The Core Valve Experience from the Siegburg Heart Center. An Update

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Disclosure Statement of Financial Interest

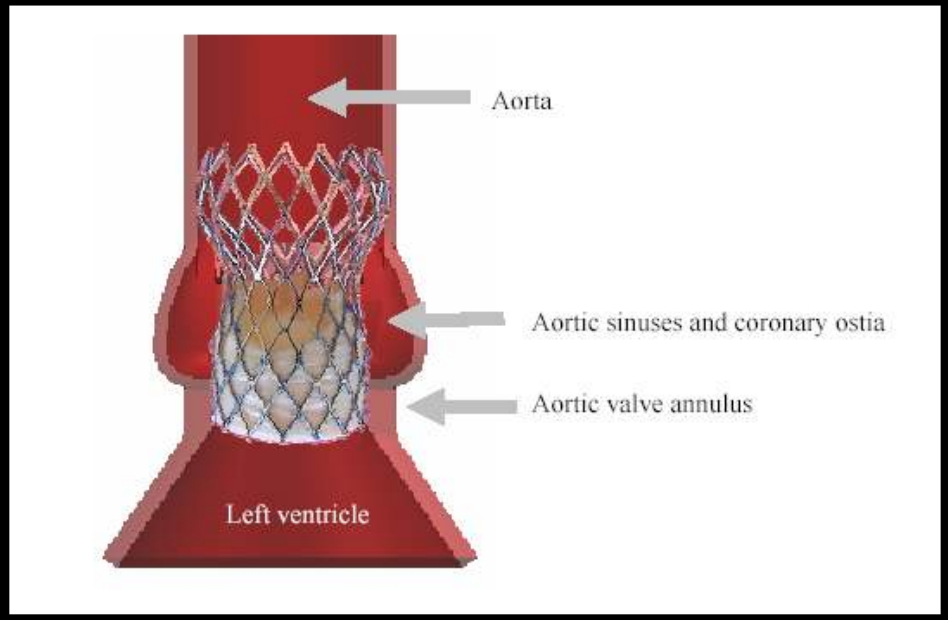
Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

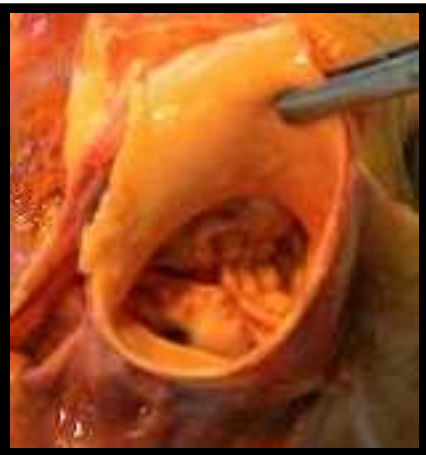
Physician Name	Company/Relationship
Eberhard Grube, MD	**Medtronic, CoreValve: C, SB** **Sadra Medical : E, C, SB** **Direct Flow: C, SB**

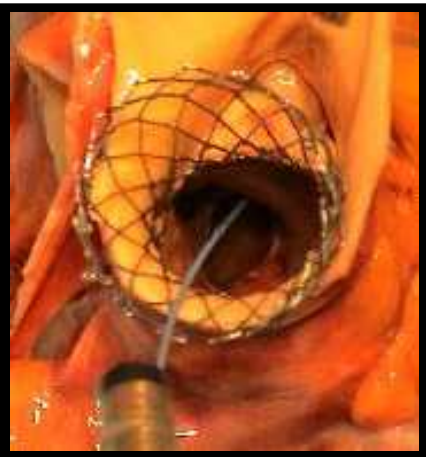
Key

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

CoreValve Prosthesis







Siegburg CoreValve TAVI Experience

Study	25 F	21 F	18 F S&E	18 F 2008	18 F 2009
Patient n	10	24	102	187	253
Time period	2004 -	2005	03/2006 to 03/2008	01/2008 to 12/2008	01/2009 to 12/2009

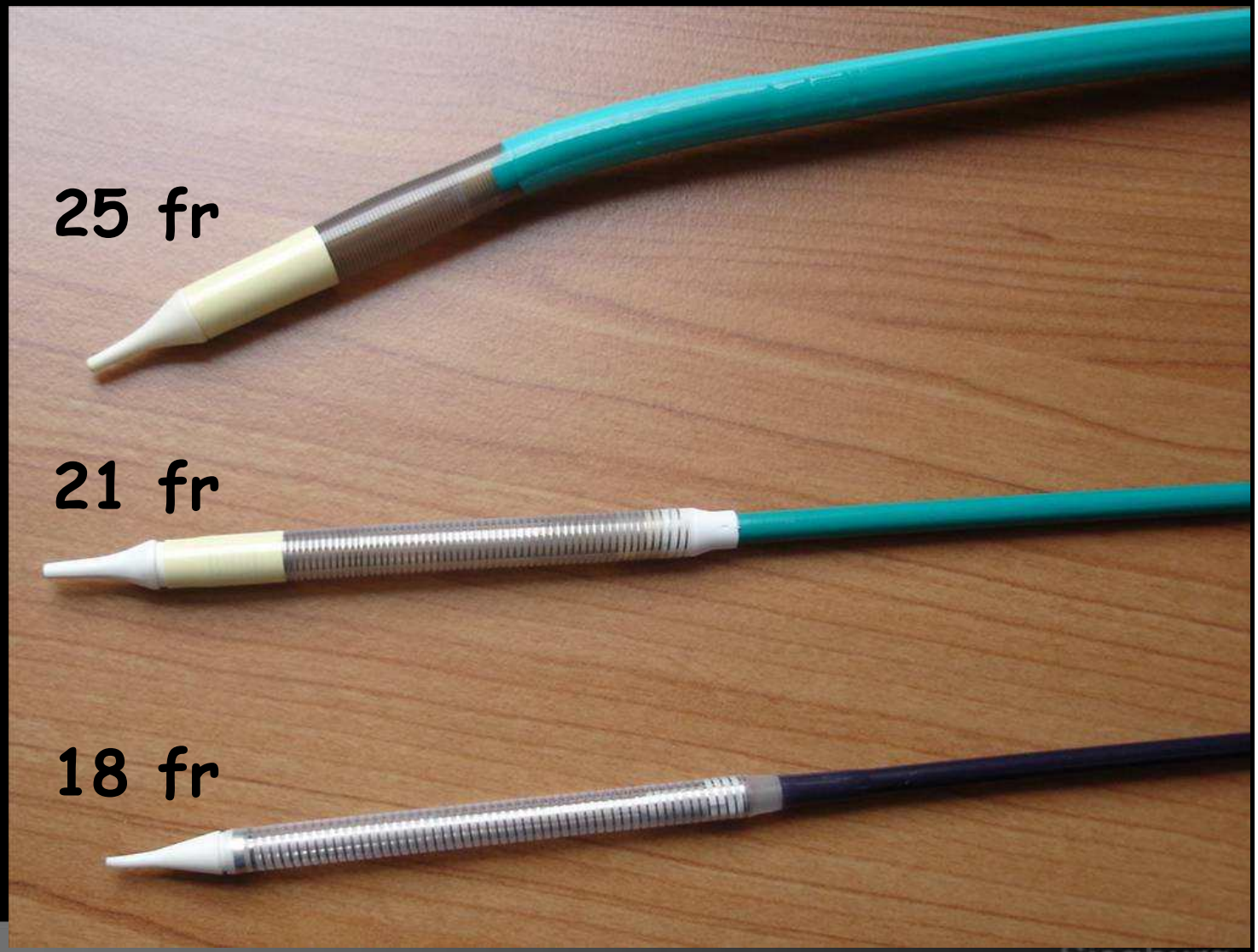
Five years, Three generations, 576 patients

CoreValve : 3 Generations

2004

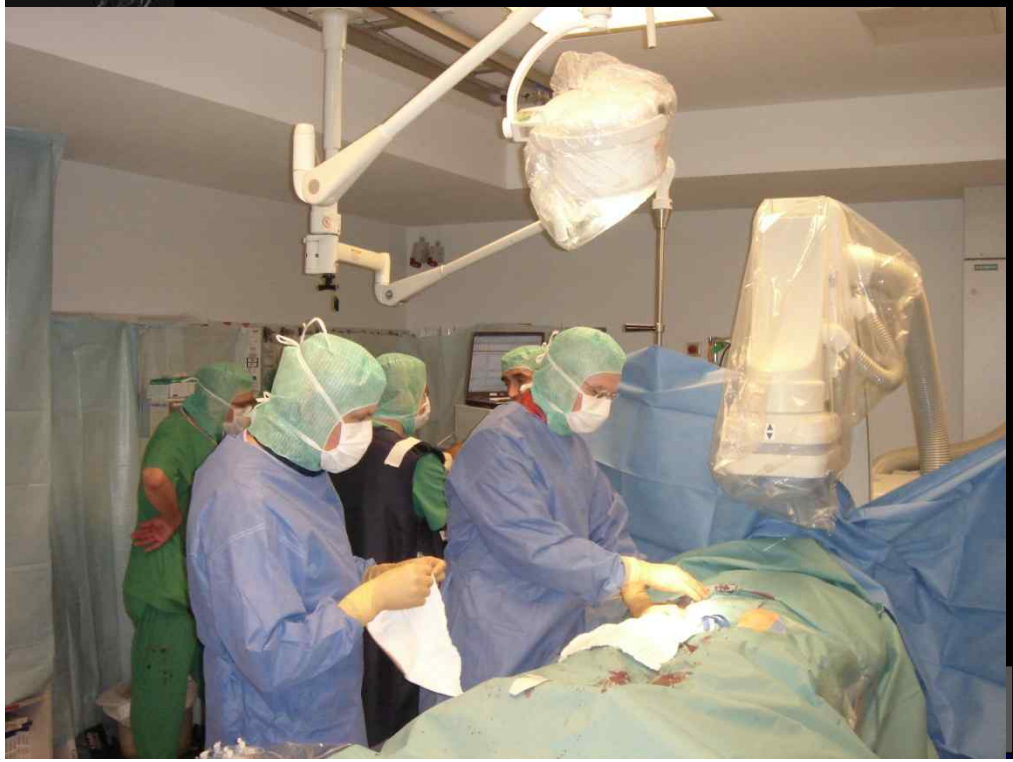
2005

2006



CoreValve 2005

- 24 F 1st Gen CoreValve
- Surgical Prep
- CPB pump
- General anesthesia

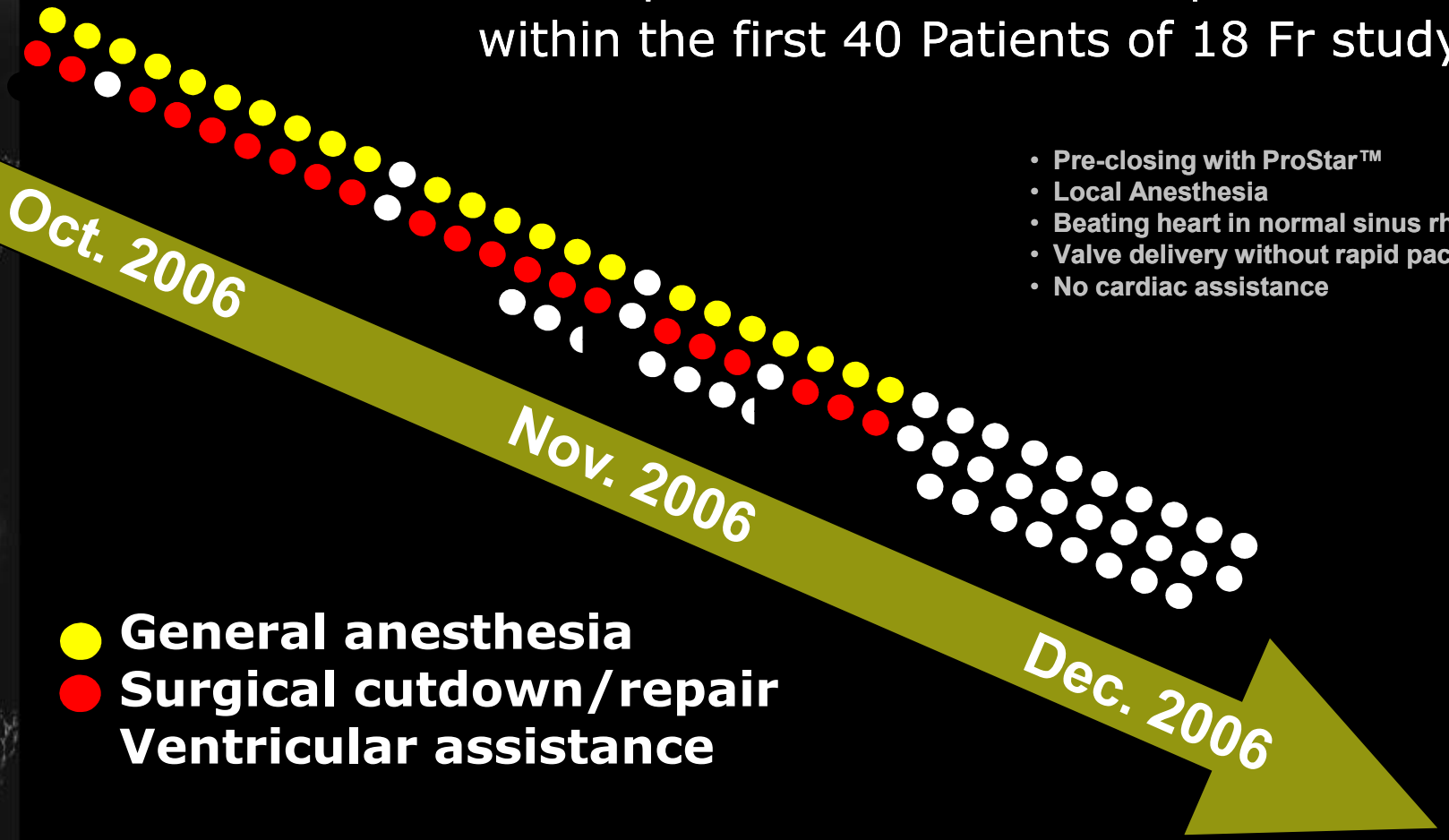


CoreValve 2010

- 18 F 3rd Gen CoreValve
- PCI-like procedure
- Conscious Sedation

18 French Procedural Progress

Evolution to a
« true percutaneous cath lab procedure »
within the first 40 Patients of 18 Fr study



- Pre-closing with ProStar™
- Local Anesthesia
- Beating heart in normal sinus rhythm
- Valve delivery without rapid pacing
- No cardiac assistance

- General anesthesia
- Surgical cutdown/repair
- Ventricular assistance

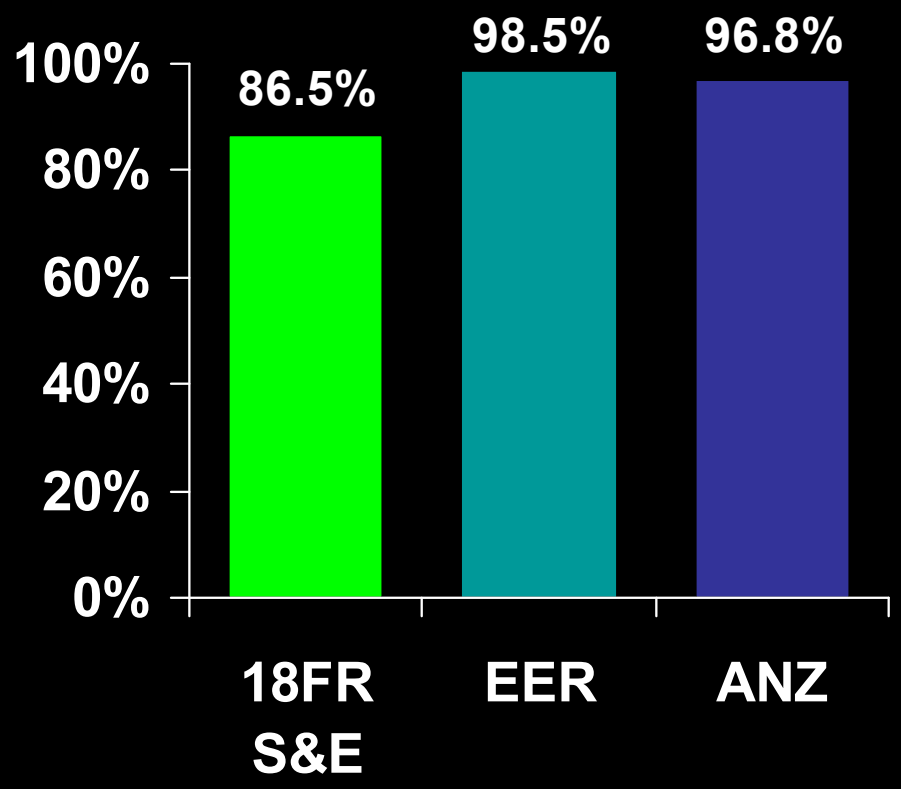
Overall Clinical Experience

Study	N	Follow-ups	Status
18 Fr Safety and Efficacy Trial	126	4 years	On-going
Australia-New Zealand Registry	140	2 years	On-going
Italian Registry	514 to date	6 months	On-going
German Series, Siegburg	>536 to date	30 days	On-going
Expanded Evaluation Registry	1483	Up to 2 years	Completed
French Registry	78 to date	6 months	On-going
Advance Study	1,000	Up to 10 years	Upcoming
US IDE Study	TBD	TBD	Upcoming

Baseline Clinical Characteristics

	18 Fr S&E (N=126)	Siegburg (N=86)	ANZ (N=62)
Age (years)	81.9 ± 6.4	82.3 ± 5.9	83.7 ± 5.4
Female	72 (57.1%)	56 (65%)	30 (48.4%)
NYHA Class I and II	32 (25.4%)	15 (17%)	11 (19.3%)
NYHA Class III and IV	94 (74.6%)	71 (83%)	46 (80.7%)
Logistic EuroSCORE (%)	23.4 ± 13.8	21.7 ± 12.6	18.7 ± 12.9 (N=58)
Peak Pressure Gradient (mmHg)	72.8 ± 23.0	70.9 ± 22.8	18.7 ± 12.9 (N=58)
Mean Pressure Gradient (mmHg)	47.8 ± 14.3	43.7 ± 15.4	48.6 ± 16.3
Aortic valve area (cm^2)	0.73 ± 0.16	0.60 ± 0.16	0.7 ± 0.2

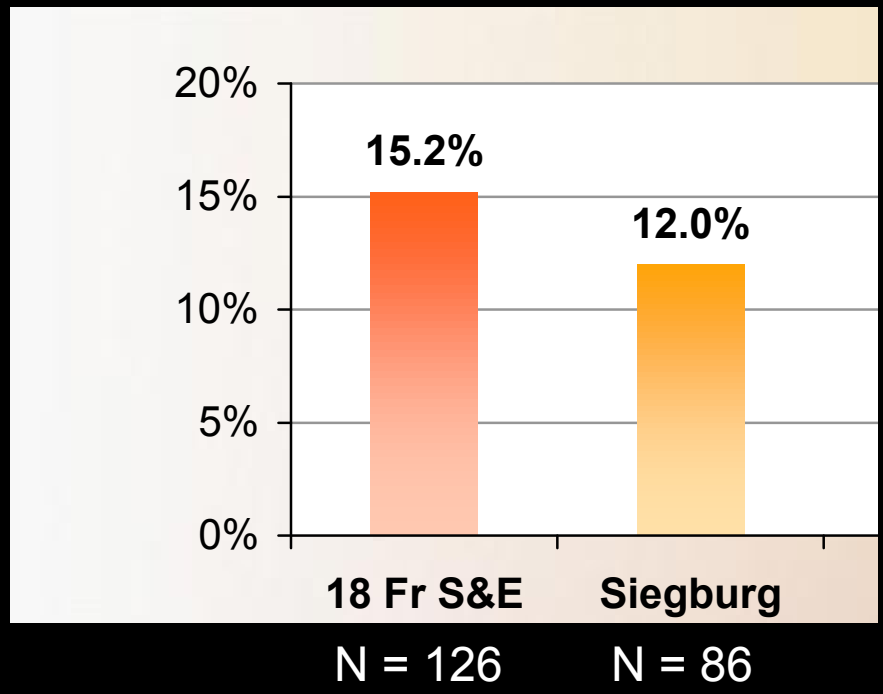
Procedural Success



Procedural success has markedly improved over time

Successful implant defined as no conversion to surgery or device-related mortality during the procedure and proper valve function immediately post-implant. The 18Fr S&E uses technical success (procedural success in re-adjudicated data was 72.6%).

30-Day All-Cause Mortality



30-day all-cause mortality has improved over time

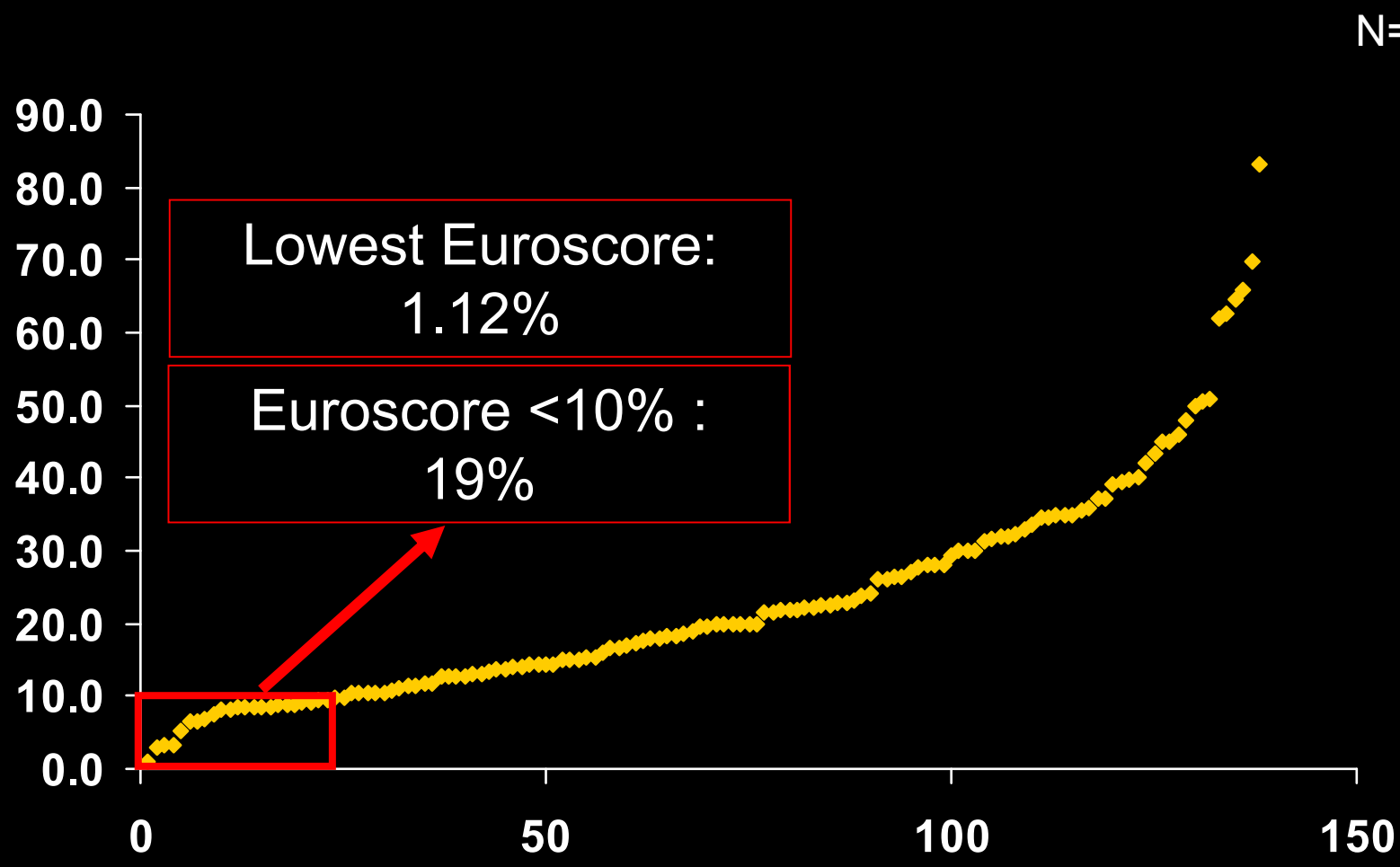
CoreValve Results
HELIOS Heart Center Siegburg

	25F	21F	18F **
Patients, (n)	10	24	102
Age (years±SD)	79.1±4.6	81.7±5.2	81.8±7.4
NYHA class III and IV, n (%)	10 (100)	23 (95.8)	97 (95.1)
Karnofsky index, mean±SD	33.3±7.1	40.7±11.5	44.9±12.4*
Logistic EuroSCORE, %, mean±SD	18.3±5.4	21.1±14.8	24.5±15.4*
STSscore — mortality,%, mean±SD	11.5±10.8	9.1±±.5	8.6±4.7
Left ventricular ejection fraction, %, mean±SD	51.2±15.8	52.8±17.5	51.0±17.3
Peak pressure gradient, mmHg, mean±SD	72.1±27.7	67.9±22.3	71.1±24.6
Mean pressure gradient, mmHg, mean±SD	45.8±20.4	42.2±17.5	41.6±16.4
Aortic valve area, cm2, mean±SD	0.70±0.14	0.74±0.24	0.64±0.18
Annulus diameter, mm	24.1±1.1	23.5±1.5	23.8±1.8
Aortic regurgitation (pre) 3+ and 4+, n (%)	0	1 (4.2)	2 (2.0)

*Significant difference 18F vs pooled 25/21F.**Statistic for the first 102 patient

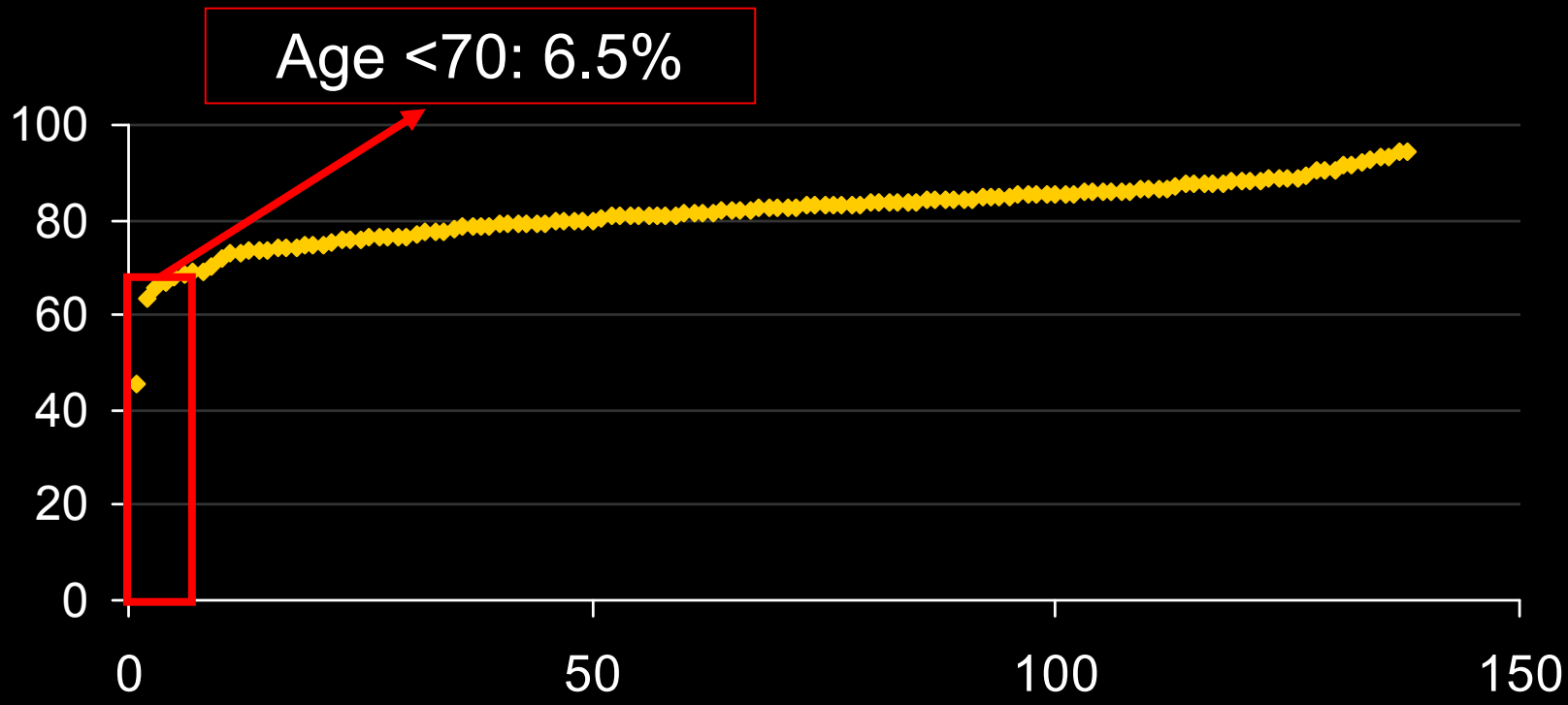
Grube E, Circ Cardiovasc Intervent 2008;1;167-175

EuroScore of CoreValve Implants 2005-2008
HELIOS Heart Center Siegburg



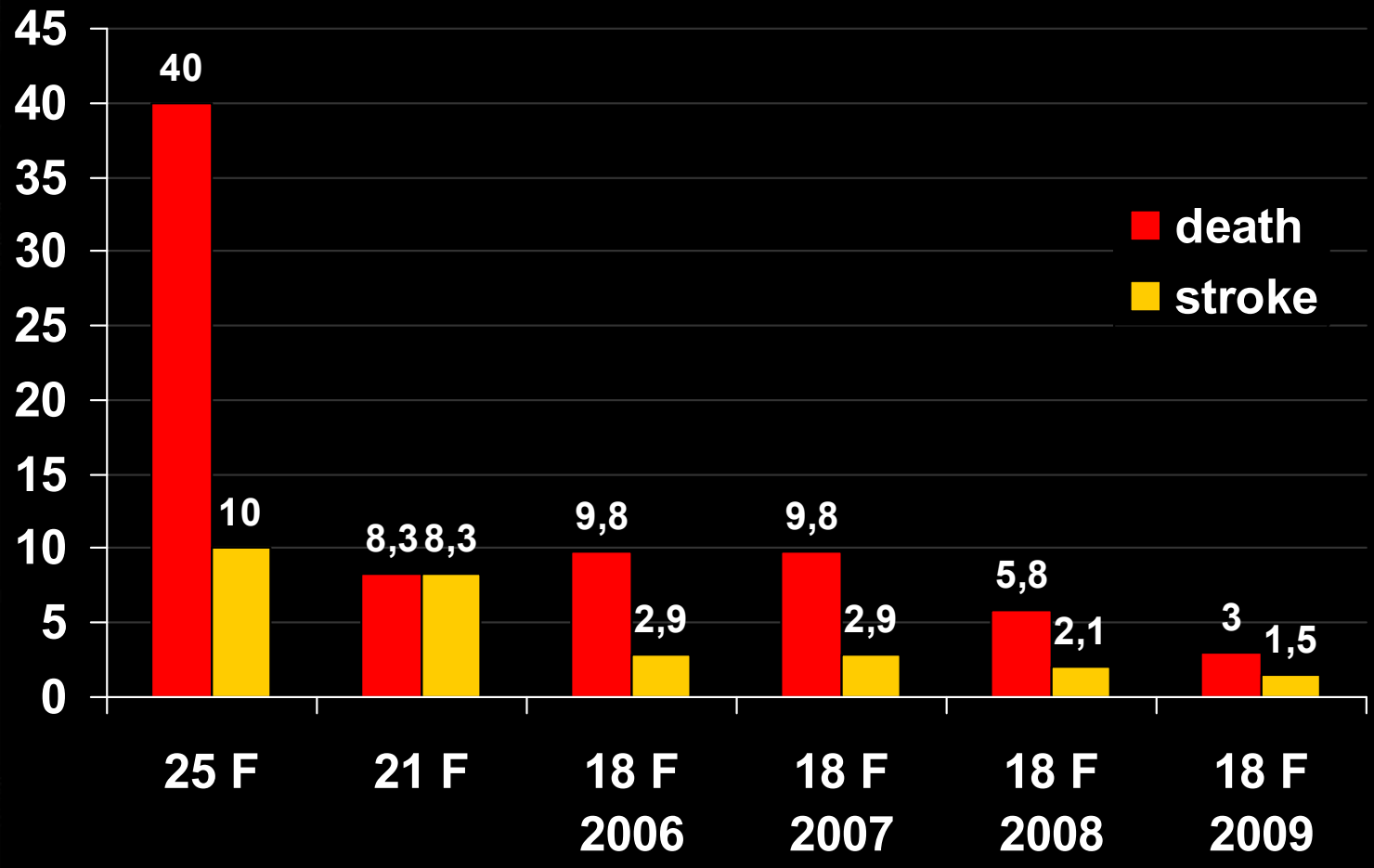
Age Distribution of CoreValve Patients 2006-2008
HELIOS Heart Center Siegburg

N=280



Youngest Pat:
45yrs

In-Hospital Clinical Outcome
HELIOS Heart Center Siegburg



CoreValve Results
HELIOS Heart Center Siegburg

	25 F	21 F	18 F initially	18 F 2008	18 F 2009
patient n	10	24	102	187	130
In-hospital					
Death, n (%)	4 (40.0)	2 (8.3)	10 (9.8)	11 (5.8)	4 (3.0)
Stroke, n (%)	1 (10.0)	2 (8.3)	3 (2.9)	4 (2.1)	2 (1.5)
Major, n (%)	1 (10.0)	0	1 (1.0)	3 (1.6)	1 (0.8)
Minor, n (%)	0	2 (8.3)	2 (2.0)	1 (0.5)	1 (0.8)
Myocardial infarction, n (%)	0	(4.2)	2 (2.0)	0	0
Pacemaker requiring, n (%)*	1 (10)	3 (13)	30 (33)	70 (37)	51 (39)

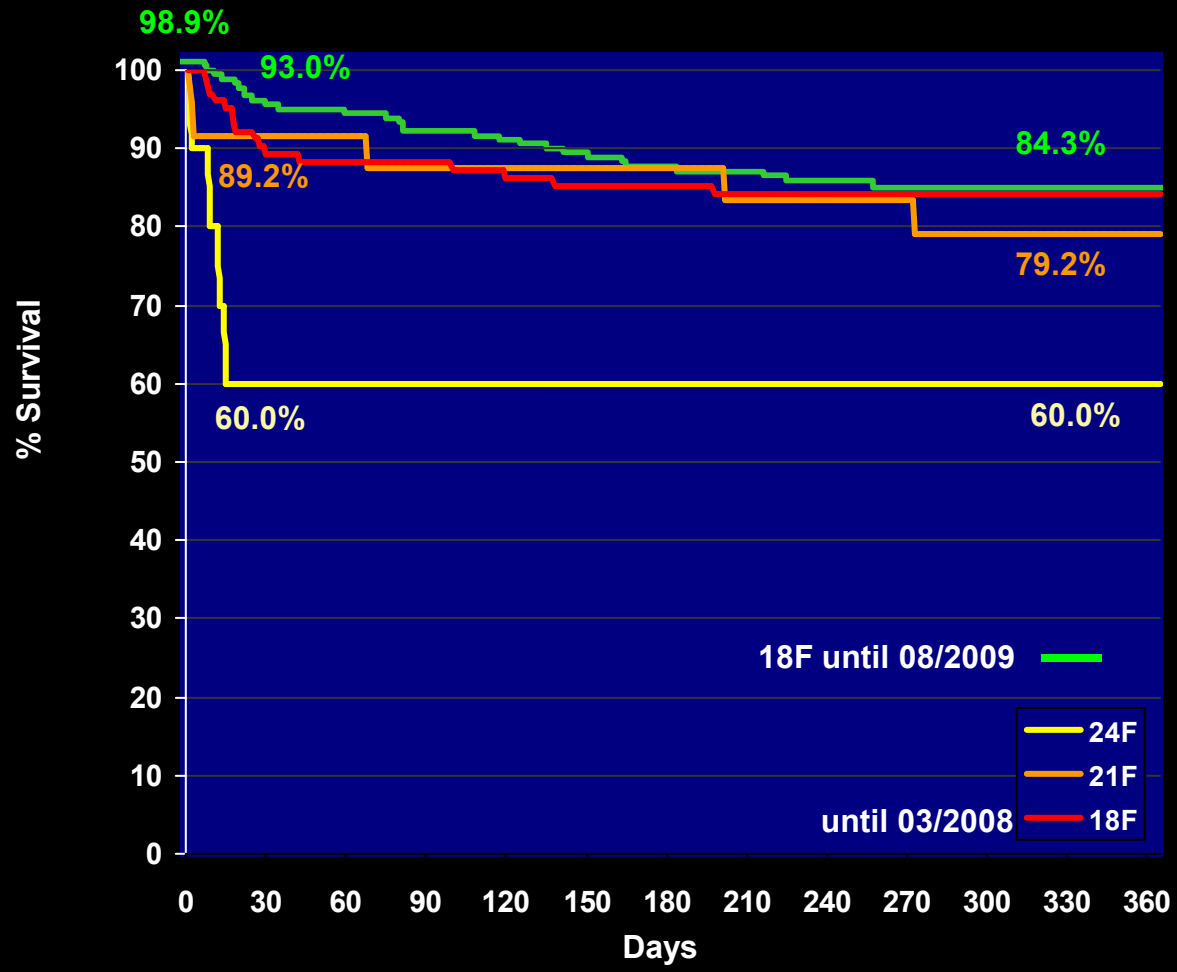
* In-hospital rate, based on patients without previous pacemaker

CoreValve Results
HELIOS Heart Center Siegburg

	25 F	21 F	18 F initially	18 F 2008	18 F 2009
patient n	10	24	102	187	130
30 days					
Death, n (%)	4 (40.0)	2 (8.3)	11 (10.8)	12 (6.3)	8 (6.1)
Stroke, n (%)	1 (10.0)	2 (8.3)	3 (2.9)	4 (2,1)	2 (1,5)
Major, n (%)	1 (10.0)	0	1 (1.0)	3 (1,6)	1 (0,8)
Minor, n (%)	0	2 (8.3)	2 (2.0)	1 (0,5)	1 (0.8)
Myocardial infarction, n (%)	0	1 (4.2)	2 (2.0)	0	0

CoreValve Clinical Results
HELIOS Heart Center Siegburg

Survival Curves up to 1 year



Inclusion Criteria

Study Criteria become Real World Criteria?

Morphological Criteria: (Mandatory)

- Native Aortic Valve Disease
- Severe AS: AVAI ≤0.6 cm^2/m^2
- 27mm ≥AV annulus ≥20mm
- Sino-tubular Junction ≤43mm

Clinical Criteria:

Logistic EuroSCORE ≥20% (21F)
≥15% (18F)

Age ≥80 y (21F)
≥75 y (18F)

Age ≥65 y plus 1+ of the following:

- Liver cirrhosis (Child A or B)
- Pulmonary insufficiency: FEV1<1L
- Previous cardiac surgery
- PHT (PAP>60mmHg)
- Recurrent P.E's
- RV failure
- Hostile thorax (radiation, burns,etc)
- Severe connective tissue disease
- Cachexia

ReDo implantation of Medtronic CoreValve

- Surgical prosthesis acts as landing zone (metallic ring)
- But sometimes no anatomical landmarks available

  1. stentless previous valve
  2. no leaflet calcification

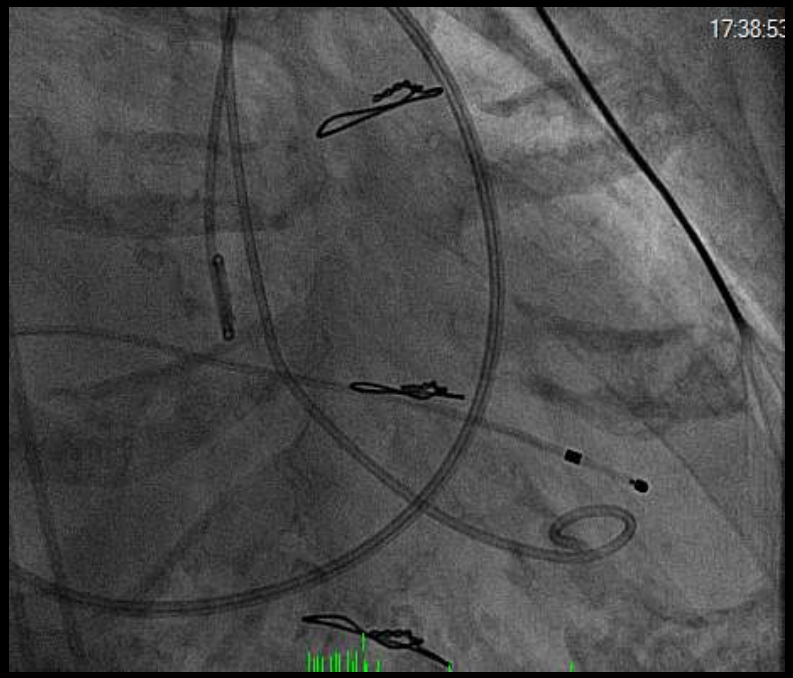
- Measurements

internal diameter >19 mm	per manufacture (also CT measured)
(thickened leaflets??→ >20 mm)	
ascending aorta width ≤40 mm	CT measured
annulus plane to aorta, angle <45	the plane of the native valve does not correspond to the orientation of the prosthetic valve

ReDo implantation of Medtronic CoreValve

Angio
Example of
no anatomical landmarks
as landing zone
ie

1. no calcium
2. stentless previous valve



ReDo implantation of Medtronic CoreValve

annulus plane to aorta

angle <45

but

the plane

of the native valve

does not correspond

to the plane

of the prosthetic valve

Case Example: Medtronic CoreValve in Degenerated Aortic Bioprosthesis

Age/Gender: **70 years, male**

Medical History:

1994 CABG
(LIMA-LAD,SVG-D1,SVG-RCA, SVG-LPL)

1999 Severe aortic stenosis – bioprosthesis

2001 PM DDD

2006 PTCA/DES RCA
+ severe degeneration of bioprosthesis

Cardiac Risk Factors:

- **Hypertension**
- **Hyperlipidemia**

Reason for Admission:
Dyspnea (NYHA IV)

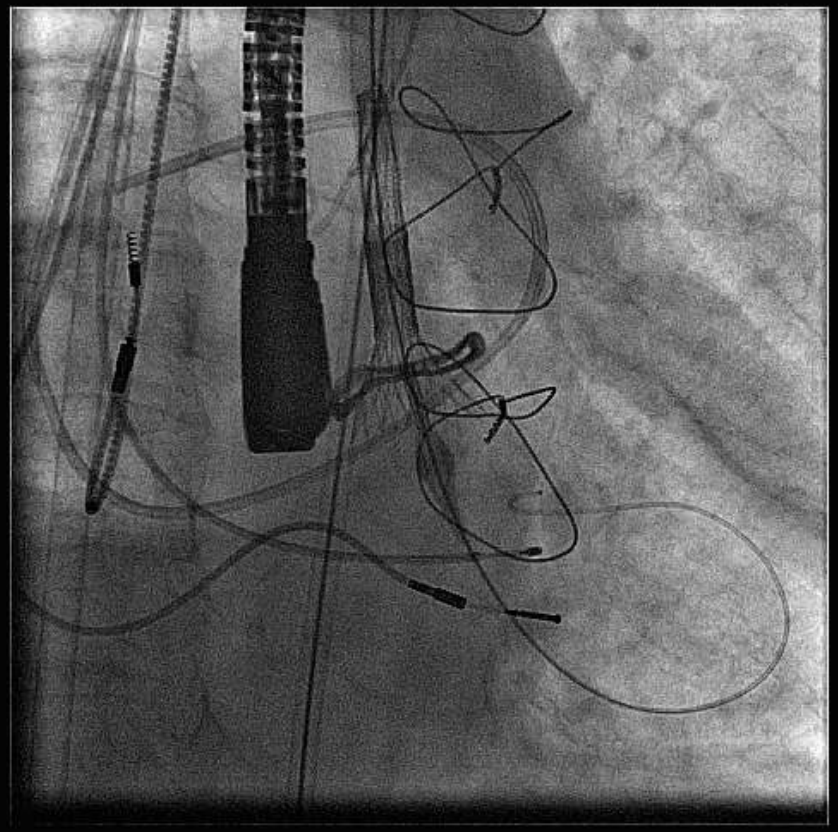
Case Example: Medtronic CoreValve in Degenerated Aortic Bioprosthesis

TEE

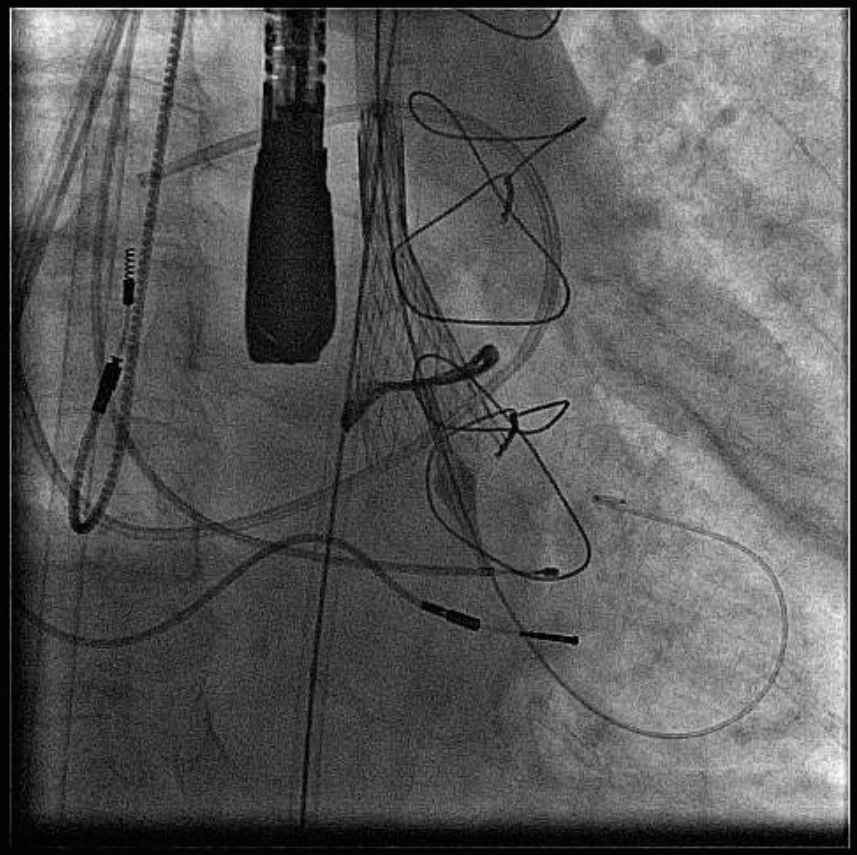
- *Aortic Bioprosthesis*
- *AI 3+/4+*
- *Gradient max/mean 25/12 mmHg*
- *Pulmonary hypertension, PAP 70 mmHg*

Logistic EuroSCORE: *45.4%*

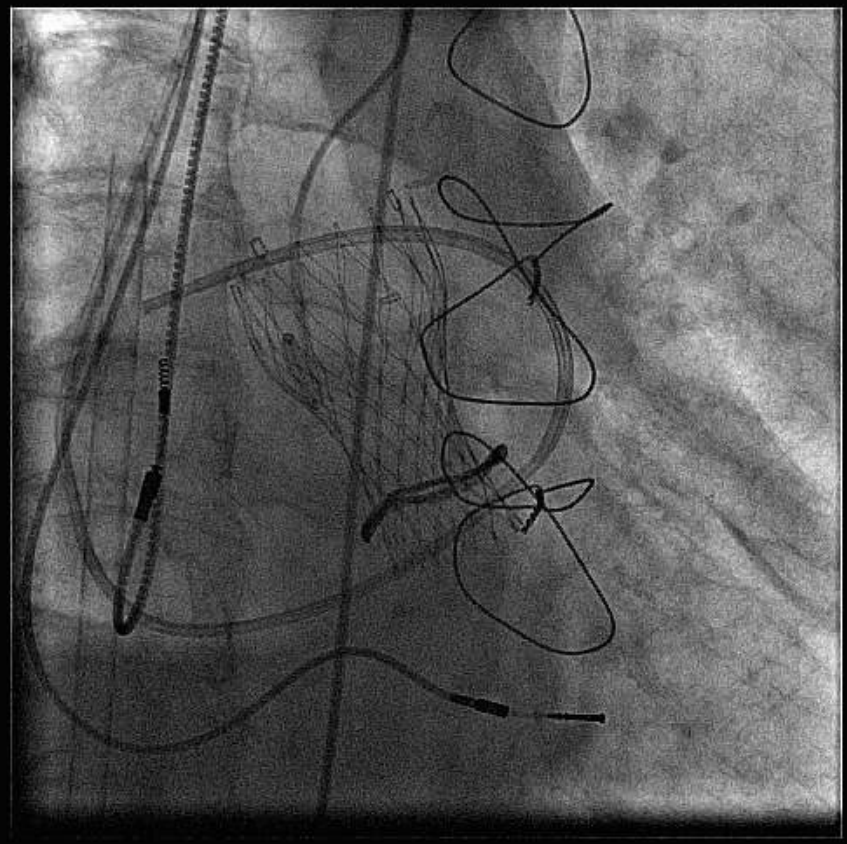
Medtronic CoreValve deployment inside degenerated prosthesis



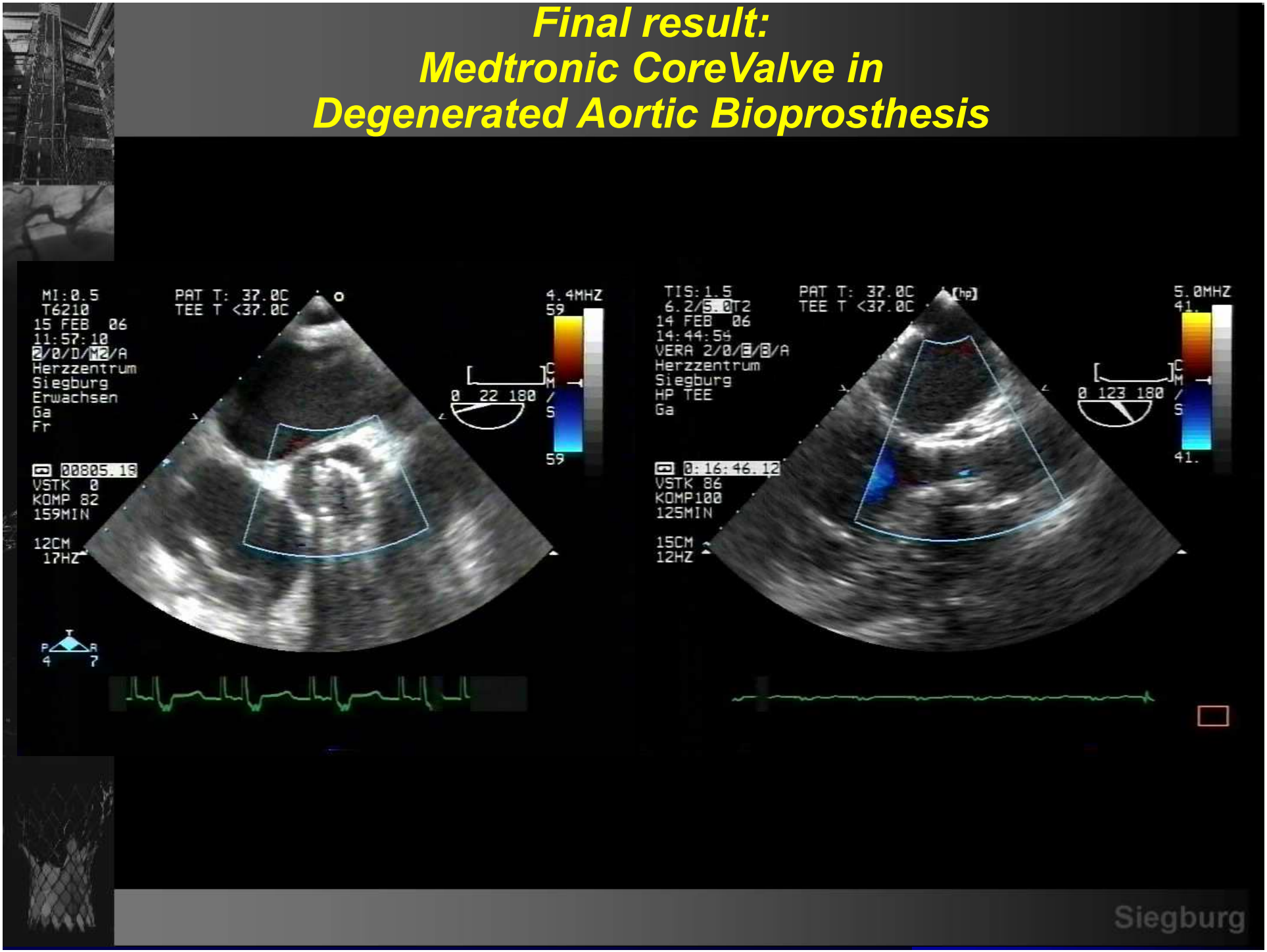
Medtronic CoreValve deployment inside degenerated prosthesis



Final result



Final result: Medtronic CoreValve in Degenerated Aortic Bioprosthesis



Medtronic CoreValve Revalving Prosthesis for Degenerated Bioprosthesis

ReDo Registry
(19 patients)
Until June. 2009

ReDo Patient Demographics

	Mean ± SD or %
Age (years)	79.9 ± 7.6
Logistic EuroSCORE (%)	28.5 ± 13.6
Female	47.4%
NYHA	I-II: 10.5% III-IV: 89.5%
Aortic Valve Area (cm^2)	0.90 ± 0.35
Peak gradient (mm Hg)	63.9 ± 25.3
Mean gradient (mm Hg)	36.3 ± 21.7
LVEF (%)	52.6 ± 11.4

Types of Previous Implants

Stented Valves

- Biocor (25 mm)
- Sorin Soprano (20 mm)
- Carpentier-Edwards (21-27 mm)
- Edwards Supra-Annular (20 mm)

Stentless Valves

- Sorin Freedom & Solo
- Cryolife O'Brien
- Homograft

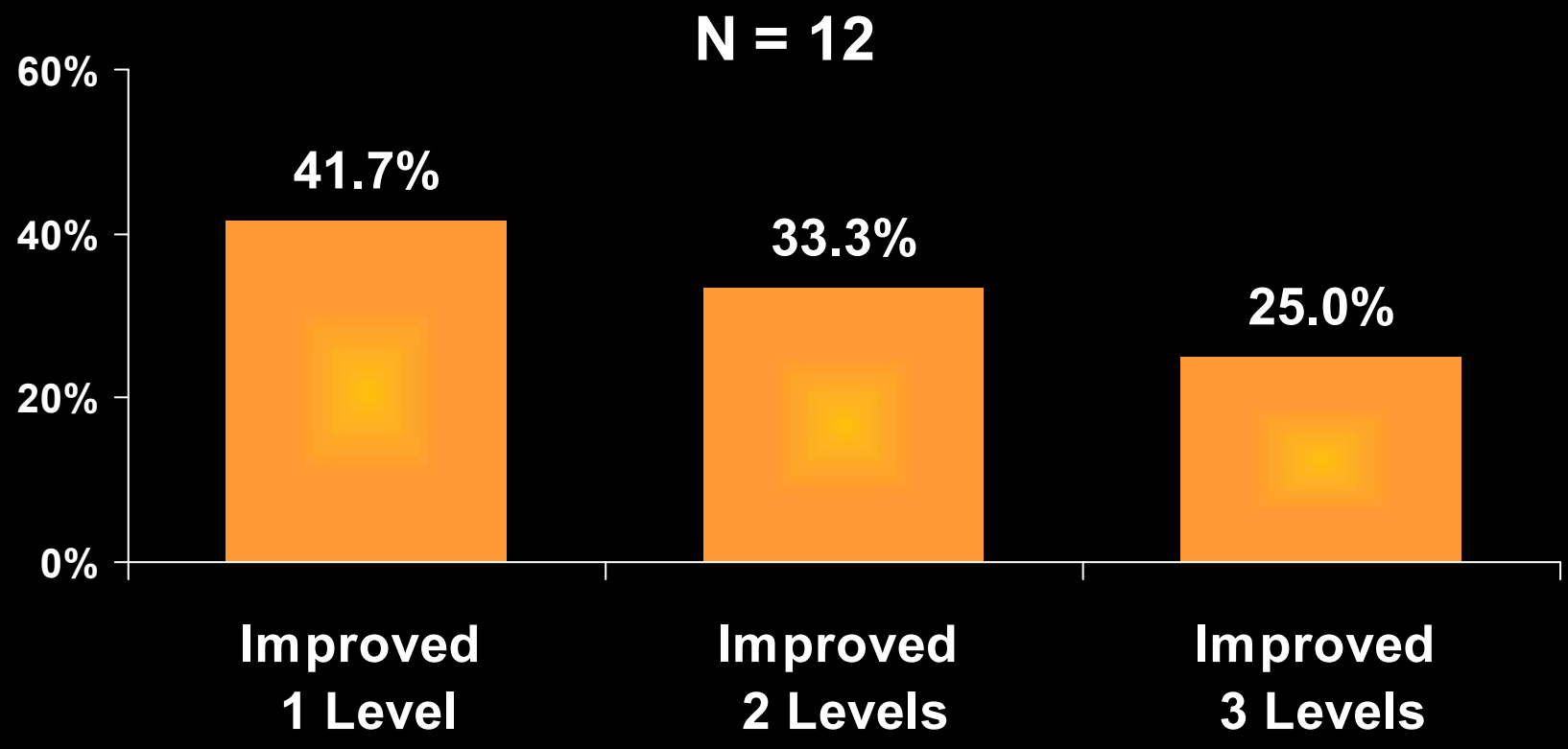
ReDo Procedural Outcomes

Procedural Success:	100.0% (19/19)
Procedural Mortality:	0.0% (0/19)
30-Day Mortality:	0.0% (0/19)

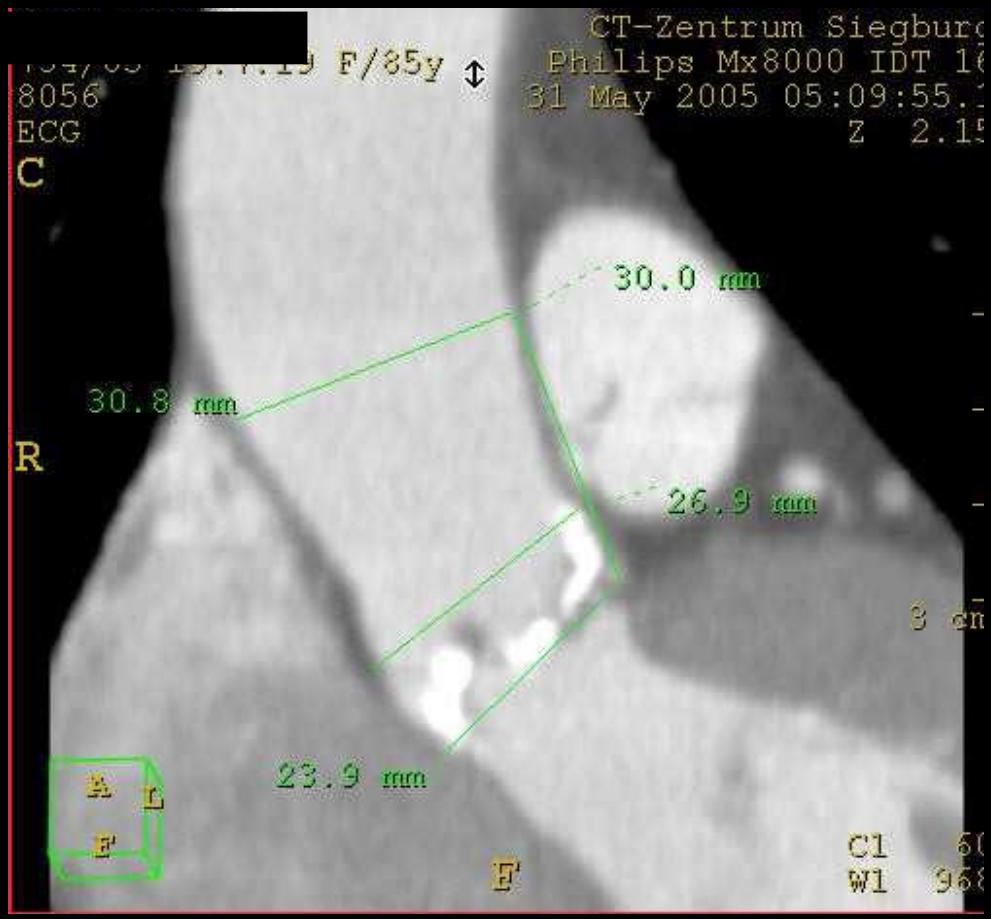
30-Day AEs*

Permanent Pacemaker:	(3/19)
Cardiac Tamponade:	(1/19)

Paired NYHA Comparison
Baseline to 30-Day Follow-Up



CT Screening for Morphologic Quantification



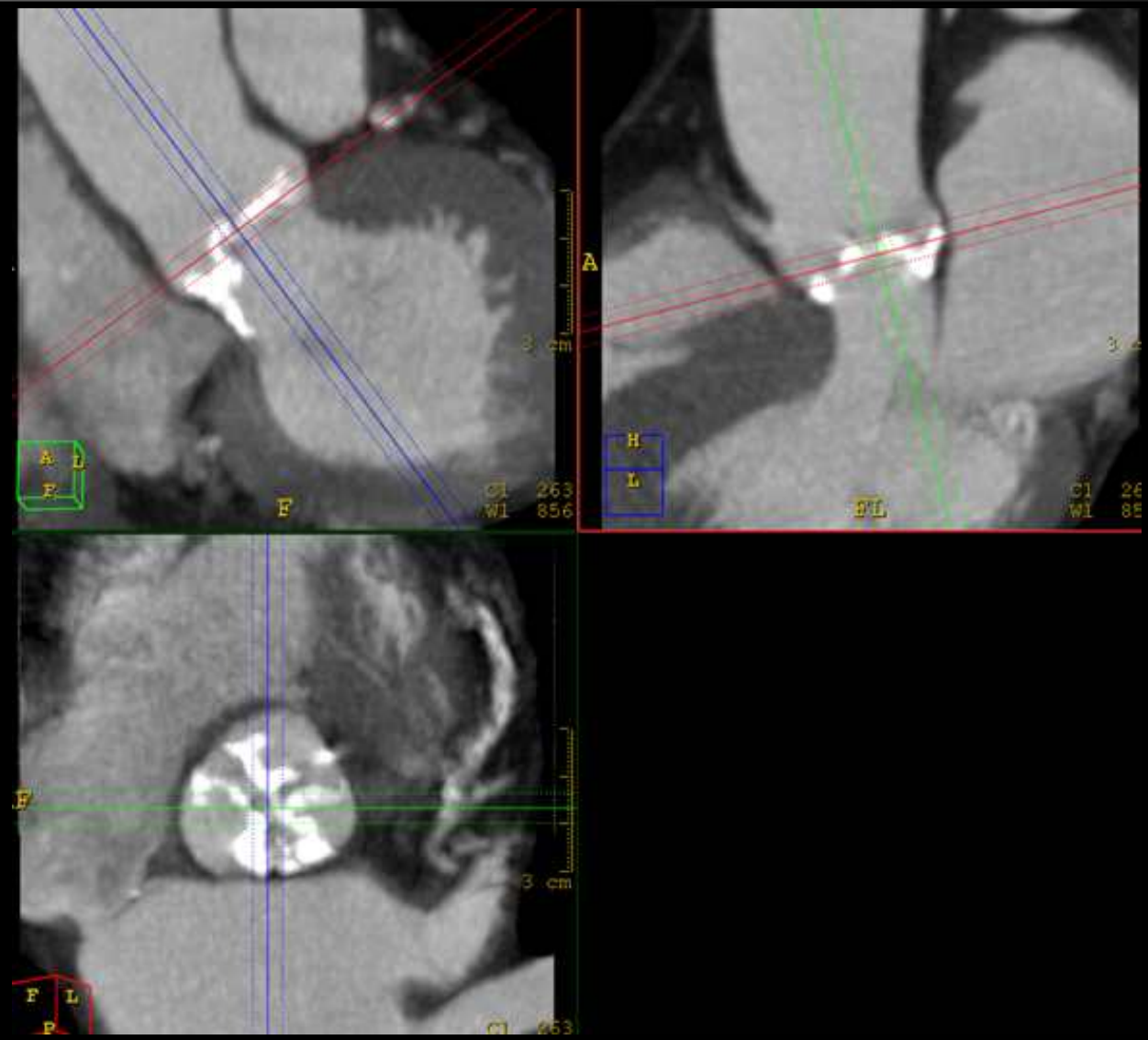
Precise screening due to

- limited amount of artifacts

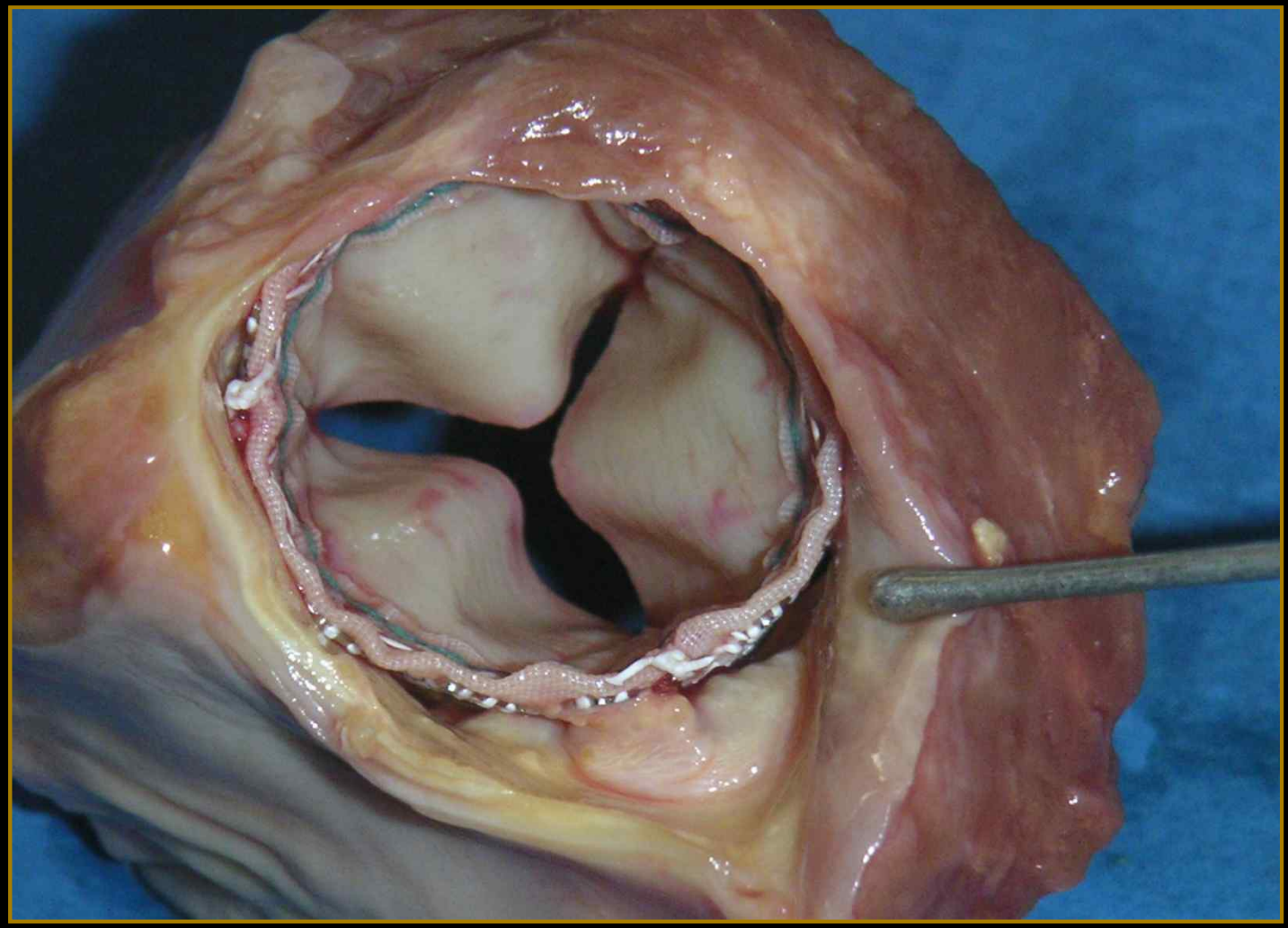
- ability for 3D reconstruction

- good resolution

Multiplanar CT Reconstruction of Correct Annulus Plane

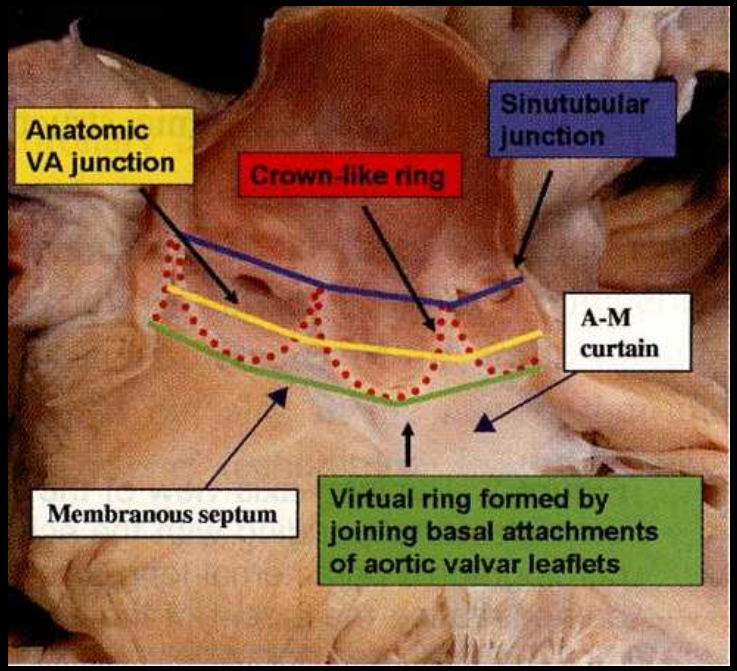


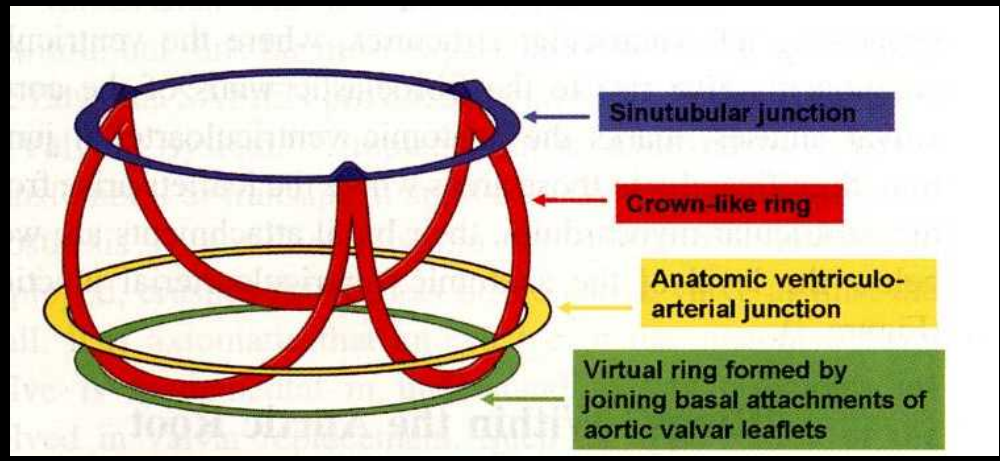
Para-Valvular Regurgitation



The Aortic Valvar Complex

Complex anatomic relationships



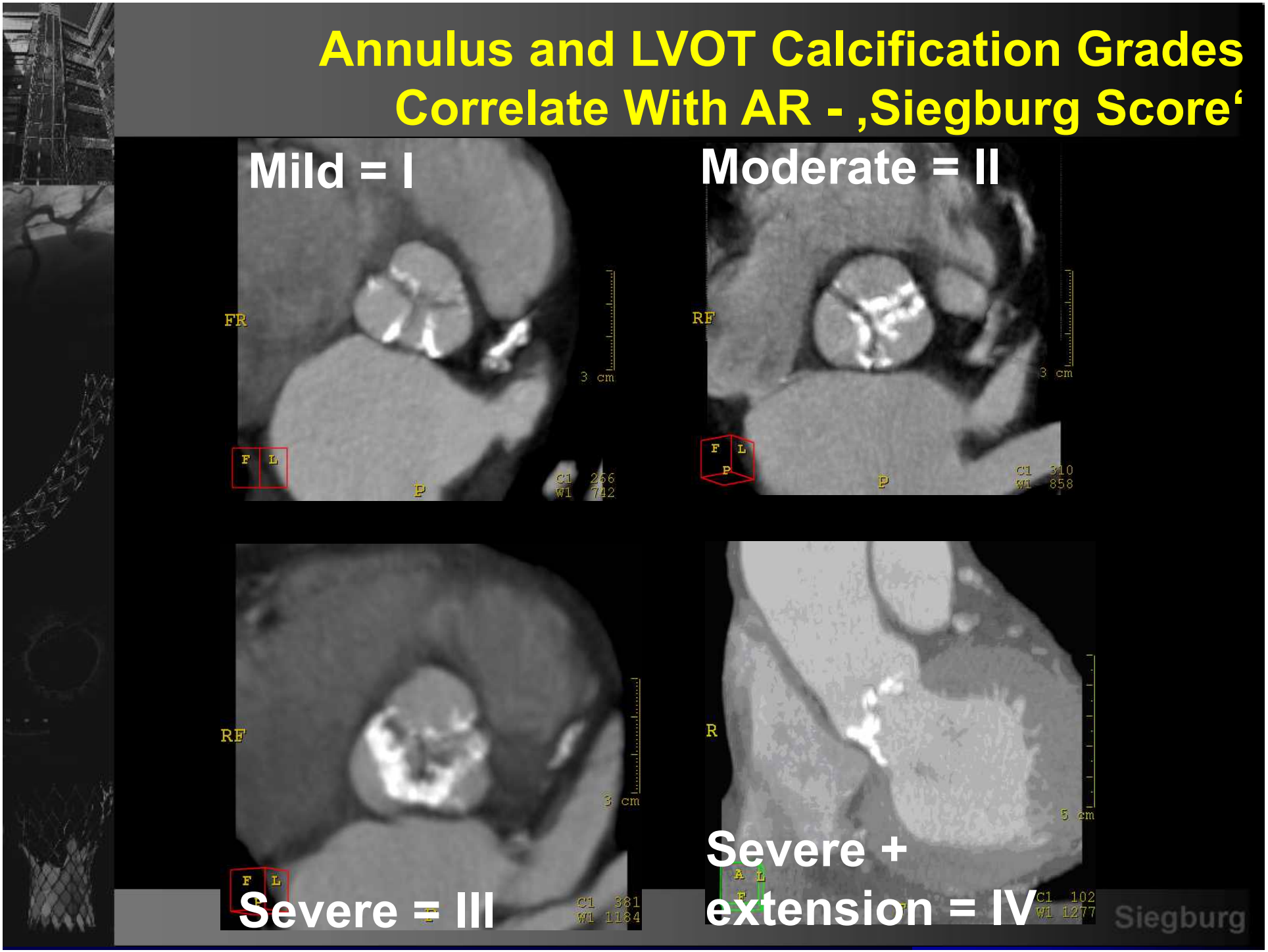


Diseased aortic valve leaflets in close proximity to…

- *aortic root (annulus)*
- *coronary ostia*
- *sinuses of Valsalva*
- *anterior mitral leaflet*
- *membranous septum (AVN)*
- *LV outflow tract*

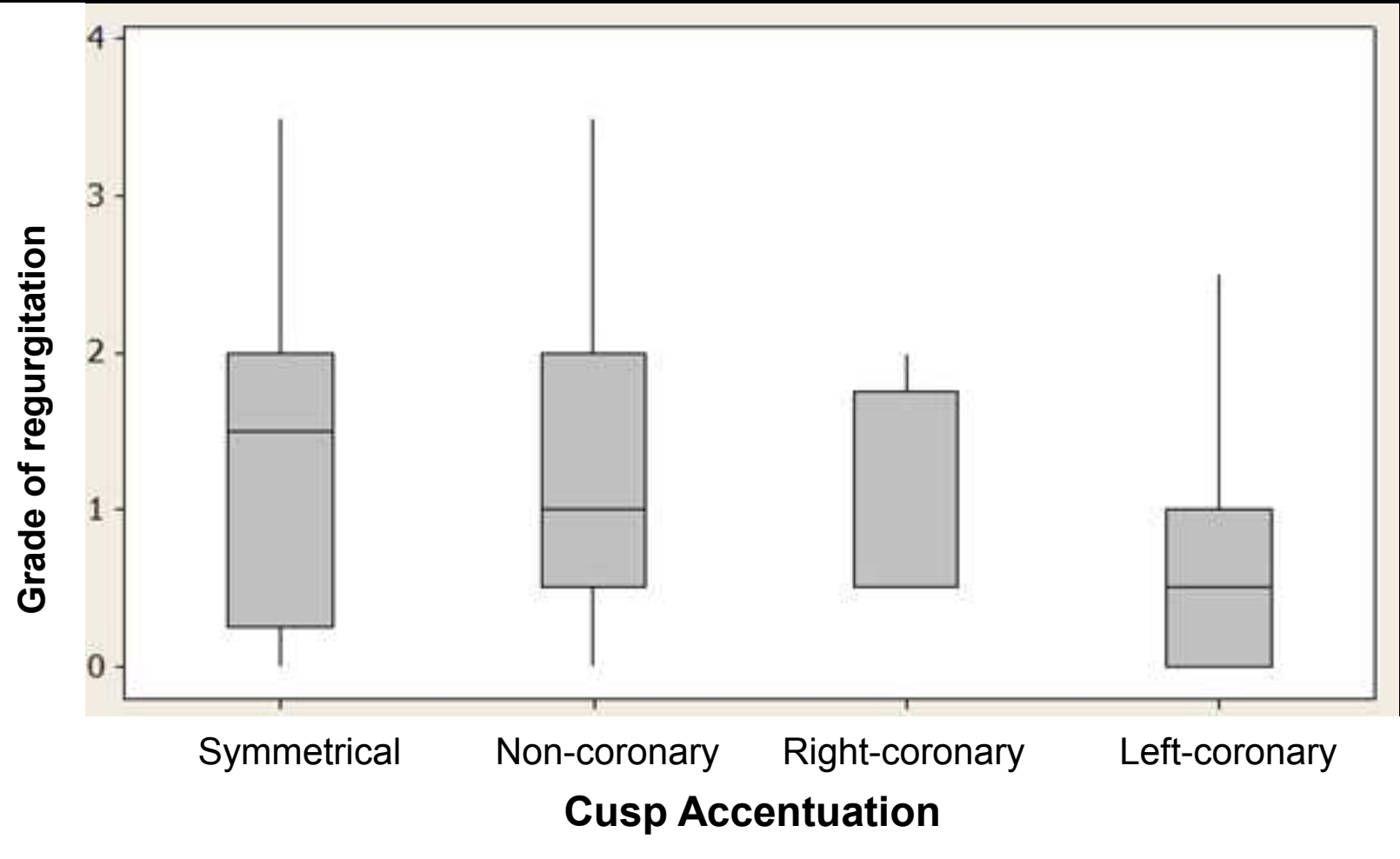
Piazza et al, *Circ Cardiovasc Intervent*. 2008;1:74-81

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



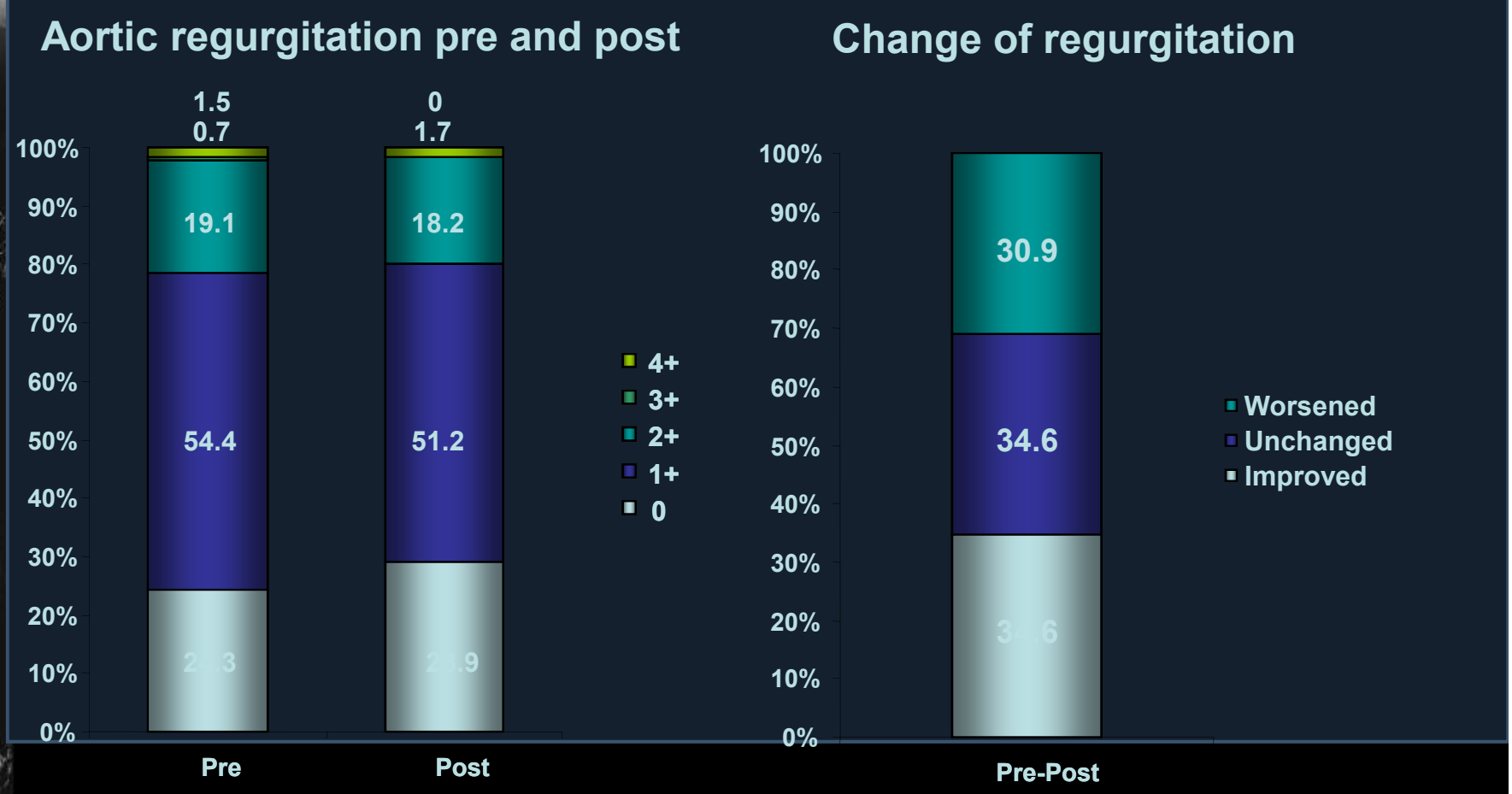
Association of Regurgitation and Distribution of Calcifications

N = 100 pts; TAVI with 3rd Gen CoreValve; Calcification assessed by MSCT, single-center (HELIOS Heart Center Siegburg)



Publication in progress

CoreValve Siegburg Experience
Aortic Regurgitation

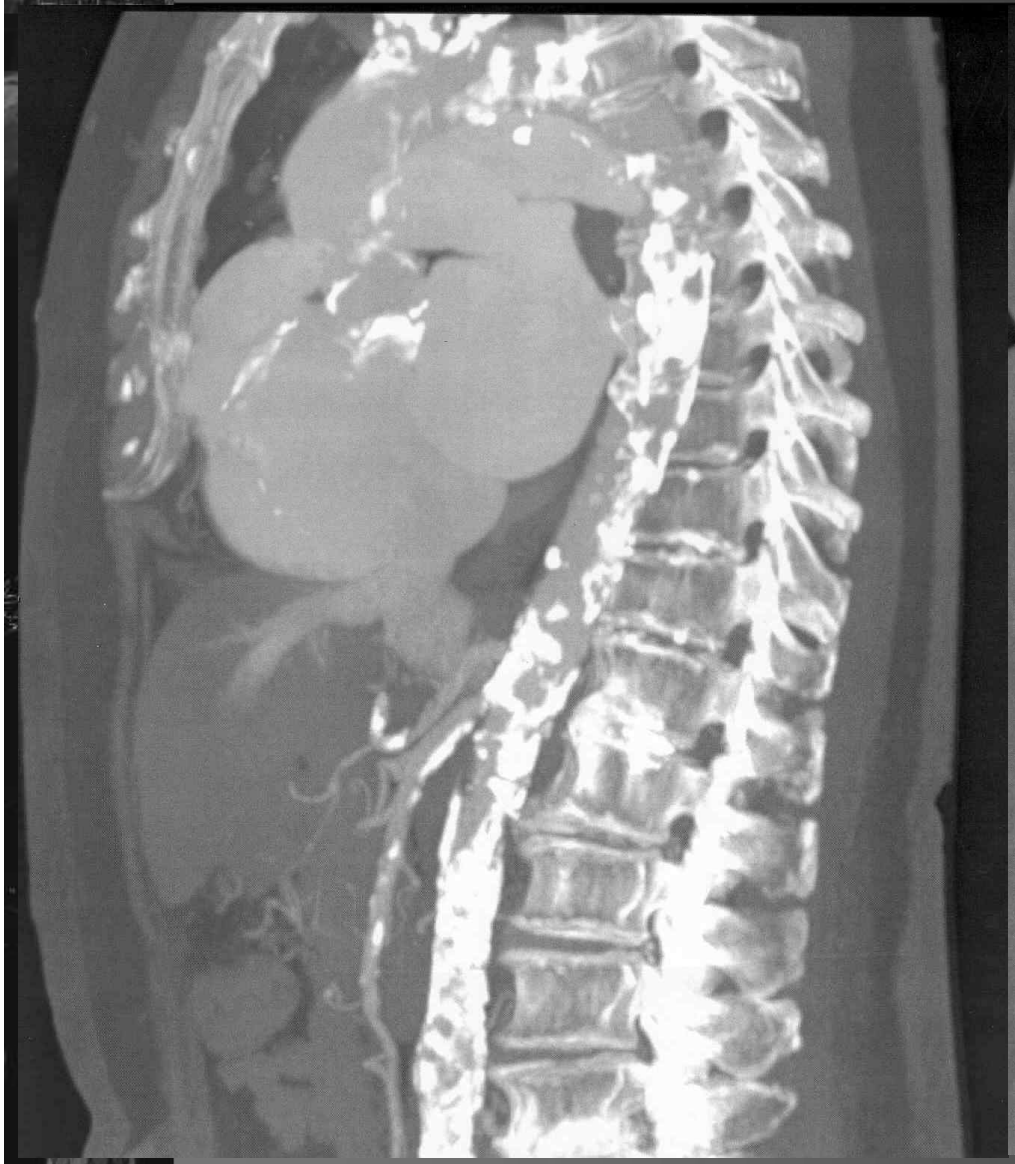


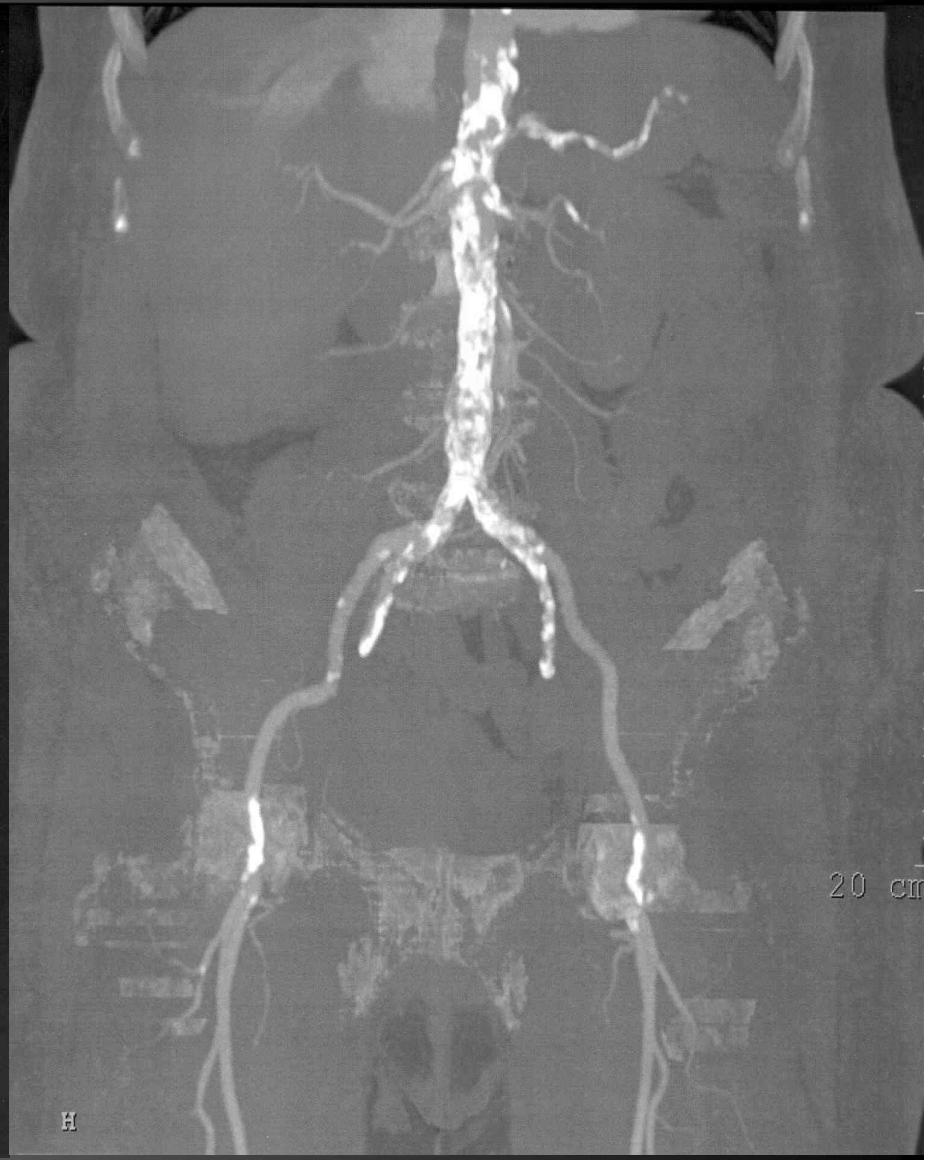
Grube E, et al. Circ Cardiovasc Intervent 2008;1:167-75.

Siegburg

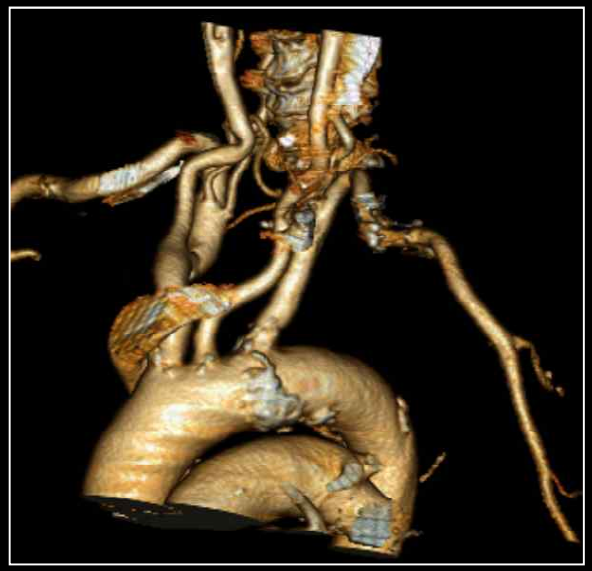
CoreValve – The Unsuitable Patient

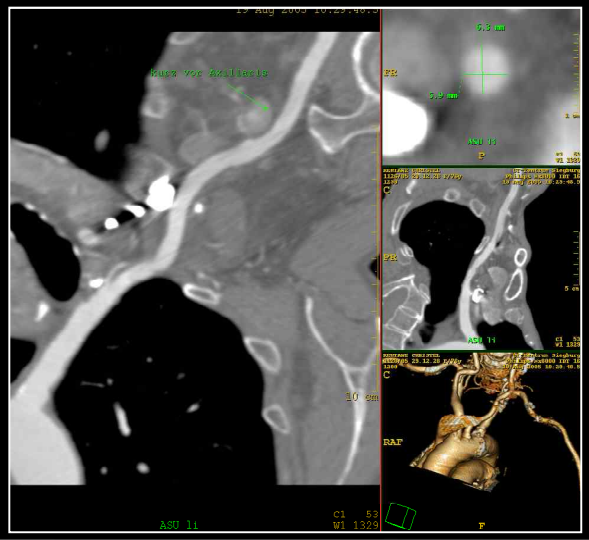
Severe Calcifications of the Access



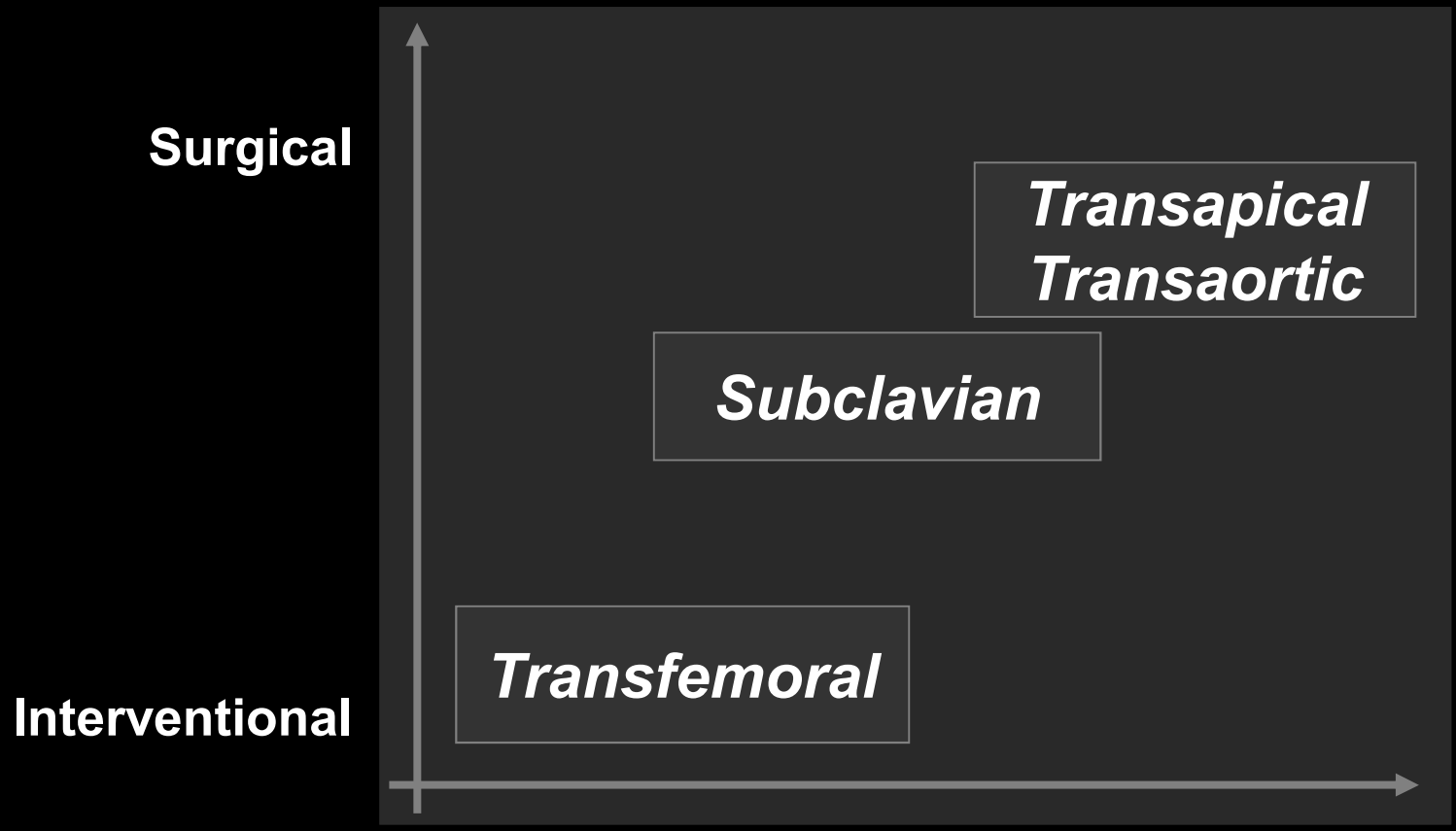


Alternative access sites
Subclavian Approach

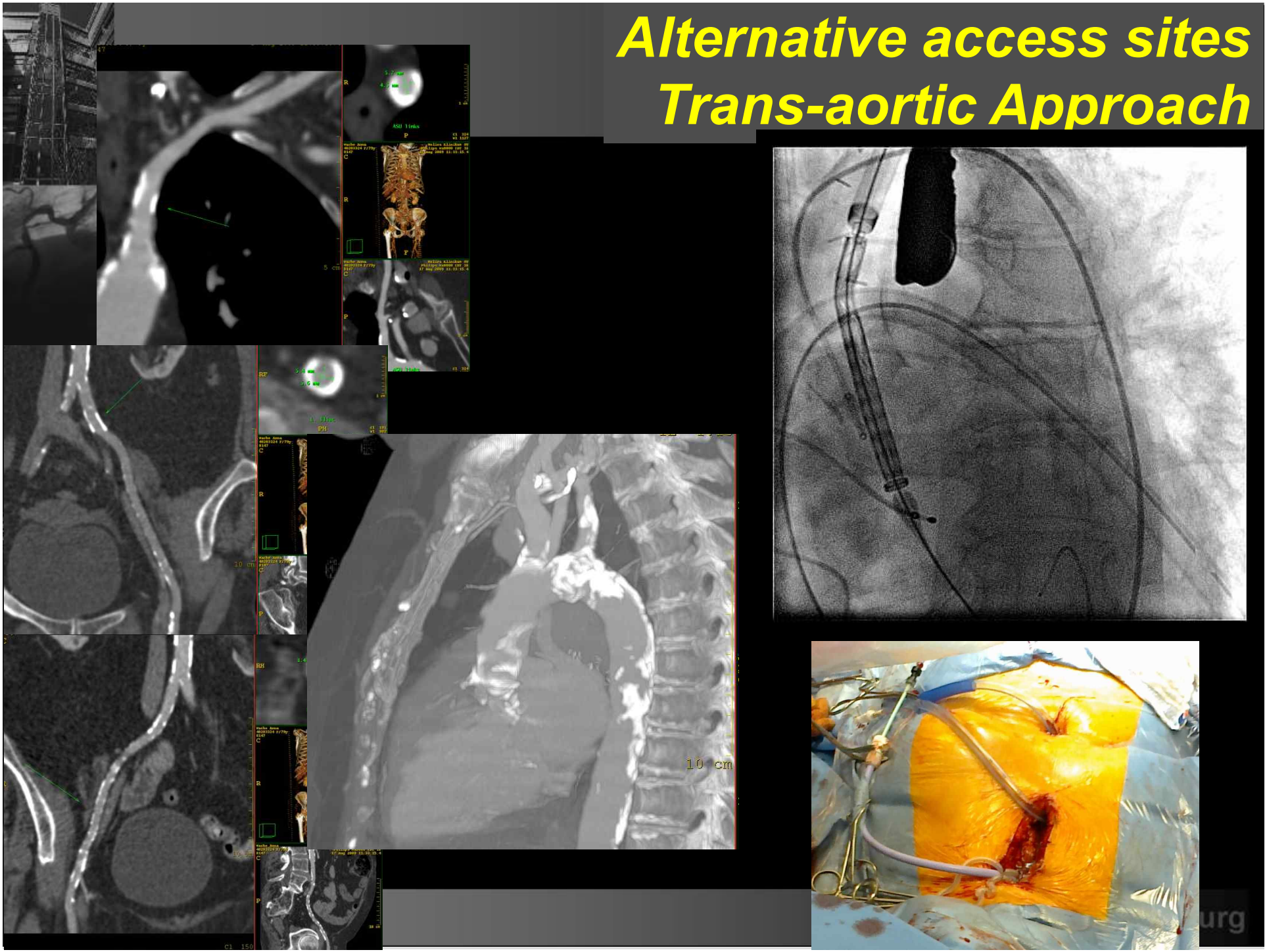




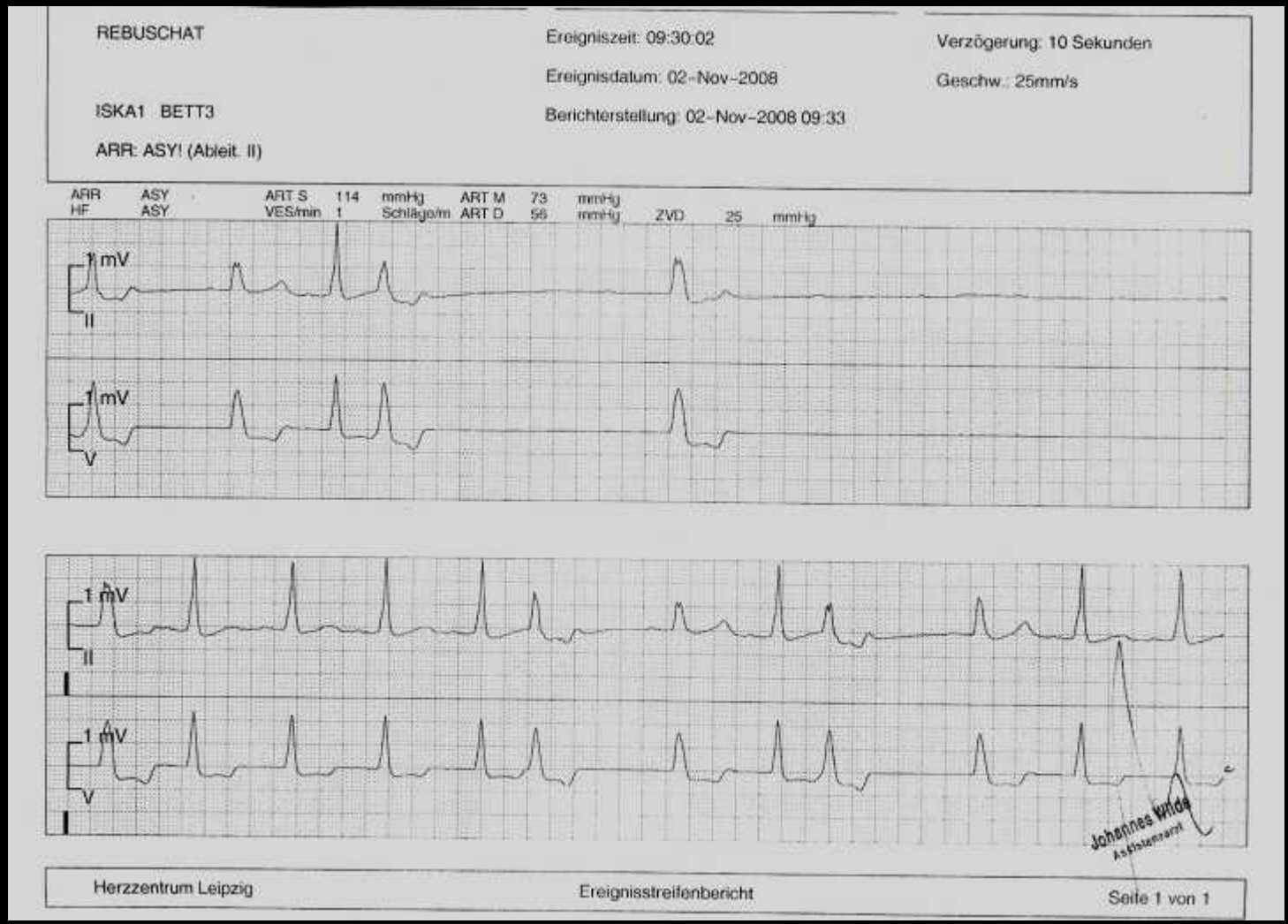
Which is the preferred access?



Alternative access sites
Trans-aortic Approach

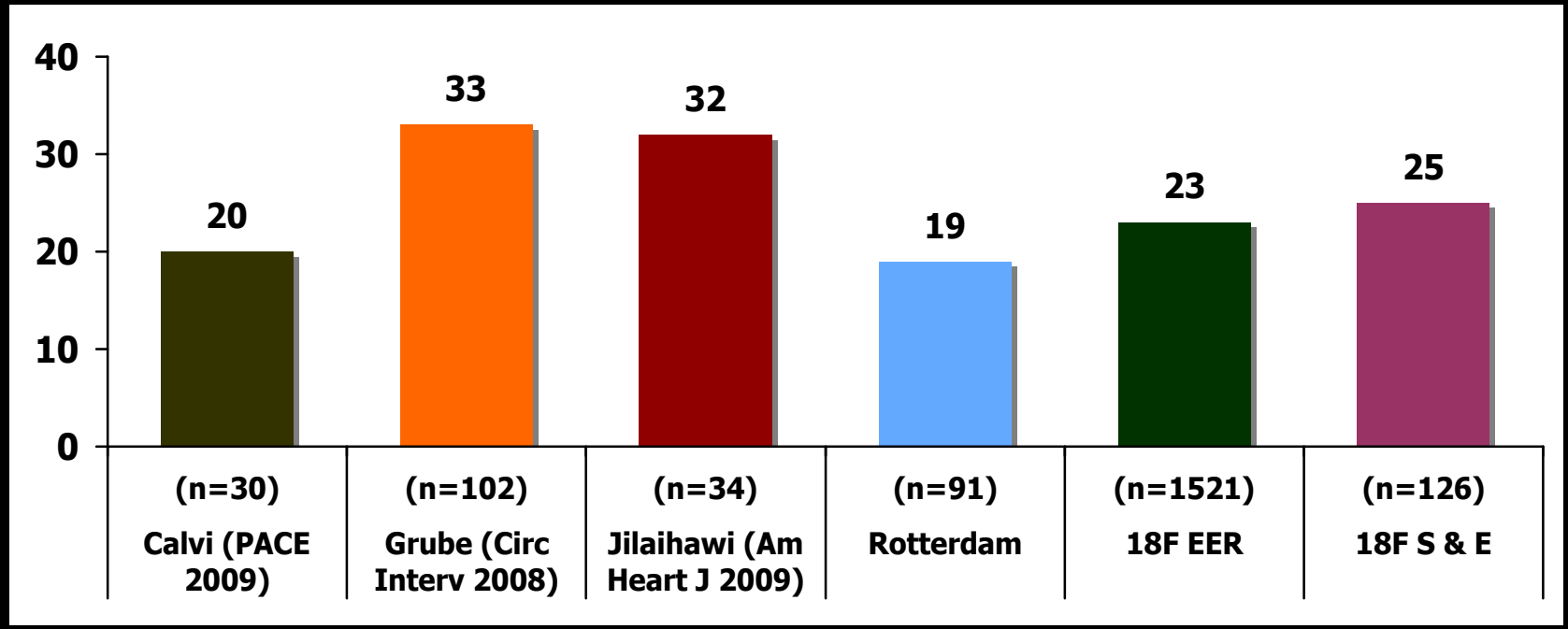


AV-Block III° Following COREVALVE Implantation



There Is a Higher Incidence of Pacemaker Implant Associated with CoreValve

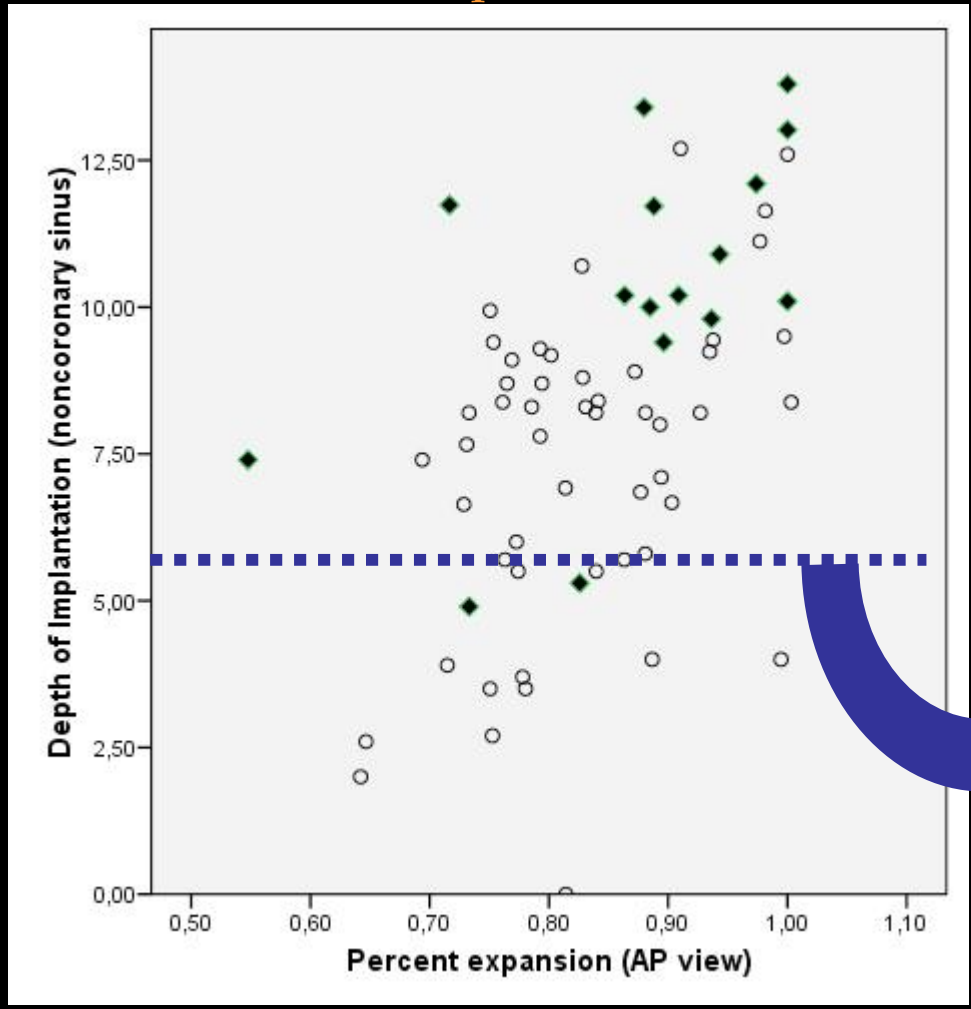
New Permanent Pacemaker within 30 Days



Weighted average = 23%
(n=1990 patients)

Depth of Implantation May Play a Role in the Onset of Rhythm Disturbances

Rotterdam Experience (n=91)



◆ New-onset LBBB acquired during or after valve implantation

10.3 mm

○ No new-onset LBBB or new-onset LBBB acquired during procedure but before valve implantation

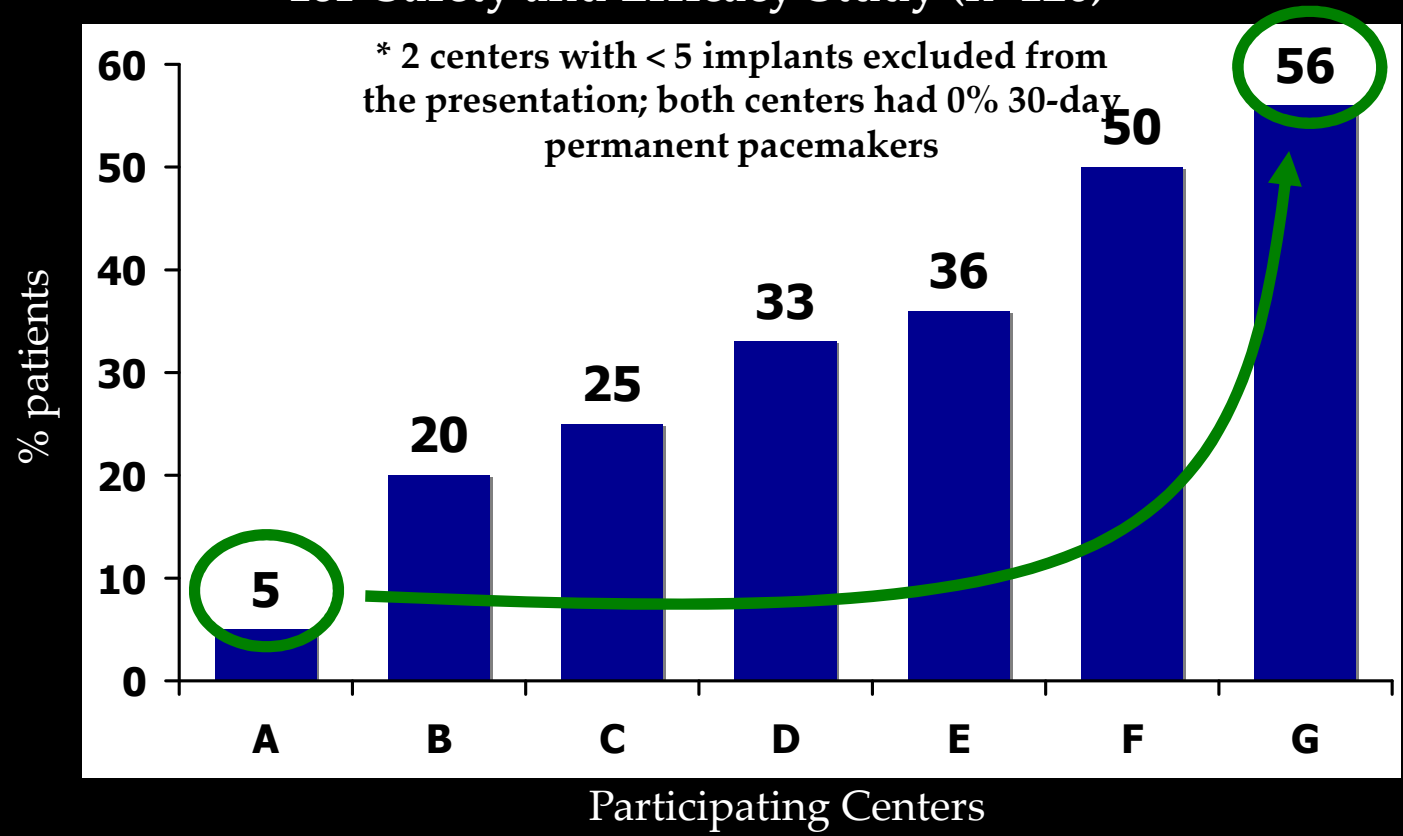
7.3 mm

6.0 mm

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

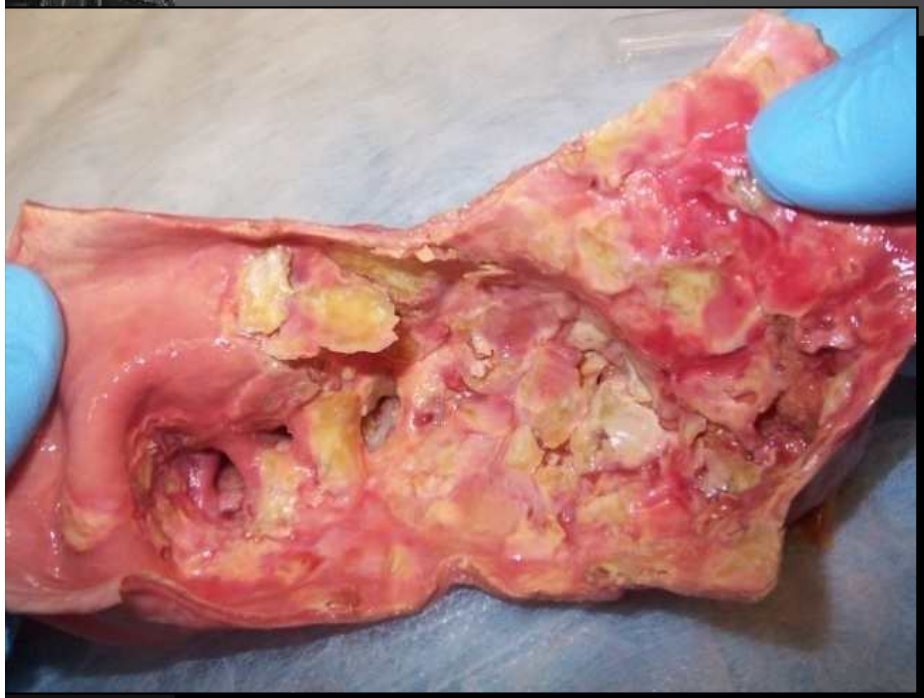
New Permanent Pacemaker within 30 Days

18F Safety and Efficacy Study (n=126)



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

Aortic Atheroma: High Risk



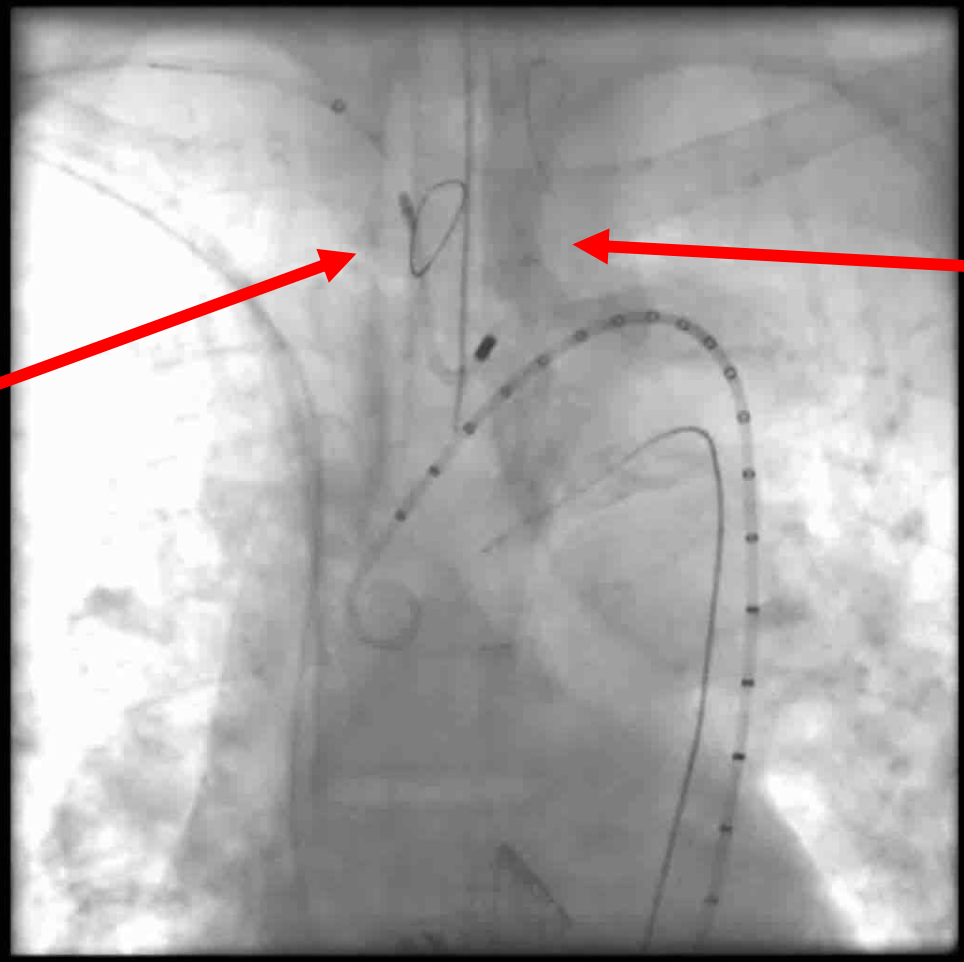
- 268 of 3404 CABG patients (8%) had
- atheroma (>/= 5 mm, or mobile)
- Defined by epi-aortic ultrasound[1]
- 15.3% of group had intra-operative stroke[1]

[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]

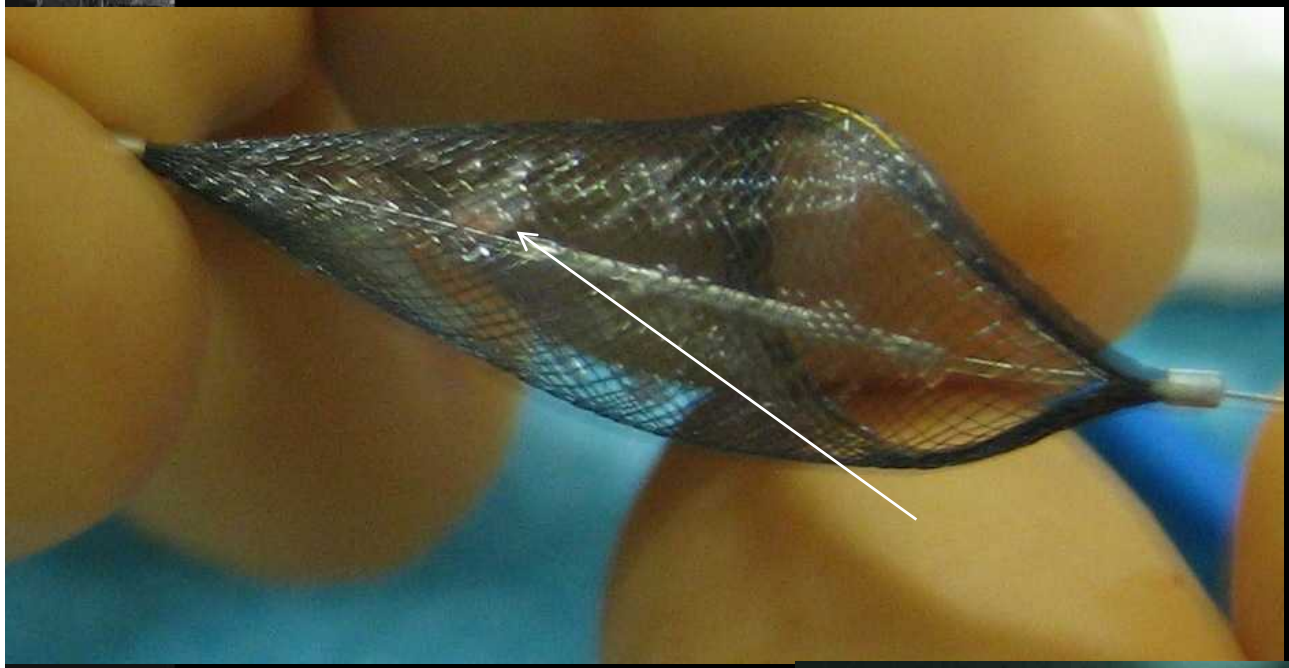
Cerebral Filter Protection
Claret



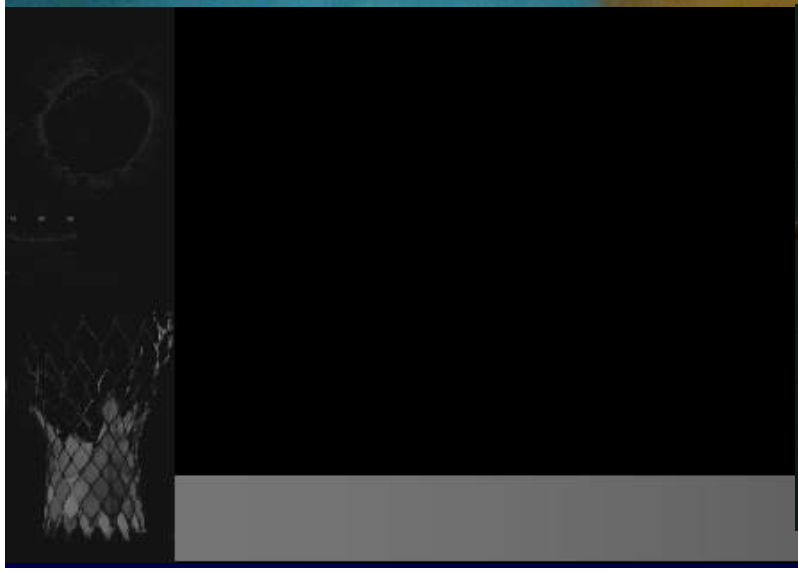
Filter in Truncus

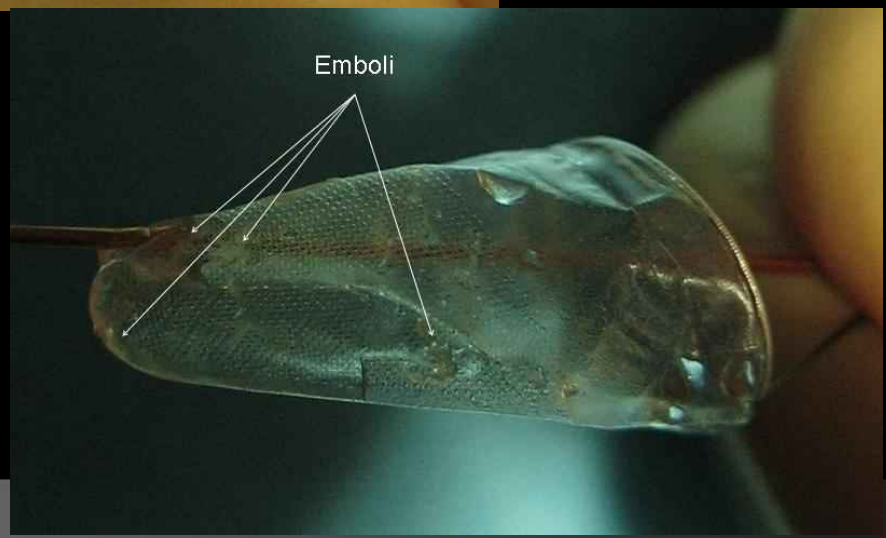
Filter in left Carotid

Claret Dual Filter



7 mm filter placed in left carotid

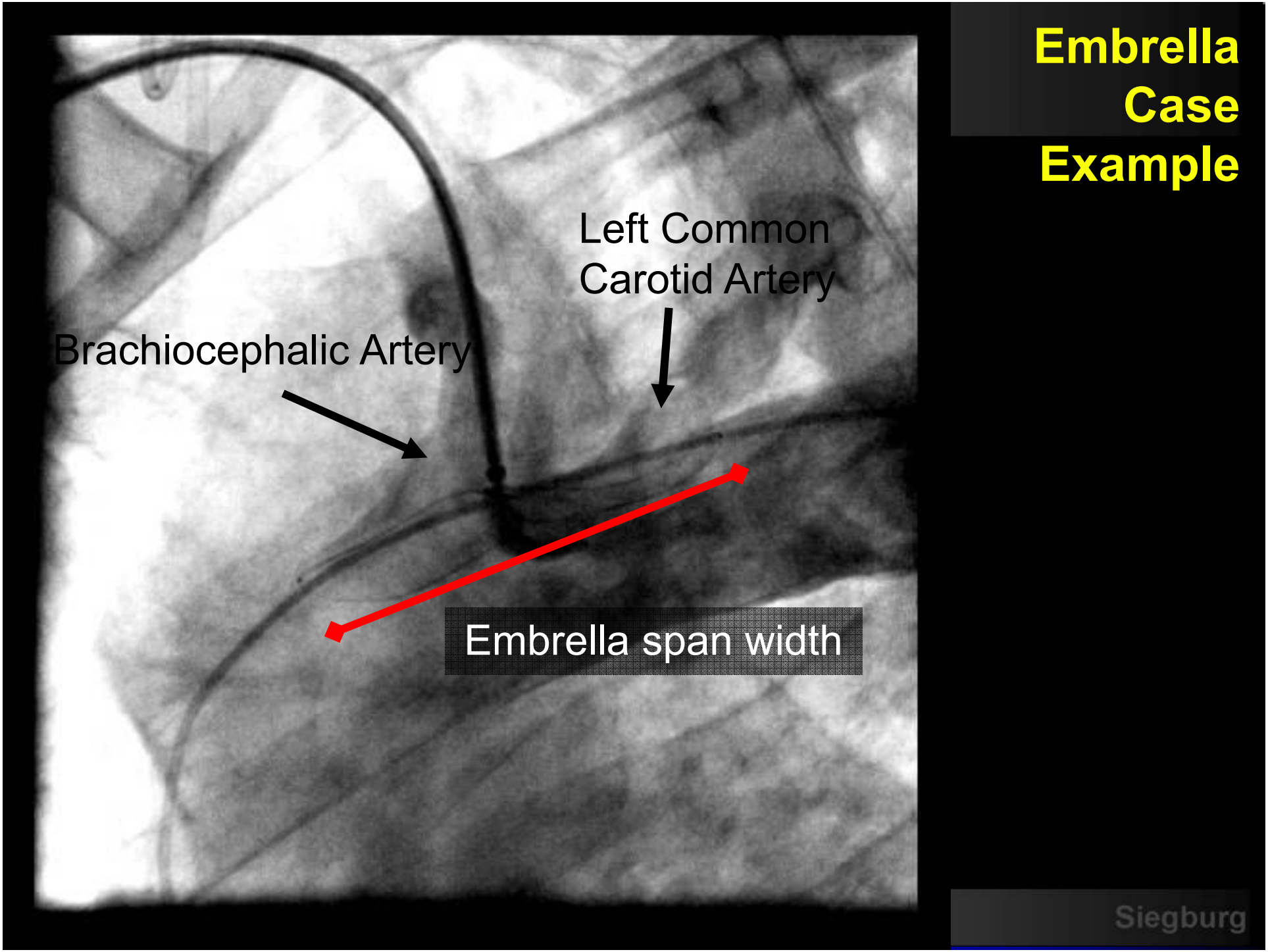




Embrella Embolic Deflector™

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

Embrella Case Example



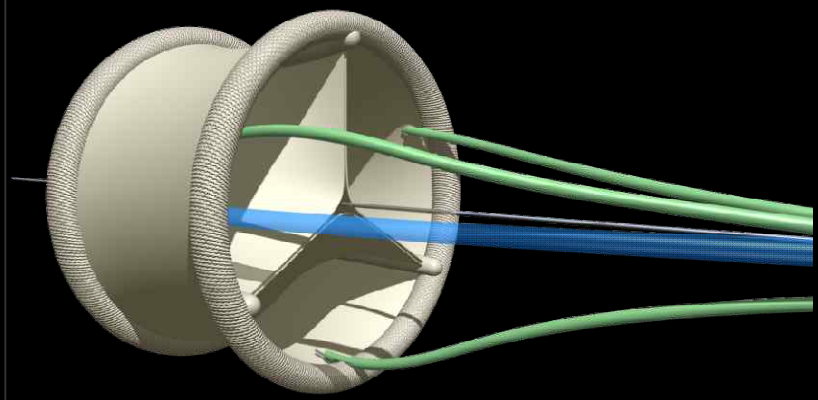
Success, but Opportunity for Improvement

- **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

Transcatheter Valve Therapy
Next Generation Devices

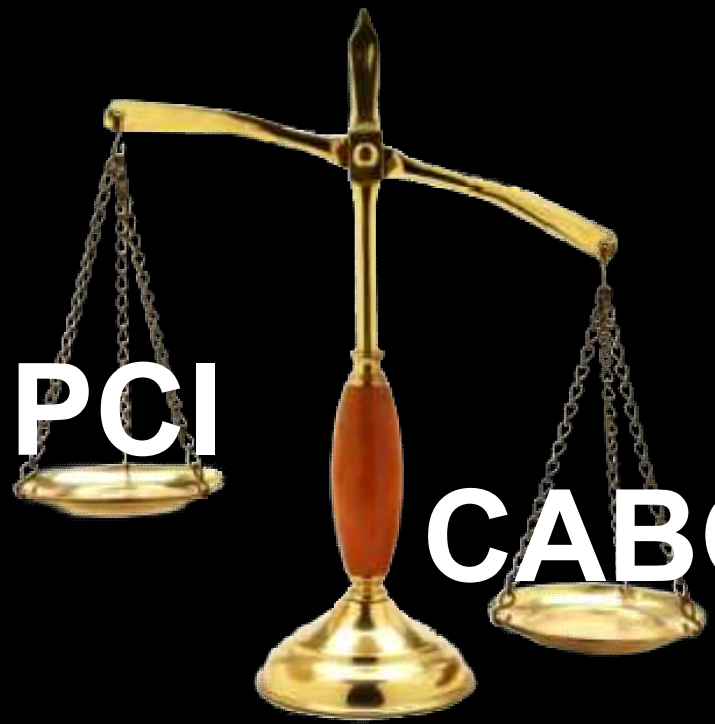
Sadra

DirectFlow



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

My Prediction: Repetition of an Old Story



1980's, 1990's

2000's, 2010's

With the same result…

Thank you