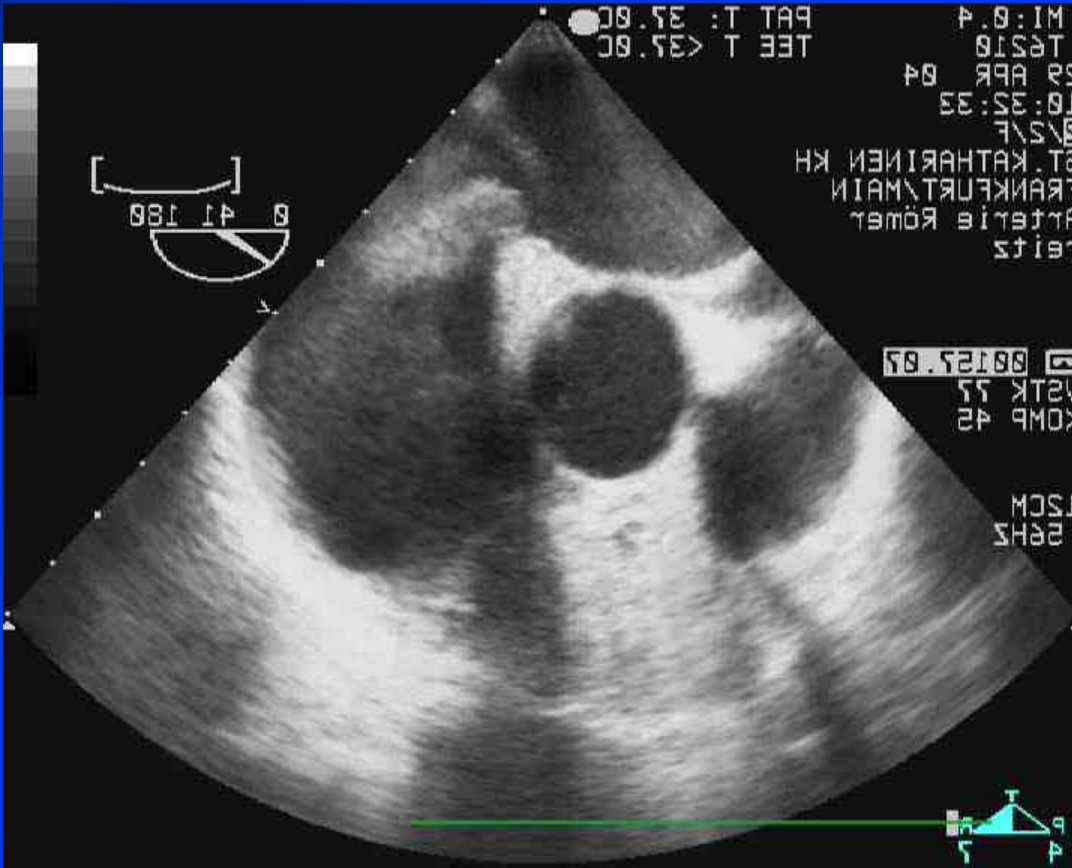


15th ANGIOPLASTY SUMMIT-TCTAP 2010
Seoul, Korea, April 28-30, 2010

Update on Percutaneous PFO Closure

Horst Sievert, Nina Wunderlich
CardioVascular Center Frankfurt
Frankfurt, Germany

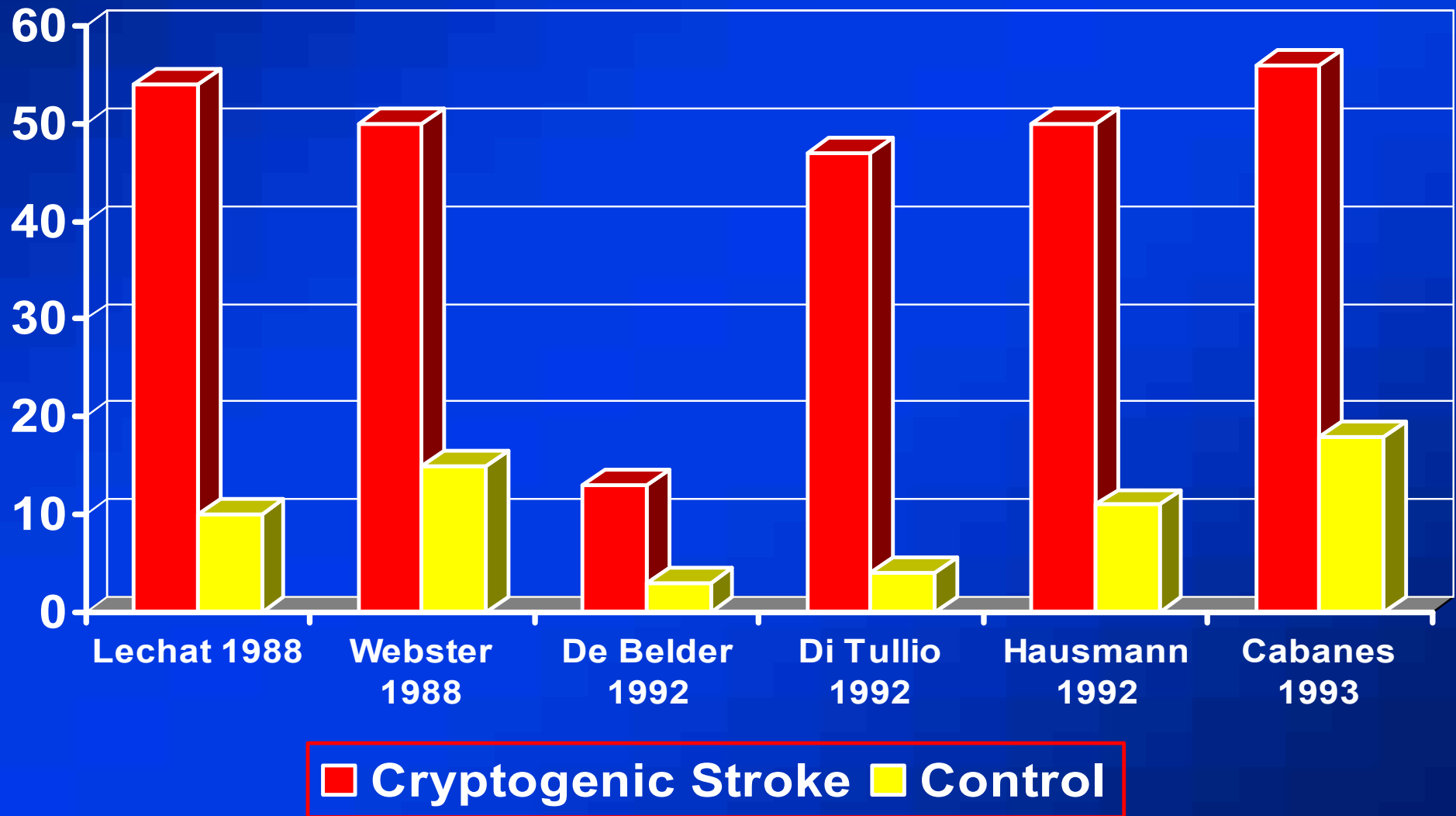
Embolus Crossing a PFO



- Peripheral embolism
- Death
- Stroke

... but the discussion is still ongoing

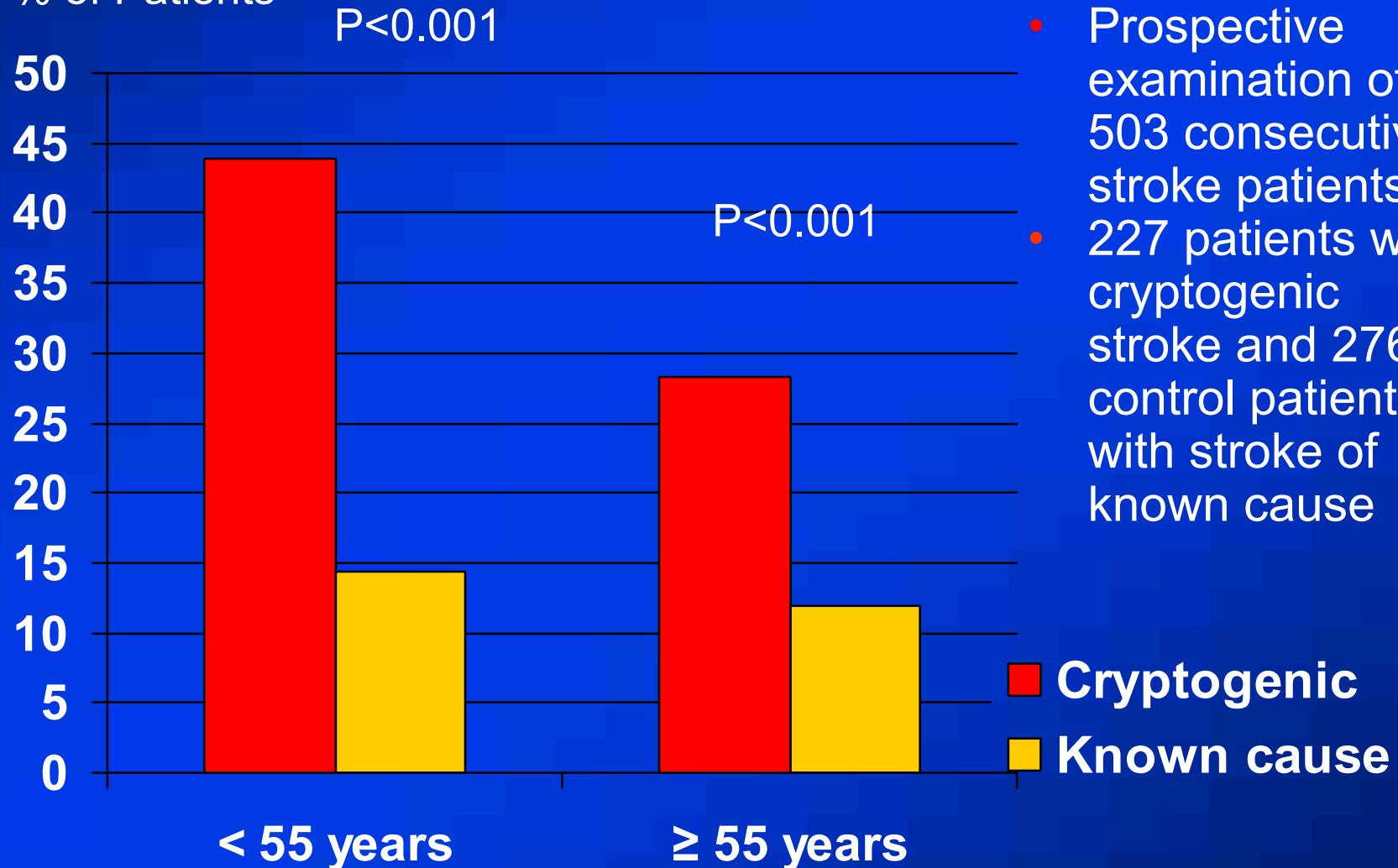
Stroke is associated with PFO



Not only in
young patients

Prevalence of Patent Foramen Ovale in cryptogenic stroke

% of Patients



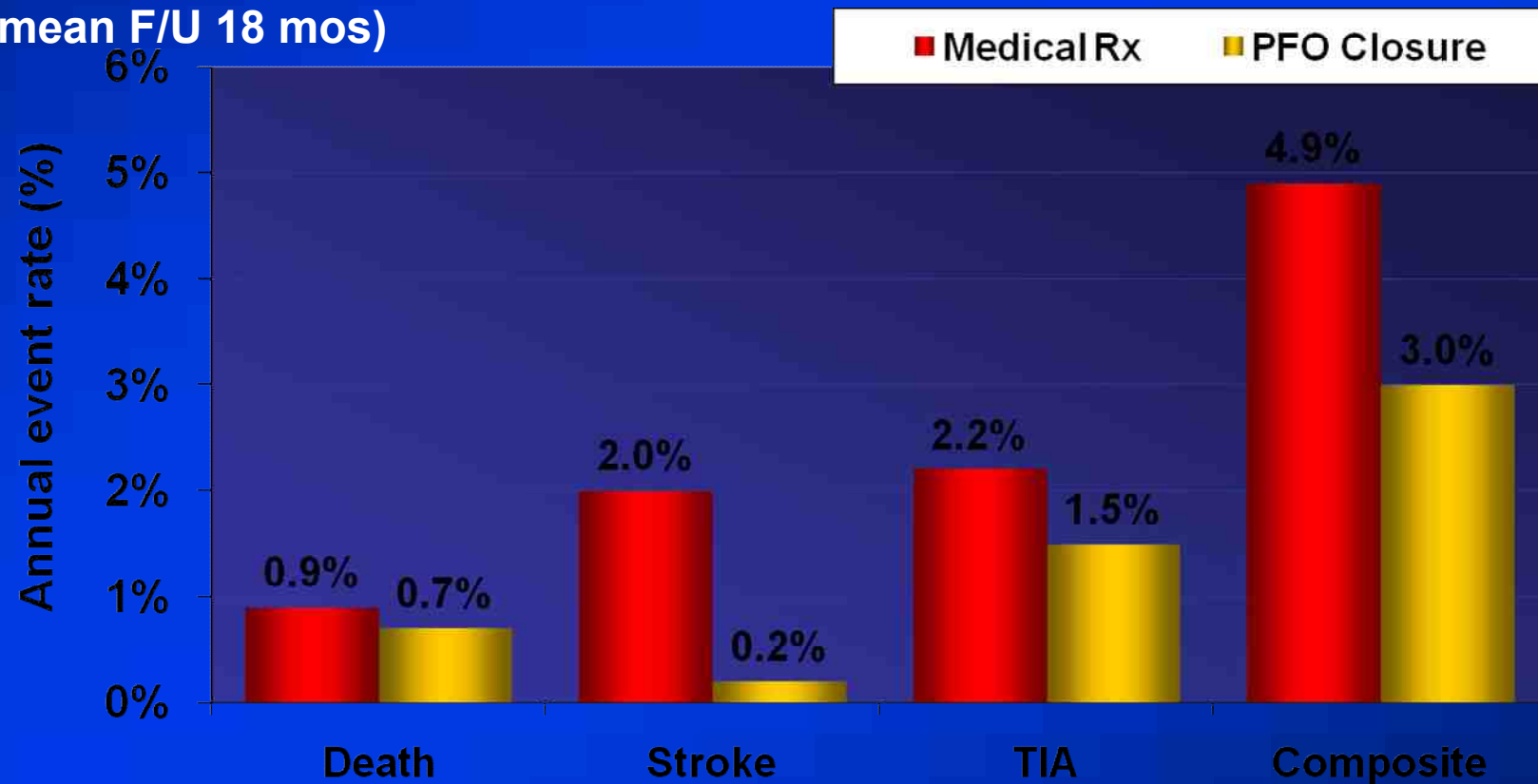
Handke et al. N Engl J Med 2007;357:2262-8.

There is general agreement...

- ... that there is a risk of recurrence after the first paradoxical embolism due to a PFO
- ... that after a paradoxical embolism there is a need for some preventive treatment
- ... that having a PFO does not have any advantages

Meta-analysis of Event Rates in Patients with Cryptogenic Stroke

- 12 studies with 943 medically treated cryptogenic stroke pts (mean age 45 years, mean F/U 34 mos)
- 12 studies with 1,430 stroke pts after PFO closure (mean age 46 years, mean F/U 18 mos)



Update on Randomized Trials

Closure I (NMT)

PFO-Closure vs Medical Therapy

- Age 18-60 yrs
- Prior TIA/stroke
- 1600 patients planned
 - in April 2007 reduced to 800
- 95 centers (US, Canada, UK)
- Enrolment completed 2008 (900 patients)
 - Results to be reported at AHA 2010

RESPECT (Amplatzer) PFO-Closure vs Medical Therapy

- Age 18-55 yrs
- Prior stroke/TIA
- 500 pts planned
 - >500 enrolled in Dec 2008
 - Enrolment is ongoing

PC Trial

PFO-Closure vs Medical Therapy

- PC Trial
 - Plan: 450 patients
 - randomized closure with Amplatzer PFO occluder vs medical therapy, FU 5 yrs
 - Study started in 2000
 - Enrolment finished?

What are the problems with these randomized trials?

- Some centers had limited experience with the procedure when they started
- Patient numbers are rather small
- Patients with a clear paradoxical embolism got their PFO closed outside of the trials
- Follow-up is rather short
- Technology outdated

So what if these trials are ...

- positive, i.e. PFO closure is better than medical therapy
 - Neurologist will not believe it
- negative, i.e. medical therapy is better than PFO closure
 - Cardiologists will not believe it
- Patients will prefer PFO closure anyway
 - because they just do not want to take anticoagulation therapy forever

PFO and Migraine

Many case series and also prospective non-randomized trials have shown a benefit of PFO closure in migraine ...

... in particular if the PFO was closed to prevent recurrent stroke

The MIST trial was the first
randomized trial PFO closure vs
sham procedure in migraine patients
who did not have a stroke ...

... and it was negative

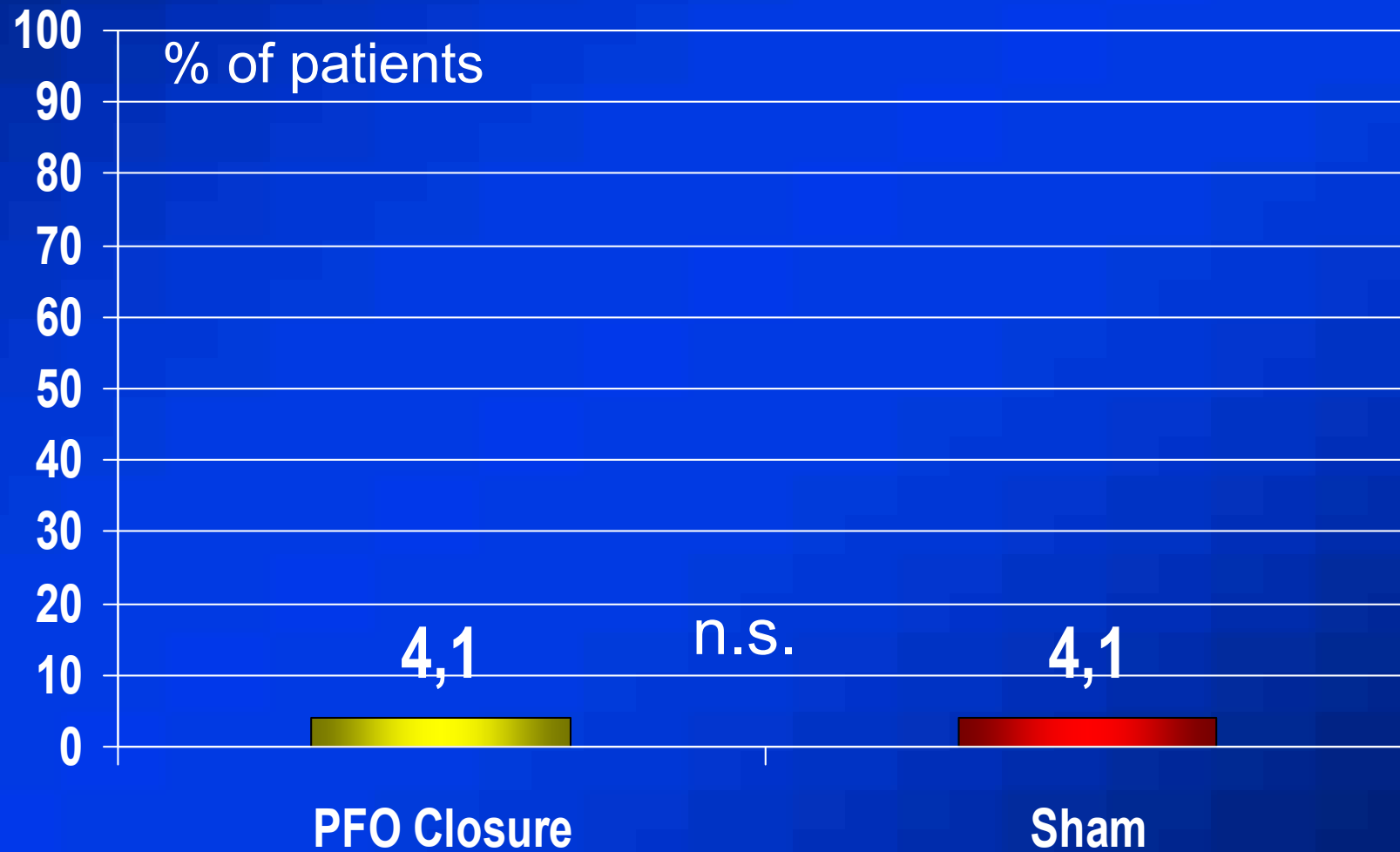
MIST: Very high prevalence of PFO in migraine

result	total #	%
total studied	432	100
small shunts (atrial and pulmonary)	72	16.7
large pulmonary shunt	22	5.1
ASD	3	0.7
large PFO	163	37.7
large shunts (all types)	188	43.5
total shunts	260	60.2

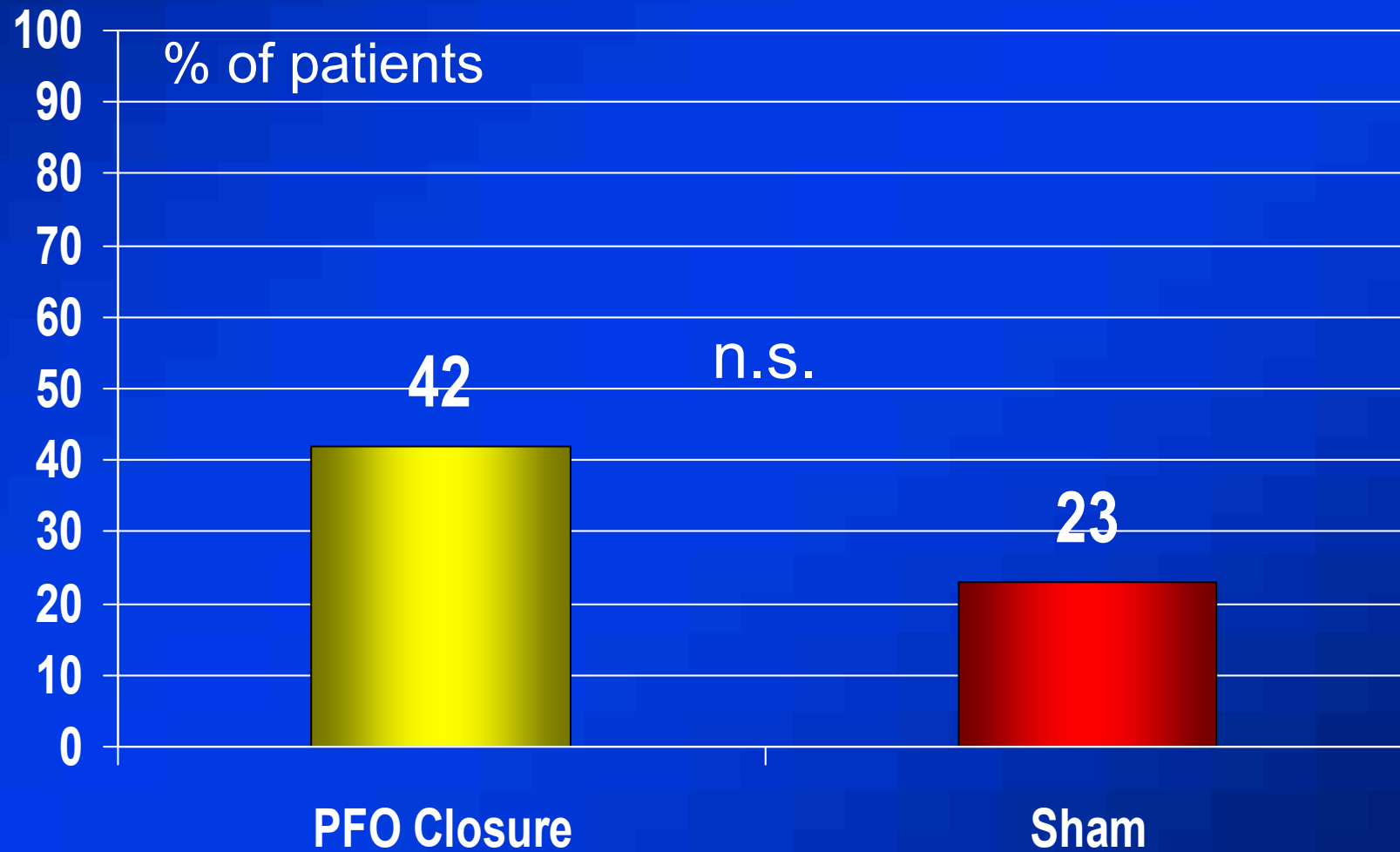
Prevalence of large shunts was approximately six times greater than in the general population

MIST - Cure of Migraine

Primary Endpoint



50% Reduction in Headache Days



Exploratory analysis

PRIMA

- Amplatzer PFO occluder for migraine therapy
- Randomized multicenter study, unblinded
- Primary endpoint: Reduction of migraine days
- Ongoing

3 other migraine trials have been stopped due to slow enrolment and/or lack of funding

- MIST II
- ESCAPE US
- ESCAPE EU

So should we close
PFOs to prevent
migraine?

Not yet!

How to Close the PFO?



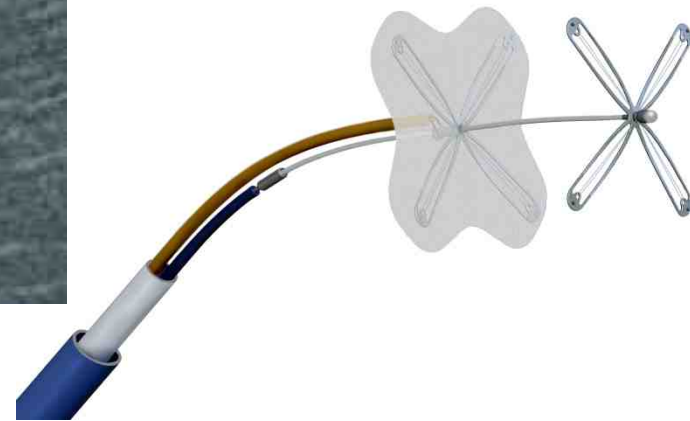
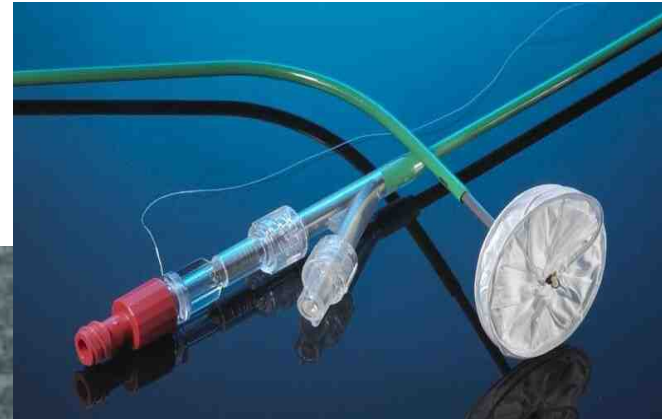
July 8 – 10, 2010 | Frankfurt, Germany

CSI – Catheter Interventions in Congenital & Structural Heart Diseases

▼
www.csi-congress.org

LIVE
CASES

A variety of different devices have been used for PFO closure



Morphology of PFO varies

- Location
 - Close to or away from the aorta
- Size
 - Up to 28mm
- Tunnel length
 - 0 to 25mm
- Single – multiple perforations
- Additional septal membranes
- Septum aneurysm
- Eustachian valve, Chiari network

The tailored approach

- Certain PFO designs fit better to certain anatomic conditions
- Others fit better to certain patient conditions
 - Clotting disorder
 - Atrial fibrillation

New Devices for PFO Closure

How can new devices and techniques improve outcome?

- Lower profile and less foreign material could reduce risk of thrombus formation
- Softer devices and in tunnel devices could reduce distortion of the septum and risk of atrial fibrillation
- Bioresorbable devices and non device closure techniques could prevent unknown long-term complications

New Devices and Techniques

- New umbrella devices
- Suture based techniques
- Non device closure
- Bioresorbable devices
- In-tunnel devices

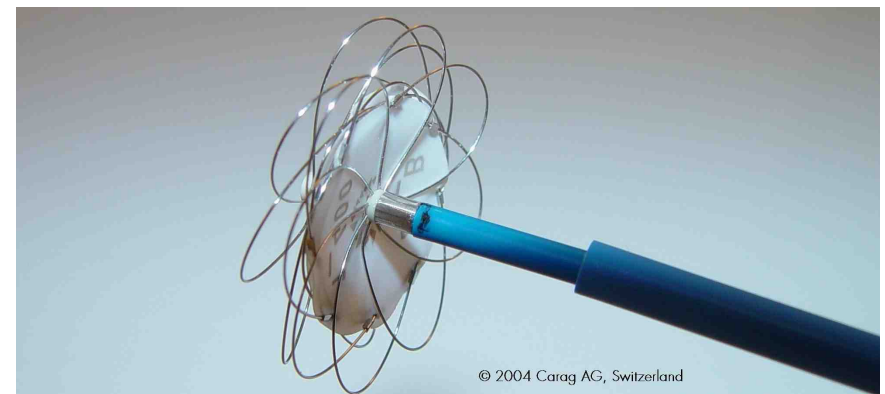
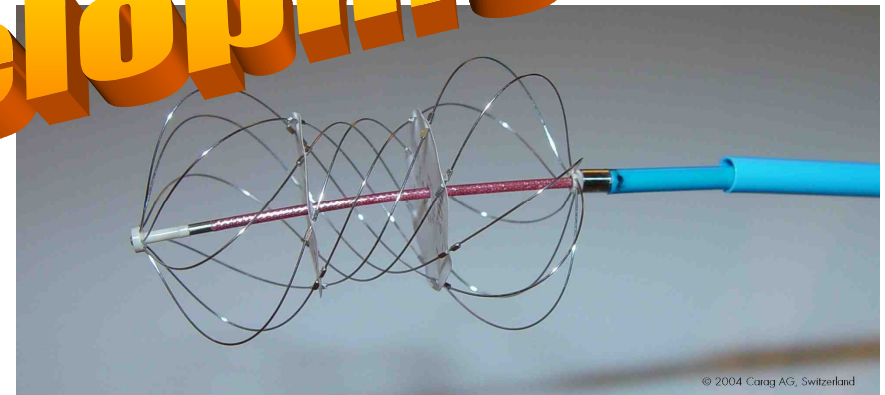
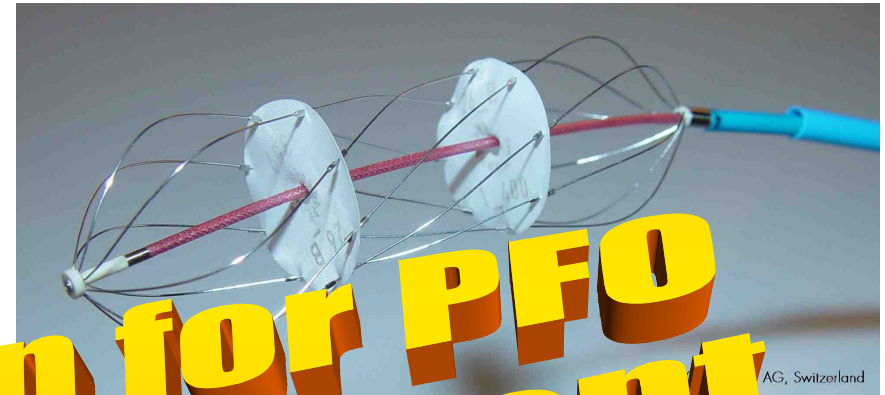
New Devices and Techniques

- New umbrella devices
- Suture based techniques
- Non device closure
- Bioresorbable devices
- In-tunnel devices

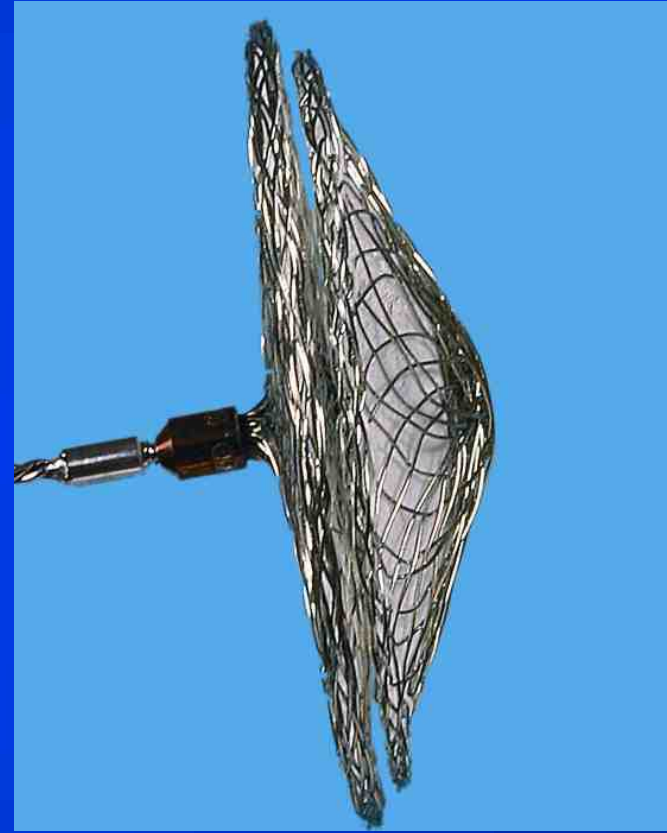
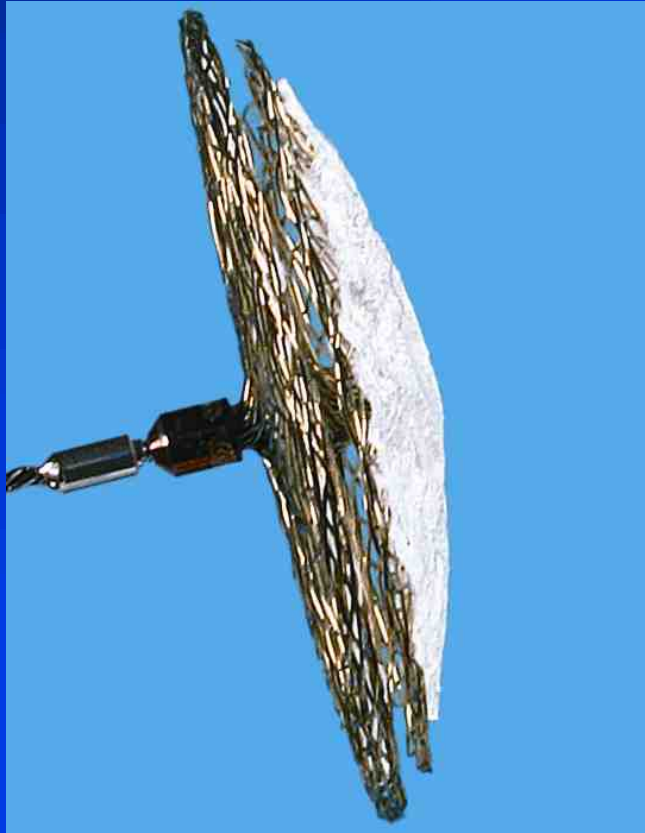
Solysafe®

- Self-centering
- Phynox wires
- Polymers patches
- In the deflated state, the wire-holders are moved towards each other
- Clicking mechanism keeps the wire-holders together
- Short 10 F introducer

**new version for PFO
under development**



Occlutech PFO Occluder



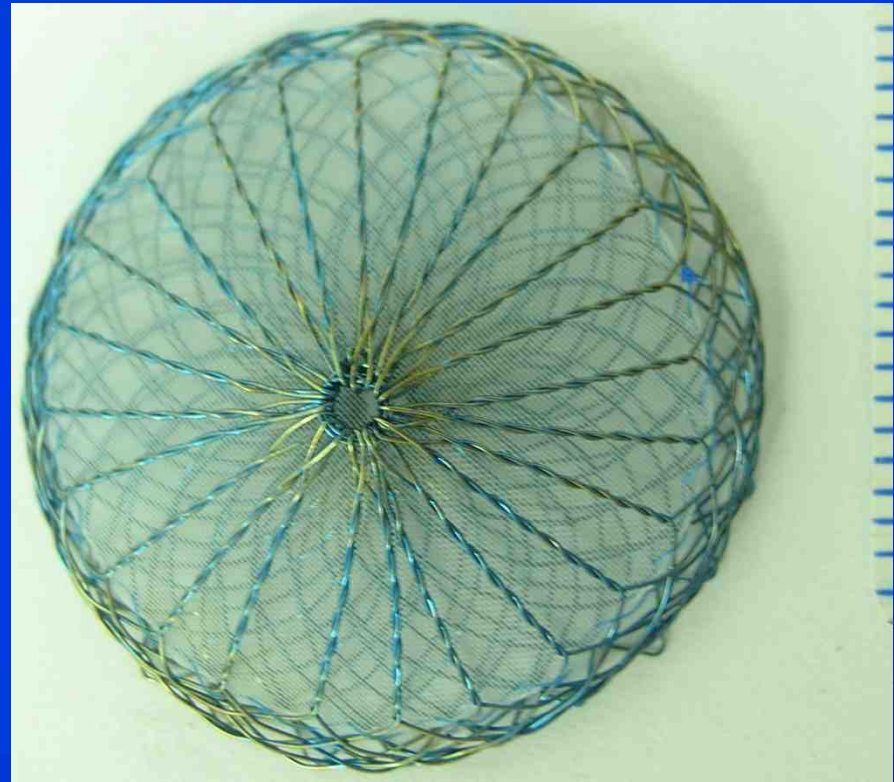
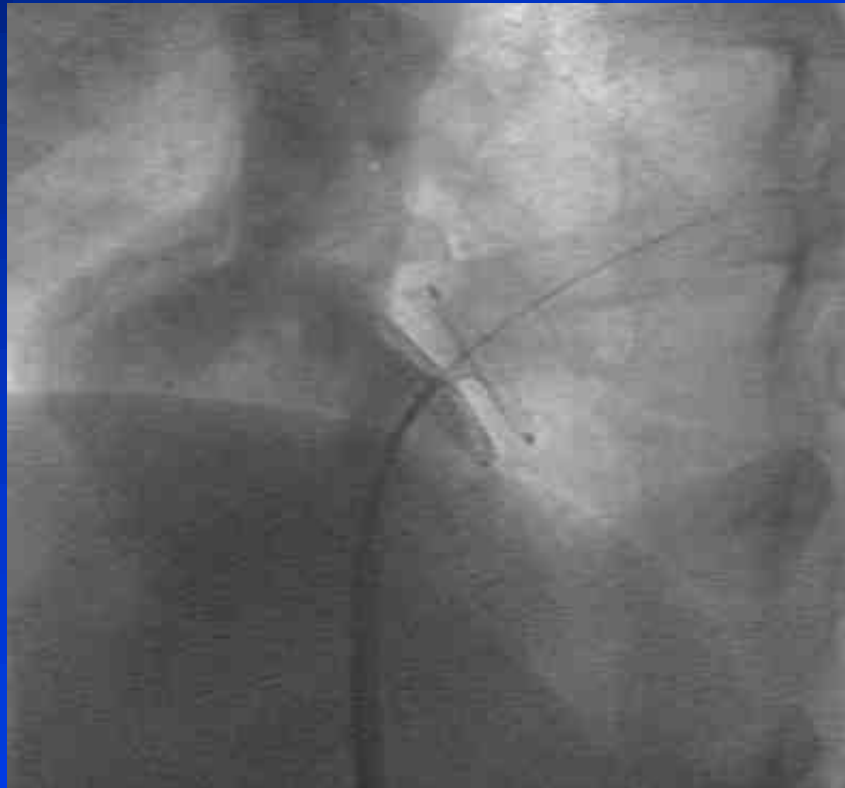
Single layer PFO Double layer PFO
Similar to Amplatzer but no left atrial hub

Nitocclud PFO (PFM)

- Nitinol
- One single wire
- Fabric on the left side
- Very flexible delivery system
 - No tension between delivery cable and device before release



Nitocclud PFO (PFM)



Courtesy F Freudenthal

EU trial has finished enrolment
Results to be presented at CSI

Spider (Lifetech)



- Right Disc: Nitinol mesh frame with ePTFE membrane
- Left Disc: Nitinol braid wire anchors covered with ePTFE patch

New Devices and Techniques

- New umbrella devices
- Suture based techniques
- Non device closure
- Bioresorbable devices
- In-tunnel devices

Suture Techniques

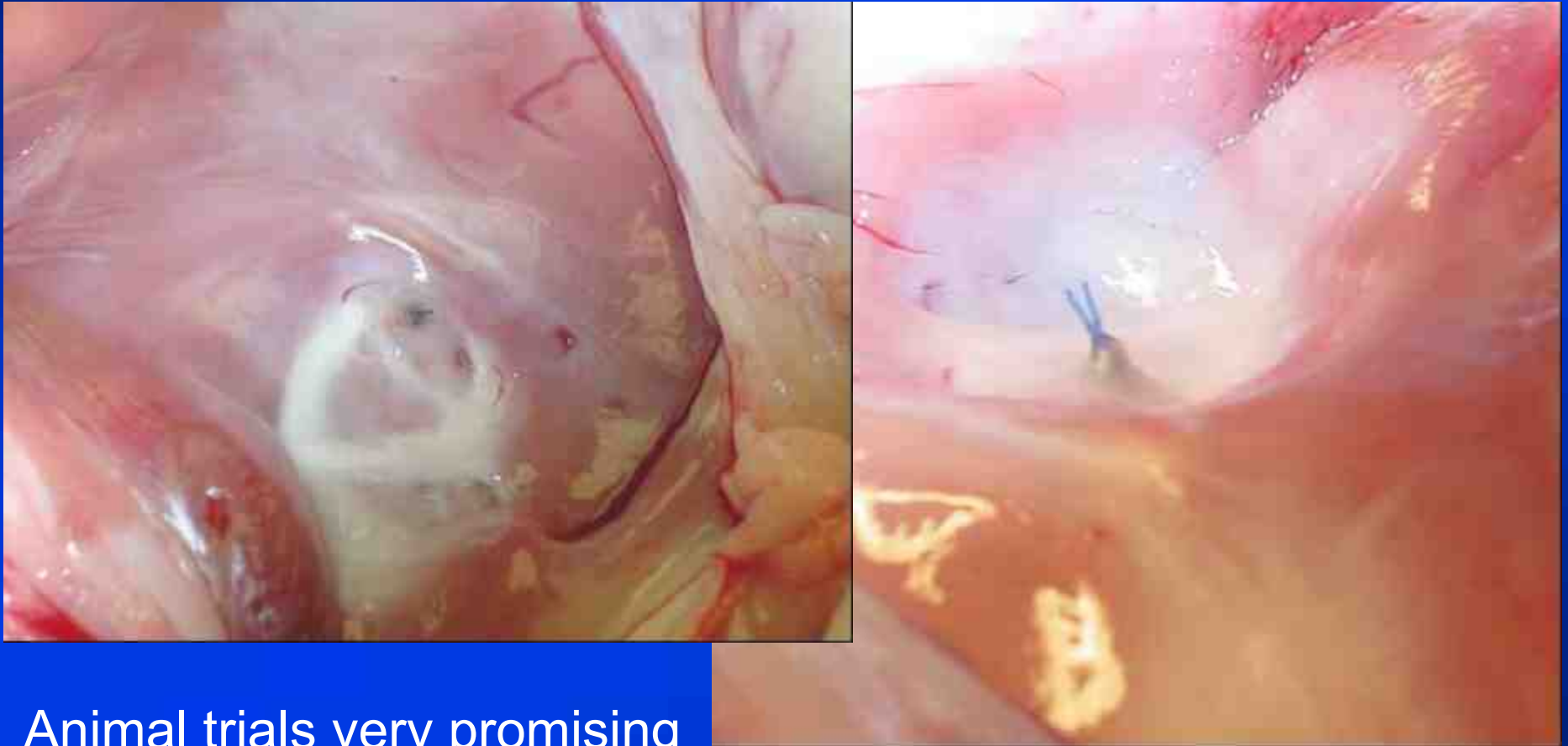
- Less foreign material
- Mimic surgery

Edwards E2E System



Therapy Catheter
Vacuum port,
needles, suture

Suture based PFO Closure



Animal trials very promising

In humans this did not work

The Sutura SuperStitch® EL

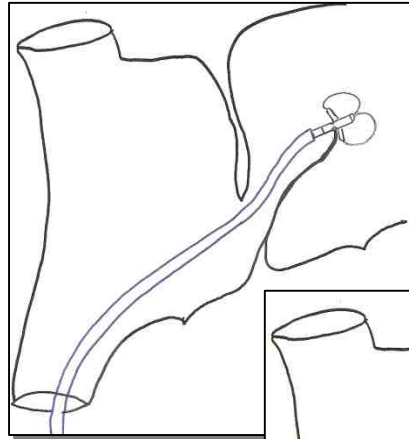
Arms and Needles

- ***Based on a puncture site closure technique***
- ***Profile: 12 Fr***
- ***Working length: 90 cm***
- ***Suture type: Polypropolene 4-0***

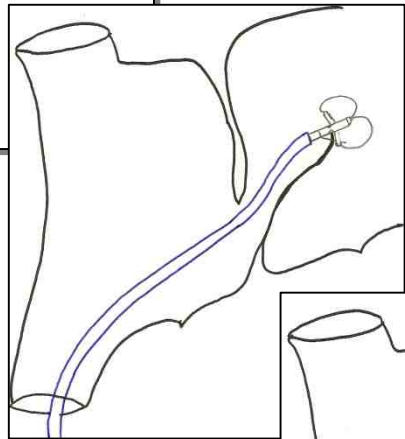


Courtesy C. Ruiz

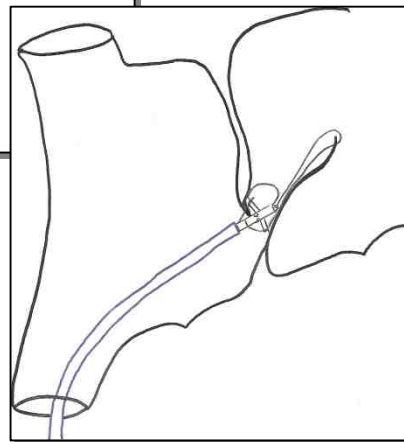
NobleStitch Suture Mediated PFO Closure



Introduce NobleStich



Suture Septum Primum



Suture Septum Secundum

**FIM results to be
presented at CSI**

New Devices and Techniques

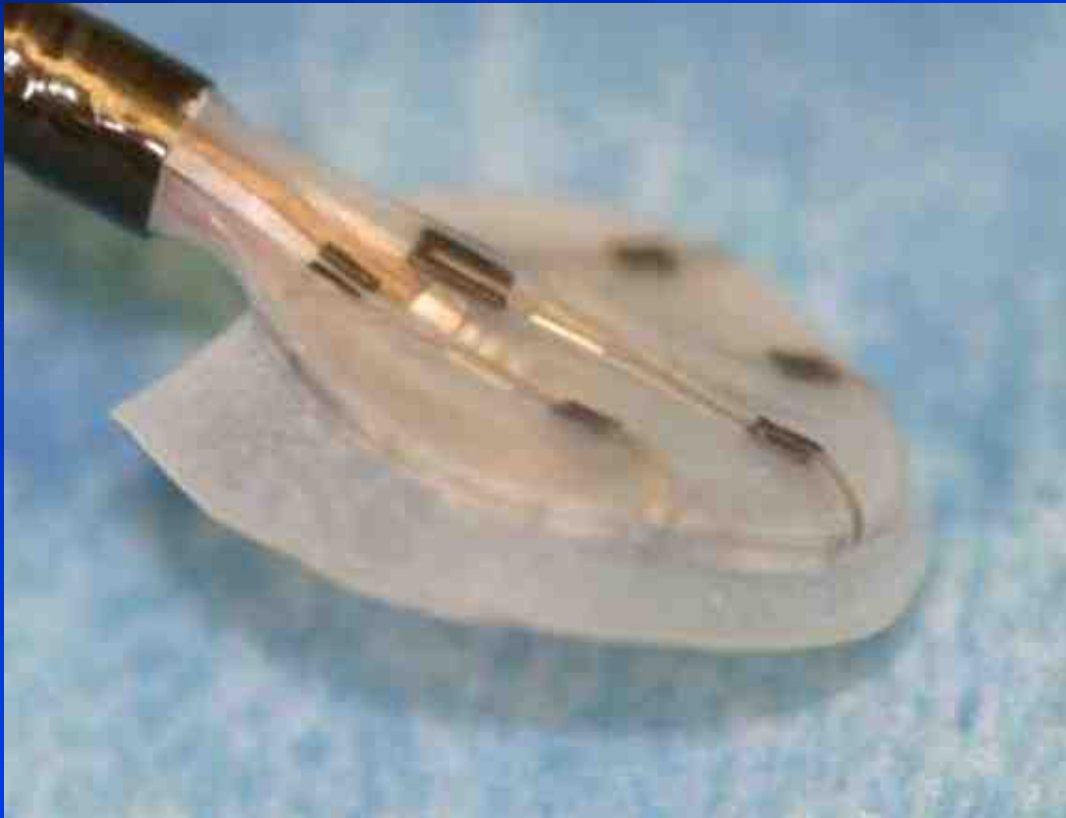
- New umbrella devices
- Suture based techniques
- Non device closure
- Bioresorbable devices
- In-tunnel devices

Non device closure

- Offer a psychological advantage
- Avoid all device related long-term complications including those not known yet

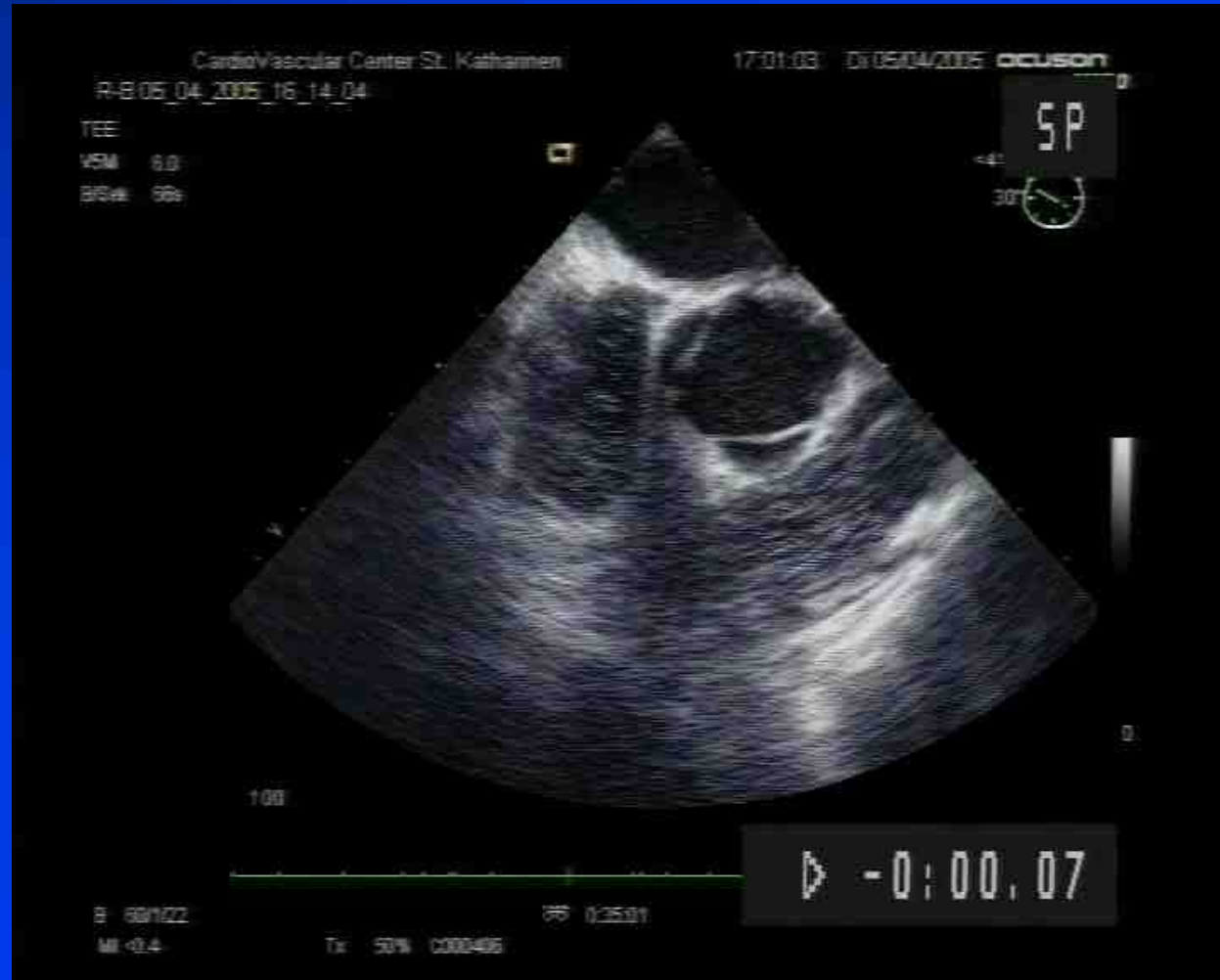
PFX™

Radiofrequency Closure System



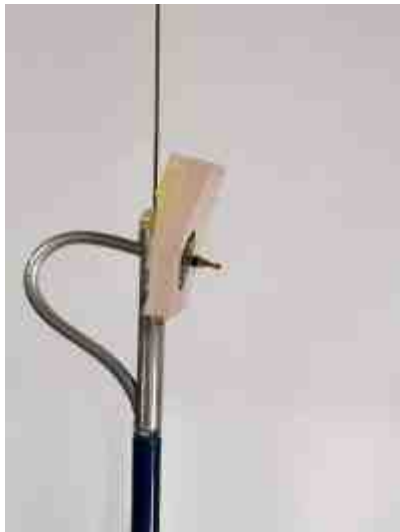
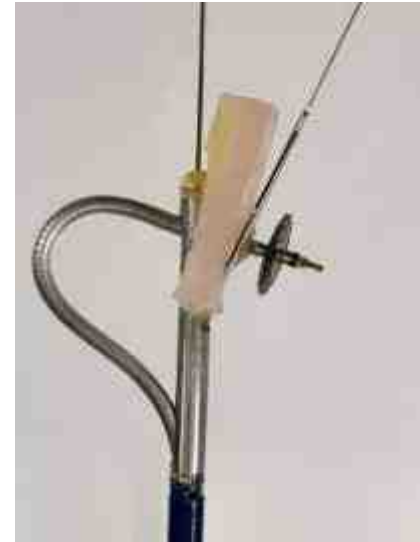
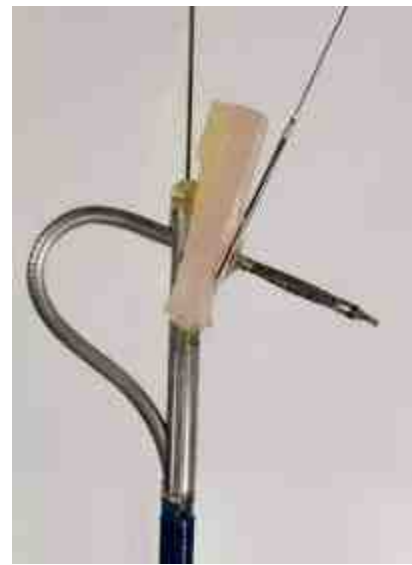
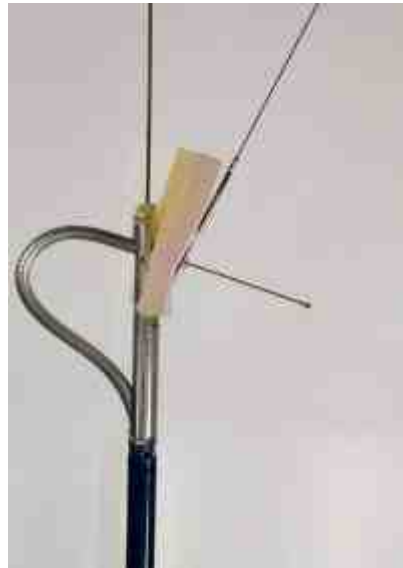
- First implant free device for intracardiac defect closure
- Leaving no foreign body behind

PFO Closure by Radiofrequency



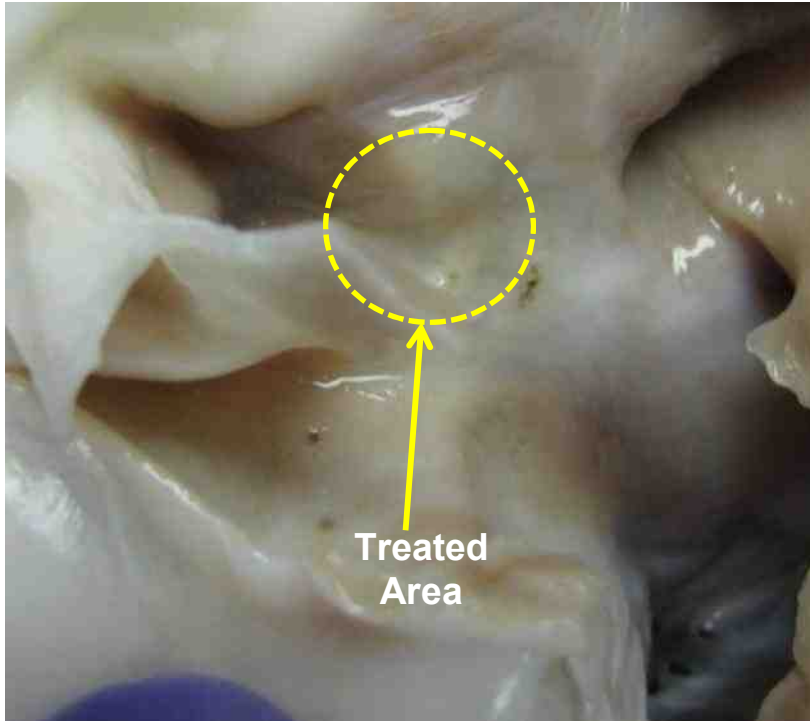
Immediately after

CoAptus: A New Approach of Non-device Closure

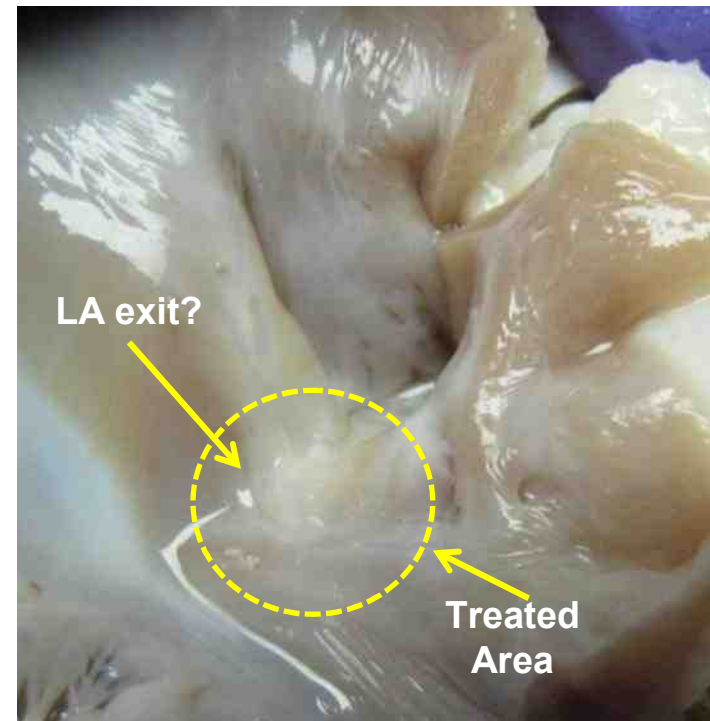


- Using radiofrequency
- Septum primum and septum secundum are coapted mechanically
- Then energy is applied
- Thereafter, the device is removed leaving nothing behind

28 day



RA



LA

New Devices and Techniques

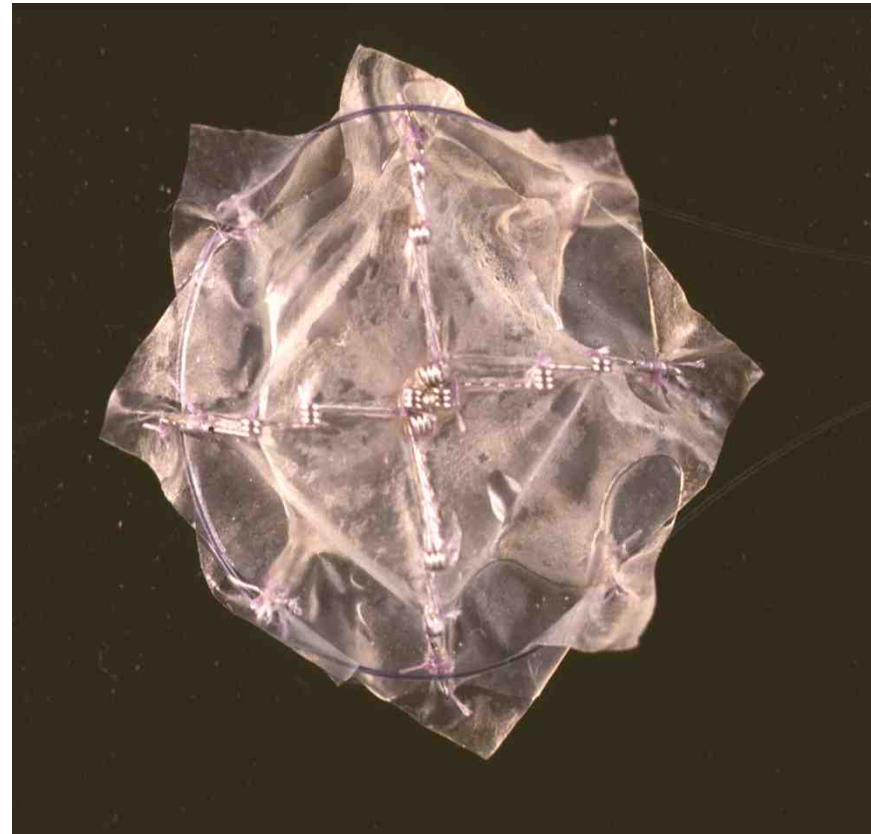
- New umbrella devices
- Suture based techniques
- Non device closure
- Bioresorbable devices
- In-tunnel devices

Resorbable devices

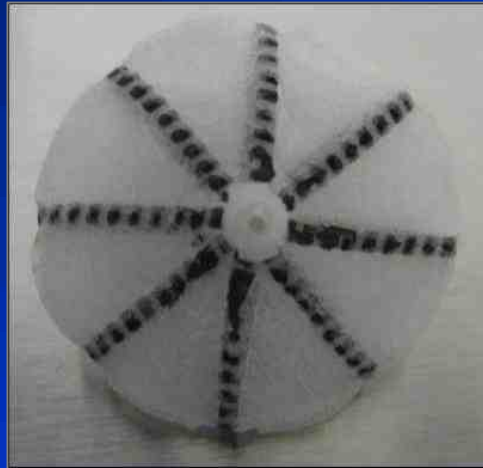
- Offer a psychological advantage
- Avoid all device related long-term complications including those not known yet

BioSTAR (NMT)

- CardioSEAL® framework
- STARFlex® self-centering mechanism
- Bioresorbable collagen matrix, heparin coating
- CE mark



BioTREK™ Bioabsorbable Septal Repair



6 months

- 100% absorption over time
- novel bioabsorbable polymer (P4HB)
 - absorbs as a non-inflammatory natural metabolite
- easily repositionable and retrievable
- radiopaque and echogenic
- currently in pre-clinical studies

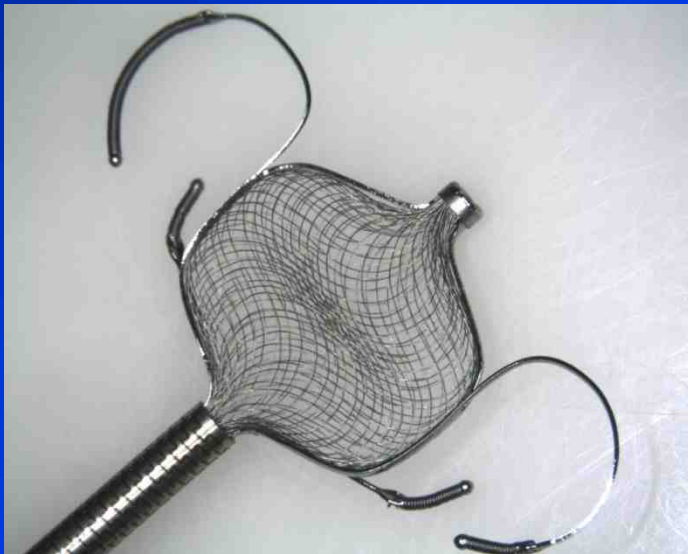
New Devices and Techniques

- New umbrella devices
- Suture based techniques
- Non device closure
- Bioresorbable devices
- In-tunnel devices

In-tunnel devices

- Minimize surface area
- Minimize risk of thrombus formation
- Minimize risk of atrial fibrillation
- Less foreign material in the body

In-Tunnel Devices



SeptRX
In clinical trials

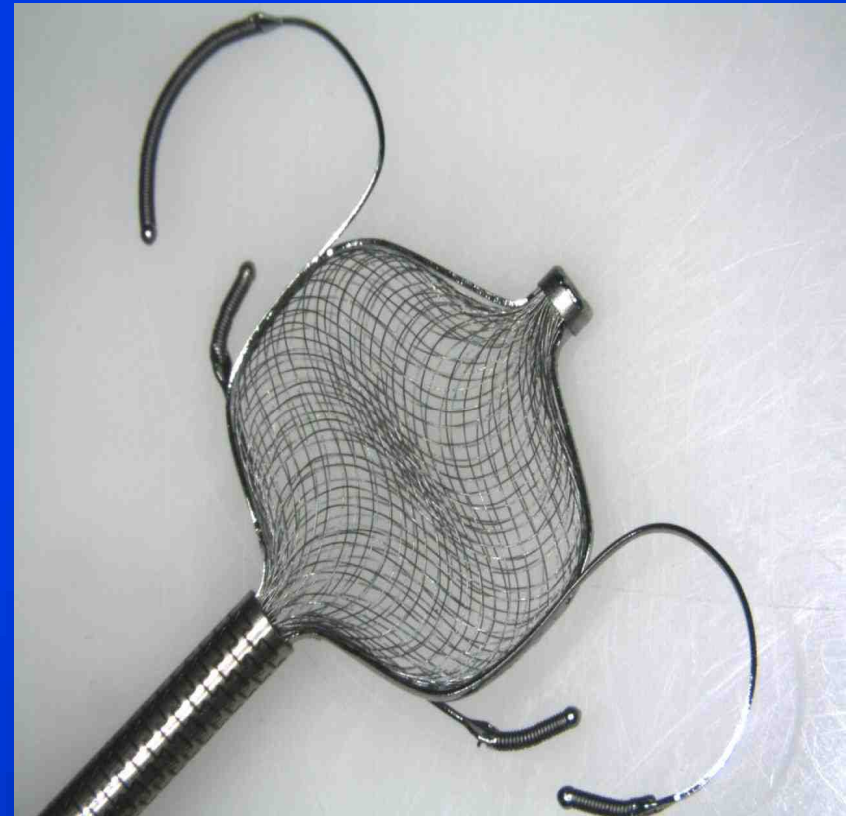


Coherex FlatStent RX
CE mark

Not FDA approved

The SeptRx- System

- Nitinol frame and Nitinol wire mesh
- Small left and right atrial anchors
- Sits almost completely within the PFO tunnel
- FIM trial finished



SeptRx



Coherex EF



Designed to "Stent" the PFO tunnel
Nitinol and Polyurethane

Coherex

- PFO closure from inside



Results of FIM to be presented at PCR and CSI

Which will be the best PFO closure device?

- There will be no "best device"
- Each PFO has its own best device
- The tailored approach is the way to go

Take Home Messages

- PFO is a frequent cause of "cryptogenic" stroke
- PFO closure prevents paradoxical embolism and stroke
 - Randomized trials will be finished very soon
- There is a need for more randomized PFO closure trials in migraine patients
- Many new PFO closure devices are under development