Percutaneous Aortic Valve Replacement with the Medtronic-CoreValve System

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Disclosure Information

Raoul Bonan, MD

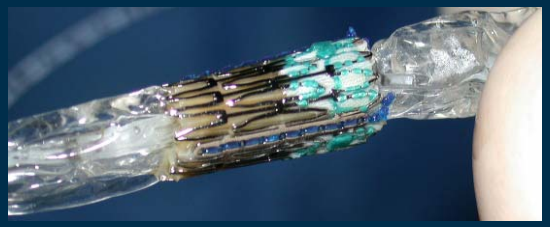
I have the following financial relationships to disclose:

Consultant for: CoreValve inc., Medtronic
Speaker's Bureau for:
Grant/Research support from: CoreValve inc.,
Stockholder in: CoreValve inc.,
Honoraria from:
Employee of:

- and -

I will discuss the following off label use and/or investigational use in my presentation: PAVR

Percutaneous Aortic Valve Replacement



Medtronic-CoreValve

- Self expandable
- Porcine pericardium
- Retrograde

- 18 Fr
- No more CP assistance

Sapien™ Edwards

- Balloon expandable
- Equine/Bovine pericardium
- Retrograde (ante.) /
- Transapical
- 24 Fr
- Rapid pacing

Medtronic-CoreValve ***ReValving*** System for PAVR

Components

1. S**elf-expanding multi-level** support frame with a tri-leaflet **porcine pericardial** tissue valve
2. **18F catheter** delivery system
3. **Disposable** loading system

Self-Expanding Multi-level Support Frame

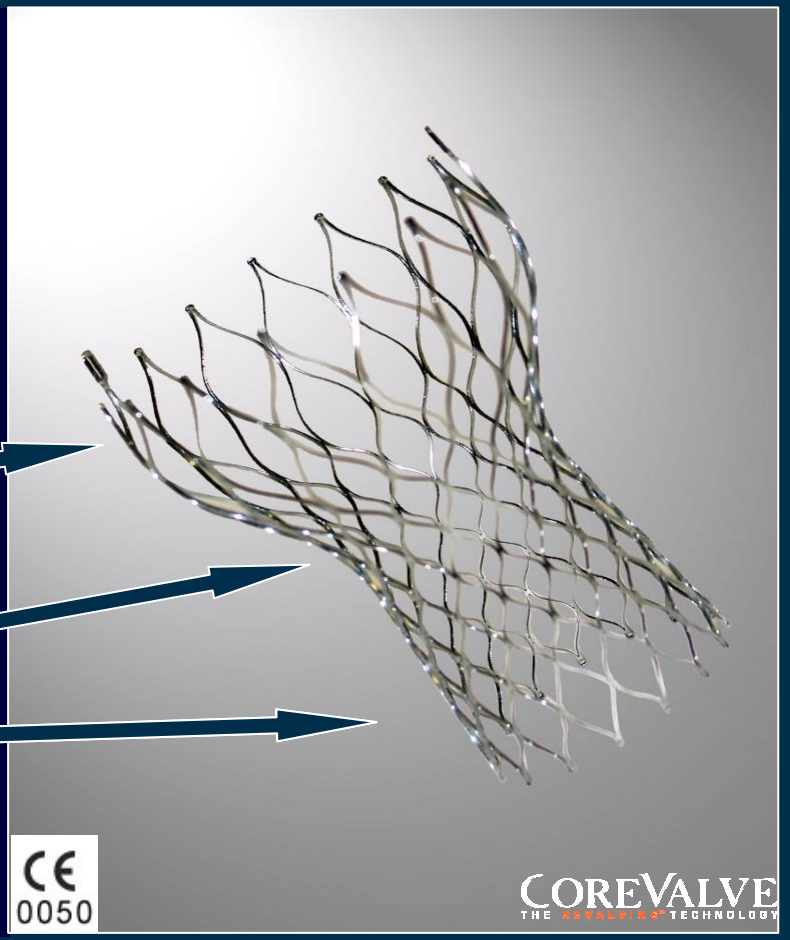
Diamond cell configuration

Nitinol: memory shaped/no recoil

Multi-level design incorporates three *different* areas of radial and hoop strength

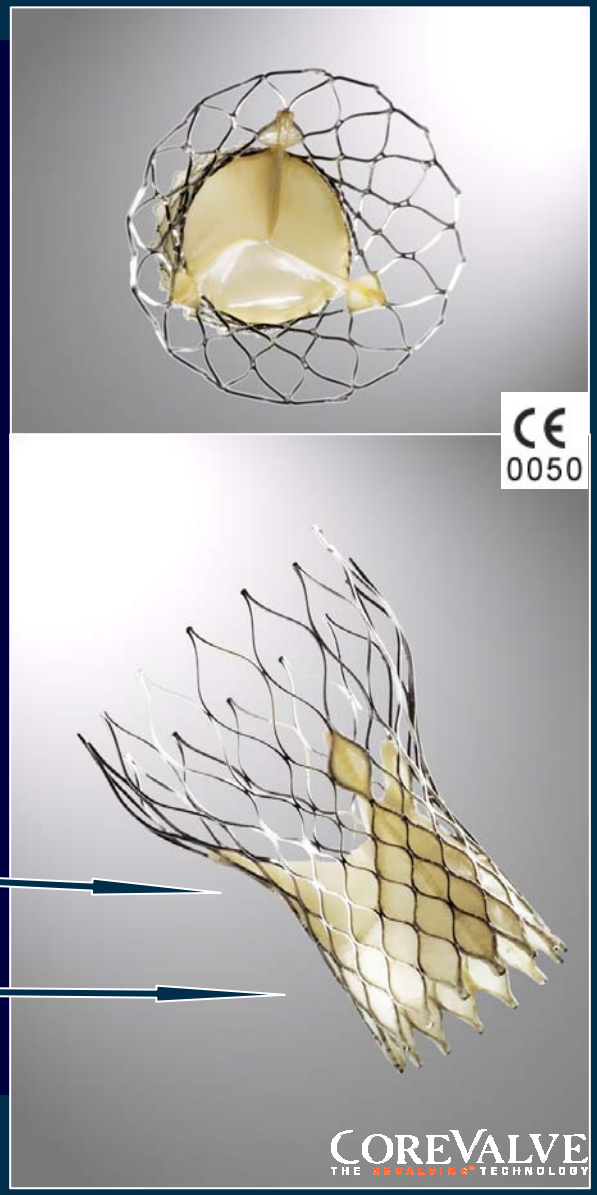
- Low radial force area orients the system
- Constrained area avoids coronaries and features supra-annular valve leaflets
- High radial force provides secure anchoring and constant force mitigates paravalvular leak

Radiopaque

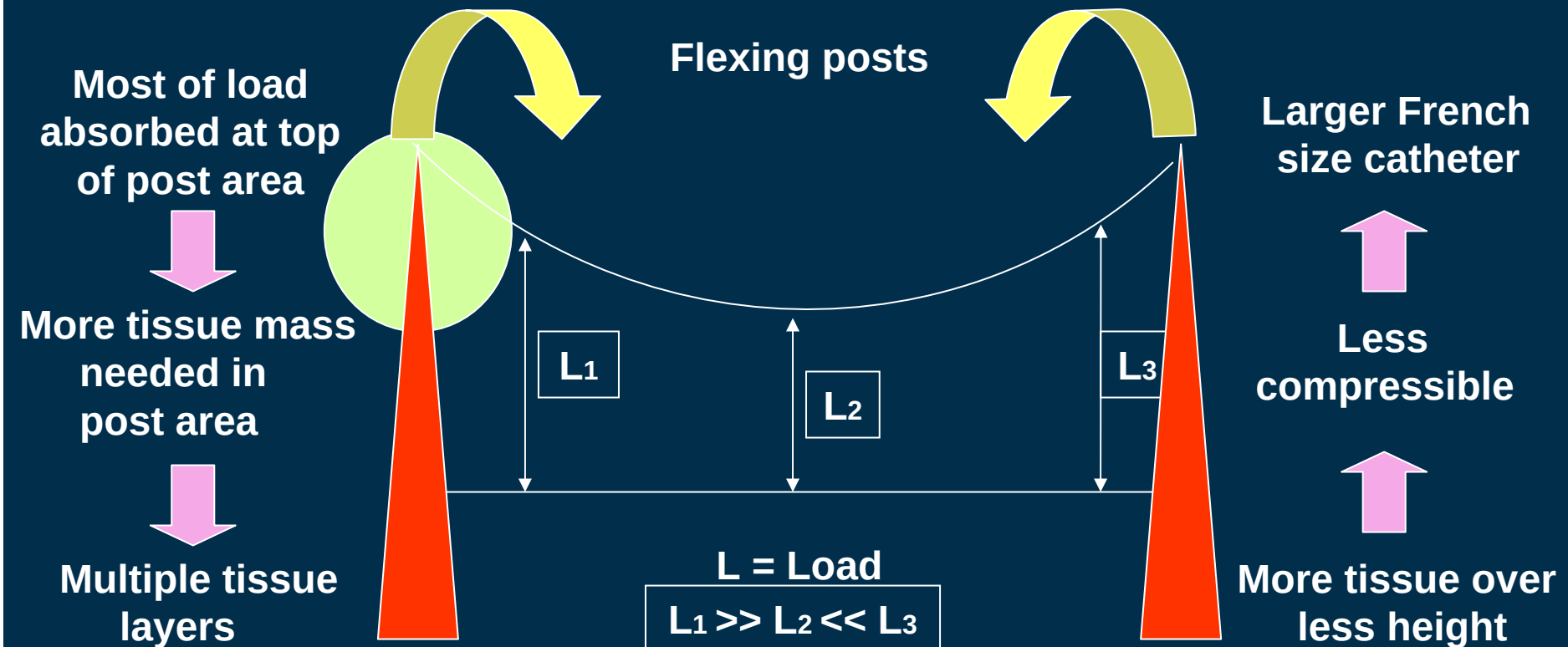


Porcine Pericardial Tissue Valve

- **Specifically designed for transcatheter delivery**
- **Single layer porcine pericardium**
- **Tri-leaflet configuration**
- **Tissue valve sutured to frame**
- **Standard tissue fixation techniques**
- **200M cycle AWT testing completed**
- **Supra-annular valve function**
- **Intra-annular implantation and sealing skirt**

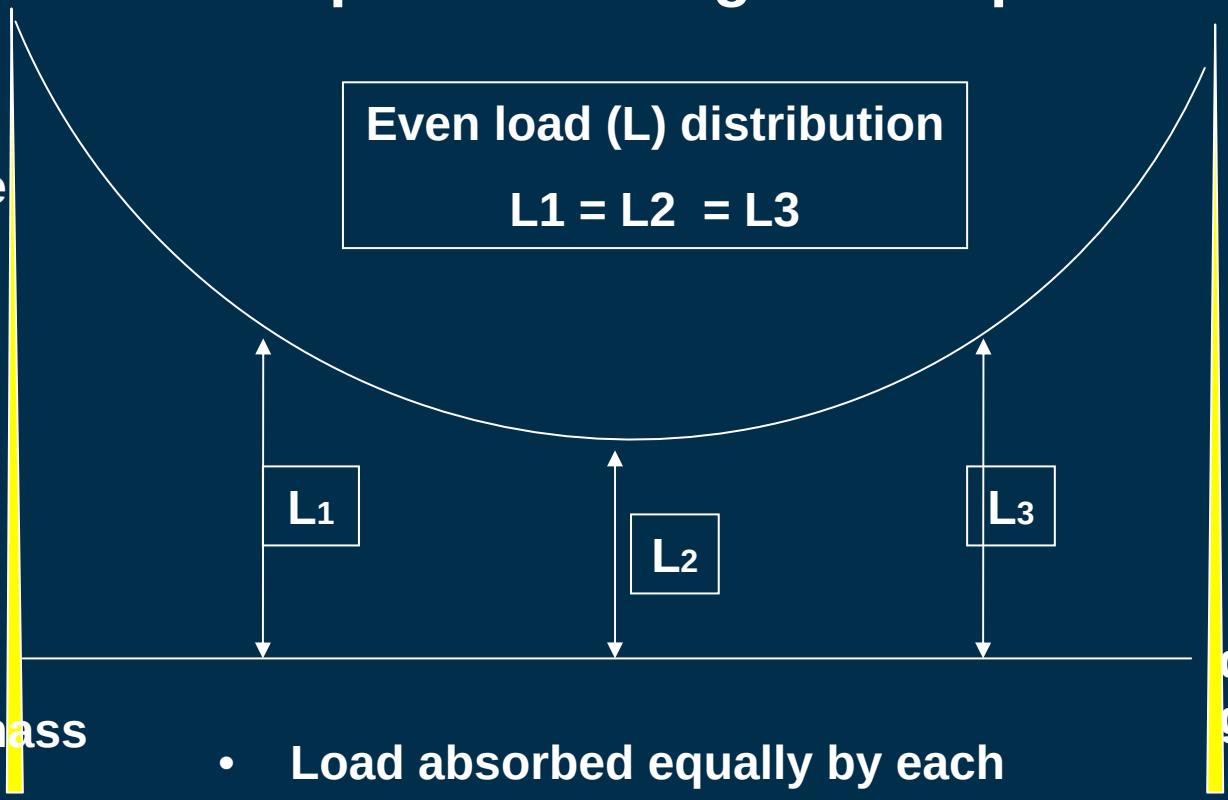


Surgical Bioprosthesis Design



Medtronic-CoreValve Bioprosthesis Design

Suspension bridge concept



Static Frame design = Fixed post equivalent

Less tissue mass needed in post area

Smaller French size catheter

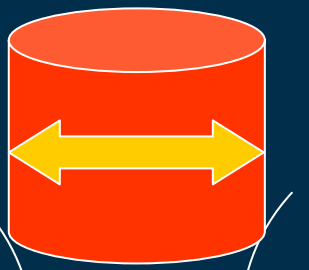
More compressible

Tissue mass distributed over greater height

- Load absorbed equally by each point on leaflet commissures
- NO frame flexing under load

Surgical implantation

Corevalve *Revalving*™

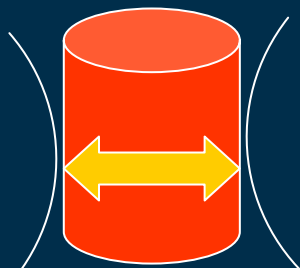


Supra-annular implantation

Supra-annular leaflet function

For same native annulus size
SA position EVA is
larger than IA position EVA

OR



Intra-annular implantation

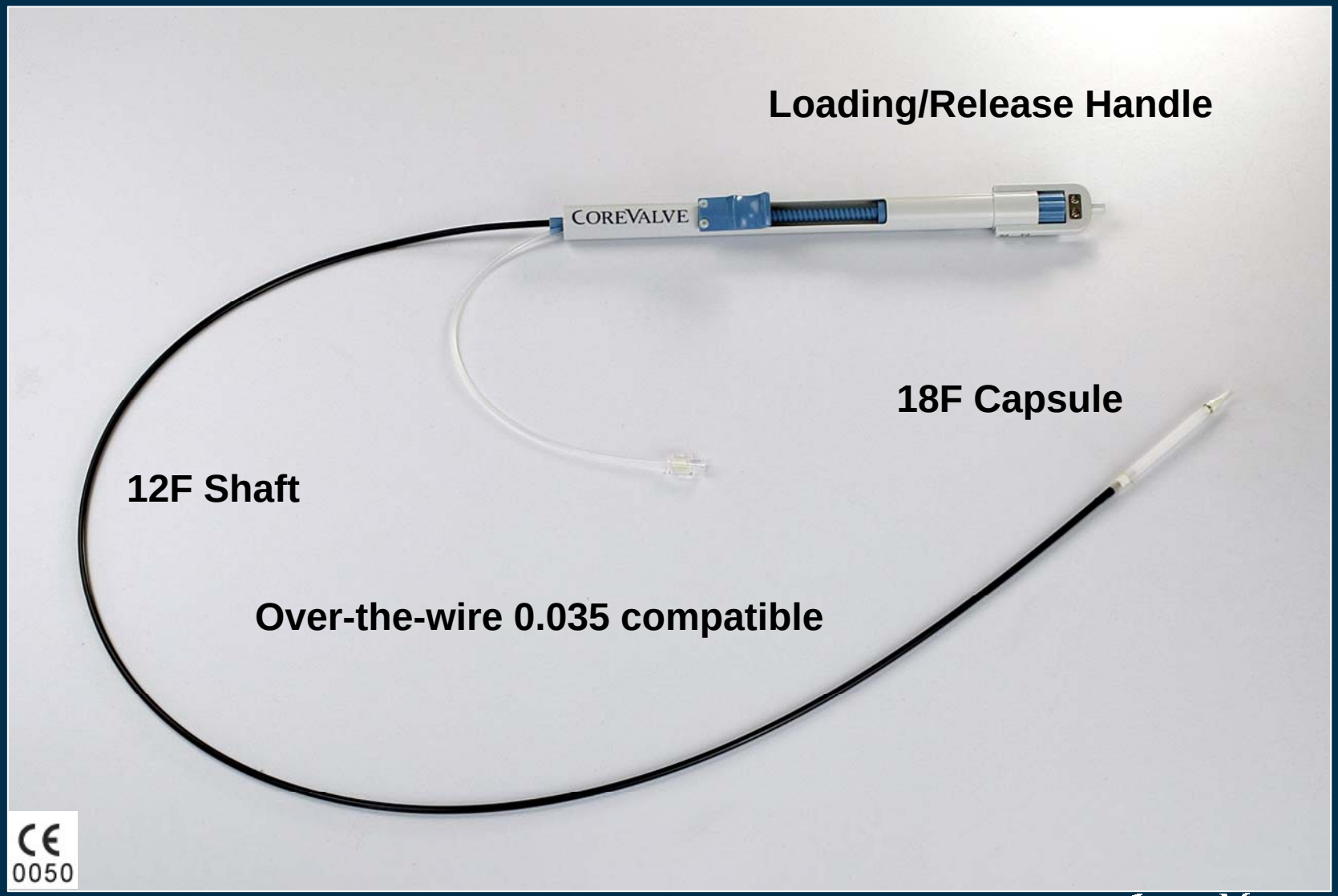
Intra-annular leaflet function

Supra-annular leaflet function

Intra-annular implantation

EVA: effective valve area

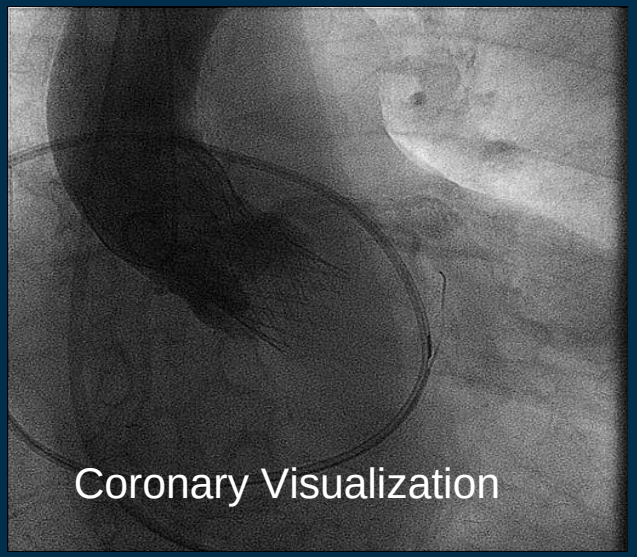
18F Delivery Catheter System



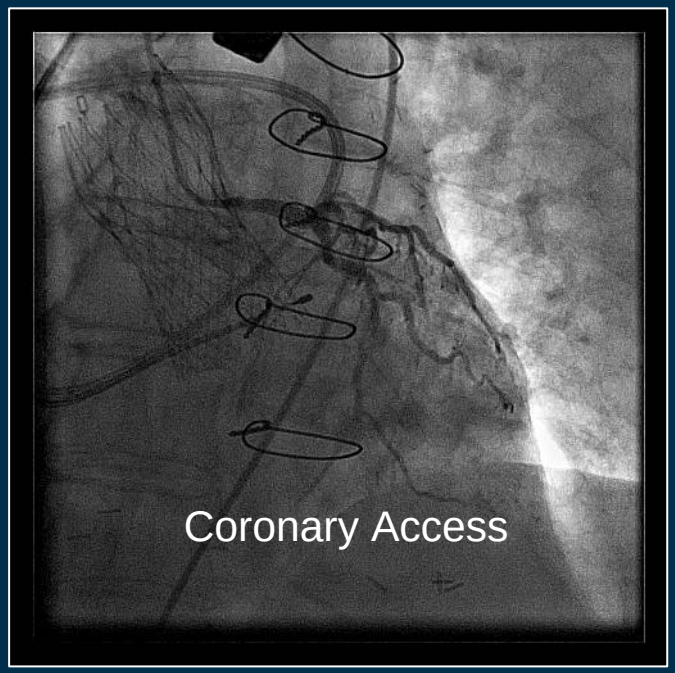
COREVALVE
THE REVALVING® TECHNOLOGY

Disposable Loading System

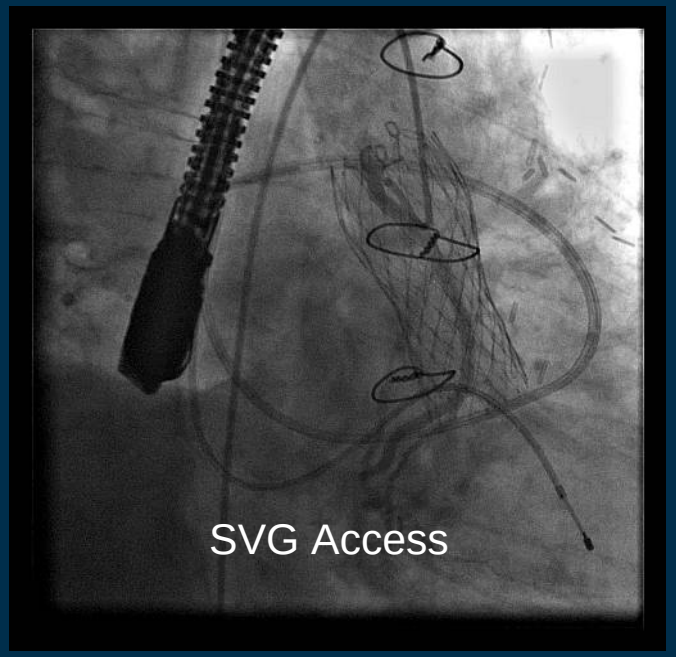
- Consistent compression of bioprosthesis into delivery catheter
- Prevents trauma to valve leaflets
- Single use



Coronary Visualization

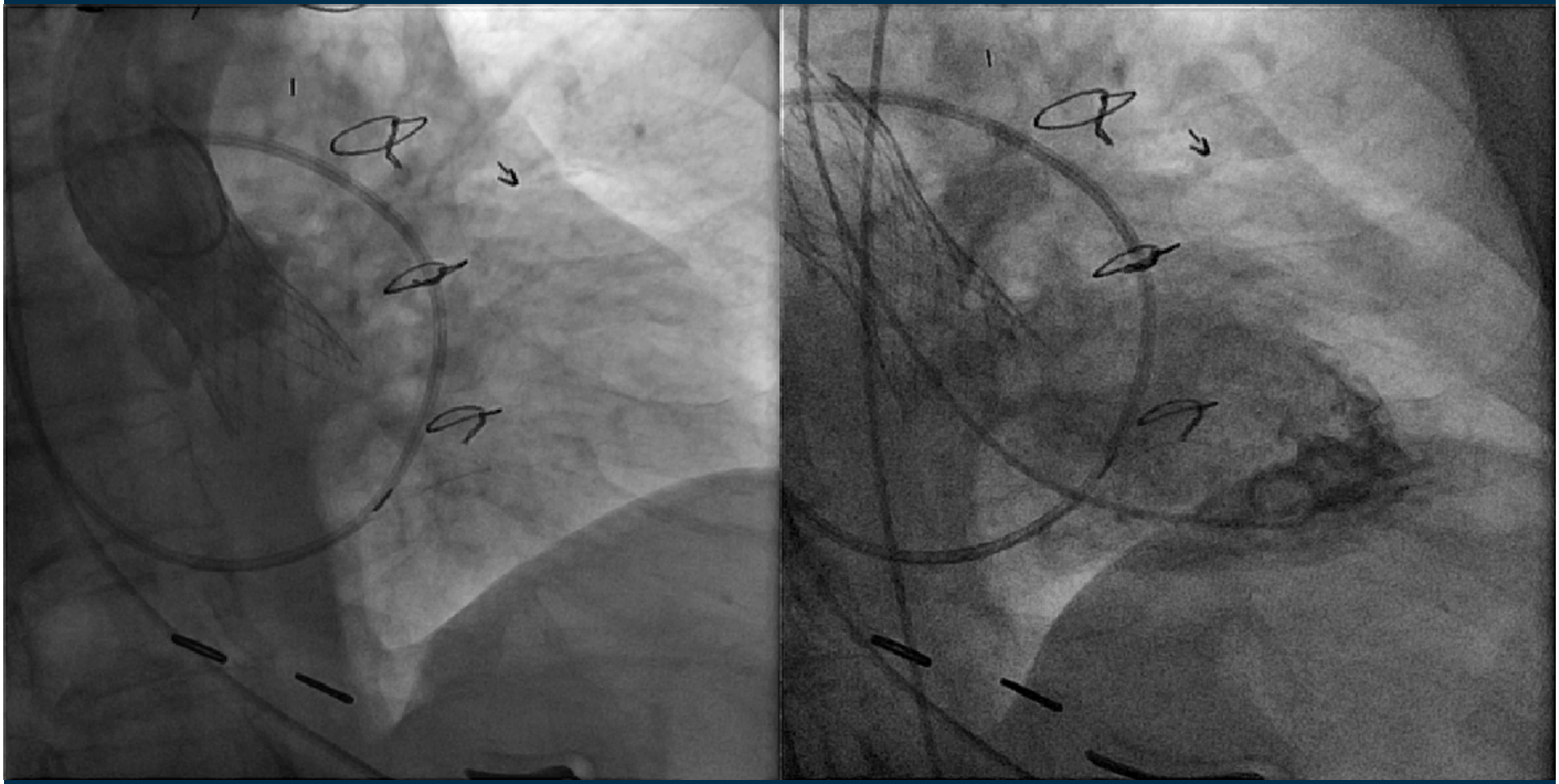


Coronary Access



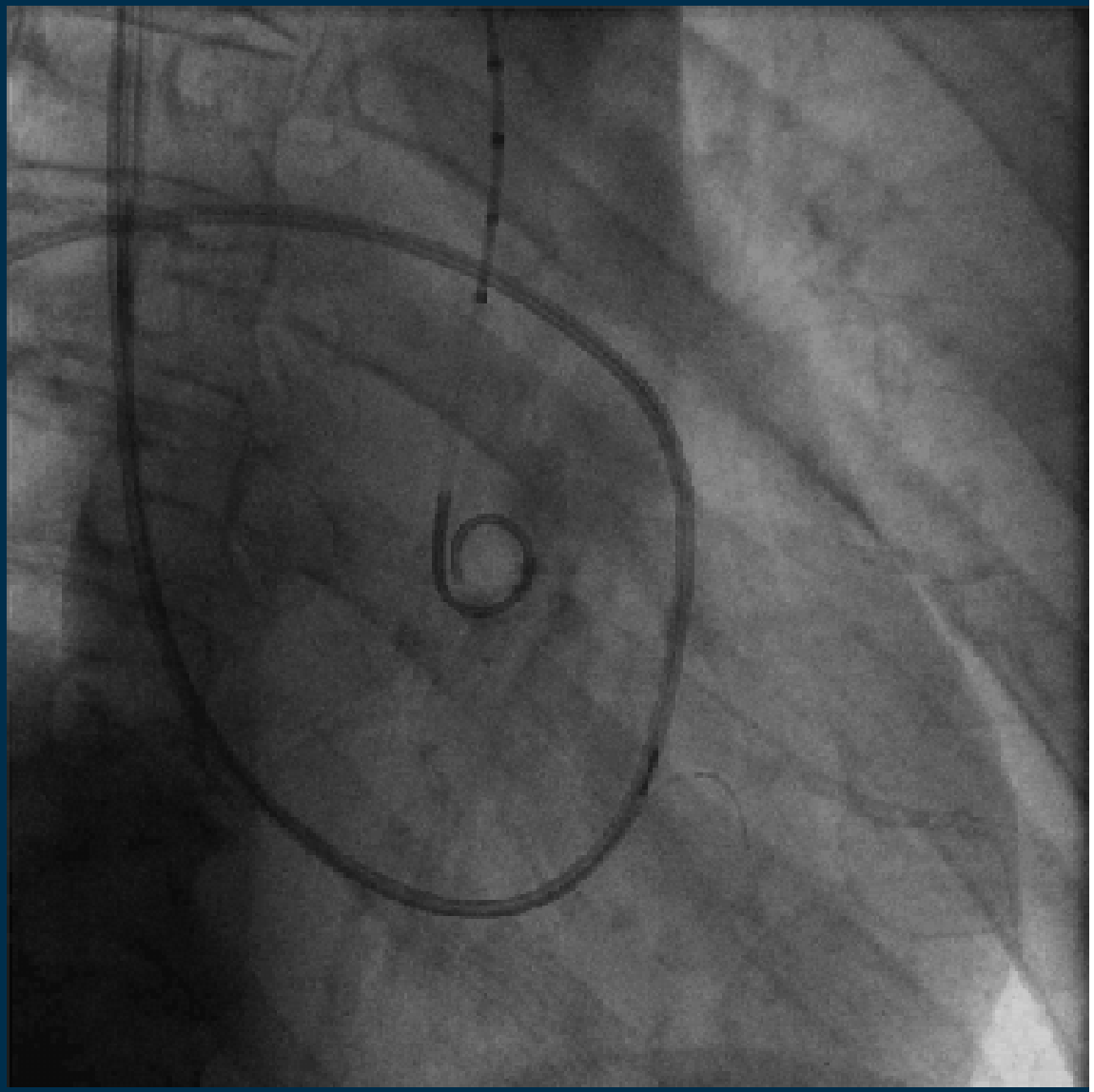
SVG Access

Medtronic-CoreValve Revalving System

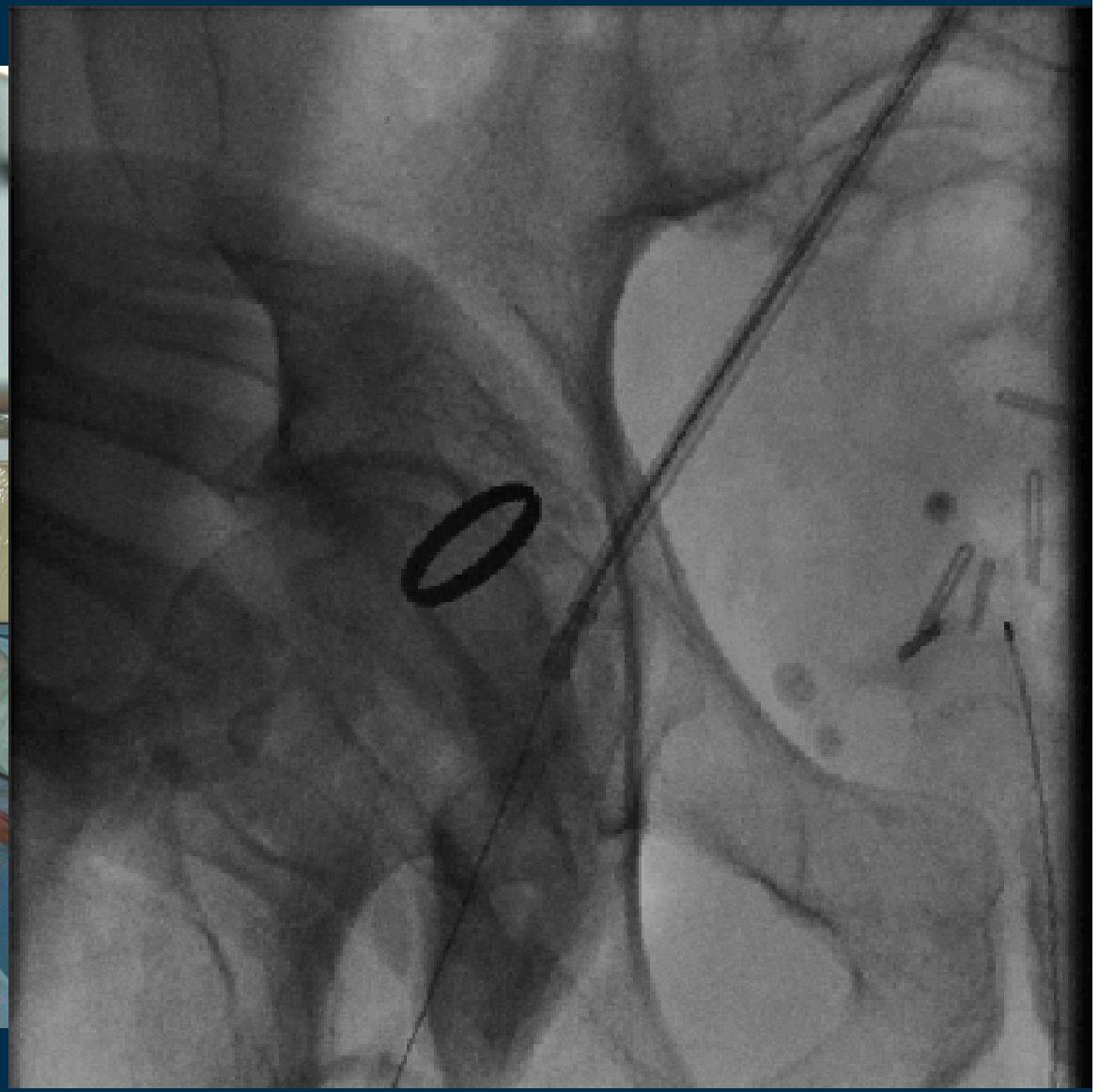


9:14 am

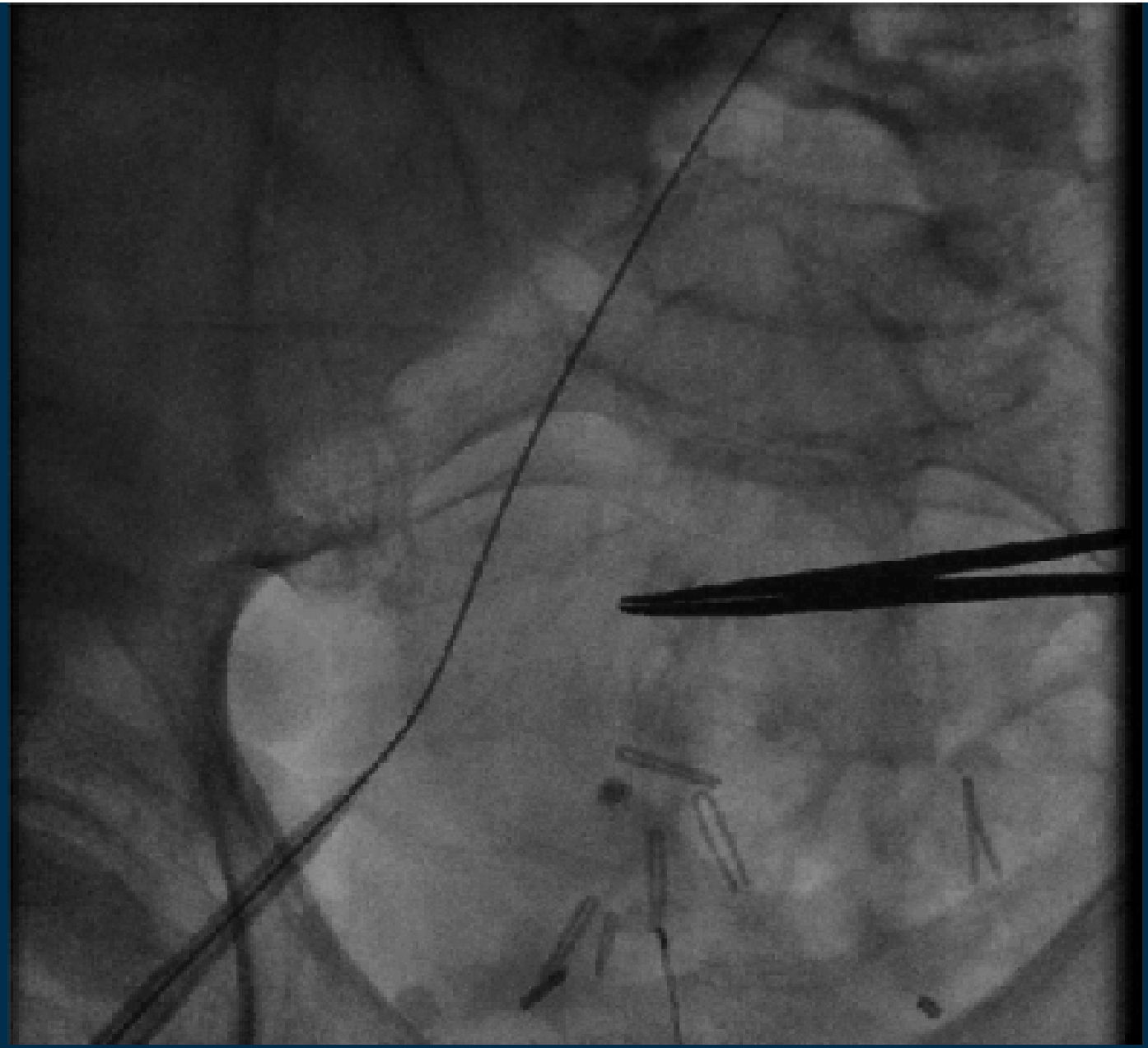
Radial approach for Angios



RAO 20° Caud. 20°: Leaflets aligned

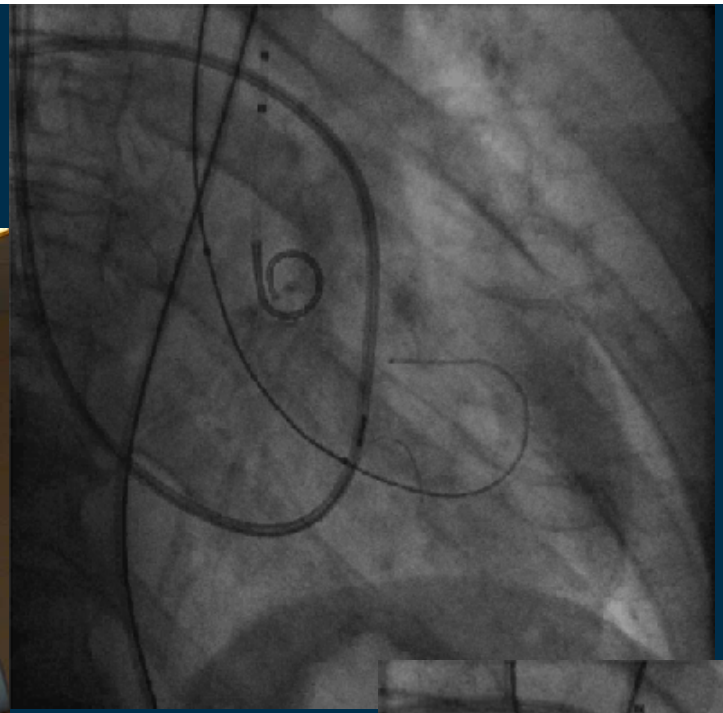


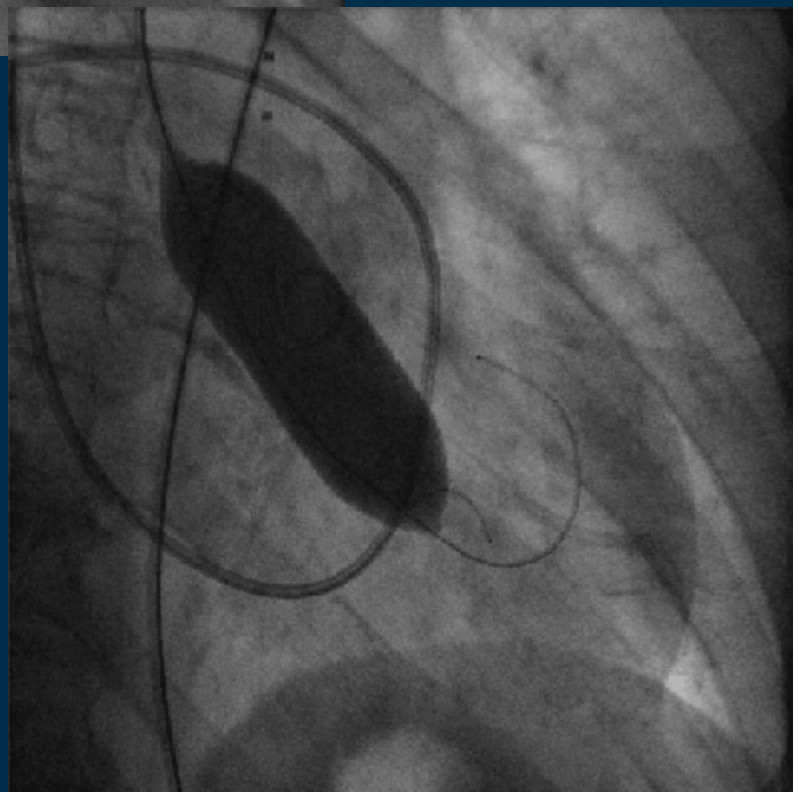
Prostar 10 Fr



Introducer 18 Fr

9:44 am

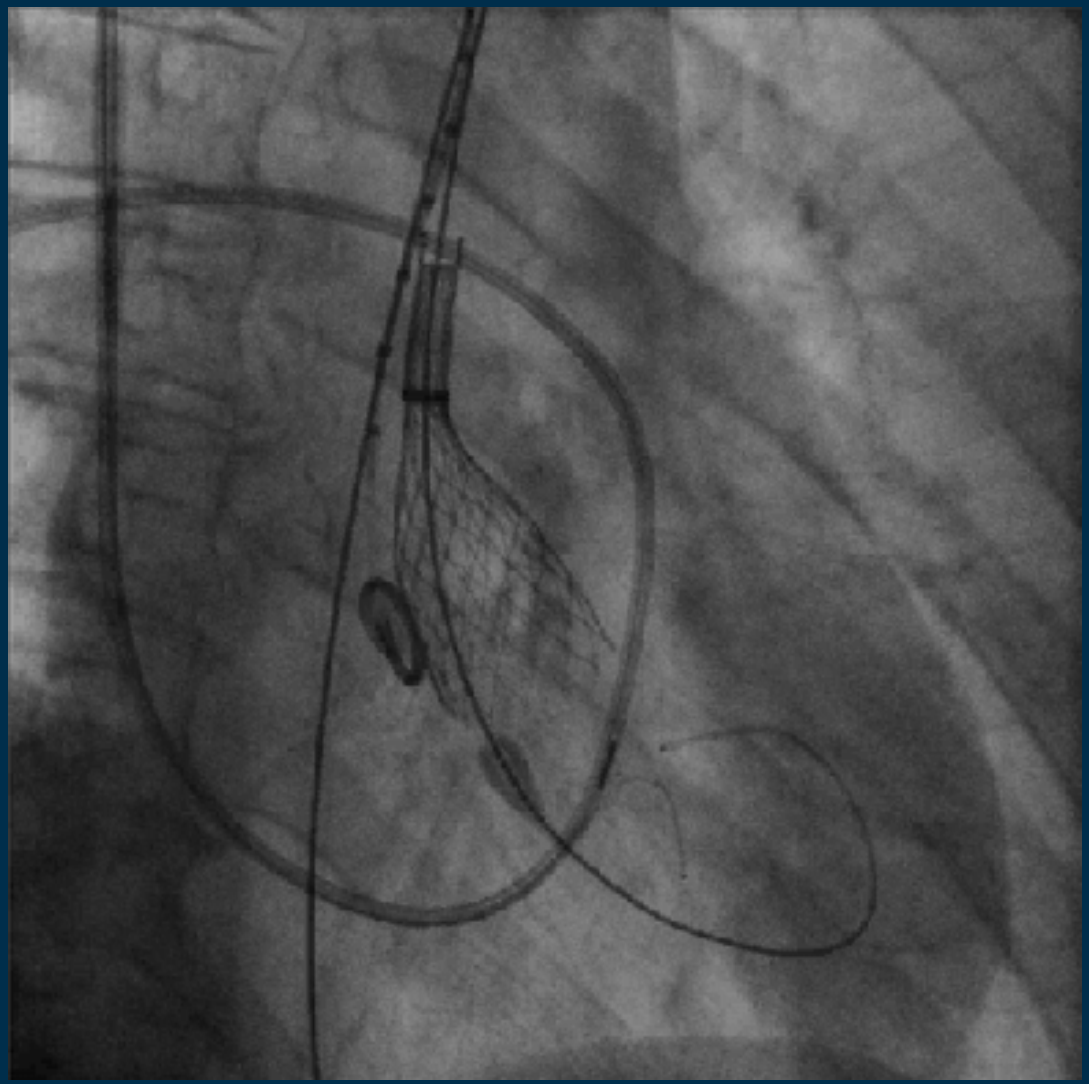




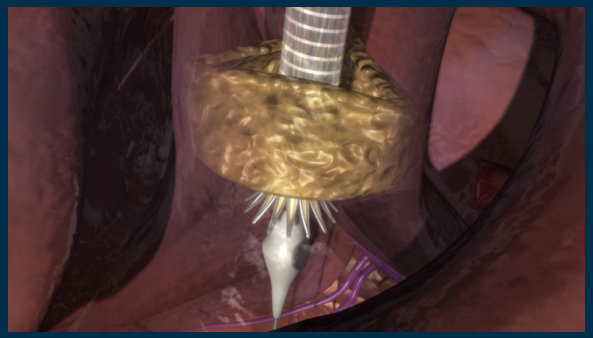
Balloon 23 mm

9:50 am

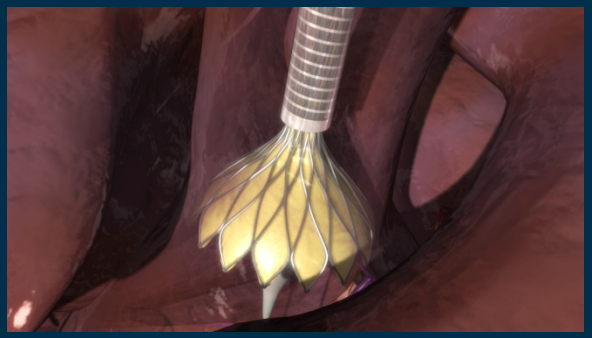
Progression of the 18 Fr catheter with the Prosthesis



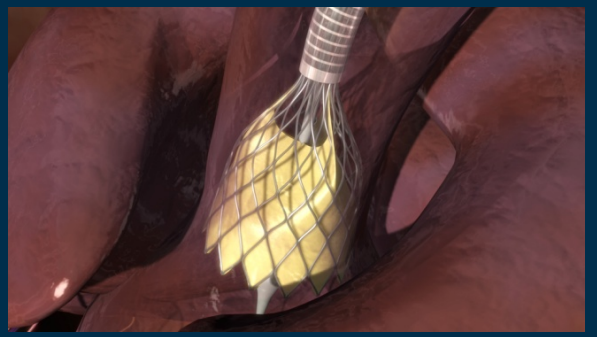
Lesson Learned
Slow and Stepwise Deployment Allows Repositionability



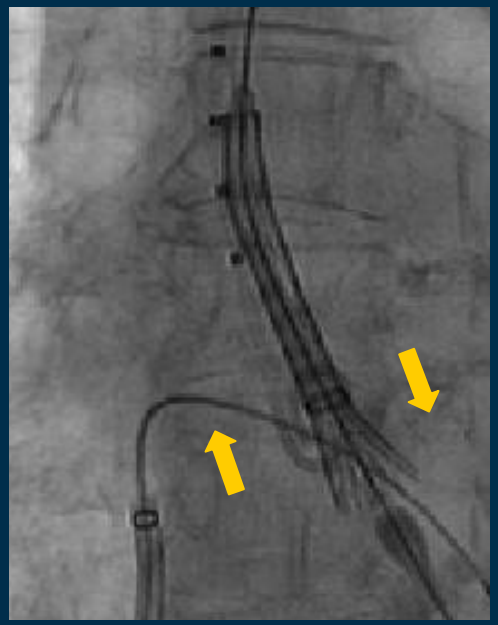
Before annular contact

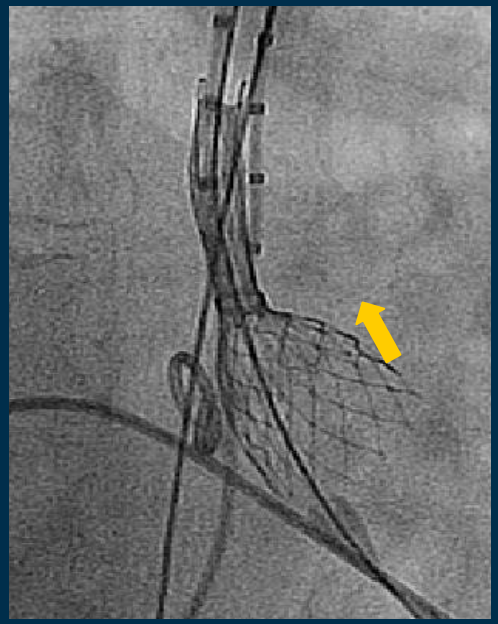


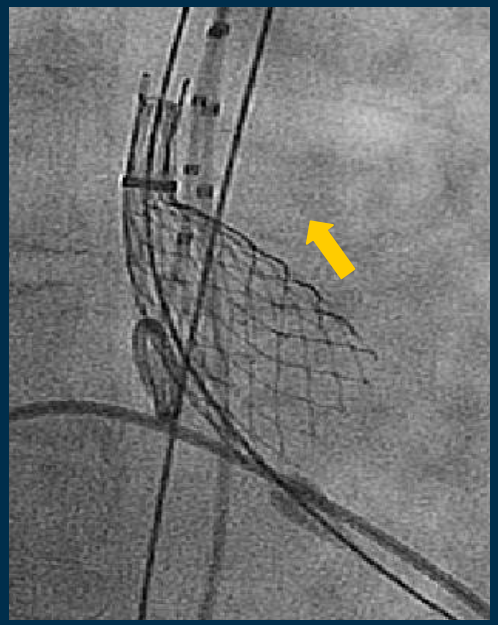
After annular contact



Before device release

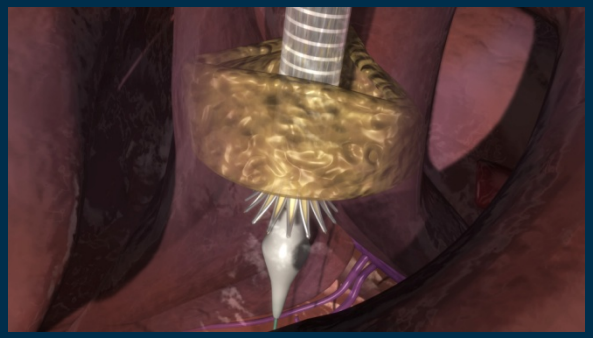




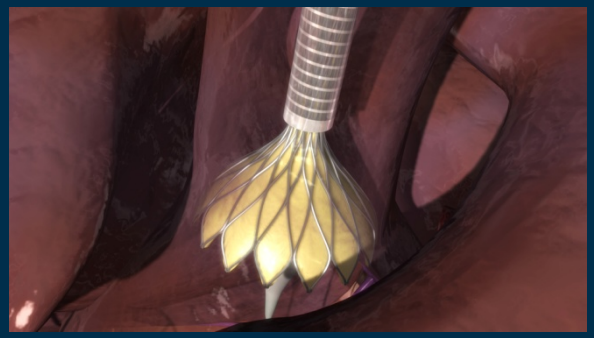


No need to “rush” since…

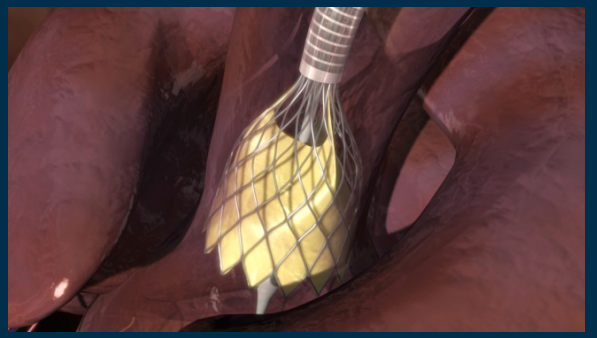
Valve Functional Before Full Deployment



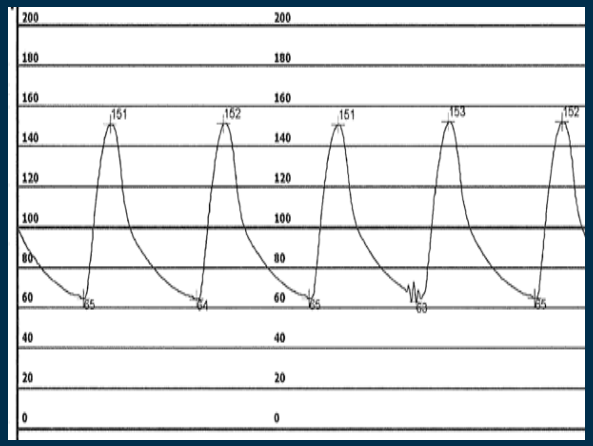
Normal blood pressure before annular contact

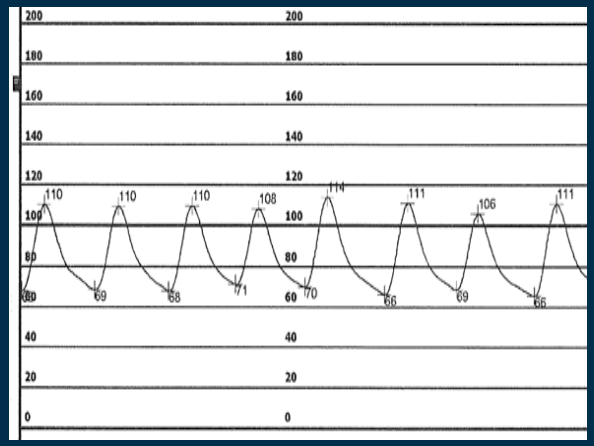


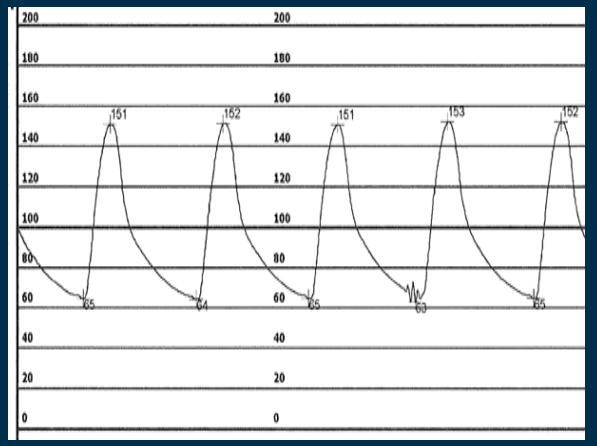
Reduced blood pressure only between 1/3 & 2/3 of the deployment

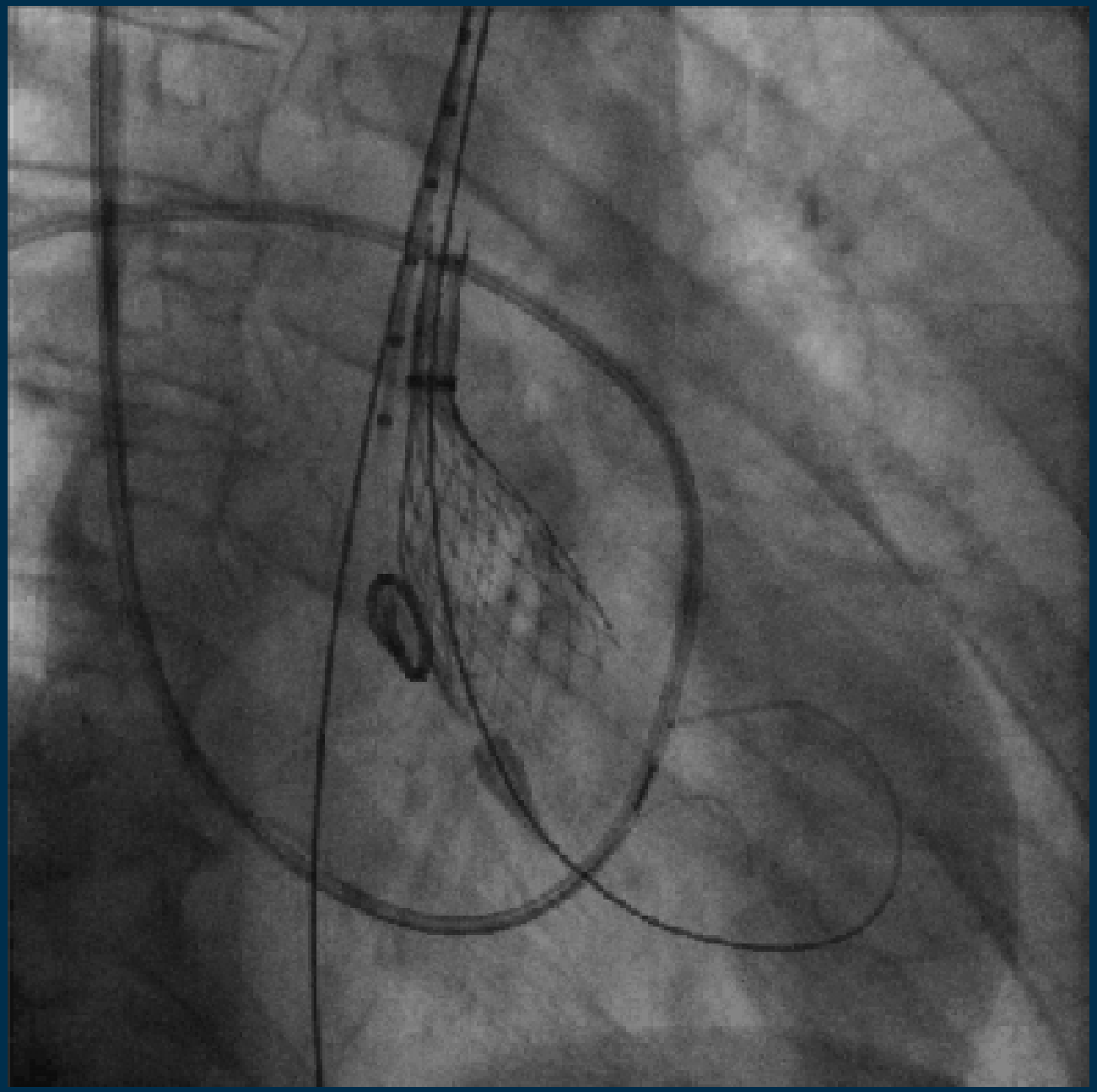


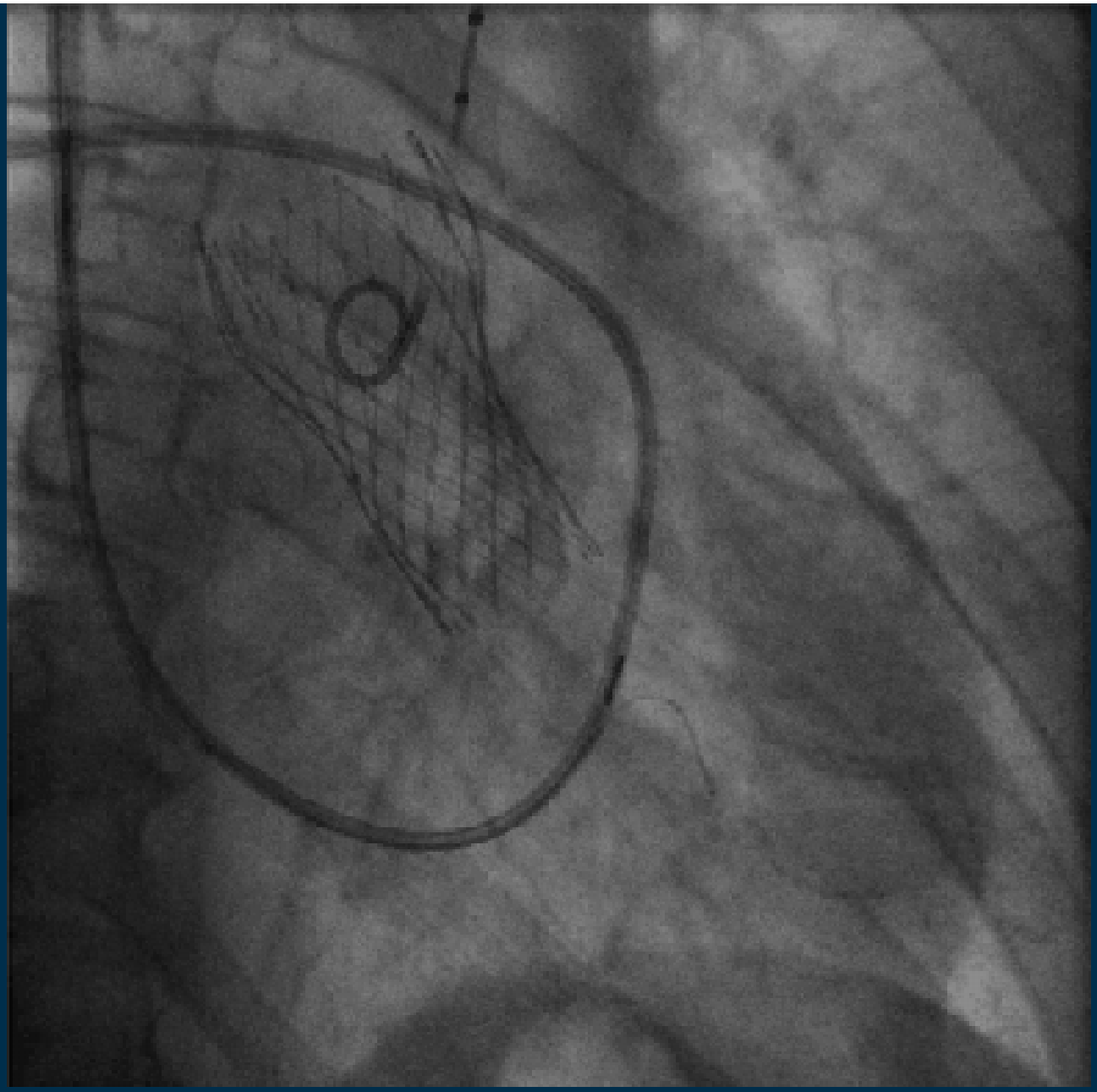
At 2/3 point, BP returns to normal and valve is still repositionable











Final Angio: AI 1

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	8.6 ± 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

18-Fr Safety & Efficacy Study

- Design
  - Prospective, multi-center, non-randomized single arm observational study.
- Enrollment
  - 112 patients (May 06 to Jun 07)
  - Additional 14 patients (Apr 08 – Nov 08) - Canada
- Inclusion Criteria
  - Severe Aortic Valve Stenosis
  - ≥ 75 Years of Age
  - Logistic EuroScore ≥ 15% or High Risk Co-morbidities
- Endpoints
  - Safety (Composite MAE and MACE)
  - Procedural Success

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

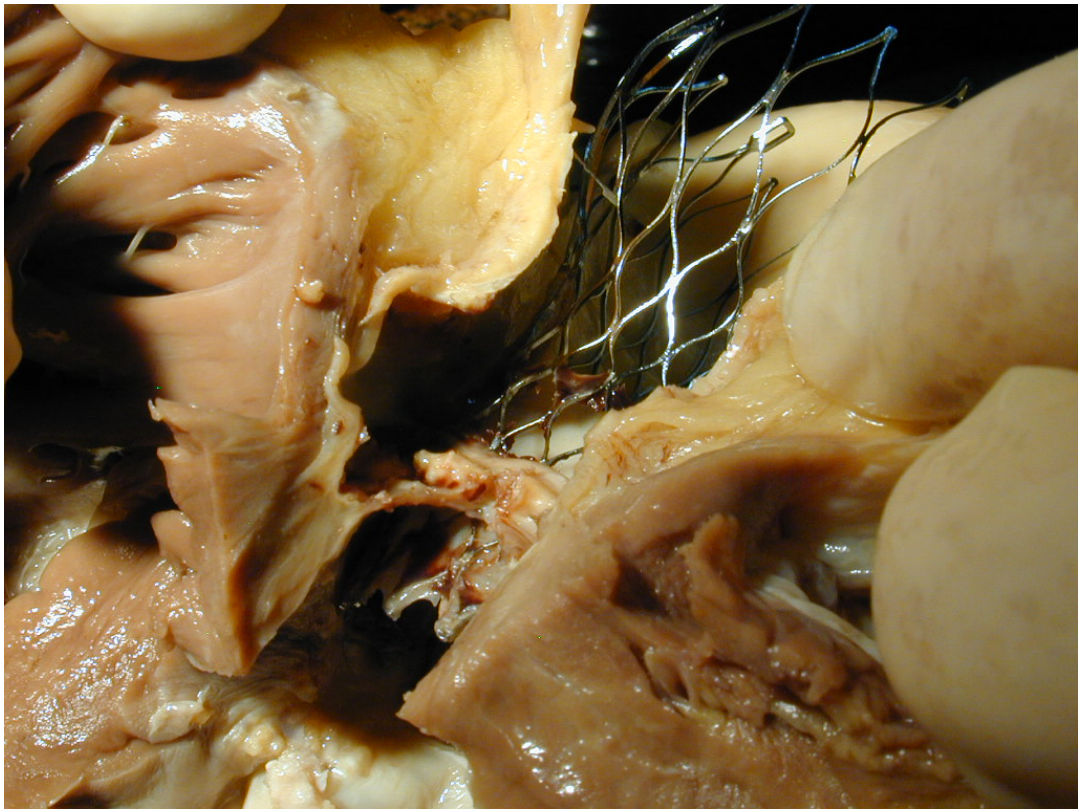
Pre-existing Co-morbidity

Morbidity	Value
Coronary artery disease	72 (64.3 %)
Prior myocardial infarction	19 (17.0 %)
Prior coronary intervention	44 (39.3 %)
Prior CABG	30 (26.8%)
Peripheral vascular disease	20 (17.9%)
Porcelain aorta	10 (8.9%)
Prior stroke or TIA	24 (21.4%)
Atrial fibrillation	48 (42.9%)
Congestive heart failure	62 (55.4%)
Renal Failure	49 (43.8%)

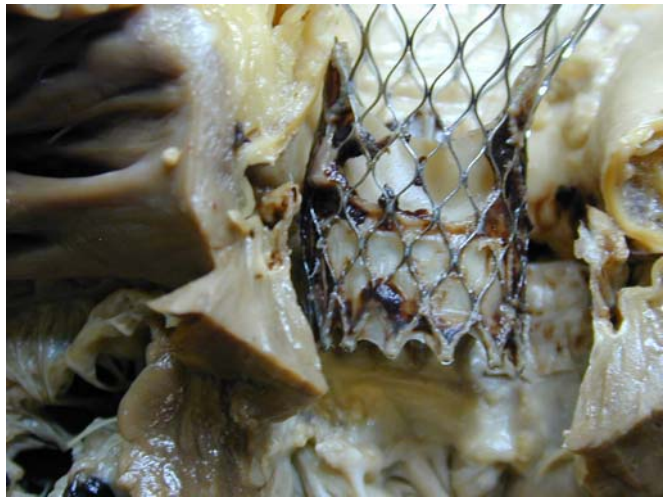
Patient Follow-up

Follow-up Period	Index	Discharge	1 Month	3 Months	6 Months	12 Months
Patients Treated	112					
Not Implanted	1					
Explanted	2					
Death/Explanted	1					
Peri-operative Death	4					
Patients Followed	**104**	**104**	**92**	**92**	**84**	**80**
Death		12	0	8	3	4
Withdrew Consents		0	0	0	1	1
Missed Follow-up Visits		0	9	8	4	3

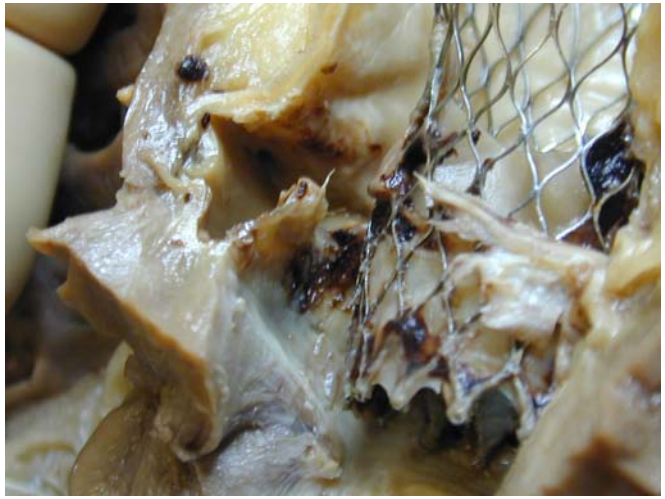
Ouverture Anterieure



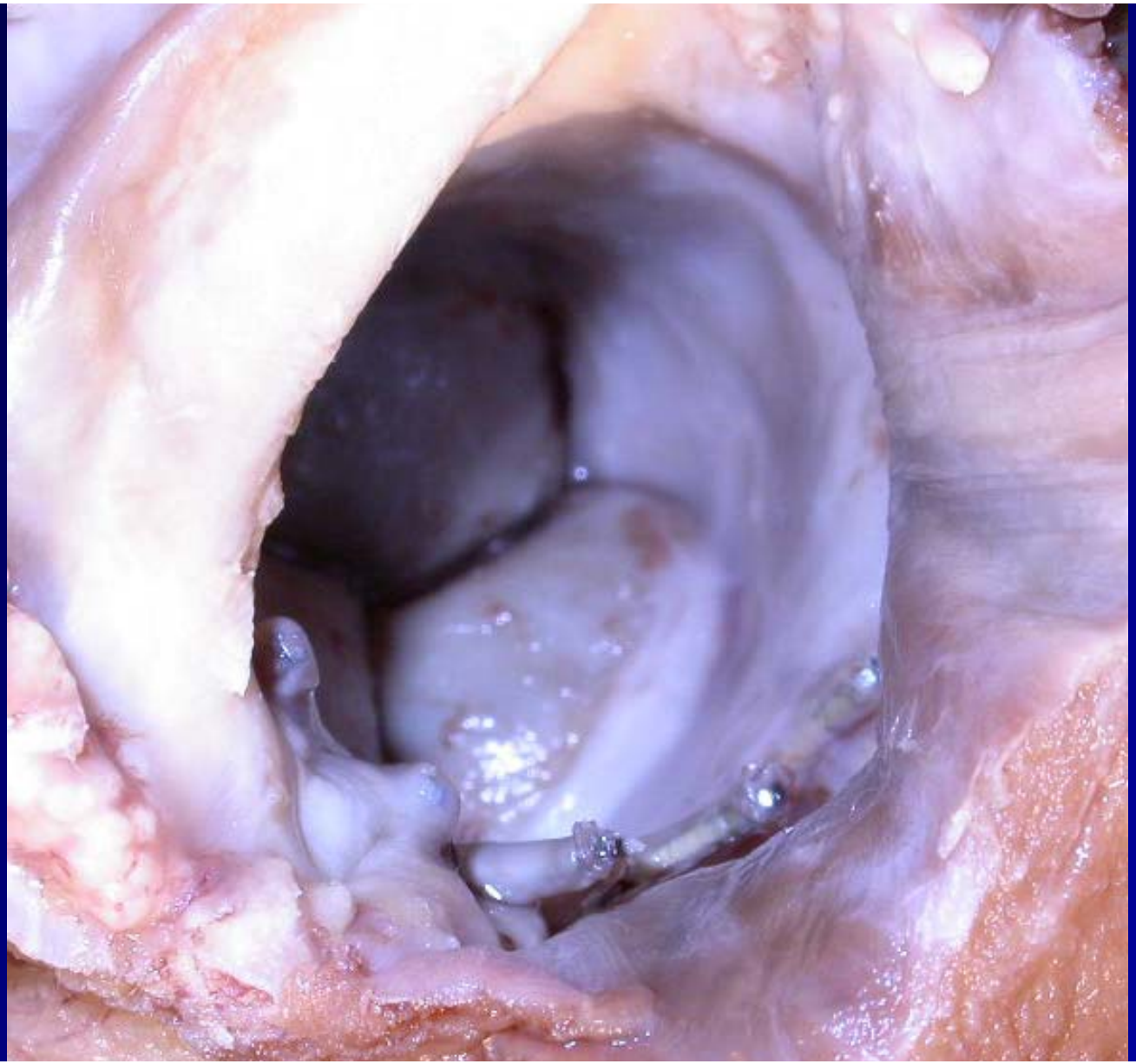
Relation Prothese
et
Feuillet Anterieur de la Mitrale



Relation Prothese
et
Feuillet Aortique Droit



CoreValve *(area 1)* 104 days post implantation



Struts completely covered by tissue

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%)

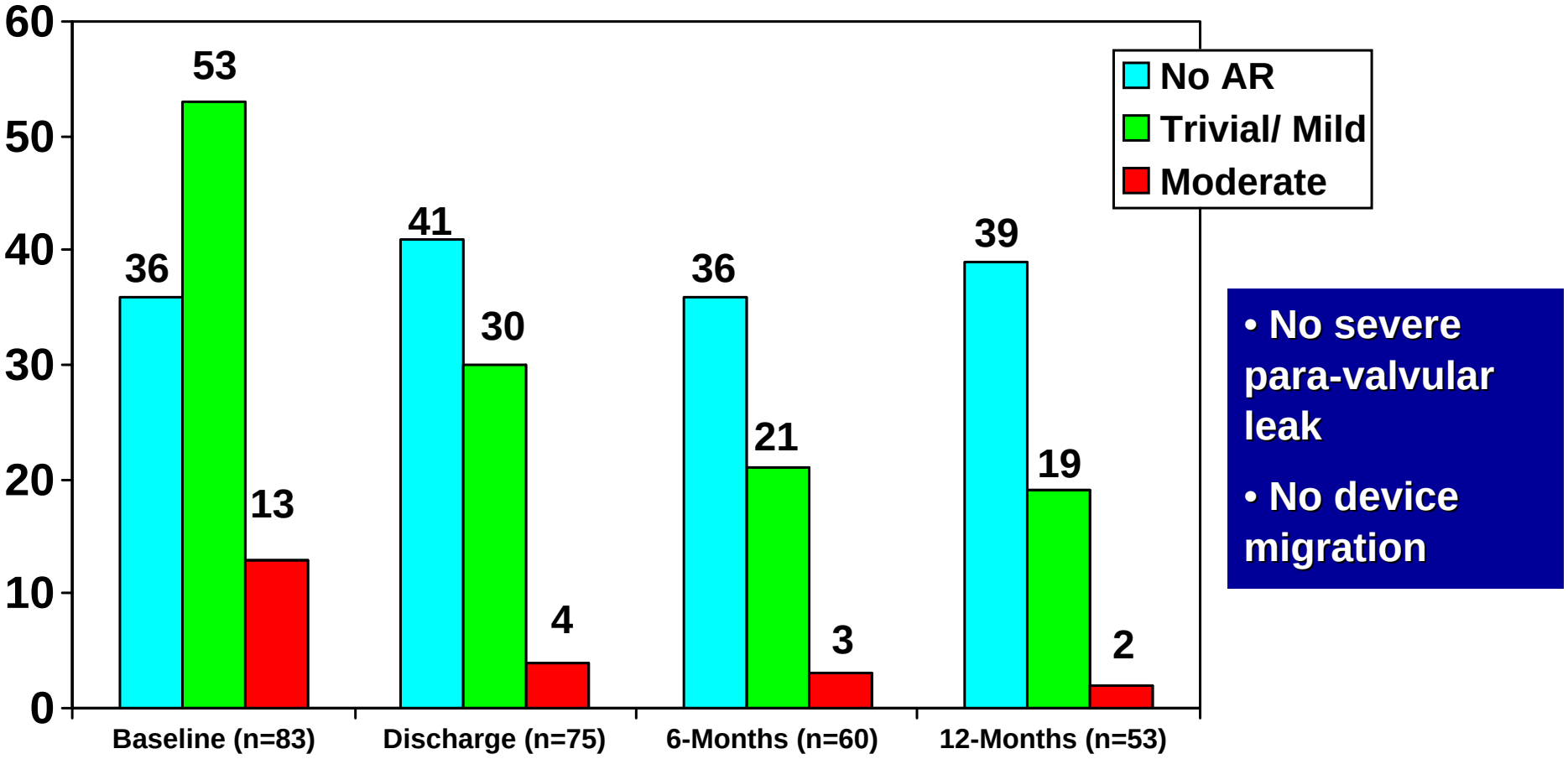
Cumulative Safety

Outcomes (n = 112)	Discharge	30-Day	12-Month
Death – All Cause	17 (15.2%)	17 (15.2%)	32 (28.6%)
Death – Cardiac	12 (10.7%)	12 (10.7%)	19 (17.0%)
Death – Non-Cardiac	5 (4.5%)	5 (4.5%)	13 (11.6%)
Thromboembolic Events	14 (12.5%)	14 (12.5%)	16 (14.3%)
Stroke	7 (6.3%)	7 (6.3%)	8 (7.1%)
TIA	7 (6.3%)	7 (6.3%)	8 (7.1%)
Myocardial Infarction	4 (3.6%)	4 (3.6%)	6 (5.4%)
Major Arrhythmia	20 (17.9%)	21 (18.8%)	25 (22.3%)
Permanent Pacemaker	26 (23.2%)	30 (26.9%)	35 (31.3%)
MACE	28 (25.0%)	30 (26.8%)	40 (35.7%)
MAE	57 (50.9%)	60 (53.6%)	73 (65.2%)

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%)

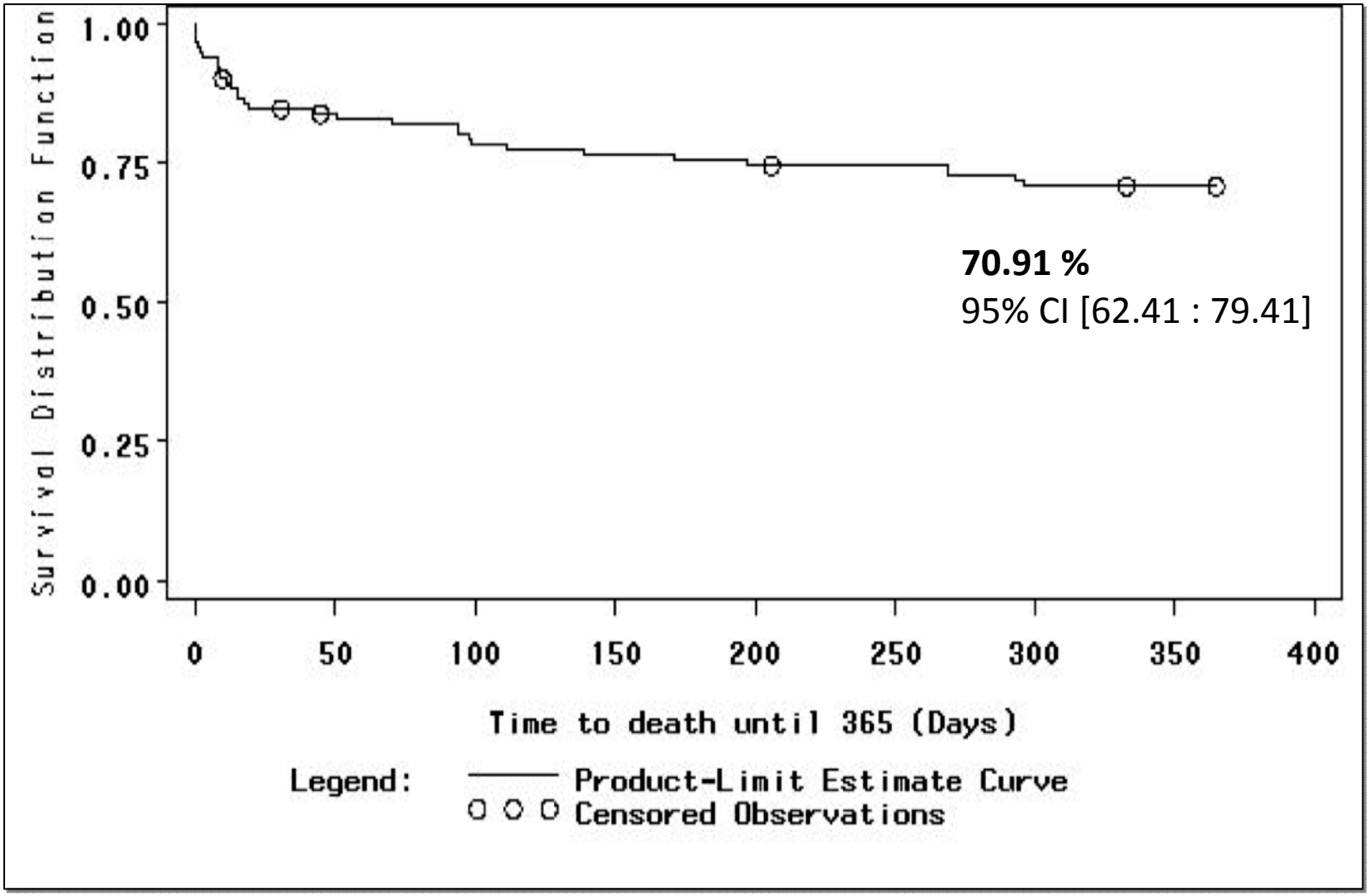
Aortic regurgitation/ Para-valvular leak



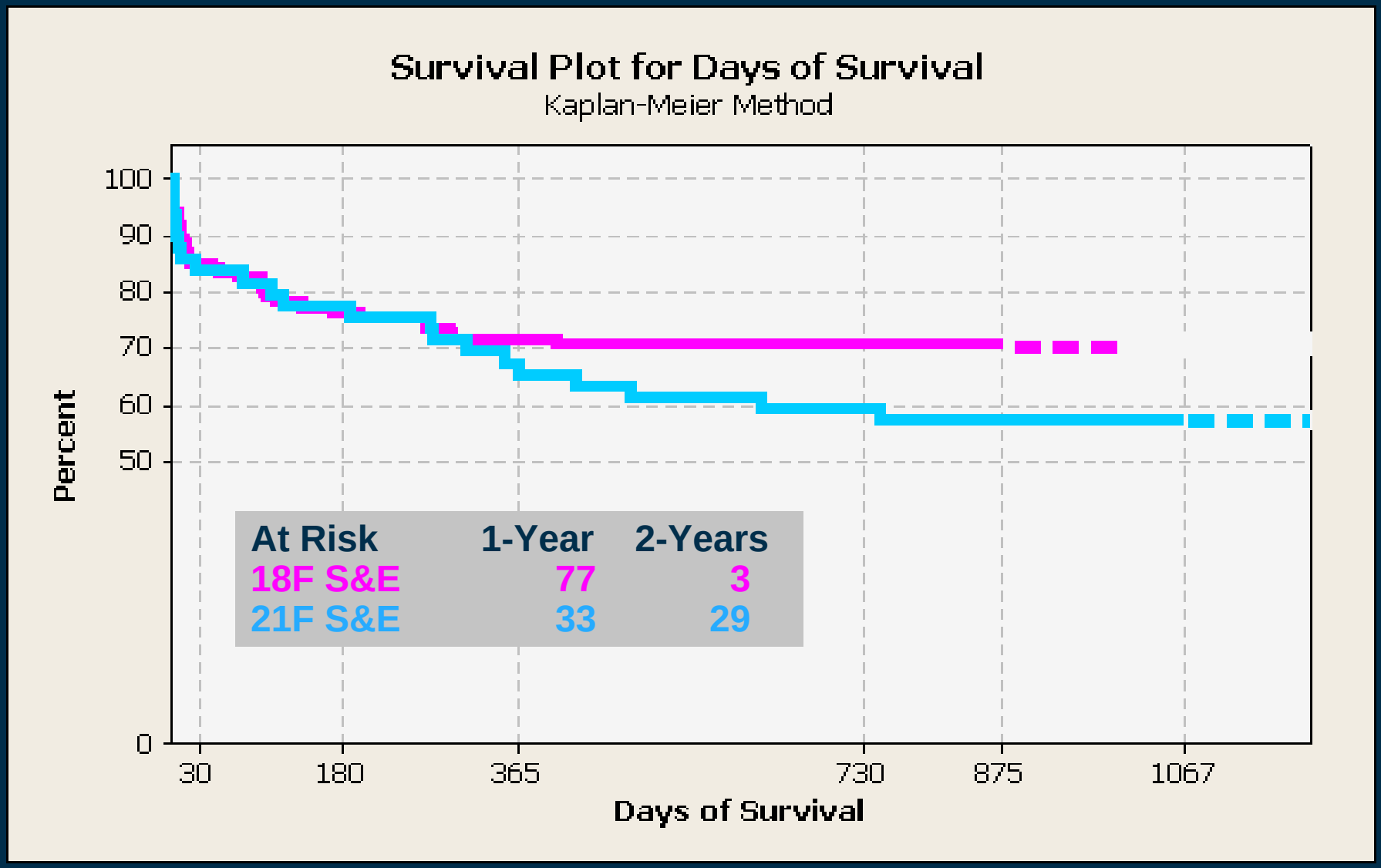
- No severe para-valvular leak
- No device migration

Trivial/ Mild vs. Moderate AR : * p= 0.086 discharge vs. BL
§ p= 0.052 12M vs. discharge

Freedom from ALL Cause Mortality



Medium Term Follow-Up



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%
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
Technical Success	86.5%	n.a.	97.3%	98.3%	98.5%	91.2%

* Site reported ✚ Un-adjudicated

Lesson Learned
Patient Selection Is A Critical Factor

- Access Site
  - Artery diameter
  - Tortuosity
  - Lesions
  - Calcification
- Abdominal and thoracic aorta
- Native valve anatomy
  - Annulus diameter
  - Valve/Aorta angulation
  - Valve Calcifications
  - Sinus dimensions
  - Sino-tubular junction
  - Ascending aorta

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Patient Selection Matrix

	NON-INVASIVE		ANGIOGRAPHY				SELECTION CRITERIA		
Anatomy	Echo	CT / MRI	LV	AO	Coro	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% (w/o cardiac support)
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 [A]	X	X					20 to 23mm → 26mm device 23 to 27mm → 29mm device		< 20mm or > 27mm
AO Root width [B]		X	X	X			≥ 27mm → 26mm device ≥ 28mm → 29mm device		< 27mm
Coronary Ostia [D] (from native leaflet)					X		≥ 14mm	13mm w/ mod. Ca^{2+} 10 to 13mm w/o Ca^{2+}	< 14mm w/ severe Ca^{2+} < 13mm w/ mod. Ca^{2+} < 10mm w/o Ca^{2+}
Coronary Disease					X		None	Mid or Distal Stenosis < 70%	Proximal Stenosis ≥ 70%
Annulus-to-Aorta (angle) †		X	X	X			< 45°	45° to 70°	> 70°
Ascending AO width [C]	X	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 & Runoff Vessels (Disease) ‡		X				X	None	Mild	Moderate to Severe
Iliac & Femoral Vessels (diameter)		X				X	≥ 7mm	Non-Diabetic Non-Dialyzed ≥ 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.

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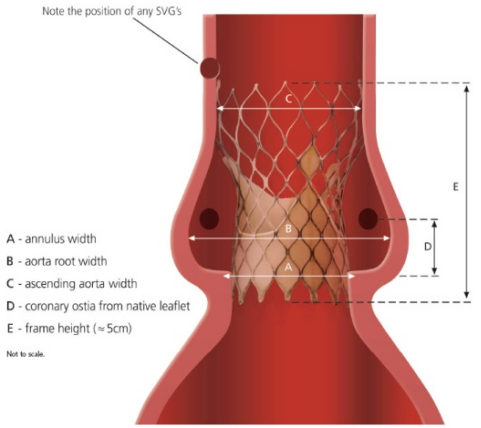

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Conclusions

PAVR with the Medtronic-CoreValve ReValving System:

- ***Has been shown to be a safe and effective procedure in high risk and inoperable patients with AS***
- ***Has evolved toward a pure percutaneous procedure***
- ***As with novel technologies, PAVR has a definite learning curve which requires an in-depth understanding of patient selection and multiple anatomical criteria analysis***
- ***Procedures by experienced teams involve:***
  - **Pre-closing (no cut-down/repair)**
  - **Mild sedation and local anesthesia possible**
  - **Valve delivery without rapid pacing**
  - **No extra-corporeal/cardiac assistance**
  - **Ample time for step wise (re-)positioning of the valve**
- ***Awaiting longer term results***