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Update on the CoreValve Experience

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Siegburg

Disclosure Statement of Financial Interest

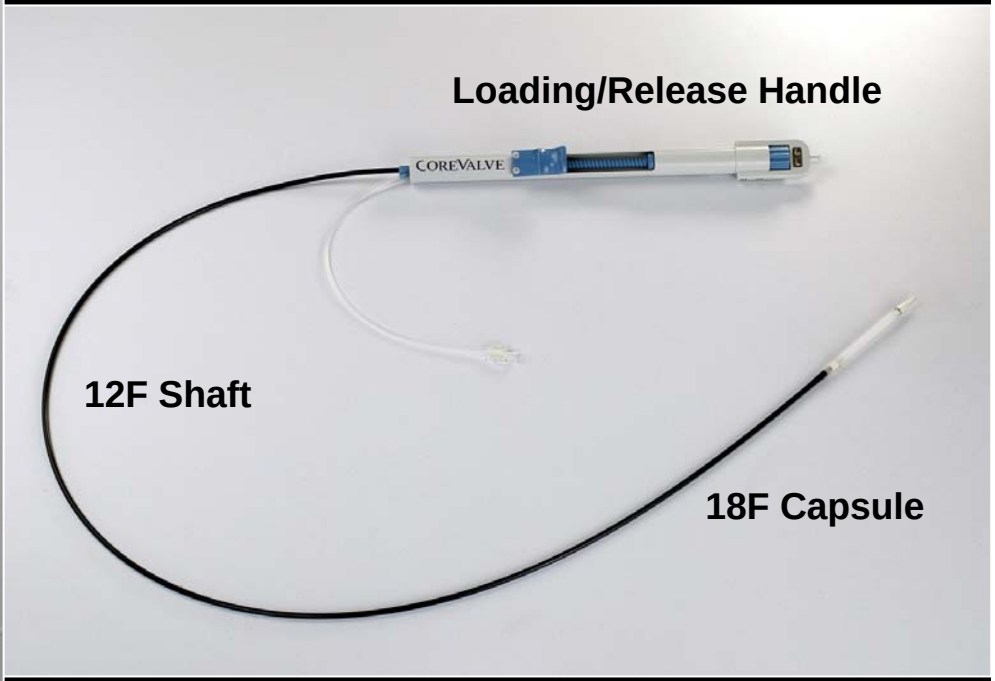
Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Physician Name	Company/Relationship
Eberhard Grube, MD	Direct Flow (C) Core Valve(C, G, SB, E,) SADRA Medical (C, SB, E) Boston Scientific (G,C,SB) Cordis JnJ (C) Abbott (C)

Key

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

CoreValve Prosthesis

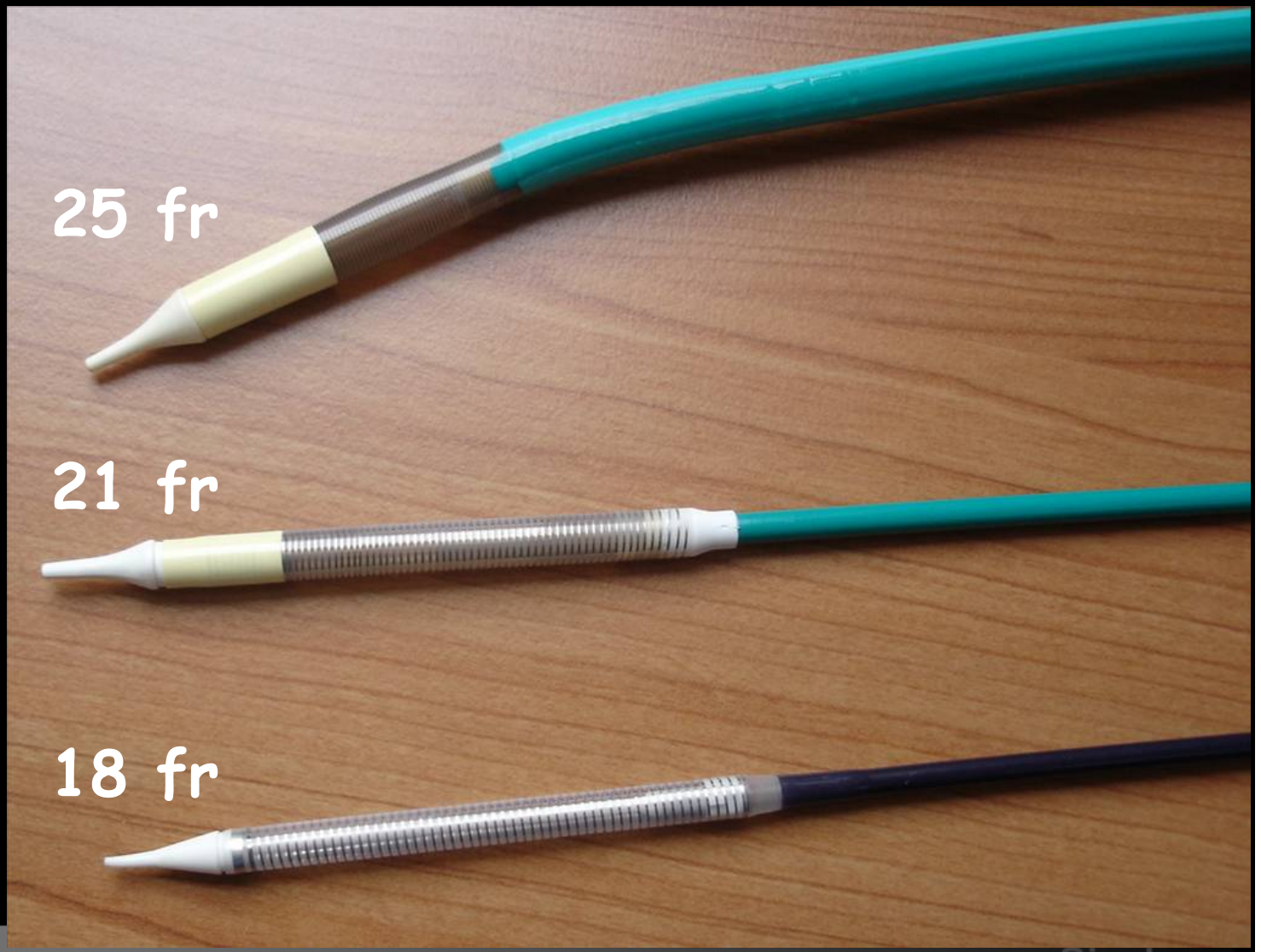


CoreValve : 3 Generations

2004

2005

2006



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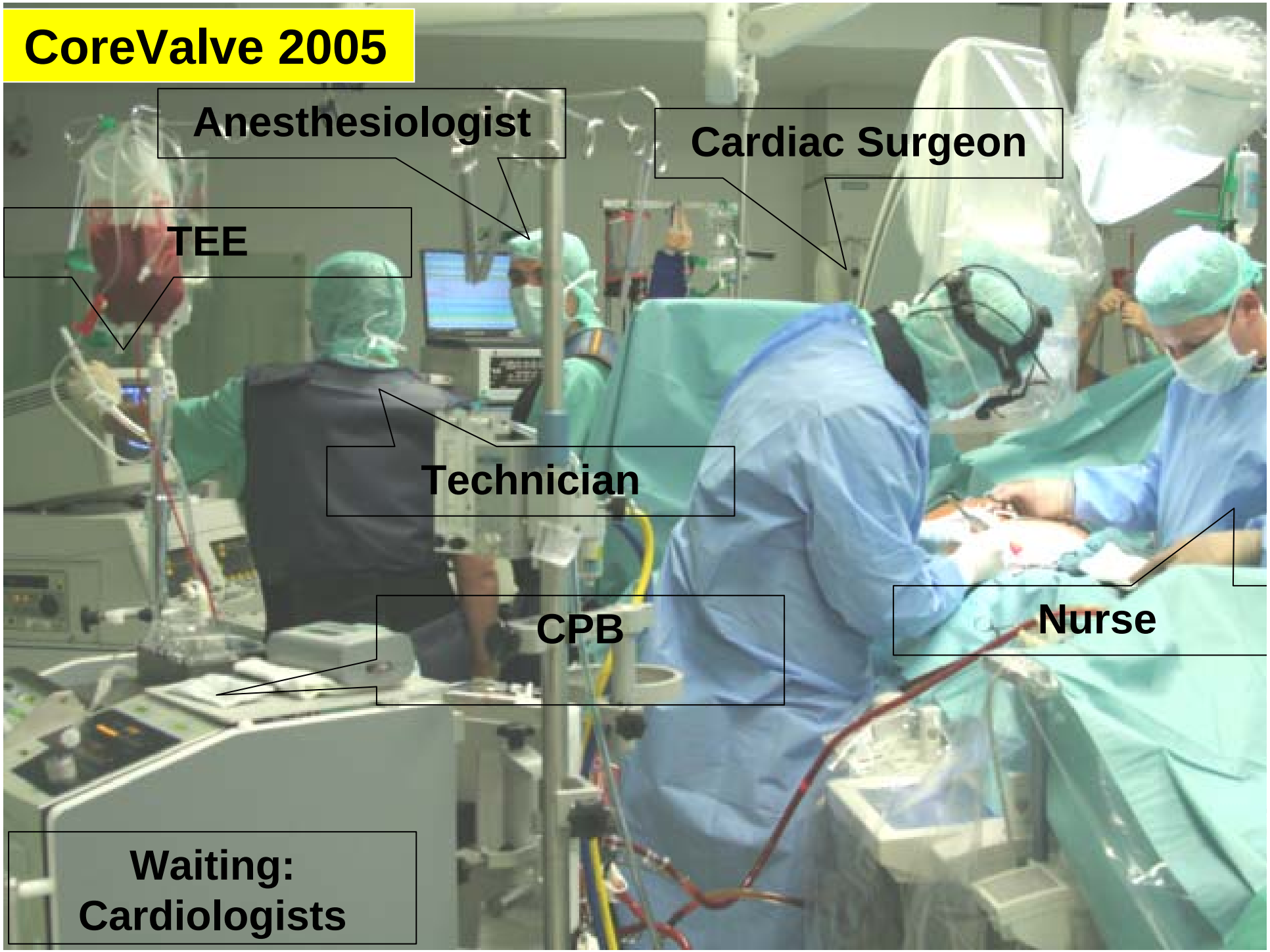

CoreValve 2005
Anesthesiologist
Cardiac Surgeon
TEE
Technician
CPB
Nurse
Waiting:
Cardiologists

CoreValve 2009

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

Global Clinical Experience

18 Fr. CVS	S&E Study CE Marking		EER (Post-CE Mark)	Australia New Zealand Trial	Published Single-Center Experience	
					Munich (Lange)[1]	Siegburg (Grube)[2]
Dates	5/06 – 6/07	4/08 – 11/08	4/07 – 12/08	8/08 - Ongoing	6/07 – 8/08	5/06 – 3/08
Patients (n)	112	14[a]	1,424	Up to 150	137	102
Logistic EuroSCORE	23.1 ± 13.4	25.7 ± 17.1	22.6 ± 13.9	17.6 ± 13.3	24.3 ± 14.9	24.5 ± 15.4
STS Score	Not collected	17.7 ± 12.3	Not collected	Being collected	23.4 ± 10.1	12.6 ± 4.7
Adjudicated	Yes	Yes	No	Yes	No	No

a. To be included in the next analysis

1. Bleiziffer, et al. *Eur J Cardiothorac Surg (in press)*
2. Grube, et al. *Circ Cardiovas Intervent*. 2008;1:167-175

Enrollment by Site

Site	Patients	Start / Stop
Siegburg	42	8 May 06 – 28 Jun 07
Leipzig	19	16 Oct 06 – 21 Jun 07
Rotterdam	12	12 Oct 06 – 25 May 07
Breda	4	22 Nov 06 – 10 Apr 07
Montreal	10	26 Sep 06 – 28 Feb 07
Edmonton	2	1 Mar 07 – 1 Mar 07
Ottawa	5	6 Feb 07 - 28 Feb 07
London	4	12 Apr 07 – 10 May 07
Leicester	14	30 Jan 07 – 14 Jun 07
Total	112	May 06 to Jun 07

Baseline Characteristics

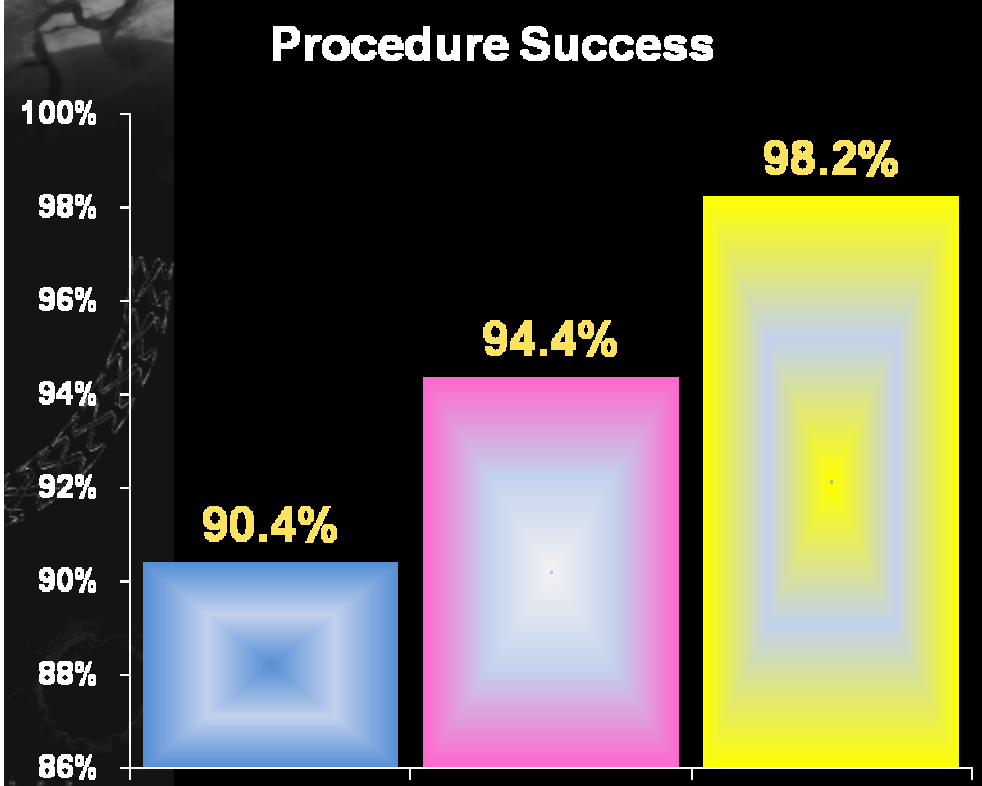
Characteristic	Value
Age, years (mean)	81.9 ± 6.4
Female gender, n (%)	64 (57.1 %)
NYHA Class I, n (%)	7 (6.3 %)
NYHA Class II, n (%)	21 (18.8 %)
NYHA Class III, n (%)	61 (54.5 %)
NYHA Class IV, n (%)	23 (20.5 %)
Cardiac Output, L/min (mean)	5.4 ± 1.3
LVEF, % (mean)	52.1 ± 12.1
Logistic EuroSCORE, % (mean)	23.2 ± 13.4
Peak pressure gradient, mmHg (mean)	73.2 ± 24.1
Mean pressure gradient, mmHg (mean)	48.7 ± 14.7
Aortic valve area, cm^2 (mean)	0.72 ± 0.17

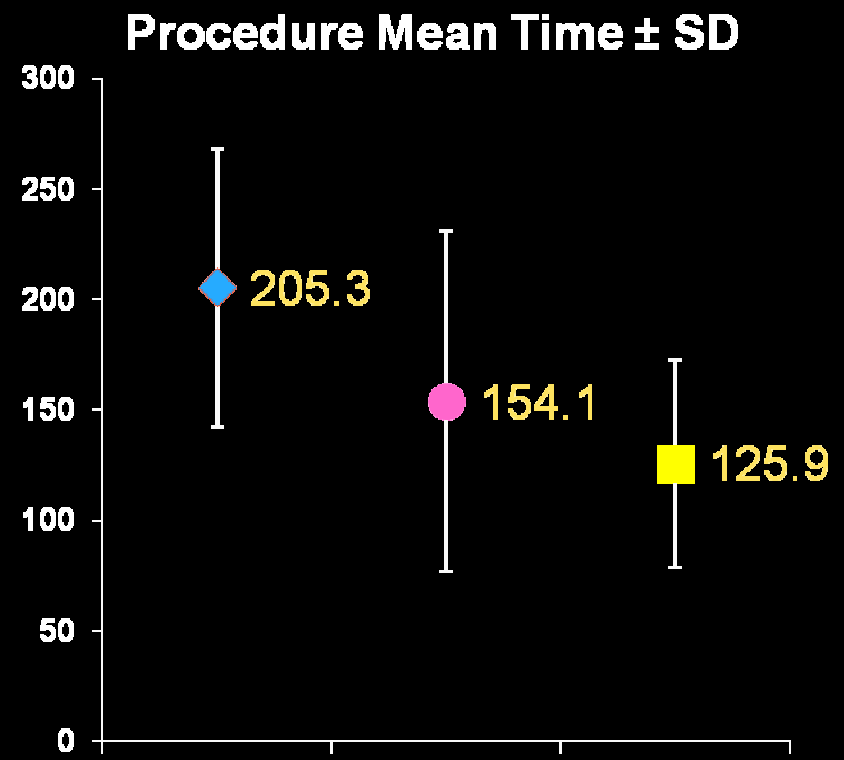
Procedural Outcomes

Procedure Information	Value
Local anesthesia	48 (42.9%)
Use of cardiopulmonary support	21 (18.8%)
Mean procedure time, min	151.0 ± 77.0
Technical success (absence of valve failure or malfunction)	86.5%
Mean hospital stay, days	15.6 ± 11.4

Complication (Discharge)	Value
Major Bleeding	13(11.6%)
Renal Failure	8 (7.1%)
Cardiac Perforation	3 (2.7%)

CoreValve Procedural Results





21F S&E 18F S&E 18F EE

Global 18-Fr Experience

18 Fr. CVS	S&E Study – CE Marking		European Registry (Post-CE Mark)*	Australian New Zealand Trial*	Single Center Experience	
					Munich (Lange)	Siegburg (Grube)
Patients (n)	112	14	1,424	37	137	102
30D Mortality – All Cause	15.2%	7.1%✚	10.4%	8.1%	12.4%	10.8%
Technical Success	86.5%	n.a.	97.3%	98.3%	98.5%	98.2%

* Site

Cause of Death

Procedure (4)

Cardiac (3)
- major bleeding (1)
- AMI (1)
- Severe hypotension (1)

Non Cardiac (1)
- major bleeding (1)

Discharge (13)

Cardiac (9)
- MOF (4)
- Severe AI (1)
- MI (2)
- cardiogenic shock (1)
- stroke (1)

Non cardiac (4)
- MOF (2)
- sepsis (1)
- subdural hematoma (1)

30-Days (0)

Cardiac (0)

Non cardiac (0)

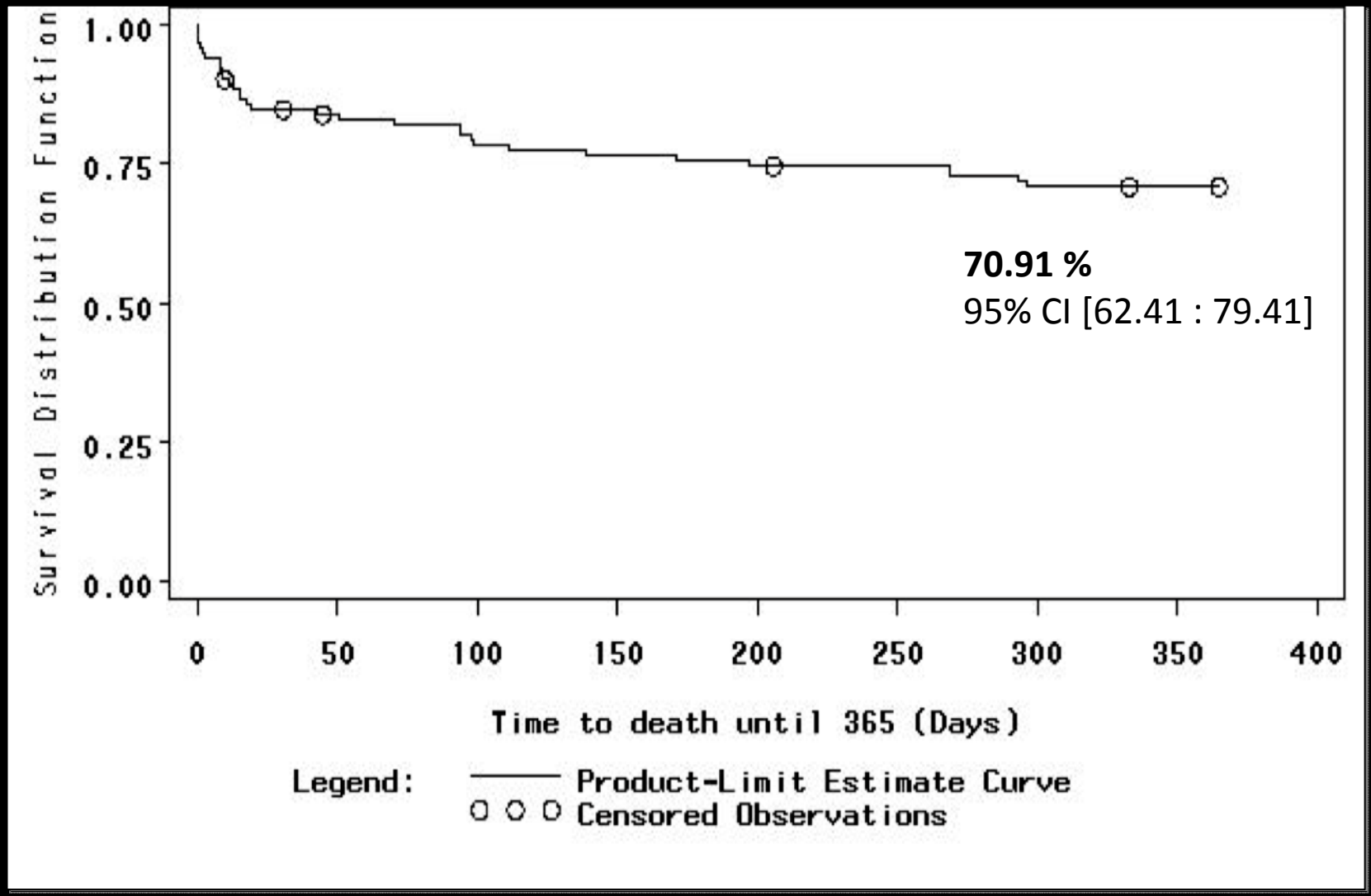
1 Year (15)

Cardiac (7)*
- unstable angina (1)
- cardiac decomp (1)
- worsening of HF (3)
- AMI (1)
- sudden death (1)

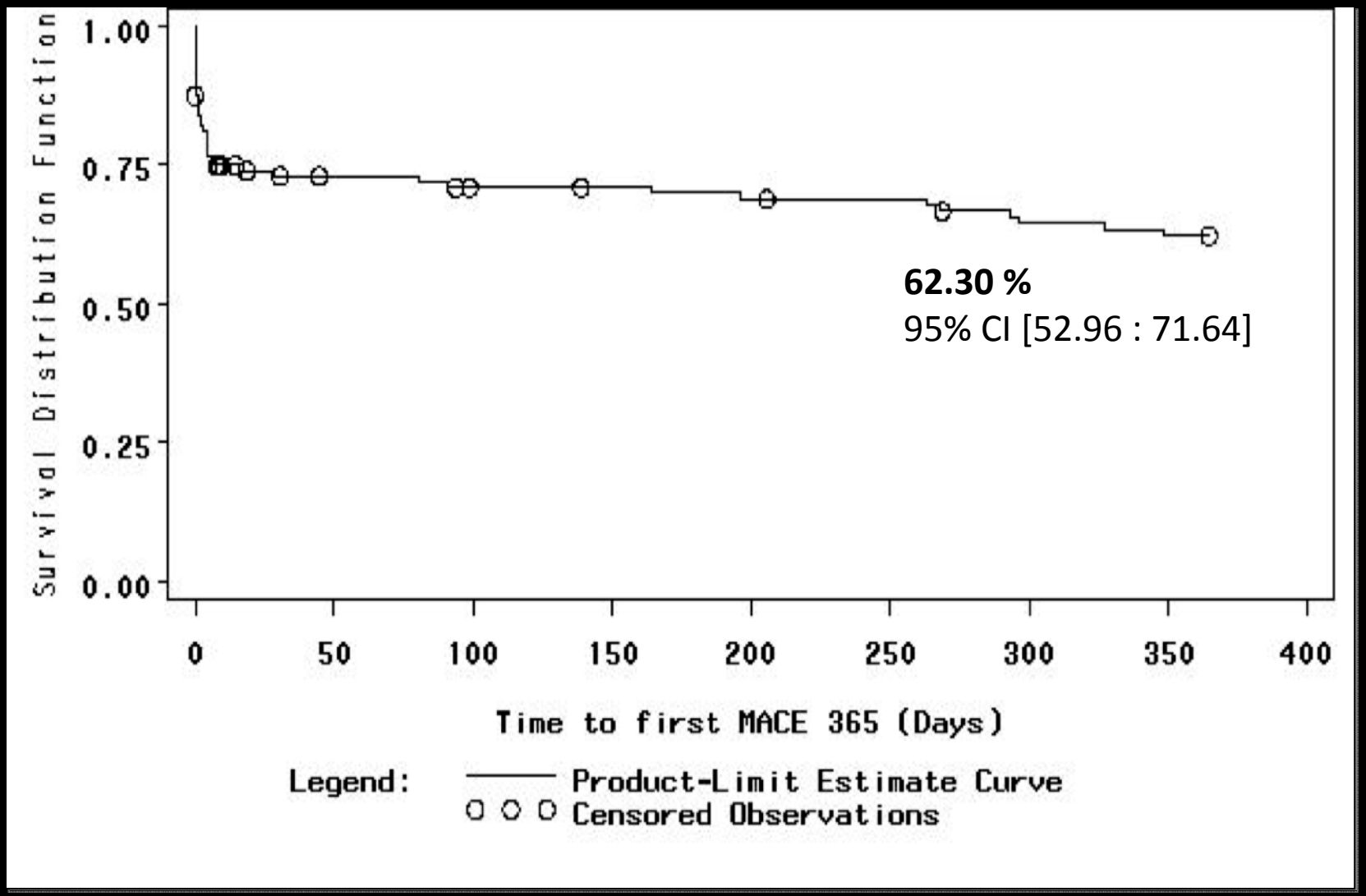
Non cardiac (8)
- pulm. embolism (2)
- MOF (1)
- sepsis (2)
- hip fracture (1)
- pneumonia (1)
- worsening of RF (1)

(* = No valve dysfunction, migration or fractures)

Freedom from ALL Cause Mortality



Freedom from MACE*

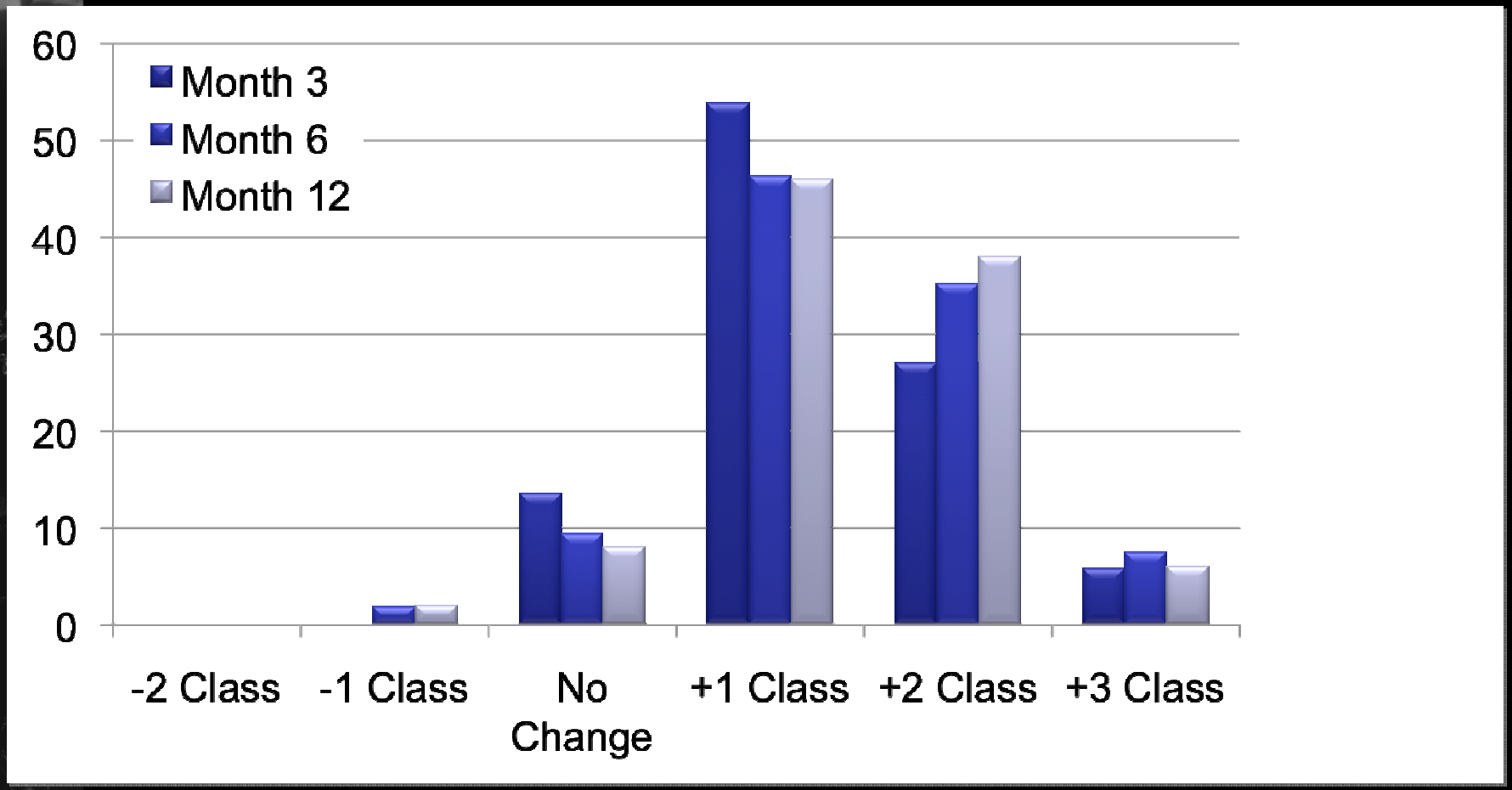


* MACE = Cardiac death, non-fatal MI, major arrhythmia, emergent revascularization

Performance Outcomes

Outcomes	Discharge	30-Day	12-Month
Peak gradient, mmHg	16.1 ± 5.4	16.0 ± 5.1	18.8 ± 6.6
Mean gradient, mmHg	10.1 ± 4.7	8.1 ± 2.6	10.3 ± 4.2
Aortic valve area, cm^2	1.83 ± 0.36	1.78 ± 0.37	1.74 ± 0.30
NYHA Class I, n (%)	28 (31.1%)	26 (33.8%)	32 (45.1%)
NYHA Class II, n (%)	50 (55.6%)	43 (55.8%)	31 (43.7%)
NYHA Class III, n (%)	11 (12.2%)	7 (9.1%)	7 (9.9%)
NYHA Class IV, n (%)	1 (1.1%)	1 (1.3%)	1 (1.4%)

Evolution NYHA-FC III-IV



Siegburg CoreValve Experience

Total number of patients*:	**321**
Gen 1 (2005)	10
Gen 2 (2005-2006)	26
Gen 3 (since 2006)	265
in 2008	208

30 Day Mortality:	
Gen 1	40.0%
Gen 2	20.8%
Gen 3	8.6%
in 2008	4.8%

*Status of Nov 2008

≤ 30-Day Adverse Events*

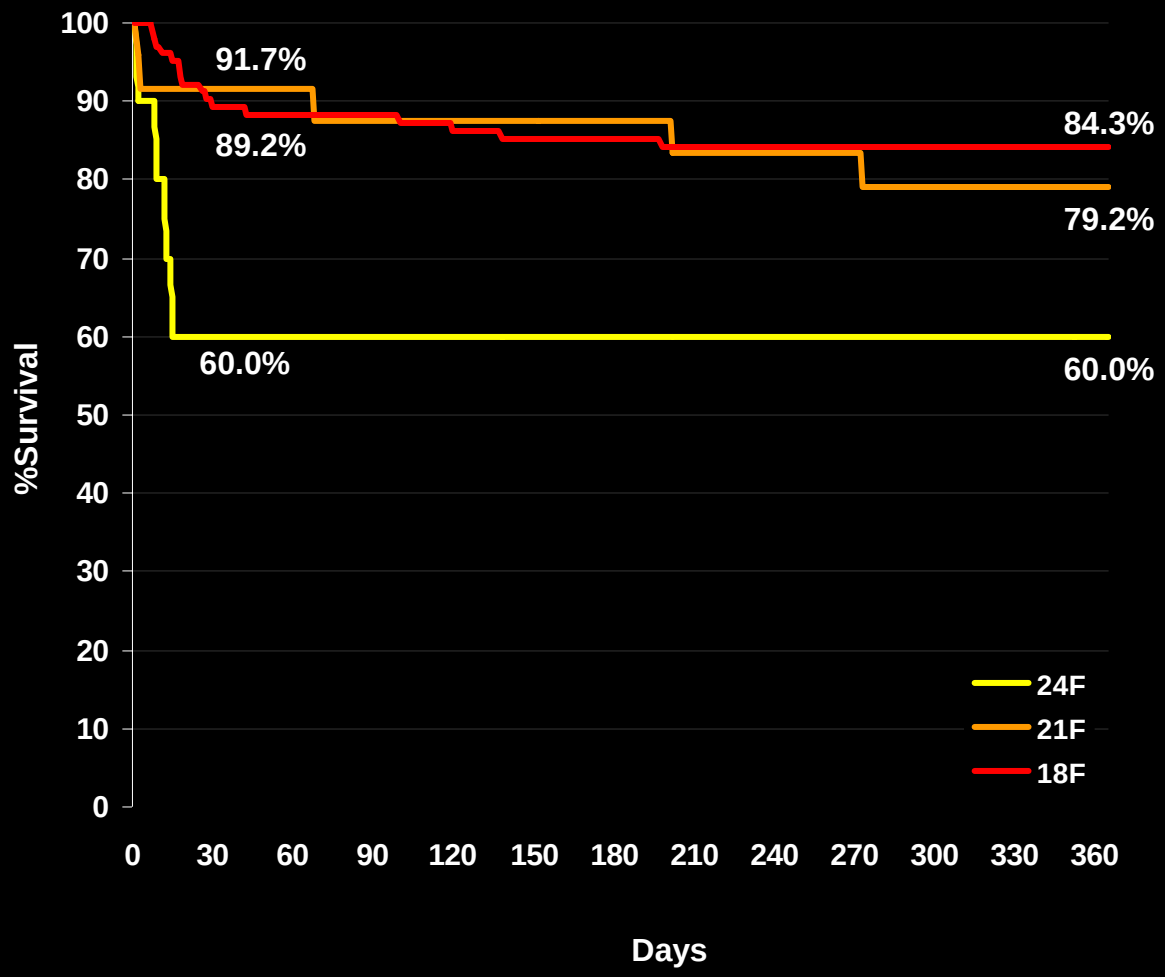
	21F S&E Study (N = 52)	18F S&E Study (N = 124)	18F EE Registry (N = 1243)
30-Day All Mortality	15.4%	14.5%	6.7%
Cardiac Deaths	7.7%	11.2%	3.9%
Myocardial Infarction	3.8%	3.4%	0.7%
Major Arrhythmias	25.0%	18.5%	4.9%
Pacemaker	17.3%	25.8%	12.2%
Renal Failure	5.8%	4.8%	1.2%
Stroke	17.3%	6.5%	1.4%
TIA	0.0%	5.6%	0.3%
Structural Valve Dysfunction	0.0%	0.0%	0.0%
Valve Migration	0.0%	0.0%	0.0%

* Multiple events in same patients = data not cumulative

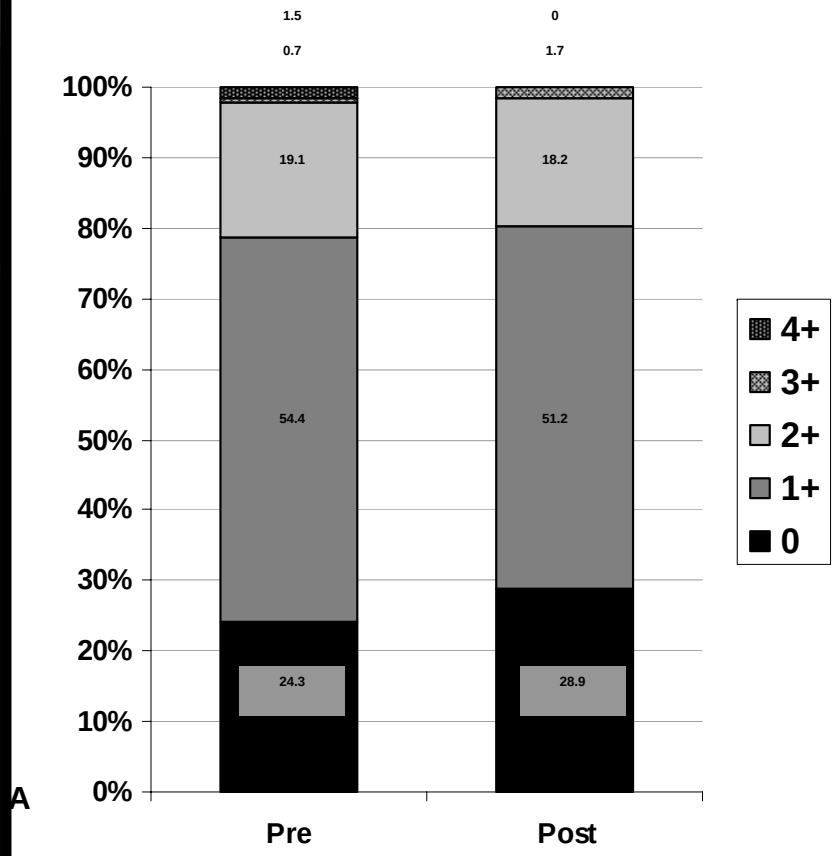
† Includes 4 deaths where cause is not known

Siegburg

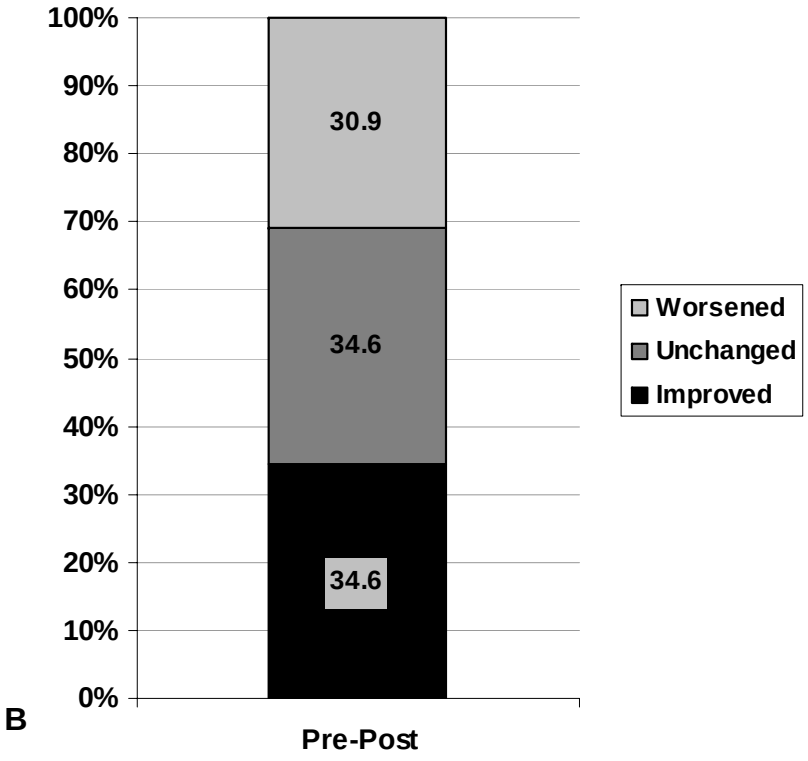
Siegburg Experience
Survival Curves



CoreValve
Aortic Regurgitation post-interventional



A



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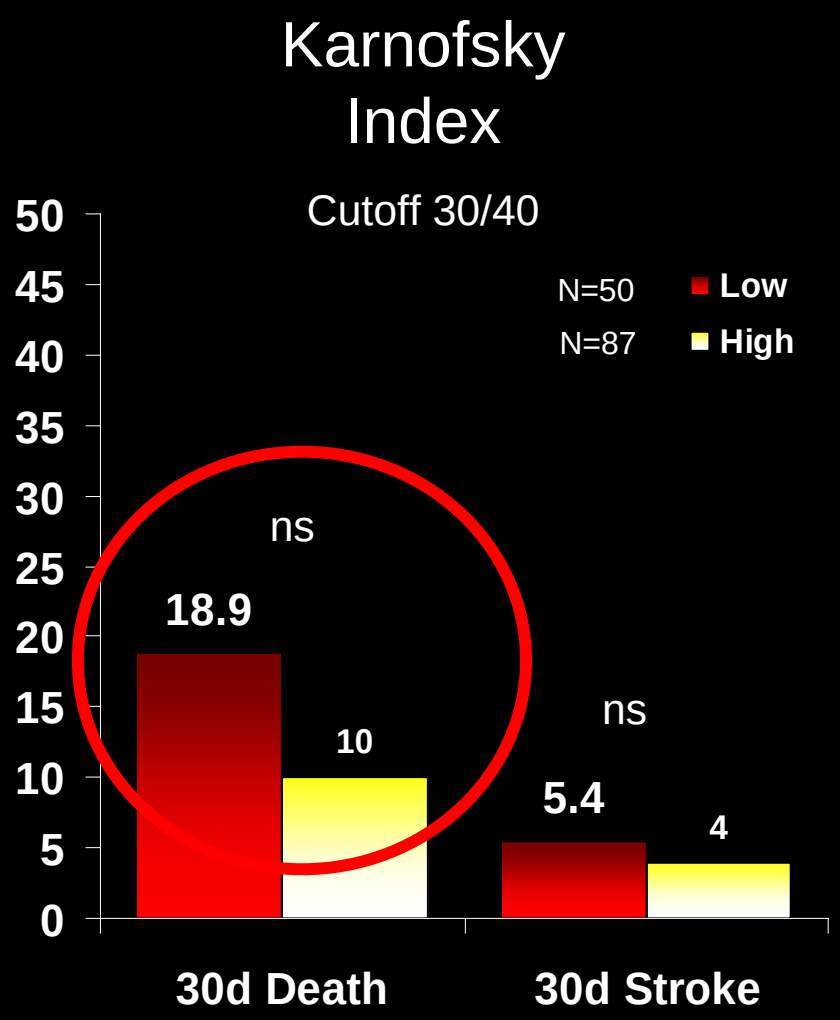
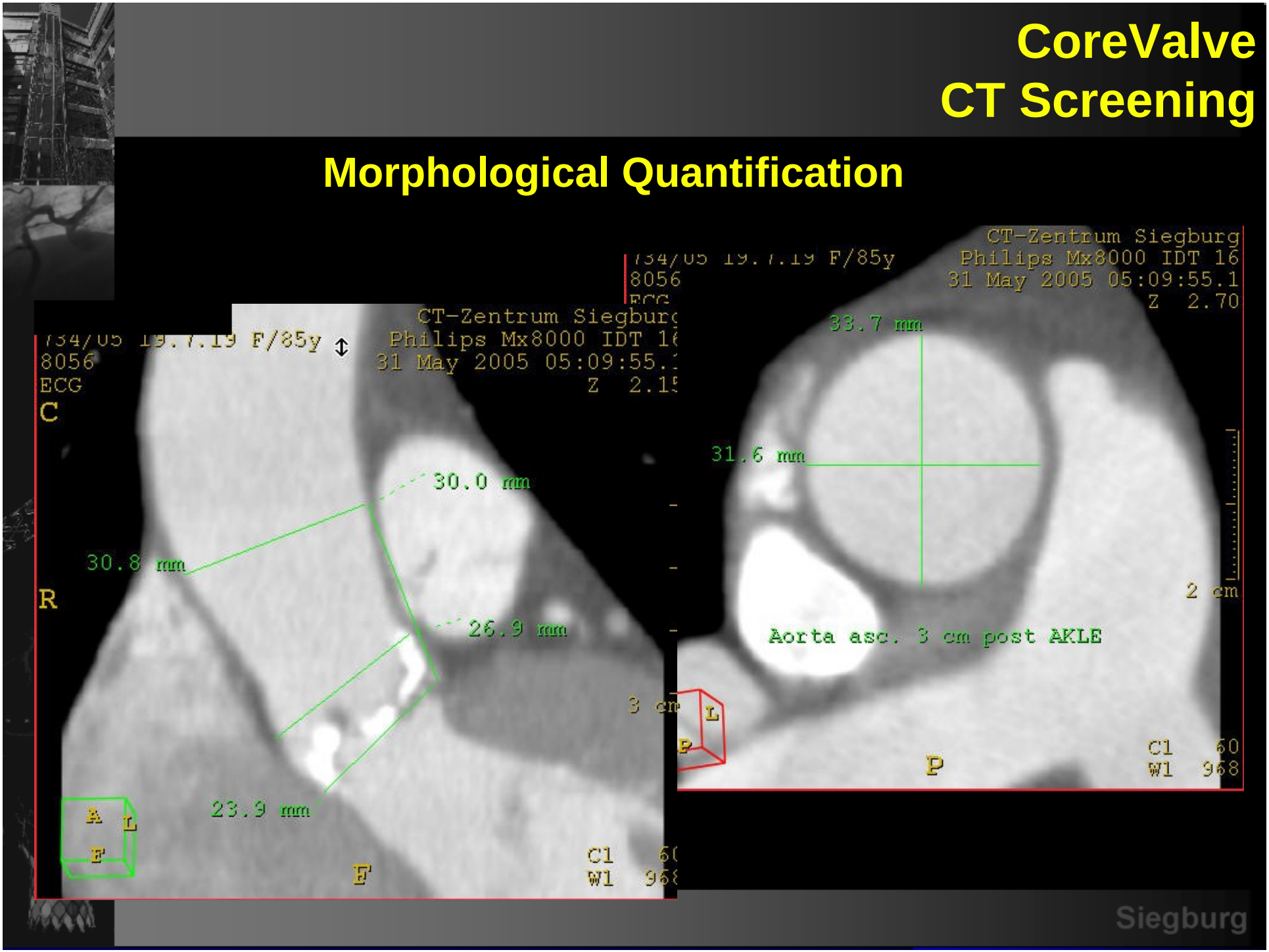
CoreValve Siegburg Experience

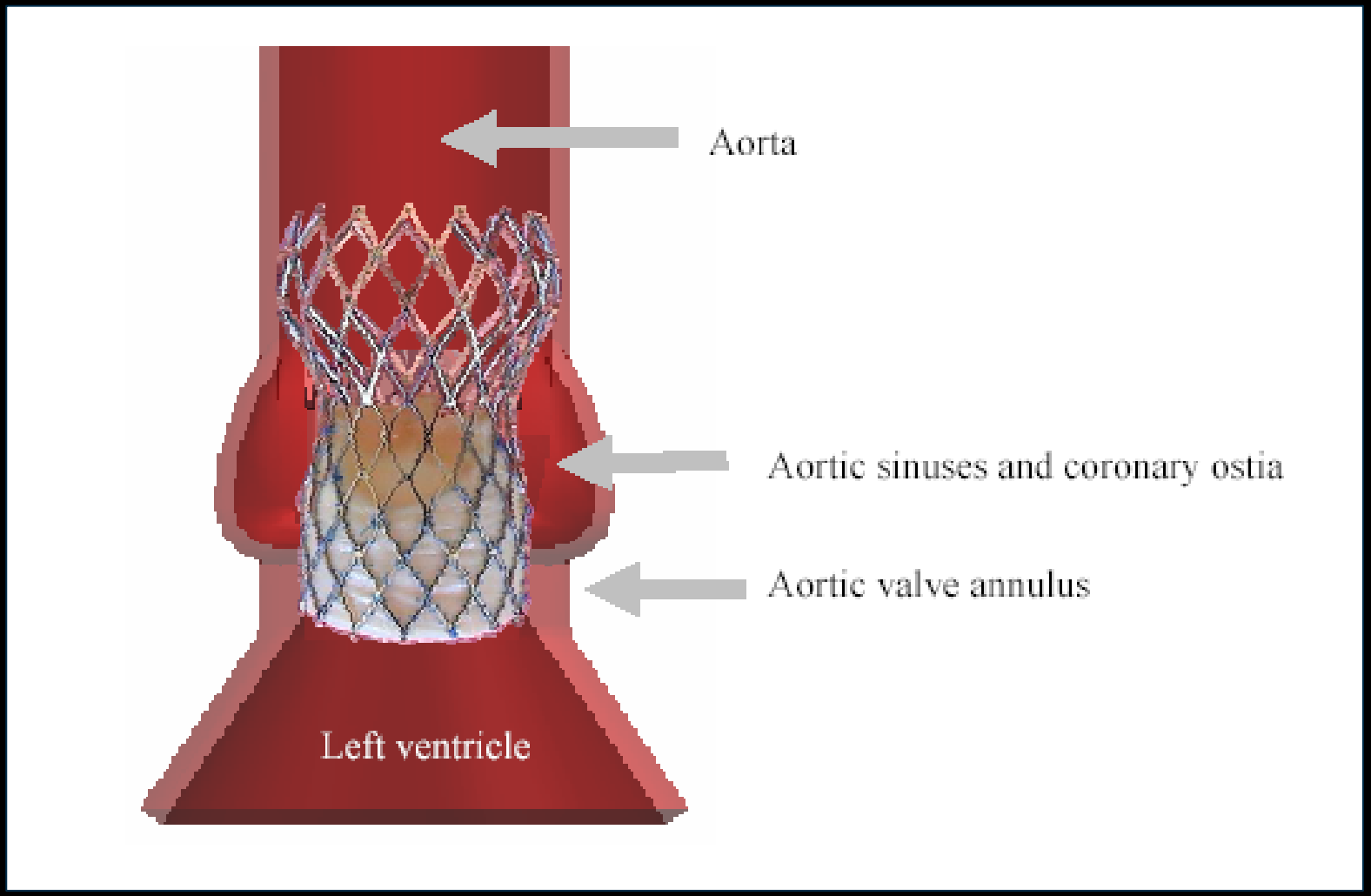


CoreValve CT Screening

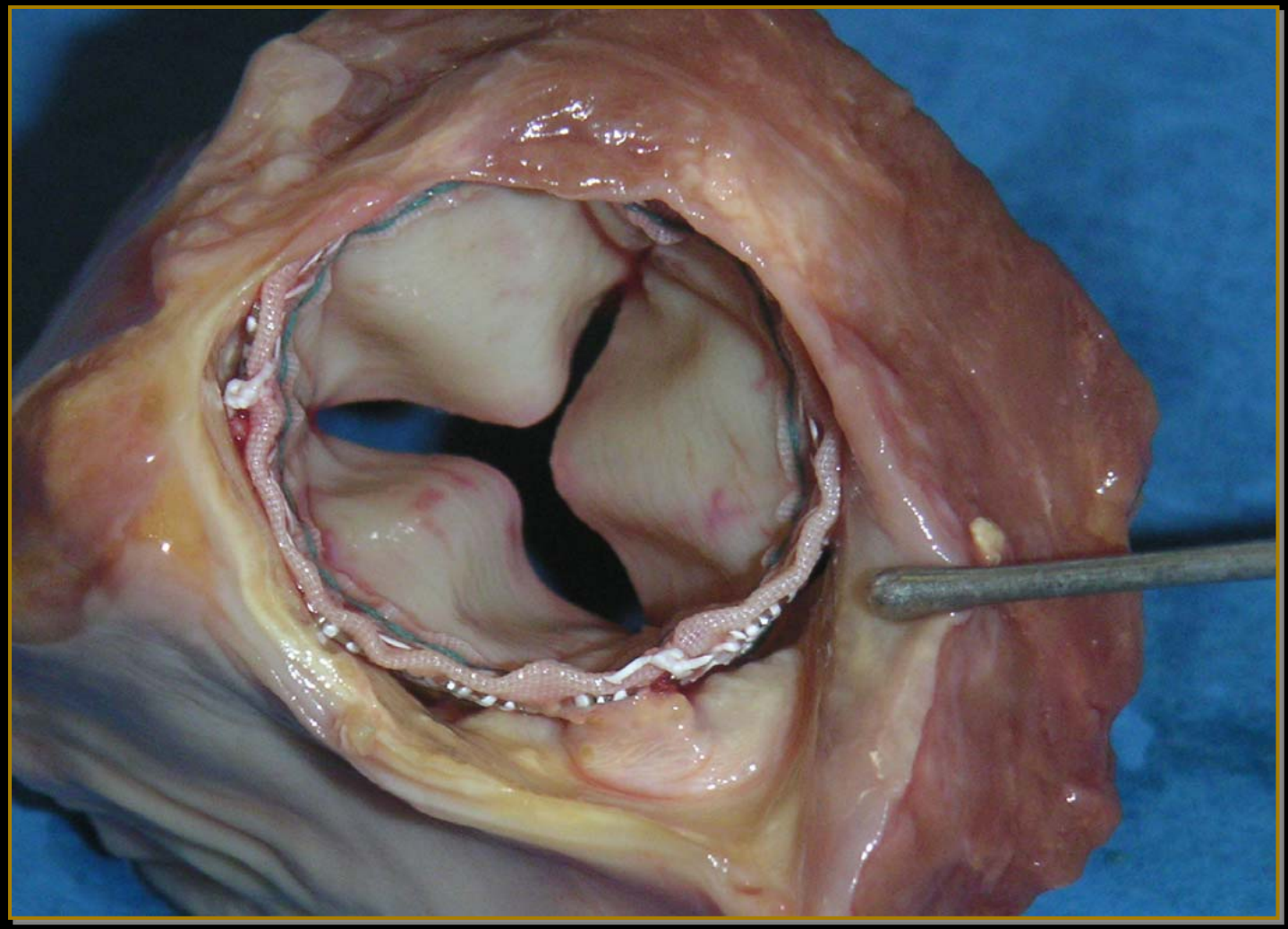
Morphological Quantification



CoreValve Prosthesis

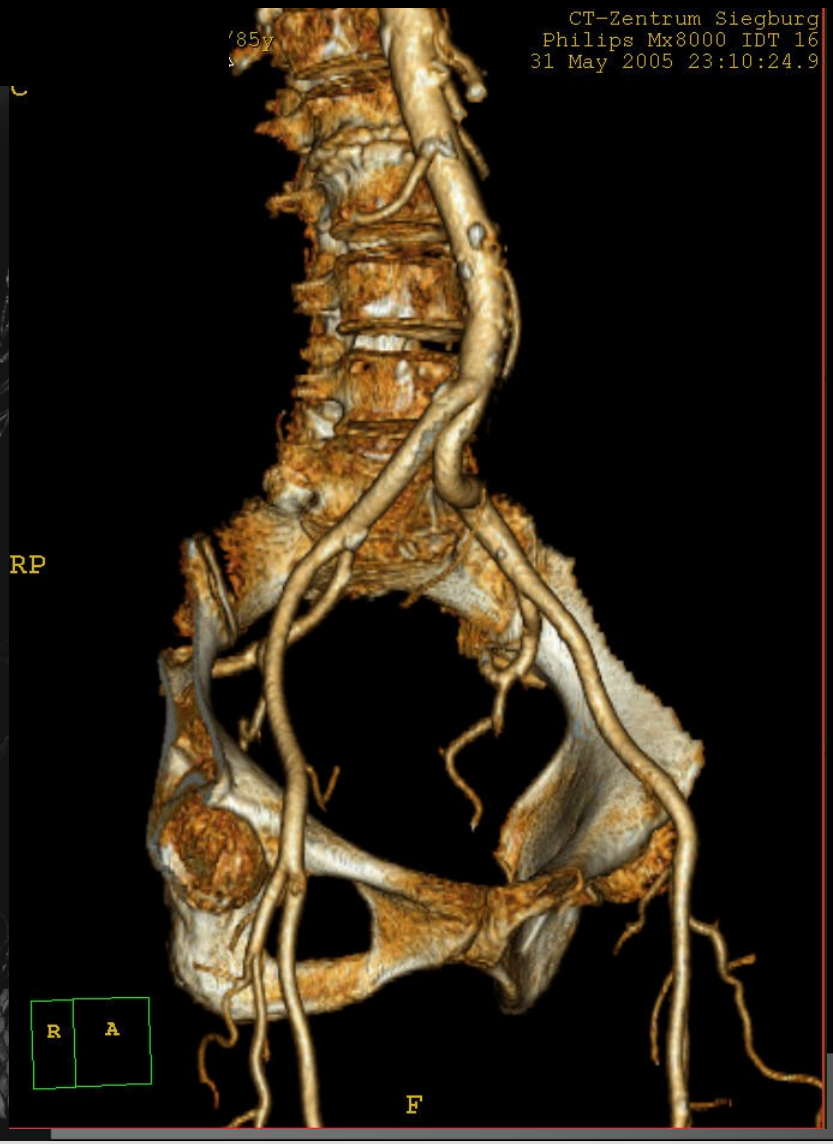


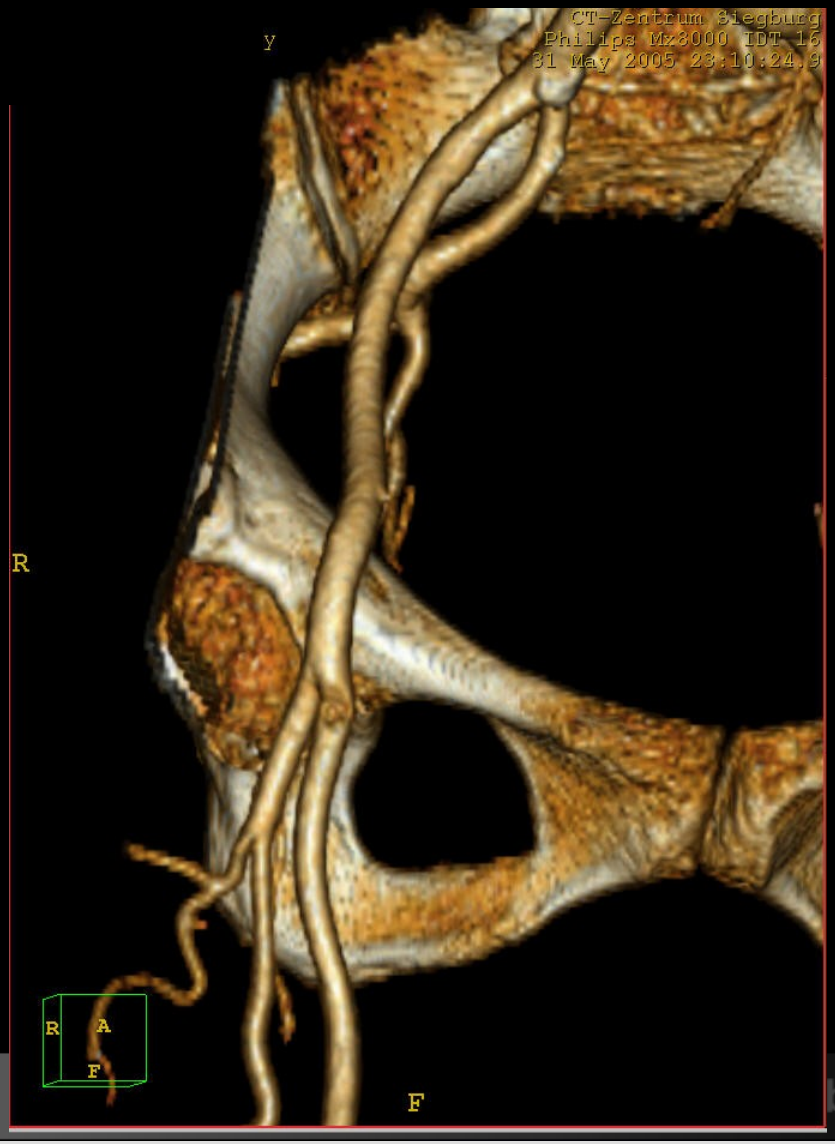
Para-valvular Regurgitation



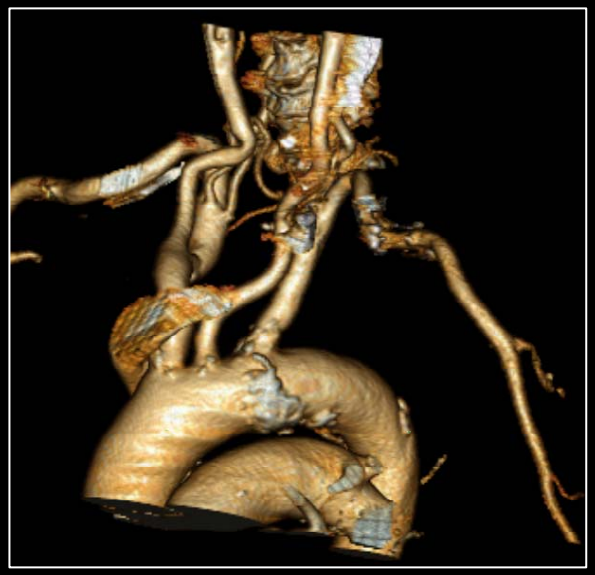
CoreValve

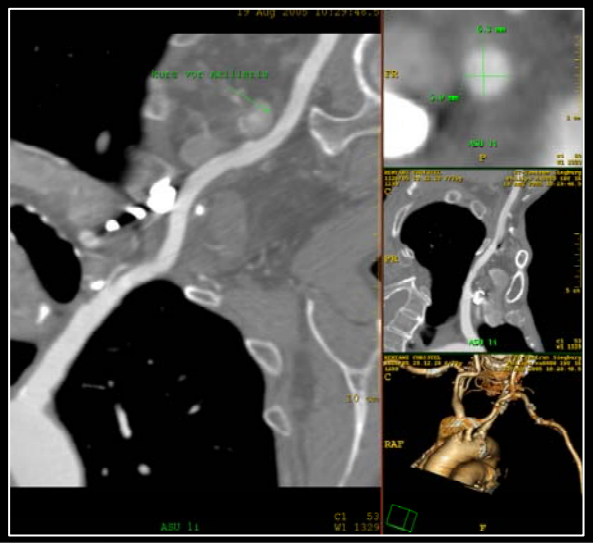
Access Site Assessment

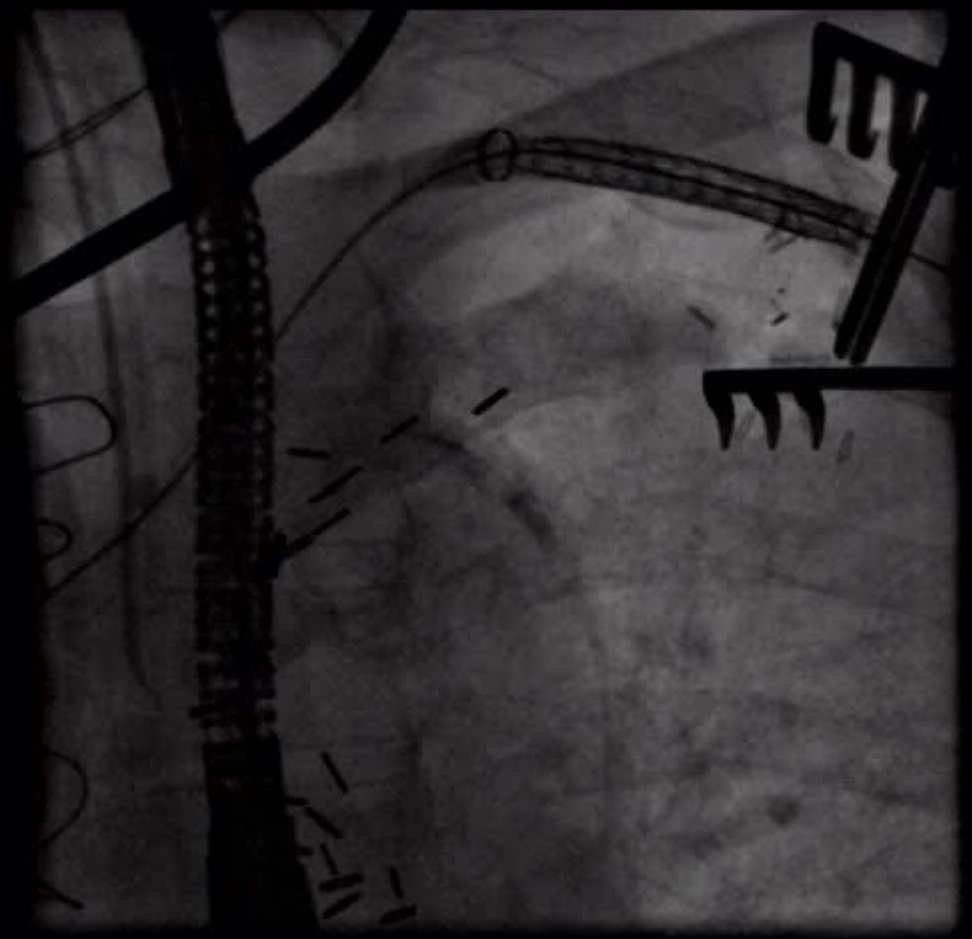




Subclavian Access







CORE VALVE
THE REVALVING TECHNOLOGY

Patient Selection Matrix

	Non-Invasive		Angiography				Selection Criteria		
Anatomy	Echo	CT / MRI	LV gram	AO gram	Coronary Angiogram	AO & Runoffs	**Preferred**	**Borderline**	**Not Acceptable**
Atrial or Ventricular Thrombus	X						**Not Present**		**Present**
Mitral Regurgitation	X						**≤ Grade 1**	**Grade 2**	**> Grade 2**
LV Ejection Fraction	X		X				**> 50%**	**30% to 50%**	**< 20%**
LV Hypertrophy (wall thickness)	X						**Normal to Mild (0.6 to 1.3 cm)**	**Moderate (1.4 to 1.6cm)**	**Severe (≥ 1.7cm)**
Sub-Aortic Stenosis	X	X					**Not Present**		**Present**
Annulus (width)	X	X					**20 to 23mm → 26mm device 24 to 27mm → 29mm device**		**< 20mm or > 27mm**
Annulus-to-Aorta (angle) †		X	X	X			**< 30°**	**30° to 45°**	**> 45°**
AO Root (width)		X	X	X			**≥ 30mm**	**27 to 29mm**	**< 27mm (if Sinus < 15mm)**
Sinuses of Valsalva (height)		X	X	X	X		**≥ 15mm**	**10 to 14mm**	**< 10mm**
Coronary Ostia Position (take-off)					X		**High**	**Mid-Sinus Level**	**Low**
Coronary Disease					X		**None**	**Mid or Distal Stenosis < 70%**	**Proximal Stenosis ≥ 70%**
Ascend Aorta (width)		X	X	X			**≤ 40mm → 26mm device ≤ 43mm → 29mm device**		**> 43mm**
AO Arch Angulation		X		X		X	**Large-Radius Turn**		**High Angulation or Sharp Bend**
Aorta & Run-Off Vessels (Disease) ‡		X				X	**None**	**Mild**	**Moderate to Severe**
Iliac & Femoral Vessels (diameter)		X				X	**≥ 7mm**	**Non-Diabetic ≥ 6mm**	**< 6mm**

† *Within the first 7cm of the ascending aorta versus a perpendicular line across the aortic valve.*
‡ *Evaluate for evidence and degree of calcification, obstruction, tortuousity, and ulceration.*

Caution: The CoreValve ReValving™ System is not available in the USA for clinical trials or commercialization.

This document is not intended to be a substitute for attending a training program for any of the products mentioned. For detailed operator training / inservice support on the CoreValve ReValving™ System, please contact your local CoreValve representative.

PN 090404 V1 June 2007

CE 0050

Conclusions

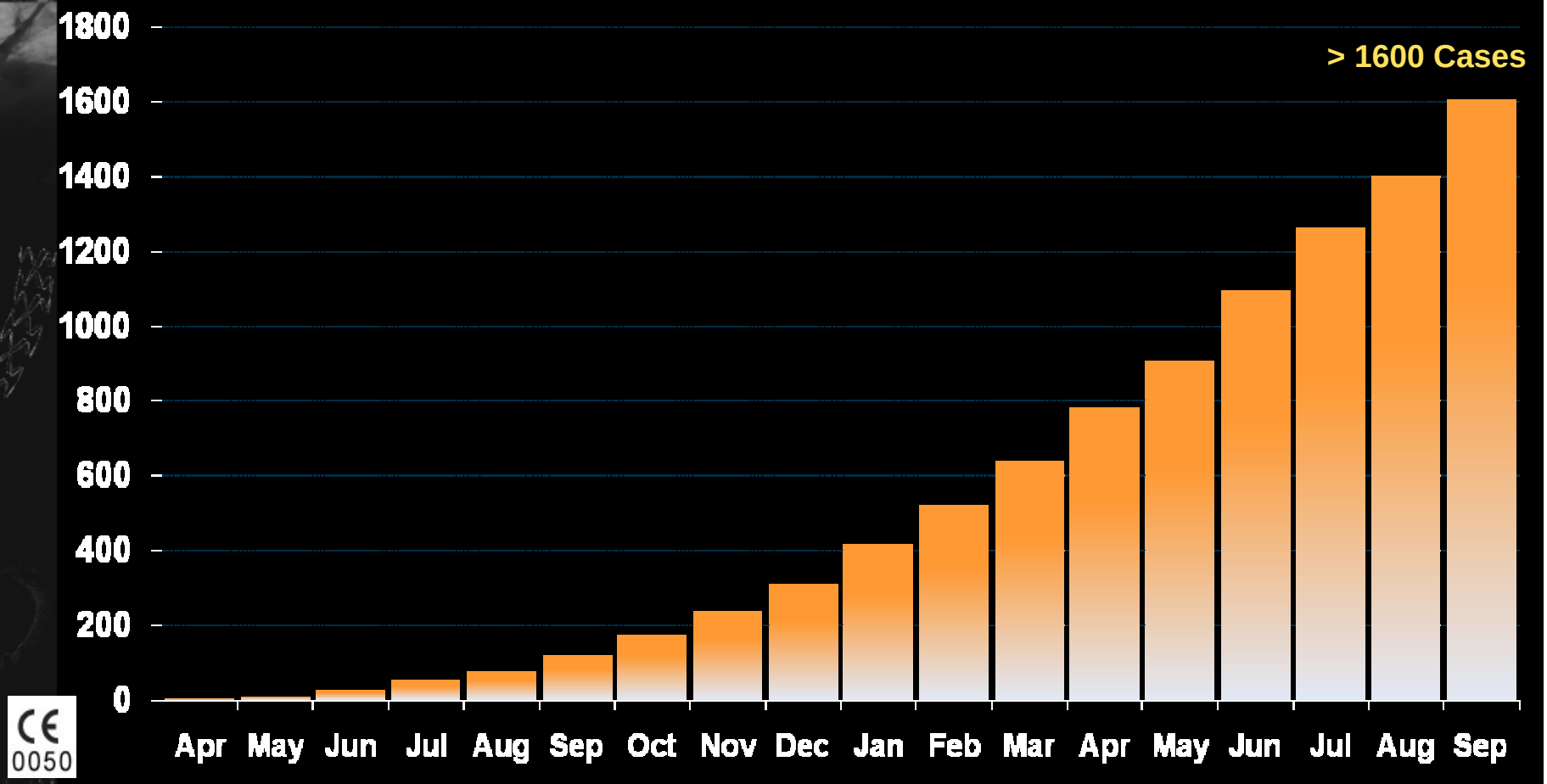
- Procedure has migrated to truly percutaneous approach, with the majority of cases done under local anesthesia without CPS
- High procedural success rate
- Adjudicated 18-Fr. S&E trial demonstrates both safety and efficacy with a concomitant improvement in NYHA-FC in high risk patients
- No valve migration or frame fractures
- Published and ongoing studies confirm transferable learning curve
- Expanded indication beyond high risk patients must be based on improved QOL and durability of the valve

Conclusions

- The initial early experience with CoreValve 18 French TAVI is encouraging.
  - Longer term follow-up data will address appropriate patient population for transcatheter valve use.
- High technical success rate with TAVI
- No evidence of frame migration
- 18 French Safety & Efficacy Data (adjudicated)
  - 81% 1 year freedom from cardiac death
  - 92% 1 year freedom from stroke
  - 80% of patients experienced at least 1 NYHA class improvement
- 18 French Safety & Efficacy data is supported by other published and ongoing studies and registries.

Thank you

Post CE Mark Cumulative
18F *ReValving* PAVR Procedures



CE 0050

Updated 01-October-2008: ~100 sites in 20 countries

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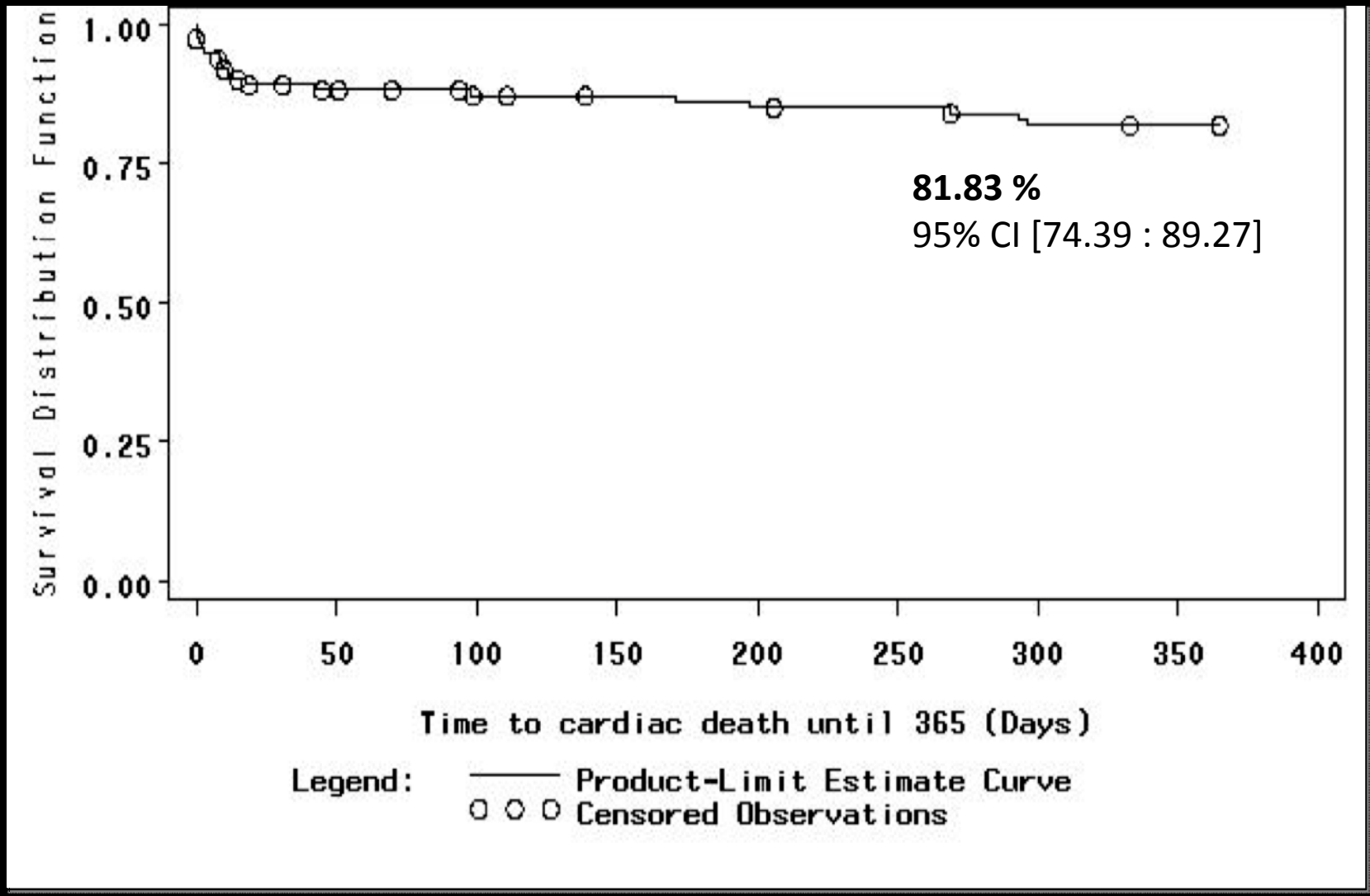
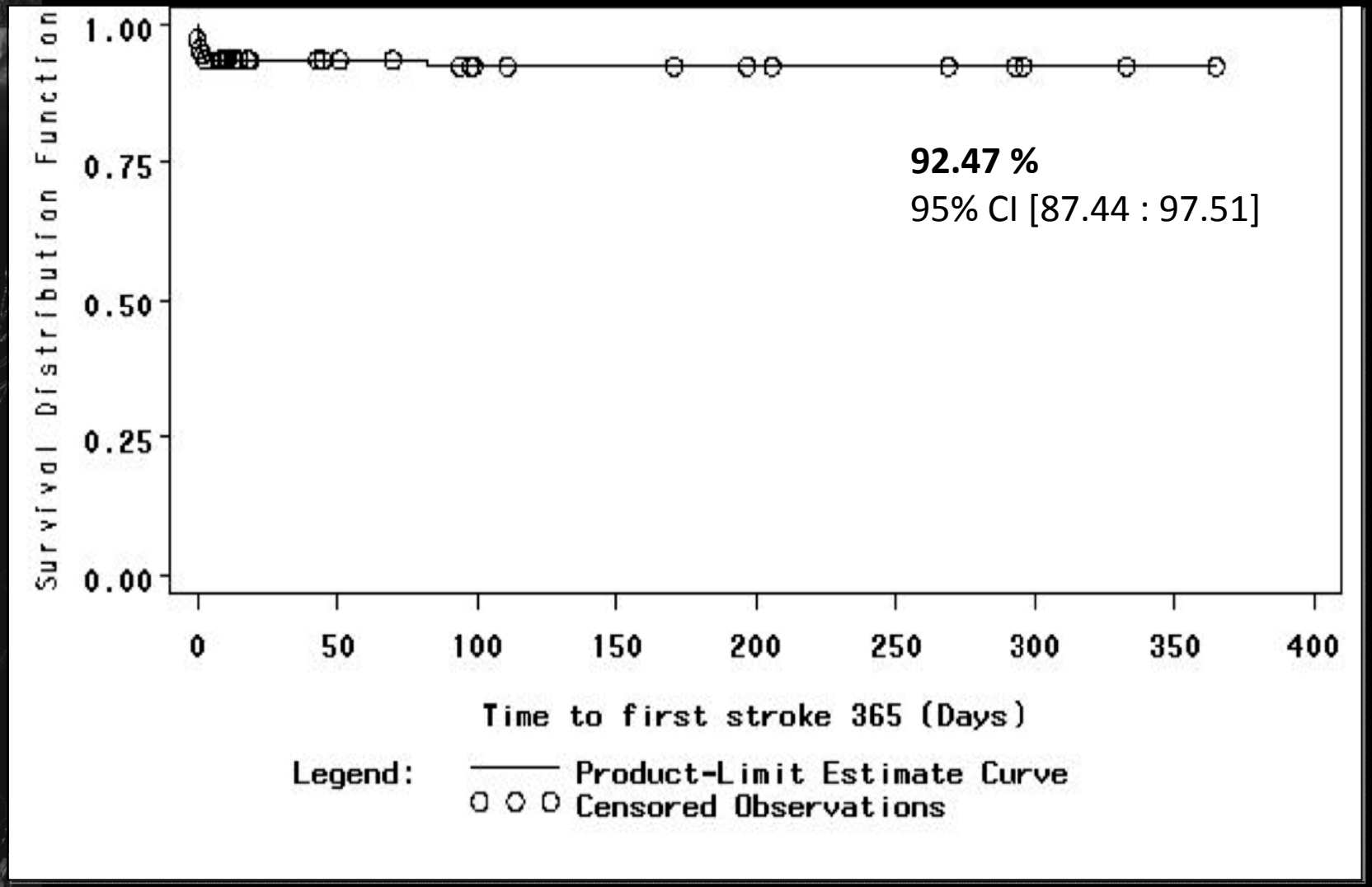
Freedom from Cardiac Mortality



Freedom from Stroke



92.47 %
95% CI [87.44 : 97.51]