

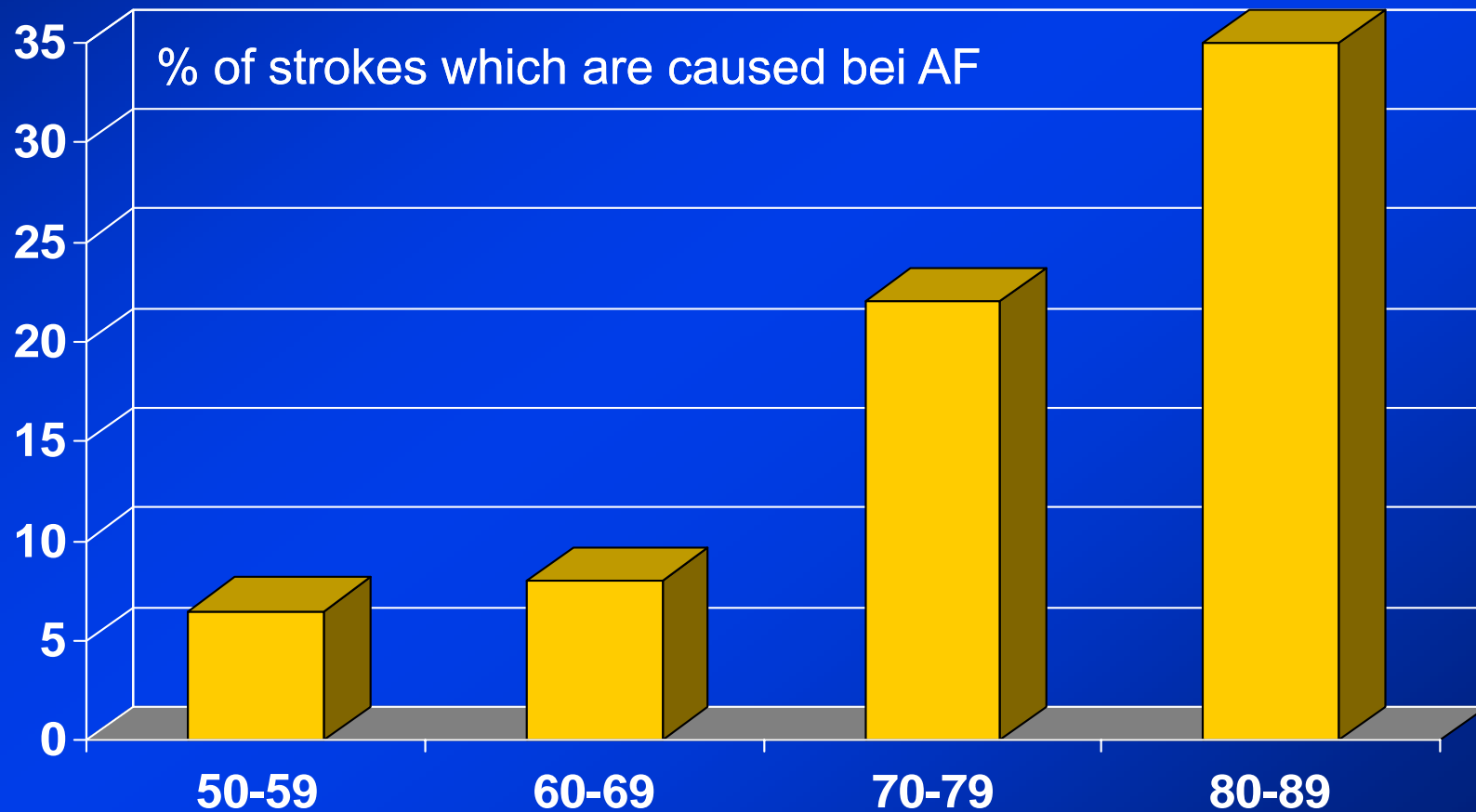
16th ANGIOPLASTY SUMMIT-TCTAP 2011
Seoul, Korea, April 27 – 29, 2011

**Percutaneous LAA Closure:
A Future Management Alternative
for Stroke Prevention in AF Patients**

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Frankfurt, Germany

Atrial fibrillation is one of the most important causes of stroke

Especially in elder patients



Framingham Study, Wolf, 1991

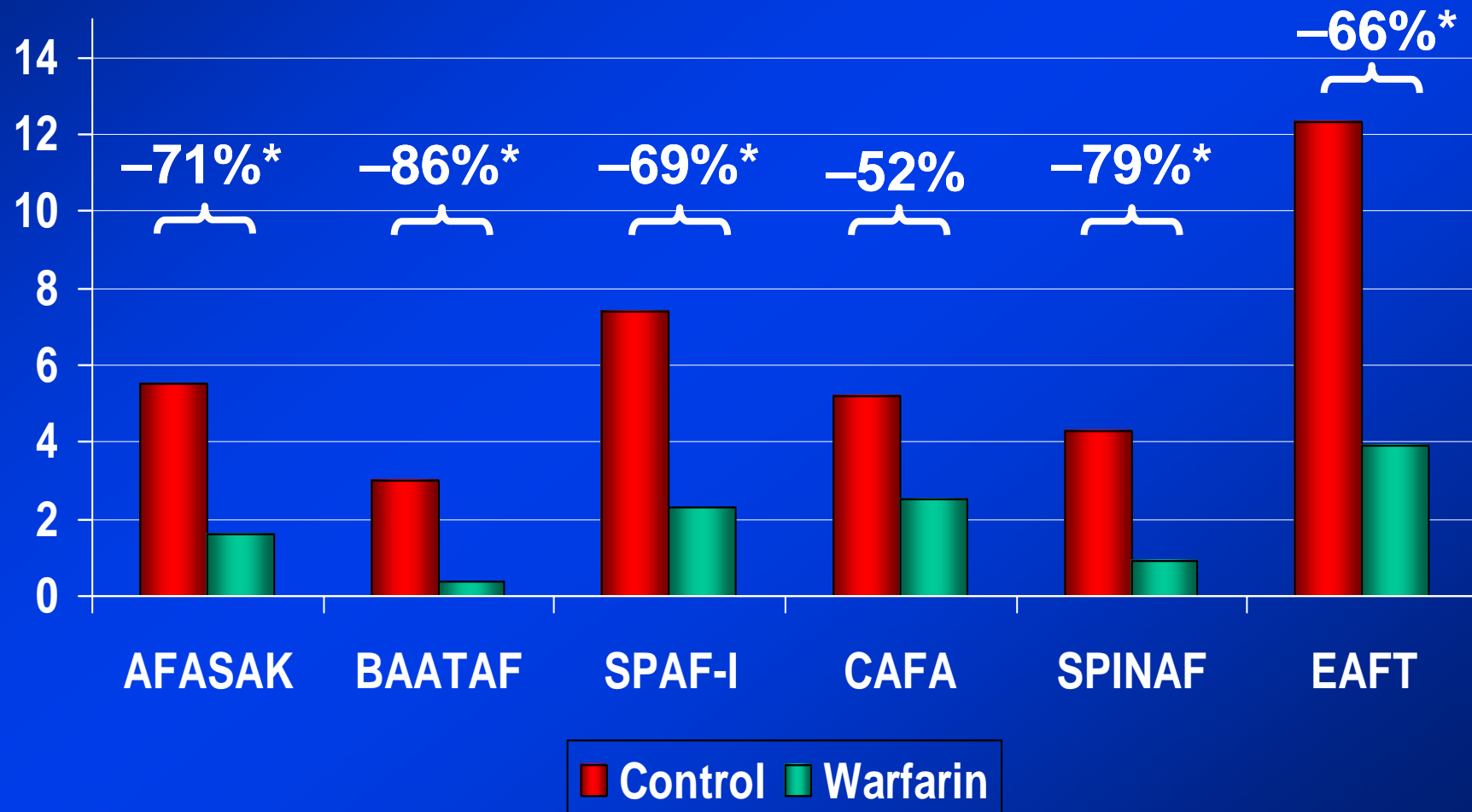
What is the Annual Risk of Stroke?

Nat. Registry of AF: CHADS₂

CHADS Score	# Pts n=1773	# Strokes n=94	NRAF adjusted Stroke Rate (95% CI)
0	120	2	1.9 (1.2-3.0)
1	463	17	2.8 (2.0-3.8)
2	523	23	4.0 (3.1-5.1)
3	337	25	5.9 (4.6-7.3)
4	220	19	8.5 (6.3-11.1)
5	65	6	12.5 (8.2-17.5)
6	5	2	18.2 (10.5-27.4)

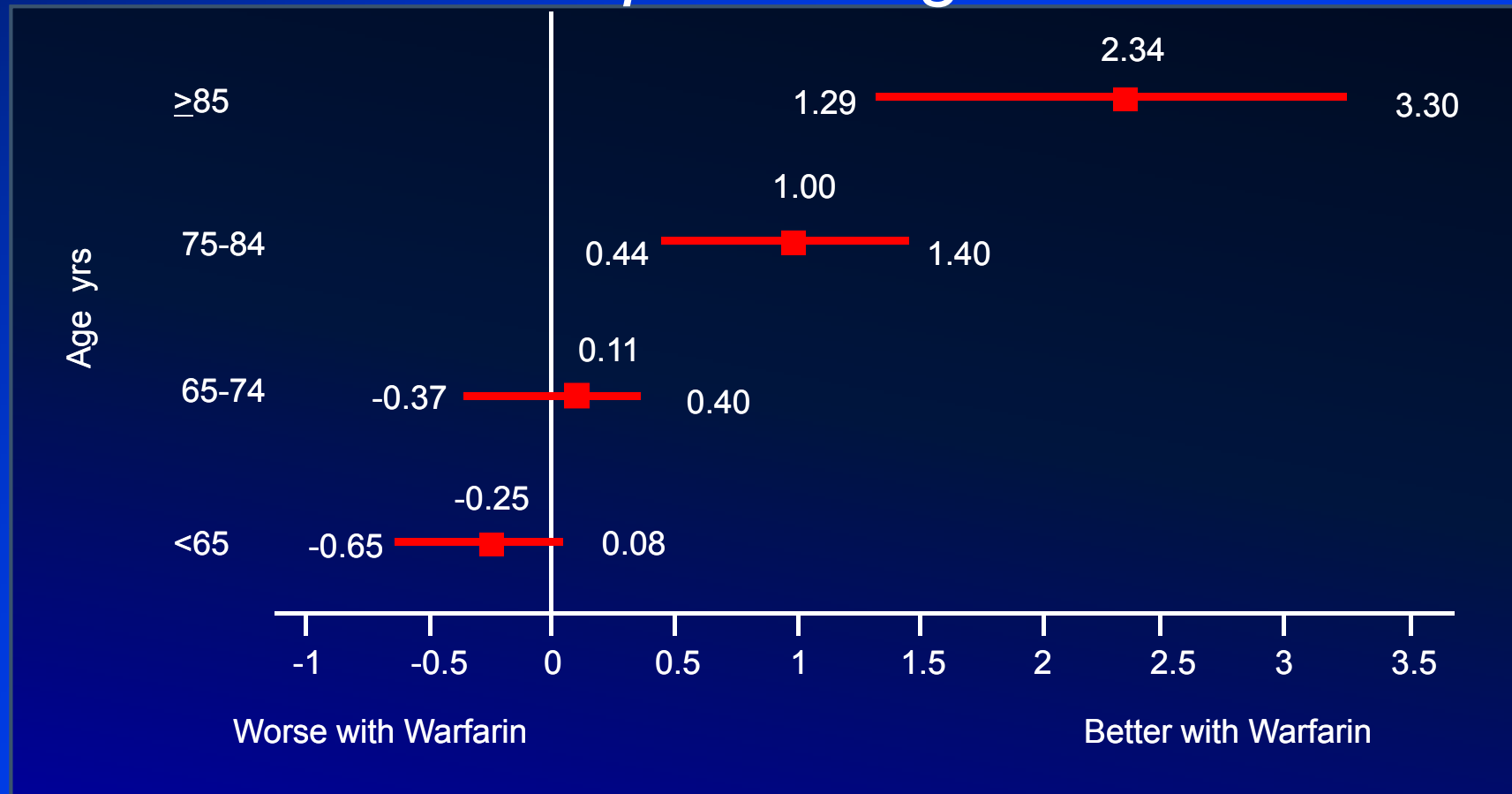
"Let's take
Coumadin!"

Randomized Clinical Trials of Coumadin in Atrial Fibrillation



* $p < 0.05$

Warfarin Net Clinical Benefit: *Impact of Age*



Net Clinical Benefit, Events Prevented per 100 Person – Years

Singer D, Ann Int Med. 2009; 2009;151:297-305

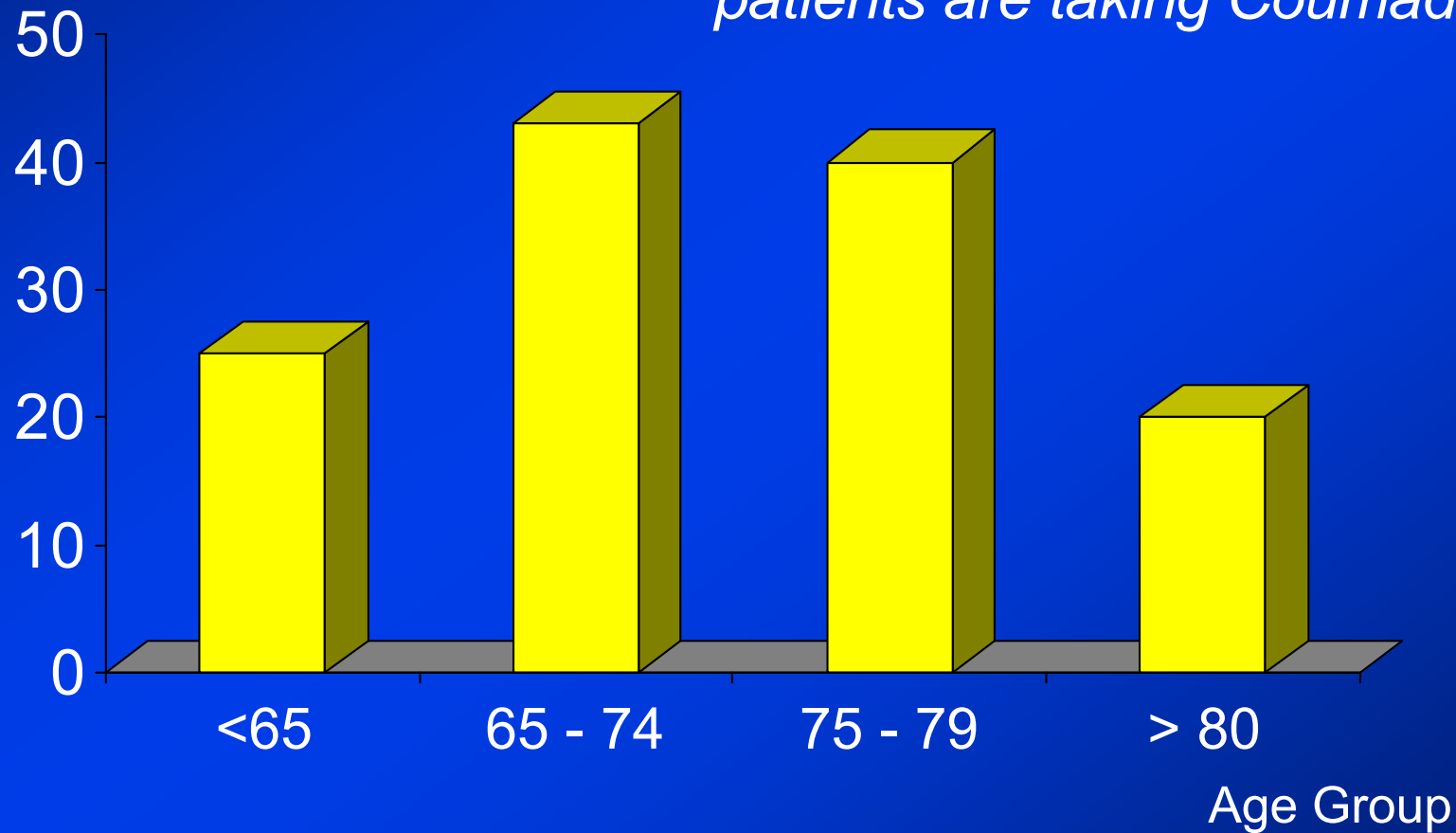
Coumadin is a
good idea,...

... if you can
take it

- 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

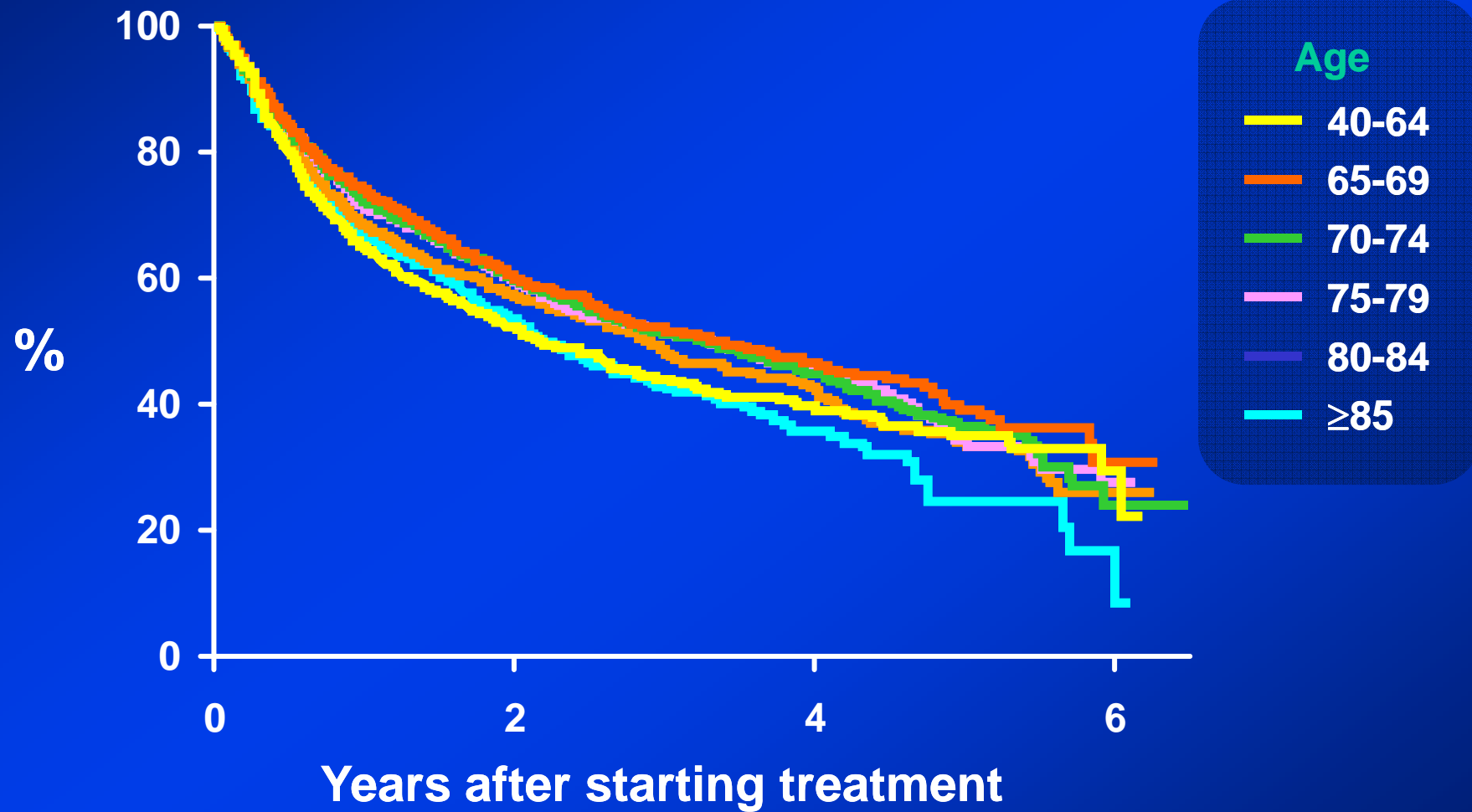
Anticoagulation Underuse

Only about 1/3 of all eligible patients are taking Coumadin



Stafford and Singer, Arch Int Med, 1996

Anticoagulation Use in General Practice Discontinuation



Gallagher AM et al: J Thromb Haemost 6:1500, 2008

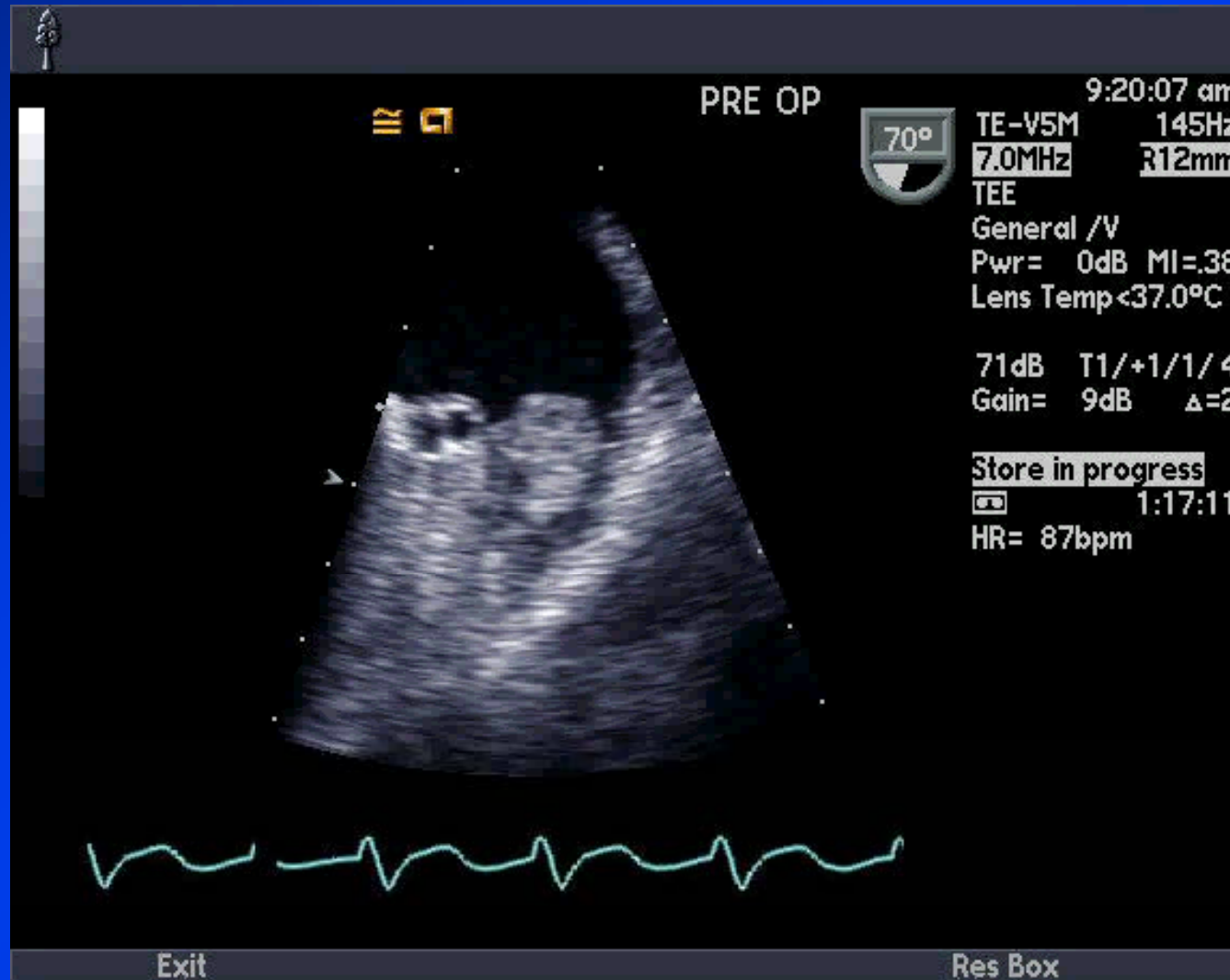
Other drugs?

All Anticoagulants

- Per definition
 - have to be given lifelong
 - have a bleeding risk
- Bleeding risk increases with age
- At some point Anticoagulants have to be stopped
- You should avoid anticoagulants in elderly patients because of higher bleeding risk
- You should avoid anticoagulants in younger patients because they would have to take it for a longer time period

Where do
the thrombi arise ?

Thrombus in the LAA

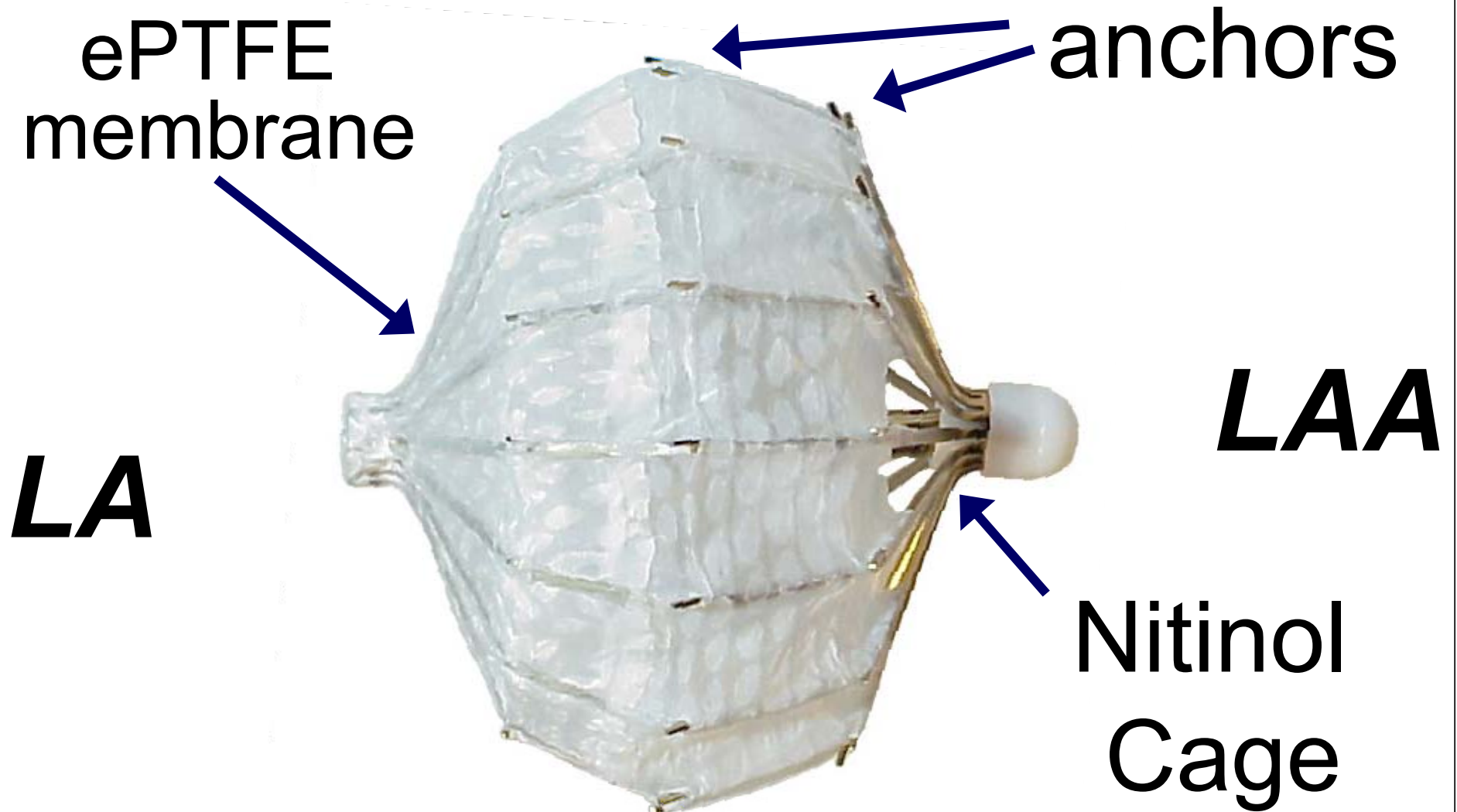


90 % of all thrombi in non-rheumatic atrial fibrillation originate in the LAA

Setting	N	Appendage (%)	LA Body (%)	Ref.
TEE	317	66 (21%)	1 (0.3%)	Stoddard; JACC '95
TEE	233	34 (15%)	1 (0.4%)	Manning; Circ '94
Autopsy	506	35 (7%)	12 (2.4%)	Aberg; Acta Med Scan '69
TEE	52	2 (4%)	2 (3.8%)	Tsai; JFMA '90
TEE	48	12 (25%)	1 (2.1%)	Klein; Int J Card Imag '93
TEE & Operation	171	8 (5%)	3 (1.8%)	Manning; Circ '94
SPAF III TEE	359	19 (5%)	1 (0.3%)	Klein; Circ '94
TEE	272	19 (7%)	0 (0.0%)	Leung; JACC '94
TEE	60	6 (10%)	0 (0.0%)	Hart; Stroke '94
Total	2018	201 (10%)	21 (1.0%)	

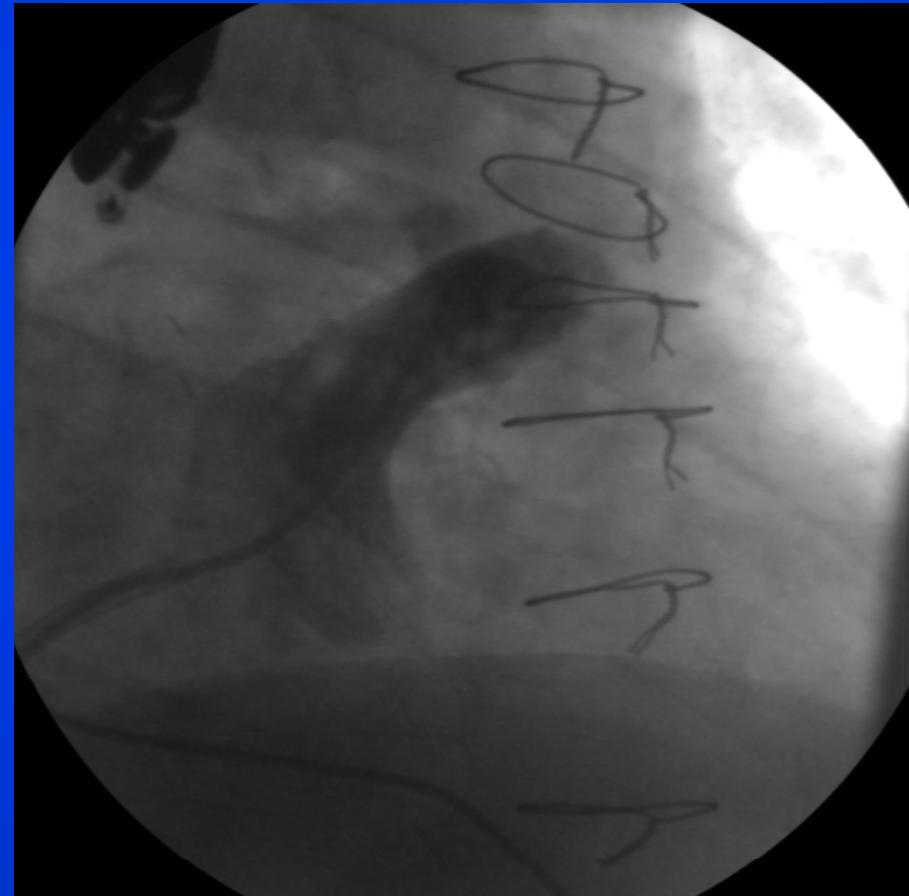
From: Blackshear & Odell; 1996

PLAATO™ Device

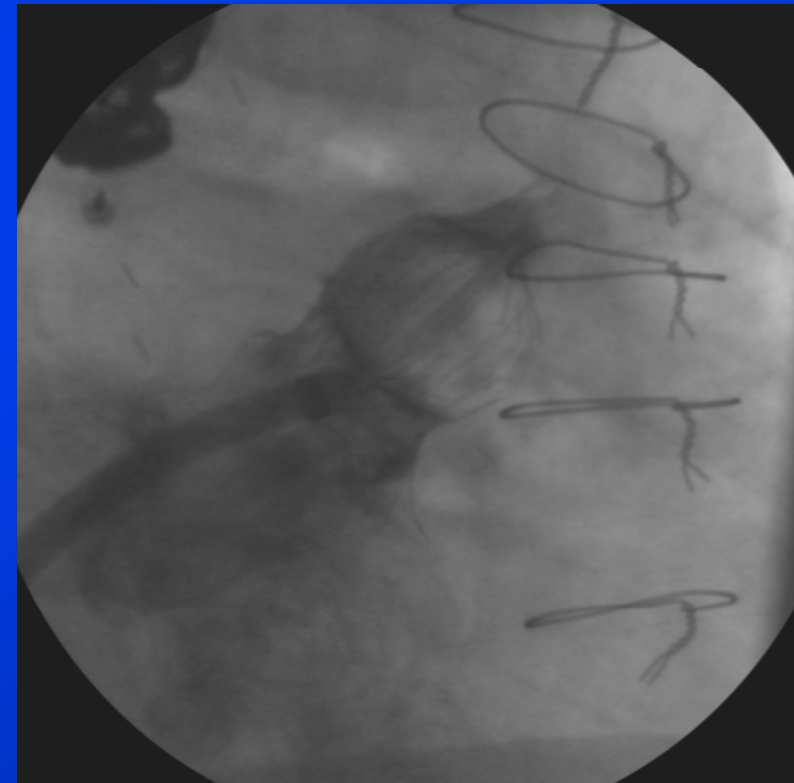


The first patient who underwent successful closure of the LAA

- Aug 30, 2001
- A.S., 72 y/o, male
- AF since 2 years
- Multiple contraindications for coumadin
- Very unstable INR
- CHADS score 3



First successful attempt of LAA closure



- Procedure time 85 min
- Complete seal
- No complications
- Coumadin off since 2001
- No neurological events
- Participated in other FIM trials
- Had his 80th birthday in Jan 2009

Watchman Device

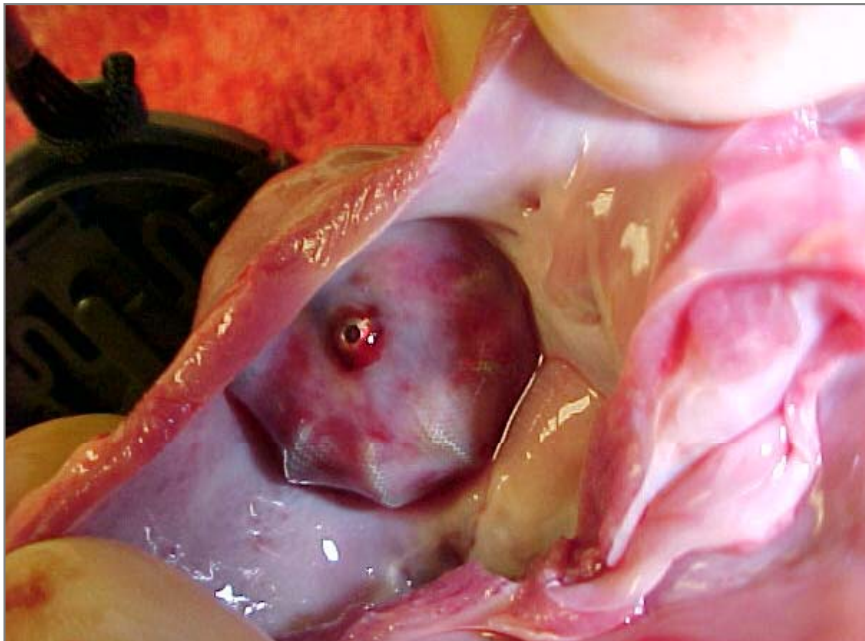


- Nitinol frame
- PET membrane
- row of fixation barbs around the mid perimeter
- 21, 24, 27, 30, 33 mm

CE mark

WATCHMAN Device

Canine Model

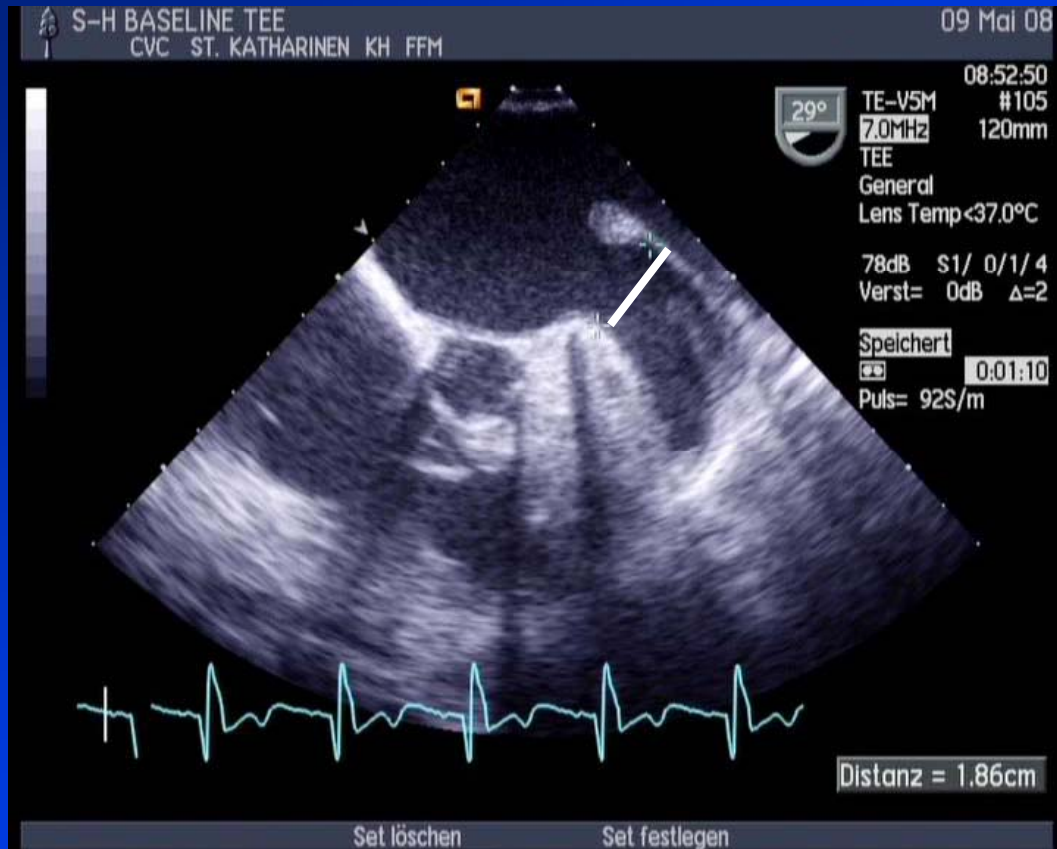


30 days

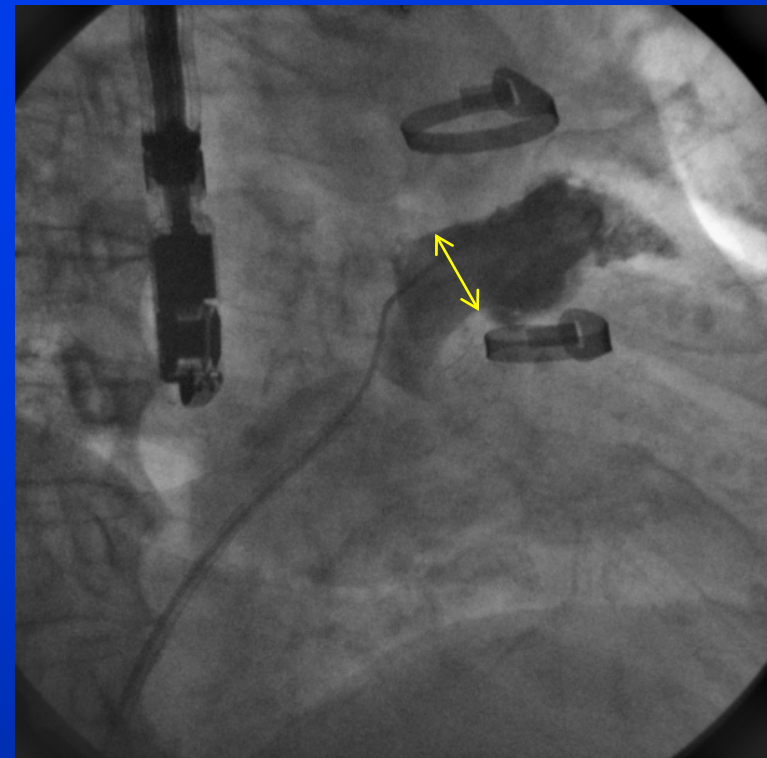


45 days

Watchman Implantation



- LAA diameter in TEE
19 mm



- anatomy of LAA in TEE
and fluoro

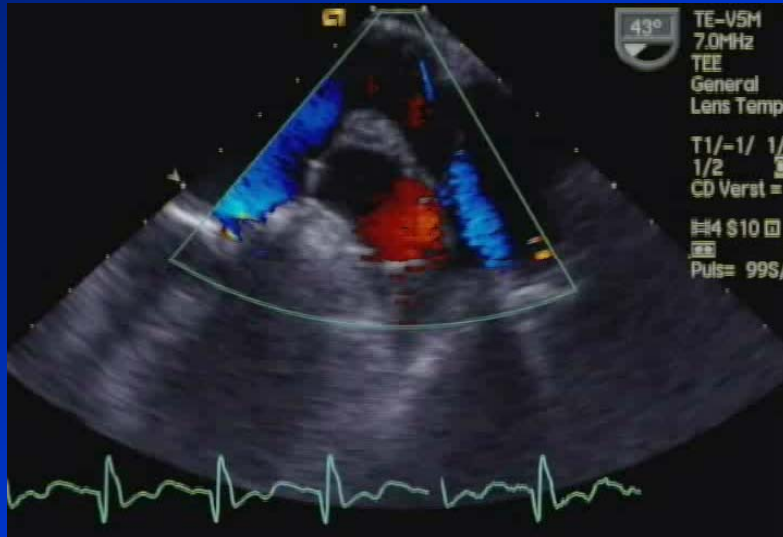
Watchman Implantation

Maximum measured LAA ostium (mm)	Implant diameter (mm)
17 - 19.5	21
20 - 22.9	24
23 - 25.9	27
26 - 28.9	30
29 - 31.9	33

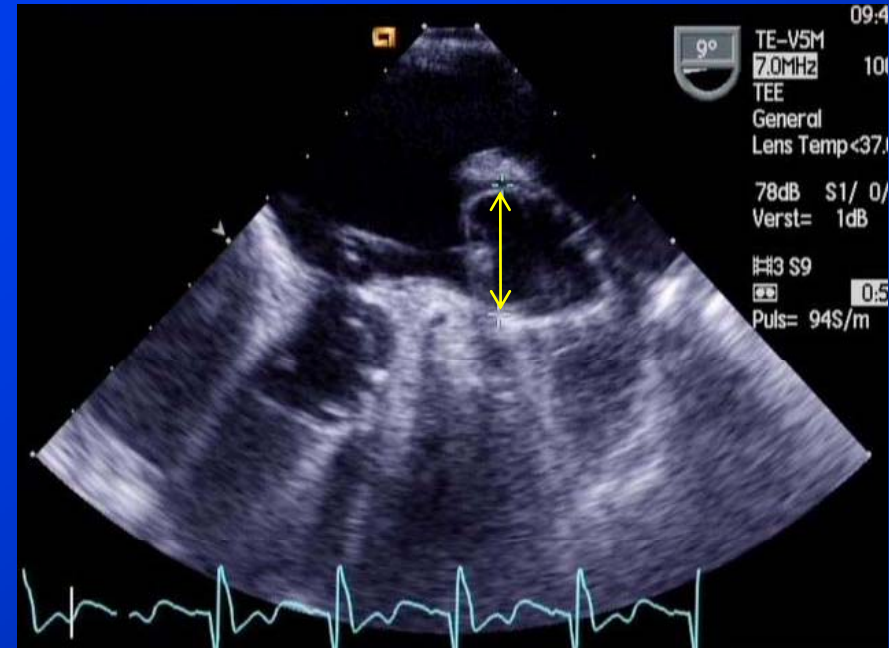
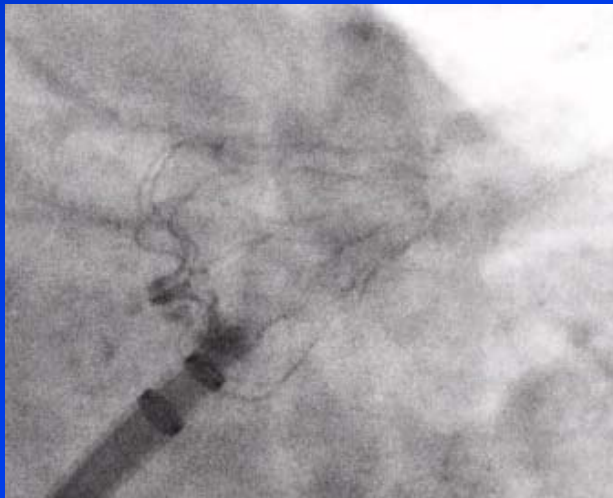


- device selection according to measurements
- Implantation of 21mm Watchman Occluder

Watchman Implantation



- Check position
- Check device compression
- Check residual flow
- Tug test
- Release



Protect AF

(System for Embolic PROTECTION
in Patients with Atrial Fibrillation)

- Multicenter
- Prospective randomized
- WATCHMAN vs coumadin 2:1
- Non-inferiority trial
- 800 pts (enrollment closed June 2008)
- > 900 patient-years

In- & Exclusion

Major inclusion criteria

- Non valvular AF with Chads2 score ≥ 1
- No contraindications to coumadin
- No co-morbidities mandating chronic warfarin use other than AF

Major exclusion criteria

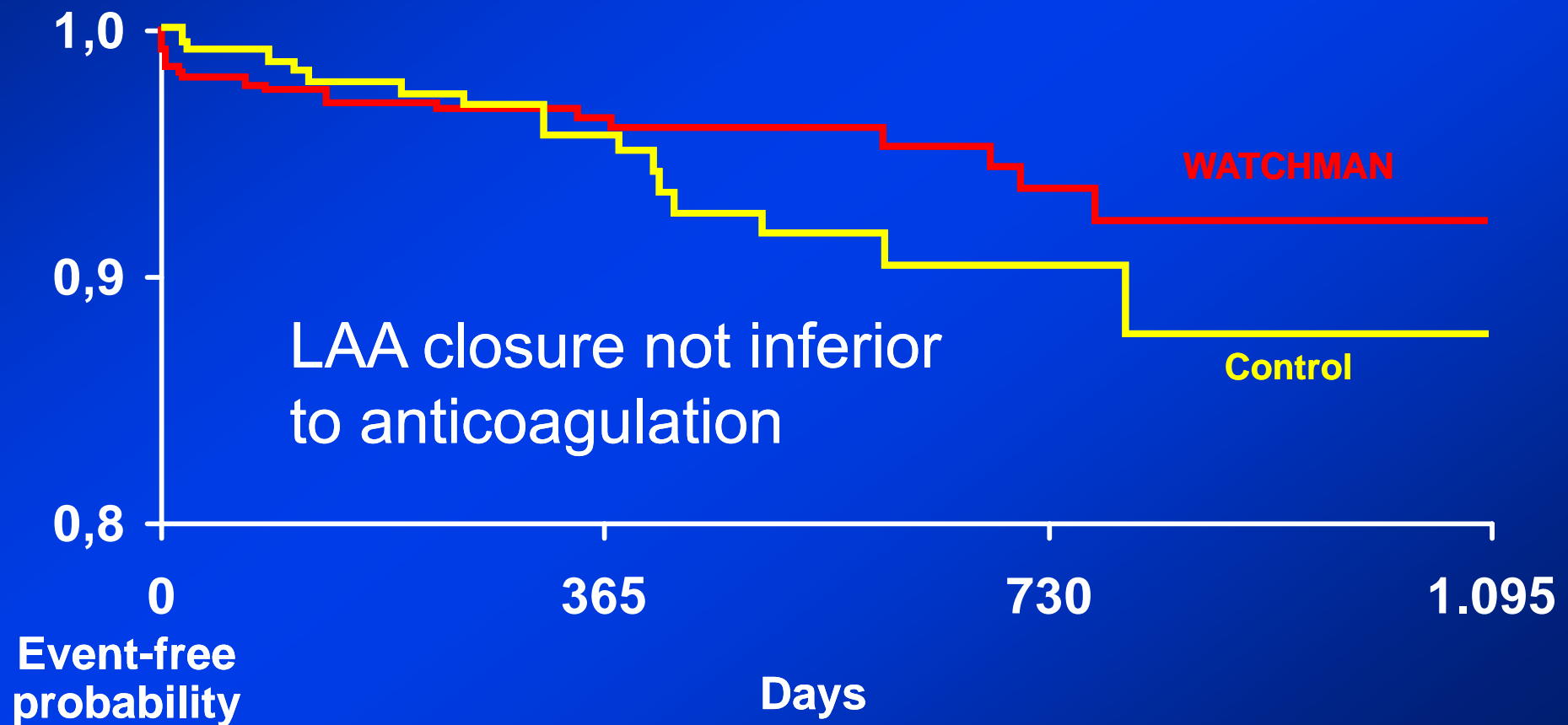
- LAA thrombus
- Large PFO with significant atrial septal aneurysm
- Mobile aortic atheroma
- Symptomatic carotid artery disease

PROTECT AF Trial Endpoints

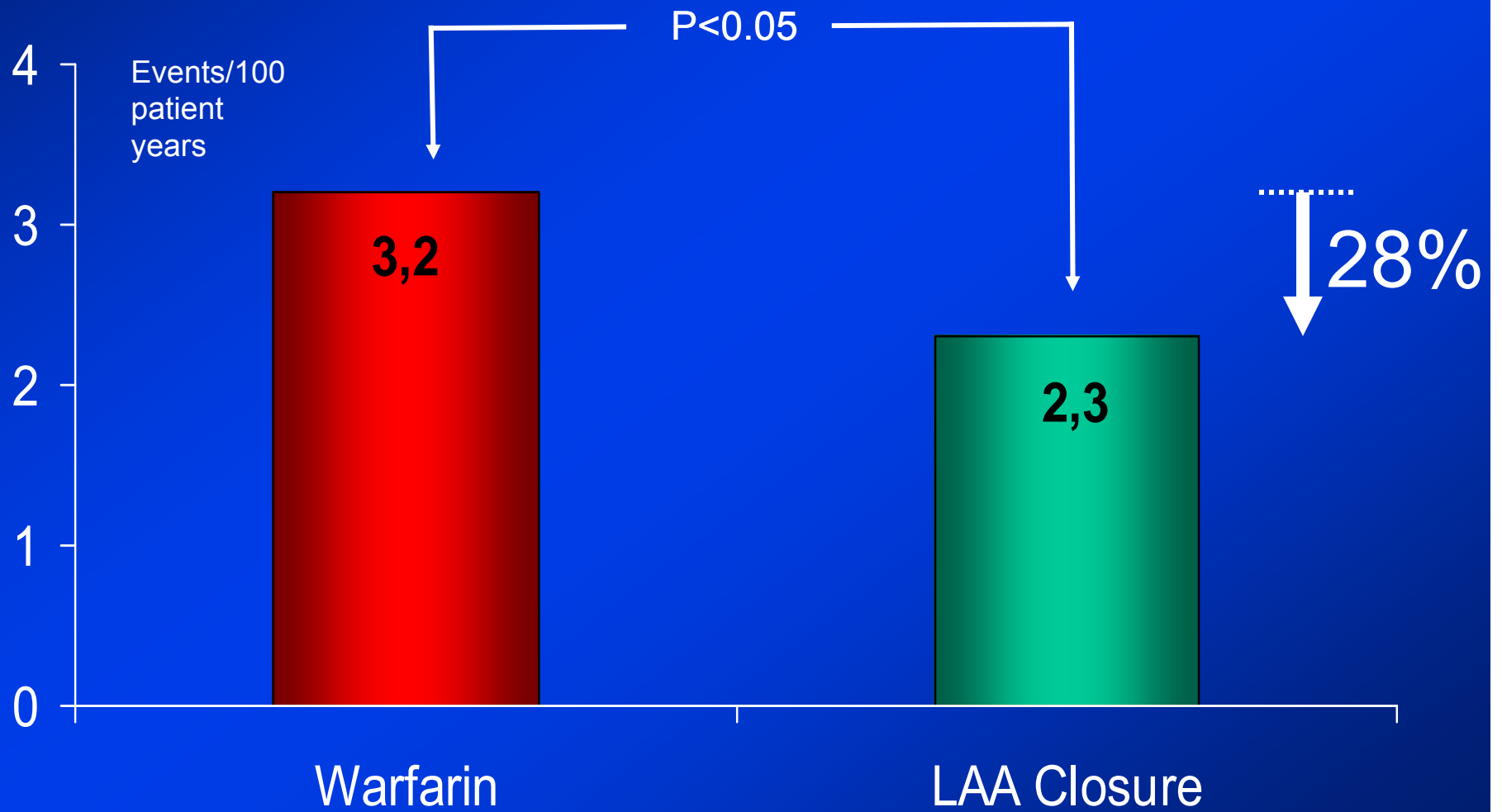
- Primary Efficacy Endpoint
 - All stroke
 - Cardiovascular and unexplained death
 - Systemic embolization
- Primary Safety Endpoint
 - Device embolization requiring retrieval
 - Pericardial effusion requiring intervention
 - Cranial bleeds and gastrointestinal bleeds
 - Any bleed that requires ≥ 2 uPRBC

Primary Efficacy Endpoint

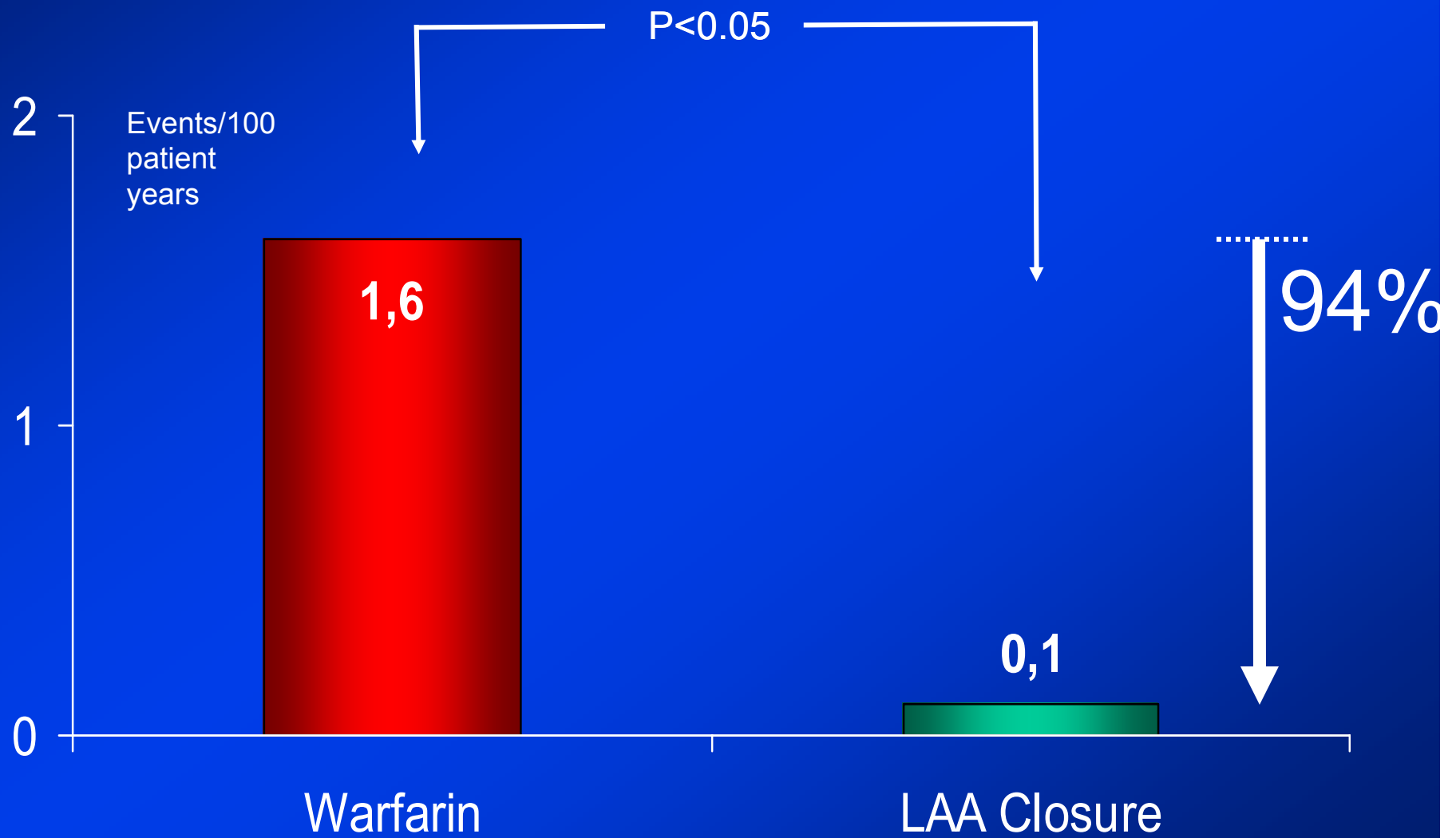
Freedom from Stroke, Death, Systemic Embolization



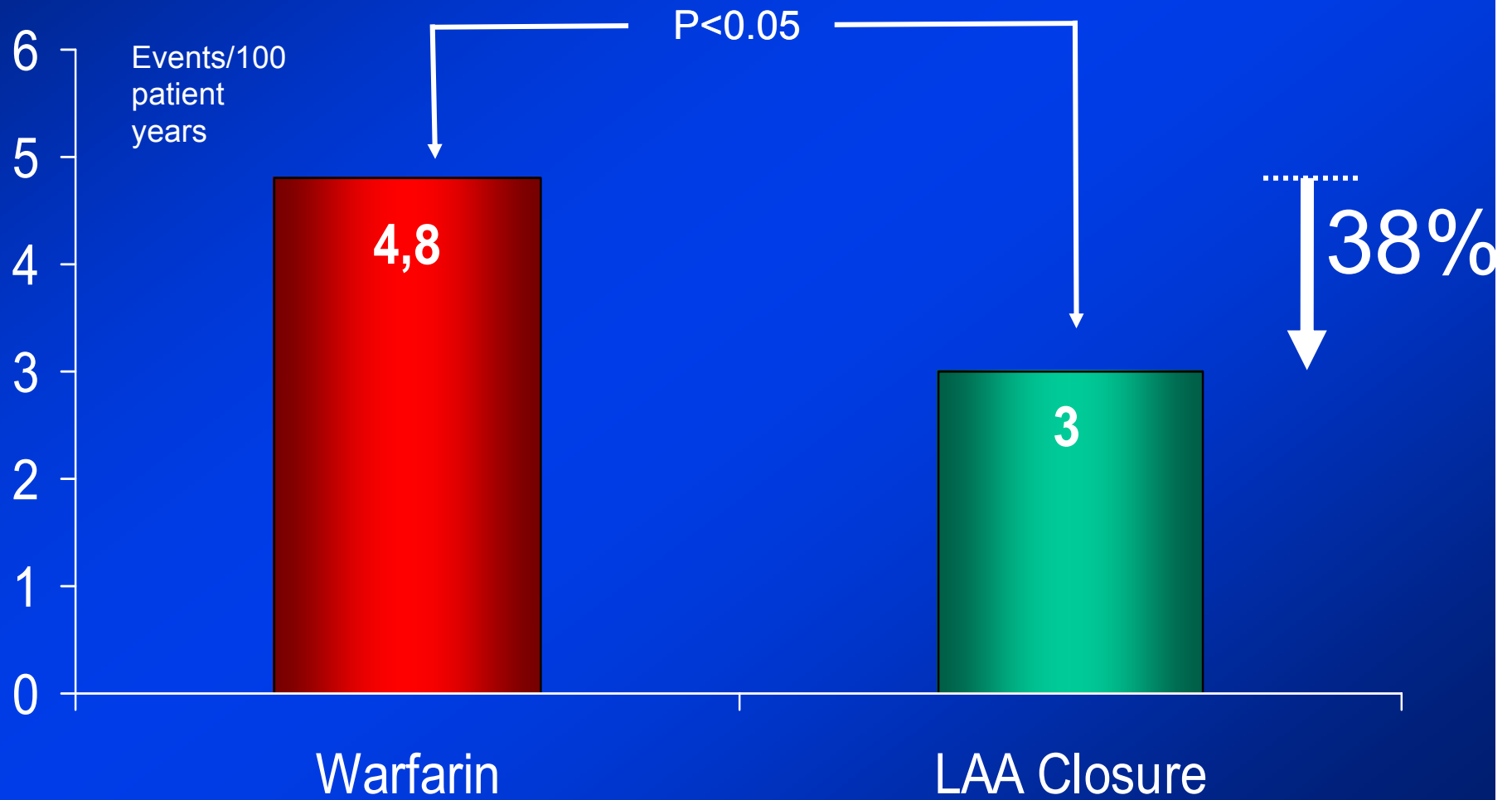
All Stroke



Hemorrhagic Stroke

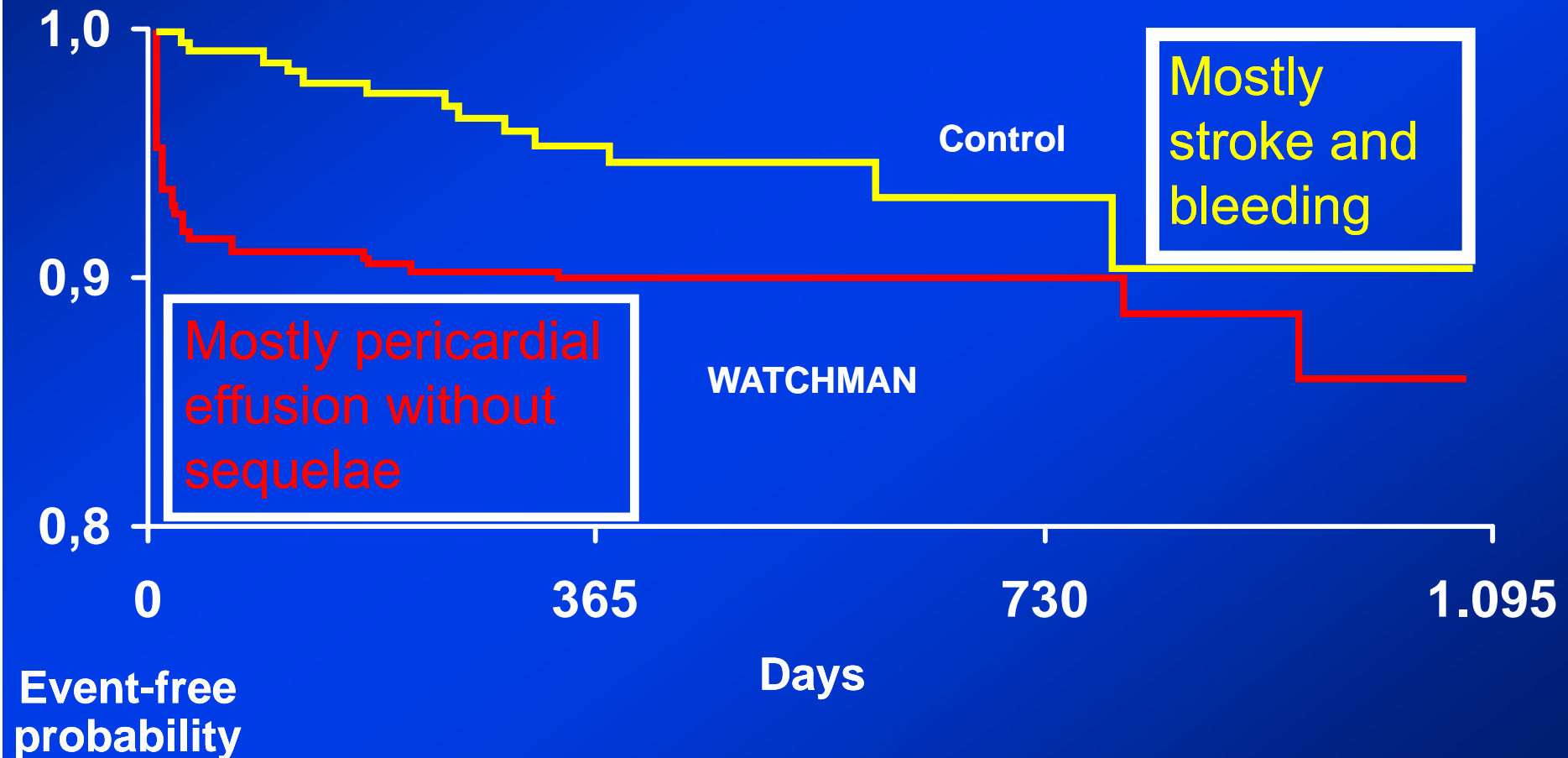


Mortality



Safety

Freedom from device embolization, pericardial effusion, Severe bleeding



PROTECT AF

- ... was the "Proof of concept":
 - Left atrial appendage closure prevents stroke
 - It is as effective as anticoagulation
- As expected there are more early safety events after LAA closure due to pericardial effusions
- Under anticoagulation therapy there are more late safety events due to stroke and bleeding

Performance Metrics PROTECT AF vs CAP

	PROTECT AF	PROTECT AF		CAP	p-value*	p-value±
		Early	Late			
Procedure Time (Mean ± SD)	62 ± 34	67 ± 36	58 ± 33	50 ± 21	<0.001	<0.001
Implant Success	485/542 (89.5%)	239/271 (88.2%)	246/271 (90.8%)	437/460 (95.0%)	0.001	0.001
45-day Warfarin Discontinuation Among Implanted	414/478 (86.6%)	194/235 (82.6%)	220/243 (90.5%)	352/371 (94.9%)	<0.001	<0.001

*From tests comparing the PROTECT AF cohort with CAP

±From tests for differences across three groups (early PROTECT AF, late PROTECT AF, and CAP)

- Improvements seen over time in PROTECT AF
 - Shorter implant time, higher implant success rate, higher warfarin discontinuation rate
- Trends confirmed in CAP



Safety Event Rates

PROTECT AF vs CAP

	PROTECT AF	PROTECT AF Early	PROTECT AF Late	CAP	p-value*	p-value±
Procedure/Device Related Safety Adverse Events within 7 Days	42/542 (7.7%)	27/271 (10.0%)	15/271 (5.5%)	17/460 (3.7%)	0.007	0.006
Serious Pericardial Effusions within 7 Days	27/542 (5.0%)	17/271 (6.3%)	10/271 (3.7%)	10/460 (2.2%)	0.019	0.018
Procedure Related Stroke	5/542 (0.9%)	3/271 (1.1%)	2/271 (0.7%)	0/460 (0.0%)	0.039	0.039

Improvements seen over time for acute safety events

Fewer total procedure/device related events

Concept of PLAATO and Watchman

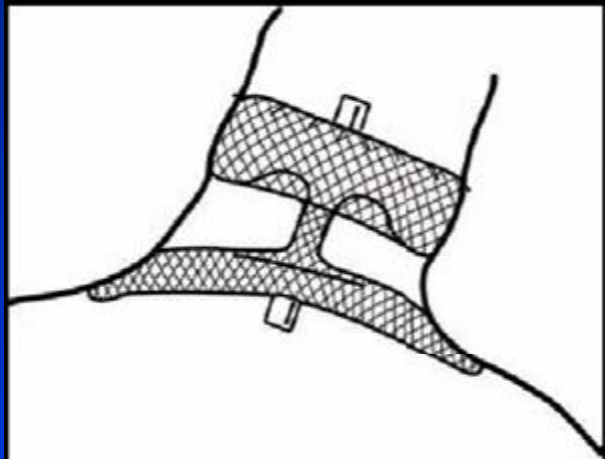
- To close the LAA like with a ball



Amplatzer Cardiac Plug ACP

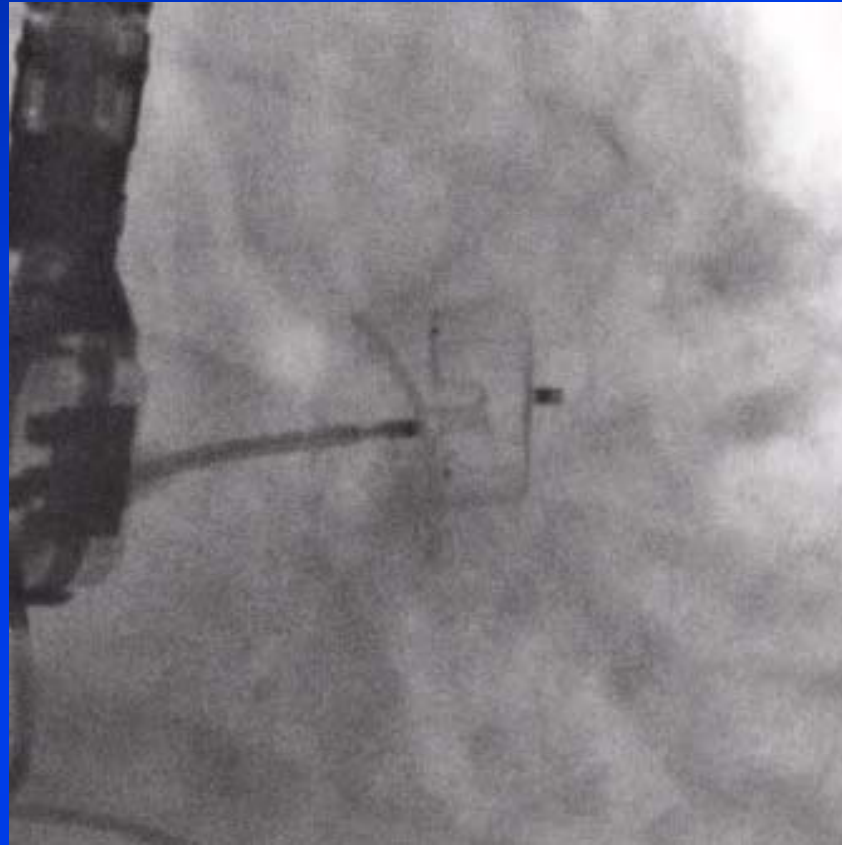


Concept of Amplatzer Cardiac Plug ACP



M.I., female, 66 years

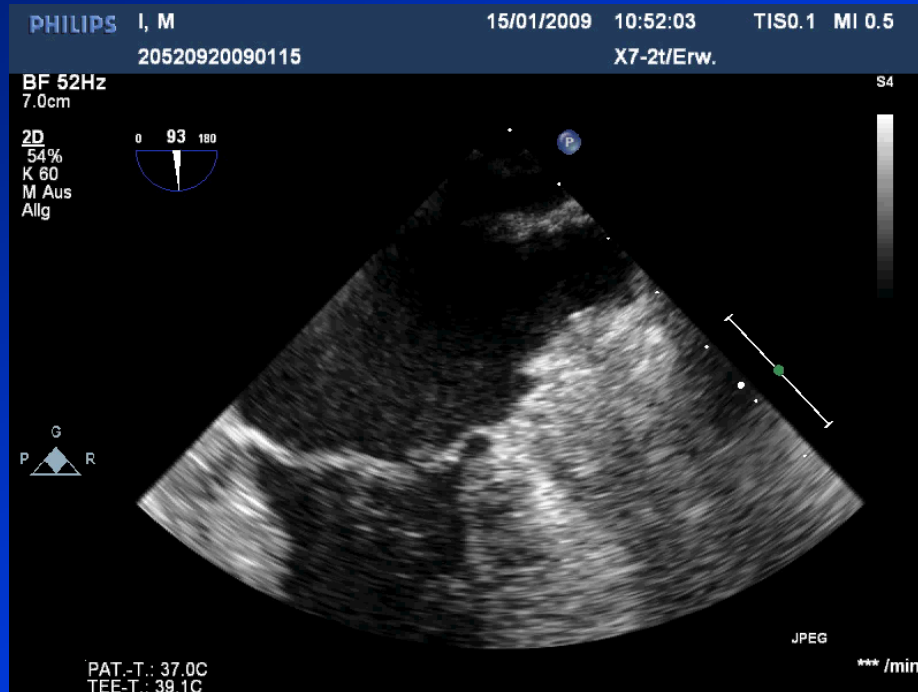
Assessment before release



- Tug test

M.I., femal, 66 years

Final position



- 2D TEE 93°

- 3D TEE: LA en-face view of the occluder



ACP

	FIM Registry	CVC Frankfurt
• N	143	67
• Technical success rate	96.4%	96%
• MAE < 24 hours		
- Tamponade	3.5%	0
- Device embolisation	1.4%	1.5%
- Stroke	2.1%	0

New Approaches

- Endocardial

- Occlutech
- Coherex
- Gore

- Epicardial

- Epitec
- AtriCure
- SentreHeart
- Aegis Medical

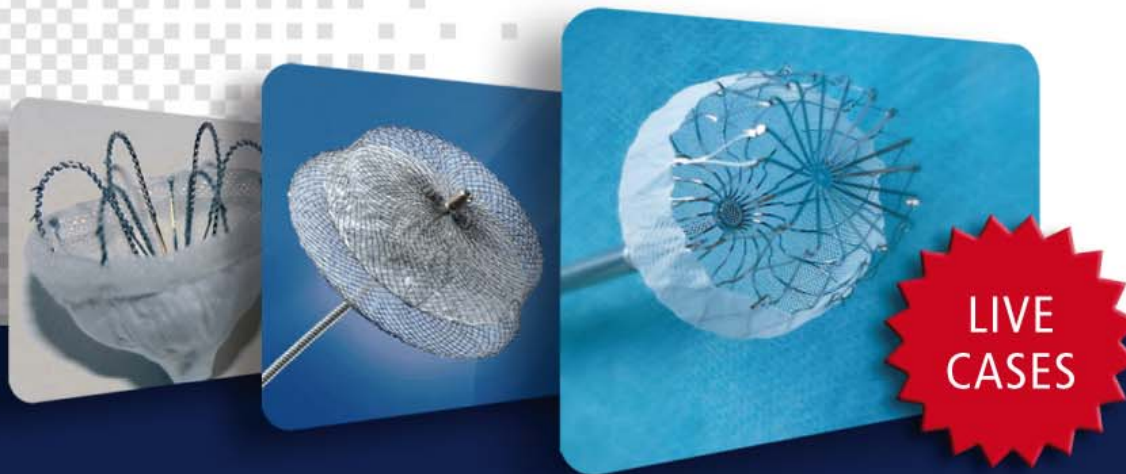


June 23 – 25, 2011 | Frankfurt, Germany

CSI 2011 – Catheter Interventions in Congenital & Structural Heart Disease

www.csi-congress.org





November 19, 2011 | Frankfurt, Germany

LAA 2011 – How to Close the Left Atrial Appendage



www.csi-laa.org

Take Home Messages

- Atrial fibrillation is a frequent cause of stroke
- Thrombi originate in the left atrial appendage
- Catheter closure of the atrial appendage is feasible and relatively safe
- The randomized trial with the Watchman device showed that the procedure is safe and effective in stroke reduction and not inferior compared to anticoagulation
- Currently two devices are available for LAA closure
- Many others are under development

Thank You