Transcatheter Aortic Valve Implantation (TAVI)
With Self Expandable Device

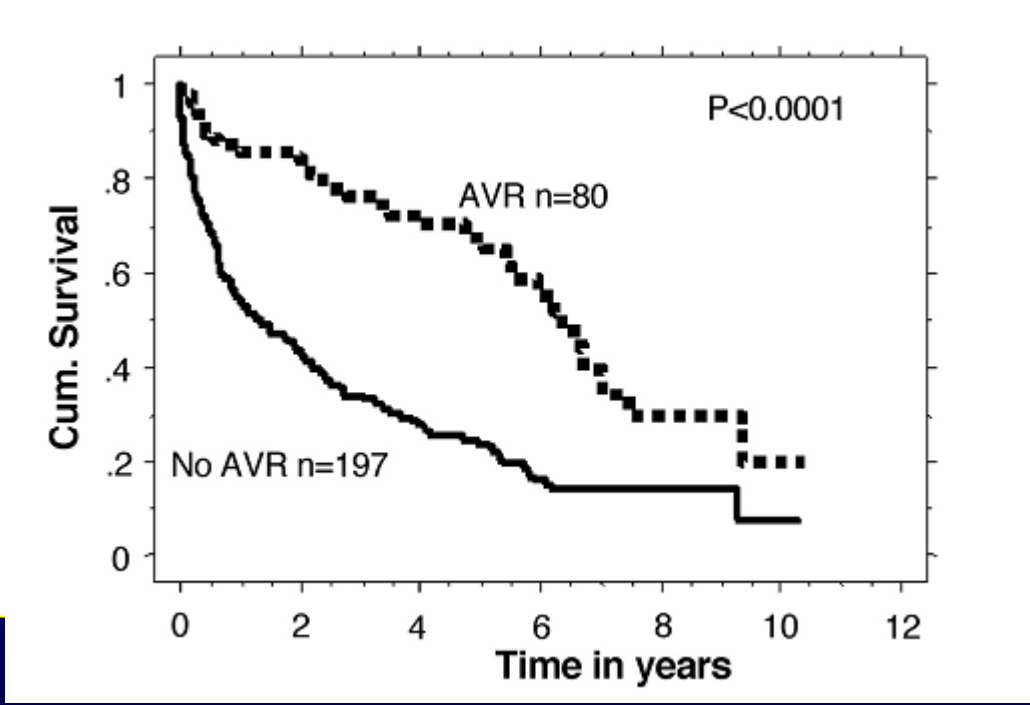
Jan Kovac, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom

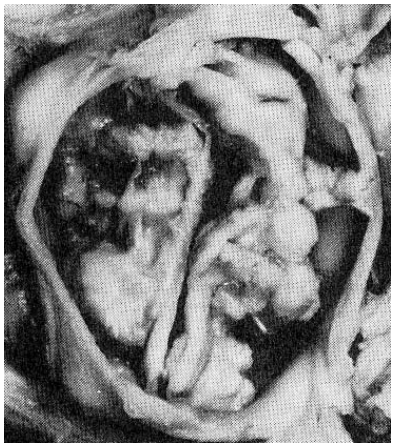
MEET, Cannes, 27 June 2008

The Allure of Aortic Stenosis

Background

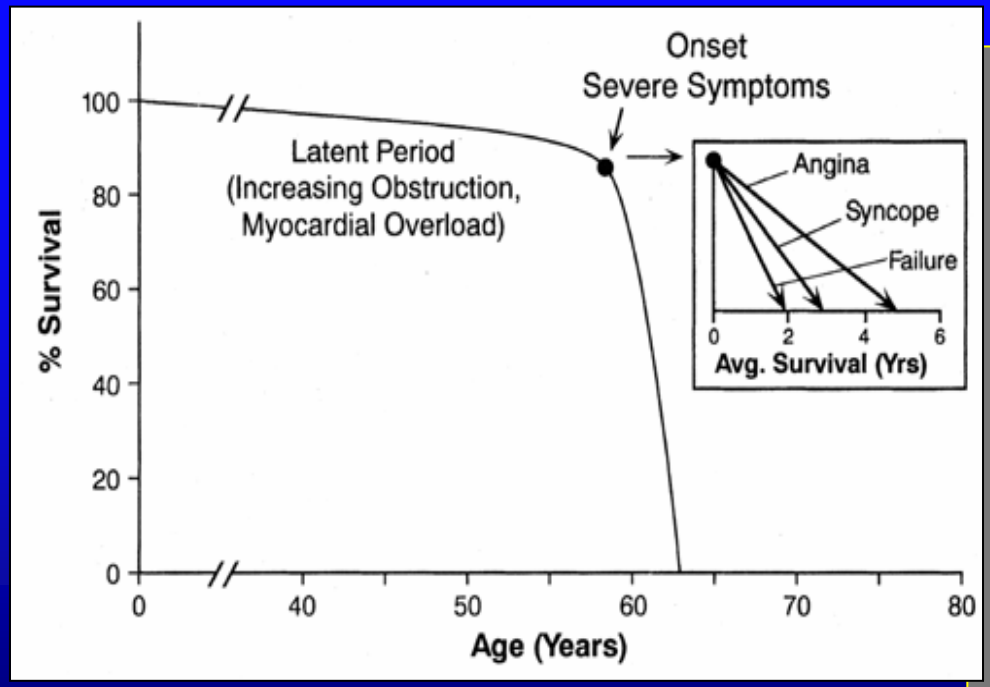
- Aortic stenosis incidence: 2-7% > 65 years
- Untreated severe AS significant mortality



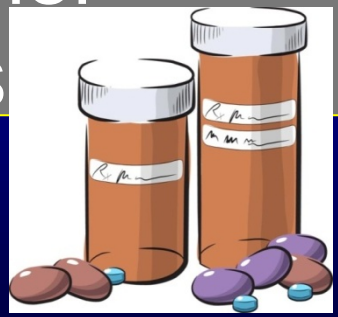


Varadajan P et al; Eur J Cardiothor Surg 2006

Severe Symptomatic Patients Require Urgent Attention



"Surgical intervention should be performed promptly once even…minor symptoms



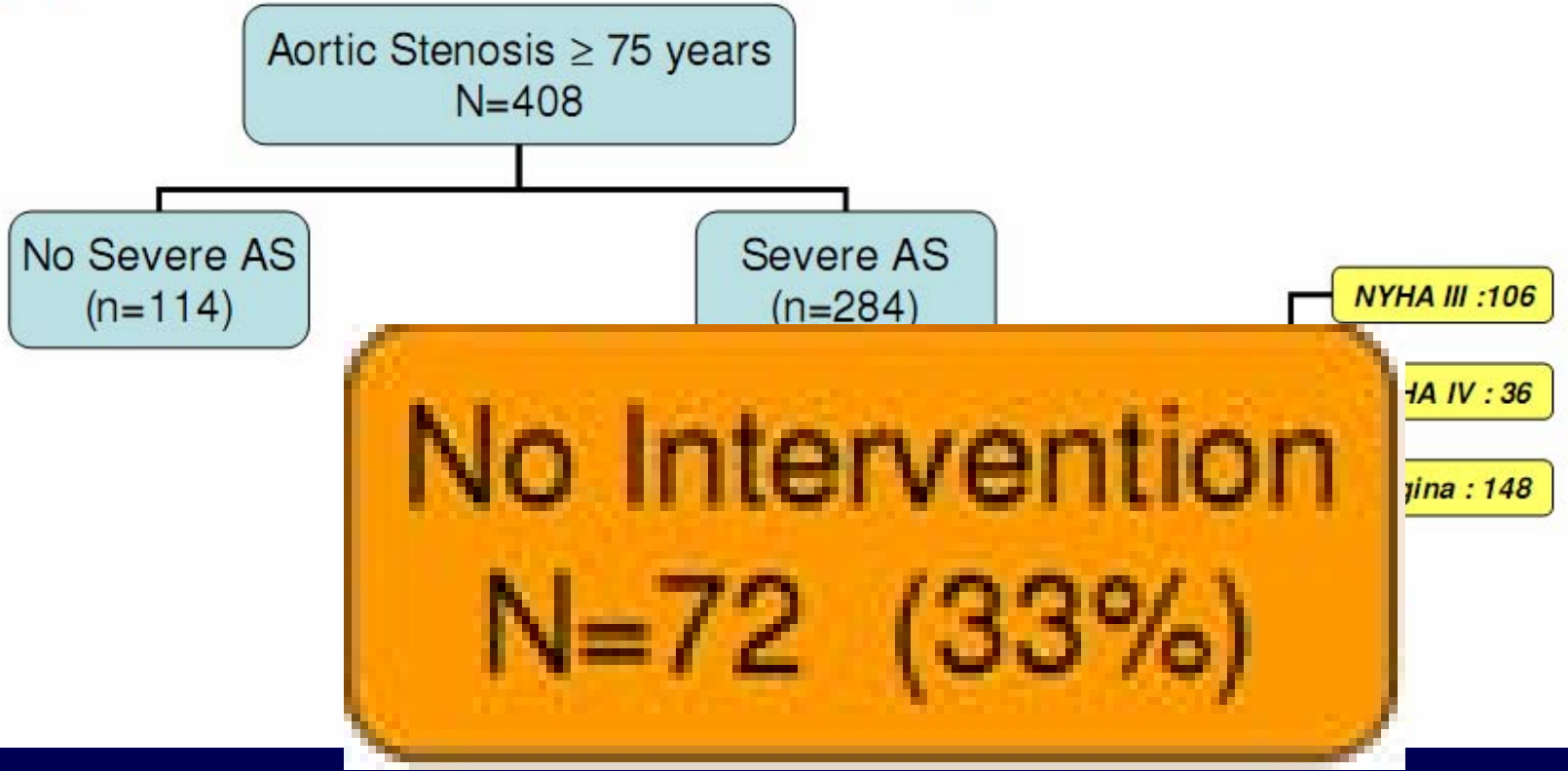
1 C.M. Otto. Valve Disease: Timing of Aortic Valve Surgery. *Heart* 2000

Chart:: Ross J Jr, Braunwald E. Aortic stenosis. Circulation. 1968;38 (Suppl 1):61-7.

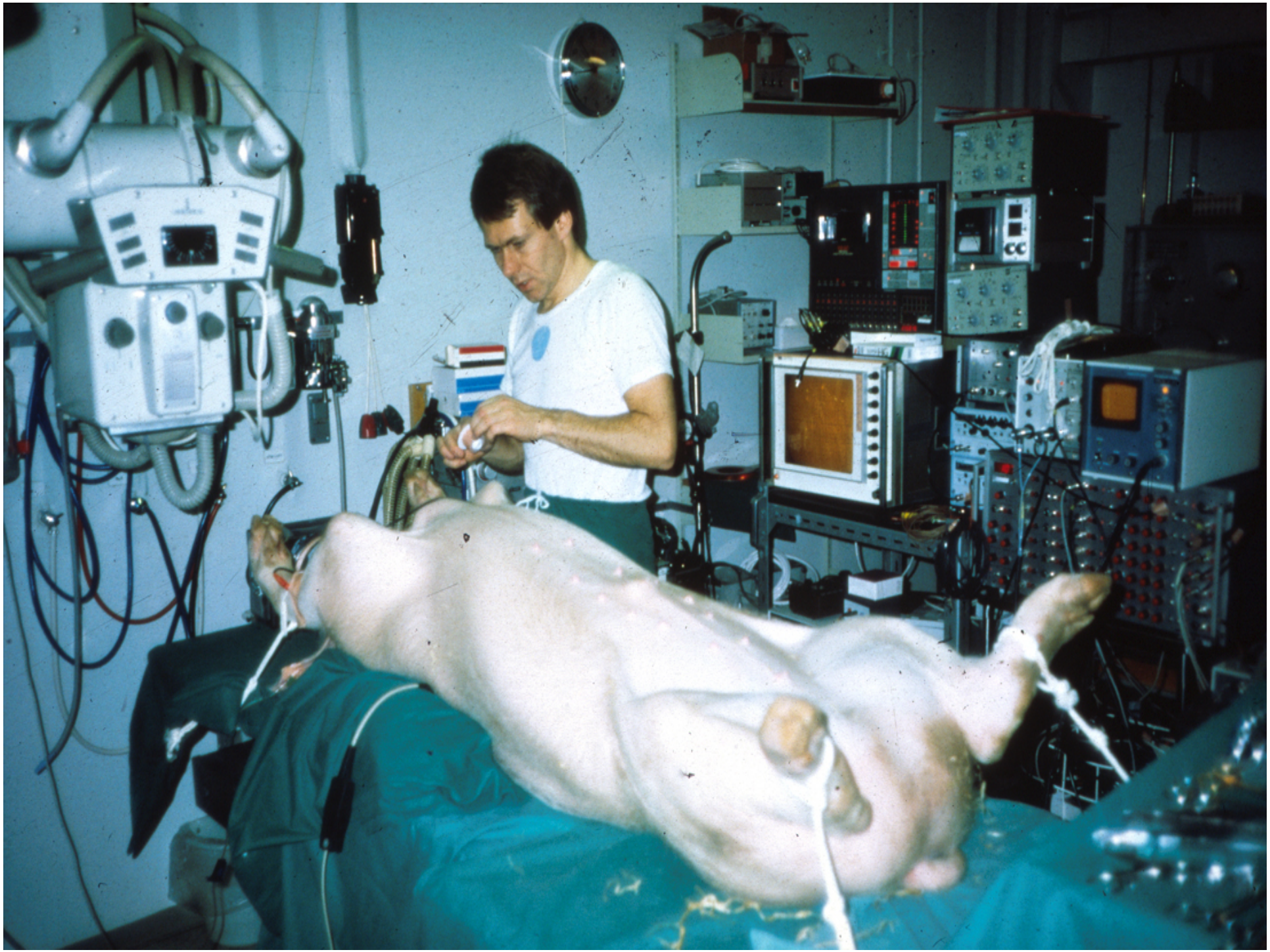
The need for PAVR: Euroheart survey

Severe AS : Valve Area ≙ 0.6 cm²/m² BSA or Mean Gradient ≥ 50 mmHg

Symptomatic AS : NYHA Class III or IV or Angina



(Iung et al. Eur Heart J 2005;26:2714-20)



GLADYS IS GLAD TO BE A WORLD HEART-OP FIRST
BY CATHY BUSS
HEALTH CORRESPONDENT

10:30 - 29 January 2008

A 90-year-old widow who made medical history by having Britain's first keyhole heart-valve replacement is celebrating the first anniversary of the operation.

Gladys Adams, from Wigston, is preparing for the wedding of her 28-year-old grandson - an event she thought she would never see.

She shows no sign of slowing down and is back to cooking for her family - including a Sunday roast for 10.

Mrs Adams was the first person in Britain to have the procedure, which replaces a patient's aortic valve without the need for open heart surgery, in January last year.

Mrs Adams said: "I feel lucky to have been able to have this operation. I never thought I would see my 90th birthday last September, let alone be getting ready to go to my grandson's wedding this August.

"I am back to cooking for my daughter and son-in-law and the usual Sunday roast for 10 people."

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

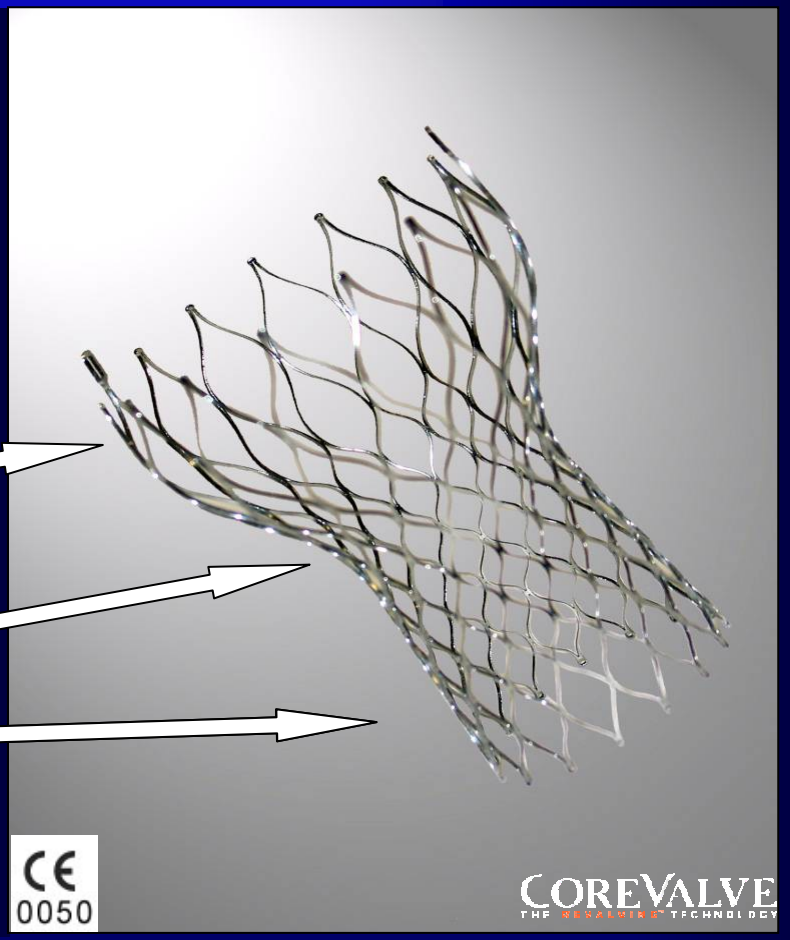
Diamond cell configuration

Nitinol: memory shaped/no recoil

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

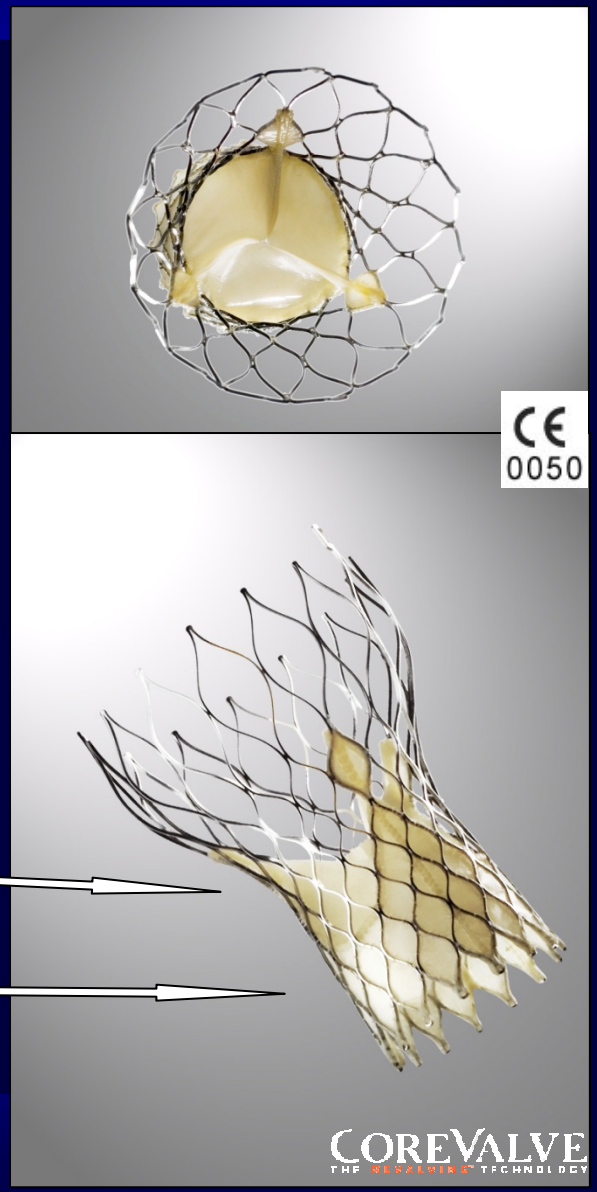
- **Low radial force area** orients the system
- Constrained area **avoids coronaries** and features **supra-annular valve** leaflets
- **High radial force** provides secure anchoring and constant force mitigates paravalvular leak

Radiopaque

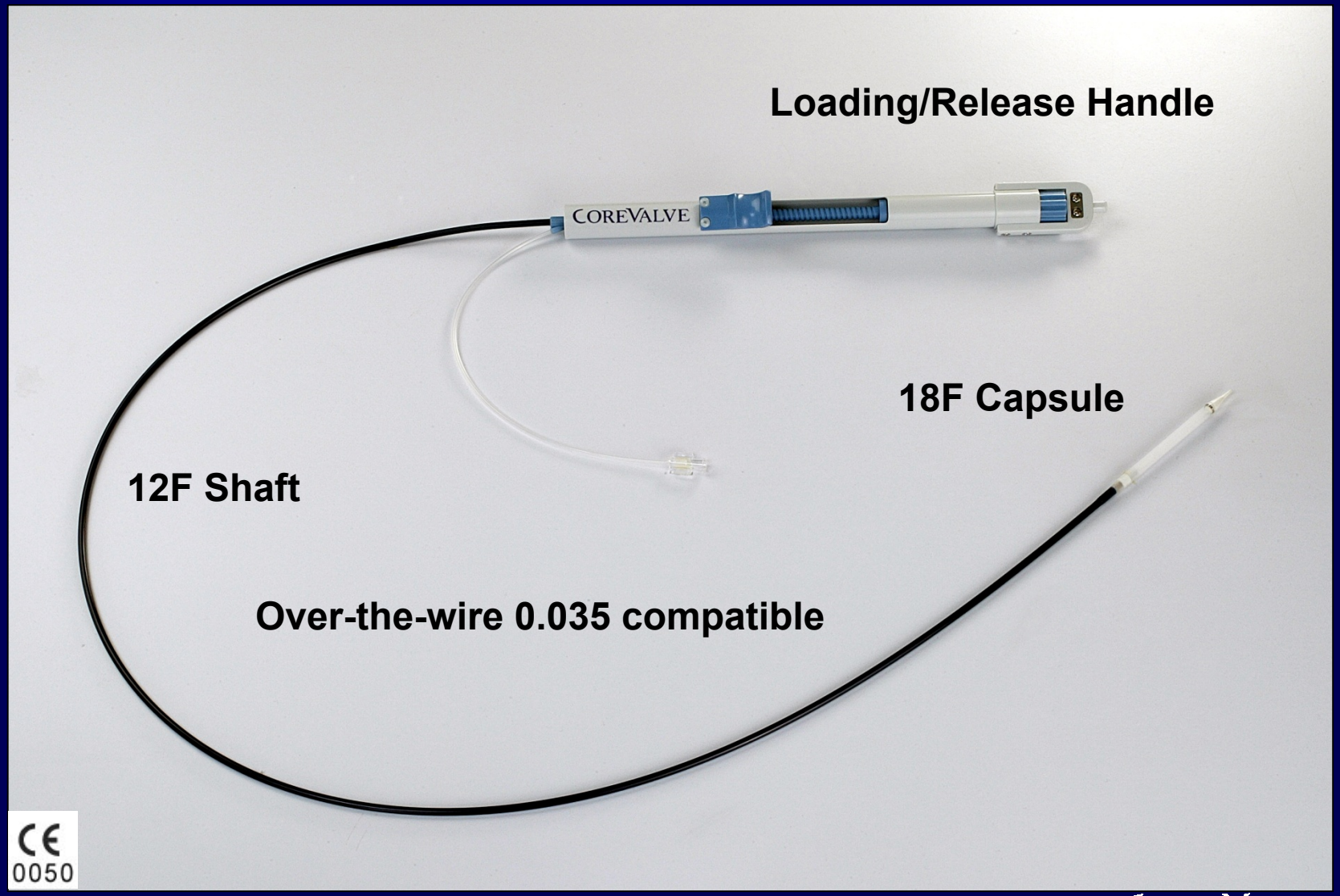


Porcine Pericardial Tissue Valve

- **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



18F Delivery Catheter System



COREVALVE
THE REVALVING™ TECHNOLOGY

CoreValve PAVR *ReValving* System
Total Experience

Time Period	Implant Phase	Device Used	Number of Patients
July 2004-July 2005	First in Man	25 French	14
May2005-August2006	21F Intl Trial Includes 2 ReDo	21 French	65
May 2006-Ongoing	18F Intl Trial	18 French	112
May 2007-Ongoing	Expanded Evaluation	CE 0050 18 French	482
Total Worldwide PAVR *ReValving* Patients Treated			673 (1200)

Updated 24 June, 2008

Safety and Efficacy Studies Criteria

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

Age ≥80 y (21F)
≥75 y (18F)

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

Age ≥65 y

+1 or more

- 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

Primary Endpoints:

- Procedural success
- 30-Day outcomes
- Long term outcomes

Post CE Mark Registry Criteria

High risk and inoperable patients with severe AS

Anatomical Criteria

- **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

CORE VALVE
RE-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.

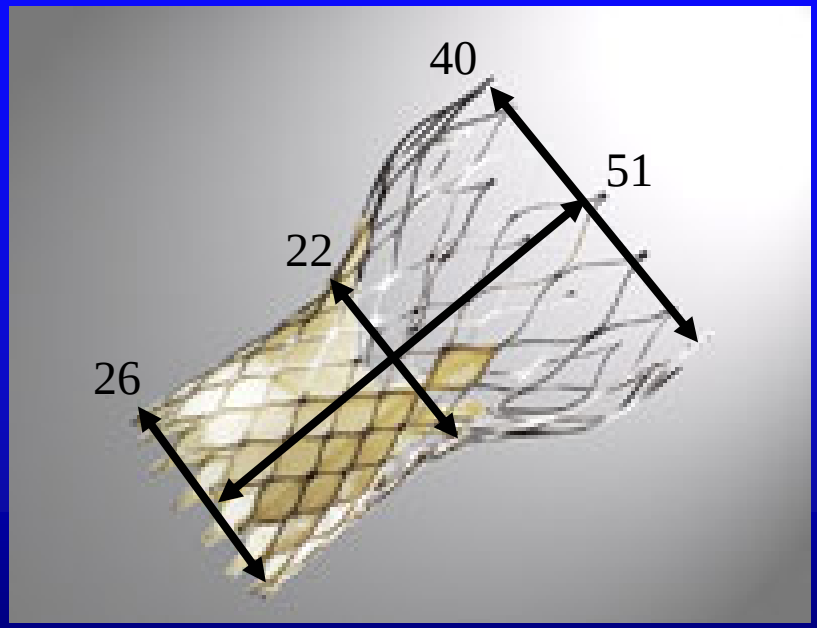
This document is not intended to be a substitute for attending a training program for any of the products mentioned. For detailed operator training / inservice support on the CoreValve ReValving™ System, please contact your local CoreValve representative.

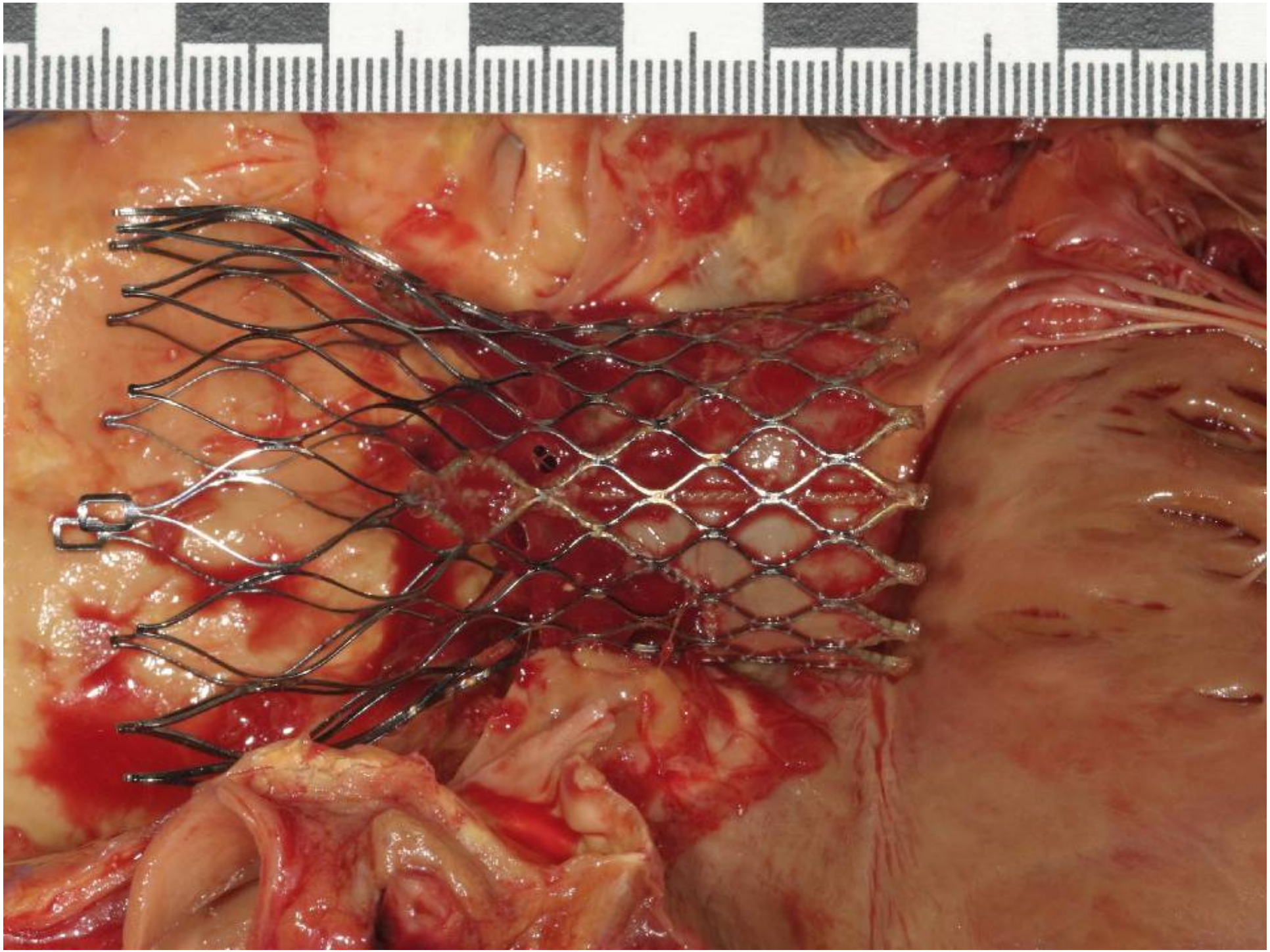
PN 090404 V1 June 2007

CE 0050

Correct size estimate vital

Imaging for Valvular Disease Interventions
23 mm CoreValve PAVR dimensions

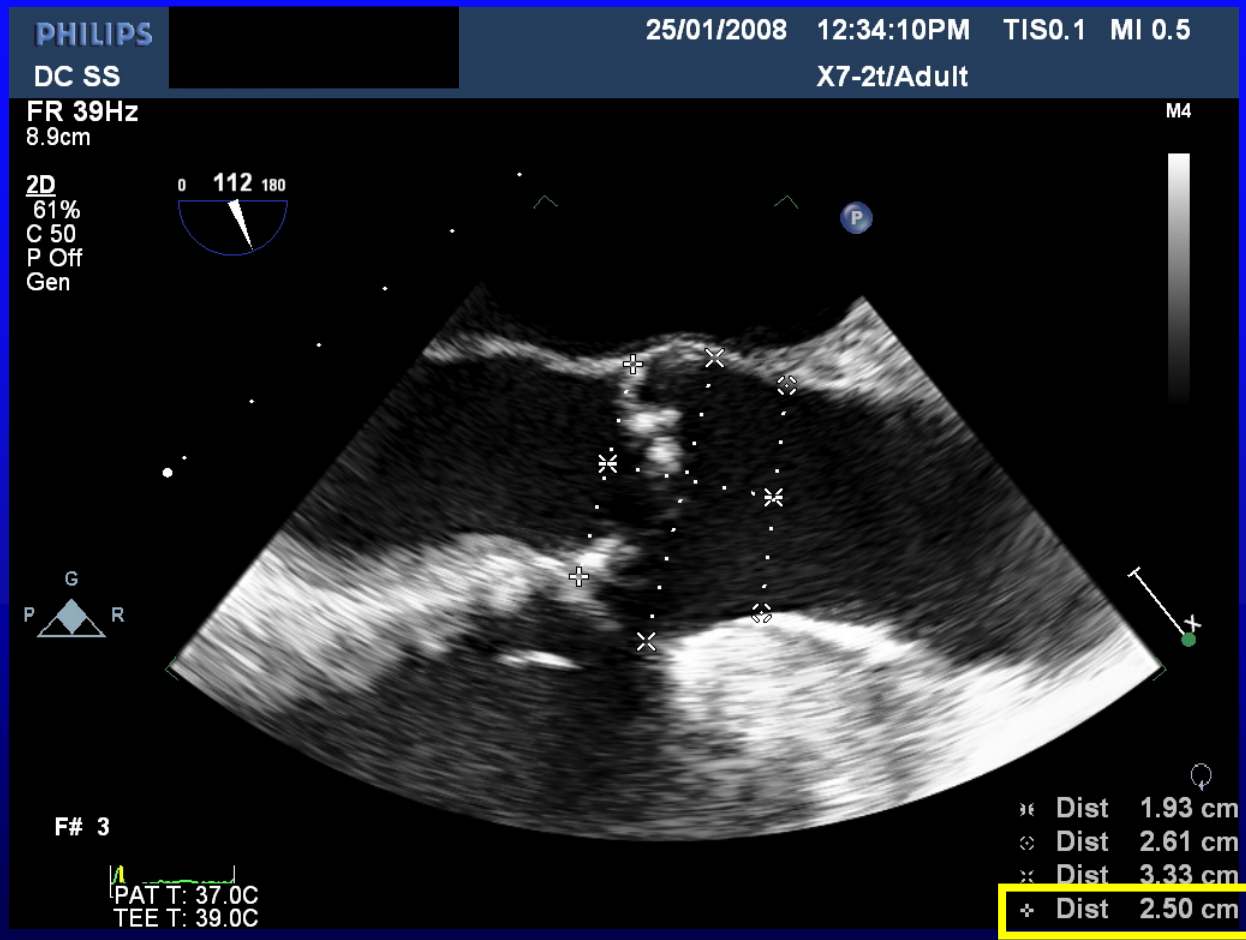




Imaging for Valvular Disease Interventions

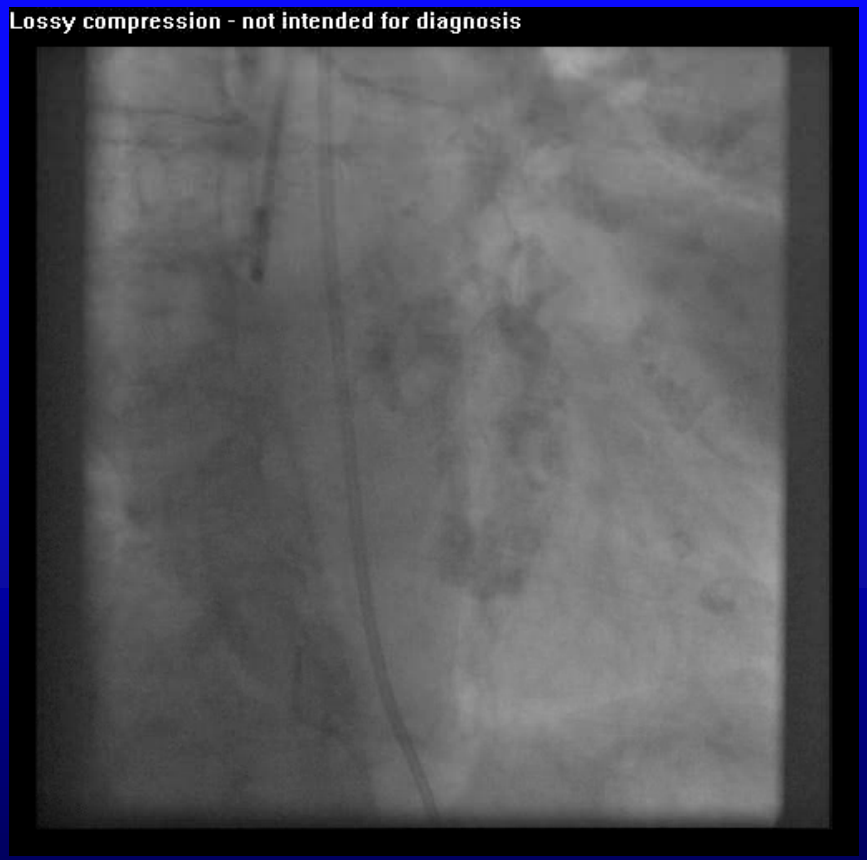
Aortic root sizing - Echo

Right angled to LAX, end-diastolic, intraluminal, hinge to wall



Imaging for Valvular Disease Interventions

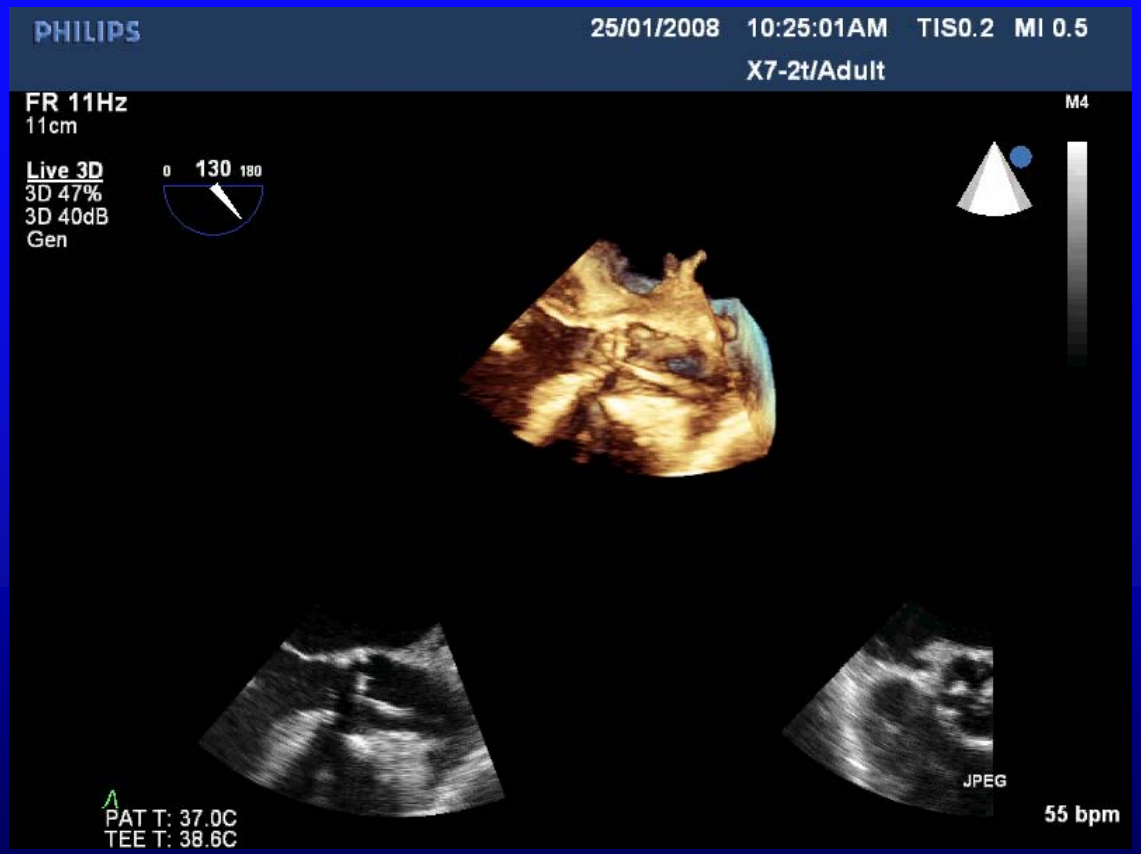
Aortic root RAO, arch LAO, coronaries, iliofemoral – Fluoro

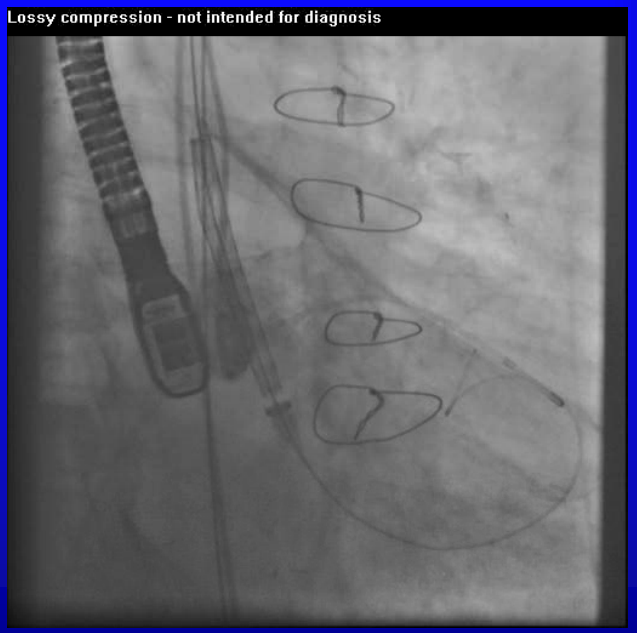


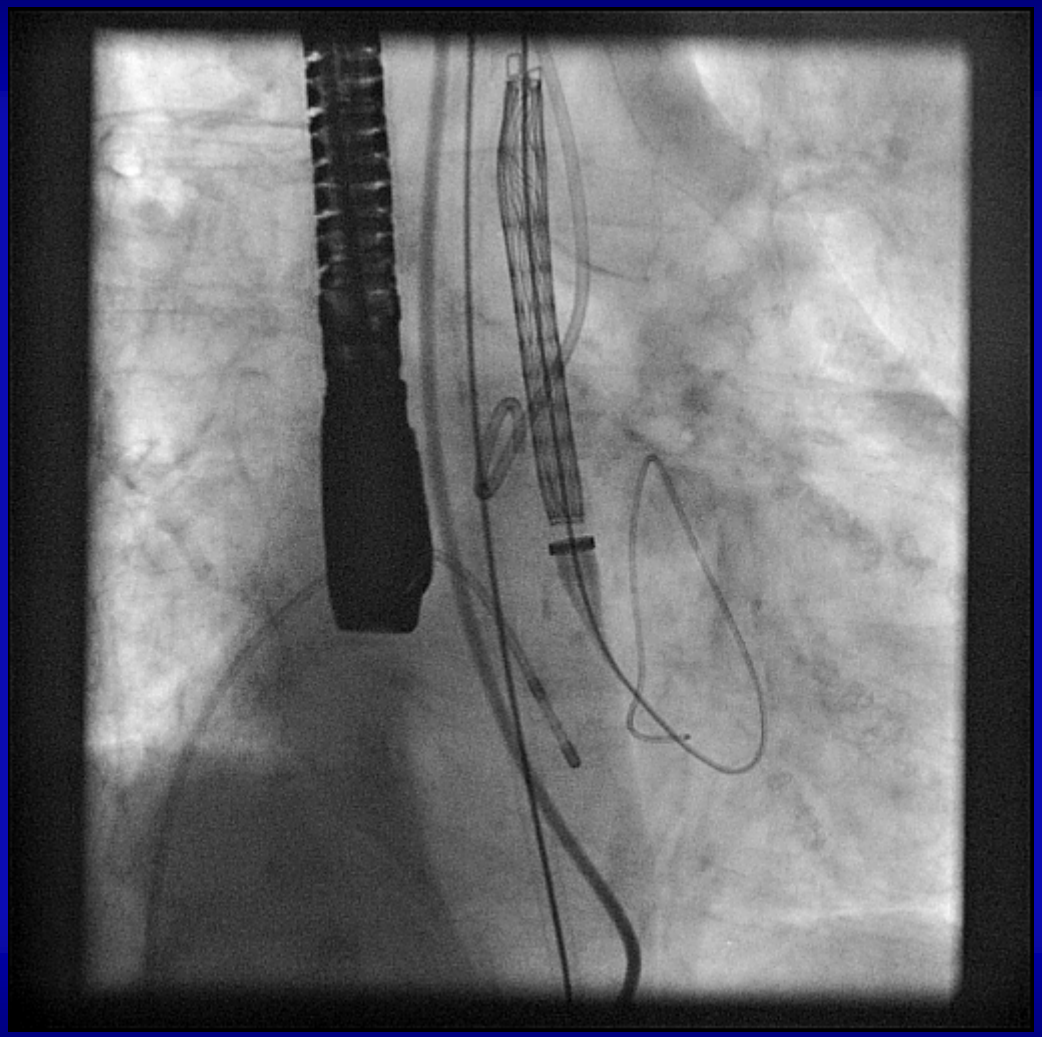
Imaging for Valvular Disease Interventions

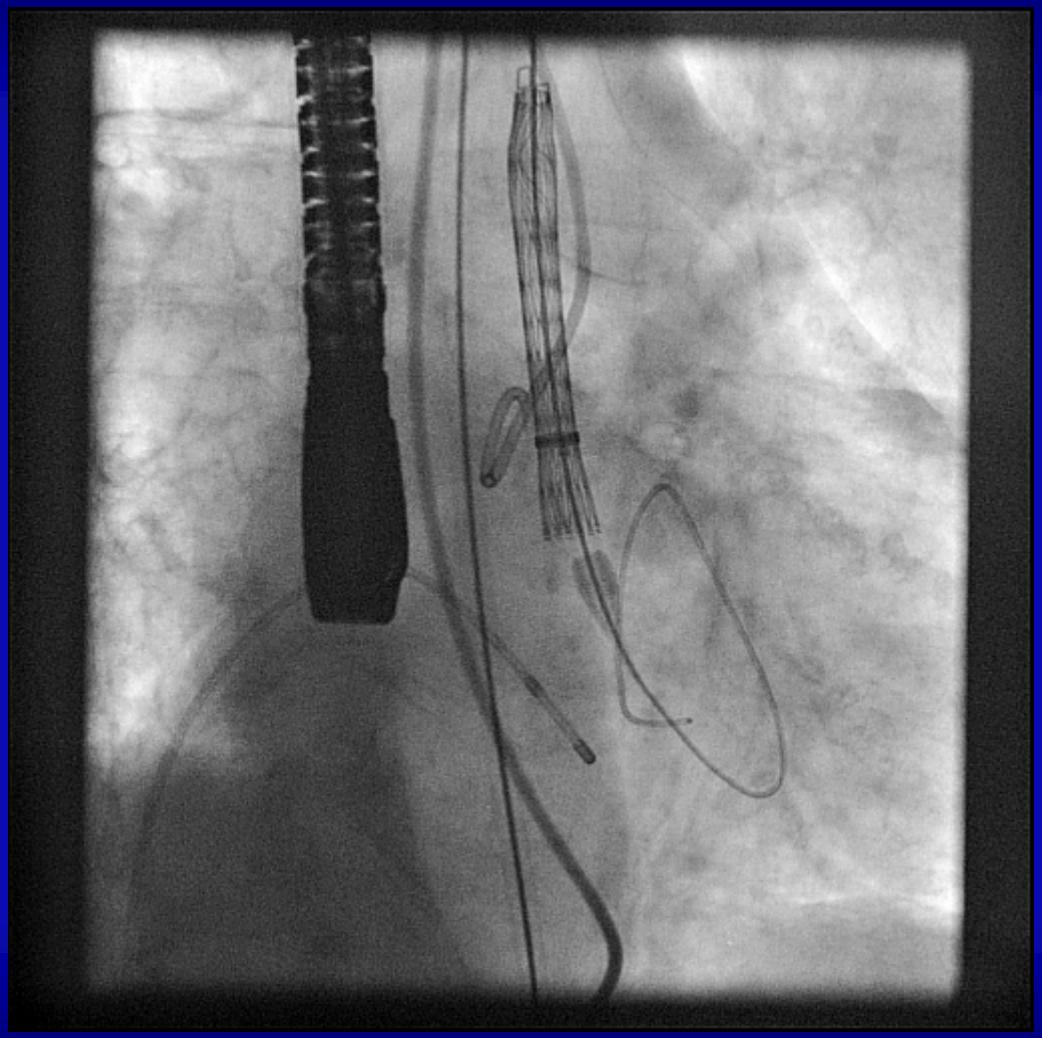
PAVR cath-annular position - Echo, Fluoro

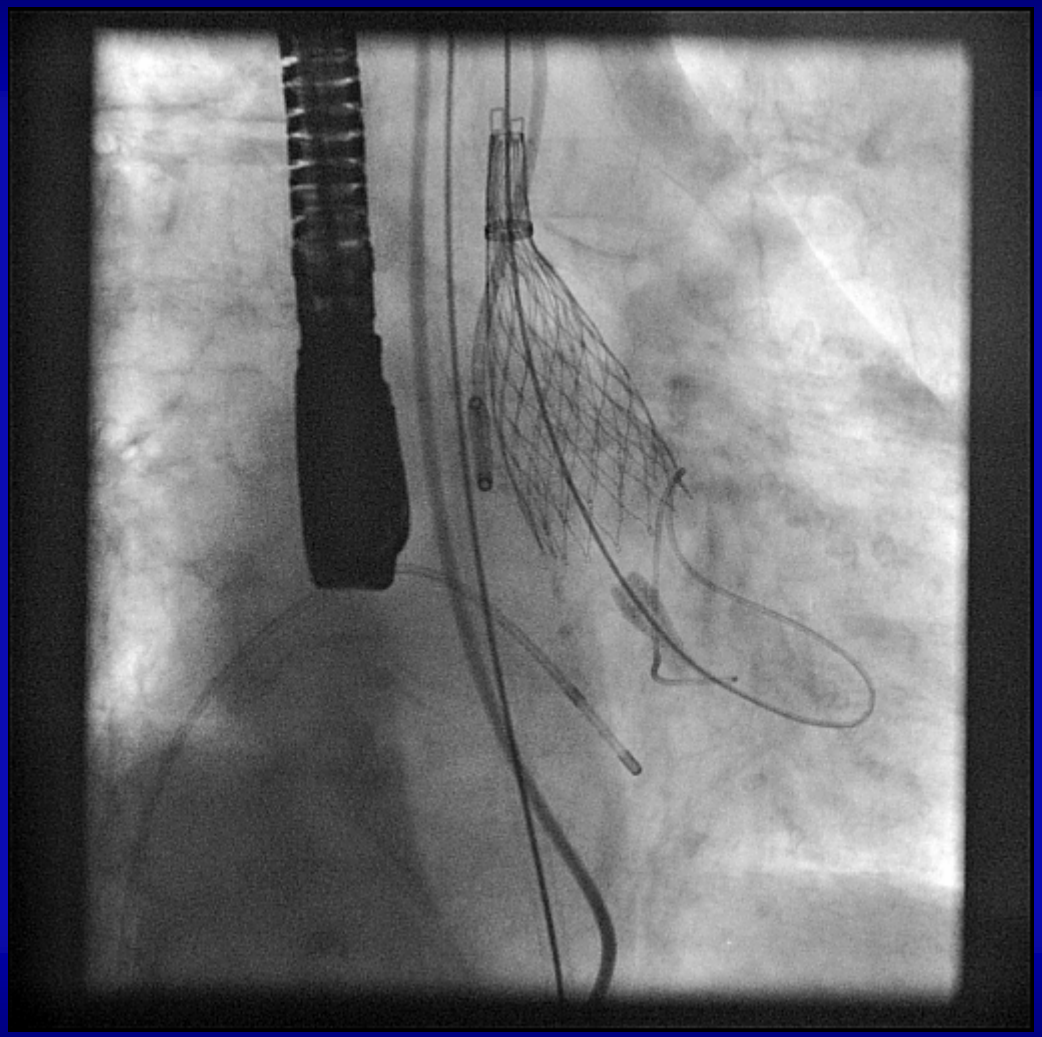
Angio4 @ rao27cau10, Angio5 @ rao27cau20

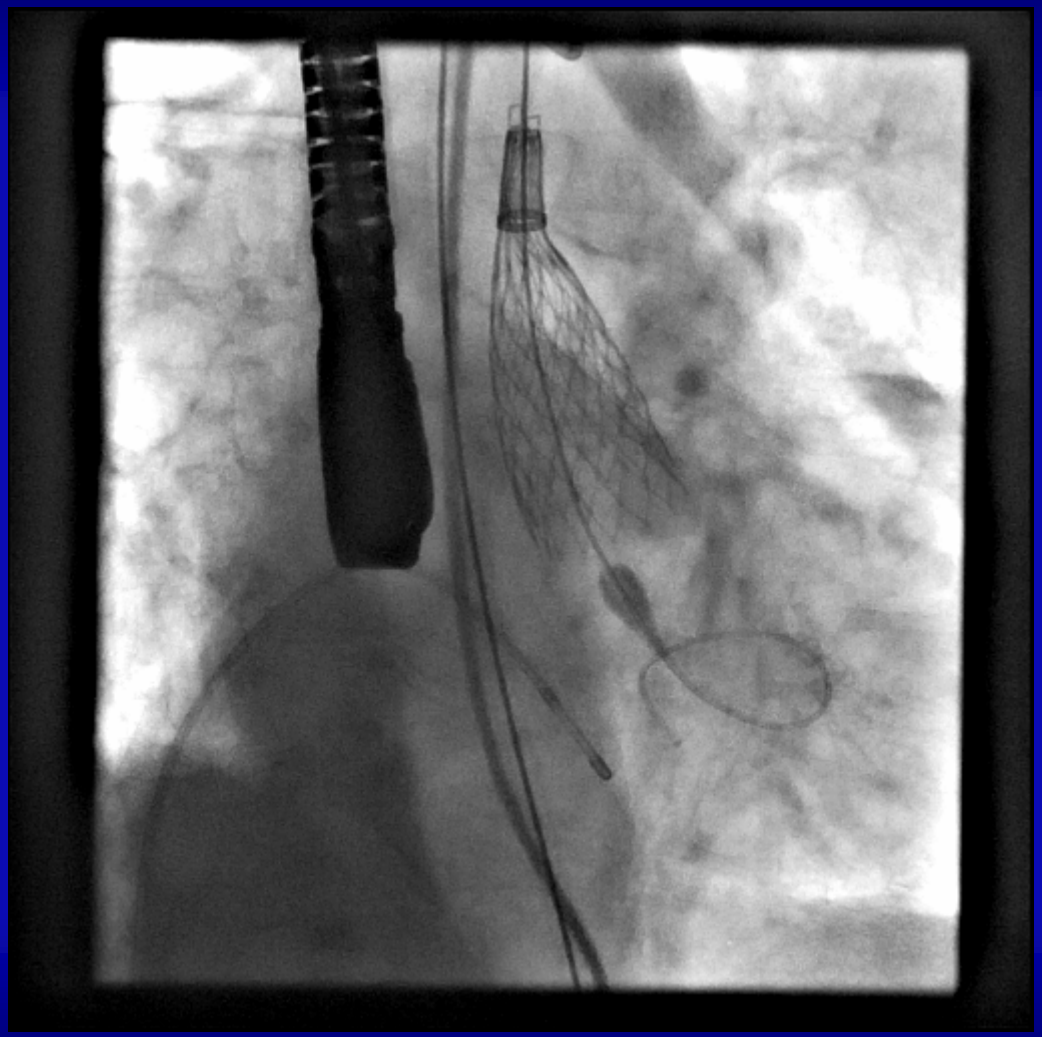


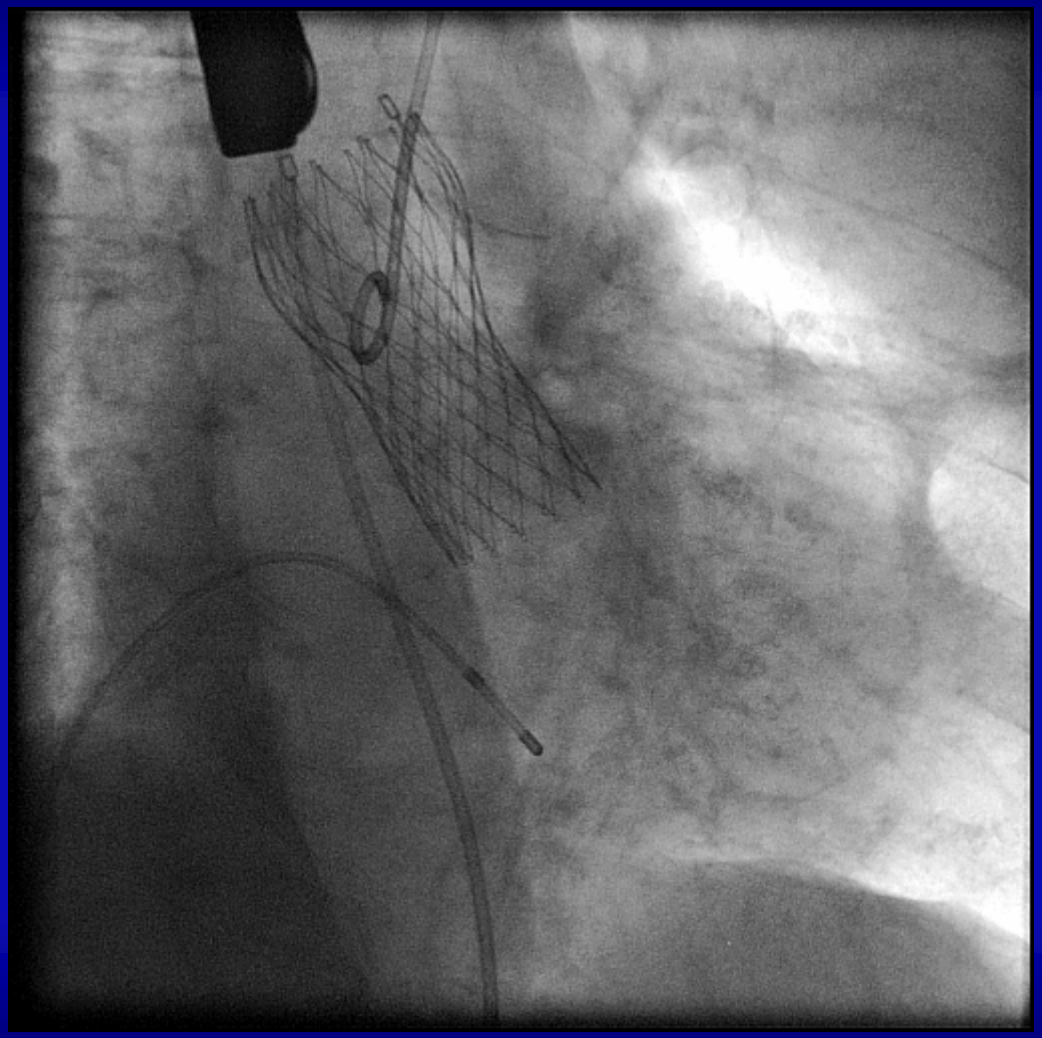




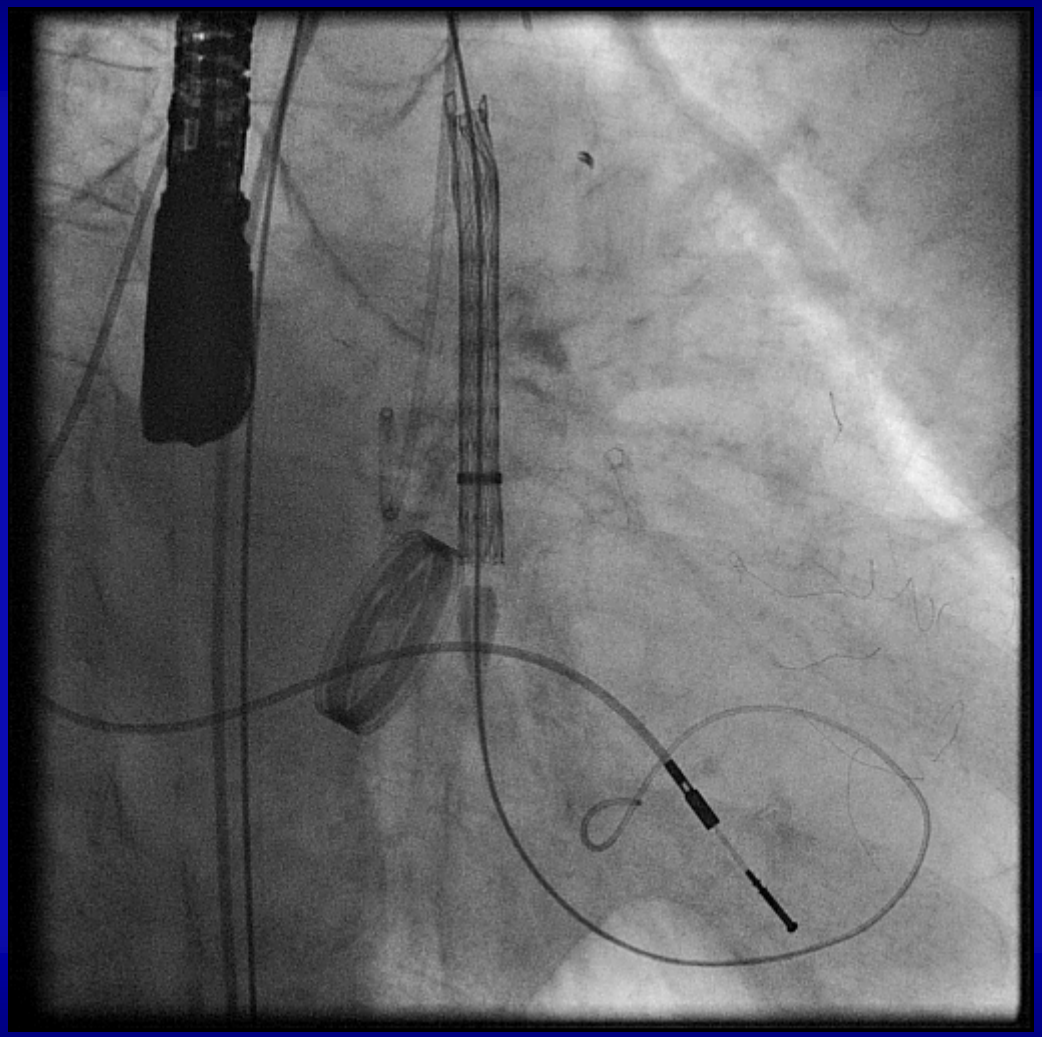


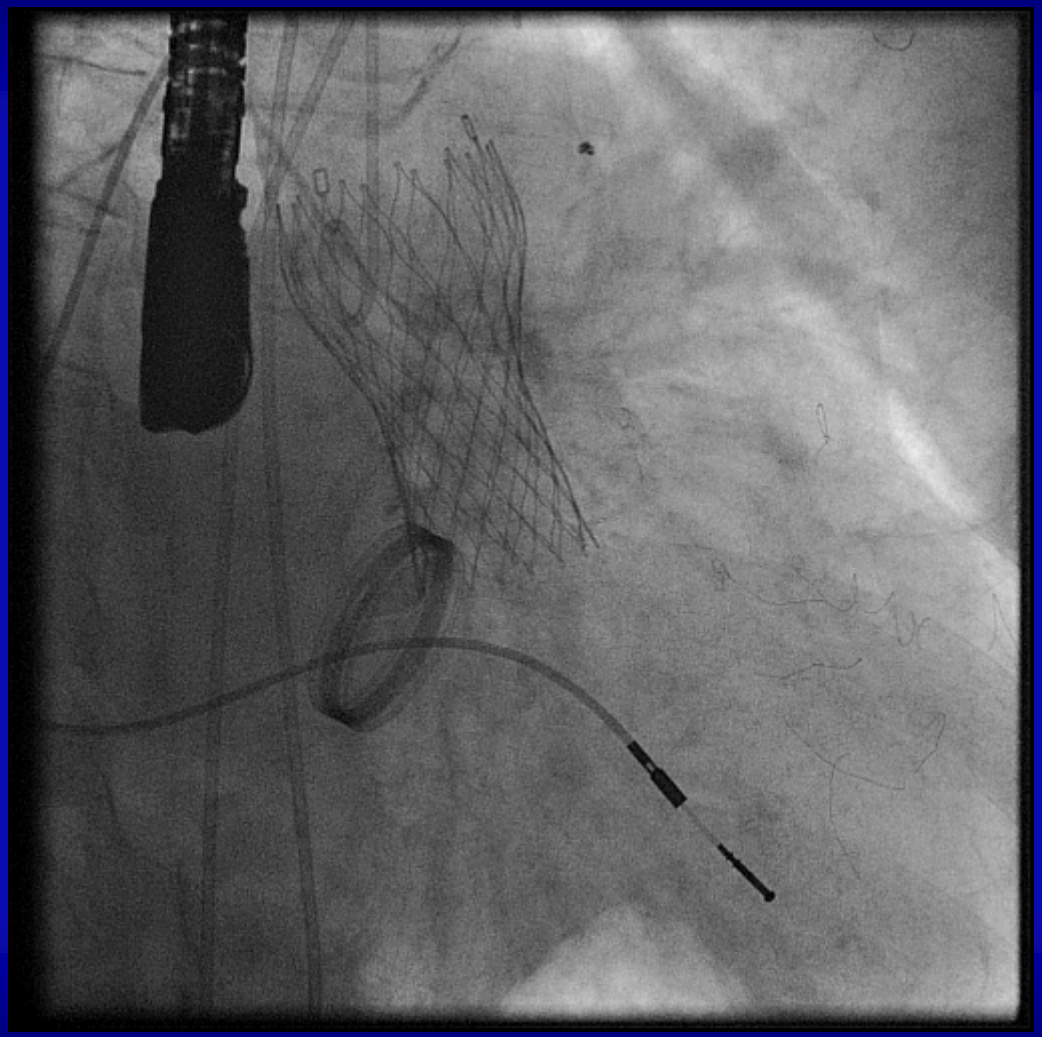


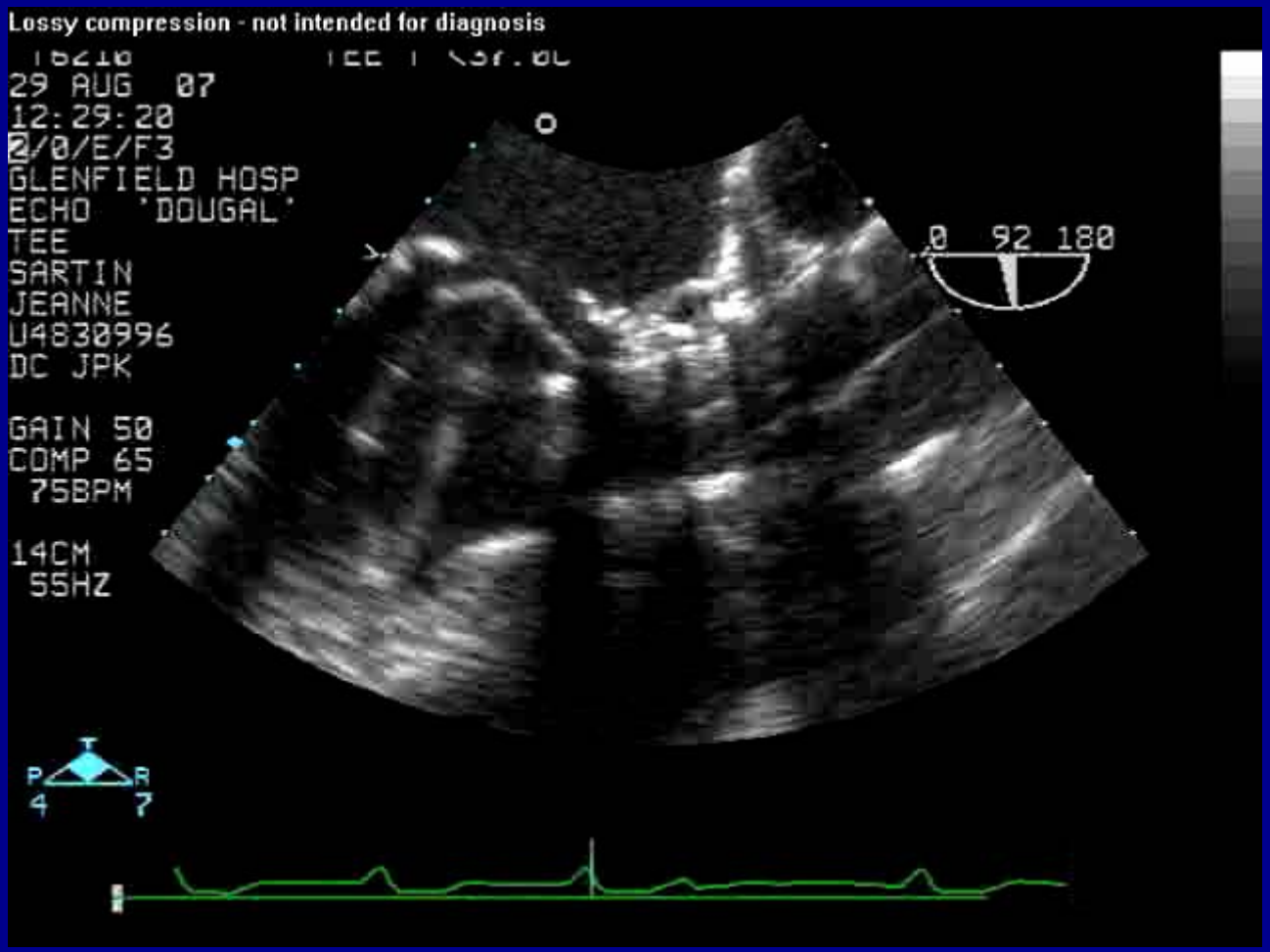




Relation to Other Structures-
Mitral Prosthesis






Lossy compression - not intended for diagnosis
29 AUG 07
12:29:20
2/0/E/F3
GLENFIELD HOSP
ECHO 'DOUGAL'
TEE
SARTIN
JEANNE
U4830996
DC JPK
GAIN 50
COMP 65
75BPM
14CM
55HZ
0 92 180
P
R
4
7

Pt 22, Male, 93 yrs

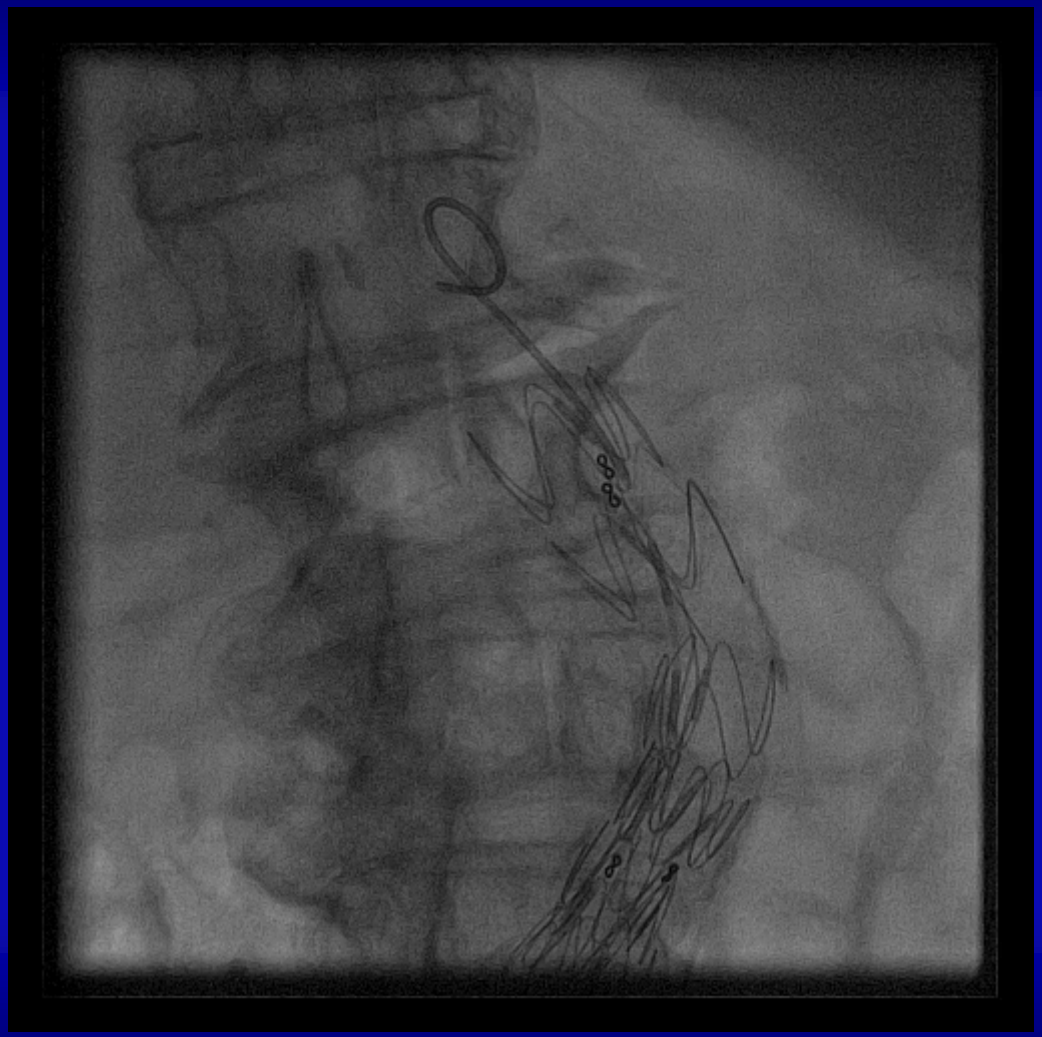
Age: 93
Diagnosis: Severe AS, mod LV, progressive dyspnoea

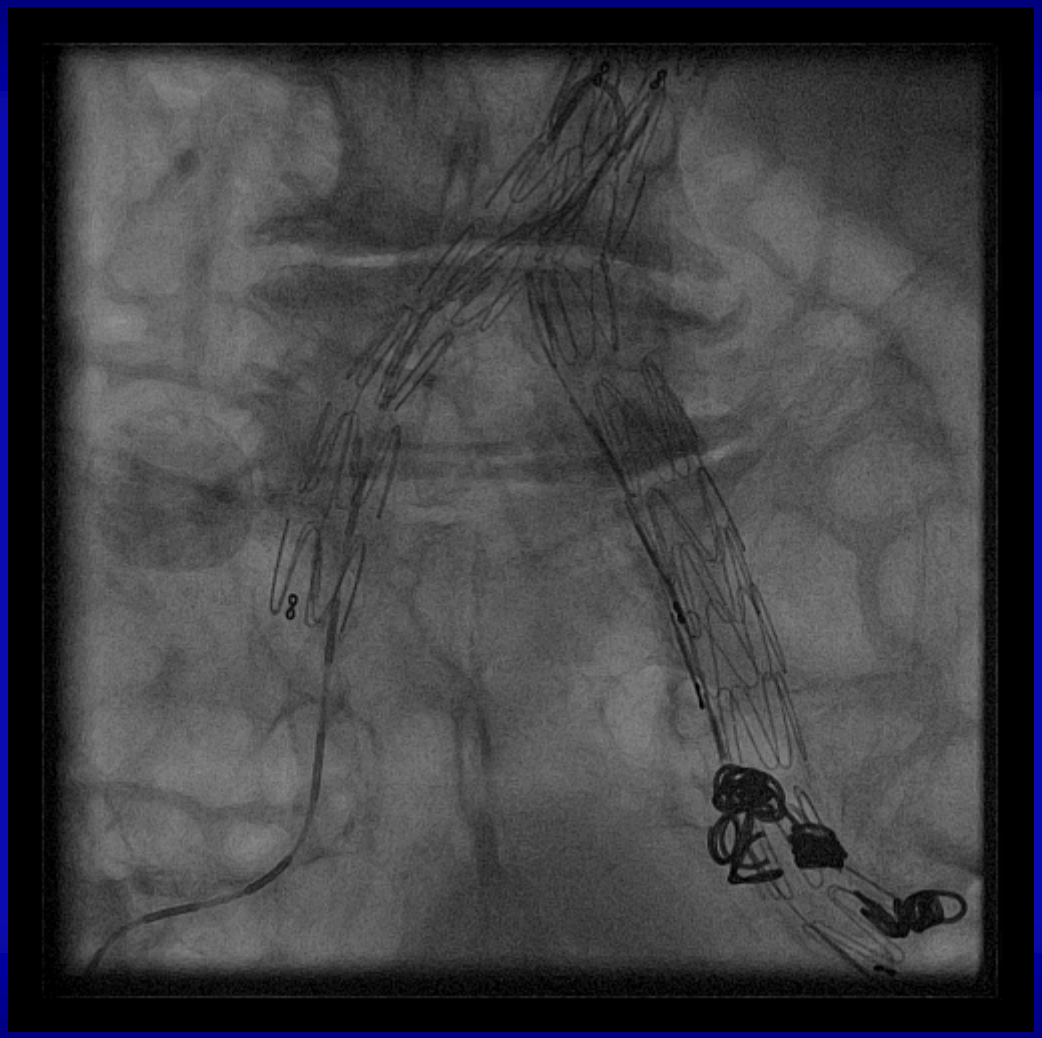
Comorbidities:
- AF
- Previously abdominal aortic aneurysm
  - Endoluminal repair 2005 – Talent stent graft
    - Occlusion of left limb of stent graft noted 2007

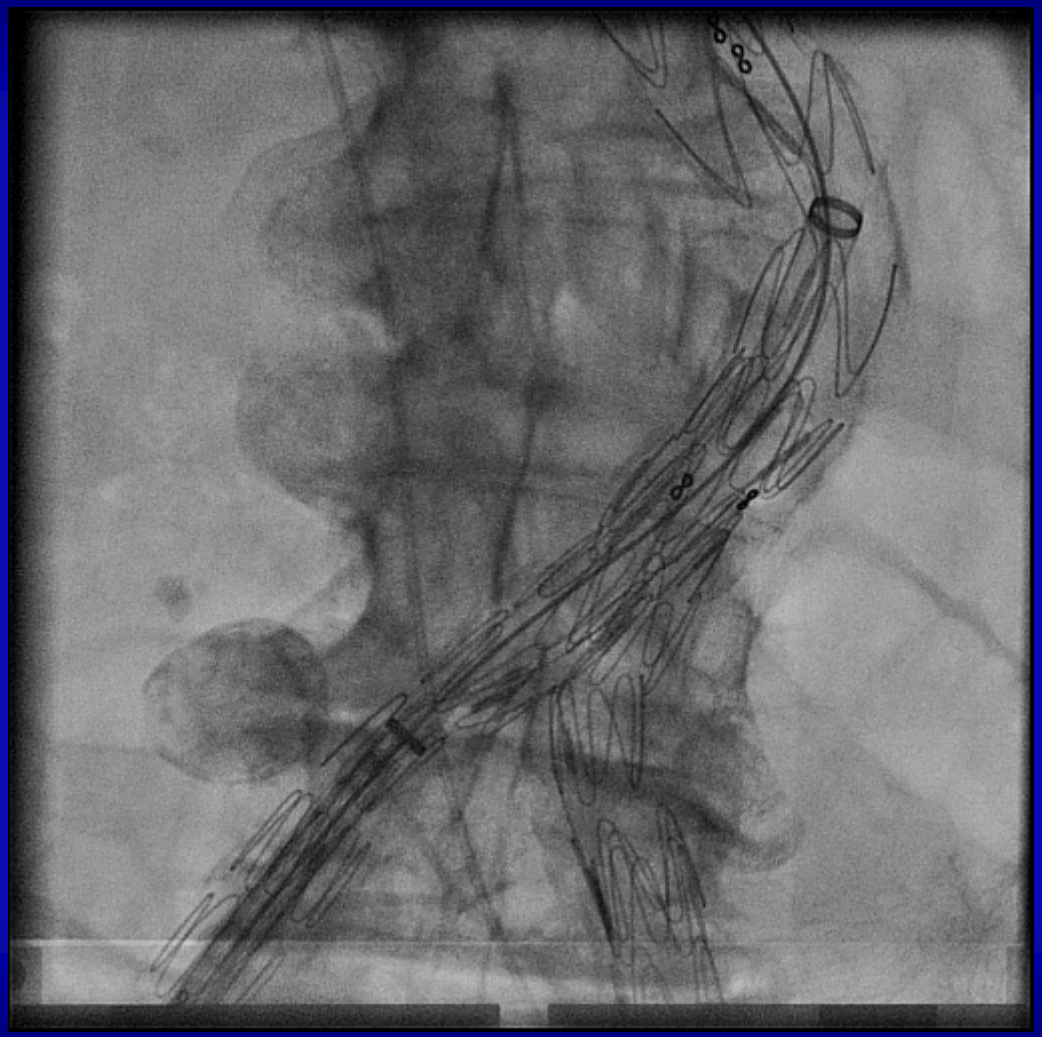
Logistic EUROSCORE : 30.15 %
NYHA: 2-3

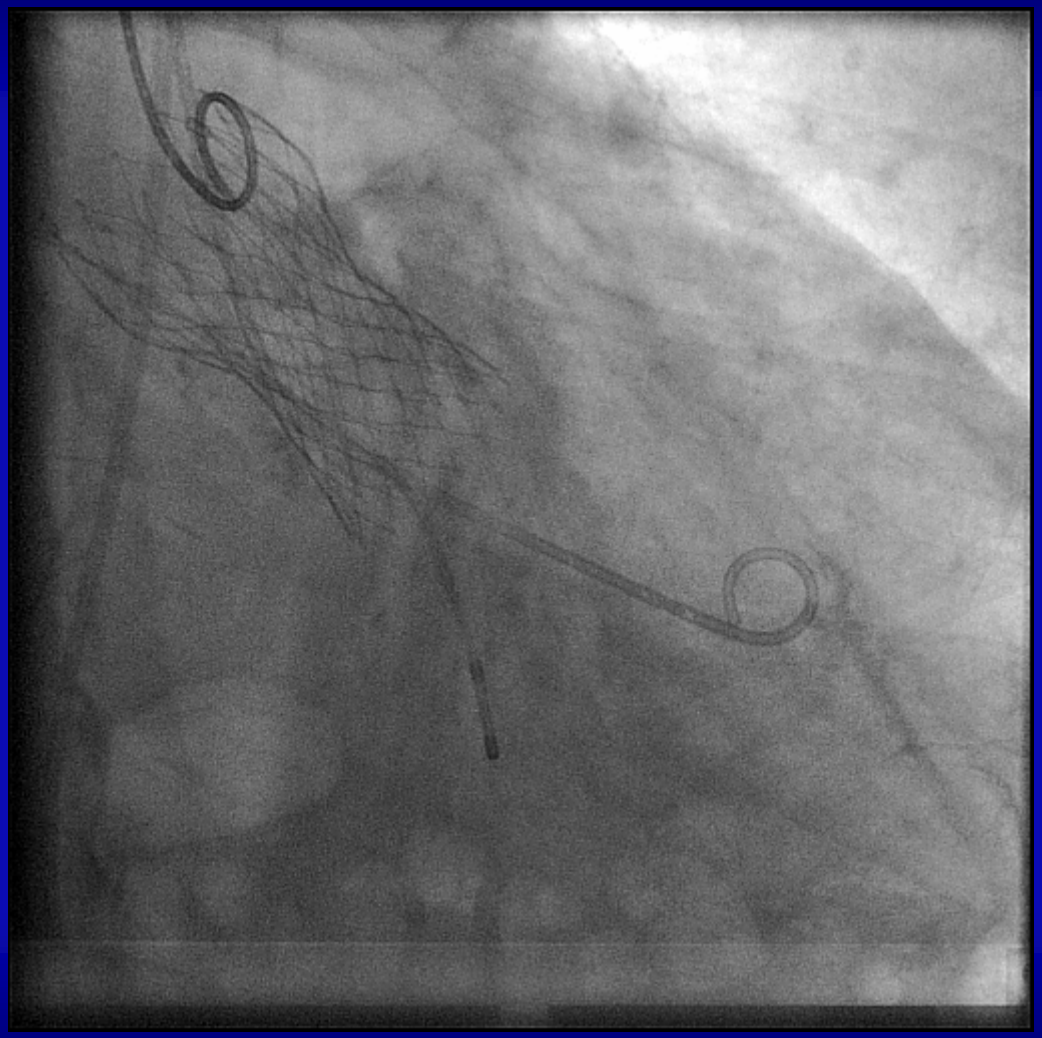
Corevalve inclusion criteria: Age, Euroscore
Corevalve exclusion criteria: None

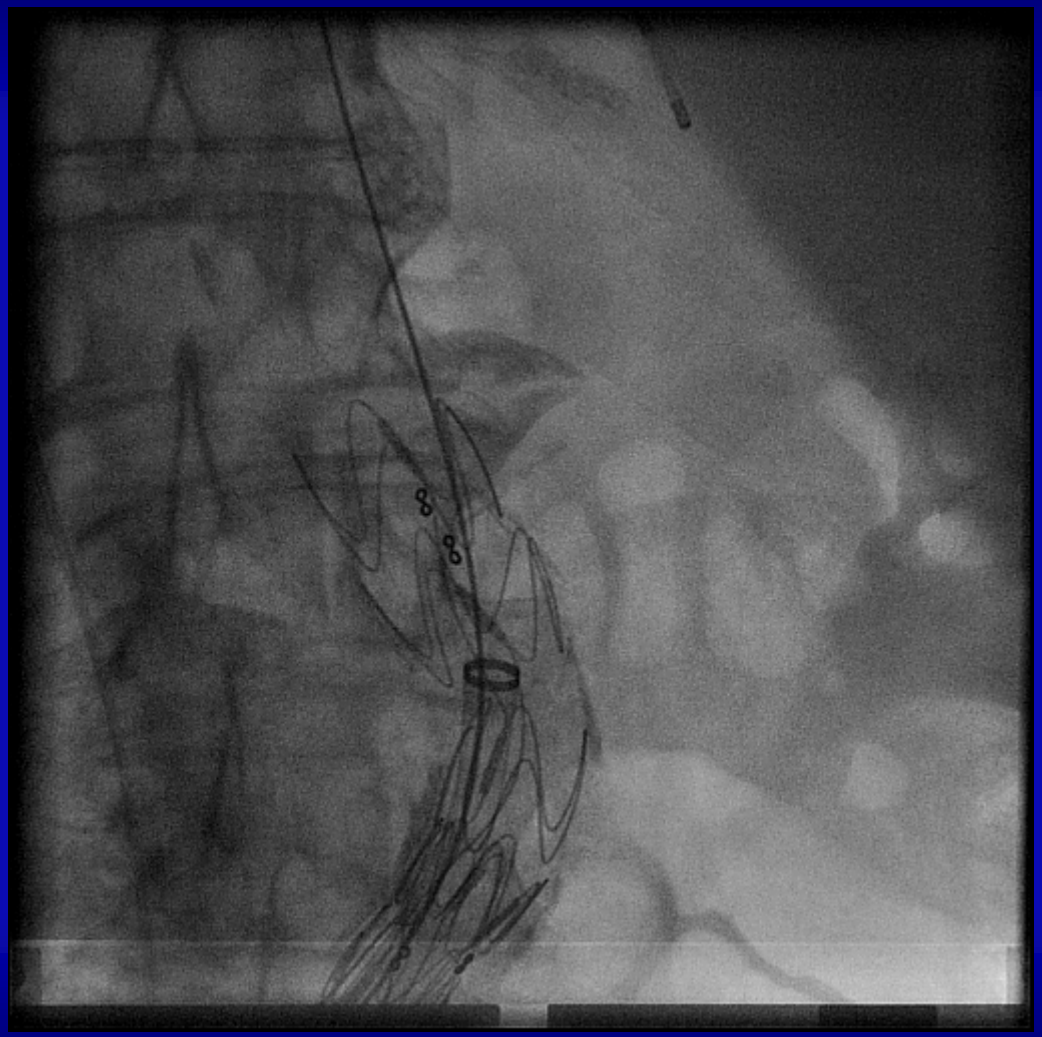
Cardiac catheter: Non obstructive RCA stenosis only
Surgical assessment: High risk, patient declined open surgery











Patient Demographics

	18F S&E (N=112)	18F Registry (N=345)
Age (years)	81.7 ±6.7 [58-92]	80.8 ±7.1 [46-95]
Female	62 (55%)	172 (55%)
Logistic EuroSCORE (%)	23.5 ±13.9 [3-69]	23.6 ±13.4 [3-83]
High Risk Co-morbidities		
Hypertension	78%	57%
Diabetes	26%	26%
CAD	61%	57%
Prior MI	19%	15%
Prior PCI	33%	33%
Prior CABG	28%	20%
AFib	41%	31%
Prior CVA	19%	7%
PVD	21%	25%

Patient Demographics (continued)

Pre-procedure	18F S&E (N=112)	18F Registry (N=345)
AVA (cm^2)	0.59 ±0.18 [0.2-1.0]	0.64 ±0.20 [0.2-1.6]
Mean Gradient (mm Hg)	47.2 ±17.9 [15-97]	50.8 ±18.2 [15-114]
Peak Gradient (mm Hg)	71.5 ±27.0 [24-150]	79.3 ±26.9 [22-169]
% in NYHA Class III/IV	75%	84%
LVEF	51% ±15 [32-78]	52% ±14 [10-80]

Procedural Results

	18 F S&E (N=112)	18F Registry (N=345)
Procedural Success	103 (92%)	337 (98%)
Mean Procedure Time	151 ±77 Min	133 ±59 Min
Discharged alive & well with CoreValve	102 (91%)	318 (92%)

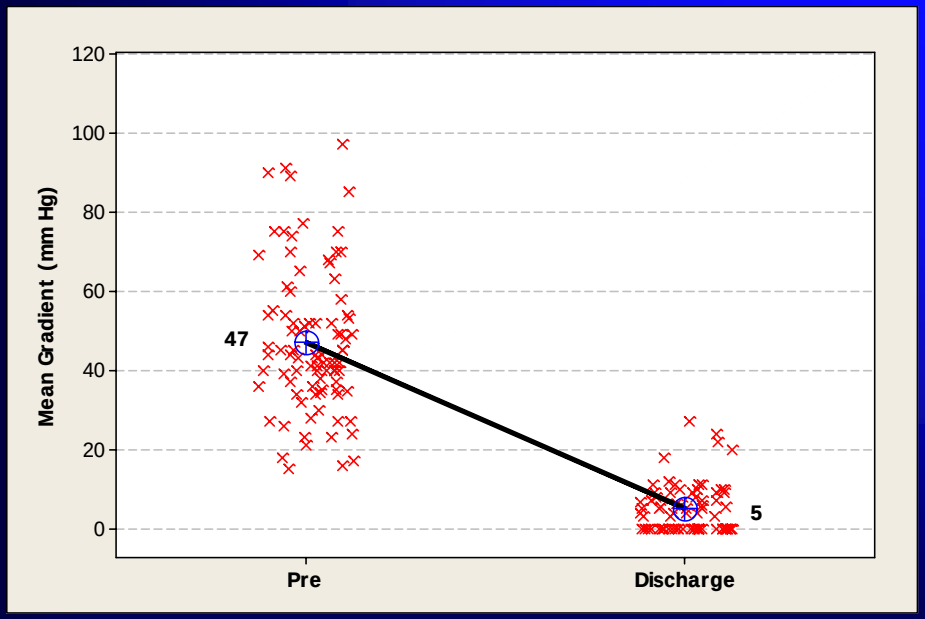
Procedural Results (continued)

Mean Gradient (mm Hg)

18F S&E
(N=112)

Pre: 47.21 ±17.98 [15-97]

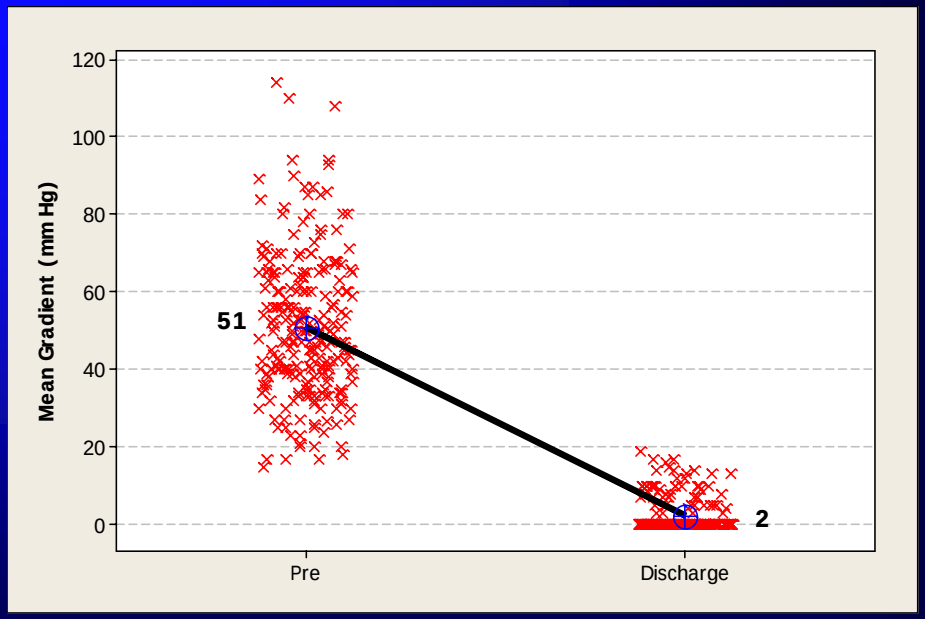
Discharge: 5.07 ±6.19 [0-27]



18F Registry
(N=345)

Pre: 50.84 ±18.23 [15-114]

Discharge: 2.26 ±4.38 [0-19]



Procedural Results (continued)

	18F S&E (N=112)	18F Registry (N=345)
Procedural Failures	**9 (8%)**	**8 (2%)**
Inability to access vessel	0 (0%)	0 (0%)
Inability to navigate vasculature	0 (0%)	0 (0%)
Inability to cross native valve	0 (0%)	0 (0%)
Malplacement	6 (5%)	0 (0%)
Aortic Root Perforation	1 (1%)	1 (<1%)
Ventricular Perforation, guidewire	2 (2%)	2 (<1%)
Ventricular Perforation, pacemaker wire	0 (0%)	2 (<1%)
Difficulty with BAV	0 (0%)	1 (<1%)
Conversion to Surgery	4 (4%)	2 (<1%)

multiple events in same patients = data not cumulative

Procedural Results (continued)

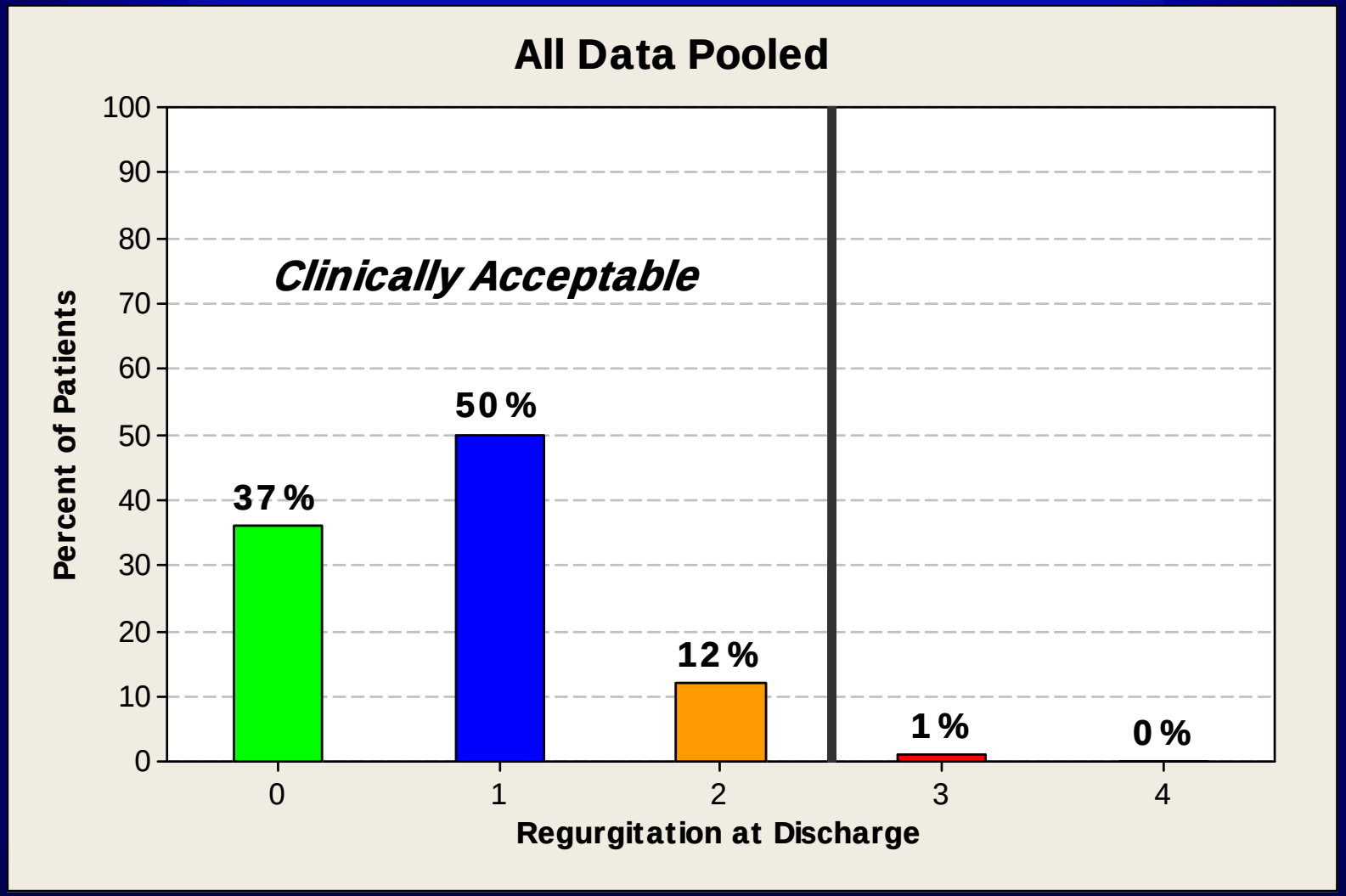
Complications (0–30 Days)*	18F S&E (112)	18F Registry (345)
AMI*	1 (1%)	1 (<1%)
Aortic dissection*	2 (2%)	1 (<1%)
Coronary impairment	1 (1%)	0 (0%)
Vascular complications	1 (1%)	4 (1%)
Stroke/TIA*	8 (7%)	6 (2%)
Pacemaker	27 (24%) **	30 (9%)
Re-op for valve failure	0 (0%)	0 (0%)

* multiple events in same patients = data not cumulative

** >1/3 prophylactic

Procedural Results (continued)

Regurgitation at Discharge



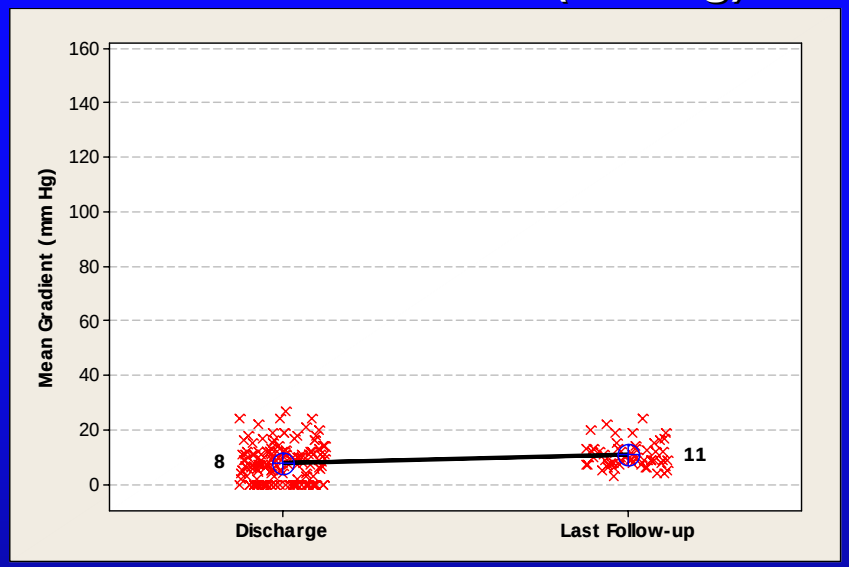
30 Day Outcomes

	18F S&E (N-112)	18F Registry (N=345)
Logistic EuroSCORE:	24%	24%
All 30-Day Mortality:	15% (17)	8% (29)
Procedure Related	10 (9%)	21 (6%)
Non-Procedure/Non-valve Related	7 (6%)	8 (2%)

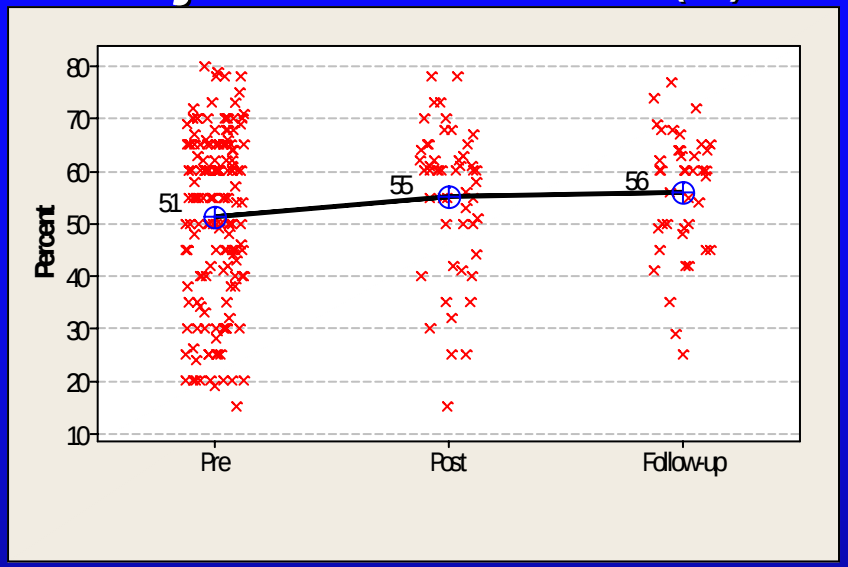
No valve dysfunction
No valve migration

Quality of Life at Follow-up
21F + 18F Safety Studies Pooled – N=175

Mean Gradient (mm Hg)



Ejection Fraction (%)



Last Follow-up NYHA

I	42%
II	43%
III	14%
IV	1%

Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI)

Alec Vahanian; Ottavio Alfieri; Nawwar Al-Attar; Manuel Antunes; Jeroen Bax; Bertrand Cormier; Alain Cribier; Peter De Jaegere; Gerard Fournial; Arie Pieter Kappetein; Jan Kovac; Susanne Ludgate; Francesco Maisano; Neil Moat; Friedrich Mohr; Patrick Nataf; Luc Pierard; Jose Luis Pomar; Joachim Schofer; Pilar Tornos; Murat Tuzcu; Ben van Hout; Ludwig K. Von Segesser; Thomas Walther

European Heart Journal 2008; doi: 10.1093/eurheartj/ehn183

Leicester Experience

- 42 TAVI cases
  - 30th January 2007 – 8th June 2008
- Logistic Euroscore 19.9 ± 11.4
- Periprocedural mortality 1/42 – tamponade/?transient aortic tear
- Additional 30 day mortality 2/41- traumatic subdural (day 19)
- Subsequent mortality 4/39
  - 1 aggressive metastatic sarcoma (day 90)
  - 1 multiple pulmonary emboli (day 94)
  - 1 renal failure/progression of leukaemia (day 94)
  - 1 mesenteric ischaemia (AF) (day 269)

Conclusions

Percutaneous Aortic Valve Replacement with the CoreValve System

- Has been shown to be a safe and effective procedure in high risk aortic stenosis patients.
- Has evolved towards a pure percutaneous procedure.
- As with novel technologies PAVR has a definite learning curve which requires an in-depth understanding of patient selection and various anatomical criteria.
- Long term efficacy and durability of PAVR in patients with aortic stenosis will be determined by future randomized trials.