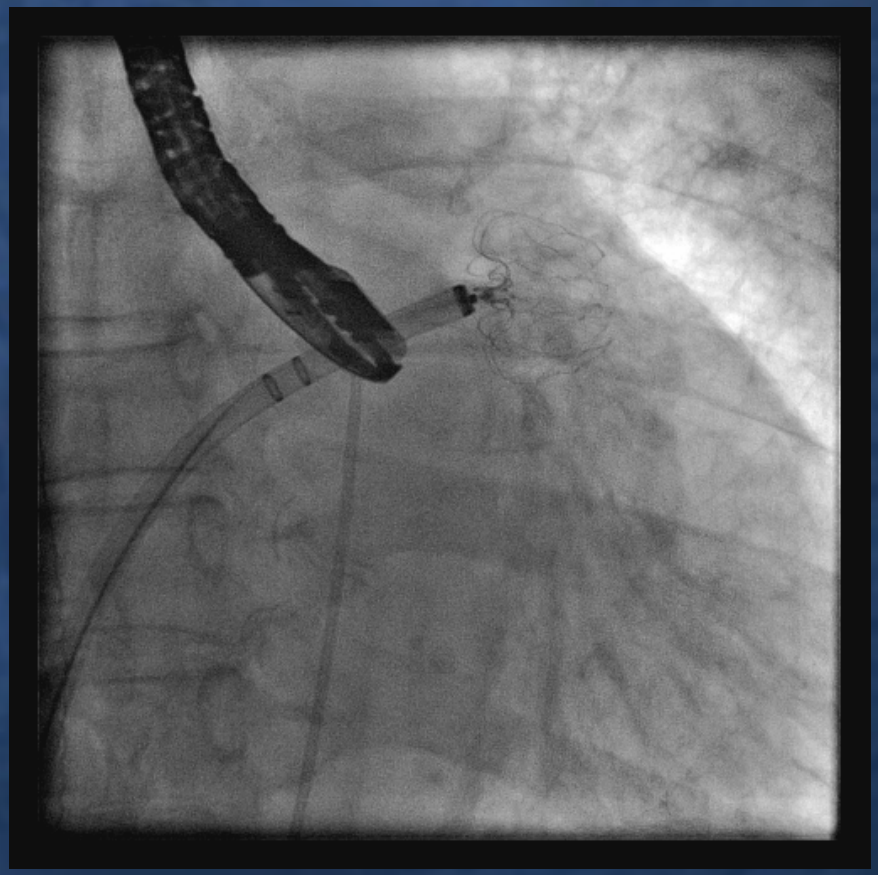


# Watchman LAA Closure


MAYO

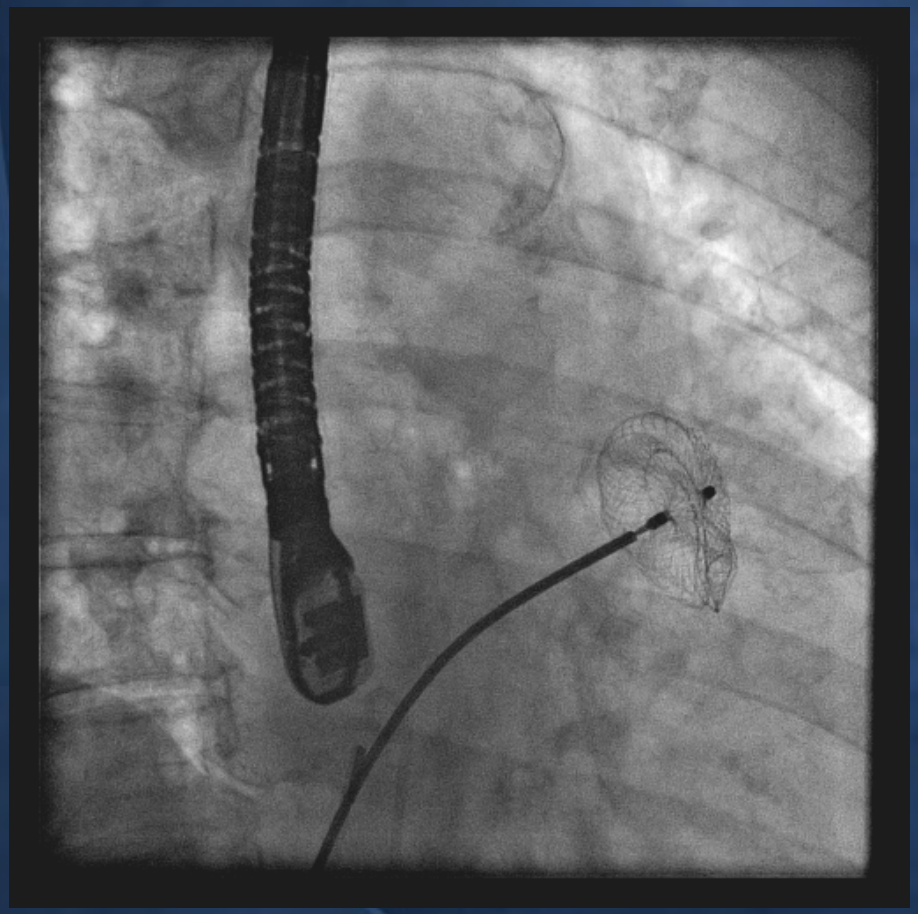
# Procedural Angio

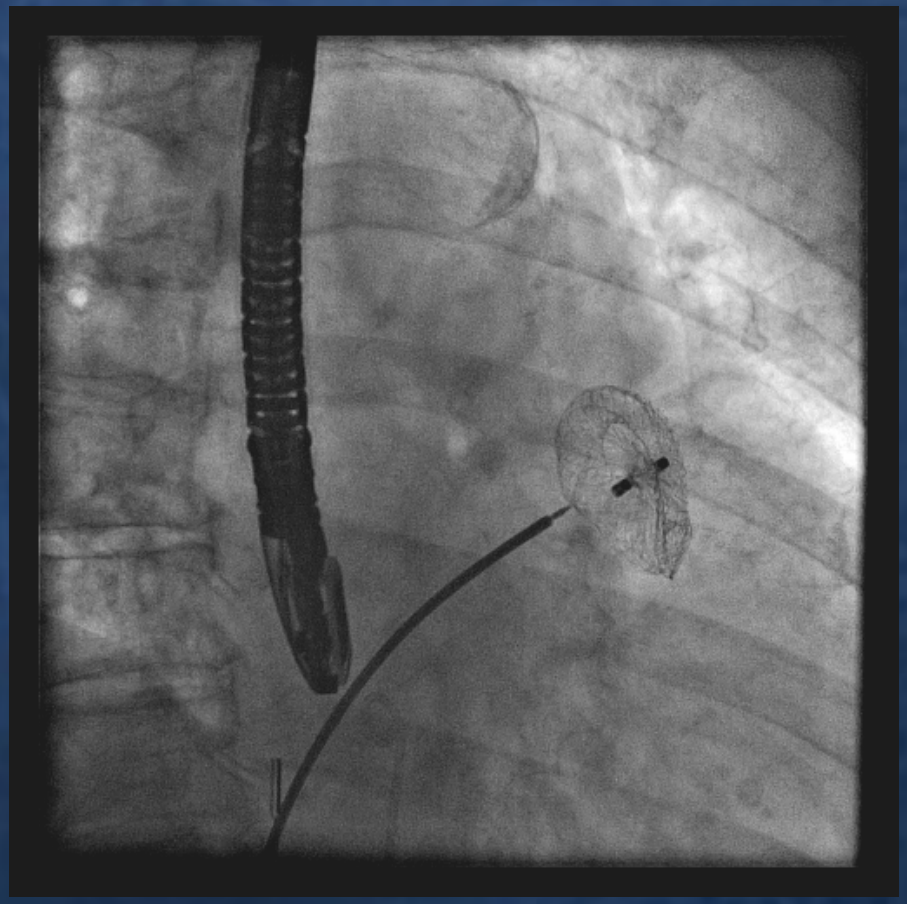




***Thoughts?***
***What to do?***

# Second Procedure





Catheterization and Cardiovascular Interventions 60:417–422 (2003)

*Original Studies*

# Transcatheter Left Atrial Appendage Occlusion With Amplatzer Devices to Obviate Anticoagulation in Patients With Atrial Fibrillation

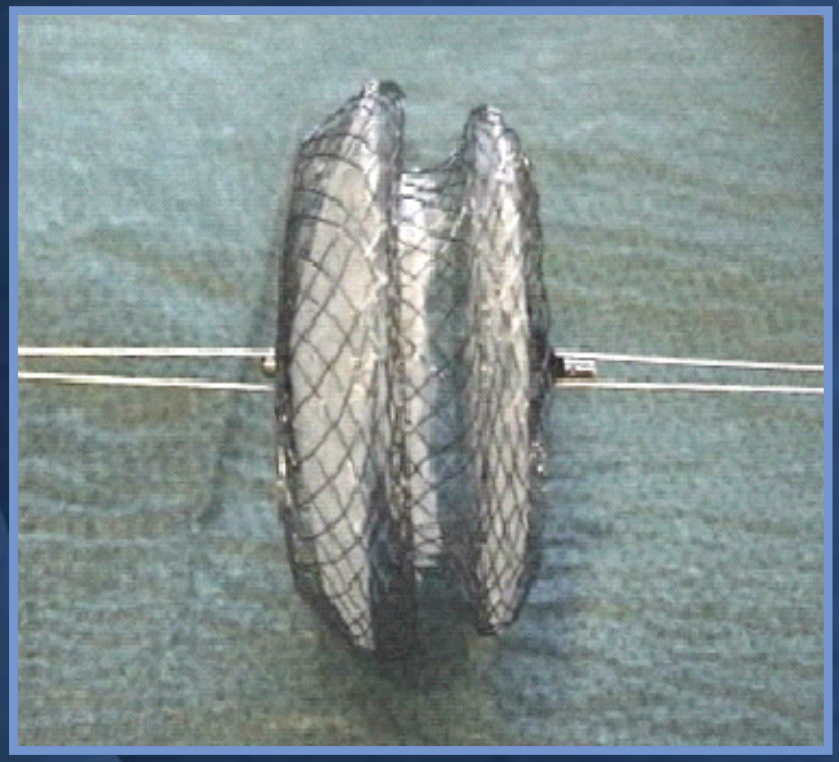
Bernhard Meier,[1*] MD, Igor Palacios,[2] MD, Stephan Windecker,[1] MD, Martin Rotter,[1] MD, Qi-Ling Cao,[3] MD, David Keane,[2] MD, Carlos E. Ruiz,[4] MD, and Ziyad M. Hijazi,[3] MD

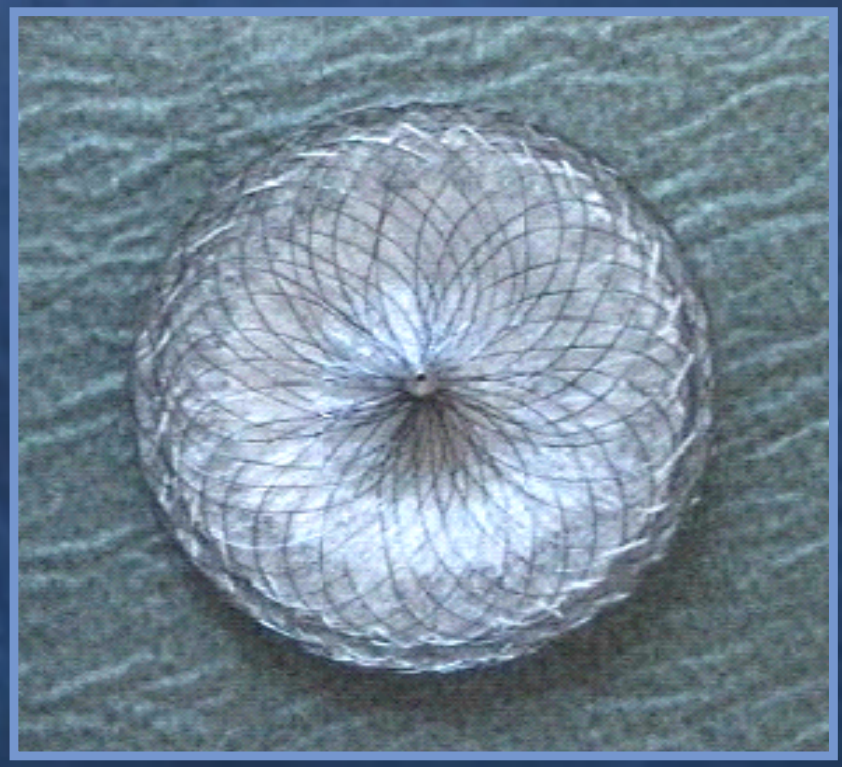
It is assumed that over 90% of clinically apparent embolisms in atrial fibrillation originate from the left atrial appendage. Recently, a percutaneous method (PLAATO technique) to occlude the left atrial appendage to the end of preventing thromboembolic complications of atrial fibrillation has been introduced into clinical practice. This technique is quite intricate and requires general anesthesia. The Amplatzer atrial septal occluder lends itself for a more simple approach to this intervention. The first 16 patients treated at four centers are described. Their age varied from 58 to 83 years. All suffered from atrial fibrillation but eight of them were in sinus rhythm at the time of implantation. All but two procedures were done under local anesthesia of the groin only. There was one technical failure (device embolization) requiring surgery. All other patients left the hospital a day after the procedure without complications. There were no problems or embolic events during an overall follow-up of 5 patient-years and all left atrial appendages were completely occluded without evidence of thrombosis at the atrial side of the device at the latest follow-up echocardiography. With the Amplatzer technique, the left atrial appendage can be percutaneously occluded with a venous puncture under local anesthesia, without echocardiographic guidance, and at a reasonable risk. It remains to be evaluated in larger series or randomized trials how the simpler Amplatzer technique compares with the complex PLAATO technique, and whether left atrial appendage closure is competitive with oral anticoagulation with warfarin or the novel ximelagatran to prevent thromboembolism in atrial fibrillation. *Catheter Cardiovasc Interv 2003;60:417–422.*



**16 patients, 1 technical failure, no complications.**

# Amplatzer devices

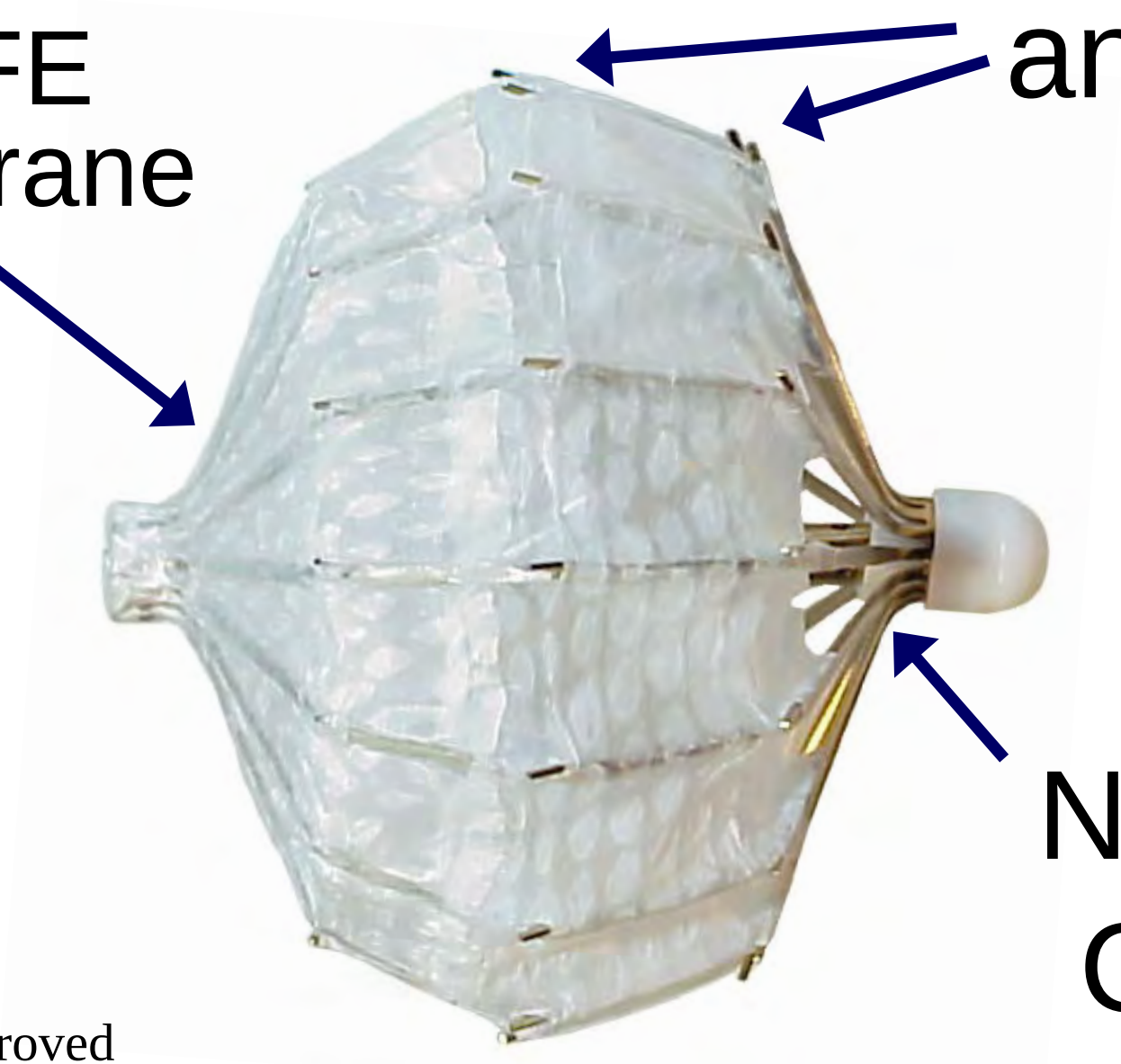




**Nitinol mesh, polyester fabric**
**Off label use**

# Dedicated LAA Device


# PLAATO™ Device



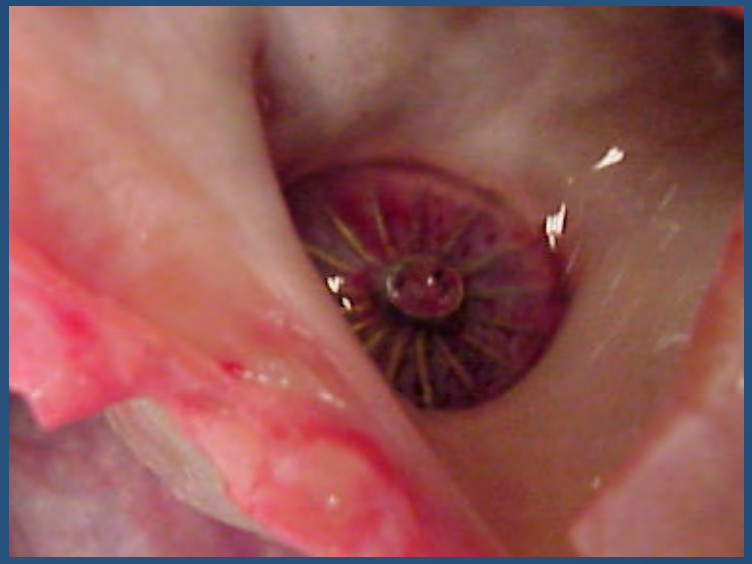

Not FDA approved

# Endothelialization

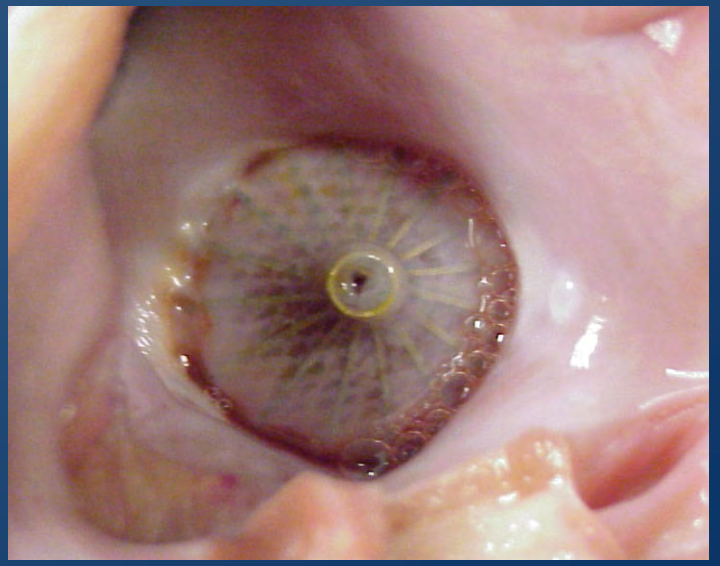
48 hours

2 weeks

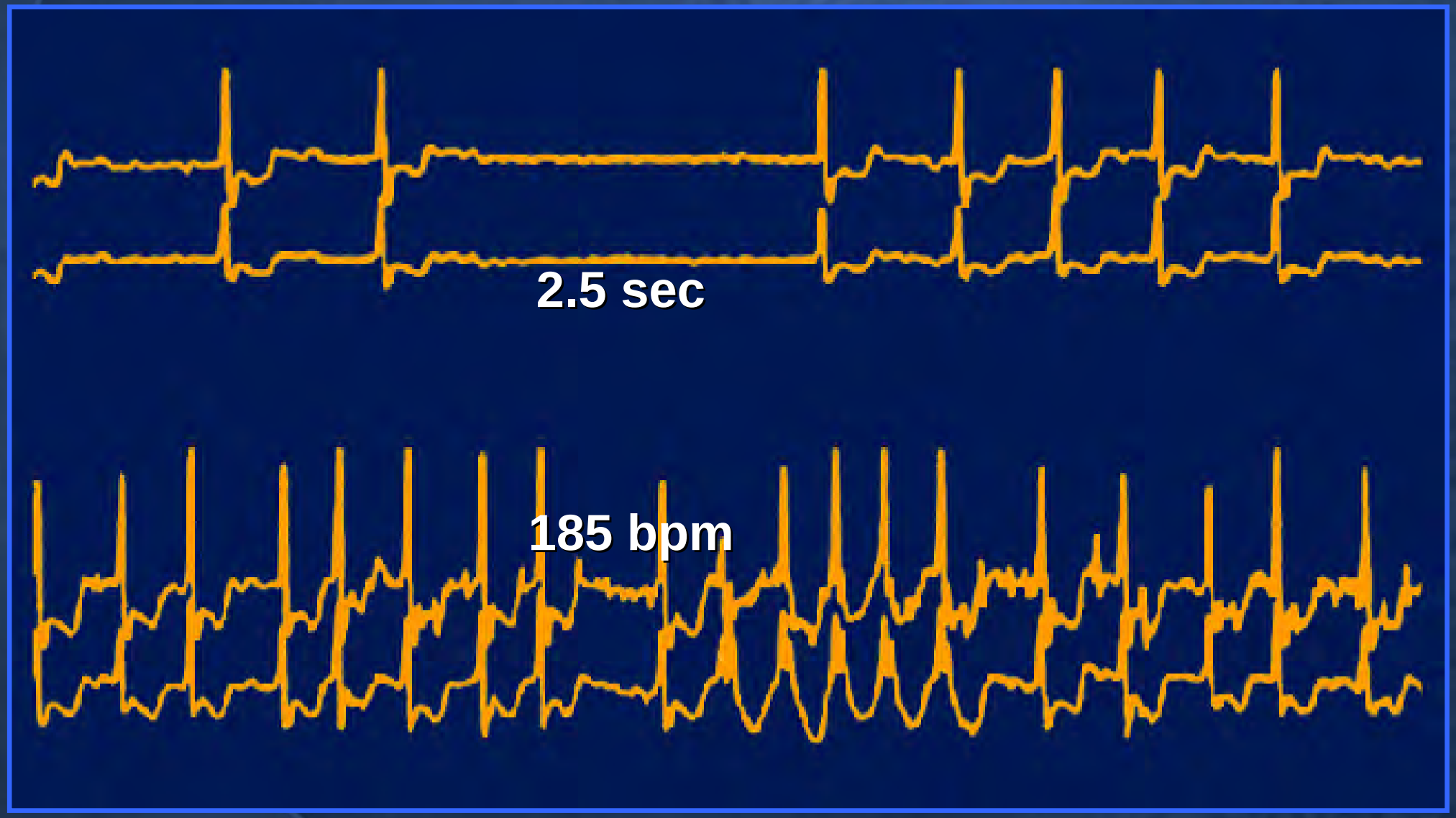
1 month



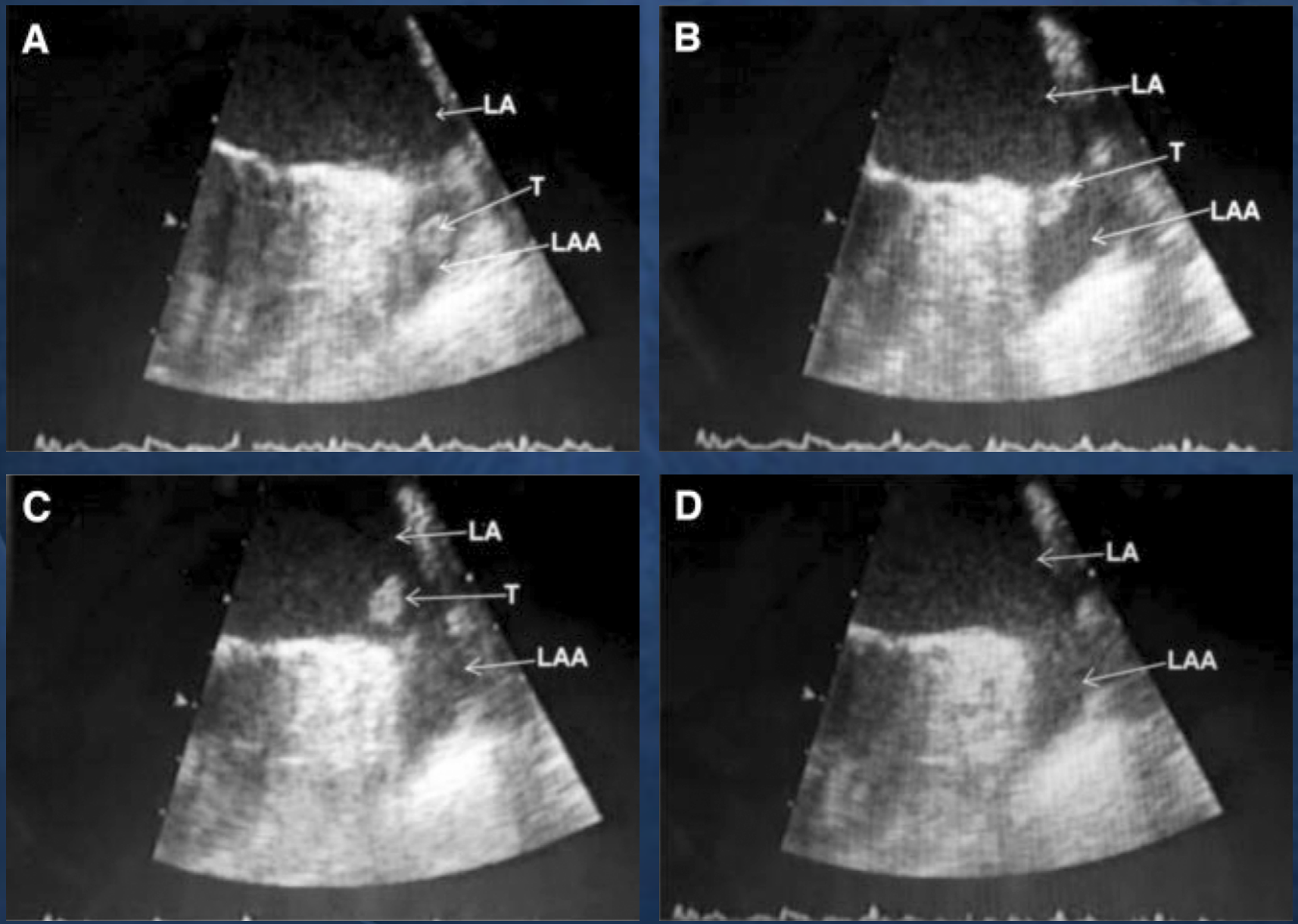
3 months



CardioVascular Center Frankfurt, Sankt Katharinen


2.5 sec
185 bpm

# LAA Thrombus is the Cause of Stroke

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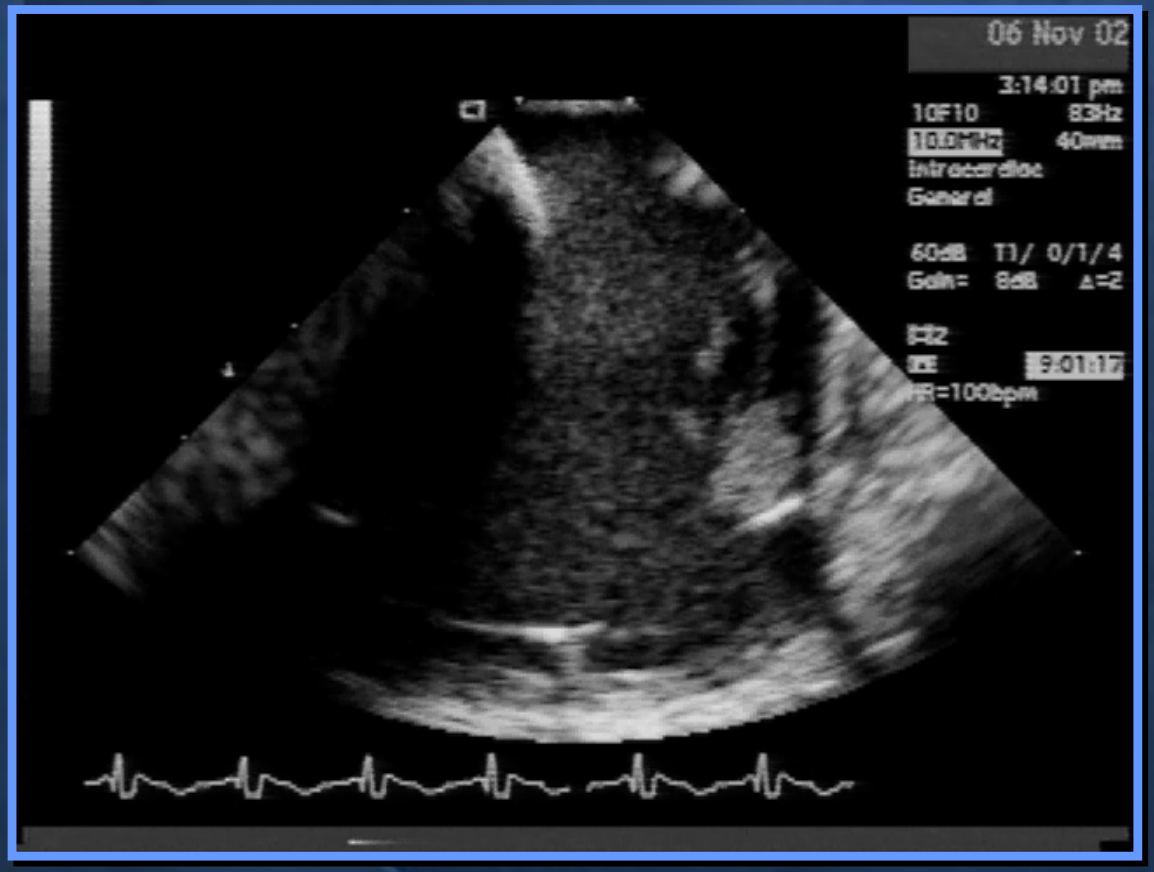
Parekh A, Ezekowitz M et al: Circ 114:e513, 2006

# Thrombus Formation




# Scope of the Problem

- AF is the most common arrhythmia
  - 3 million people in the U.S.
  - 16 million by 2050
- Lifetime risk is 1 in 4
- 5 x higher risk of stroke
  - 90% of strokes are thromboembolic
  - 90% of thrombus originates in LAA

# Scope of the Problem

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  - 3 million people in the U.S.
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- Lifetime risk is 1 in 4
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  - 90% of strokes are thromboembolic
  - 90% of thrombus originates in LAA

- Stroke is the #1 cause of long-term disability and the third leading cause of death in patients with AF

# Stroke in AF

- Paroxysmal, persistent and permanent AF all appear to increase the risk of ischemic stroke to a similar degree
- Risk increases with age

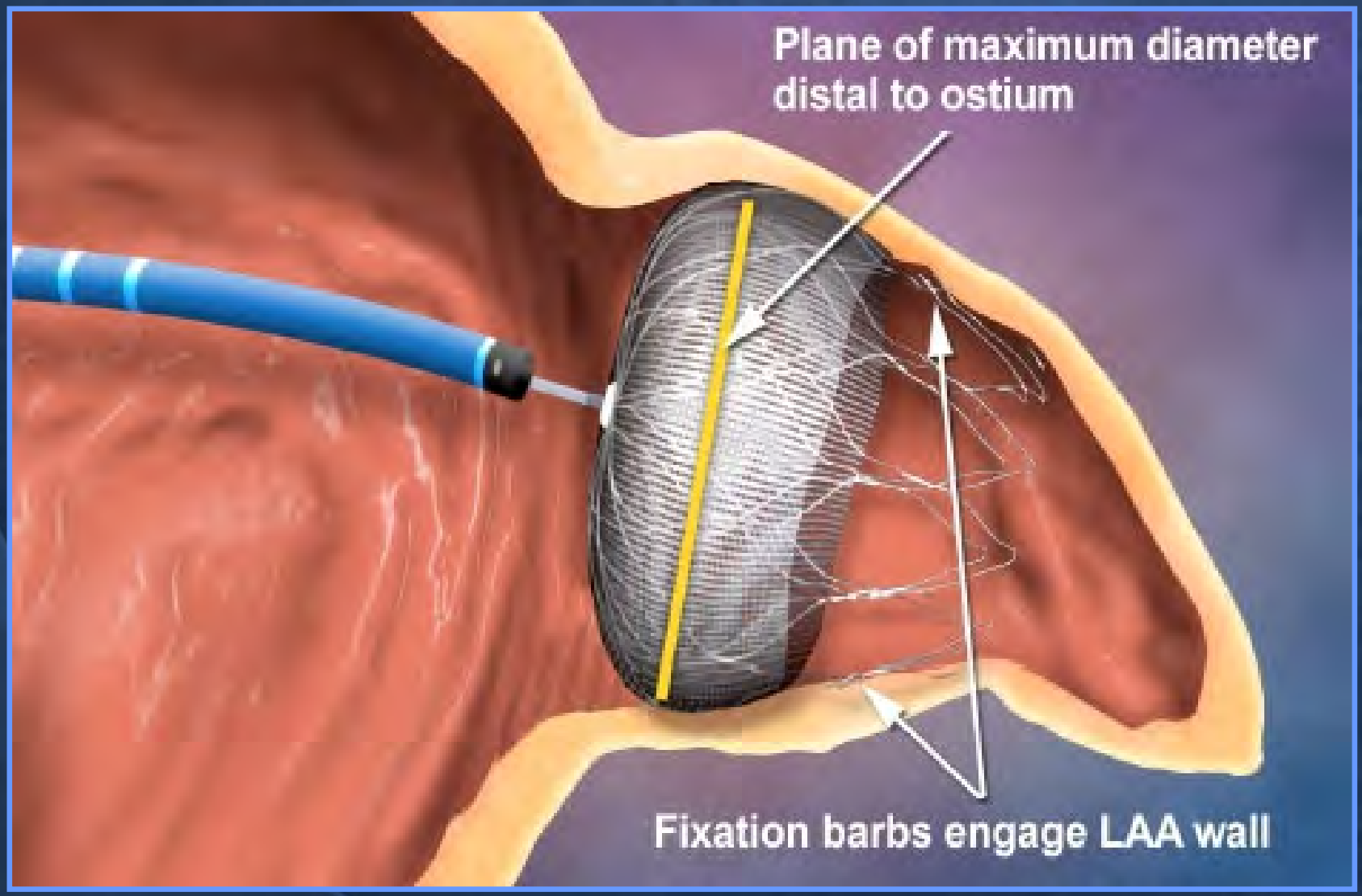
  In the Framingham study, risk of ischemic stroke attributable to atrial fibrillation increased from 1.5% at age 50-59, to 23.5% at age 80-89

# Location of thrombi in non-rheumatic atrial fibrillation

| Setting | Total thrombi | LAA | | LA | | Reference |
|---|---|---|---|---|---|---|
| | | No. | % | No. | % | |
| TEE | 67 | 66 | 99 | 1 | 1.5 | Stoddard: JACC, '95 |
| TEE | 35 | 34 | 97 | 1 | 2.9 | Manning: Circ, '94 |
| Autopsy | 47 | 35 | 74 | 12 | 25.5 | Aberg: Acta Med Scan, '69 |
| TEE | 4 | 2 | 50 | 2 | 50.0 | Tsai: JFMA, '90 |
| TEE | 13 | 12 | 92 | 1 | 7.7 | Klein: Int J Card Imag, '93 |
| TEE & operation | 11 | 8 | 73 | 3 | 27.3 | Manning: Circ, '94 |
| SPAF III & TEE | 20 | 19 | 95 | 1 | 5.0 | Klein: Circ, '94 |
| TEE | 19 | 19 | 100 | 0 | 0.0 | Leung: JACC, '94 |
| TEE | 6 | 6 | 100 | 0 | 0.0 | Hart: Stroke, '94 |
| Total | 222 | 201 | 91 | 21 | 9.5 | |

Ann Thor Surg 61:755, 1996

# WATCHMAN LAA Closure Device in Situ



# 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

See Editorial page 501

See Comment page 504

*Members listed at end of paper

**Mayo Clinic College of Medicine, Rochester, MN, USA** (Prof D R Holmes MD); **Mount Sinai School of Medicine, New York, NY, USA** (V Y Reddy MD); **Cooper Hospital, Camden, NJ, USA** (Z G Turi MD); **Pacific Heart Institute/St Johns Hospital, Santa Monica, CA, USA** (S K Doshi MD); **CardioVascular Center Frankfurt, Sankt Katharinen, Frankfurt, Germany** (Prof H Sievert MD); **Foundation for Cardiovascular Medicine, La Jolla, CA, USA** (M Buchbinder MD); **Integra Group, Brooklyn Park, MN, USA** (C M Mullin MS); **and Krankenhaus der Barmherzigen Bruder, Regensburg, Germany** (P Sick MD)

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Prof David R Holmes, Mayo Clinic, 200 First Street SW, SMH MB 4-523, Rochester, MN 55905, USA
**holmes.david@mayo.edu**

## Summary

**Background** In patients with non-valvular atrial fibrillation, embolic stroke is thought to be associated with left atrial appendage (LAA) thrombi. We assessed the efficacy and safety of percutaneous closure of the LAA for prevention of stroke compared with warfarin treatment in patients with atrial fibrillation.

**Methods** Adult patients with non-valvular atrial fibrillation were eligible for inclusion in this multicentre, randomised non-inferiority trial if they had at least one of the following: previous stroke or transient ischaemic attack, congestive heart failure, diabetes, hypertension, or were 75 years or older. 707 eligible patients were randomly assigned in a 2:1 ratio by computer-generated randomisation sequence to percutaneous closure of the LAA and subsequent discontinuation of warfarin (intervention; n=463) or to warfarin treatment with a target international normalised ratio between 2·0 and 3·0 (control; n=244). Efficacy was assessed by a primary composite endpoint of stroke, cardiovascular death, and systemic embolism. We selected a one-sided probability criterion of non-inferiority for the intervention of at least 97·5%, by use of a two-fold non-inferiority margin. Serious adverse events that constituted the primary endpoint for safety included major bleeding, pericardial effusion, and device embolisation. Analysis was by intention to treat. This study is registered with Clinicaltrials.gov, number NCT00129545.

**Findings** At 1065 patient-years of follow-up, the primary efficacy event rate was 3·0 per 100 patient-years (95% credible interval [CrI] 1·9–4·5) in the intervention group and 4·9 per 100 patient-years (2·8–7·1) in the control group (rate ratio [RR] 0·62, 95% CrI 0·35–1·25). The probability of non-inferiority of the intervention was more than 99·9%. Primary safety events were more frequent in the intervention group than in the control group (7·4 per 100 patient-years, 95% CrI 5·5–9·7, *vs* 4·4 per 100 patient-years, 95% CrI 2·5–6·7; RR 1·69, 1·01–3·19).

**Interpretation** The efficacy of percutaneous closure of the LAA with this device was non-inferior to that of warfarin therapy. Although there was a higher rate of adverse safety events in the intervention group than in the control group, events in the intervention group were mainly a result of periprocedural complications. Closure of the LAA might provide an alternative strategy to chronic warfarin therapy for stroke prophylaxis in patients with non-valvular atrial fibrillation.

# PROTECT AF Trial: Hypothesis

Left atrial appendage occlusion can decrease all stroke, death, systemic embolization and avoid the need for chronic anticoagulation in patients with non-rheumatic valvular atrial fibrillation

# Safety and Efficacy Events

## Efficacy events

Stroke – ischemic

Systemic embolism

Sudden death

## Stroke – hemorrhagic

## Stroke – procedural related

## Both efficacy and safety

## Safety events

Device embolization

Major bleeding events

Pericardial effusions

"Primary effectiveness endpoint captures the events that would also be considered significant safety events (ie, stroke, death and systemic embolism)."

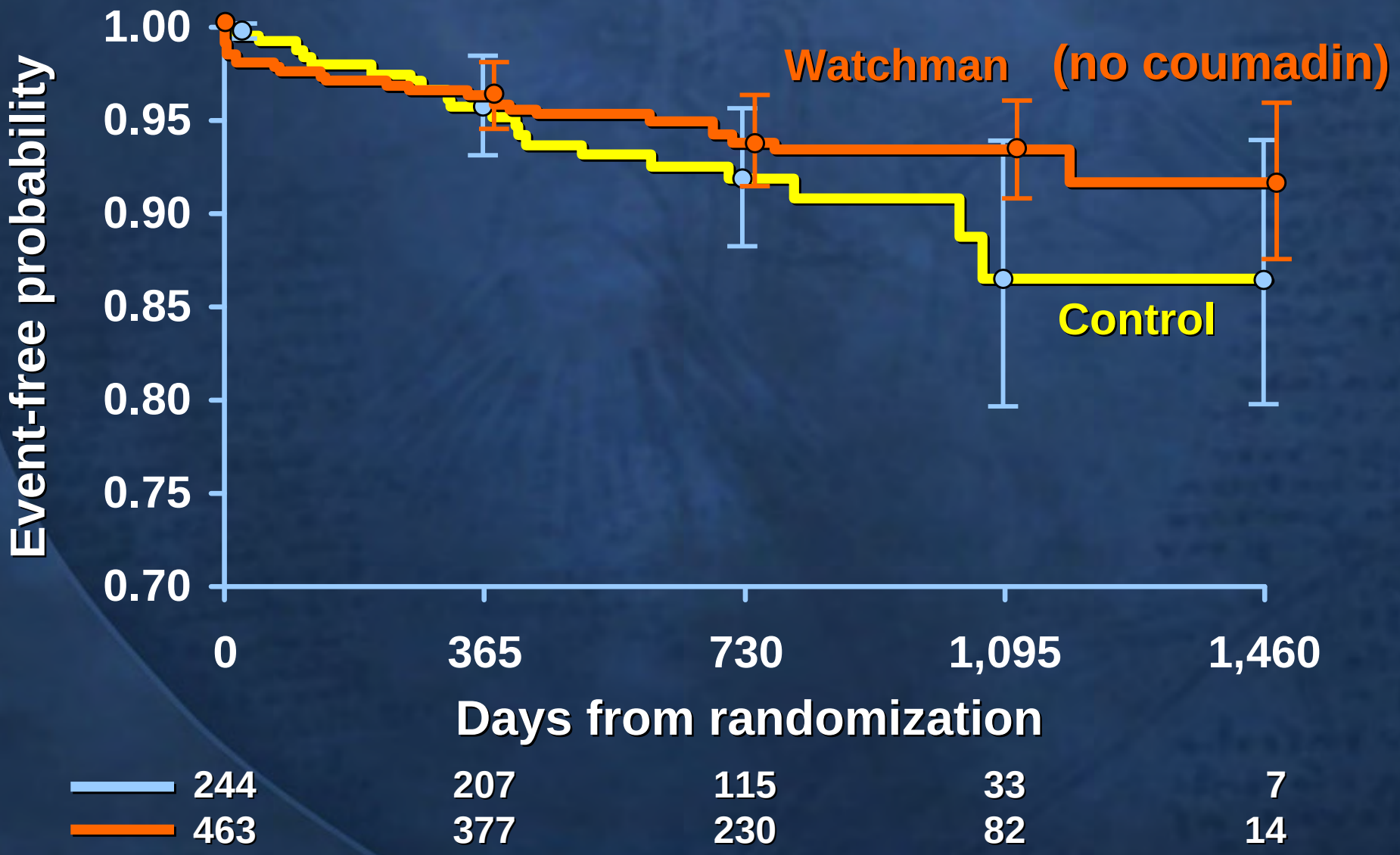
# Intent-to-Treat: Primary Efficacy Results

| Cohort | WATCHMAN Rate (95% CI) | Control Rate (95% CI) | Rel risk (95% CI) | Posterior probabilities Noninferiority | Superiority |
|---|---|---|---|---|---|
| 600 pt-yr | 4.4 (2.6-6.7) | 5.8 (3.0-9.1) | 0.76 (0.39-1.67) | 0.992 | 0.734 |
| 900 pt-yr | 3.4 (2.1-5.2) | 5.0 (2.8-7.6) | 0.68 (0.37-1.41) | 0.998 | 0.837 |
| 1,065 pt-yr | 3.0 (1.9-4.5) | 4.9 (2.8-7.1) | 0.62 (0.35-1.25) | >0.999 | 0.900 |
| 1,350 pt-yr | 2.9 (2.0-4.3) | 4.2 (2.5-6.0) | 0.69 (0.42-1.37) | >0.999 | 0.830 |
| 1,500 pt-yr | 3.0 (2.1-4.3) | 4.3 (2.6-5.9) | 0.71 (0.44-1.30) | >0.999 | 0.846 |

- Noninferiority criteria met
- 29% lower relative risk in WATCHMAN group –

**WITHOUT COUMADIN**

# Primary Efficacy Over Time



# Primary Efficacy Kaplan-Meier Estimates


| Cohort | 1-year event rate (95% CI) | 2-year event rate (95% CI) | 3-year event rate (95% CI) |
|---|---|---|---|
| WATCHMAN | 3.7 (1.9-5.4) | 6.1 (3.8-8.5) | 7.9 (5.0-10.9) |
| Control | 4.3 (1.7-6.9) | 8.0 (4.5-11.6) | 12.5 (6.9-18.1) |

1,500 patient-year analysis

# Intent-to-Treat: All Stroke

| Cohort | WATCHMAN Rate (95% CI) | Control Rate (95% CI) | Rel risk (95% CI) | Posterior probabilities* Noninferiority | Superiority |
|---|---|---|---|---|---|
| 600 pt-yr | 3.4 (1.9-5.5) | 3.6 (1.5-6.3) | 0.96 (0.43-2.57) | 0.927 | 0.488 |
| 900 pt-yr | 2.6 (1.5-4.1) | 3.5 (1.7-5.7) | 0.74 (0.36-1.76) | 0.998 | 0.731 |
| 1,065 pt-yr | 2.3 (1.3-2.6) | 3.2 (1.6-5.2) | 0.71 (0.35-1.64) | 0.993 | 0.769 |
| 1,350 pt-yr | 2.1 (1.3-3.3) | 2.7 (1.4-4.3) | 0.78 (0.41-1.75) | 0.989 | 0.685 |
| 1,500 pt-yr | 2.0 (1.3-3.1) | 2.7 (1.5-4.1) | 0.77 (0.42-1.62) | 0.995 | 0.728 |

- 23% lower relative risk in WATCHMAN group

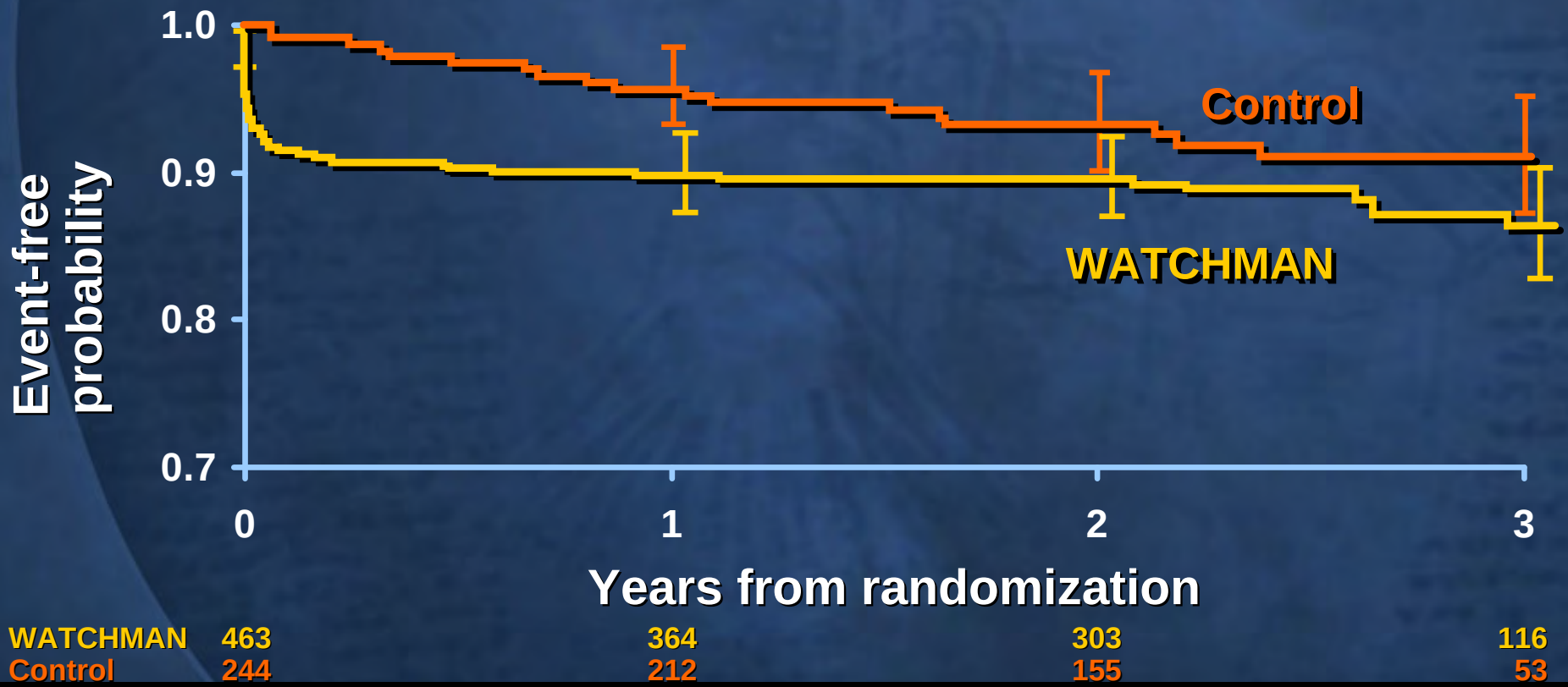
**WITHOUT COUMADIN**

# Intent-to-Treat: All-Cause Mortality

| Cohort | WATCHMAN Rate (95% CI) | Control Rate (95% CI) | Rel risk (95% CI) | Posterior probabilities* Noninferiority | Superiority |
|---|---|---|---|---|---|
| 600 pt-yr | 3.4 (1.8-5.4) | 4.9 (2.3-7.8) | 0.69 (0.33-1.66) | 0.991 | 0.779 |
| 900 pt-yr | 2.9 (1.7-4.4) | 4.7 (2.5-7.1) | 0.61 (0.32-1.32) | 0.999 | 0.889 |
| 1,065 pt-yr | 3.0 (1.9-4.5) | 4.8 (2.8-7.1) | 0.62 (0.34-1.24) | >0.999 | 0.907 |
| 1,350 pt-yr | 3.1 (2.1-4.4) | 4.4 (2.6-6.1) | 0.70 (0.43-1.36) | >0.999 | 0.823 |
| 1,500 pt-yr | 3.2 (2.3-4.5) | 4.5 (2.8-6.2) | 0.71 (0.46-1.28) | >0.999 | 0.852 |

- 29% lower relative risk in WATCHMAN group

# Primary Safety Kaplan-Meier Estimates




**Upfront risk of procedural complications is real and Relates to experience with transseptal and structural techniques And is directly related to operator learning curve.**

# Pericardial Effusions

| | Events (%) |
|---|---|
| Initial transseptal puncture | 2/22 (9%) |
| From adjunctive device to enter LAA (such as a guidewire or catheter) | 4/22 (18%) |
| Manipulating delivery system within LAA | 3/22 (14%) |
| Protruding delivery sheath from transseptal access sheath | 2/22 (9%) |
| Watchman deployment process | 4/22 (18%) |
| No definitive cause identified | 7/22 (32%) |

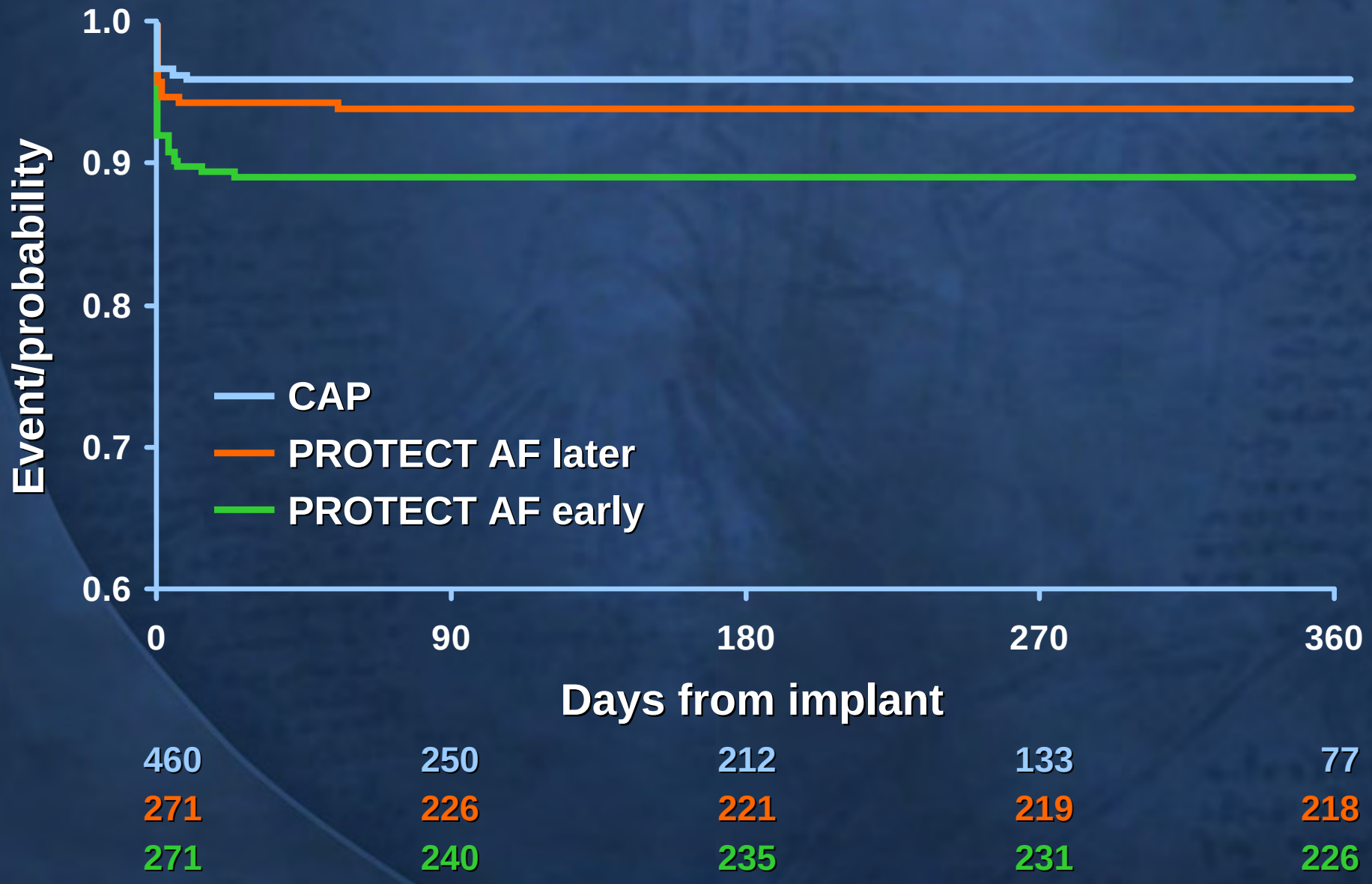


Reddy: Circ (in press)

# Intent to Treat: Primary Safety Results

| Cohort | WATCHMAN Rate (95% CI) | Control Rate (95% CI) | Rel risk(95% CI) |
|---|---|---|---|
| 600 pt-yr | 11.6 (8.5-15.3) | 4.1 (1.9-7.2) | 2.85 (1.48-6.43) |
| 900 pt-yr | 8.7 (6.4-11.3) | 4.2 (2.2-6.7) | 2.08 (1.18-4.13) |
| 1,065 pt-yr | 7.4 (5.5-9.7) | 4.4 (2.5-6.7) | 1.69 (1.01-3.19) |
| 1,350 pt-yr | 6.2 (4.7-8.1) | 3.9 (2.3-5.8) | 1.60 (0.99-2.93) |
| 1,500 pt-yr | 5.5 (4.2-7.1) | 3.6 (2.2-5.3) | 1.53 (0.95-2.70) |

# PROTECT AF & CAP Registry Safety Events

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# Warfarin Discontinuation – WATCHMAN Group

- 76% of **randomized** patients discontinued warfarin at 45 days
- 87% of **implanted** patients discontinued warfarin at 45 days

| Visit | Warfarin discontinuation Total implanted | |
|---|---|---|
| | No. | % |
| 45 day | 348/401 | 86.7 |
| 6 month | 355/385 | 92.2 |
| 12 month | 345/370 | 93.2 |
| 24 month | 293/311 | 94.2 |

| Reason for continuation/reinitiation | At 45 days | | At 6 months | |
|---|---|---|---|---|
| | No. | % | No. | % |
| Observation of flow in the LAA | 30 | 7.5 | 14 | 3.6 |
| Physician discretion | 23 | 5.7 | 16 | 4.2 |

# Anticoagulation

- Very narrow therapeutic range
- Close therapeutic drug monitoring is required
- Frequent dose adjustments are necessary
- Hard to antagonize
- Multiple side effects
- Food/drug interactions
- Increased risk of bleeding: 5-10% annually
  severe 1-2% annually

- ***< 40 %*** **of all AF patients receive anticoagulation therapy!**

- Any localized or general physical condition in which the hazard of hemorrhage might be greater than the potential clinical benefits of anticoagulation
- Any personal circumstance in which the hazard of hemorrhage might be greater than the potential clinical benefits of anticoagulation
- Pregnancy
- Hemorrhagic tendencies
- Blood dyscrasias.
- Recent or contemplated surgery of central nervous system
- Recent or contemplated surgery of the eye
- Recent or contemplated traumatic surgery resulting in large open surfaces
- Gastrointestinal bleeding
- Genitourinary tract bleeding
- Respiratory tract bleeding
- Cerebrovascular hemorrhage

- **Cerebral aneurysms**
- **Dissecting aorta**
- **Pericarditis**
- **Pericardial effusions**
- **Bacterial endocarditis**
- **Threatened abortion**
- **Eclampsia**
- **Preeclampsia**
- **Inadequate laboratory facilities**
- **Unsupervised patients**
- **Senility**
- **Alcoholism**
- **Psychosis**
- **Lack of patient cooperation**
- **Spinal puncture**
- **Other diagnostic procedures with potential for uncontrollable bleeding**
- **Therapeutic procedures with potential for uncontrollable bleeding**
- **Major regional anesthesia**
- **Lumbar block anesthesia**
- **Malignant hypertension**

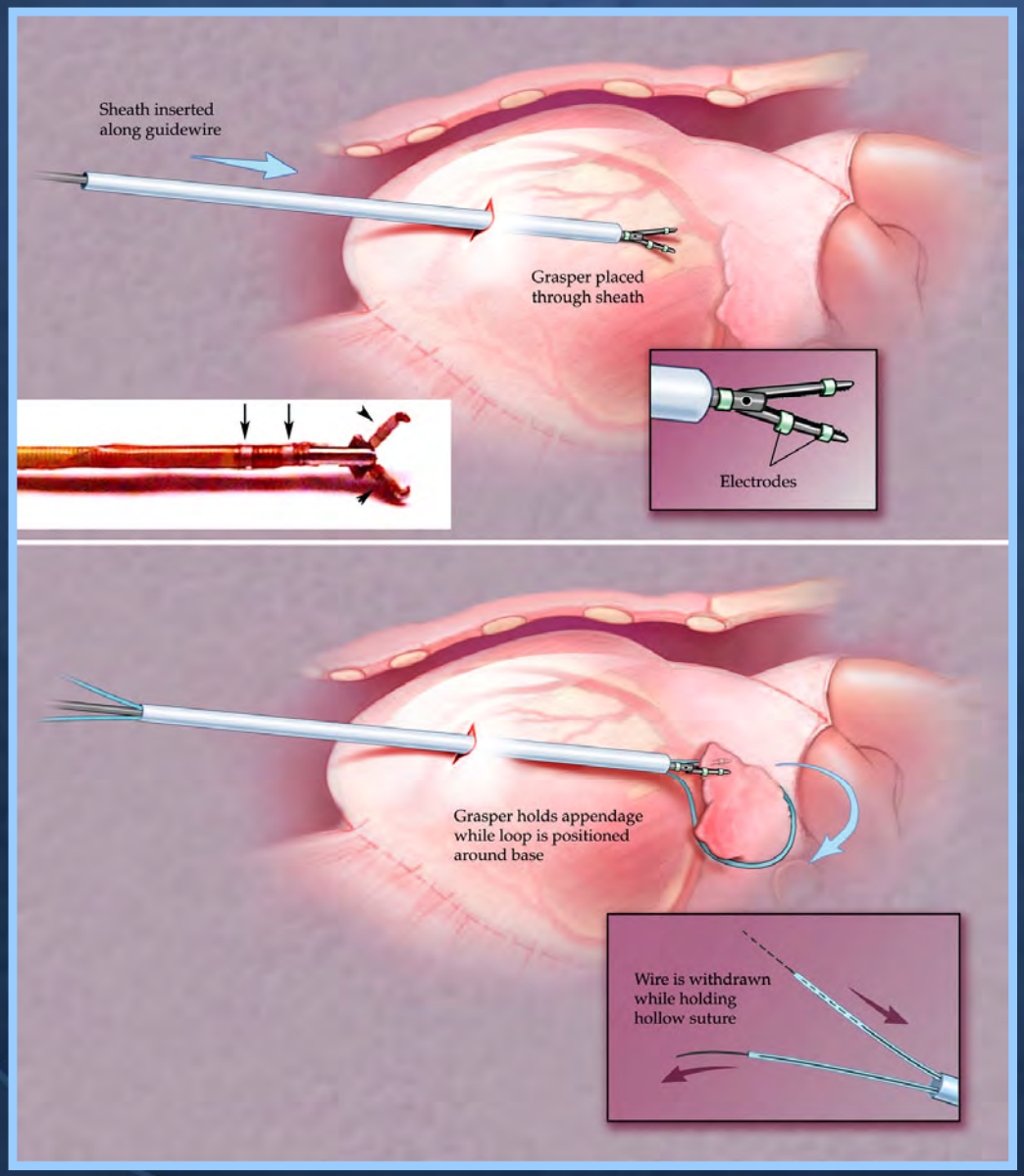

# Warfarin will always have its indications

# LAA Closure

## *Innovations*

# TigerPaw

# Percutaneous LAA Ligation

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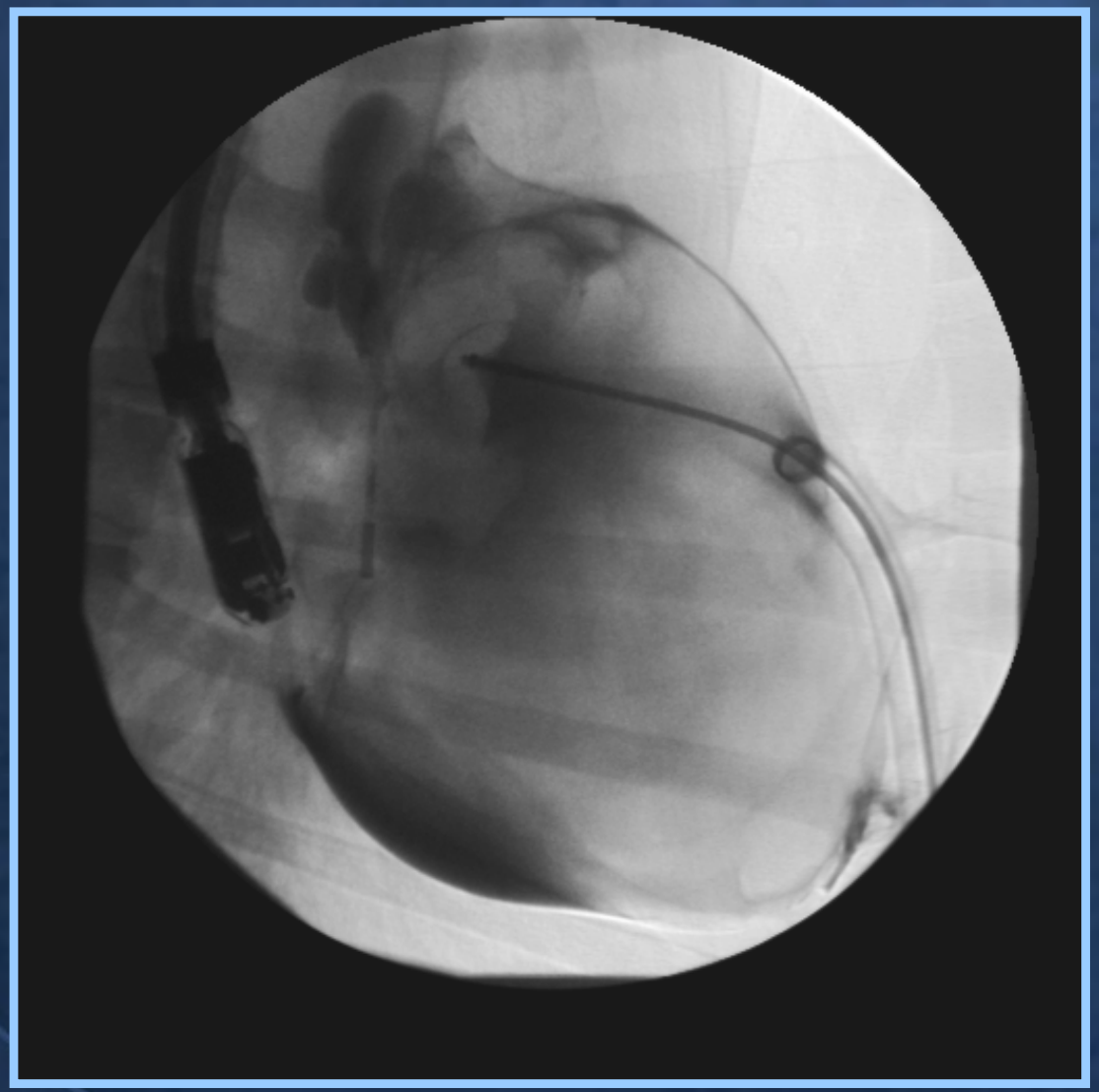
# Percutaneous LAA Ligation



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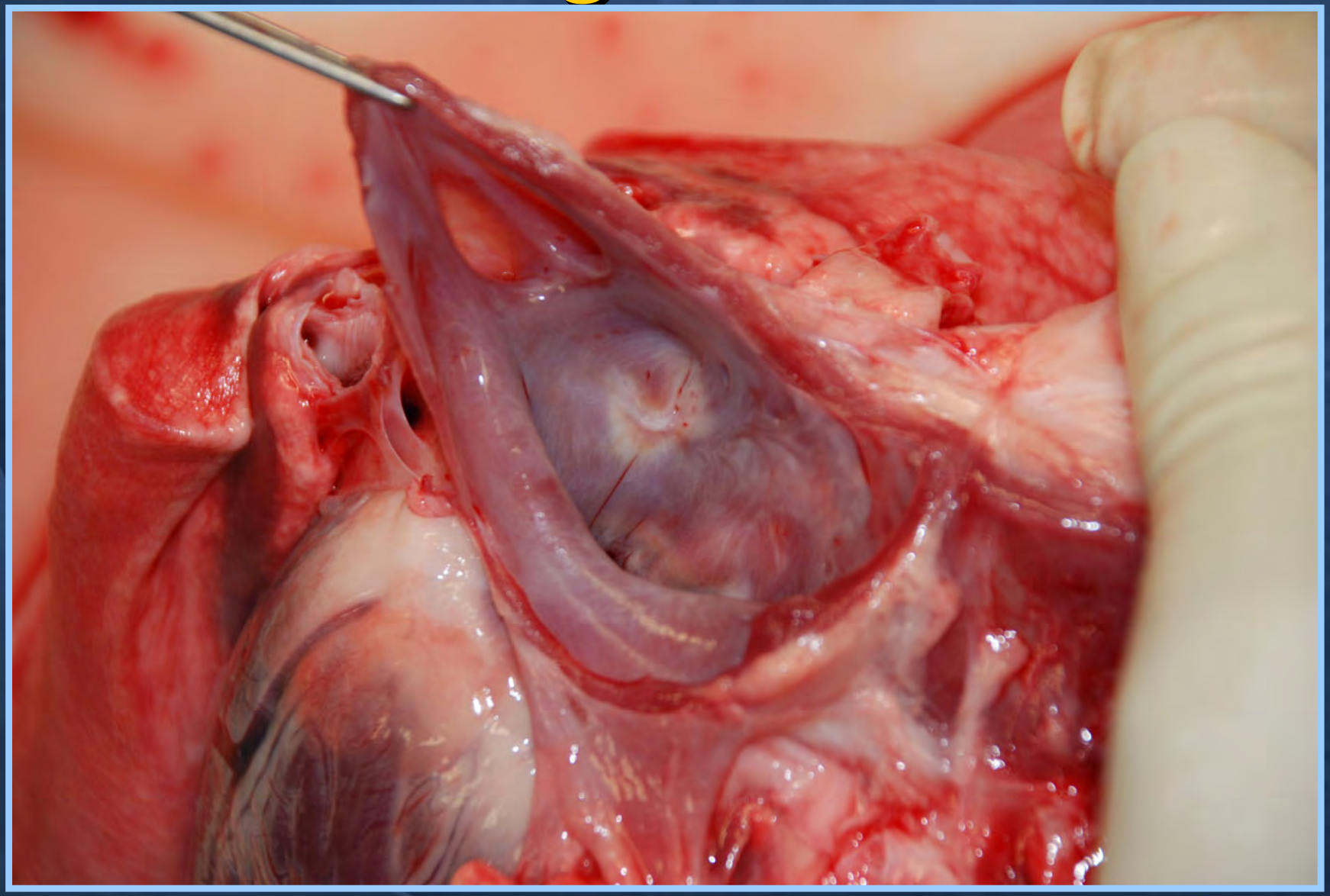

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