New TAVI Devices:
More of the Same or Meaningful Differences?

Eberhard Grube MD

Intl. Heart Center Rhein – Ruhr, Essen, Germany
Hospital Oswaldo Cruz - Dante Pazzanese, São Paulo, Brazil
Stanford University, Palo Alto, California, USA

Disclosure Statement of Financial Interest

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Physician Name	Company/Relationship
Eberhard Grube, MD	Medtronic, CoreValve: C, SB, AB, OF Sadra Medical: E, C, SB, AB Direct Flow: C, SB, AB Mitralign: AB, SB, E Boston Scientific: C, SB, AB Biosensors: E, SB, C, AB Cordis: AB Abbott Vascular: AB Capella: SB, C, AB Devax: SB, AB,

Key
G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker's Bureau O – Ownership OF – Other Financial Benefits'

Transcatheter AVR

Current Generation Devices

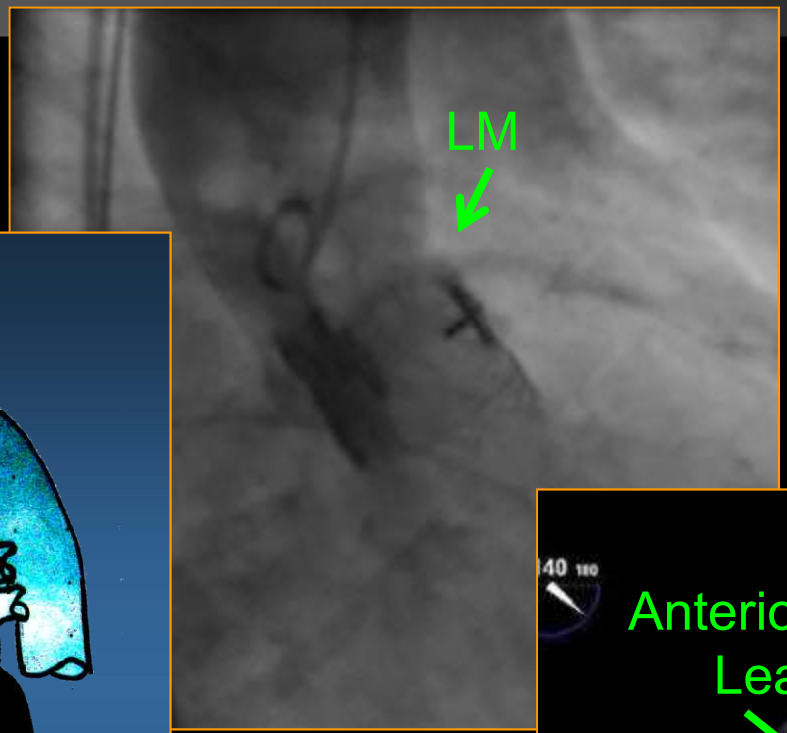
Edwards
~5,500 patients

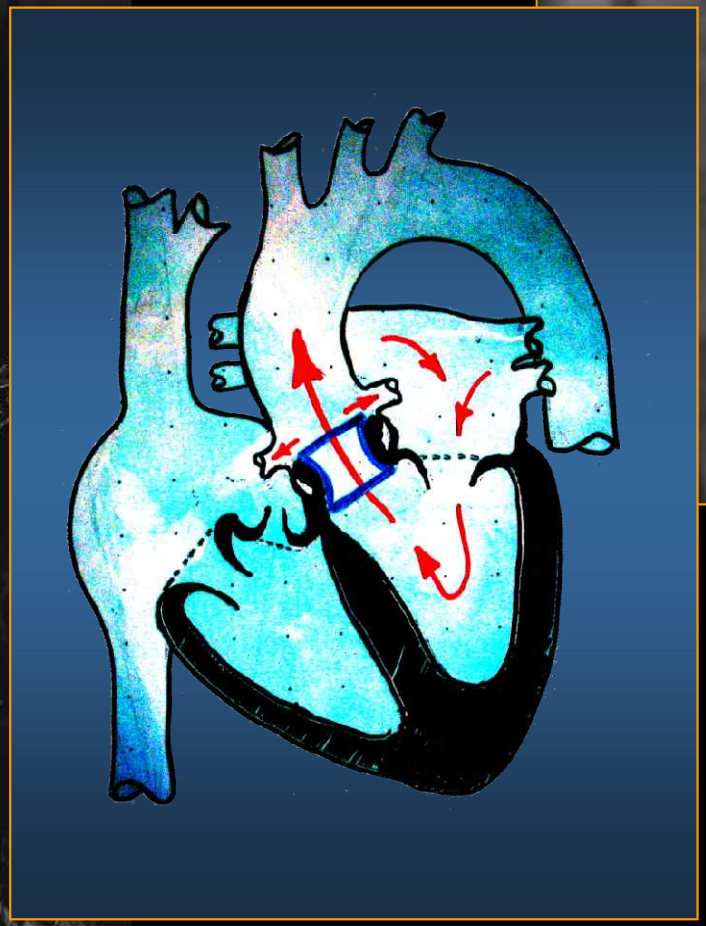
CoreValve
~5,500 patients

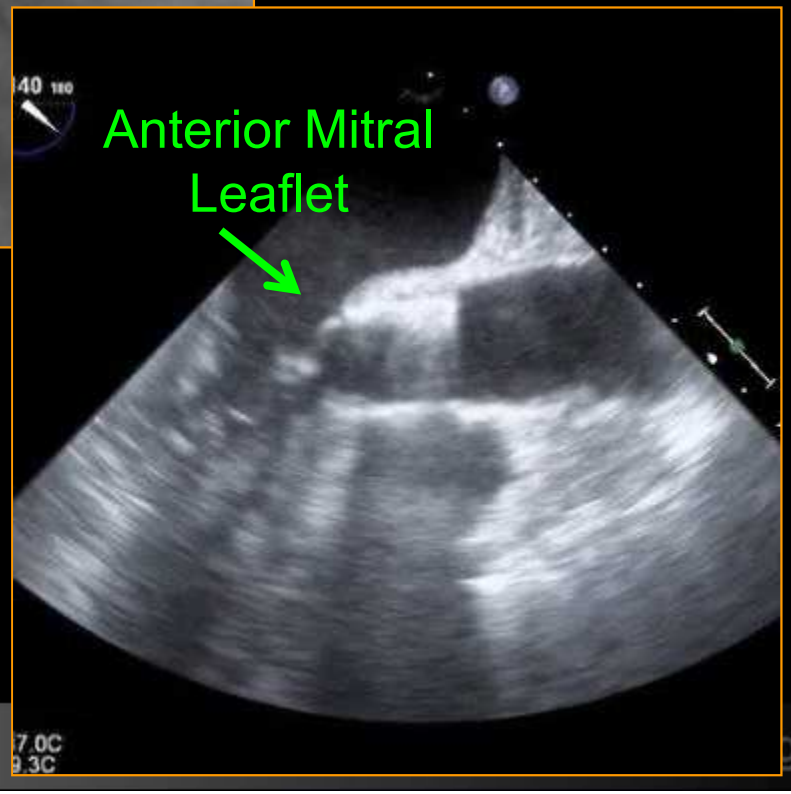
Success, but Opportunity for Improvement

- **Percutaneous Aortic Valve Replacement (PAVR) has established itself as a viable therapy**
  - Solid clinical results
  - Expanding number of MD's performing PAVR
- **Challenges remain with current devices**
  - Steep, unforgiving learning curves
  - Difficult to place with precision
  - Cannot be easily repositioned for optimization
  - Cannot be atraumatically removed if needed
  - Perivalvular Leaks
  - Permanent Pacemaker Implant
  - Stroke

Positioning is Critical

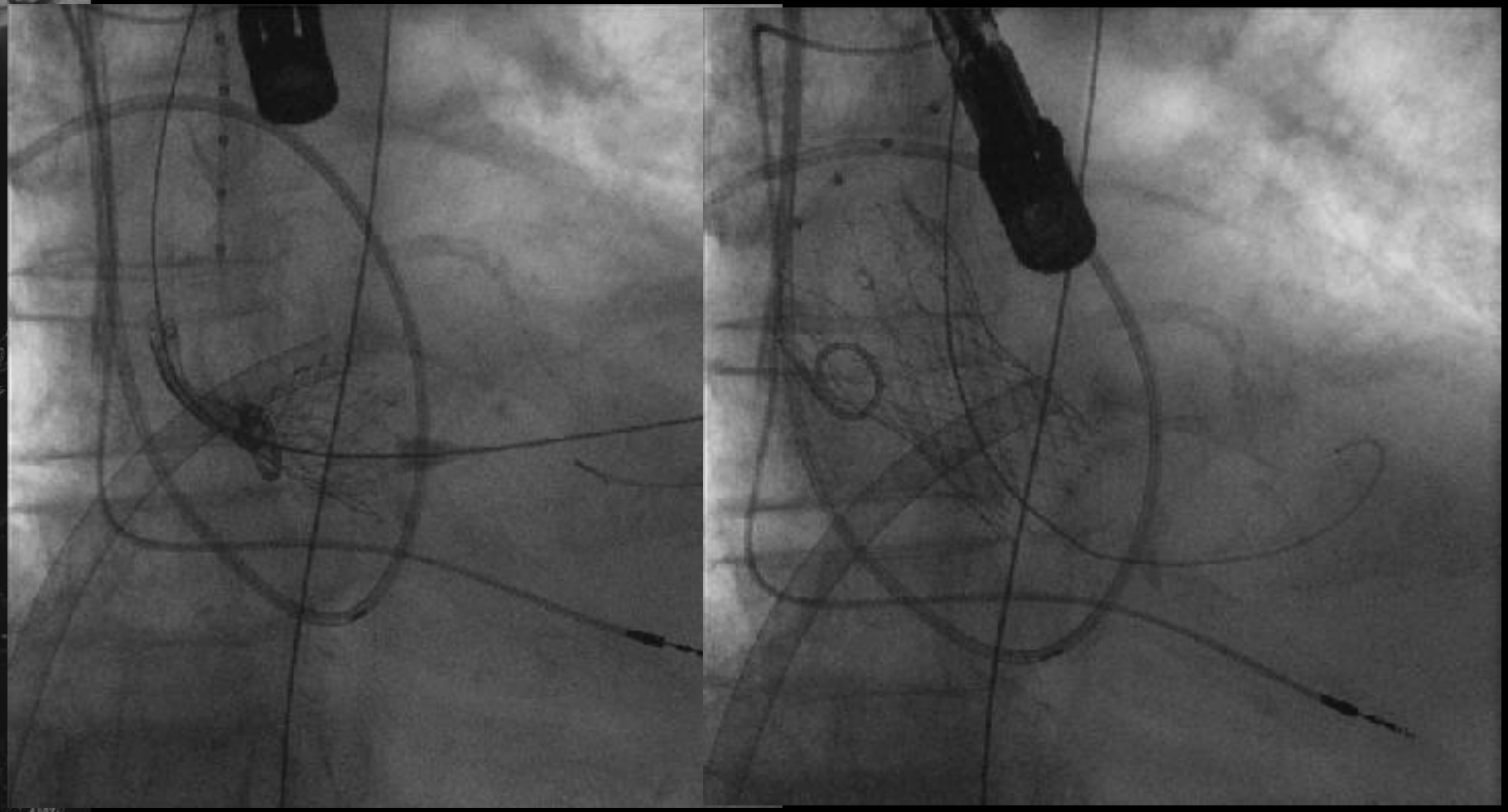






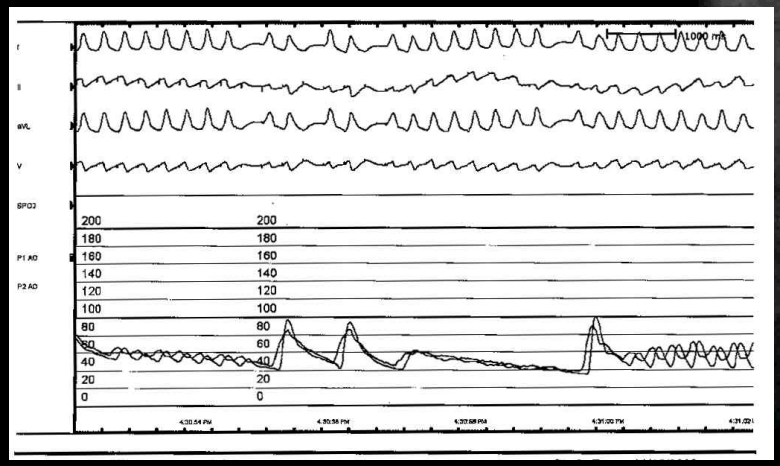
MDT Corevalve Positioning Challenges

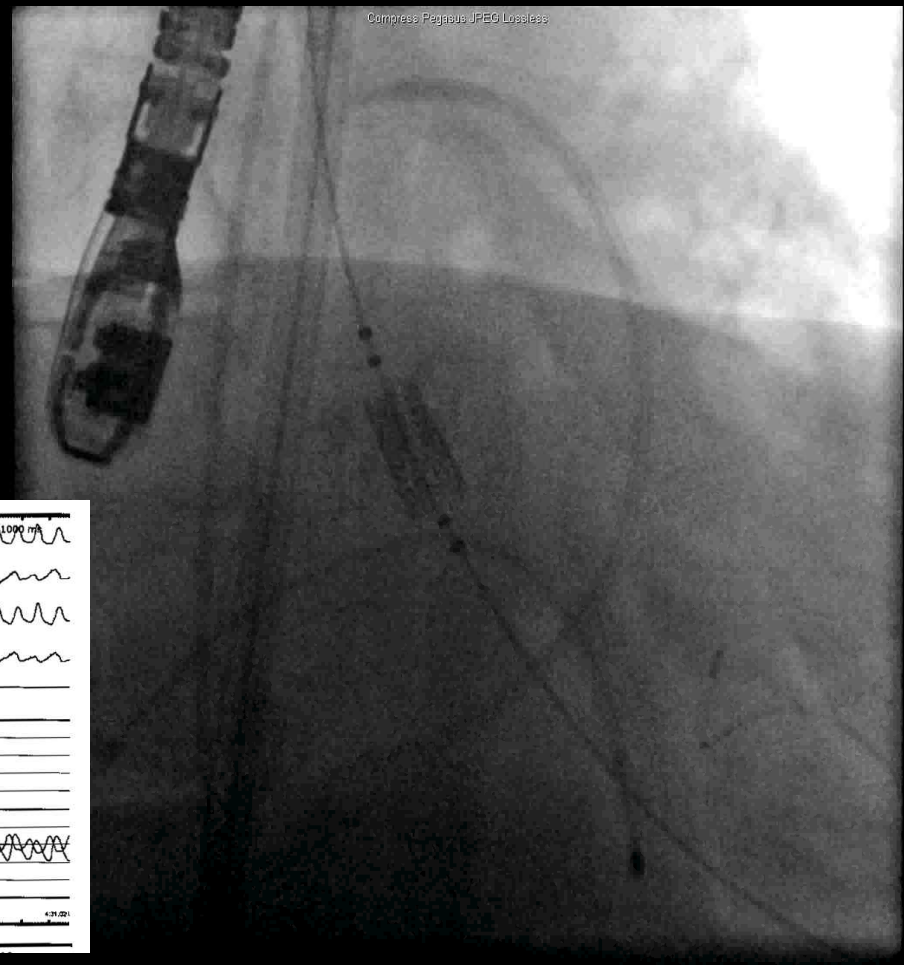
- Challenging deployment in horizontal aorta



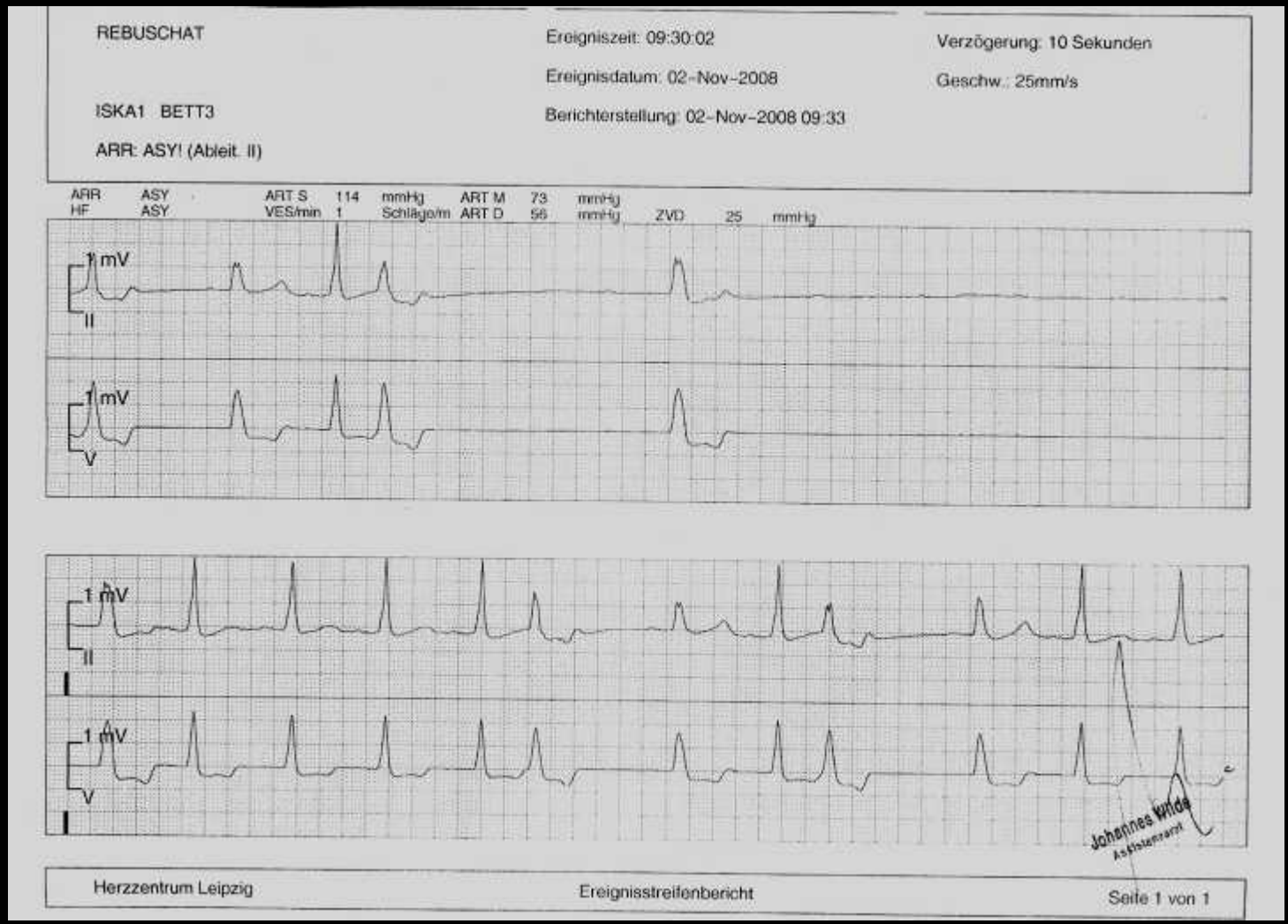
Edwards – Positioning Challenges

Migration of valve during deployment due to escape beats

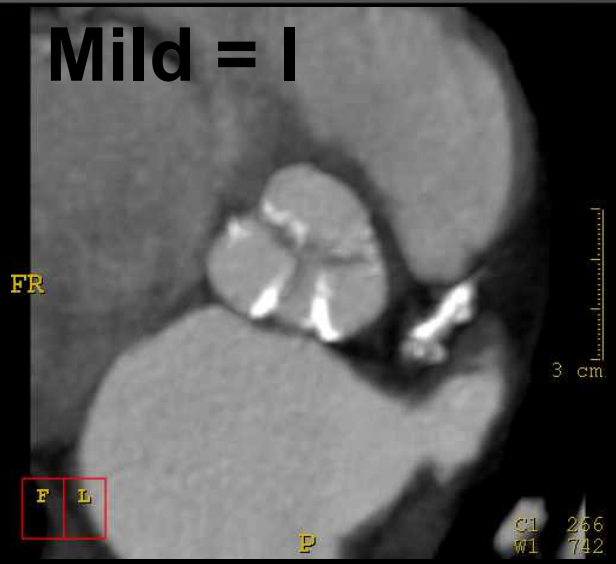


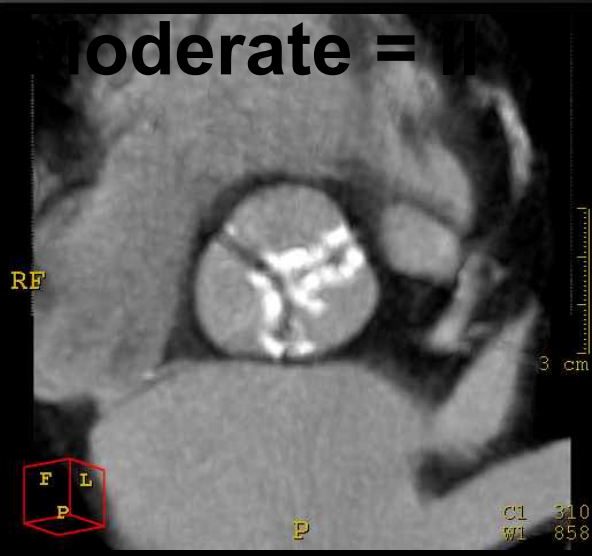


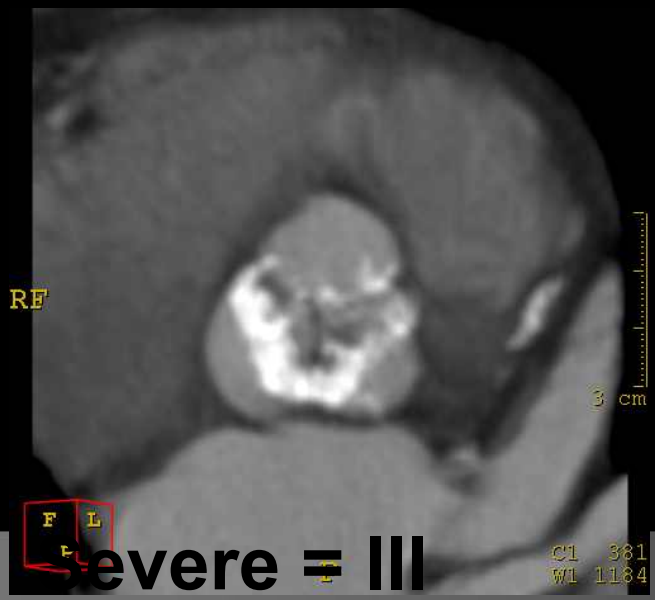
AV-Block III° Following COREVALVE Implantation

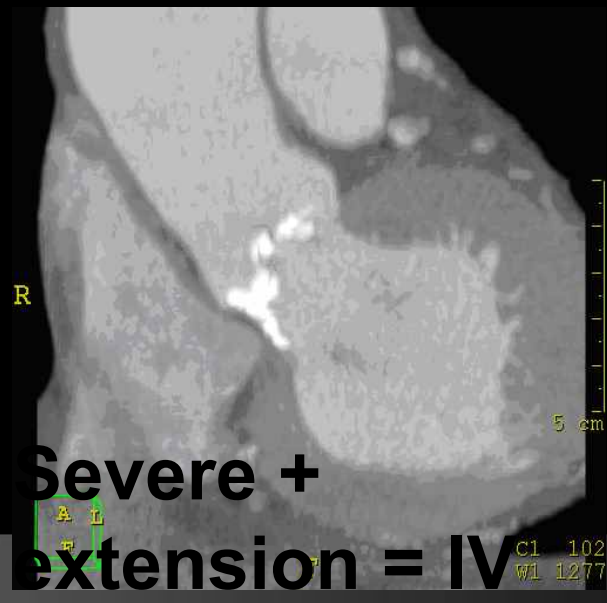


Annulus and LVOT Calcification Grades Correlate With AR - ‚Siegburg Score‘

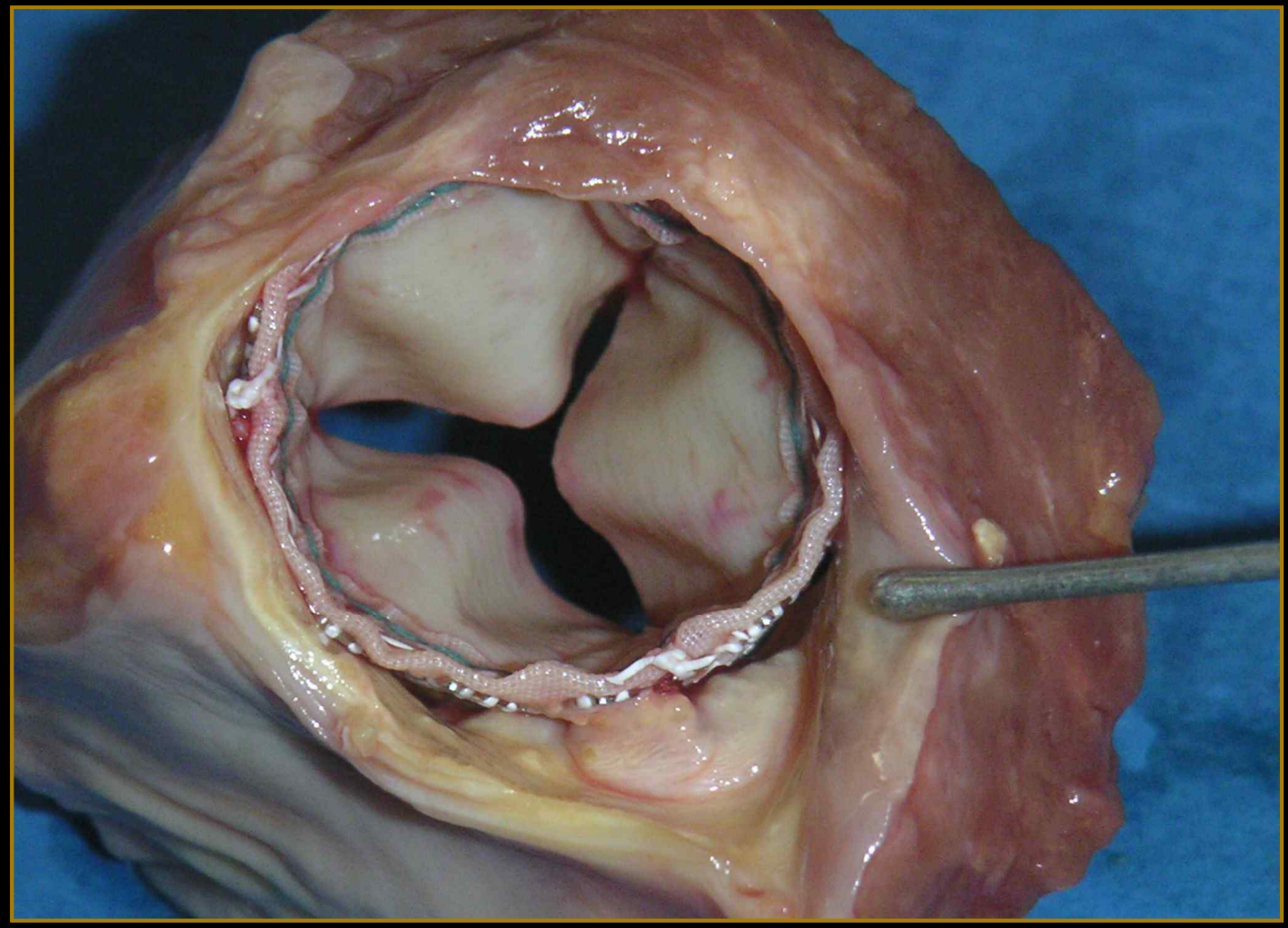






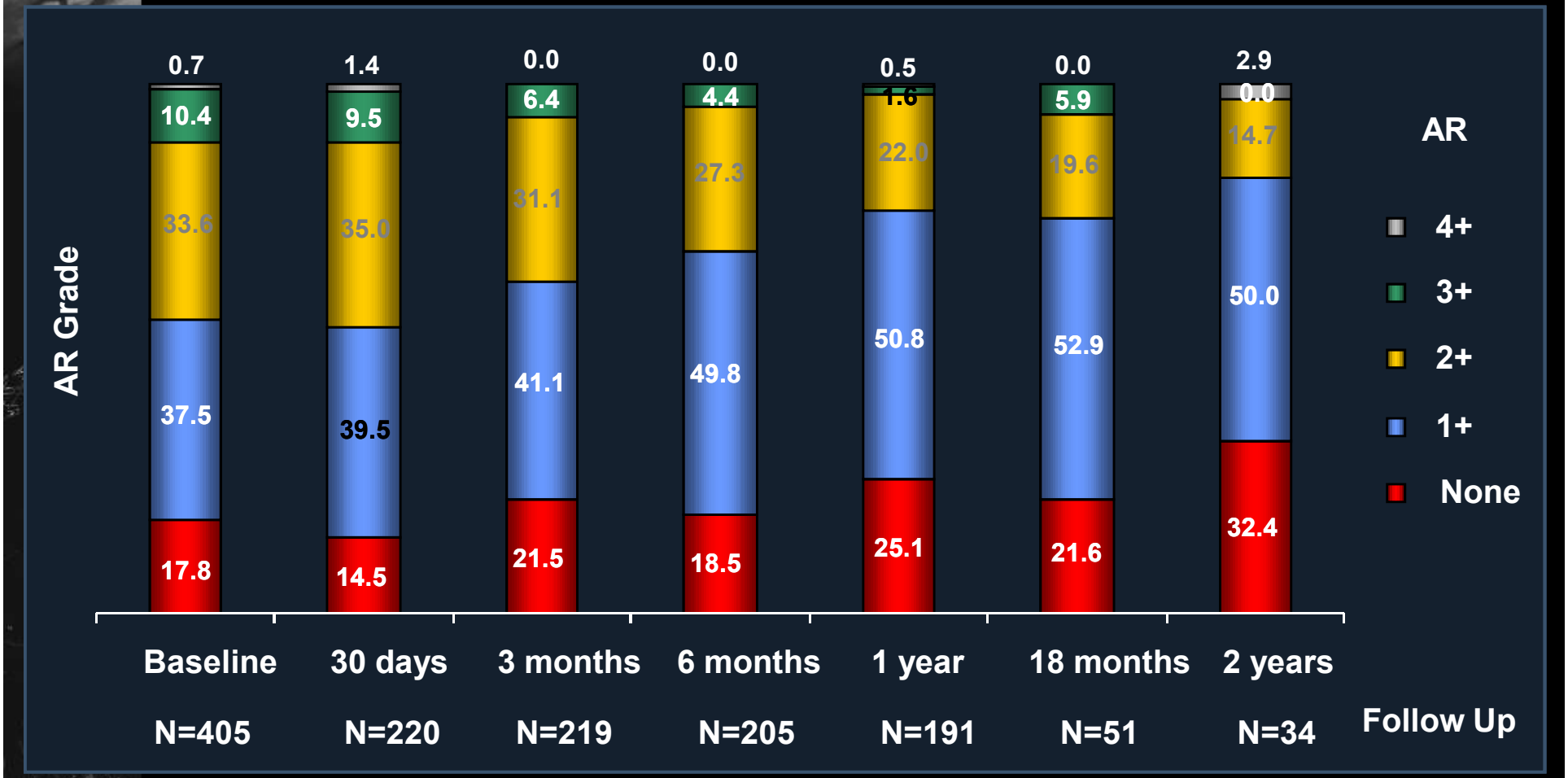


Para-Valvular Regurgitation



POOLED* Monitored Edwards TAVI

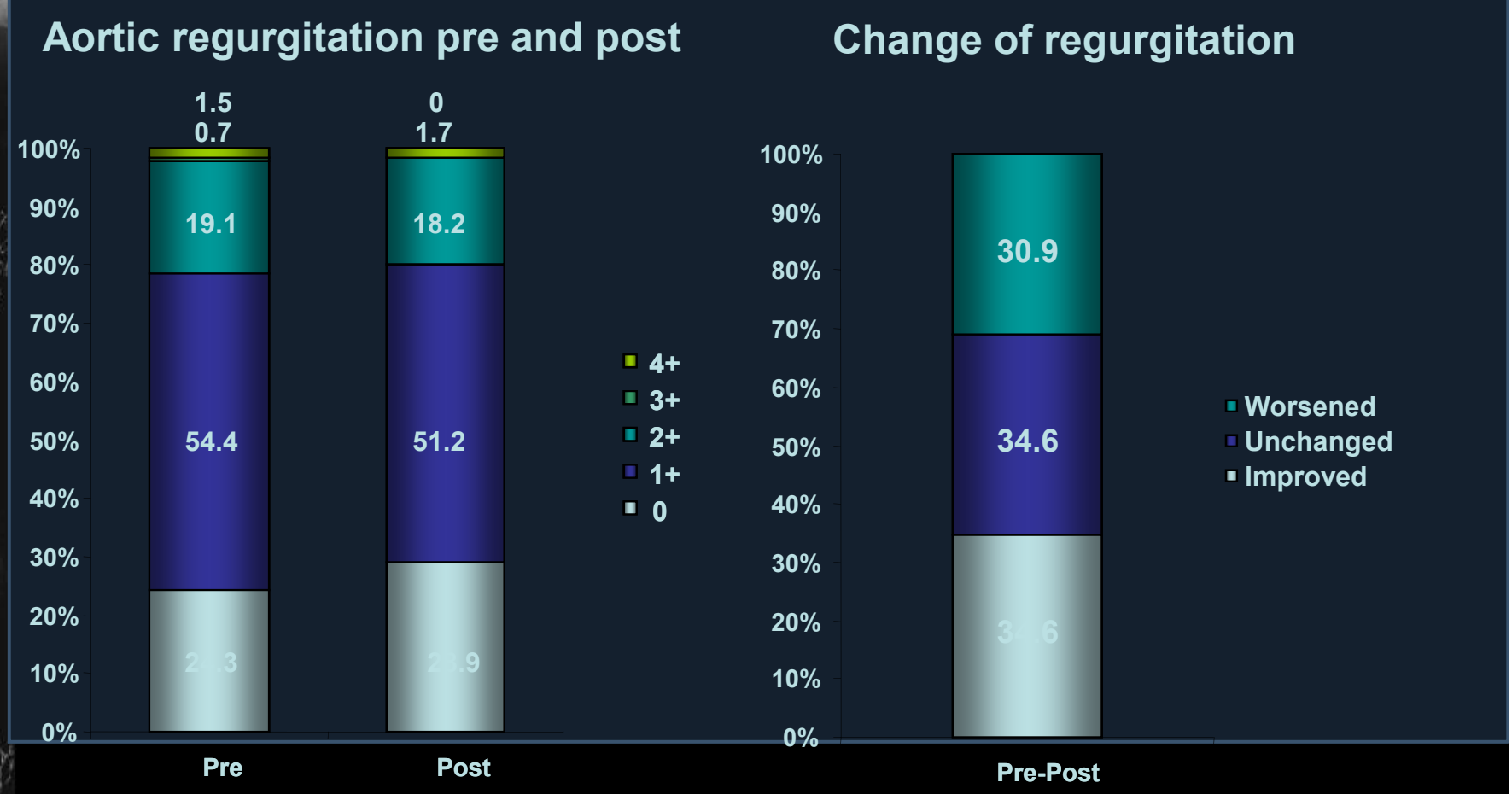
Echo AR Results



** REVIVE, REVIVAL, TRAVERCE and PARTNER EU*

Siegburg

CoreValve Siegburg Experience
Aortic Regurgitation

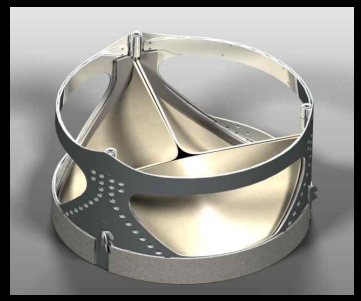


Grube E, et al. Circ Cardiovasc Intervent 2008;1:167-75.

Siegburg

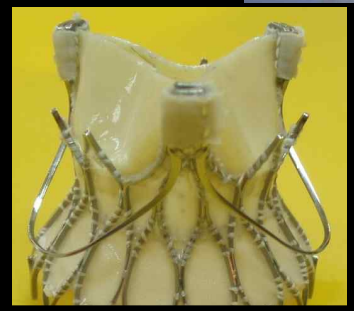
Future Aortic Valve Concepts

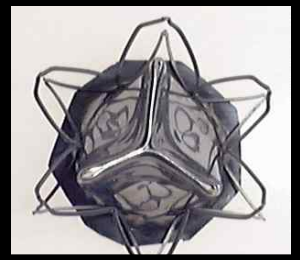
- Direct Flow
- Sadra
- AorTx
- Jena Valve
- HLT
- ABPS PercValve
- EndoTech
- Ventor Embracer





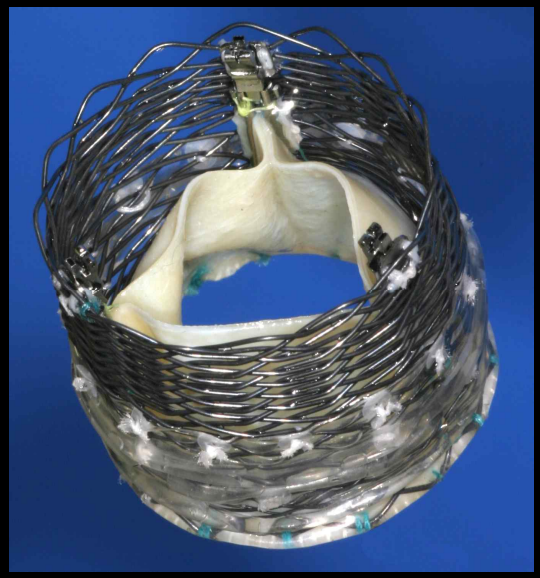




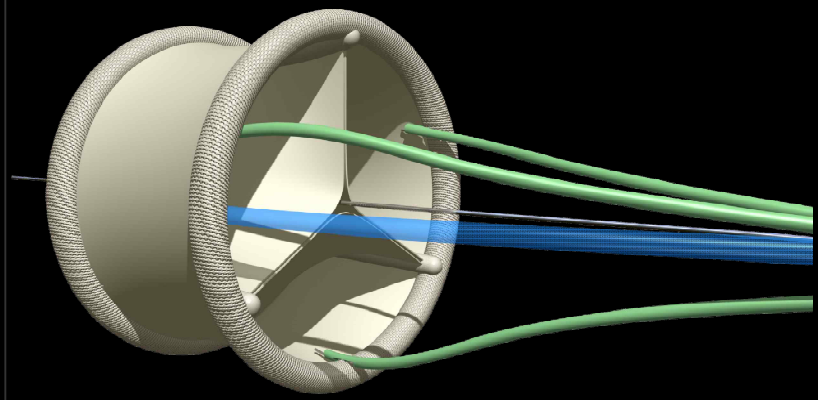


Transcatheter Valve Therapy
Next Generation Devices

Sadra



DirectFlow

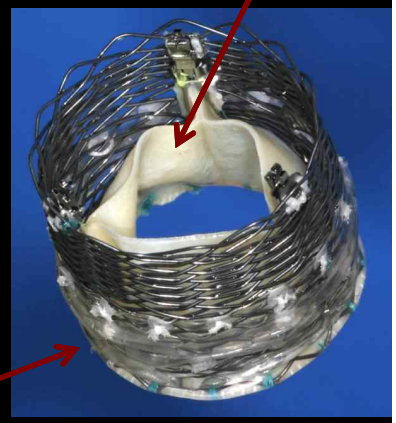


Low profile, repositionable,
(?) less peri-valvular AR

Sadra Medical Lotus Valve System

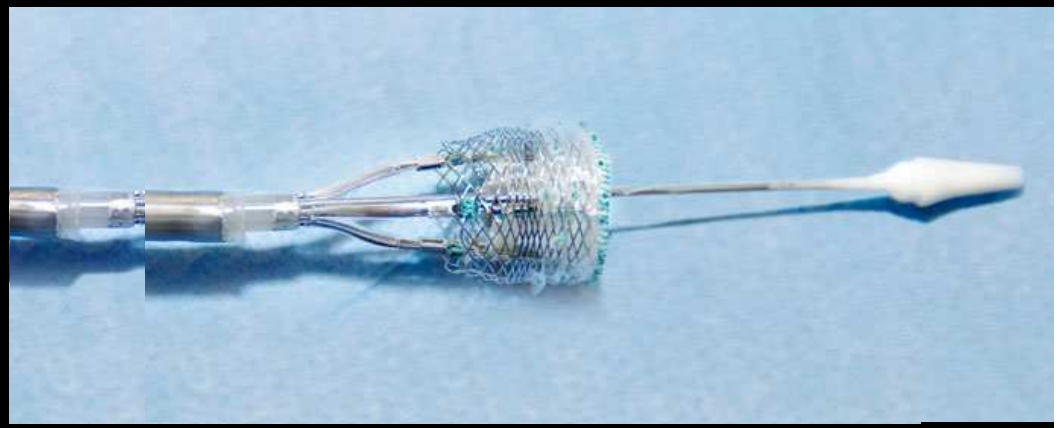
Designed for optimized aortic valve replacement with a user-friendly delivery system

- **Highly accurate, controlled prosthesis positioning**
  - **Self-centering**
- **Easy repositioning, distally or proximally**
- **Retrievability**
- **Minimal Perivalvular Leakage**



Lotus Valve – Accurate Positioning

- Control in the MD's hands
  - Rate of deployment
  - Ability to pause, unsheath, re-sheath, lock, unlock
  - Fully repositionable, distally and proximally
- Accurate positioning facilitated by
  - Self-centering
  - Predictable locking around central marker



Procedure – Controlled Positioning

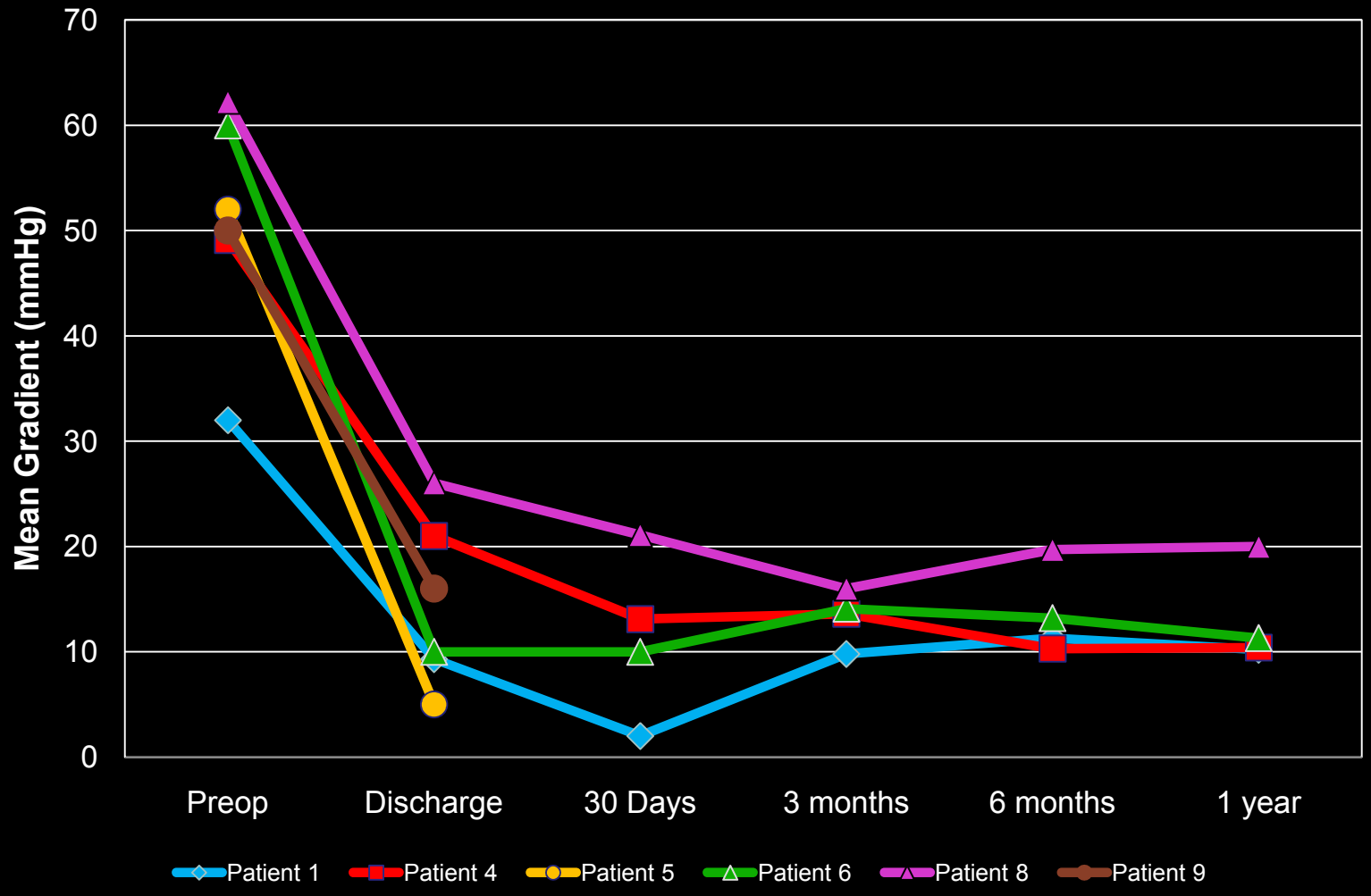
Clinical Experience to Date

- Clinical experience
  - 10 patients enrolled – July 2007 – October 2008
  - 6 patients implanted, 5 surviving
- Intra-procedural results
  - Procedure time <20 minutes
  - No perivalvular leaks
  - No migration issues
- Follow-up at 1 year to be presented
- European Trial with new Device started in April 2010

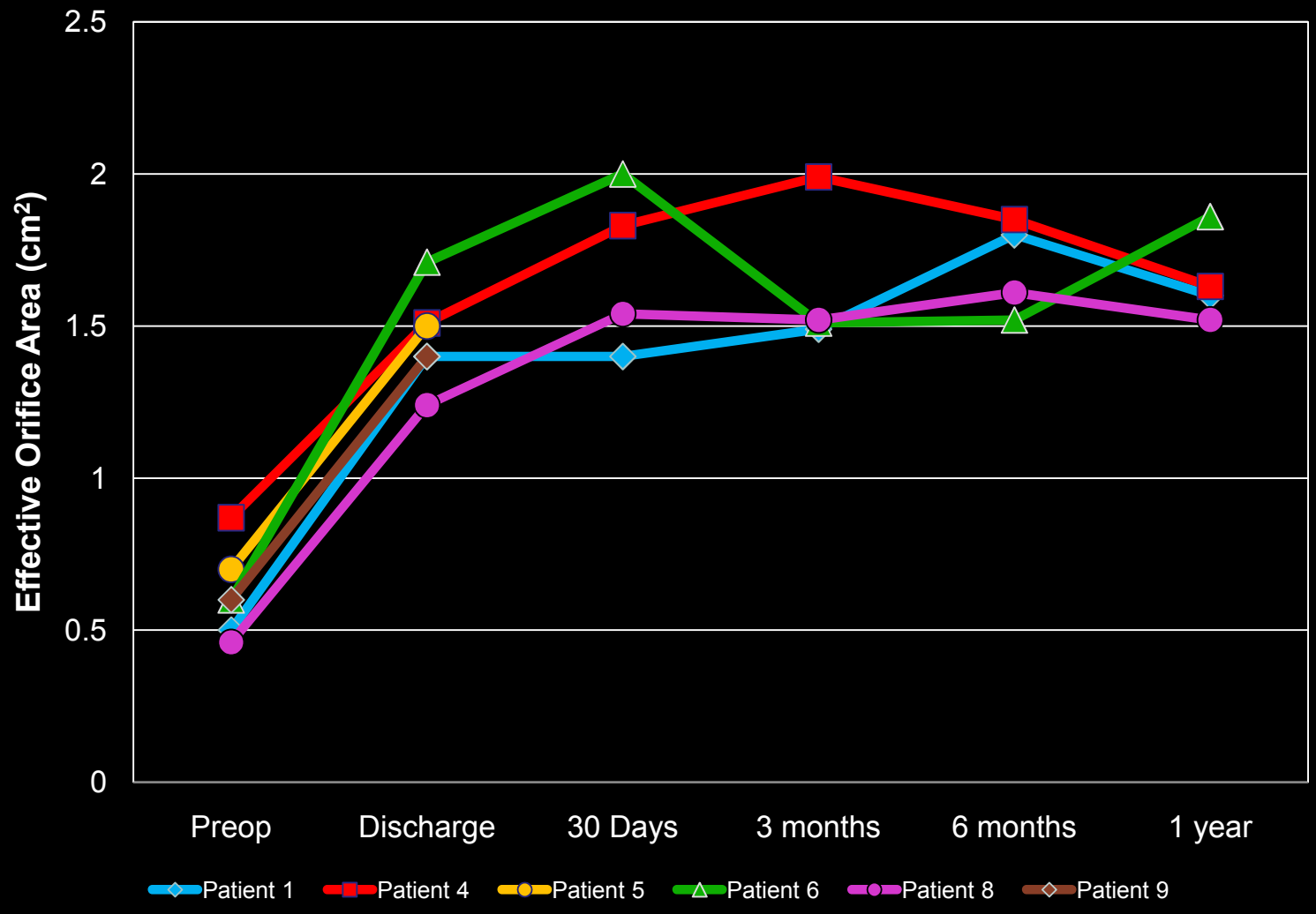
Clinical Data Summary – Enrollment/Demographics

Number of Patients Enrolled Gender Age	10 80% Female 84.2±5.9 years
EuroScore (n=8) STS Score (n=8)	17.3%±7.8% (9.7 - 28.9%) 9.6%±6.0% (2.3 - 22.1%)
Common Pre-existing Conditions	COPD, Hypertension, hyperlipidemia, CHF, PVD, mitral valve disease
Pre-op Annulus Diameter (per CT) (n=10)	21.4±1.2 mm (20.1 – 23.7)
Pre-op Mean Gradient (n=10)	55.7±15.6 mmHg (32 – 80)
Pre-op AVA	0.58±0.08 cm^2 (0.4 – 0.85)

Long Term Follow-up – Gradient



Long Term Follow-up – Valve Area



Lessons from First Clinical Experience

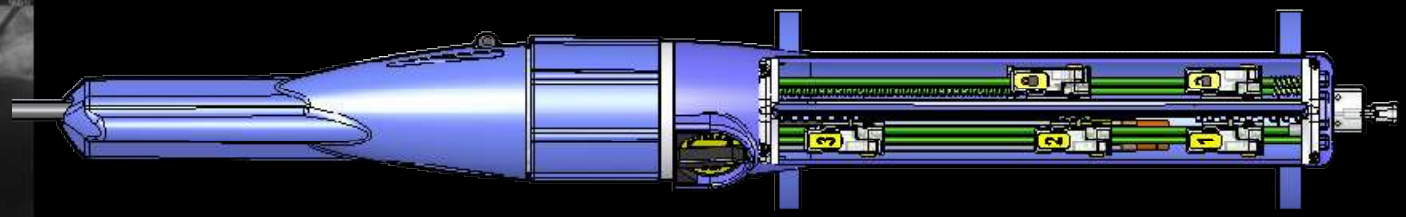
- **Lotus Valve Implant function is excellent, but opportunities identified to improve delivery system:**
  - Valve attachment to and release from delivery system needed to be simplified.
  - Handle needed to be redesigned with ease of use a foremost consideration
  - Delivery System size limited use – needed to be reduced.

Simplified Attachment: 15 → 3 fingers

Previous 15 finger design

New 3 finger design

Redesigned Handle: 7 → 2 controls



- Fewer controls – easier to use
- Ensures correct deployment sequence
- Reduced force required to lock

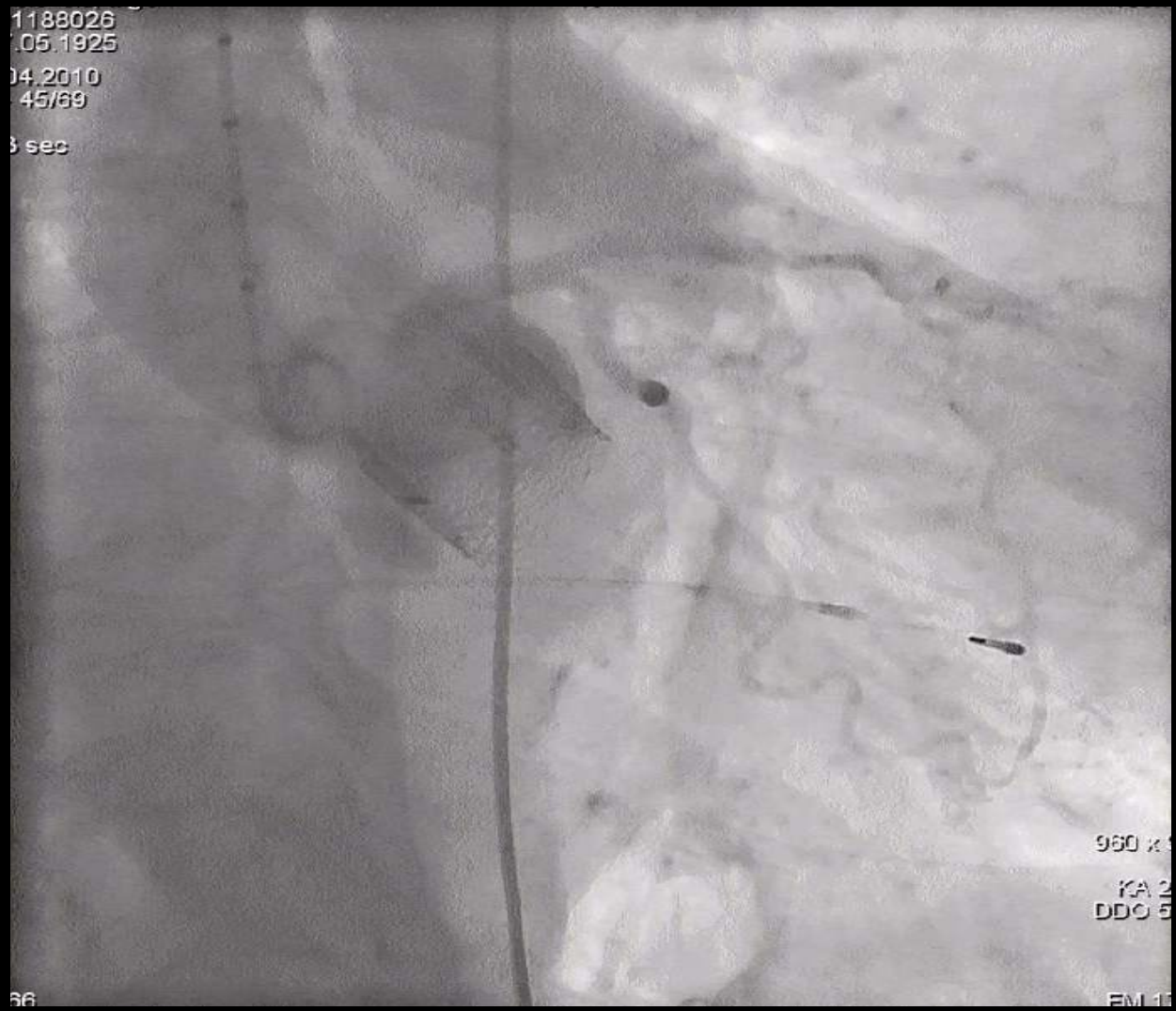
Profile Reduction: 21 → 18 Fr

- Sadra-developed thin-wall introducer enables fully percutaneous procedure:
  - Same outer diameter as Cook 18Fr
  - Reinforced for excellent kink resistance

Cook 18Fr Introducer Sheath

Sadra Custom Introducer Sheath

Latest Patient Implant – April 13, 2010

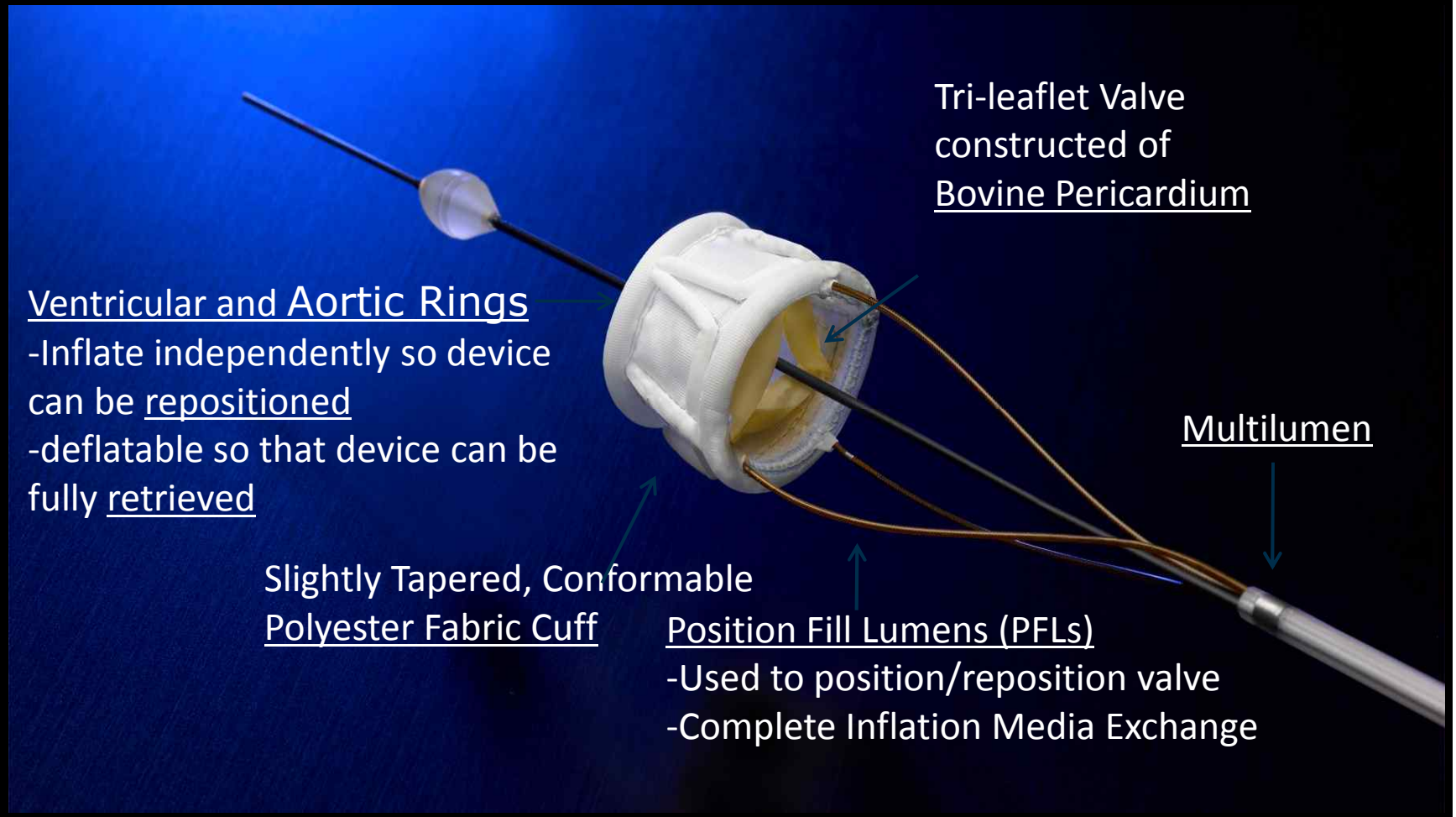


Timeline

- **Multicenter European Trial started 13.April 2010 (PI. E.Grube)**
  - Intl. Heart Center Rhein Ruhr (E.Grube)
  - University Hospital Essen (R.Erbel)
  - Heart Center Siegburg (R.Mueller)

- **First 3 Patients enrolled with excellent acute hemodynamic and angiographic results**
  - Zero Gradient
  - No Aortic Insufficiency
  - No Pacemaker Implant
  - Av. Implant Time 14 Minutes

The Direct Flow Medical (DFM) Aortic Valve Prosthesis



18F System Features

3 sizes matching valvuloplasty balloons

22F Design

18F Design

European Feasibility Trial

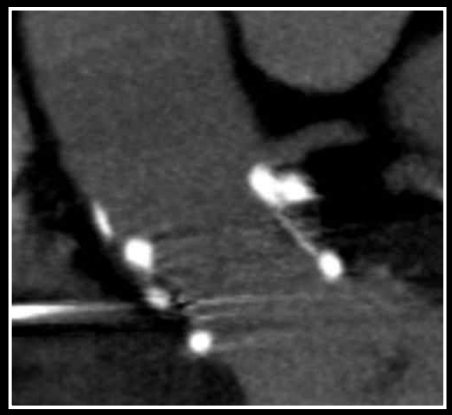
Design: Prospective, non-randomized clinical evaluation of the DFM PAV at two centers in Germany

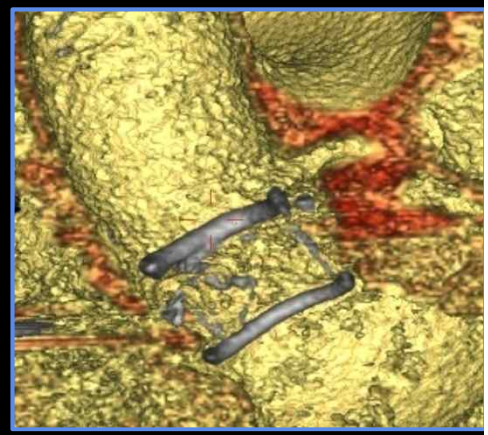
Hamburg University Cardiovascular Center (n=25)

Siegburg, Helios Heart Center (n=6)

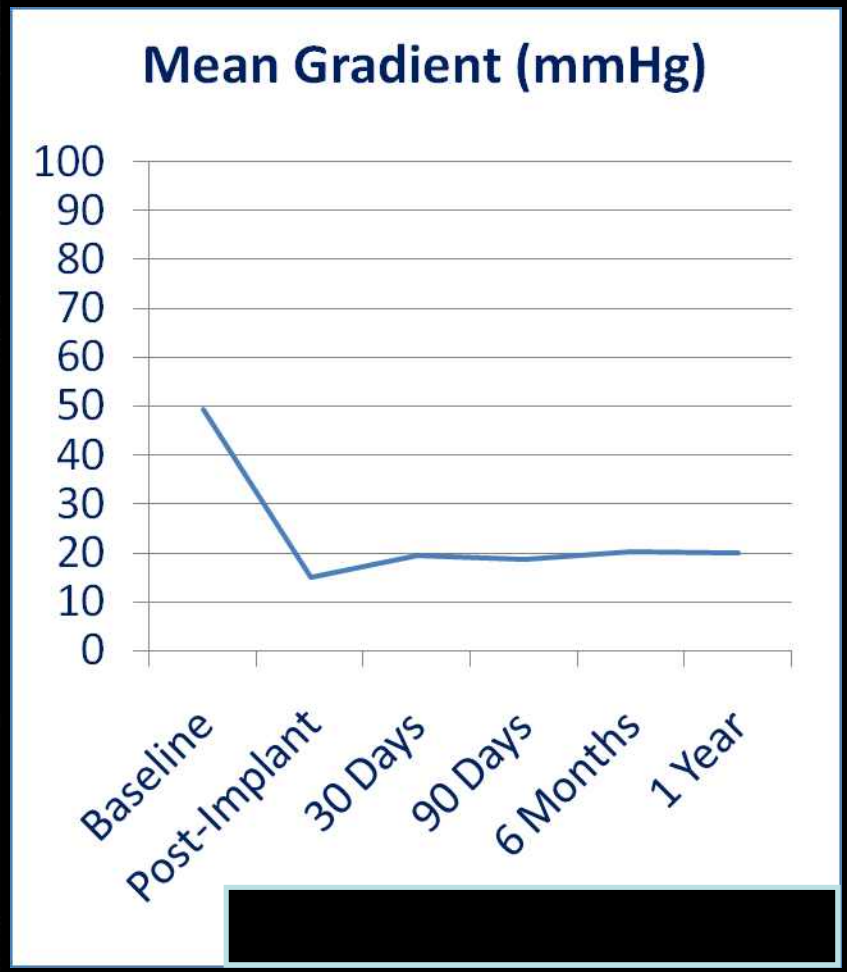
Purpose: Determine clinical feasibility and safety of treating patients high-risk for cardiac surgery:

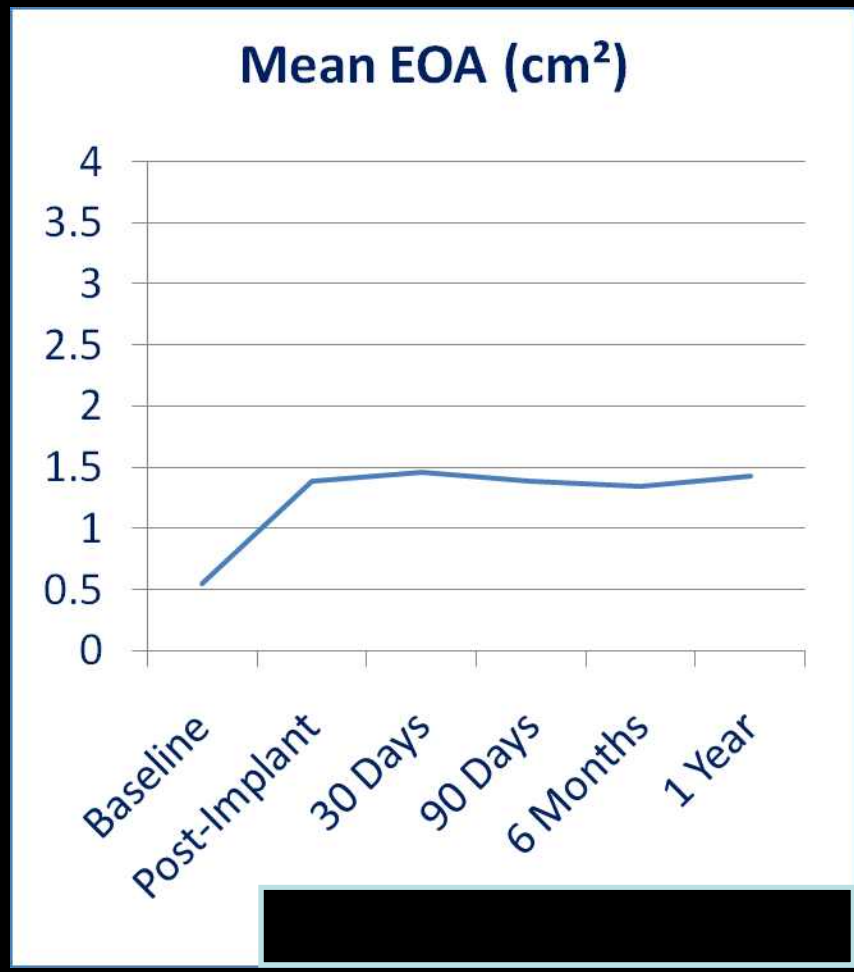
- EuroSCORE ≥ 20%
- Age ≥ 70
- Severe aortic valve stenosis





The DFM AV Prosthesis
European Clinical Trial

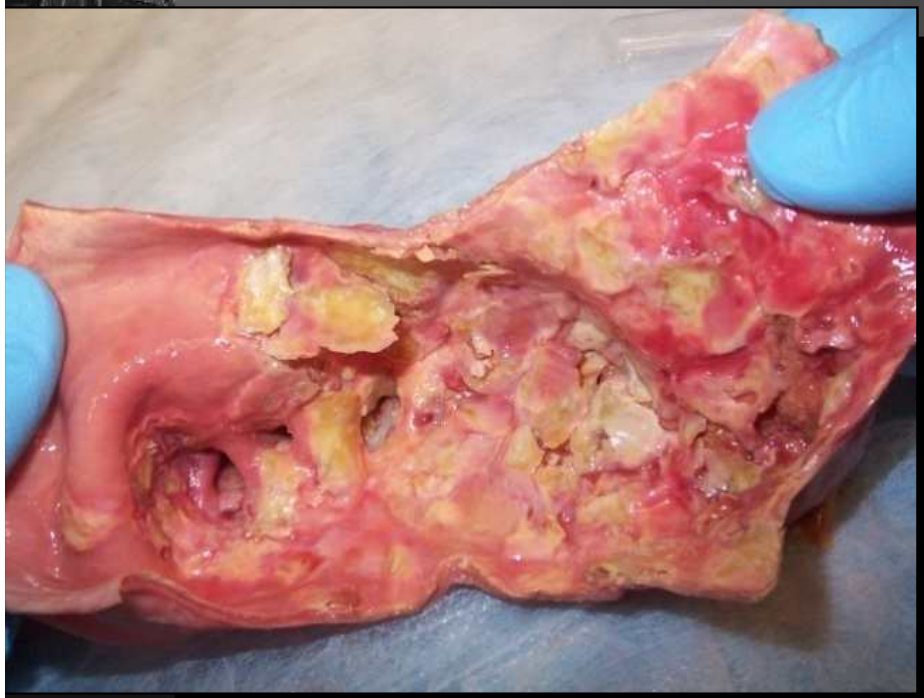




Summary Thoughts…

- Next generation TAVR *devices* are rapidly evolving, providing substantial benefits over the first generation devices
- Issues addressed are repositionability, risk of paravalvular leakage, profile size etc.
  - Valve + platform *durability* still must be conclusively demonstrated!
  - Once durability is established, we can expand clinical trials and indications for TAVR to most (not all) patients with severe AS!

Aortic Atheroma: High Risk



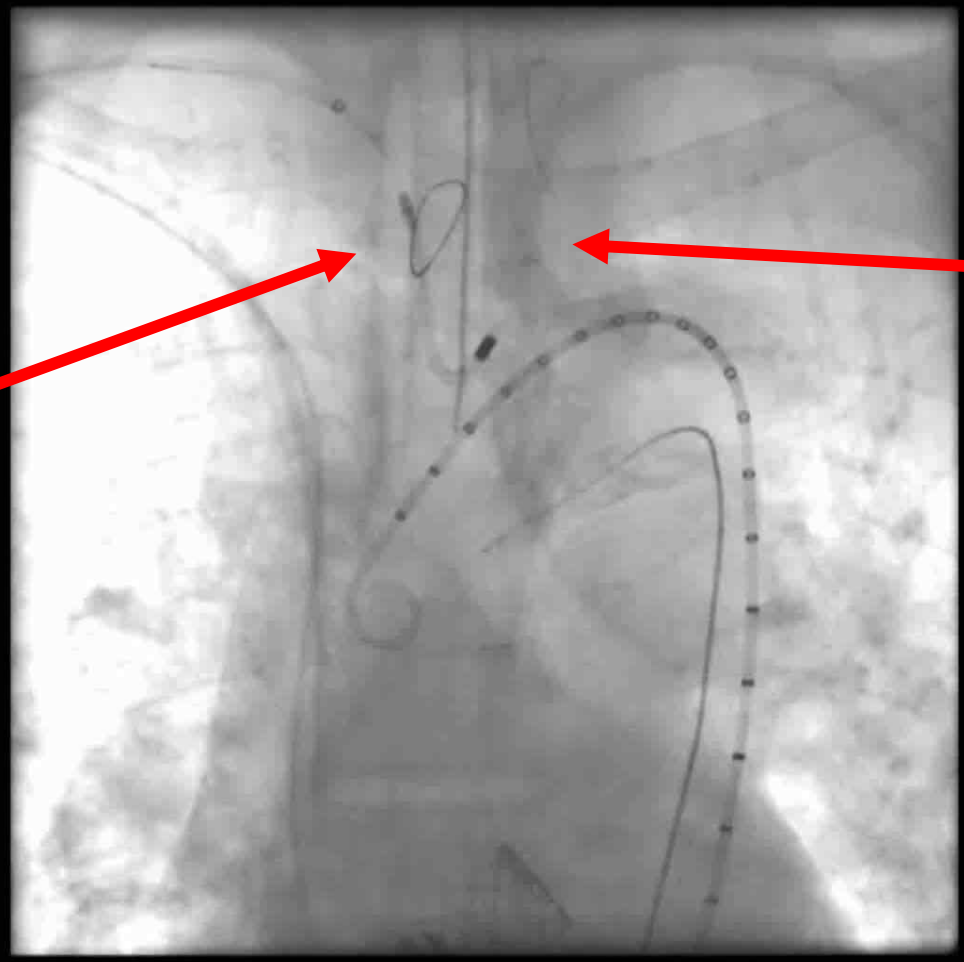
- 268 of 3404 CABG patients (8%) had
- atheroma (>/= 5 mm, or mobile)
- Defined by epi-aortic ultrasound[1]
- 15.3% of group had intra-operative stroke[1]

[1]Protruding aortic arch atheromas: risk of stroke during heart surgery with and without aortic arch endarterectomy. Stern et al. American Heart Journal Oct. 1999.

- **High Risk for:**
  - Intra-operative stroke
  - Multiple morbidity
  - Prolonged hospital stay,
  - Death resulting from heart surgery.[1]

- **Risk Factors for Aortic Atheroma:**
- > 70 years old
- Diabetes Mellitus
- Hyperlipidemia
- Arterial hypertension
- Aortic calcifications on chest X-ray
- Elevated serum levels of C-reactive protein
- Other inflammatory markers
- Activated coagulation[3]

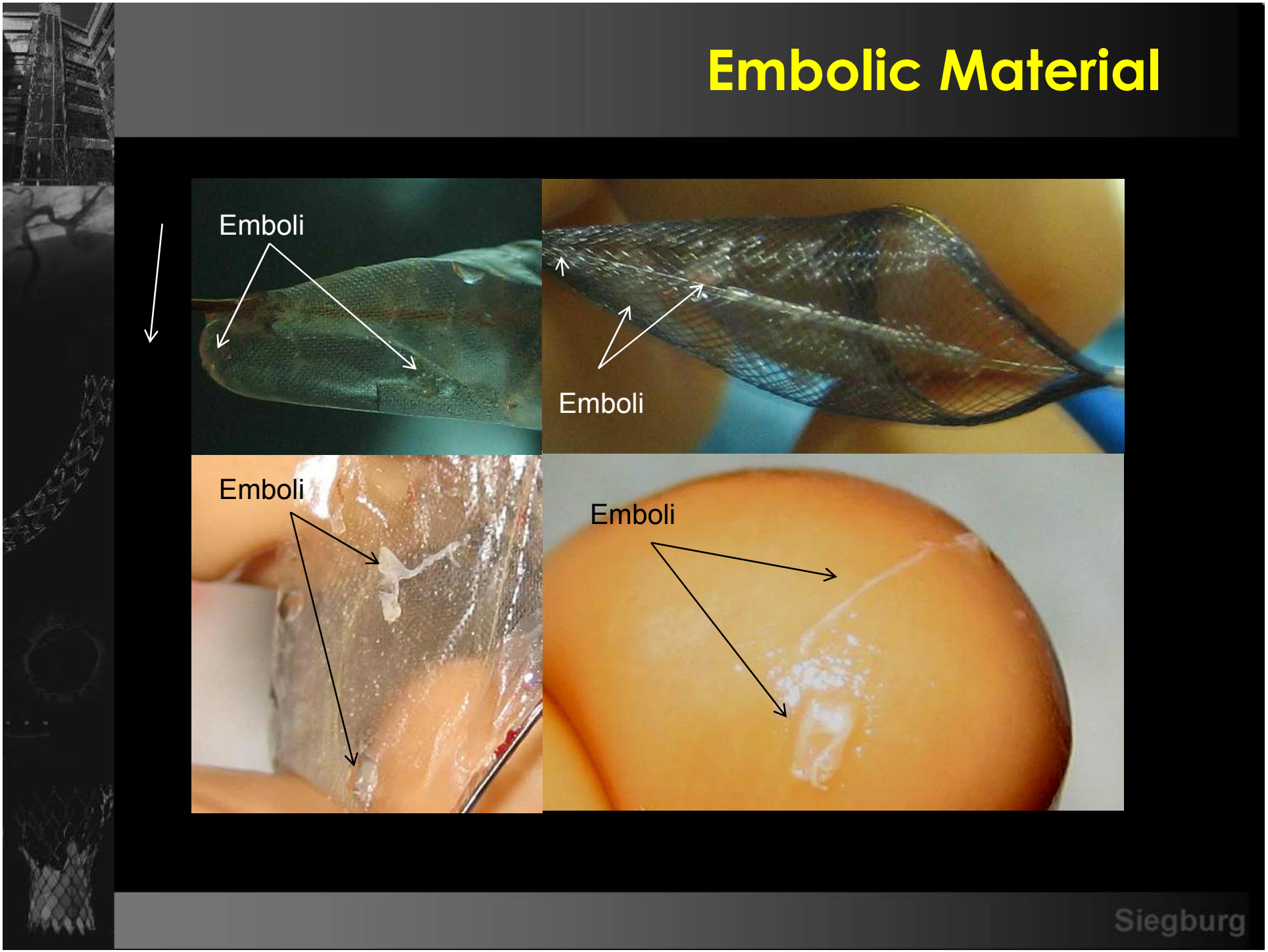
Cerebral Filter Protection
Claret



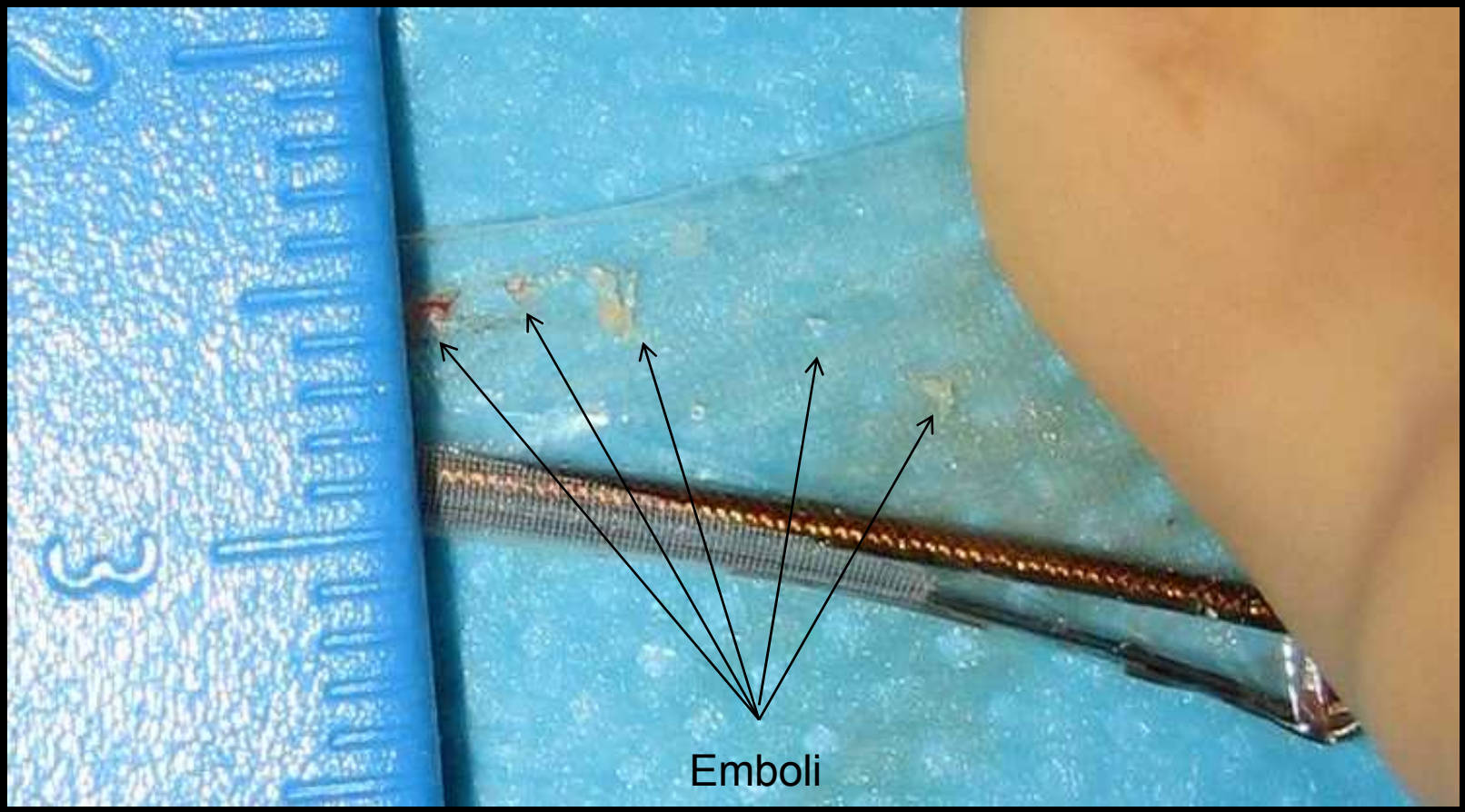
Filter in Truncus

Filter in left Carotid

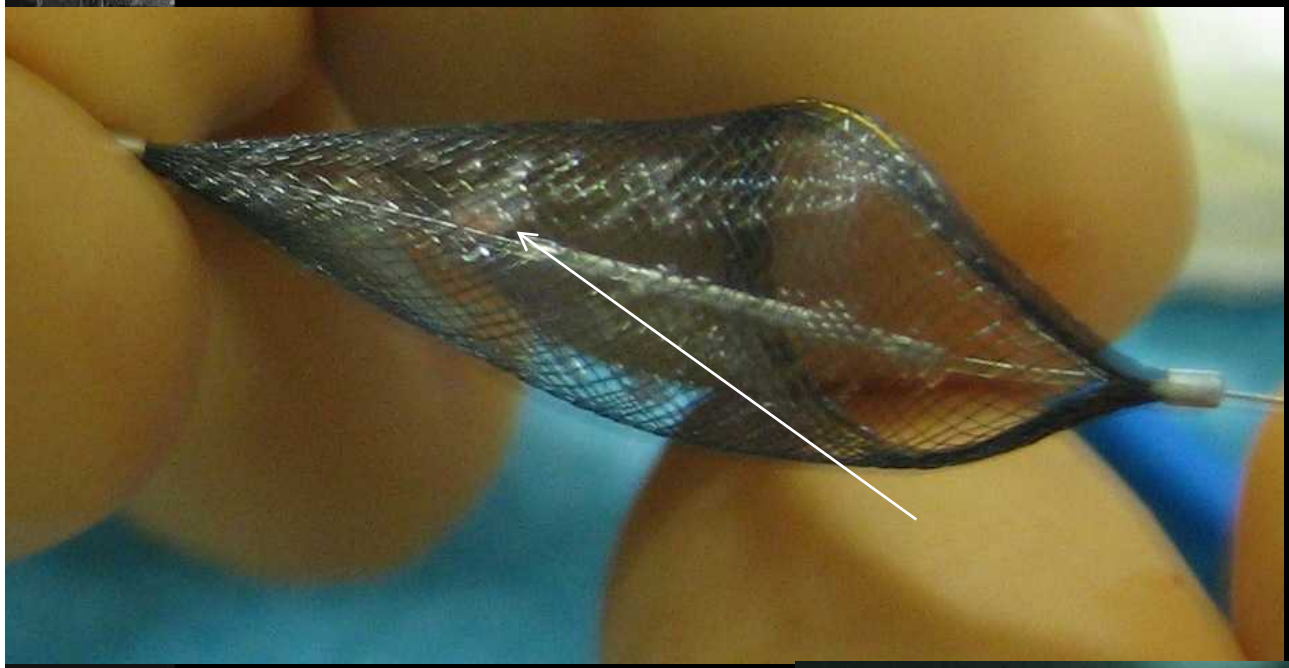
Embolic Material



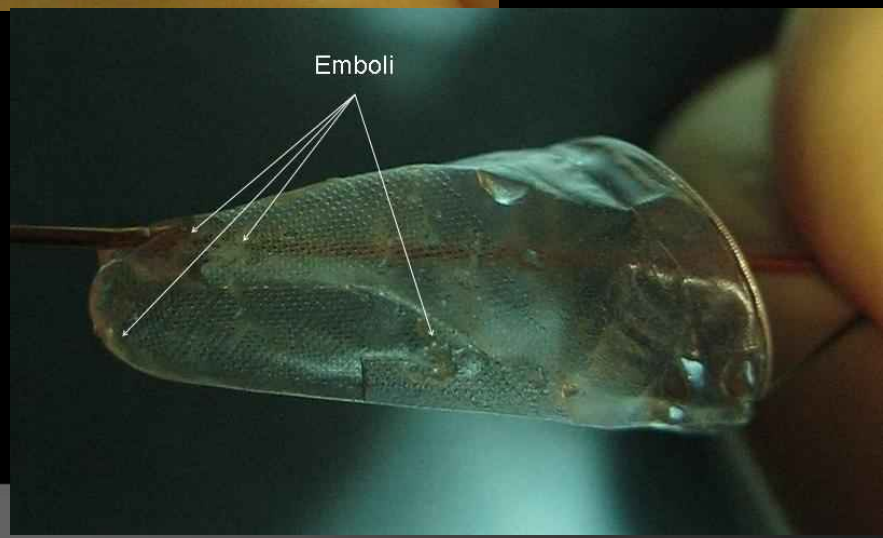
Embolic Material



Claret Dual Filter



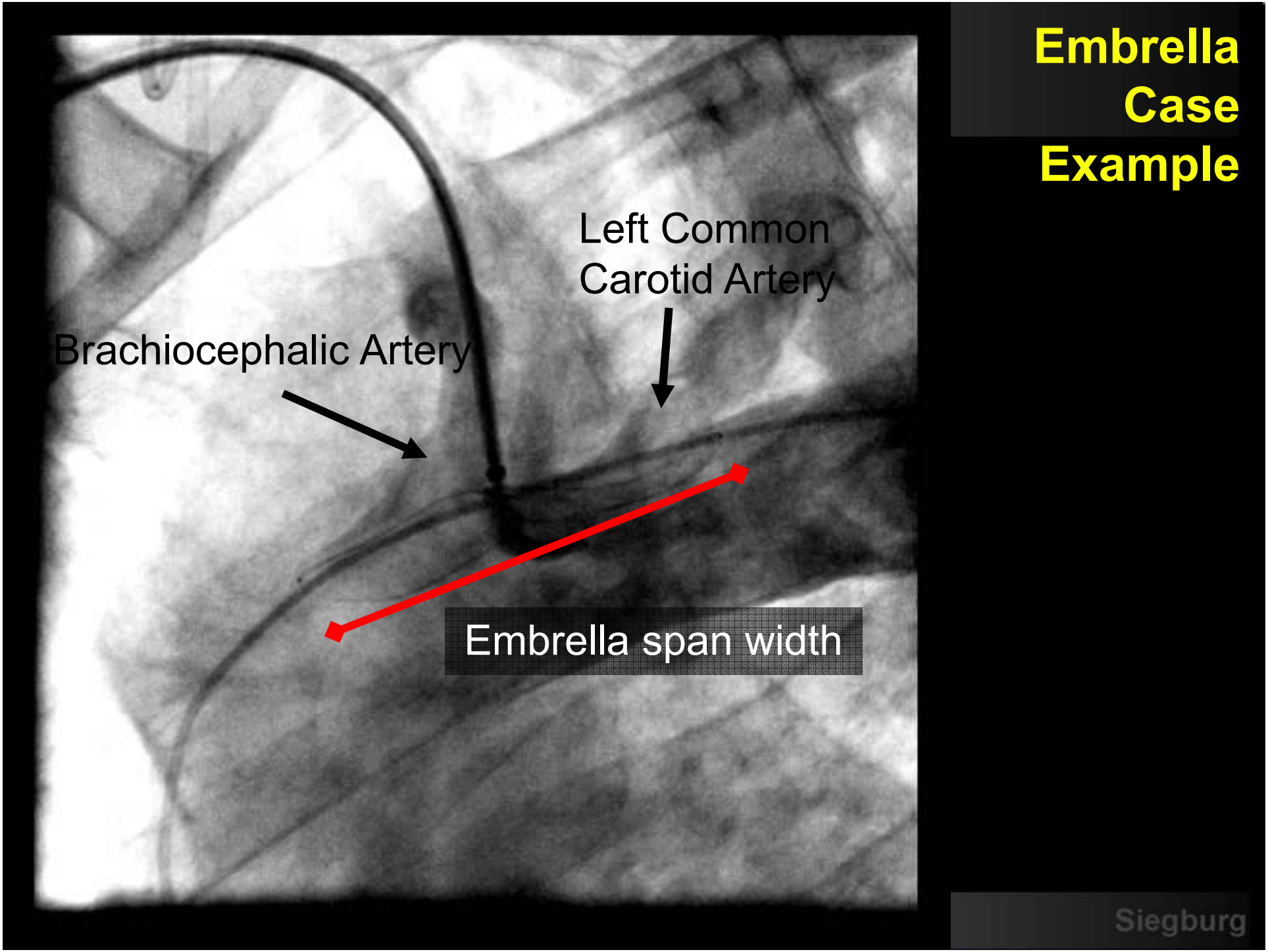
7 mm filter placed in left carotid



Embrella Embolic Deflector™

- Porous membrane designed to deflect embolic debris
- Nitinol® Frame & Shaft
- Polyurethane Porous Membrane
- Heparin Coating
- 3 Radiopaque Markers
- Suture; Monofilament Nylon

Embrella Case Example

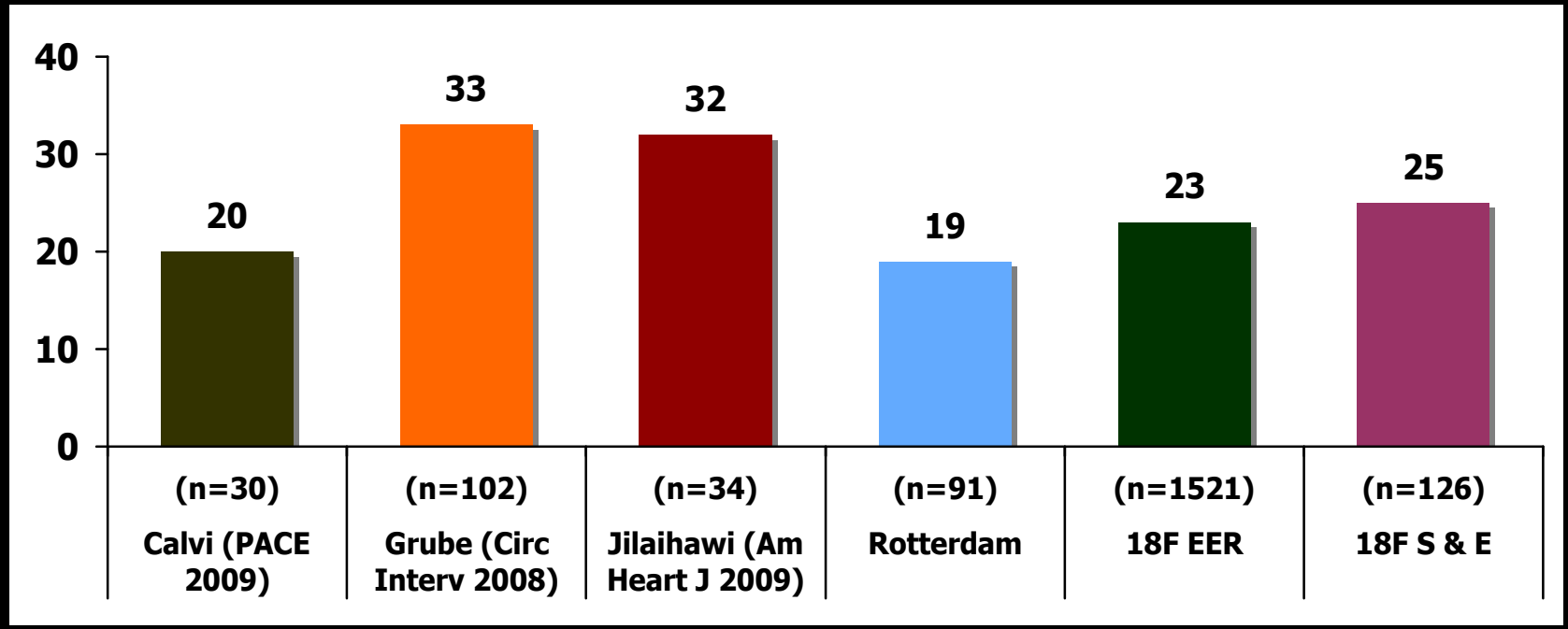


Thank you for your attention !

Thank you

There Is a Higher Incidence of Pacemaker Implant Associated with CoreValve

New Permanent Pacemaker within 30 Days

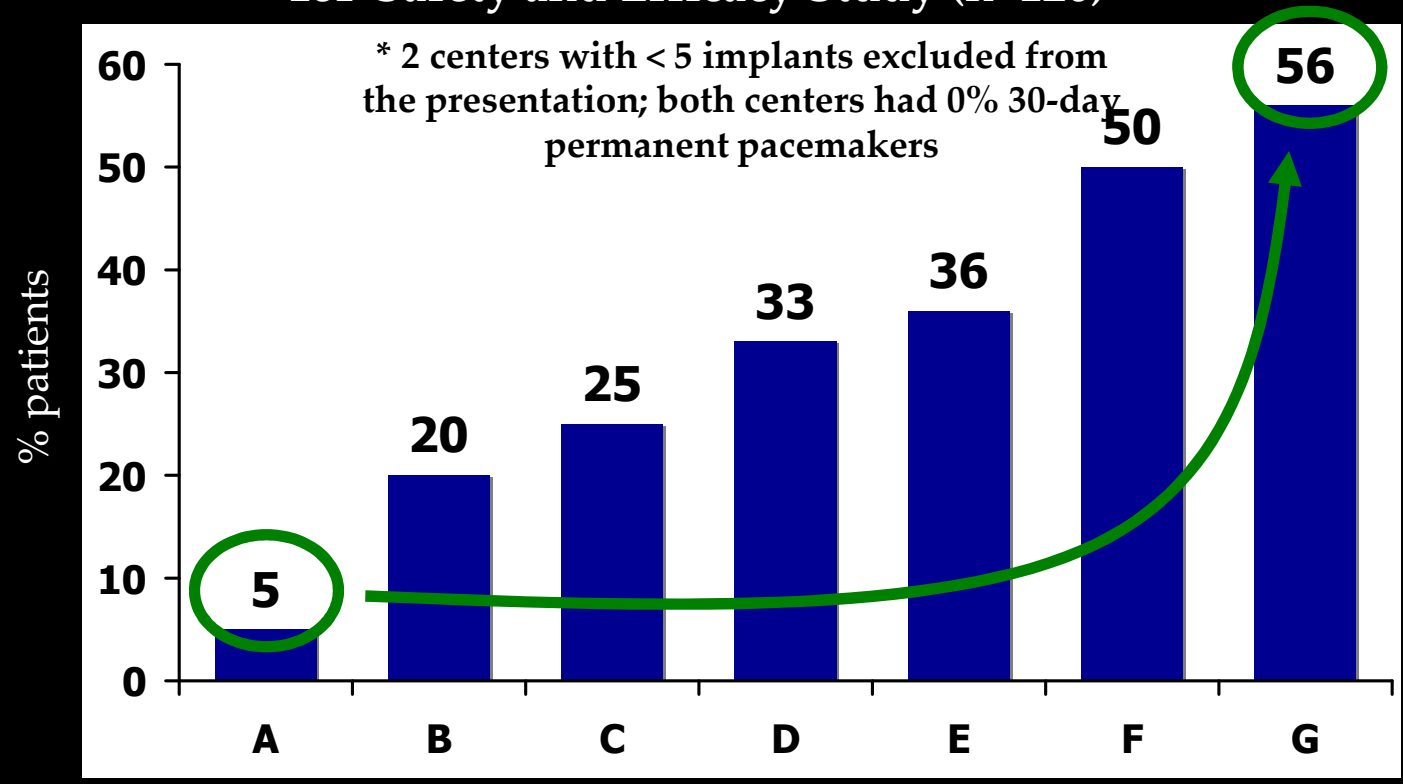


Weighted average = 23%
(n=1990 patients)

It is important to remember that pacemaker implantation may not mean pacing need

New Permanent Pacemaker within 30 Days

18F Safety and Efficacy Study (n=126)



Physicians' decision to prophylactically implant play a big role in the variability among centers

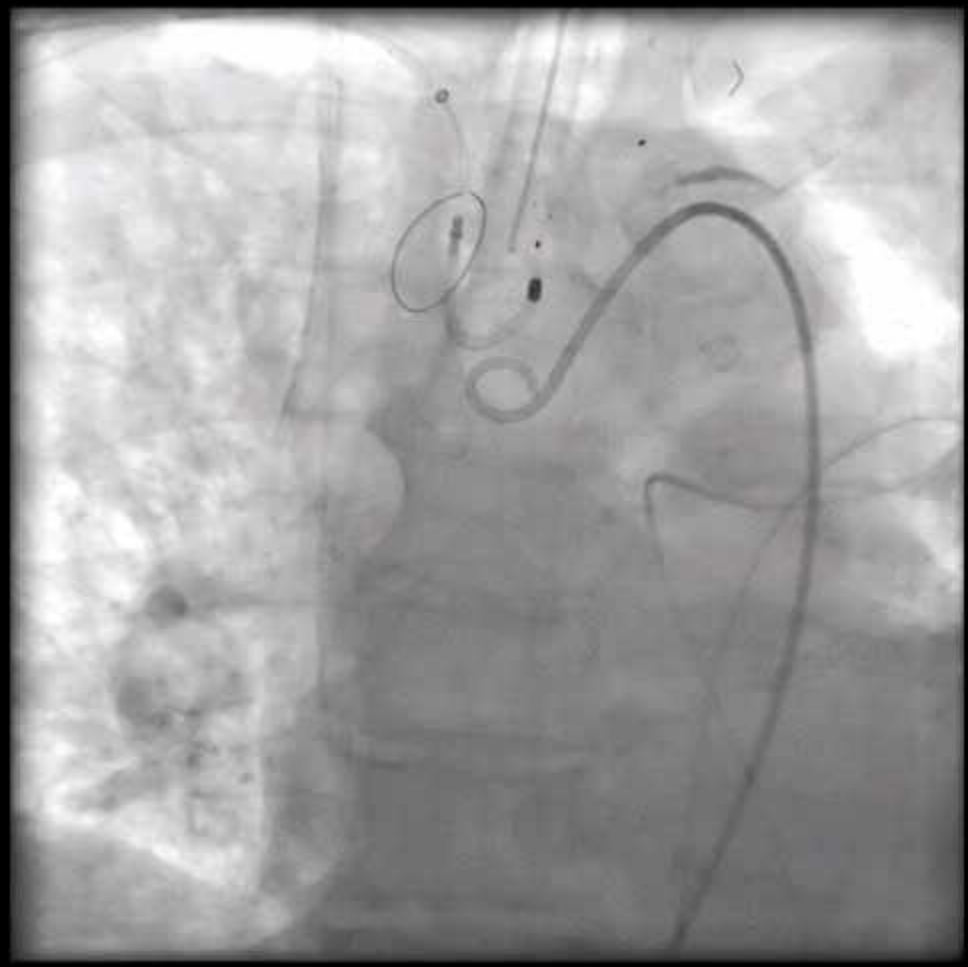
Claret Dual Filter

The Device:

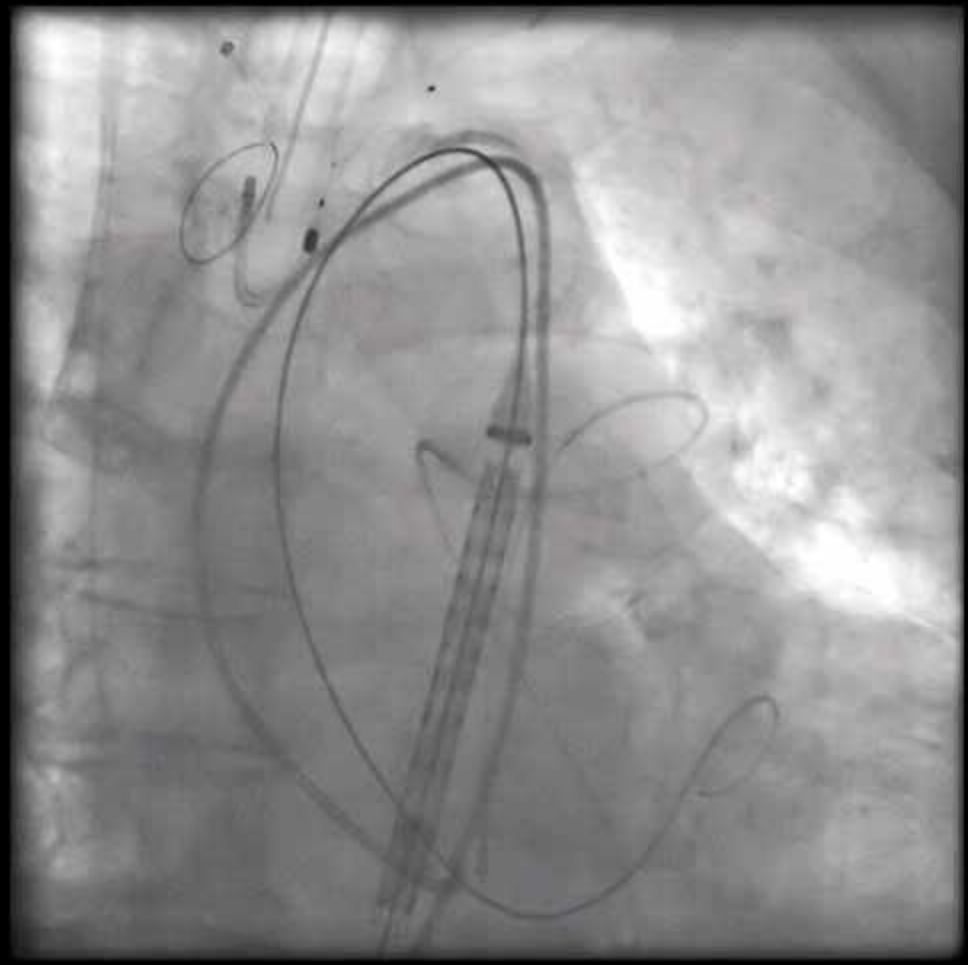
- **Must be easy to use!**
- The filter device should **not** be present in the aorta
- Catheter 6F (5F in development)
- 140 micron pore size
- Right radial/brachial delivery
- System will accommodate variable aortic anatomy

Claret

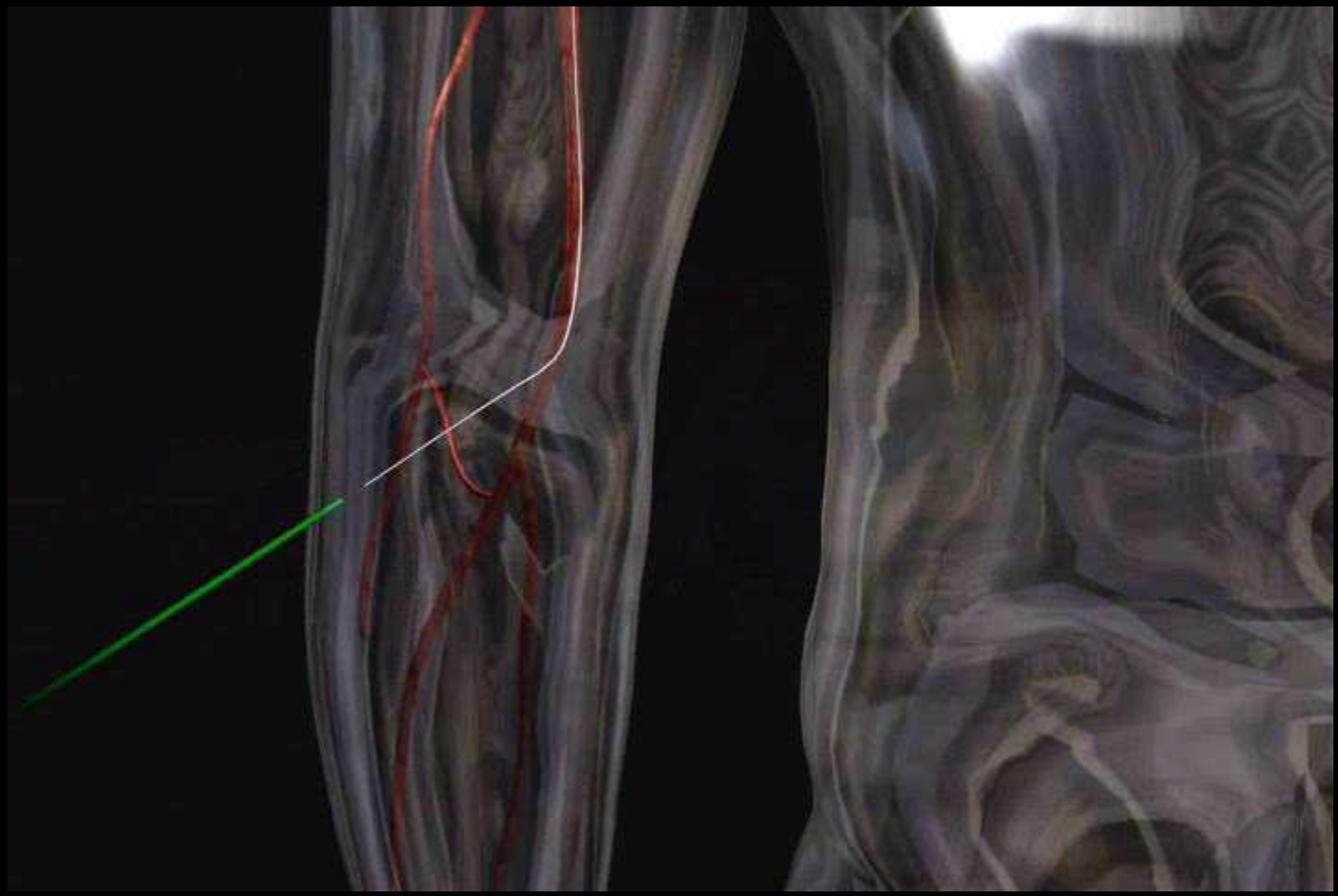
Claret Dual Filter Device



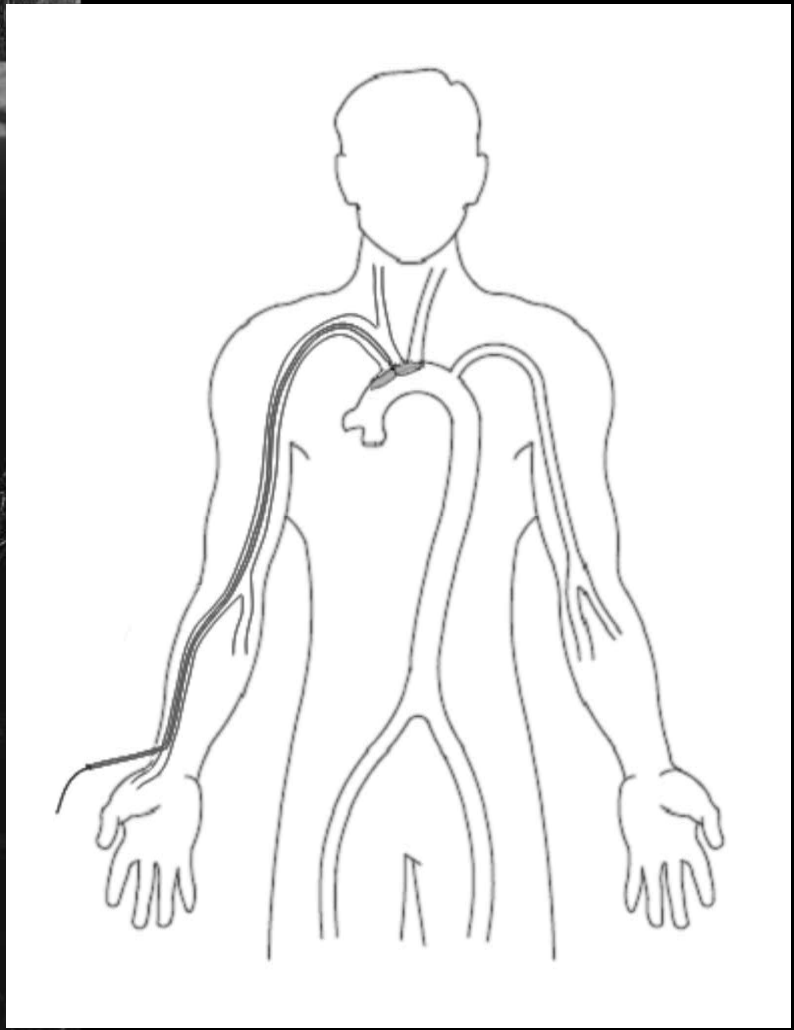
Claret Dual Filter Device



Embrella

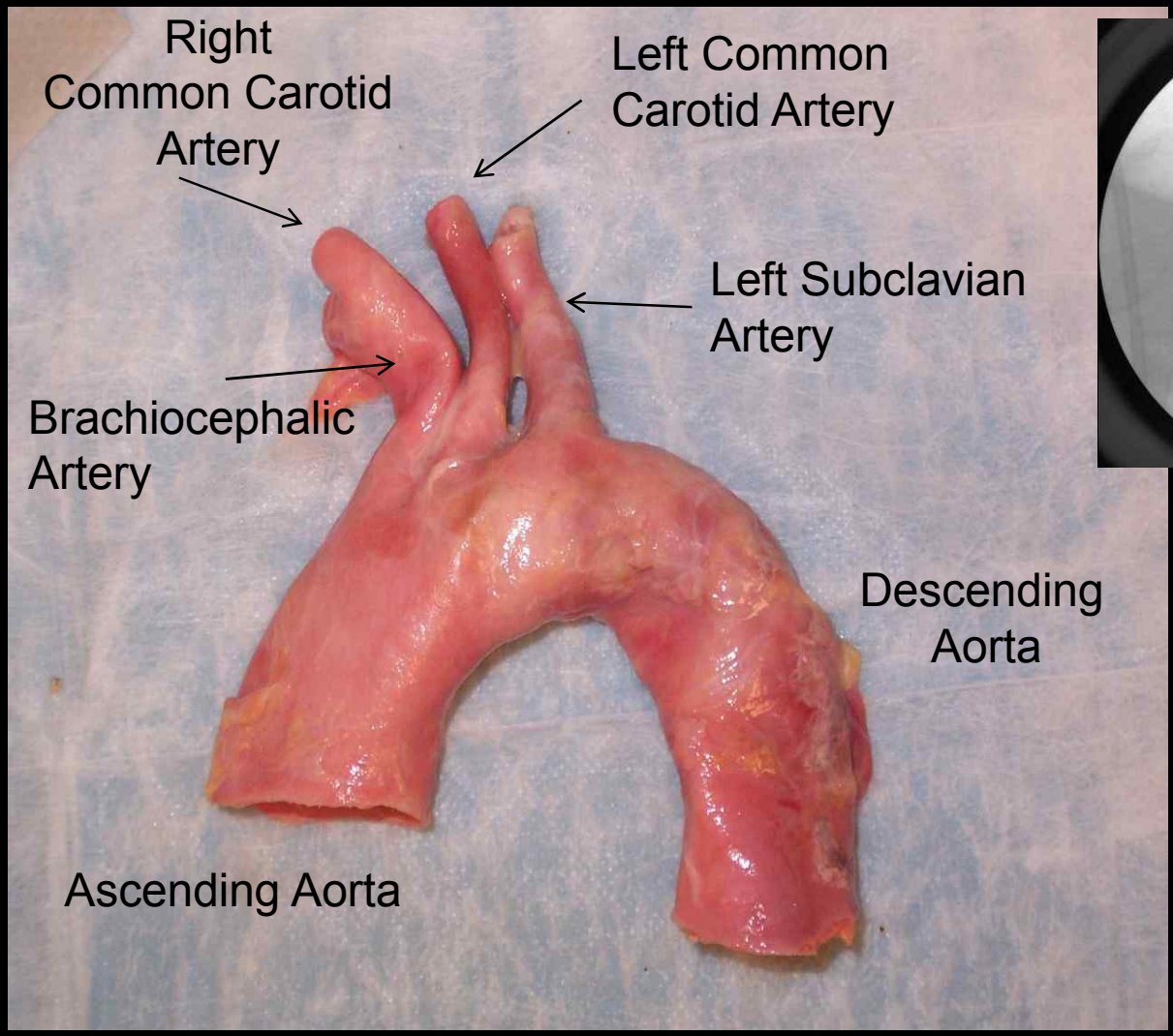


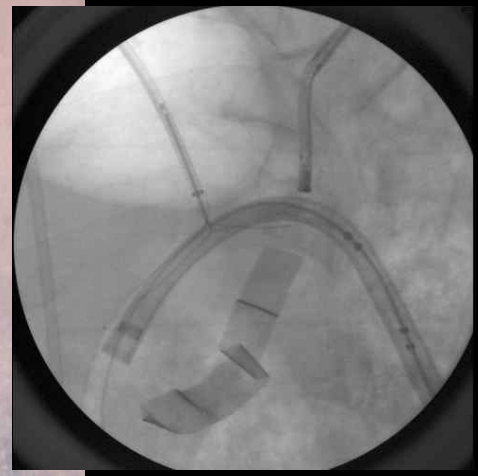
Concept of Embrella Product Requirements



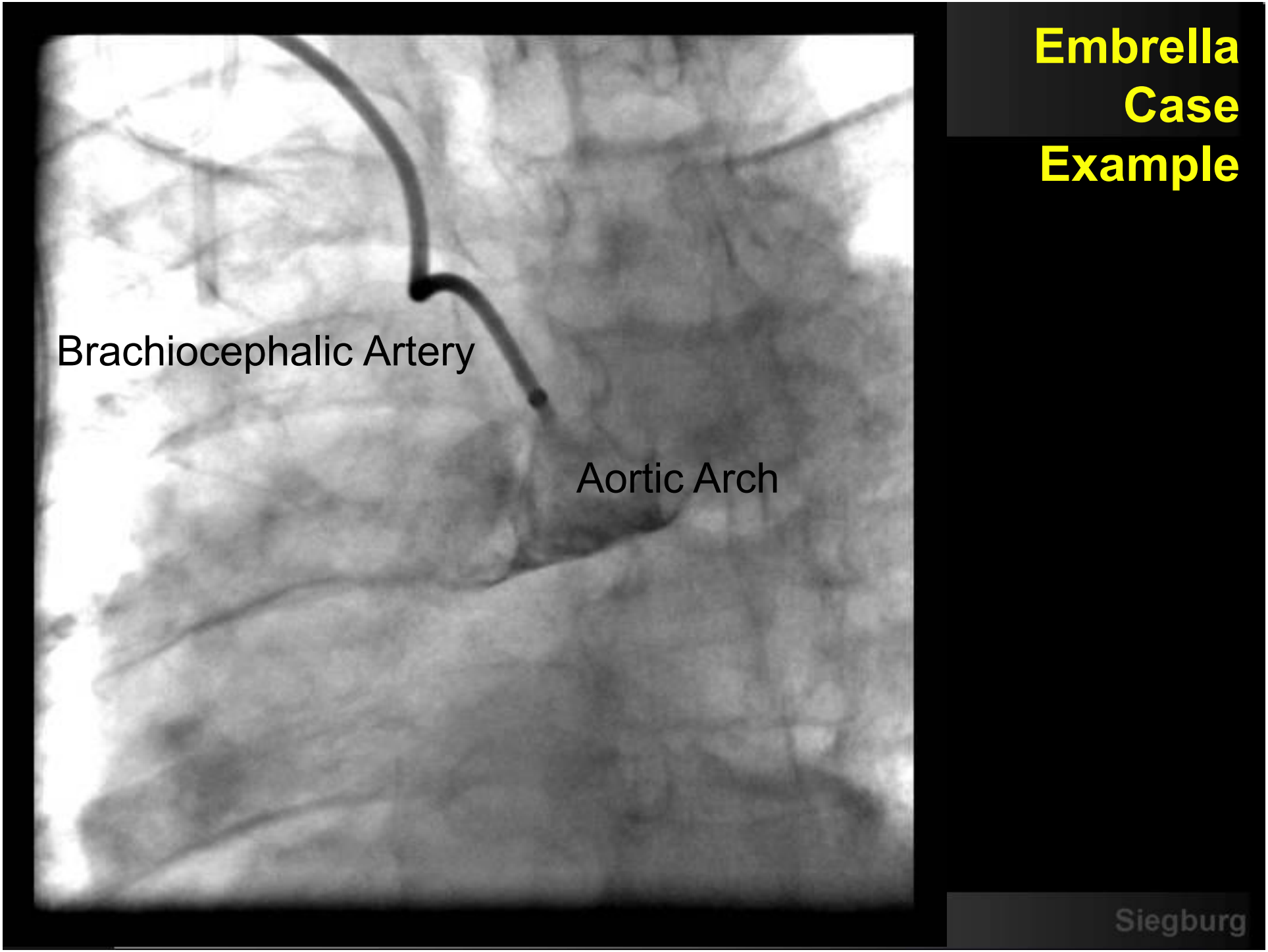
- Separate access site from main procedure; radial or brachial artery
- Fits through a 6F sheath
- Minimal orientation
- Ease of use, no new techniques
- Low profile
- One size fits all
- Deflect debris

Concept of Embrella
Human Aorta

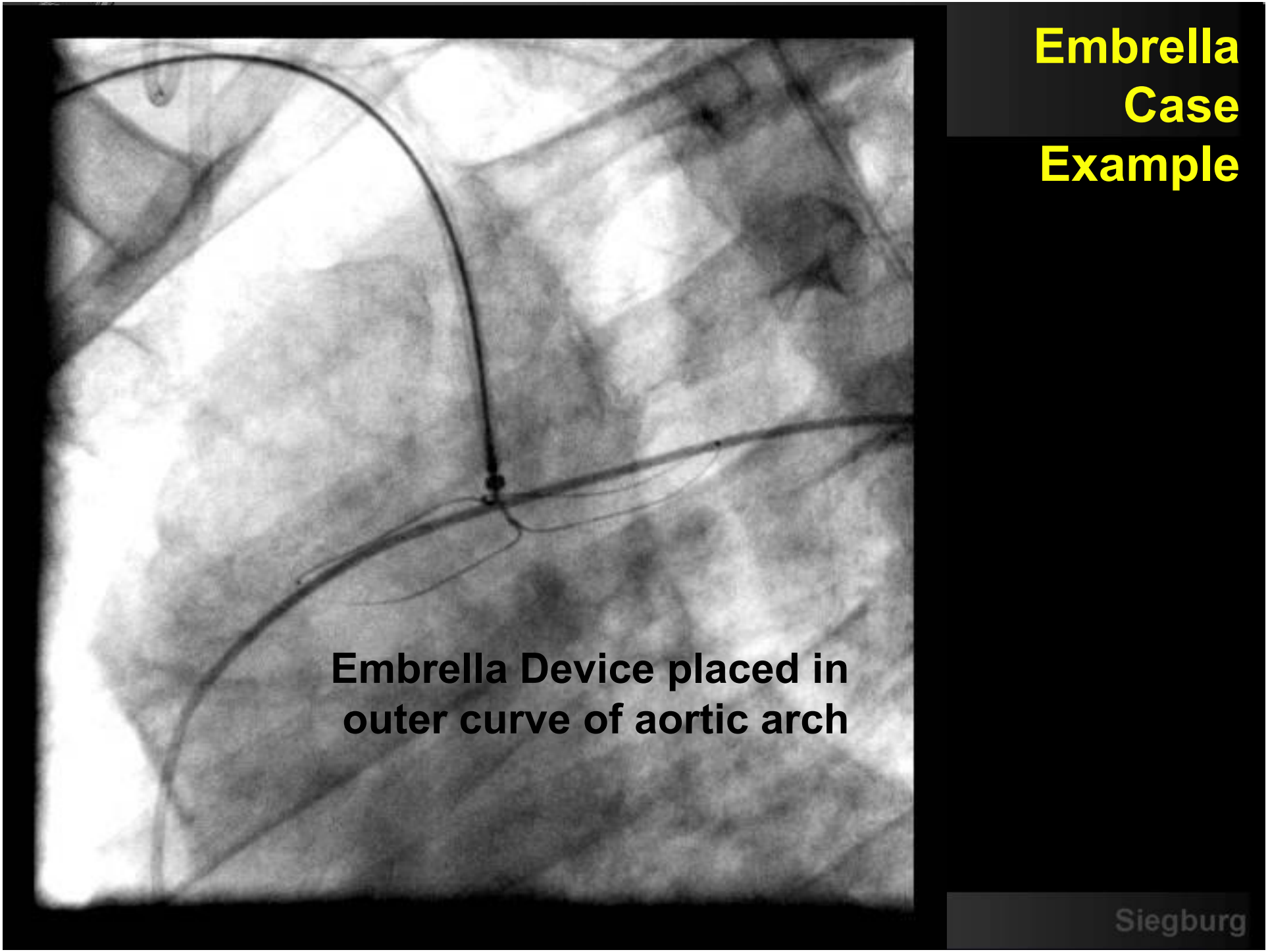




Embrella Case Example



Embrella Case Example



Embrella Case Example