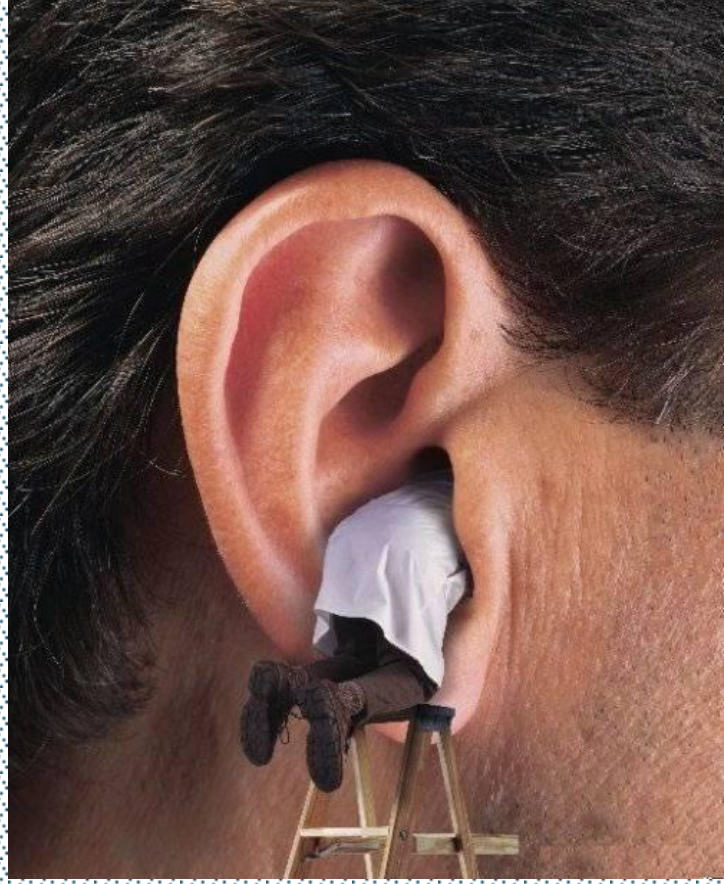
LAA Closure Devices:

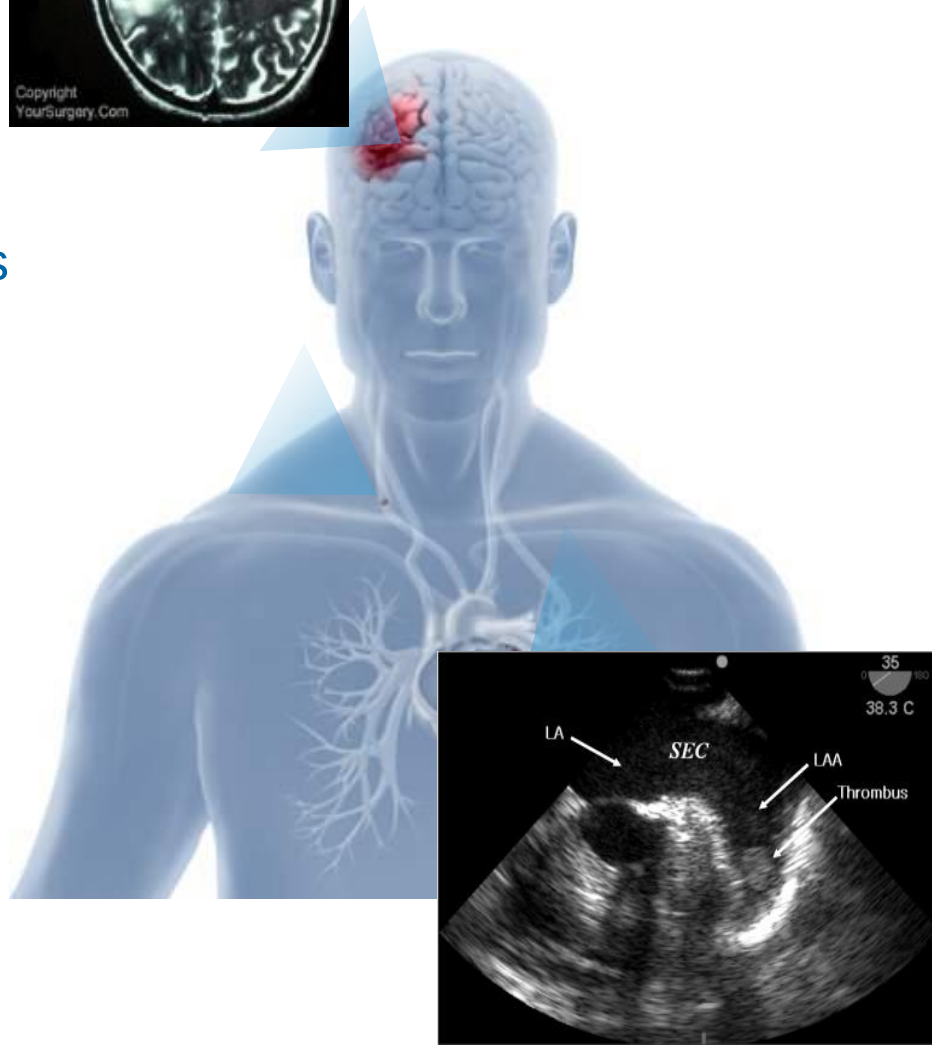


Protecting Against Stroke in Non-valvular Atrial Fibrillation

Alexander Feldman MD

AF confers an increased thromboembolic risk, notably in the brain

- AF confers a **near 5-fold risk** of stroke[1] and a 2-fold risk of death.
- Strokes associated with AF tends to reoccur and are frequently disabling.
- It is estimated that 20% of all strokes are caused by AF[2]
- AF is often asymptomatic[3]
- The absence of symptoms (e.g. palpitations) does not imply a lower risk of thromboembolism[3]
- **Oral Anticoagulants (OAC) therapy reduced stroke risk by 3-5 fold.**

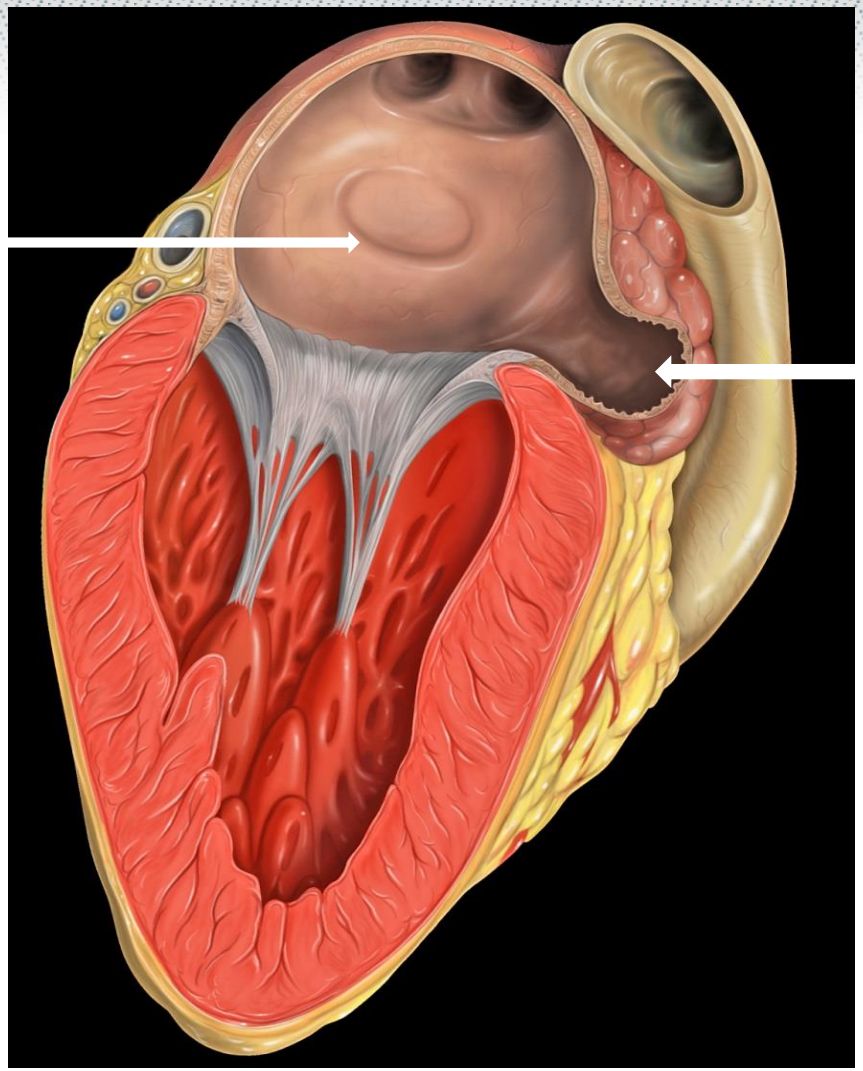


1. Wolf et al. Stroke 1991;22:983-8.
2. Friedman et al. Circulation 1968;38:533-541.
3. Flaker et al. Am Heart J 2005:149:657-63.

Prevention of Stroke and Bleeding in Non-valvular Atrial Fibrillation

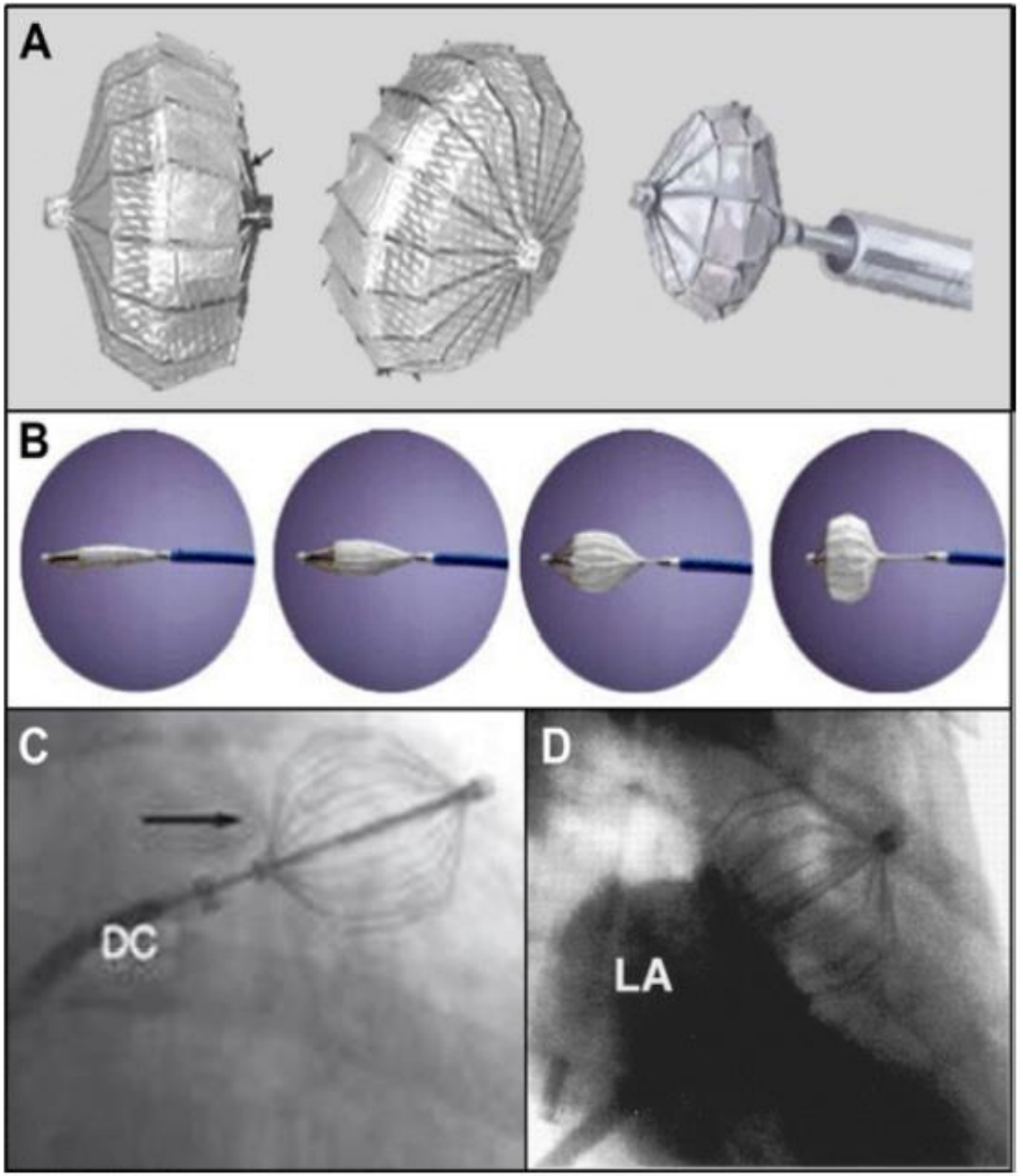
- Anticoagulation is indicated for all AF patients who are older than 65 or with a risk factor.
- In patients with a higher risk of stroke, the risk of bleeding tend to be higher as well.
- Single antiplatelet therapy doubles bleeding risk with OAC, Dual antiplatelet therapy quadruple bleeding risk.
- Prevention of stroke following major bleeding is challenging.

Left Atrial Appendage

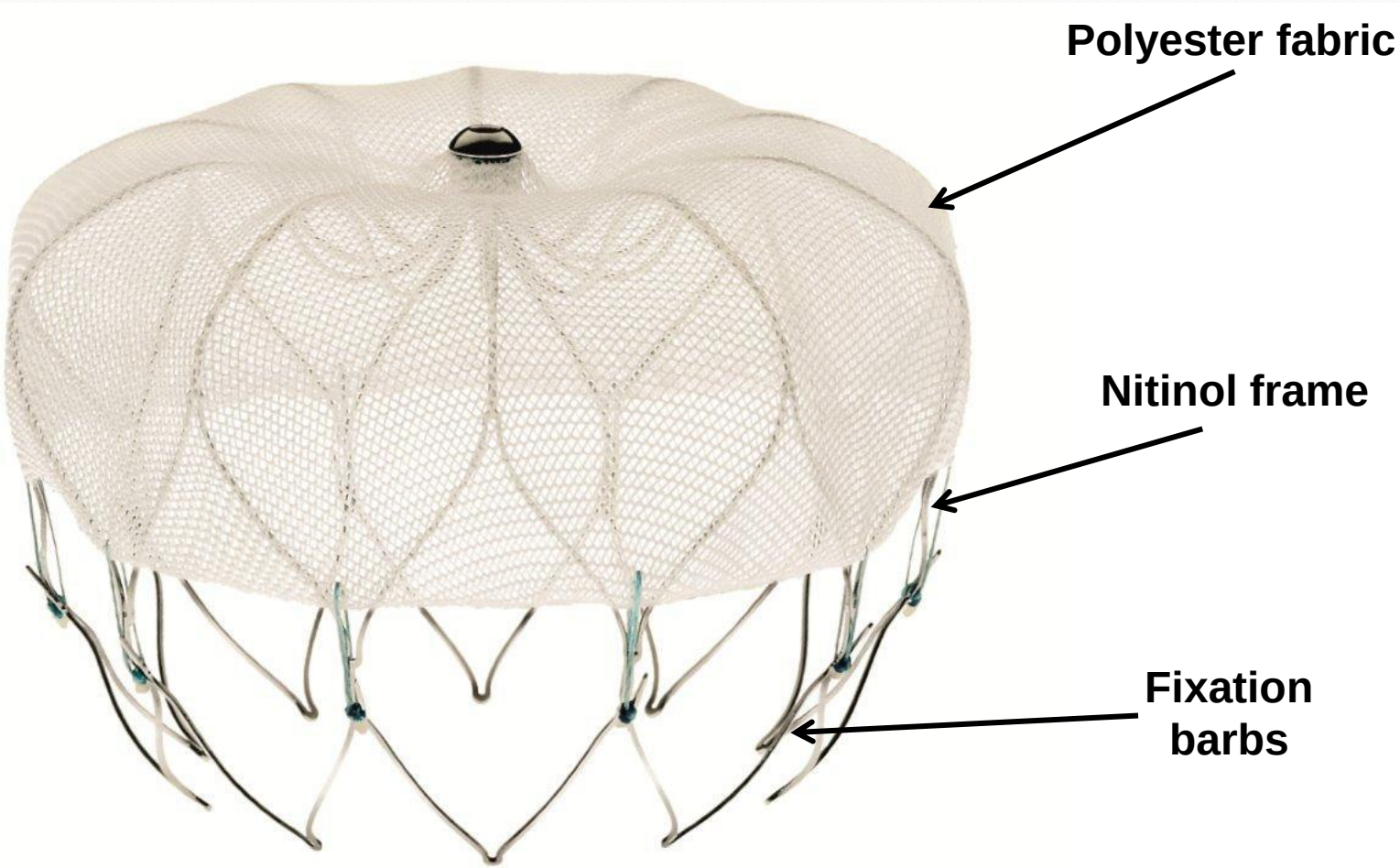


a. Blackshear JL, et al. *Ann Thorac Surg*. 1996;61:755-759.[5]

The PLAATO the first device developed for LAA closure

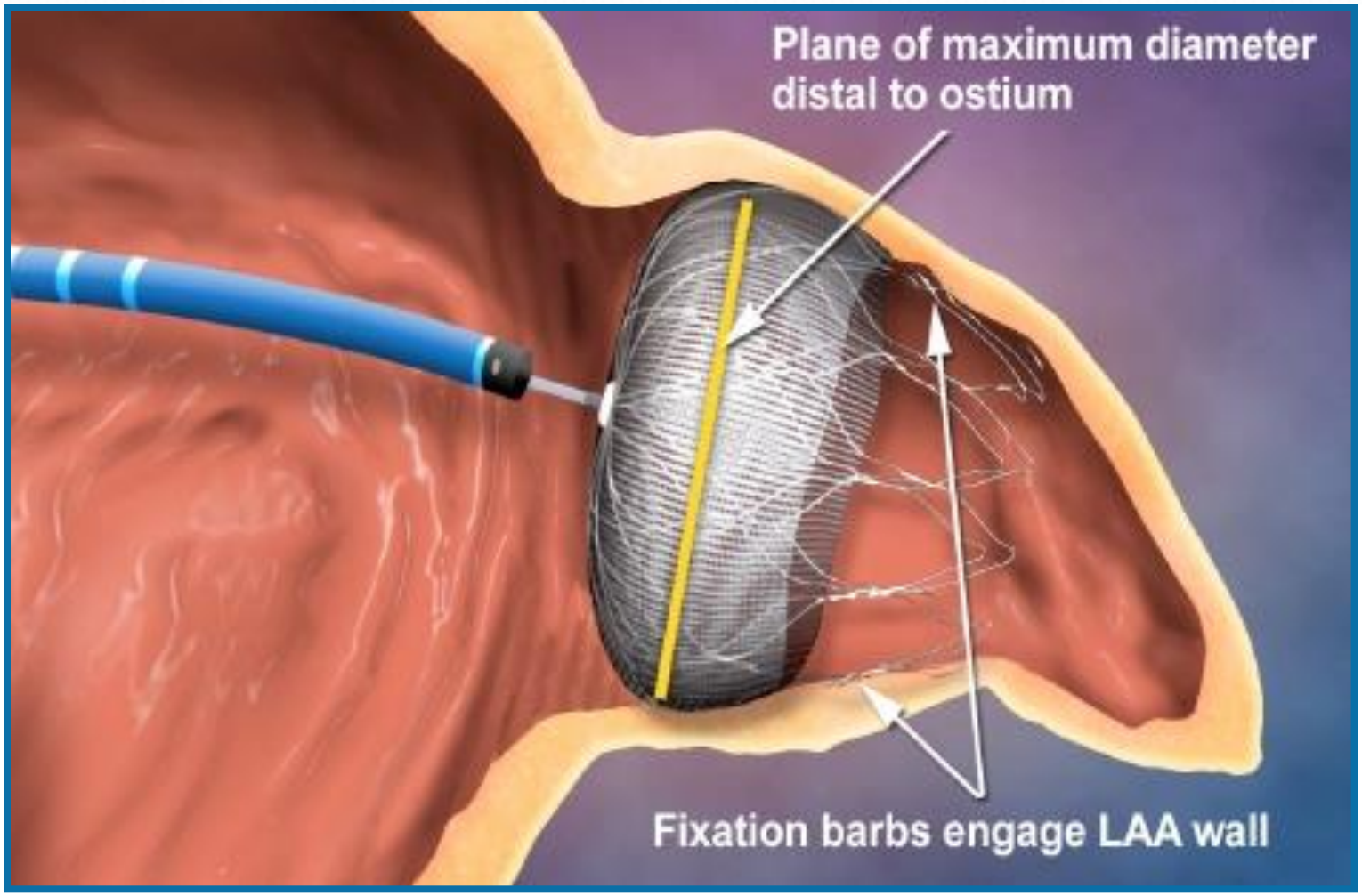


WATCHMAN™ Device

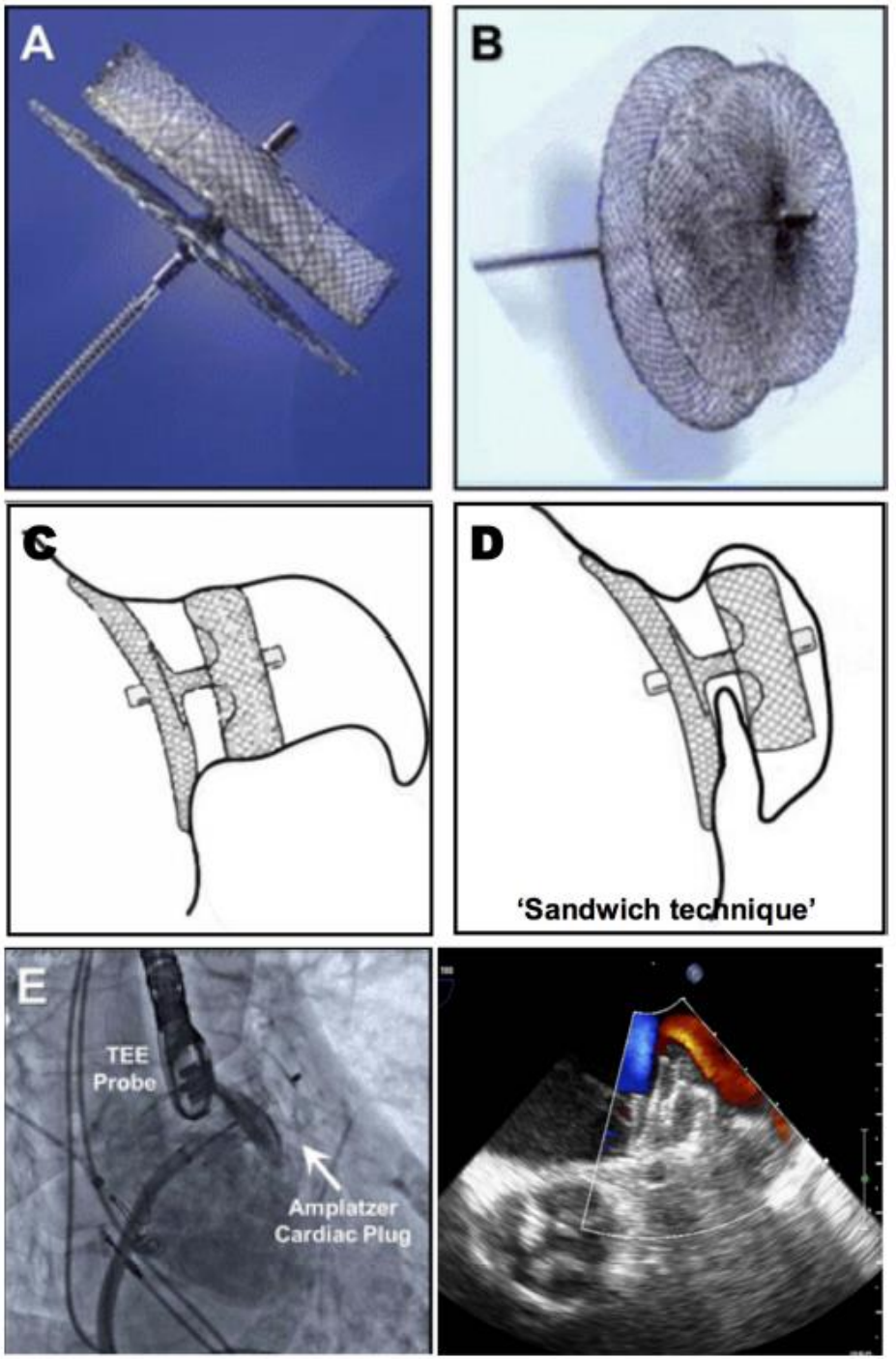


The WATCHMAN LAA closure technology has CE Mark approval and is currently available for investigational use only in the United States.
Image courtesy of Boston Scientific Corp.

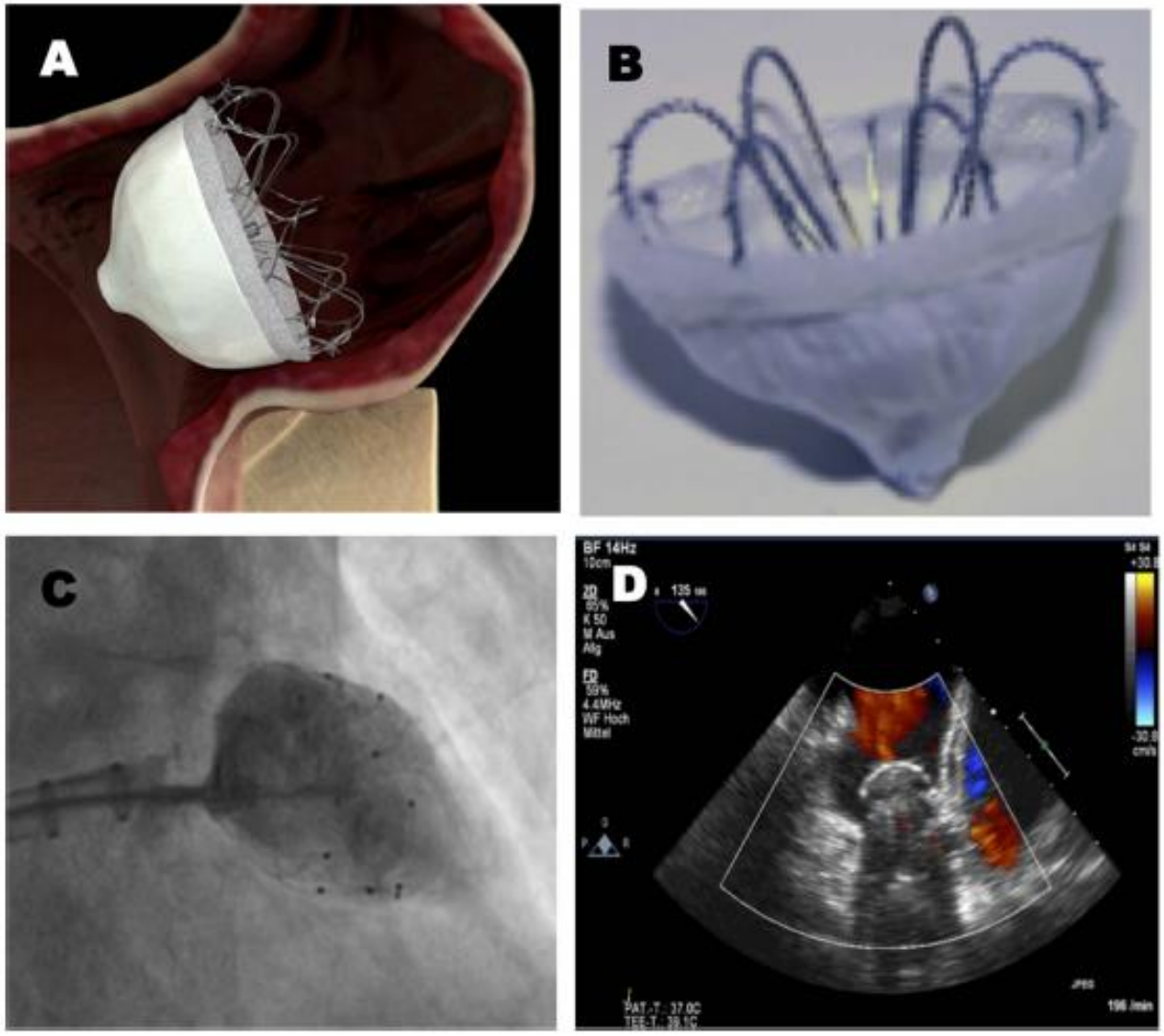
WATCHMAN
LAA Closure Device in situ



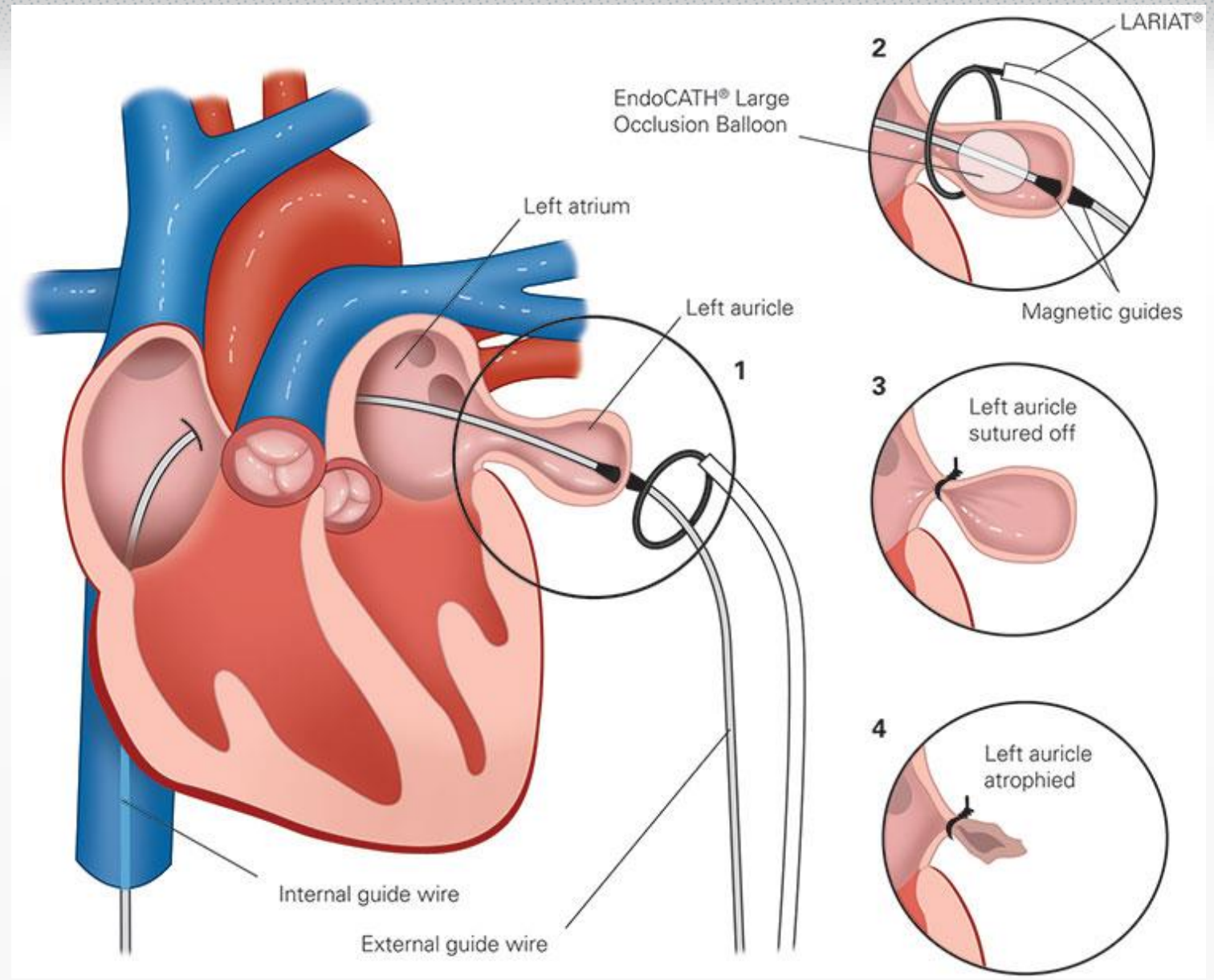
ACP – Amplatzer Cardiac Plug



Coherex WaveCrest Device (Medtronic)



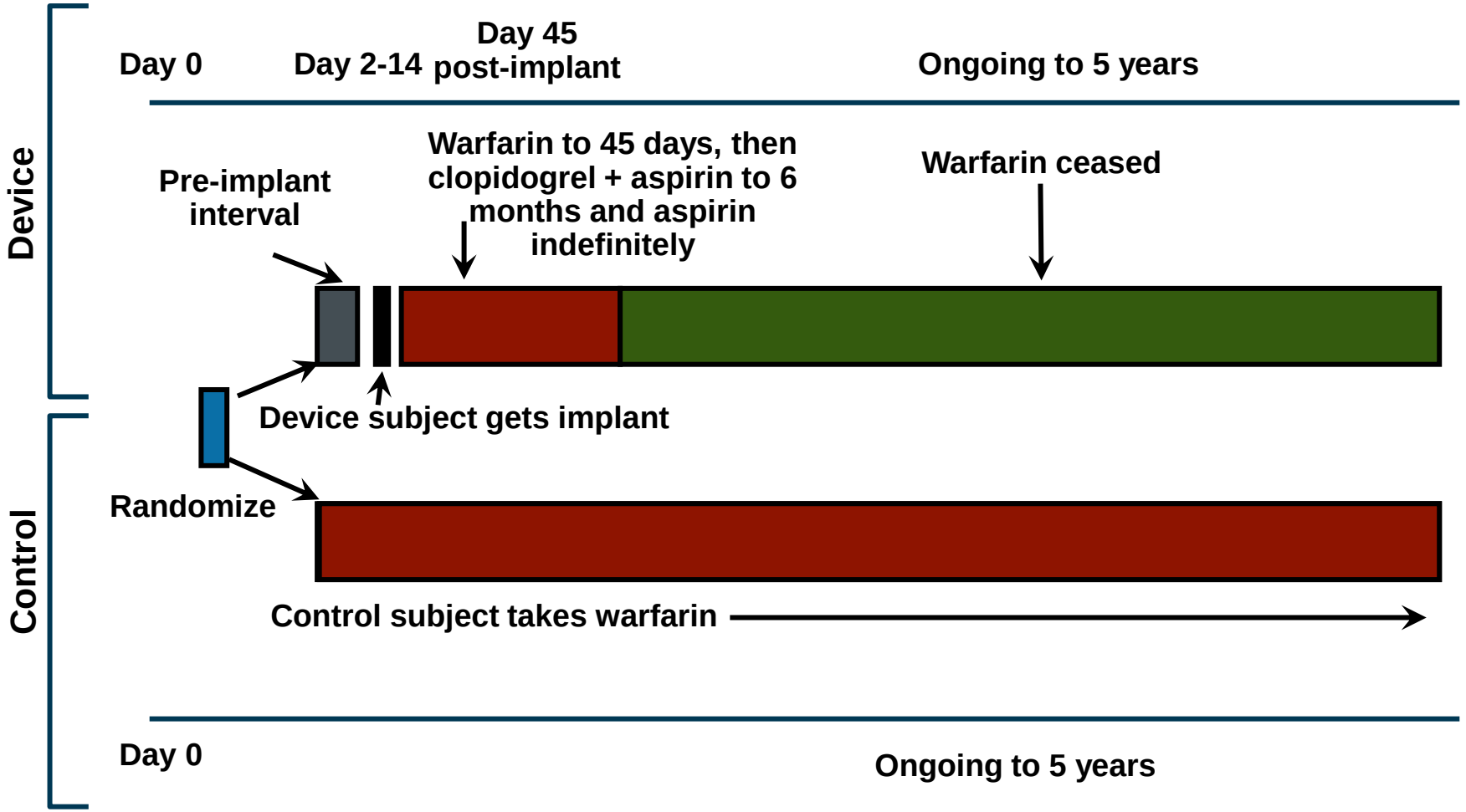
LARIAT – Pericardial LAAC



Complication:

- **Periprocedural complication:**
  - Cardiac perforation – Tamponade
  - Vascular complication – Bleeding
  - Device embolization
  - Trans-septal complication
  - Stroke
  - Bleeding (due to heparinization. DAPT therapy)
- **Late complication:**
  - Incomplete appendage closure – thrombotic nidus - stroke
  - Late pericardial effusion (subacute perforation).

PROTECT AF
Design



Fountain RB, et al. *Am Heart J*. 2006;151:956-961.[6]

Key Participation Criteria

- Key Inclusion Criteria
  - Age 18 years or older
  - Documented non-valvular AF
  - Eligible for long-term warfarin therapy, and no other conditions that would require long-term warfarin therapy
  - Calculated CHADS2 score > 1
- Key Exclusion Criteria
  - NYHA Class IV Congestive Heart Failure
  - ASD and/or atrial septal repair or closure device
  - Planned ablation procedure within 30 days of potential WATCHMAN Device implant
  - Symptomatic carotid disease
  - LVEF < 30%
  - TEE Criteria: Suspected or known intracardiac thrombus (dense spontaneous echo contract)

Patient Demographics

Baseline Demographics			
Characteristic	**WATCHMAN N= 463**	**Control N= 244**	**P-value**
Age (years)	**71.7 ± 8.8** **463 (46.0, 95.0)**	**72.7 ± 9.2** **244 (41.0, 95.0)**	**0.1800**
Height (inches)	**68.2 ± 4.2** **462 (54.0, 82.0)**	**68.4 ± 4.2** **244 (59.0, 78.0)**	**0.6067**
Weight (lbs)	**195.3 ± 44.4** **463 (85.0, 376.0)**	**194.6 ± 43.1** **244 (105.0, 312.0)**	**0.8339**
Gender			
Female	**137/463 (29.6)**	**73/244 (29.9)**	**0.9276**
Male	**326/463 (70.4)**	**171/244 (70.1)**	

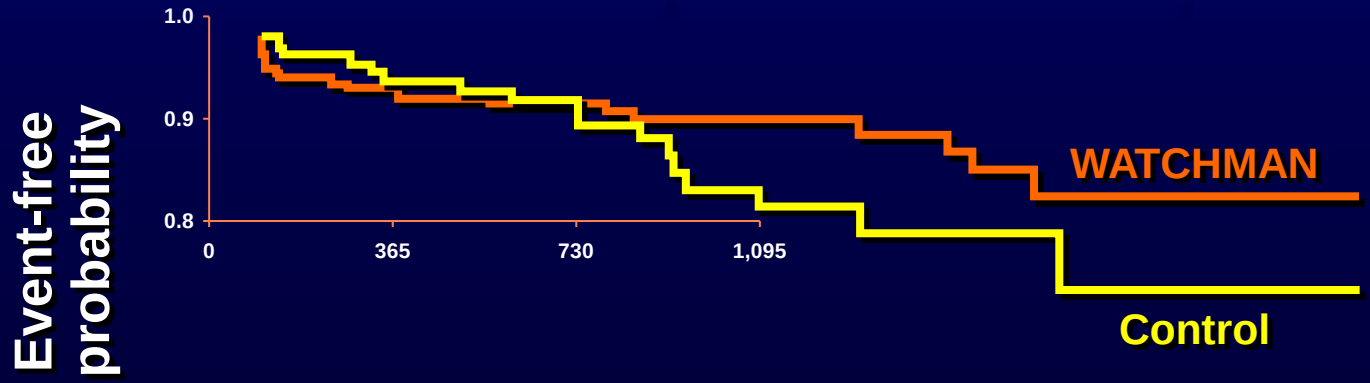
Patient Demographics - 2

Baseline Risk Factors			
	WATCHMAN N= 463	Control N= 244	P-value
CHADS2 Score			
1	158/463 (34.1)	66/244 (27.0)	0.3662
2	157/463 (33.9)	88/244 (36.1)	
3	88/463 (19.0)	51/244 (20.9)	
4	37/463 (8.0)	24/244 (9.8)	
5	19/463 (4.1)	10/244 (4.1)	
6	4/463 (0.9)	5/244 (2.0)	
AF Pattern			
Paroxysmal	200/463 (43.2)	99/244 (40.6)	0.7623
Persistent	97/463 (21.0)	50/244 (20.5)	
Permanent	160/463 (34.6)	93/244 (38.1)	
Unknown	6/463 (1.3)	2/244 (0.8)	
LVEF %	57.3 ± 9.7	56.7 ± 10.1	0.4246
	460 (30.0, 82.0)	239 (30.0, 86.0)	

Intent-to-Treat
Primary Efficacy Results

Randomization allocation (2 device : 1 control)

	Device			Control				Posterior Probabilities	
Cohort	Events (no.)	Total pt-yr	Rate (95% CI)	Events (no.)	Total pt-yr	Rate (95% CI)	Rel. Risk (95% CI)	Non-inferiority	Superiority
900 pt-yr	20	582.3	3.4 (2.1, 5.2)	16	318.0	5.0 (2.8, 7.6)	0.68 (0.37, 1.41)	0.998	0.837

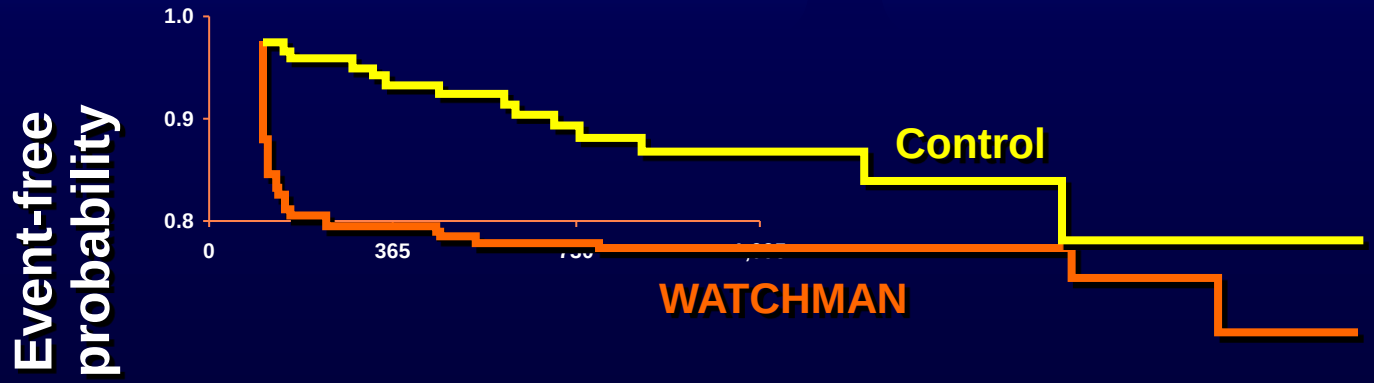


ITT Cohort: patients analyzed based on their randomly assigned group (regardless of treatment received)

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)



ITT Cohort: patients analyzed based on their randomly assigned group (regardless of treatment received)

PROTECT AF
2.3-Year Follow-up Safety Results

- Procedure-related events
  - eg, pericardial effusion that required intervention or hospitalization, procedure-related stroke, or device embolization
- Major bleeding
  - eg, intracranial bleeding/GI bleeding that required transfusion

	Safety Events %/Year (95% CI)	RR (95% CI)
WATCHMAN Group	5.5 (4.2-7.1)	
Control	3.6 (2.2-5.3)	1.53 (0.95-2.70)

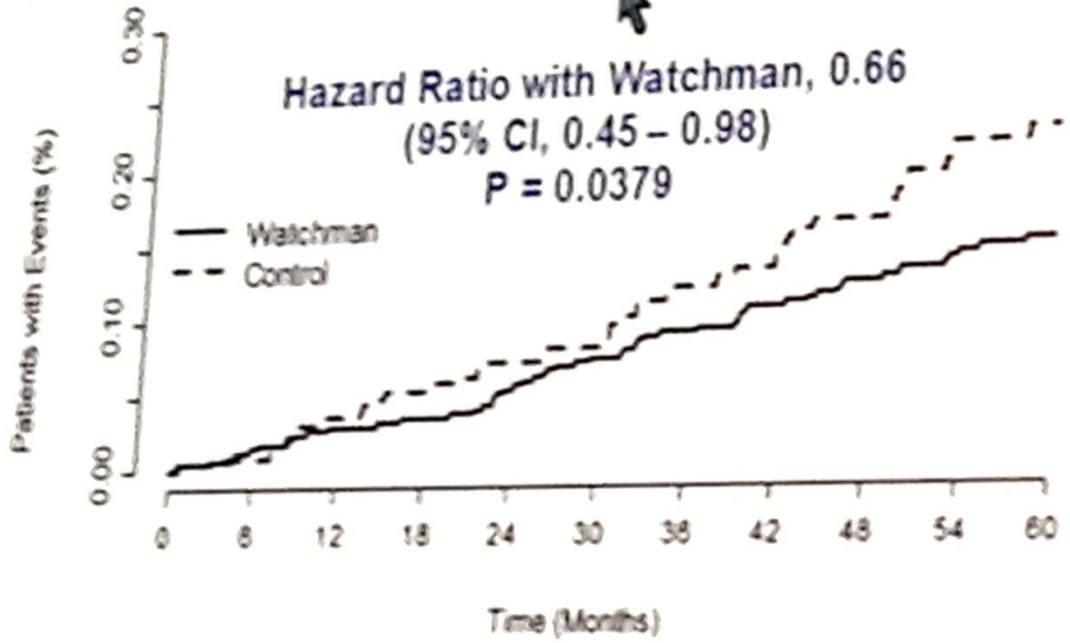
Conclusions:

- LAA closure is noninferior to OAC
- LAA implicated in the pathogenesis of stroke in AF

Reddy VY, et al. *Circulation.* 2013;127:720-729.[7]

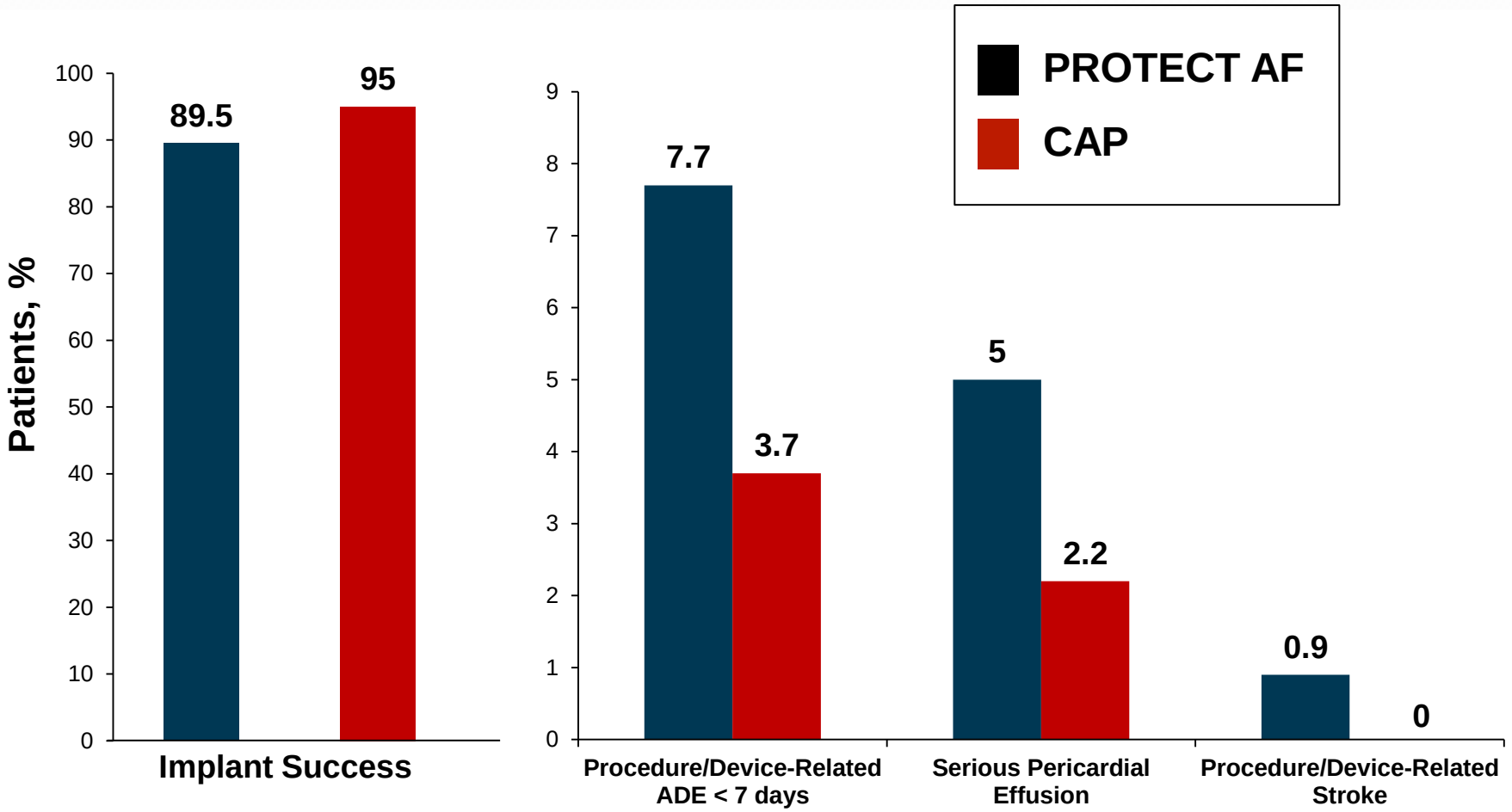
Long term results of Protect AF

- WATCHMAN was superior to Warfarin
  - 40% reduction of stroke / systemic embolism / CV death
  - 60% reduction in Cardiovascular Mortality
  - 34% reduction in All-Cause Mortality



Reddy V. Oral presentation HRS 2013

PROTECT AF and CAP



Reddy VY, et al. *Circulation.* 2011; 123:417-424.[8]

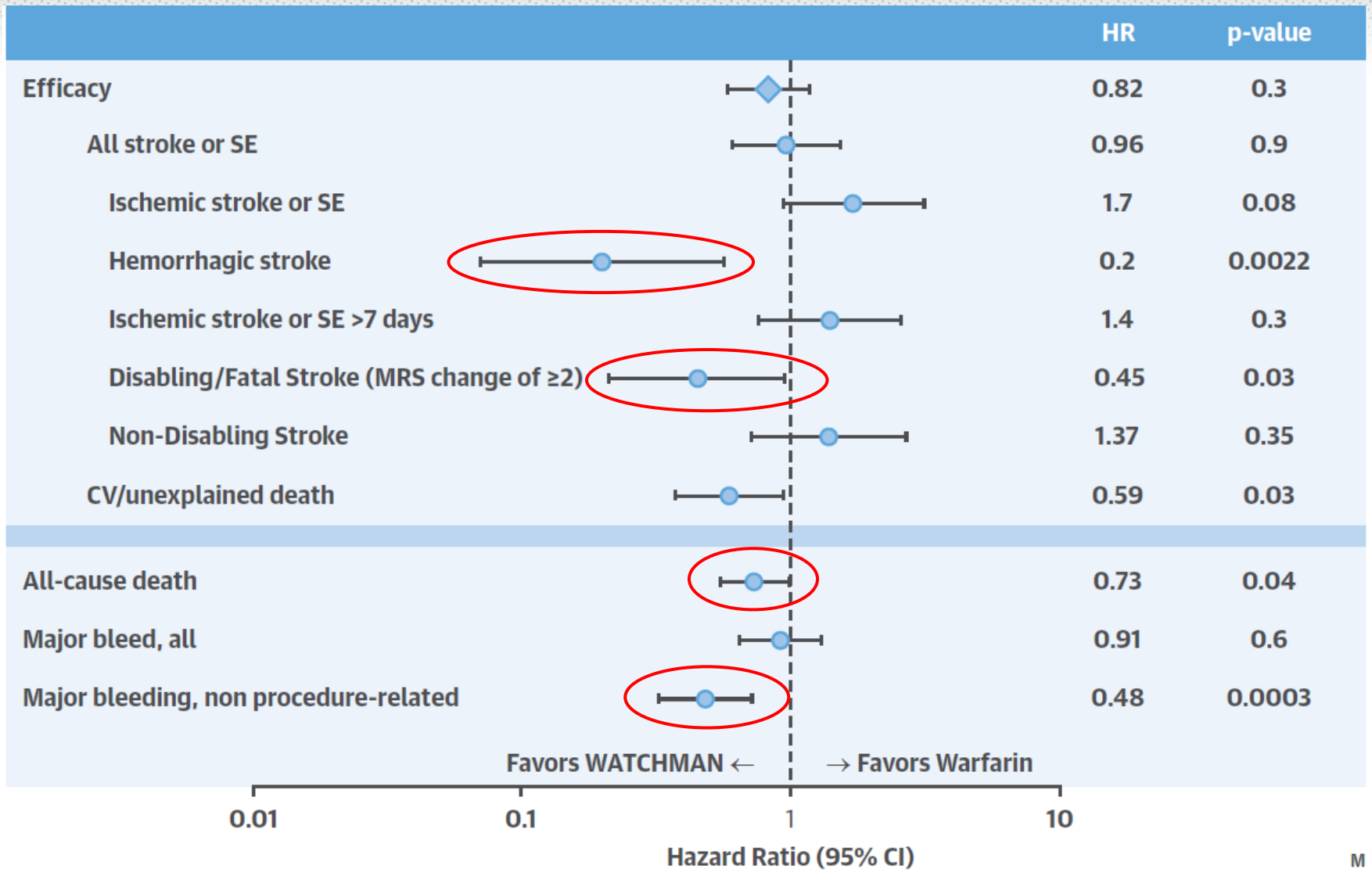
Comparison of LAAC, OAC and NOAC for NonValvular A Fib

Table 1 Comparison of some clinical data from the PROTECT AF versus new oral anticoagulant trials *

	PROTECT AF[55] LAA closure	PROTECT AF[55] warfarin	Dabigatran[14] (RELY)	Rivaroxaban[15] (ROCKET AF)	Apixaban[16] (ARISTOTLE)
Age, years	71.7	72.7	71.5	73	70
$CHADS_2$	2.2	2.3	2.1	3.5	2.1
$CHADS_2$>2 (%)	52.9	57.6	32.7	87	30.2
Major or minor bleeding (%)	–	–	16.4	14.9	18.1
Major bleeding (%)	3.5	4.1	3.1	3.6	2.1
Stroke/systemic embolism (%)	2.3	2.7	1.1	1.7	1.3
Treatment abandoned at >1 year (%)	–	16–34	21	24	–

*Adapted from López-Mínguez *et al.*[72]

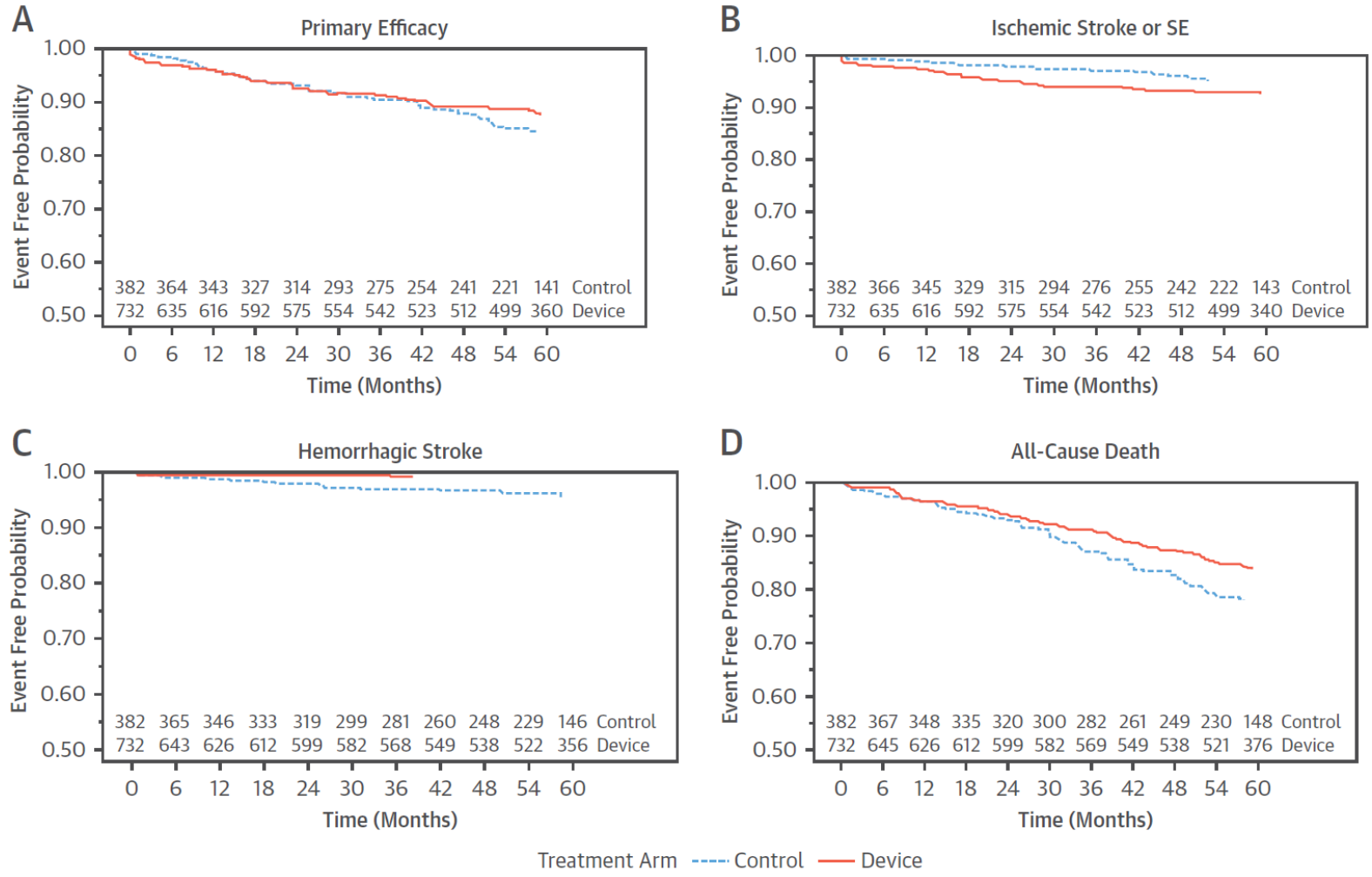
Five year FU of Protect AF & Prevail Studies



Reddy VY et al. J Am Coll Cardiol 2017;70:2964-2975.

Five year FU of Protect AF & Prevail Studies

FIGURE 1 PROTECT AF/PREVAIL Combined: Kaplan-Meier Curves of the Major Efficacy Endpoints



Reddy VY et al. J Am Coll Cardiol 2017;70:2964-2975.

Indication for LAAC Device Implantation

- **Patients (pts) at high stroke risk who had suffer a major bleeding.**
- ***Pts with high risk of bleeding on OAC:***
  - Uncontrolled severe hypertension.
  - Coagulopathies.
  - Severe renal or hepatic dysfunction
  - Vascular disease or malformation (amyloid angiopathy etc.).
  - Insufficiently treatable GIT disease with bleeding.
  - Recurrent severe trauma.
- ***Ischemic stroke despite well controlled OAC therapy.***
- ***Contraindication to all OAC therapy.***
- ***Obligatory long term dual antiplatelet therapy.***

Contraindication for Percutaneous LAA Closure

- Low risk for stroke (CHADS-VAS=0).
- Significant mitral stenosis
- Indication for long-term OAC therapy.
- Contraindication for transseptal catheterization (LA thrombus or tumor, active infection, presence of ASD/PFO closure device).

התוויות סל הבריאות 2015 לחוסם אוזנית

- **חולים הסובלים מפרפור עליות בדרגת סיכון בינוני עד גבוה לשבץ מוחי (CHADS≥2).**
- **ושאינם יכולים להיות מטופלים בנוגדי קרישה.**
- **ושסבלו מאירוע דימום משמעותי:**
  - מסכן חיים או מסכן איבר
  - שהתרחש עם או ללא טיפול בנוגדי קרישה המוגדר על פי דירוג BARC בחומרה 3a ומעלה.

BARC 3a:

Overt bleeding Hb drop 3-5 g%

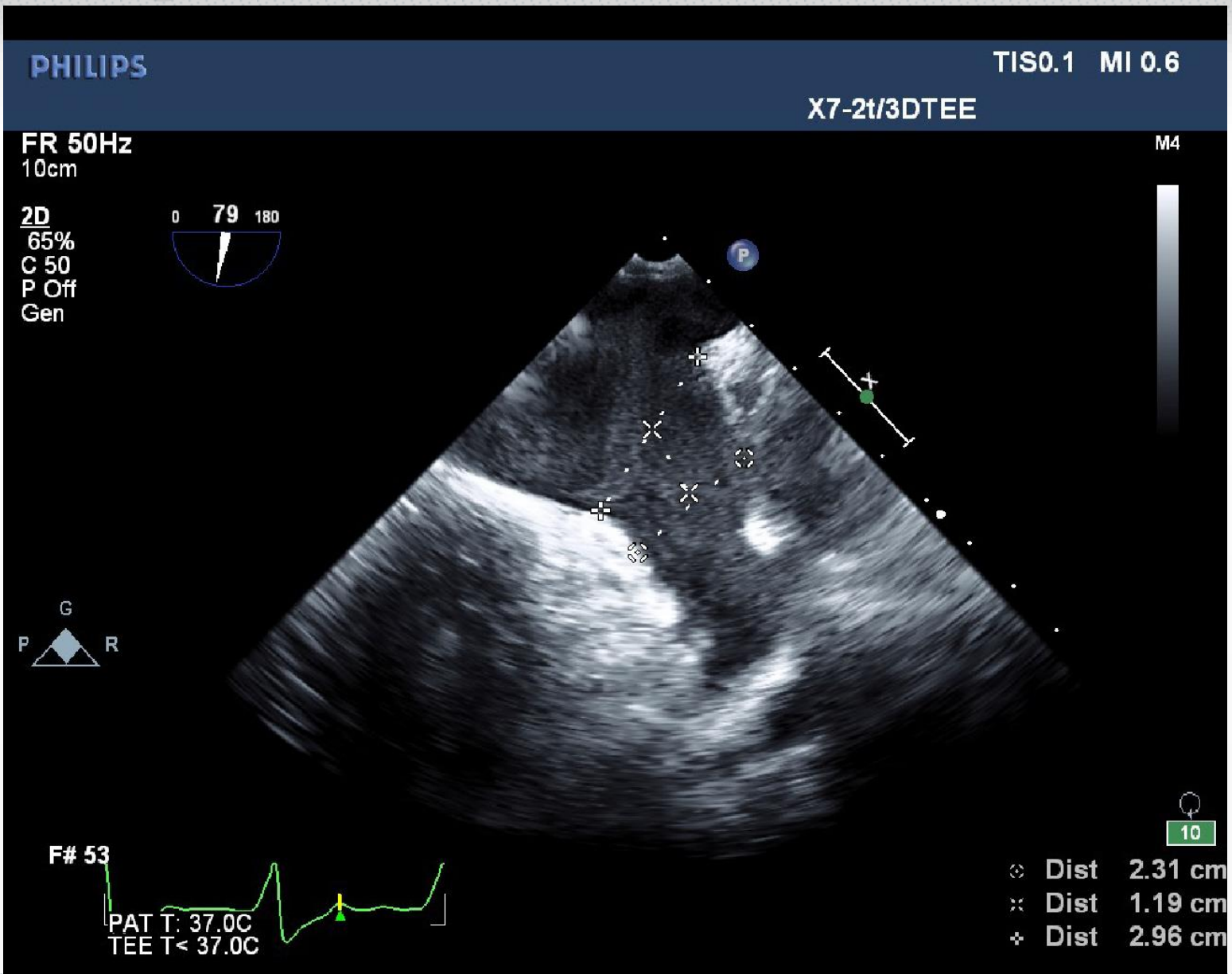
Any transfusion with overt bleeding

BARC 3b-3c דימומים בדרגות חומרה גבוהות יותר – קיפוח המודינמי, טמפונדה, דימום מוחי, דימום עמוד שדרה, דימום עיני הפוגע בראיה, דימום המצריך התערבות ניתוחית

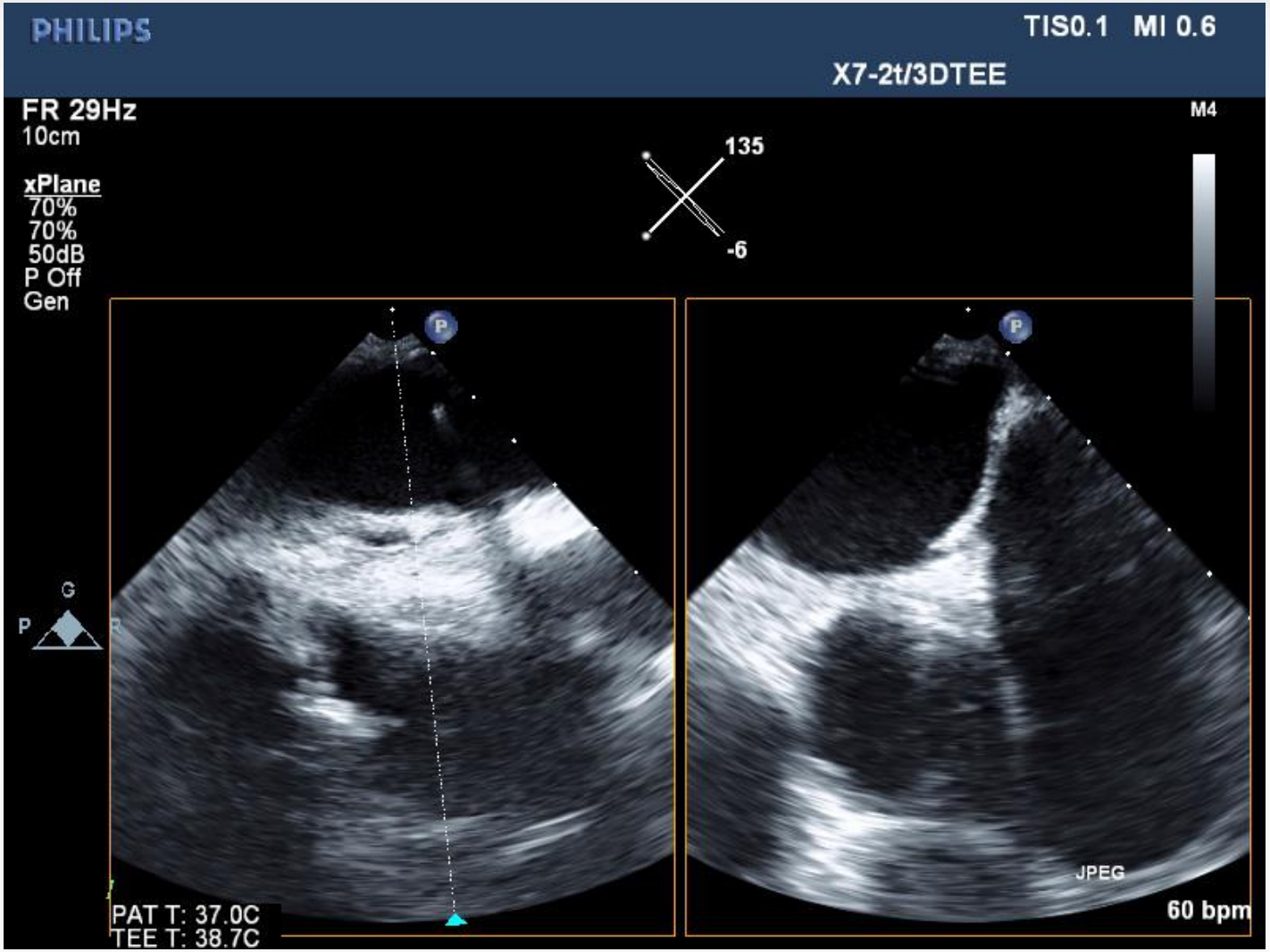
נסיון במרכז רפואי העמק

- 21 פעולות בסדציה ללא מרדים.
- הנחיית אקו TEE (מקרה אחד עם ICE)
- בכל הפעולות ההתקן מוקם בהצלחה.
- ללא אירועים מוחיים וללא טמפונדה.
- מעקב TEE יציבות של התקן ללא דלף וללא קרישים על ההתקן.
- אירוע אחד של השתחררות ההתקן למחרת הפעולה, זוהה בשיקוף שגרתי למחרת הפעולה. החולה הייתה אסימפטומטית
- ההתקן נתקע באזור סוב מיטרלי.
- עקב המיקום לא נעשה ניסיון הוצאת מילעורית (ניסיון של מרכזים אחרים סיכון רב לפגיעה קטלנית במסתם המיטרלי).
- הועברה לניתוח במרכז רפואי שיבא.

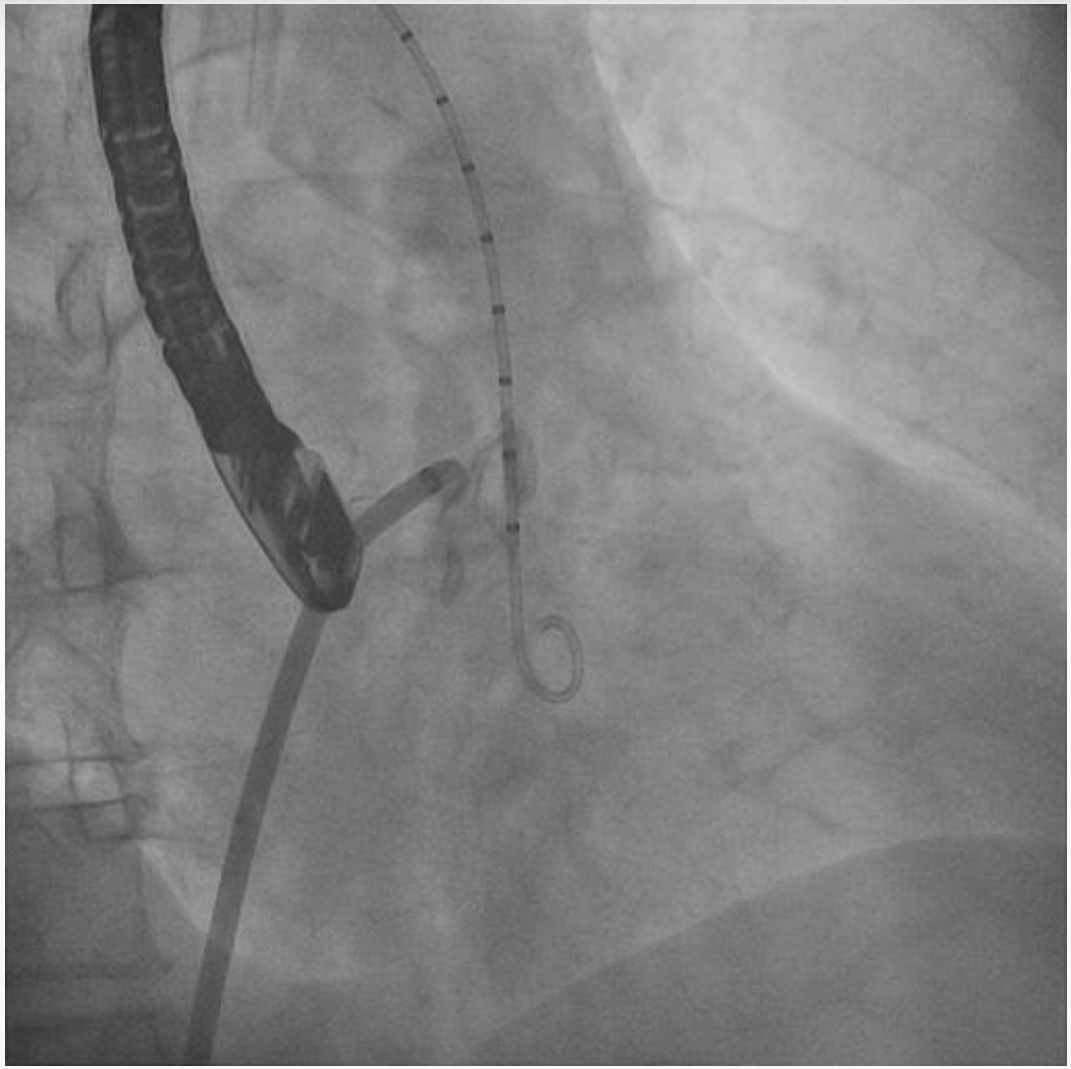
Measurements of LAA outlet and landing zone diameters in TEE



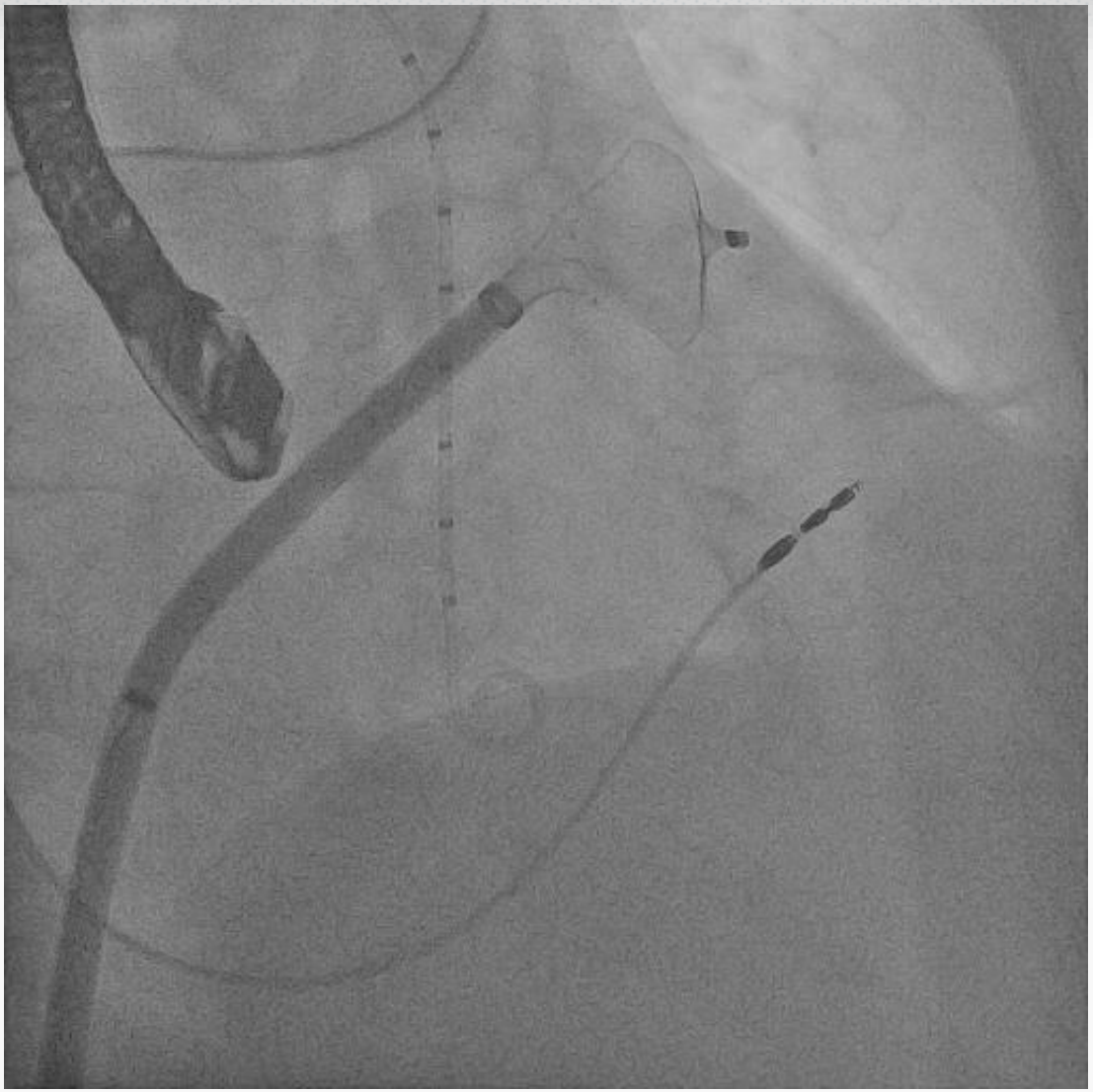
Trans septal puncture – infero-posterior aspect, TEE guided



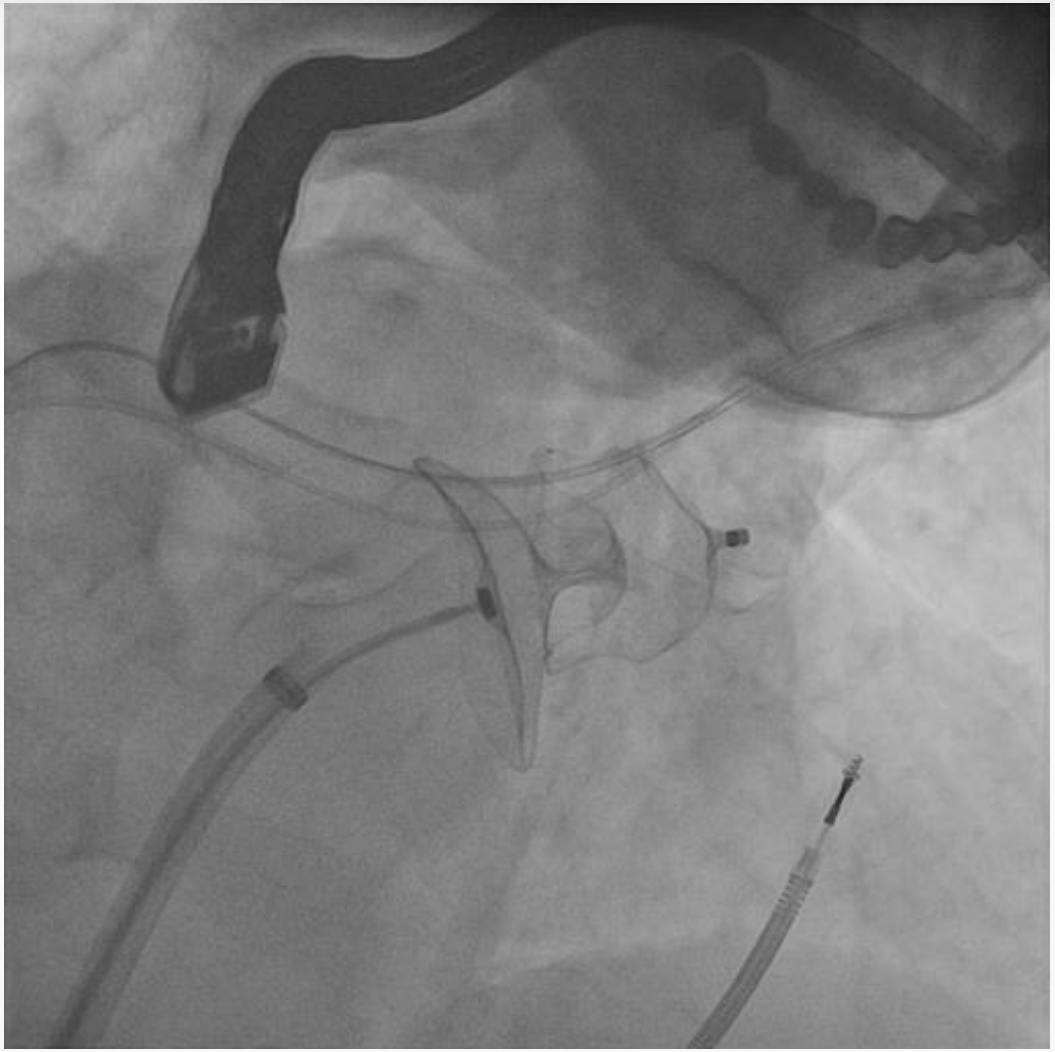
Visualization of LAA from sheath



Release of distal ACP part into LAA body

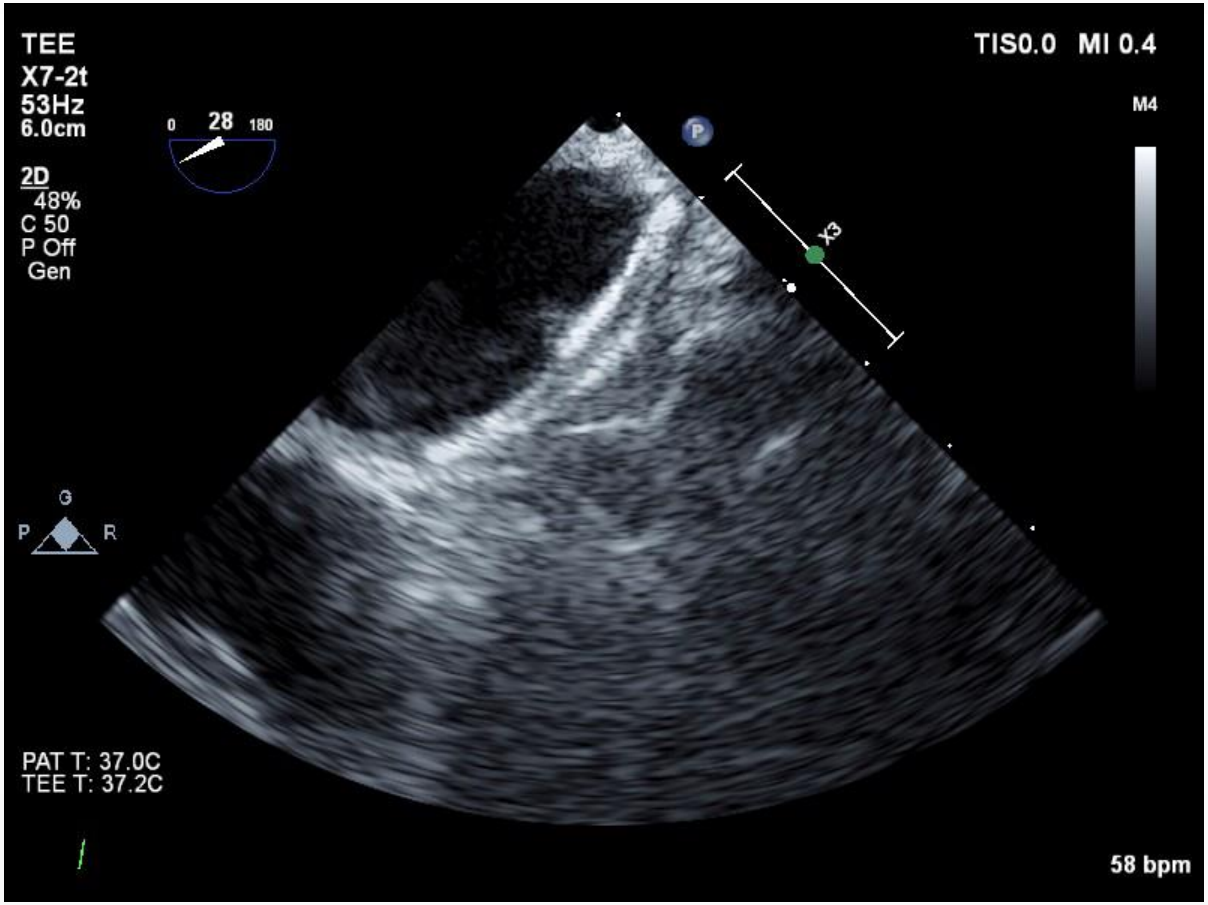


LAA occluded well

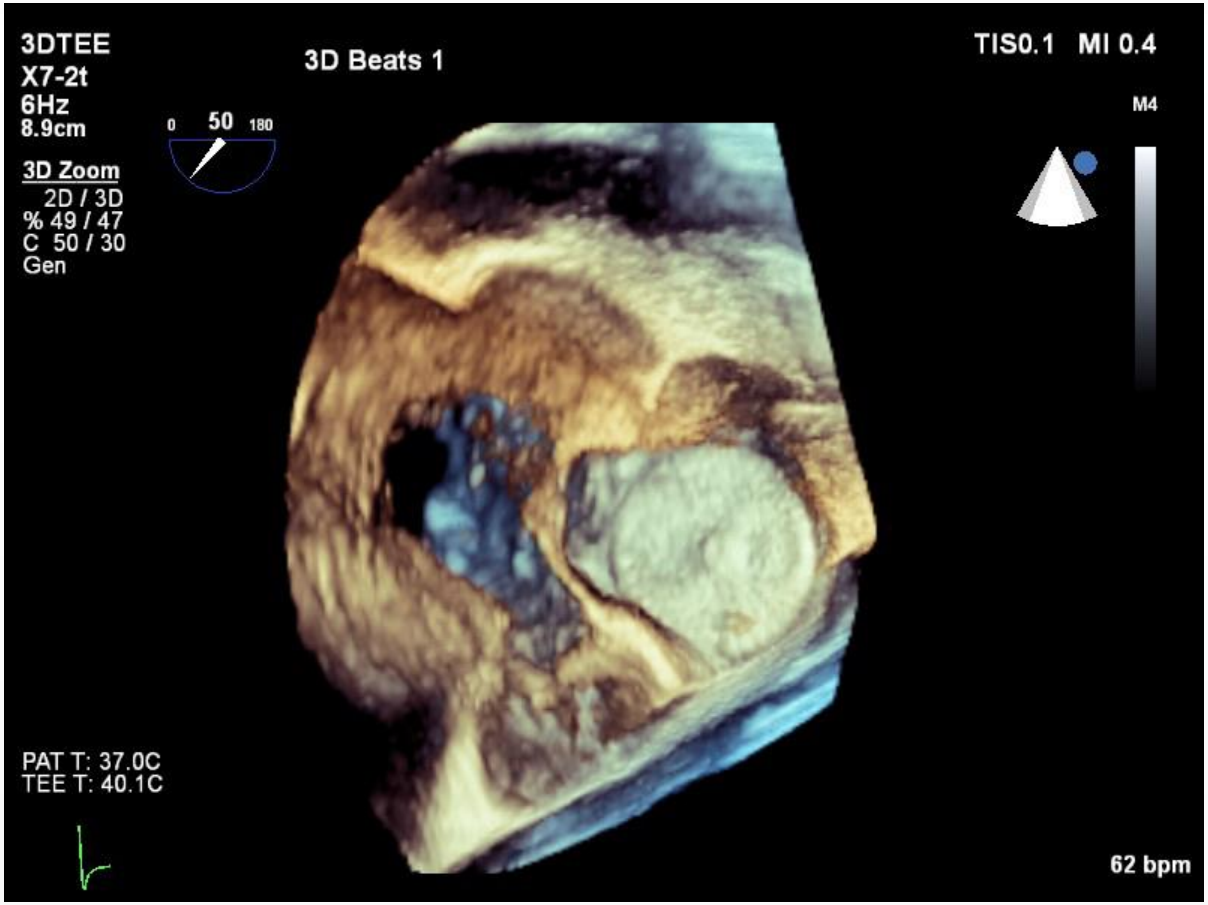


Final result

Final by Echo



Final by echo 3D



מסקנות

- בחולים עם פרפור פרוזדורים ככל שהסיכון לאירוע מוחי גדל כך גם הסיכון לדימום.
- חולים עם פרפור פרוזדורים לא מסתמי בהם יש הוראת נגד לטיפול נוגד קרישה עקב דימום משמעותי שלא ניתן למניעה, יש לשקול החדרת חוסם אוזנית.
- מחקרים שהשוו התקנת חוסם אוזנית מול טיפול בקומדין הראו ירידה משמעותית בתמותה ודימום מוחי במעקב של חמש שנים.
- ניתן לבצע החדרת חוסם אוזנית תחת סדציה ללא רופא מרדים בשיעור סיבוכים נמוך.
- במעקב ארוך טווח חסימת אוזנית מונעת אירועים אמבולים מהעלייה השמאלית בטיפול באספרין בלבד

Thank you for your attention!