TURIN, 20TH—21ST NOVEMBER 2008

GREAT INNOVATIONS IN CARDIOLOGY

4TH JOINT MEETING WITH MAYO CLINIC

4TH TURIN CARDIOVASCULAR NURSING CONVENTION

SESSION VI: **HOT TOPICS**
NEW TREATMENTS FOR AORTIC VALVE DISEASES

A. Colombo (Milano)

Lecture: State of art

4th Joint Meeting with Mayo Clinic
GREAT INNOVATIONS IN CARDIOLOGY
Torino – 20 – 22 November 2008

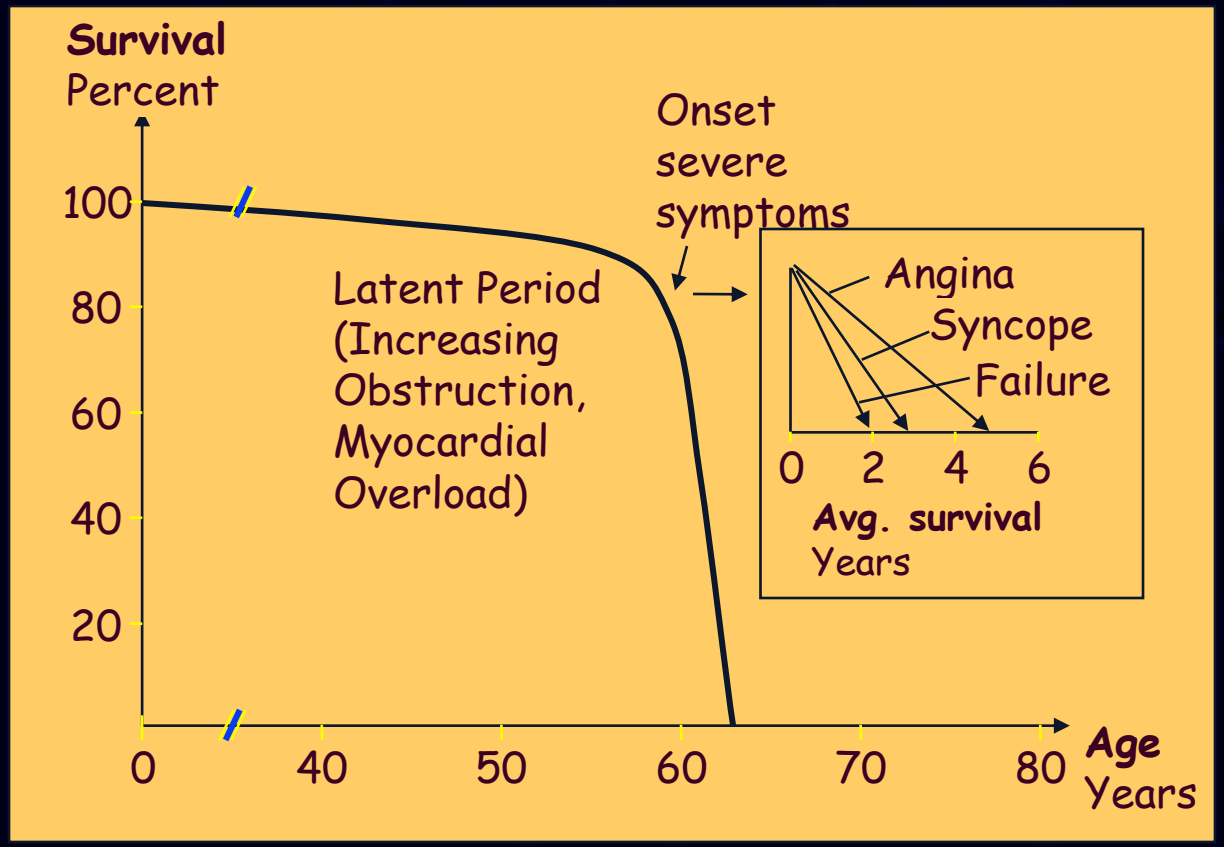
Terapia Interventistica Della Valvola Aortica

40min

Antonio Colombo

Centro Cuore Columbus Milan, Italy
S. Raffaele Hospital Milan, Italy

Aortic stenosis is life-threatening and progresses rapidly



"Survival after onset of symptoms is 50% at two years and 20% at five years."[1]

"Surgical intervention [for severe AS] should be performed promptly once even … minor symptoms occur."[2]

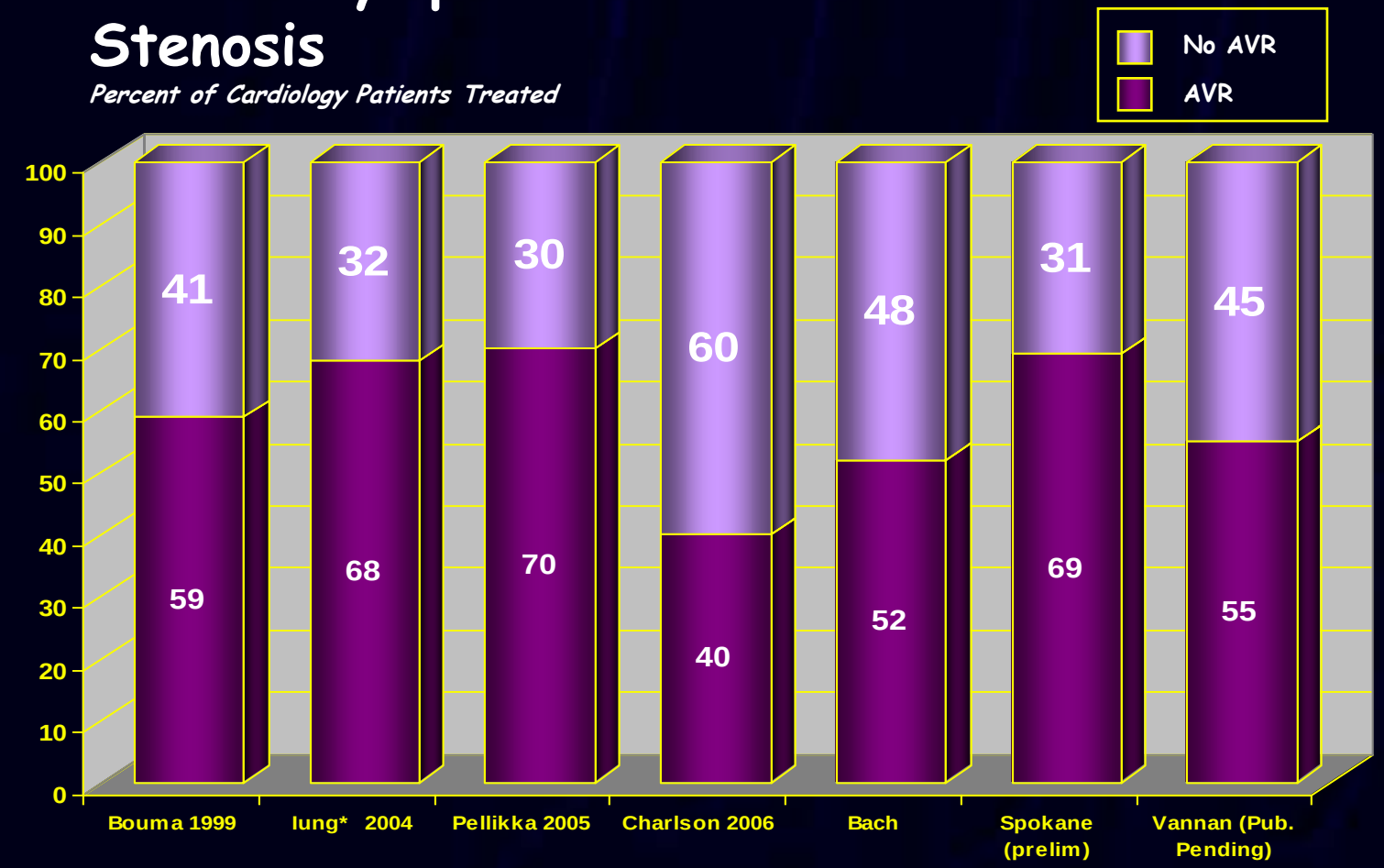
Sources: [1] S.J. Lester et al., "The Natural History and Rate of Progression of Aortic Stenosis," *Chest* 1998
[2] C.M. Otto, "Valve Disease: Timing of Aortic Valve Surgery," *Heart* 2000

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

At least 30-40% of Cardiologists' AS Patients Go Untreated

Severe Symptomatic Aortic Stenosis

Percent of Cardiology Patients Treated



Under-treatment especially prevalent among patients managed by *Primary Care* physicians

1. Bouma B J et al. To operate or not on elderly patients with aortic stenosis: the decision and its consequences. Heart 1999;82:143-148
2. Iung B et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. European Heart Journal 2003;24:1231-1243 (*includes both Aortic Stenosis and Mitral Regurgitation patients)
3. Pellikka, Sarano et al. Outcome of 622 Adults with Asymptomatic, Hemodynamically Significant Aortic Stenosis During Prolonged Follow-Up. Circulation 2005
4. Charlson E et al. Decision-making and outcomes in severe symptomatic aortic stenosis. J Heart Valve Dis2006;15:312-321

Transcatheter Aortic Valve Implantation

In 2008, surgical AVR remains the gold standard treatment of calcific degenerative AS:

- Improves hemodynamics
- Improves symptoms
- Increases life expectancy
- Low mortality rate in the vast majority of pts

Indications for transcatheter AVR

Symptomatic patients with severe AS

- High risk for surgery
- Inoperable

THV currently used

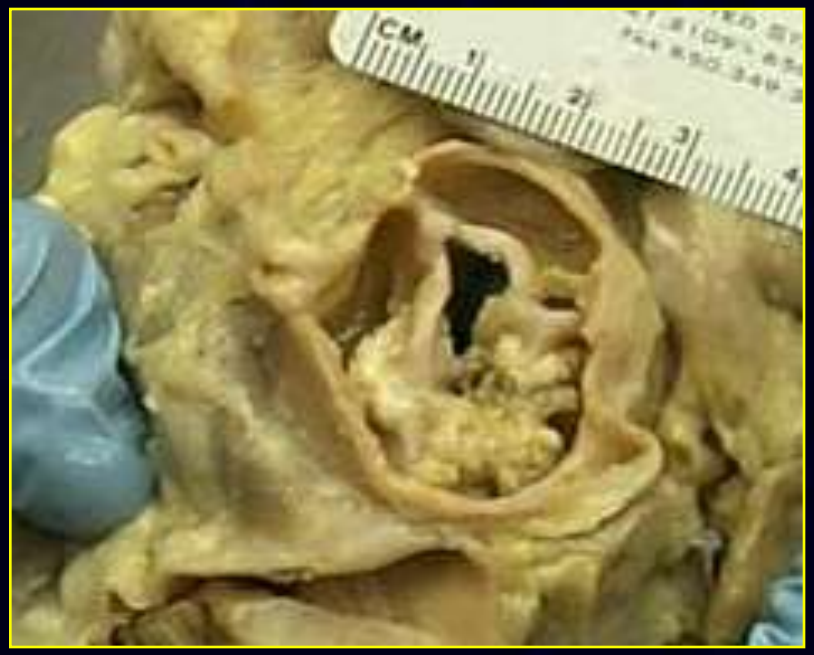
CE MARK: 2007

Edwards-Sapien ™

> 3000 patients

CoreValve Revalving ™

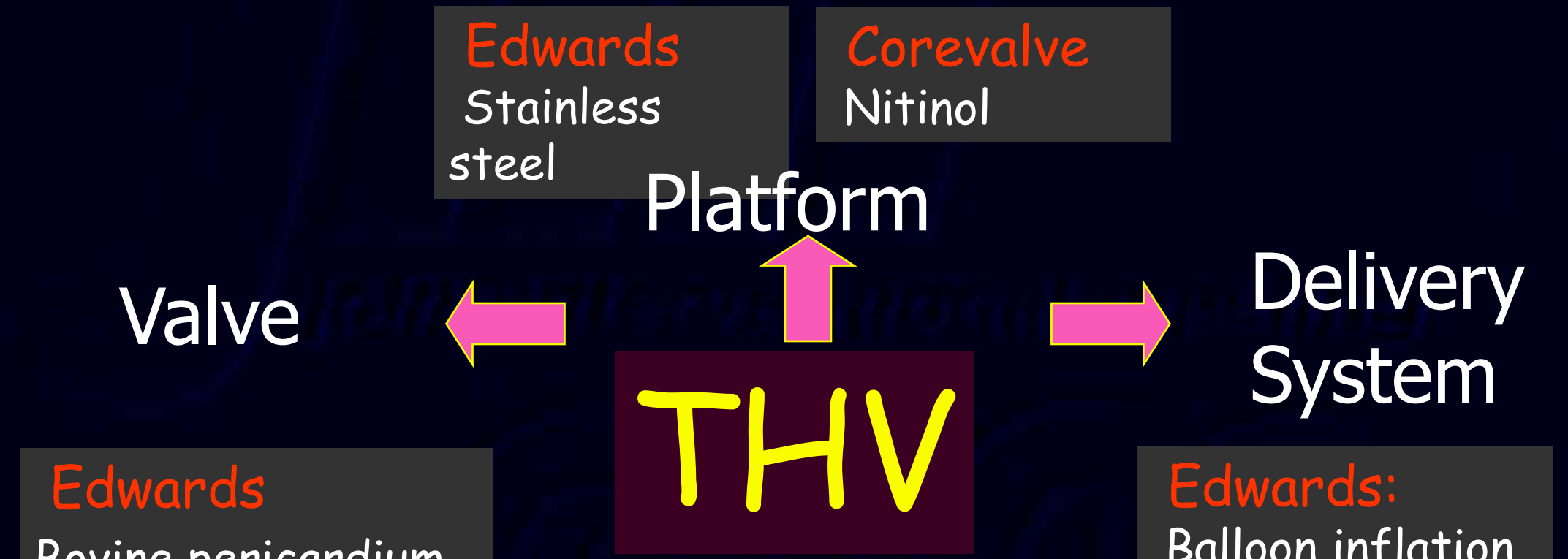
> 4000 patients



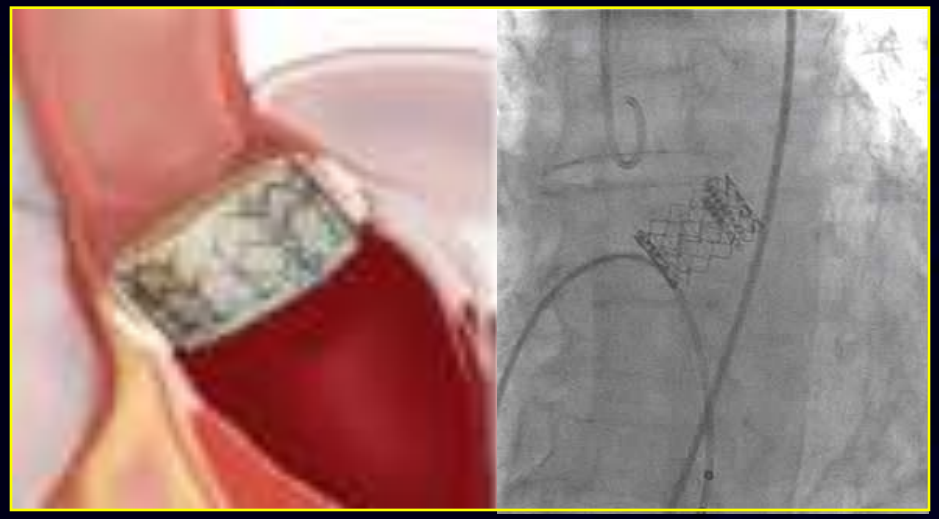
Stenotic aortic valve[1]

Edwards SAPIEN THV frame[1]

Transcatheter Heart Valve

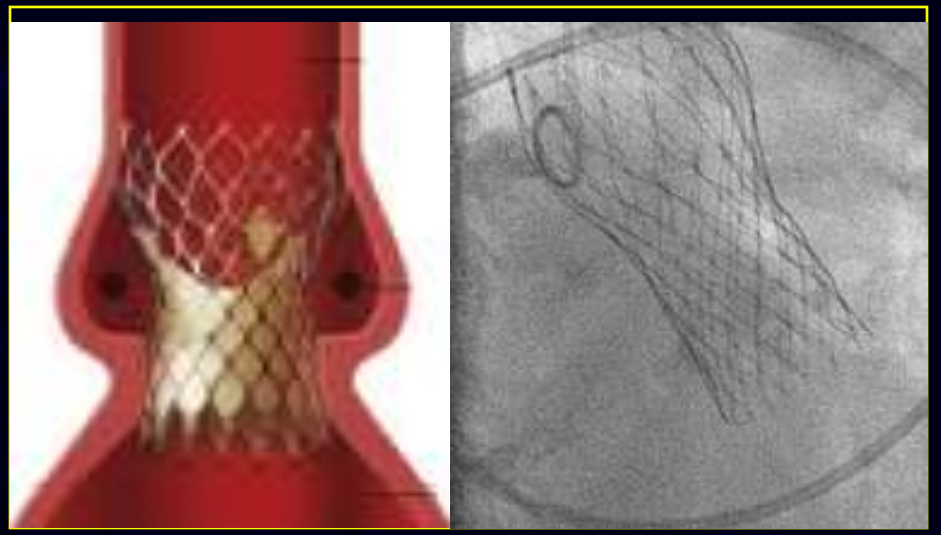


	Stent Ø	Height	Annulus Ø
Edwards-Sapien ™	23 mm	14.5mm	18-21 mm
	26 mm	16 mm	21-25 mm
CoreValve Revalving ™	26 mm	53 mm	20-23 mm
	29 mm	55 mm	23-27 mm



Edwards-Sapien

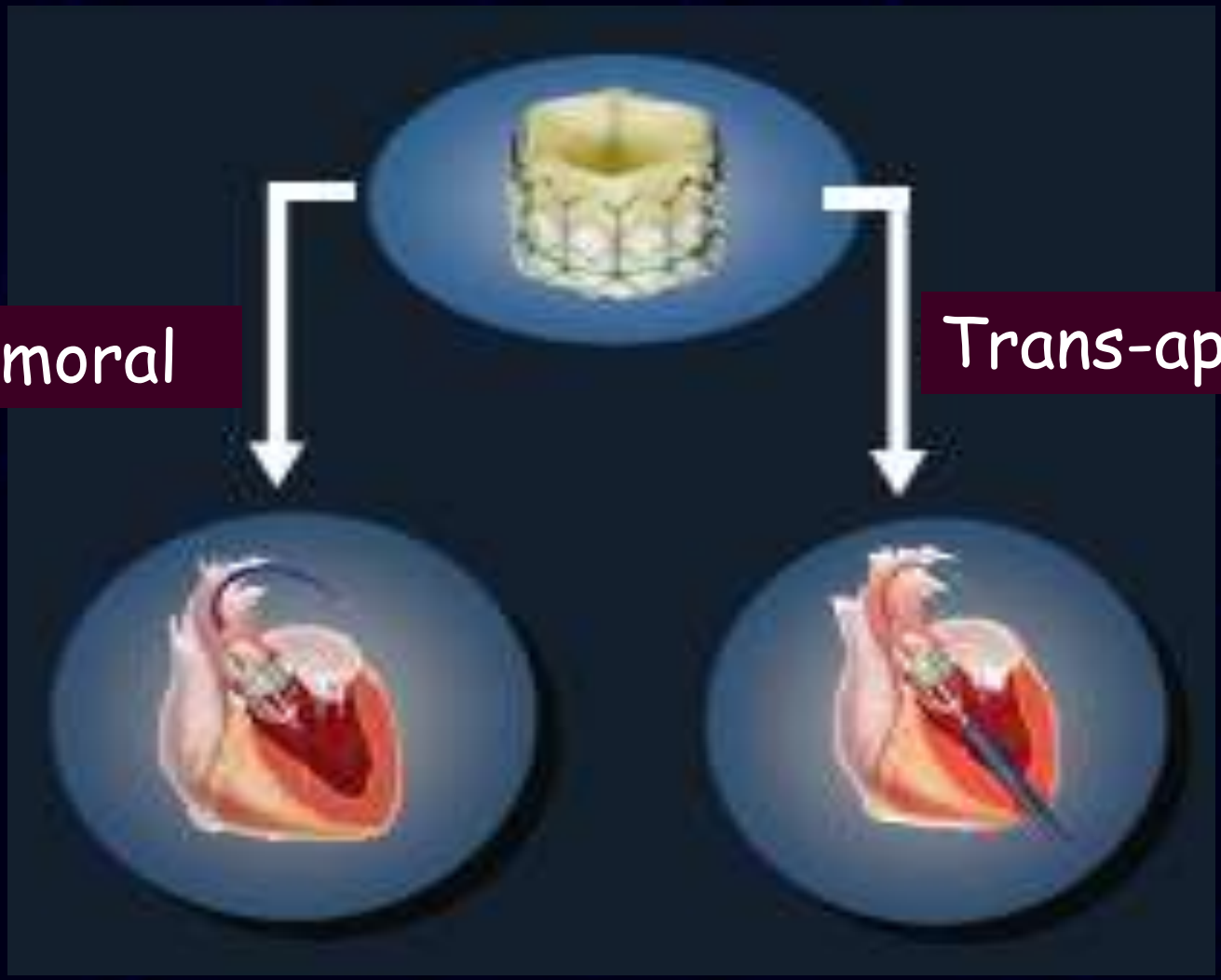
Transfemoral (22F or 24F)
Trans-apical



CoreValve Revalving

Transfemoral (18F)

EDWARDS-SAPIEN™



Transfemoral

Trans-apical

The CRIBIER-EDWARDS/EDWARDS-SAPIEN™ TRANSCATHETER BIOPROSTHESIS

Cribier-Edwards™
23mm

Edwards SAPIEN™
23mm, 26mm

Untreated
Equine pericardium

Treated (anti-Ca)
Bovine Pericardium

Stainless steel stent

Transfemoral retrograde

Transapical

EMO GVM
CENTRO
CUORE COLUMBUS s.r.l.

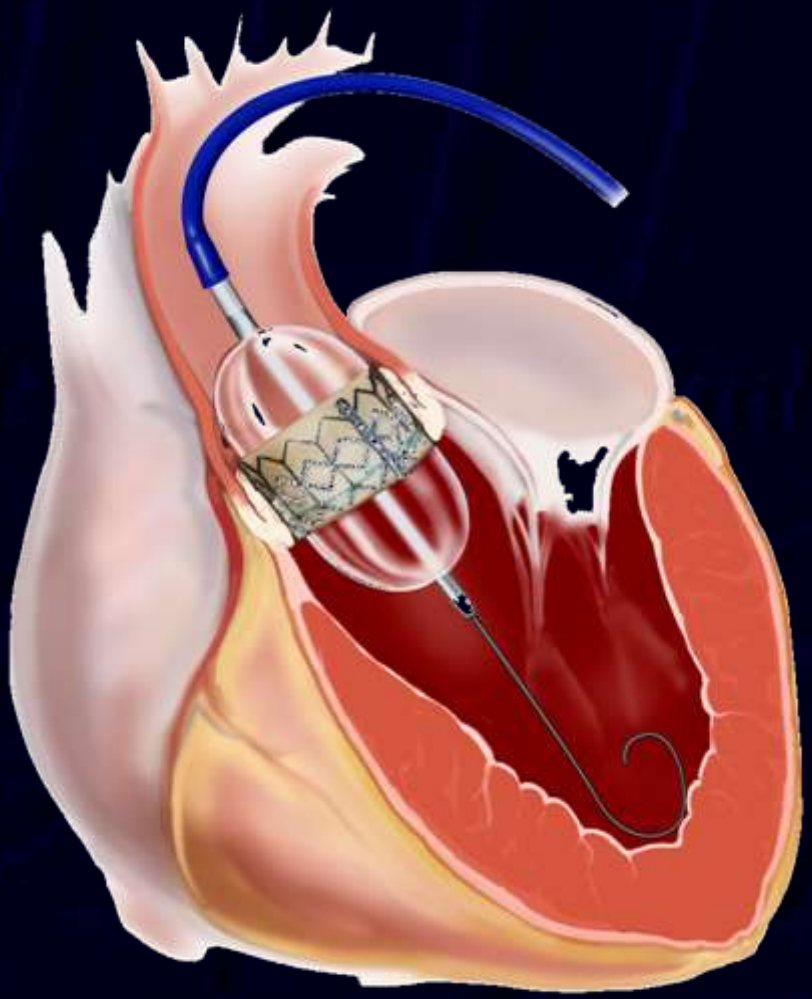
> 1200 Patients
2002-2008

- Transfemoral (n=628)
  - Antegrade n=59
    - RECAST n = 24
    - iREVIVE n = 22
    - REVIVE n = 4
    - REVIVAL I n = 7
    - US Compassionate n=2
  - Retrograde n=569
    - REVIVE II (EU) n = 106
    - REVIVAL II (USA) n = 55
    - Canadian Special Access n = 125
    - PARTNER EU n=63
    - PARTNER IDE n > 200 (>100 TF)
    - SOURCE Registry n > 200
- Transapical (n=457)
  - TRAVERCE (EU) n=172
  - REVIVAL II (USA) n =40
  - Canadian Special Access n =90
  - US Compassionate n=2
  - PARTNER EU N =67
  - SOURCE Registry (EU) N > 200

EARLY TRIALS

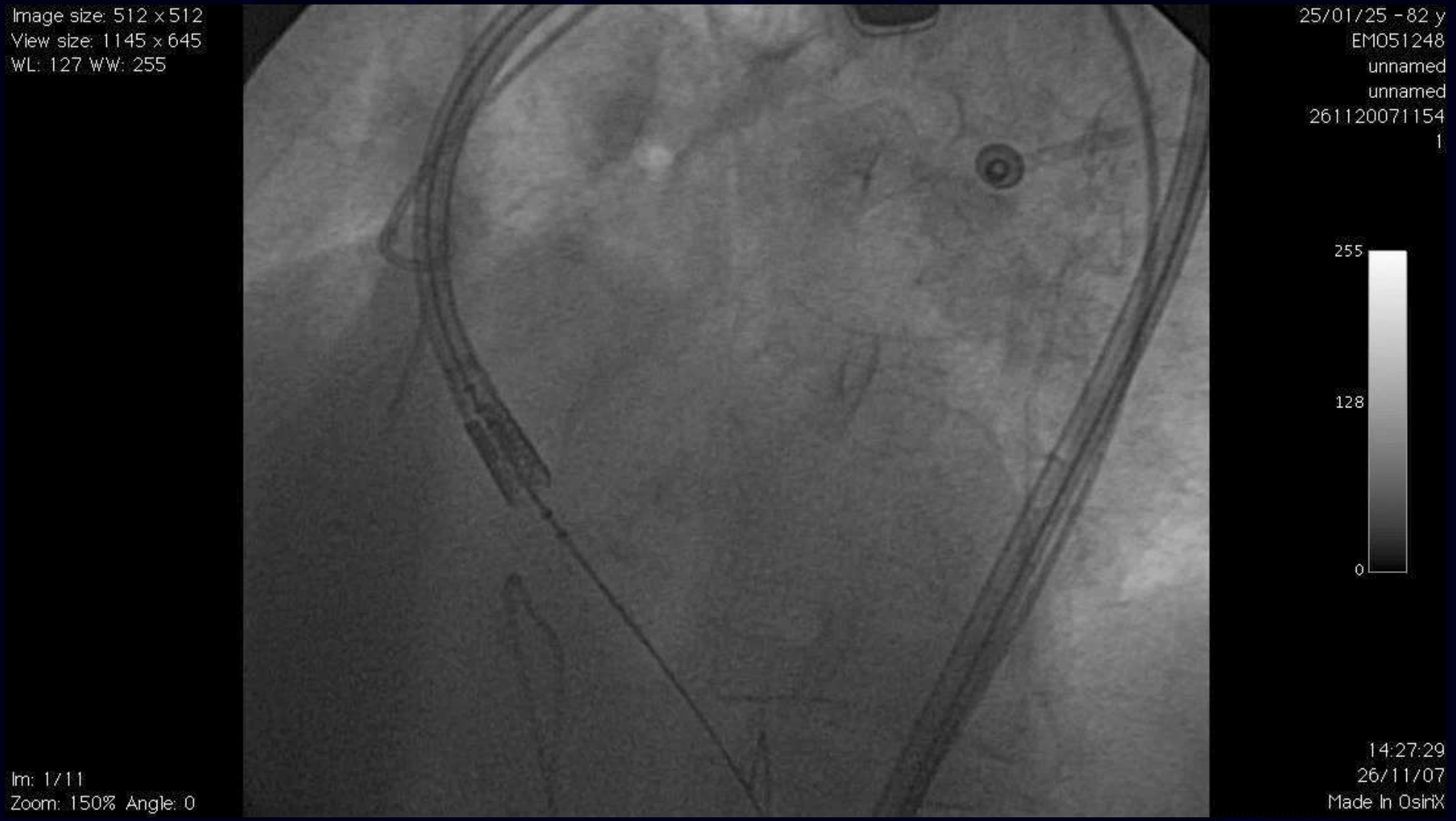
May 2008

Transfemoral approach

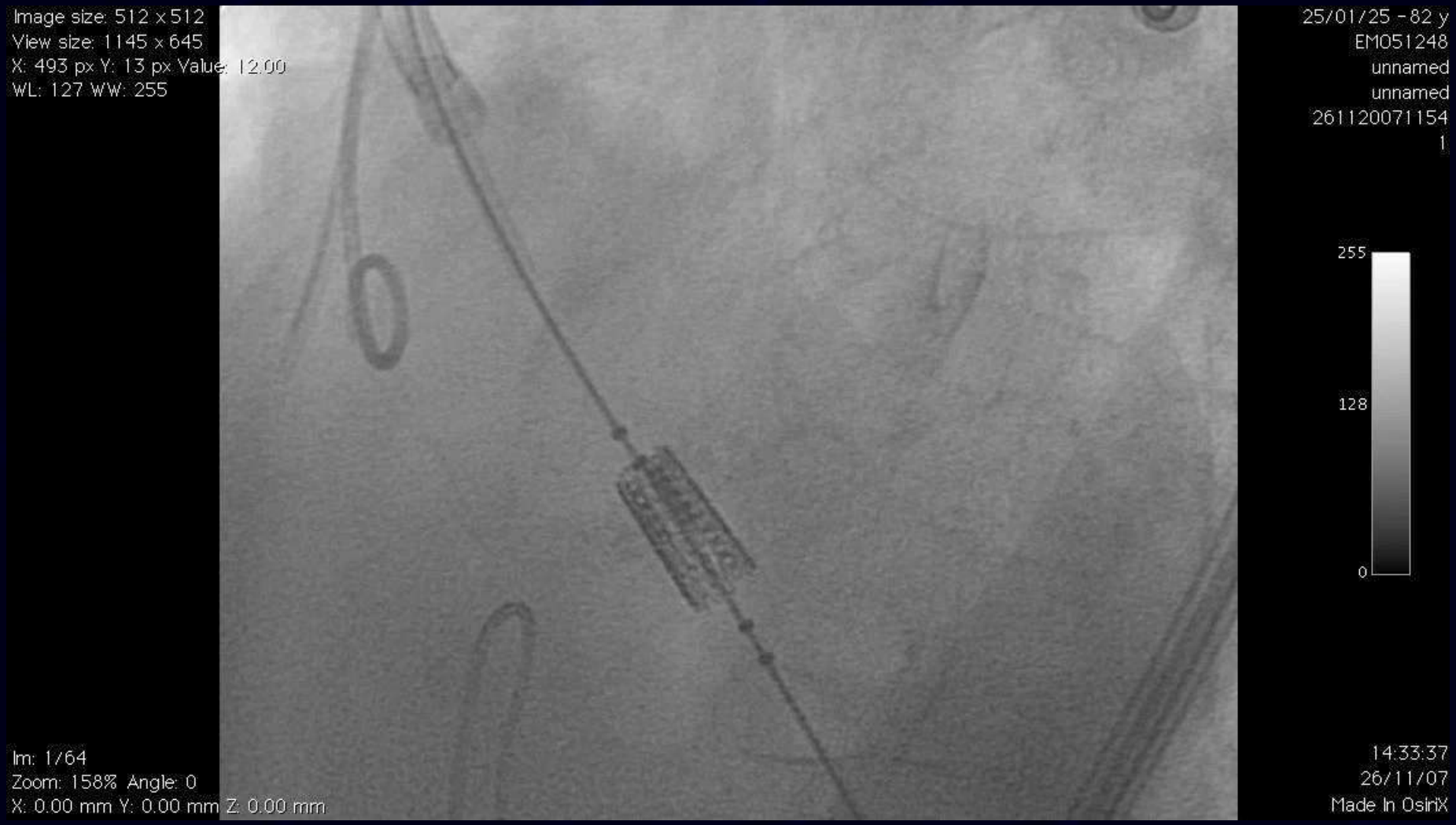


Local anesthesia, sedation, no TEE

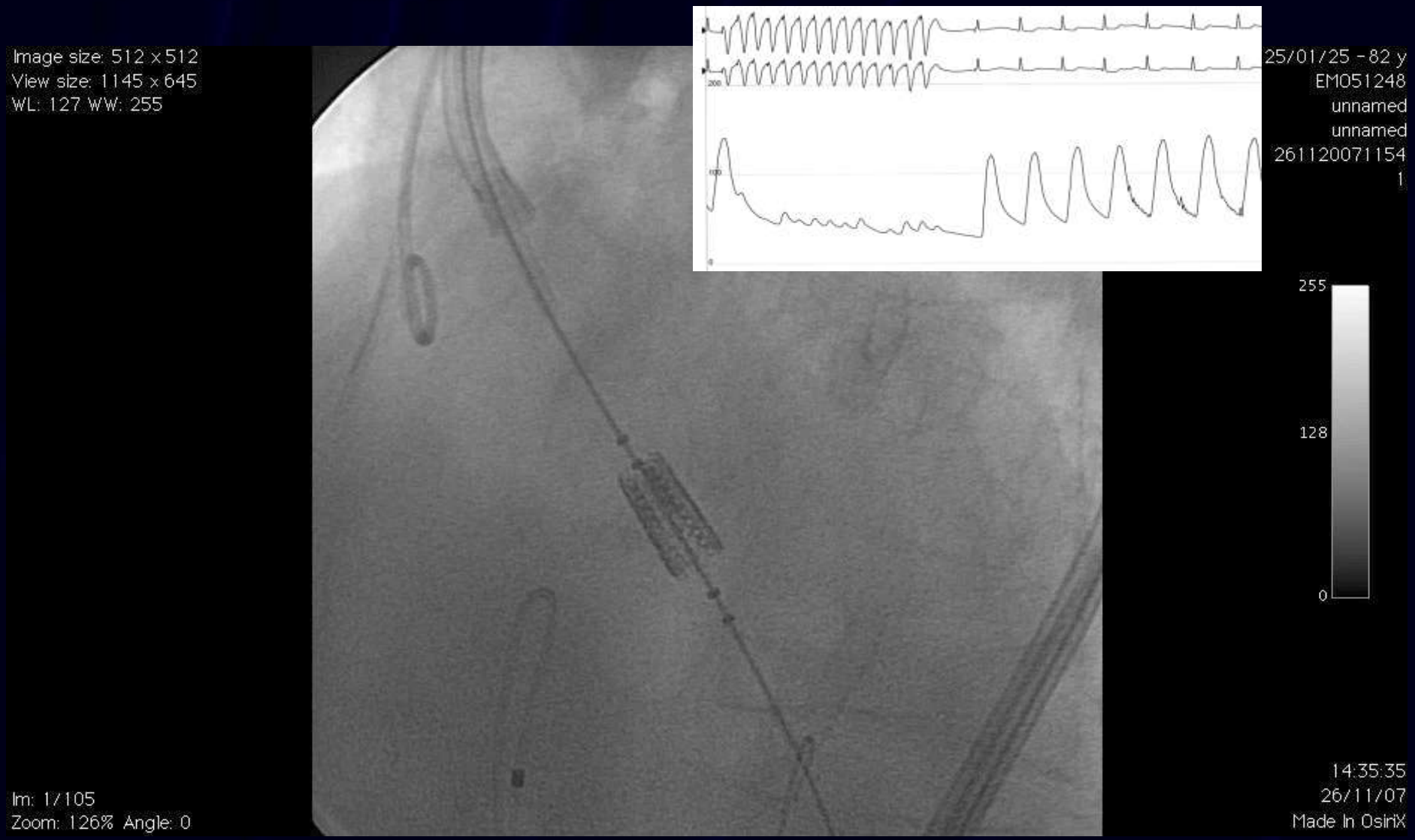
flex cateter



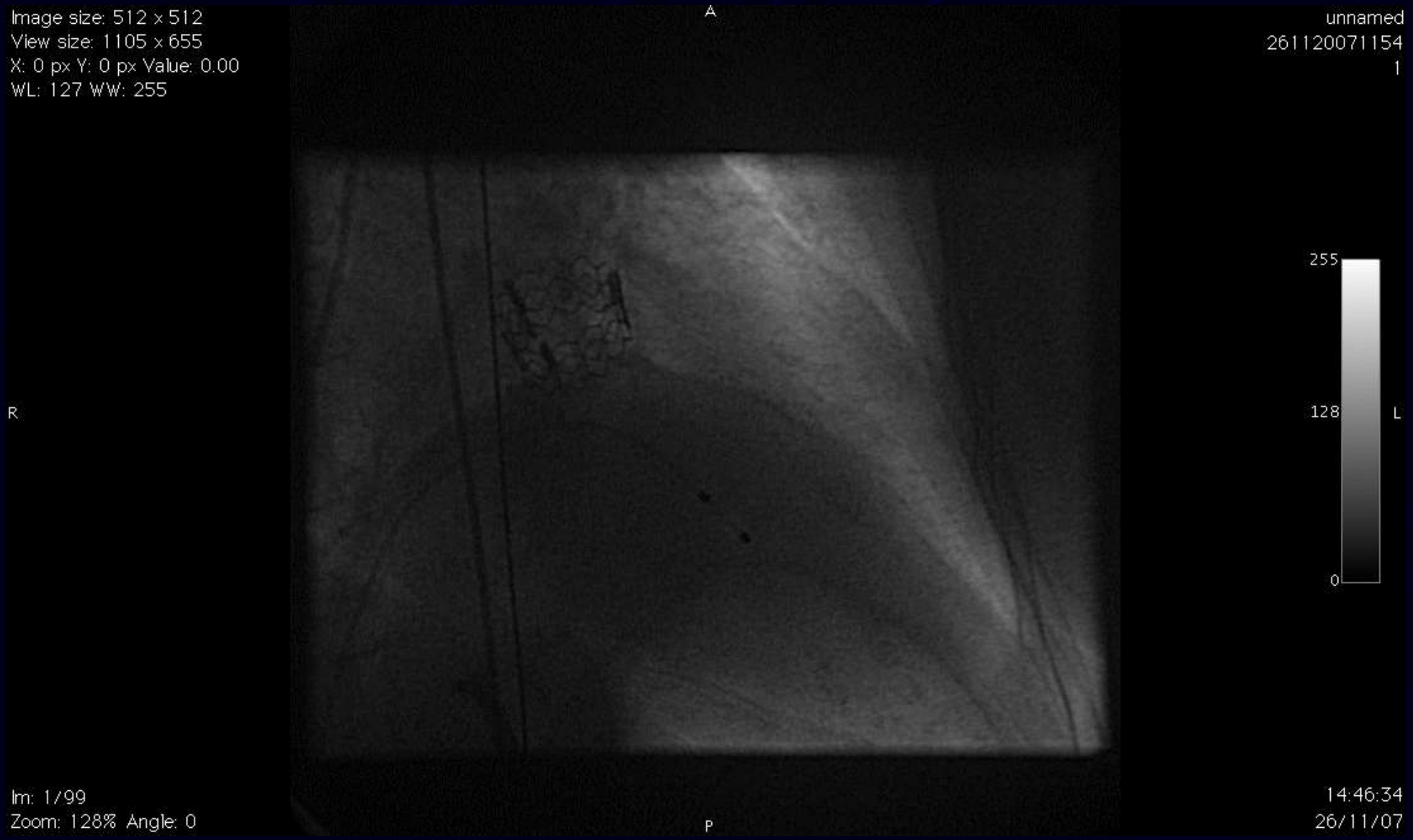
VALVE POSITIONING



VALVE INFLATION



VALVE POST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X: 0 px Y: 0 px Value: 0.00
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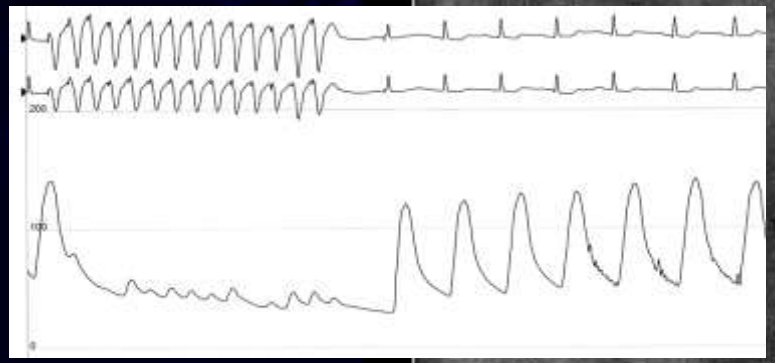
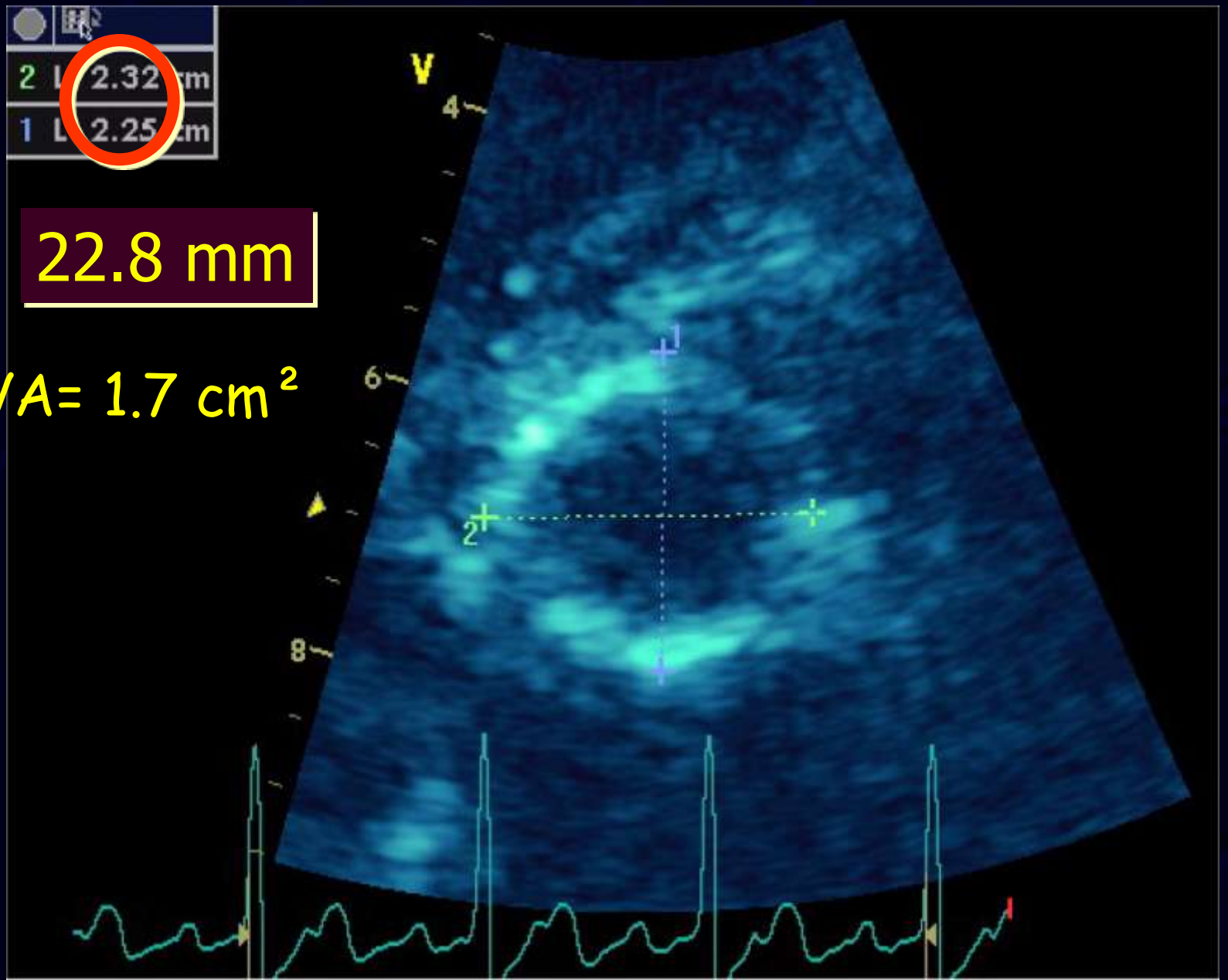
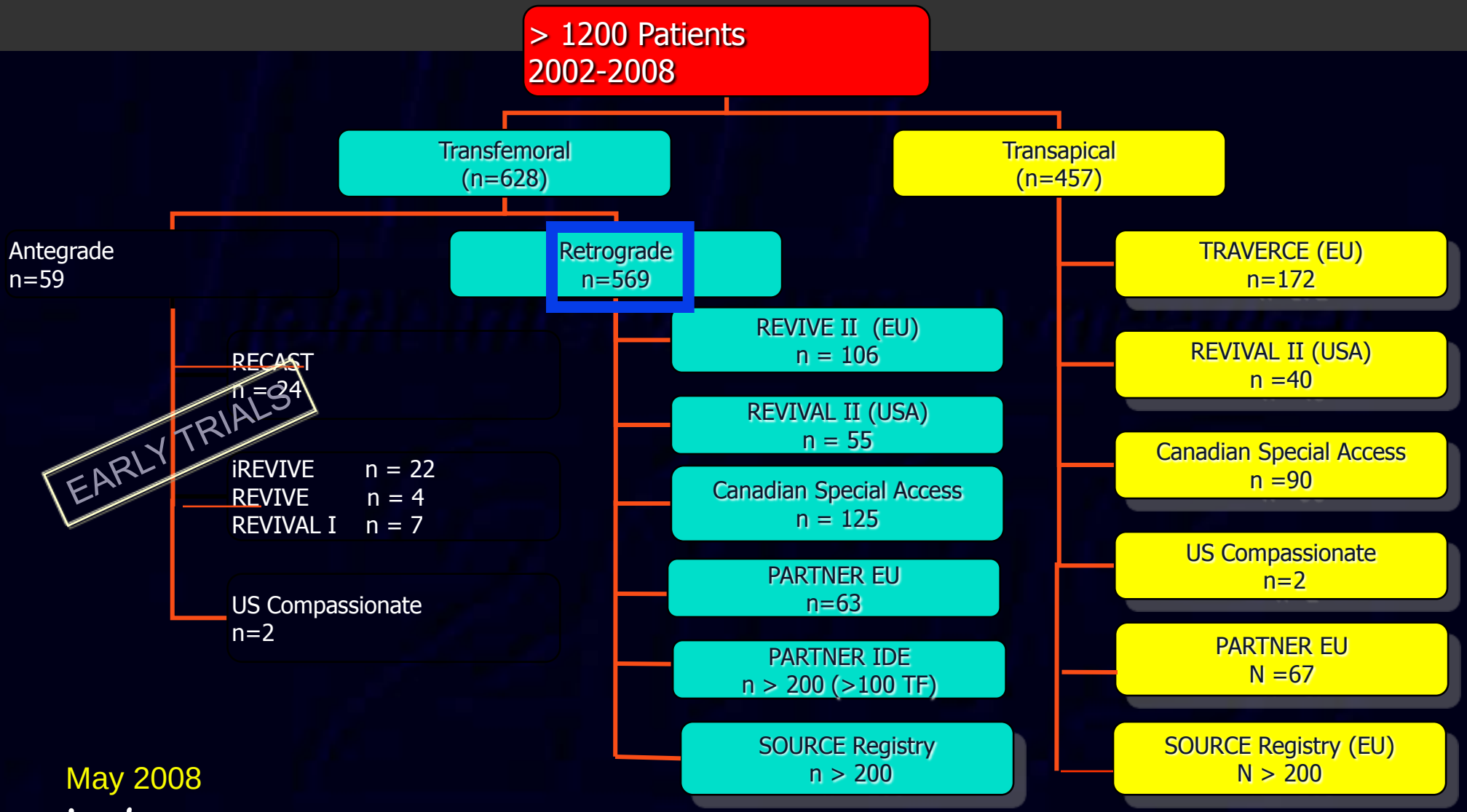
THV delivery under rapid pacing



Gradient post-THV

TTE, Day 1 post-THV: cross-section





May 2008

CoreLab assessment

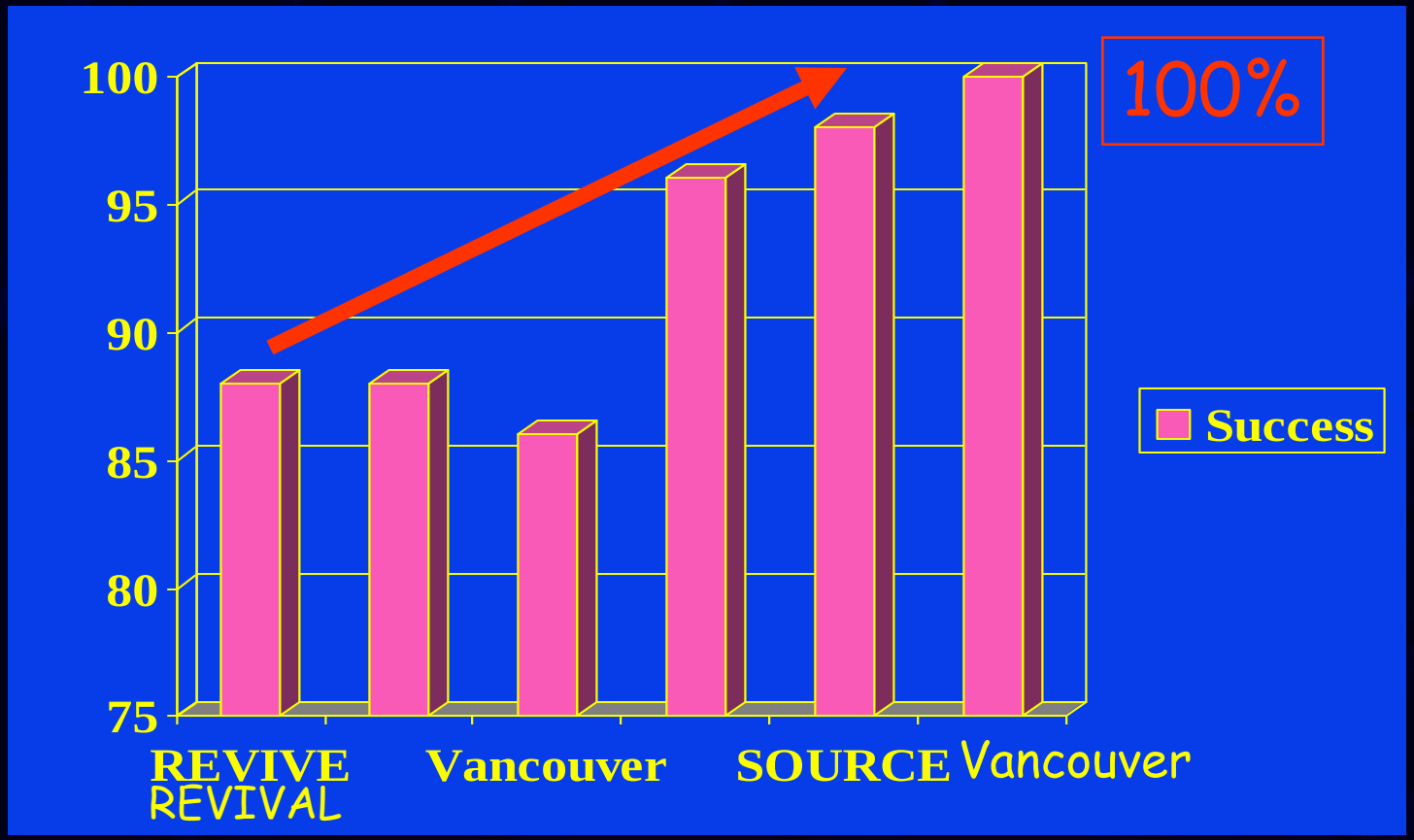
REVIVE II (Europe) and REVIVAL II (US) TF trials

	REVIVE II (n=106)	REVIVAL II (n = 55)
Logistic EuroSCORE		
Mean ± SD	29.9 ± 13.2	34.1 ± 18.0
Range (Min - Max)	16 – 43	8 – 83
STS Score		
Mean ± SD	Not collected	13.1 ± 7.2
Range (Min – Max)	Not collected	4 – 31

High risk patients

Trans-femoral Edwards PHV implantation

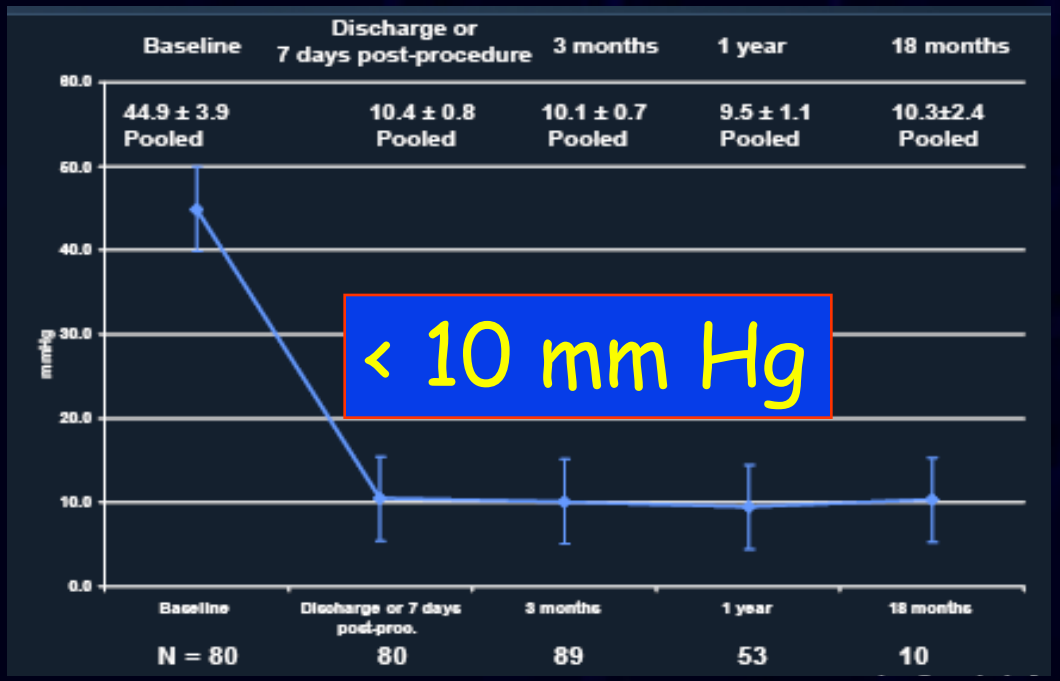
Procedural success

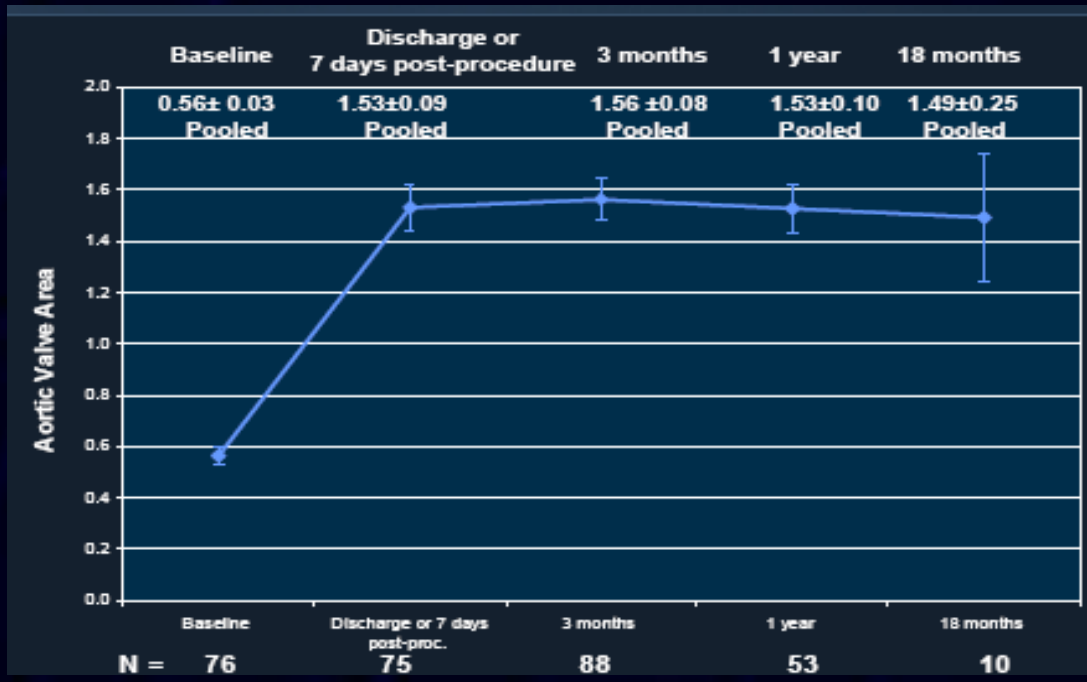


2006 REVIVAL 2008

REVIVE II and REVIVAL II TF

Mean Gradient* and Echo EOA* Over Time

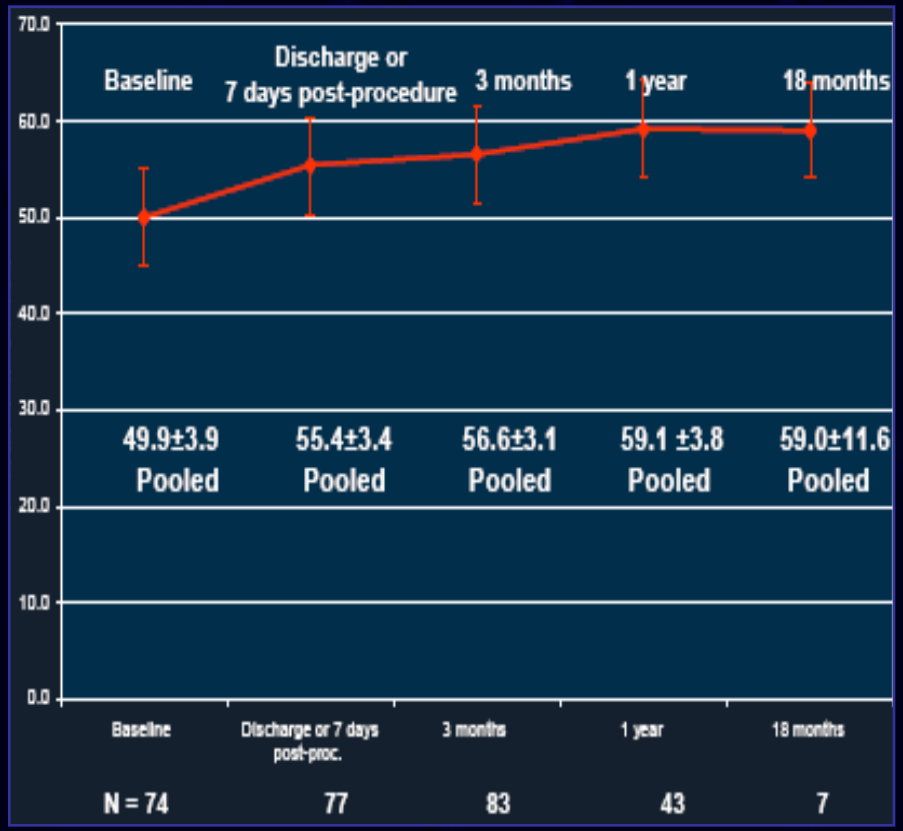




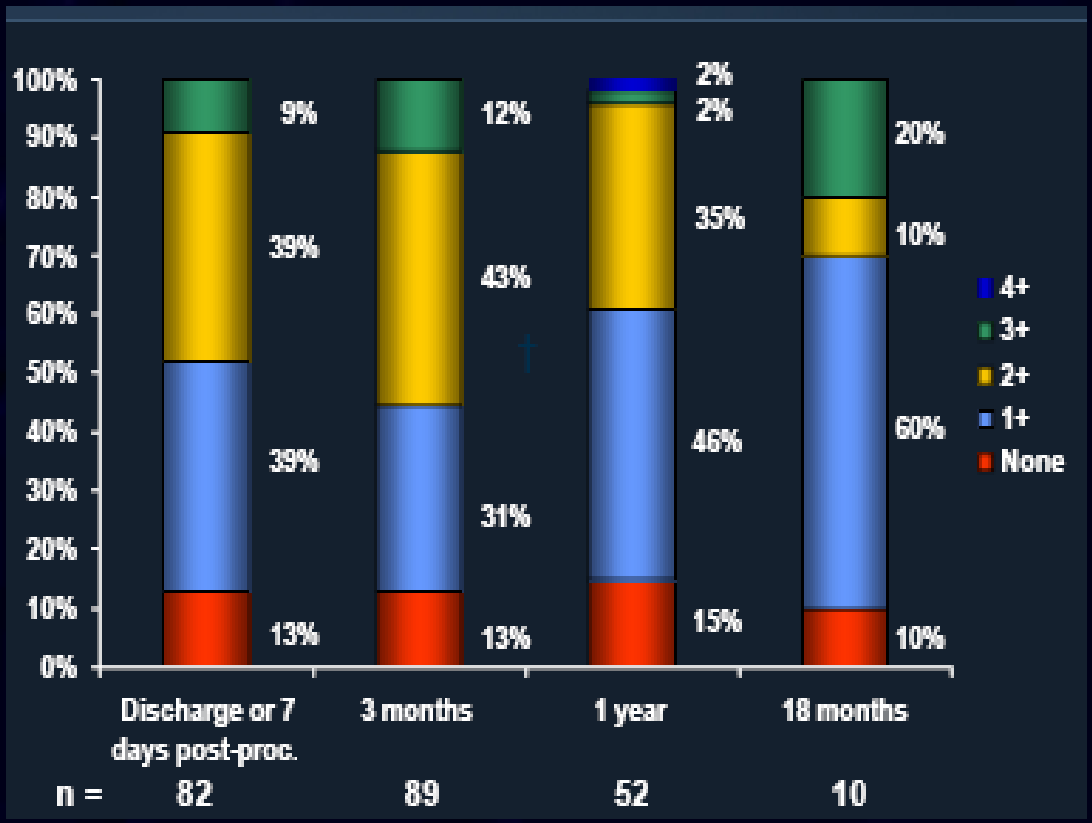
** Core Lab analysis*

REVIVE II and REVIVAL II TF

Ejection Fraction*



Aortic Regurgitation*



** Core Lab analysis*

REVIVE II and REVIVAL II TF

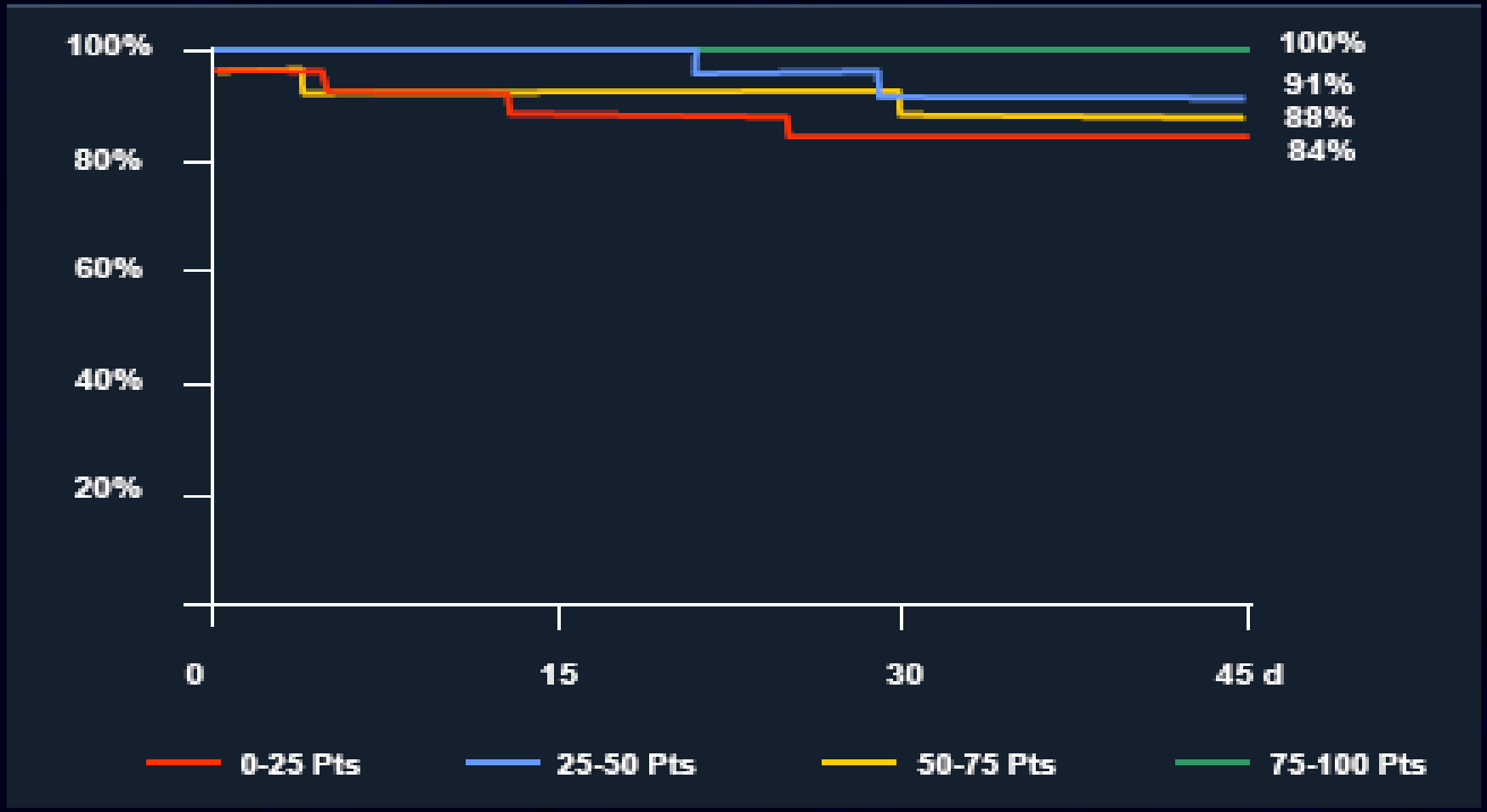
30-Day Clinical Events

	REVIVE II (n=106)	REVIVAL II (n = 55)
30-Day Mortality	14 (13.2%)	4 (7.3%)
MI	9 (8.5%)	9 (16.3%)+
Emergency Cardiac Events	1 (0.9%)	1 (1.8%)
Neurologic Events	3 (2.8%)	8 (9.0%)
Vascular / Access Complications	13 (13.0%)	7 (12.7%)

+ MI defined as >2X nml CK with elevated CKMB; 7/9 patients had no Sx or ECG changes.

Complete AV block requiring pacemaker: 5.7%
(Webb et al – JACC Intv 2008)

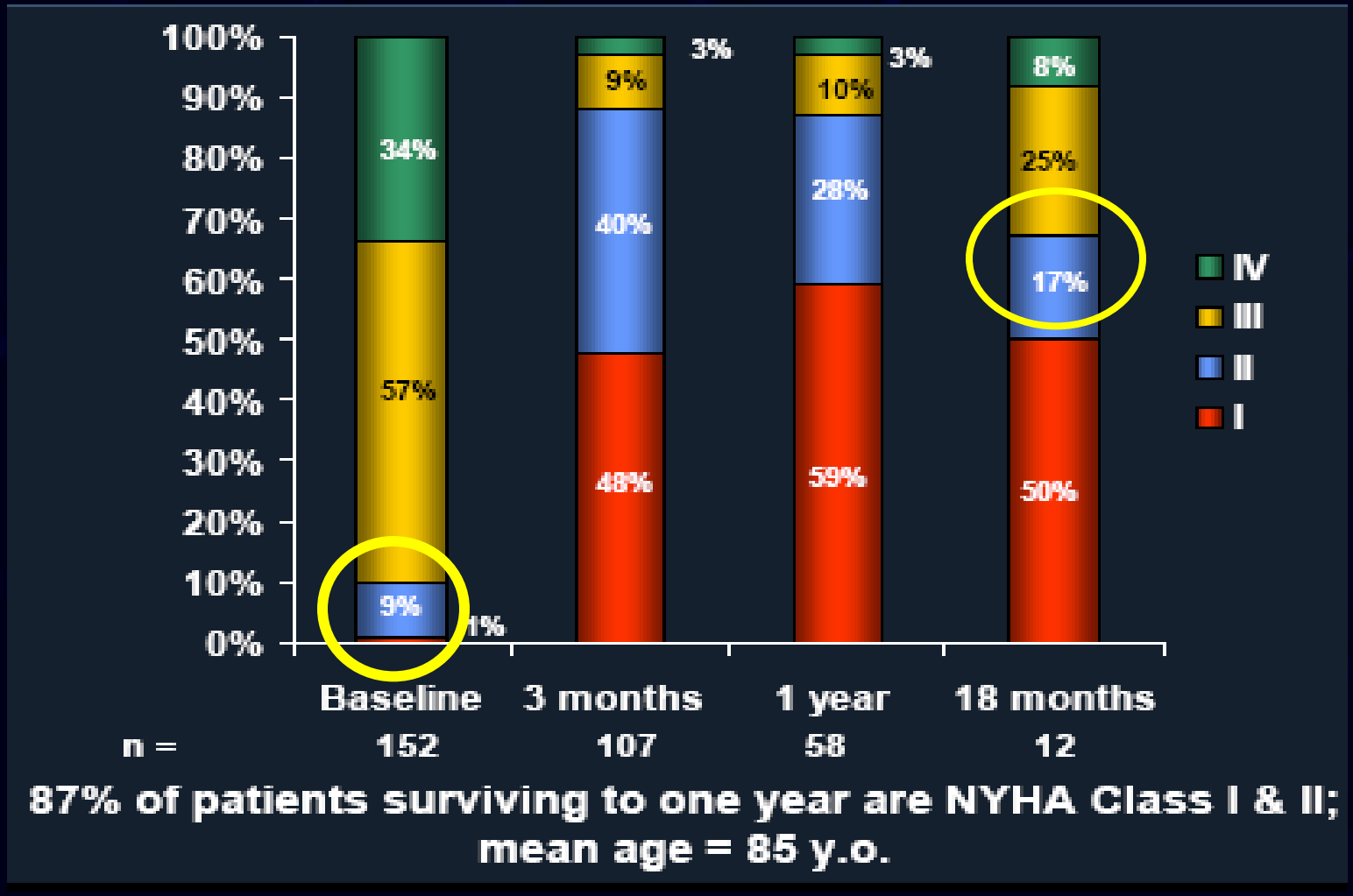
Early survival (45 days)
Vancouver data



30-day mortality = 0 in the last patients

REVIVE II and REVIVAL II TF

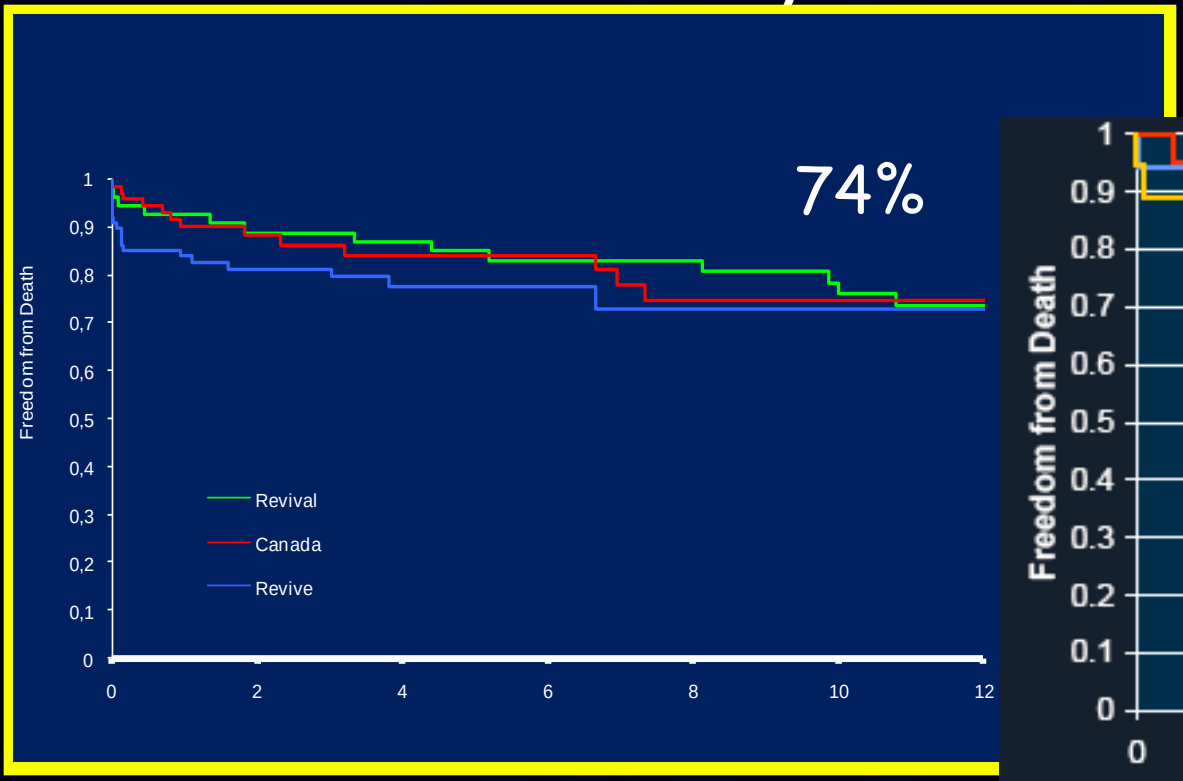
NYHA Symptoms Overtime



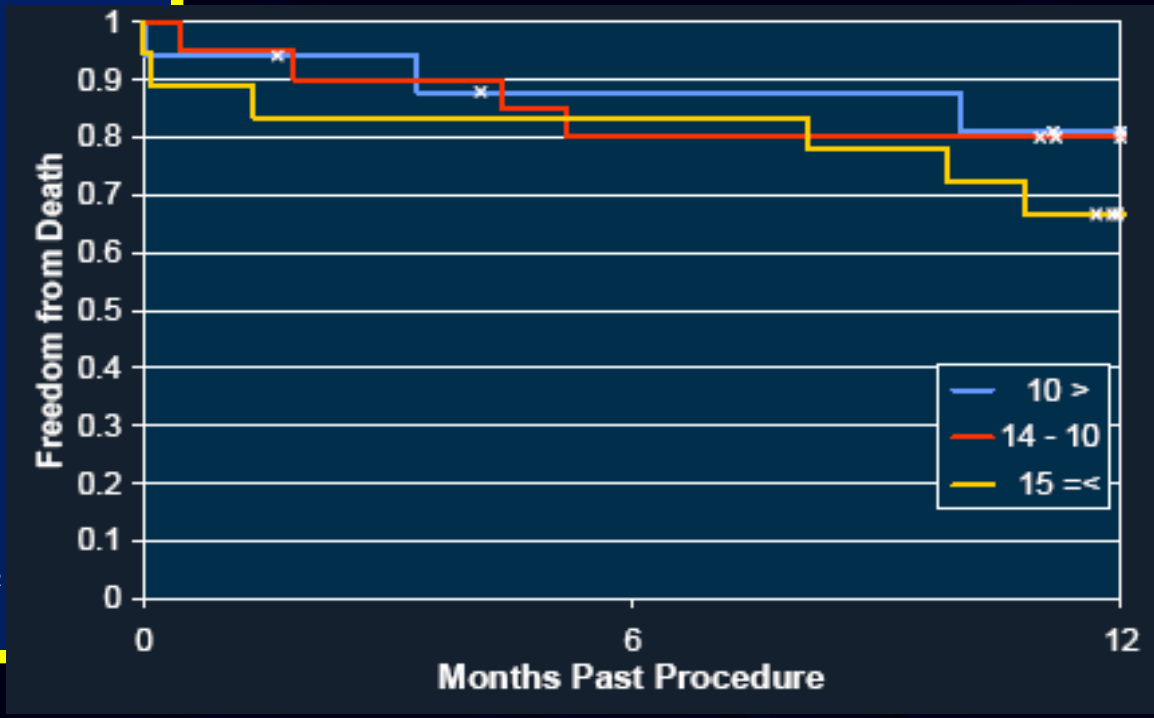
87% of patients surviving to one year are NYHA Class I & II; mean age = 85 y.o.

REVIVE II and REVIVAL II TF

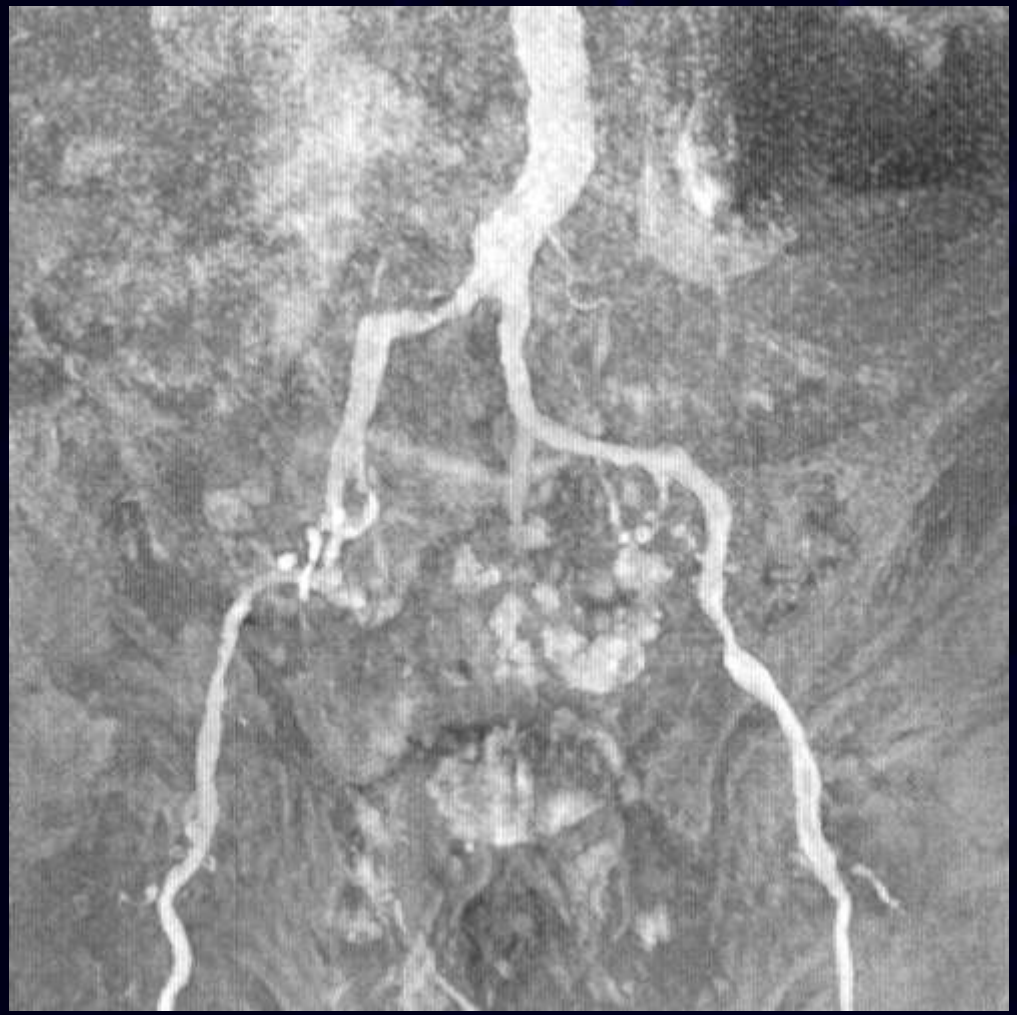
All Cause Mortality

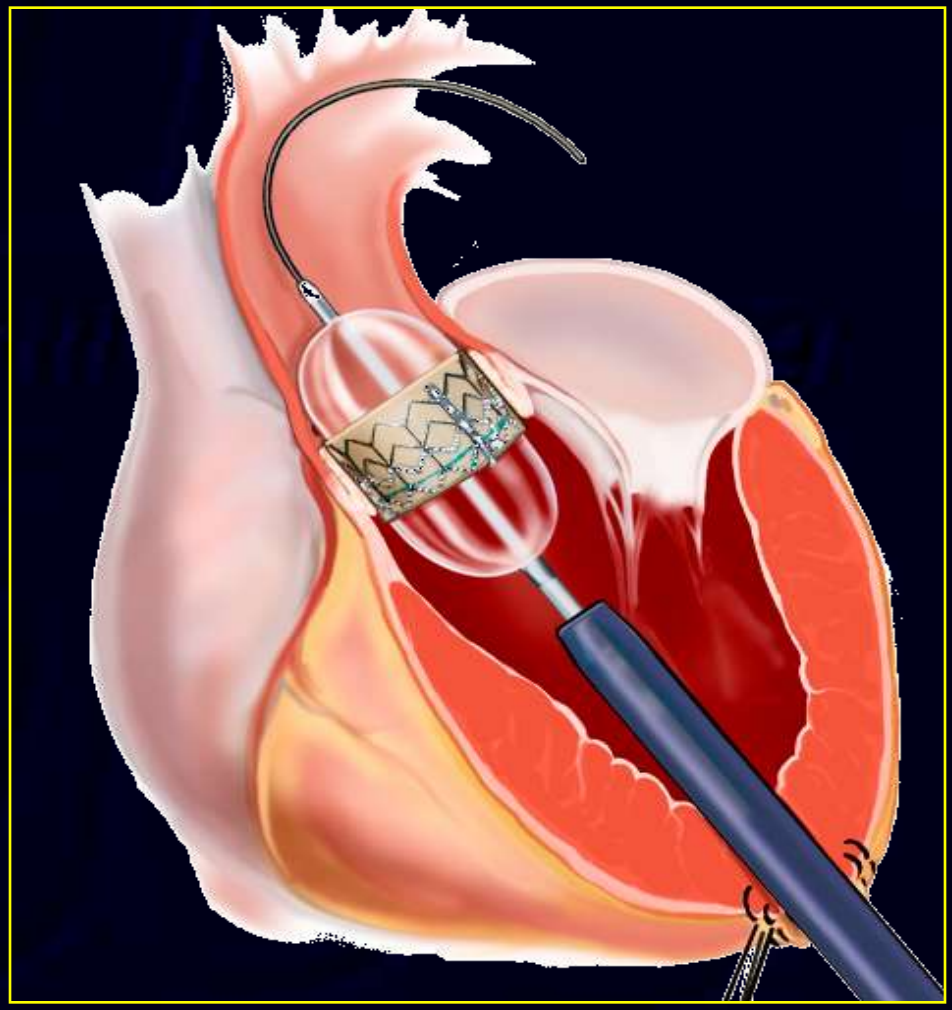


Event-free Survival by Echo-Score



When Arterial Access is an Issue: The Trans-Apical Surgical Approach





Ongoing PARTNER US Randomized Trial

High risk symptomatic critical aortic stenosis

1ary endpoint: Mortality at one-year

Operable ?

NO:

Medical management

Superiority

350 Pts

- Best Medical TT
- THV

YES:

Surgical management

Non inferiority

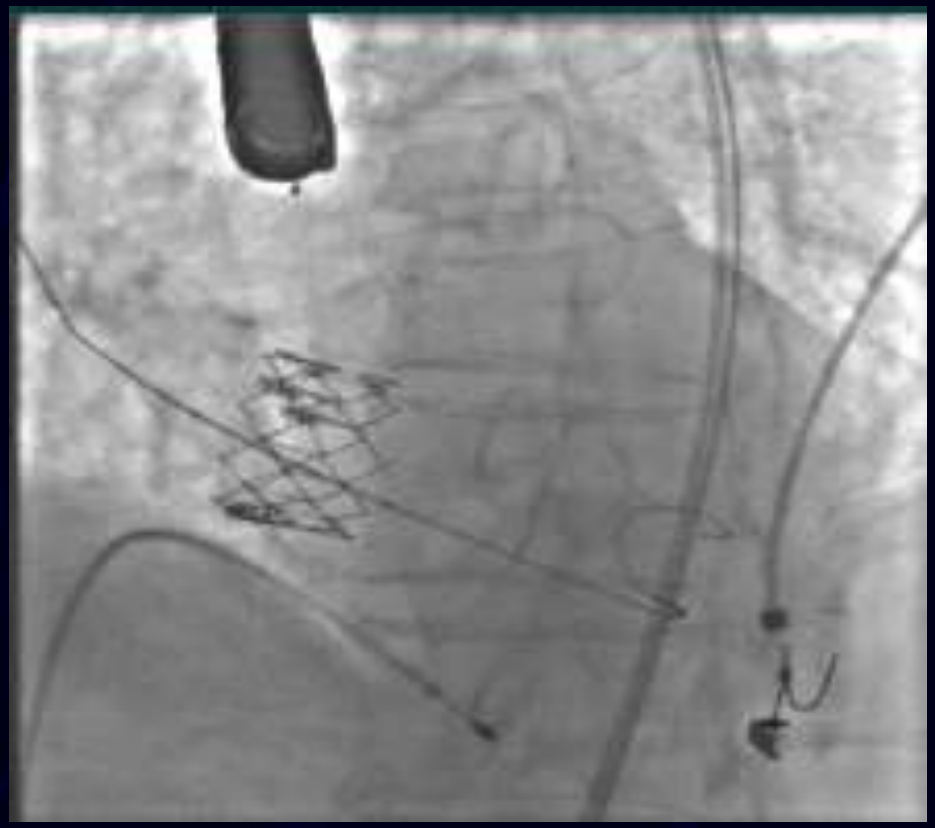
850 Pts

- Conventional AVR
- THV

Edwards next generation THV

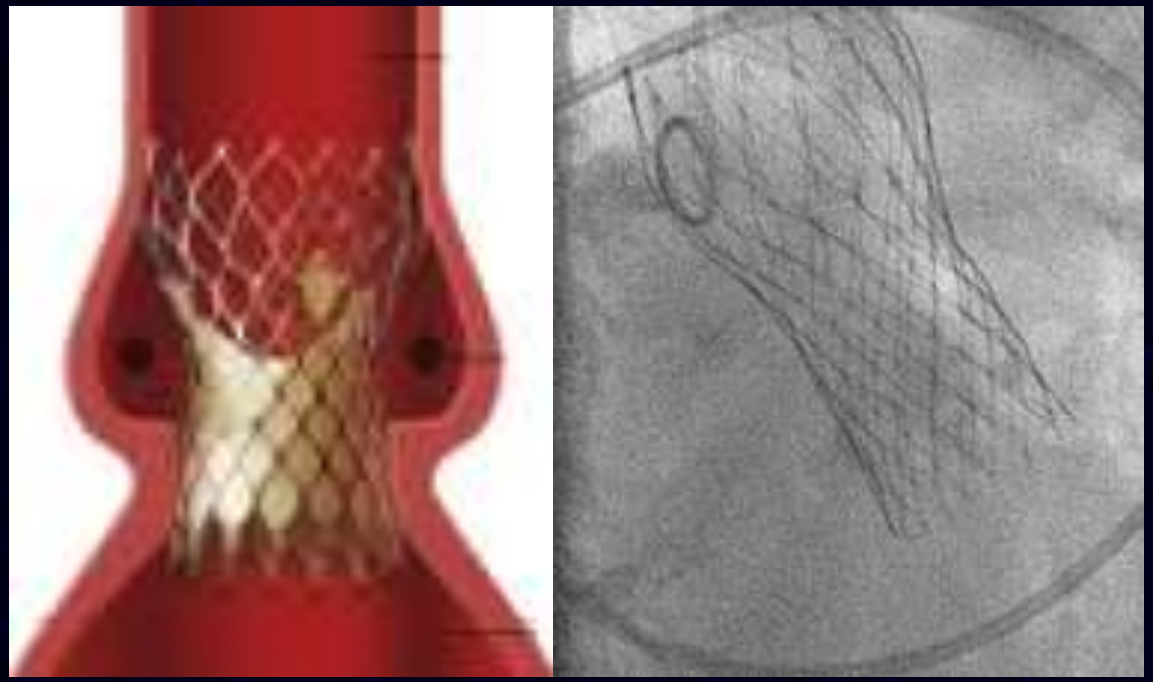
Design features

- Cobalt alloy frame
- Refined bovine pericardial leaflets (geometry for long valve performance)
- Overall system profile reduced by 4-5F
- Additional sizes: 20, 23, 26 and 29mm



COREVALVE REVALVING

Self-expanding
multilevel
nitinol frame

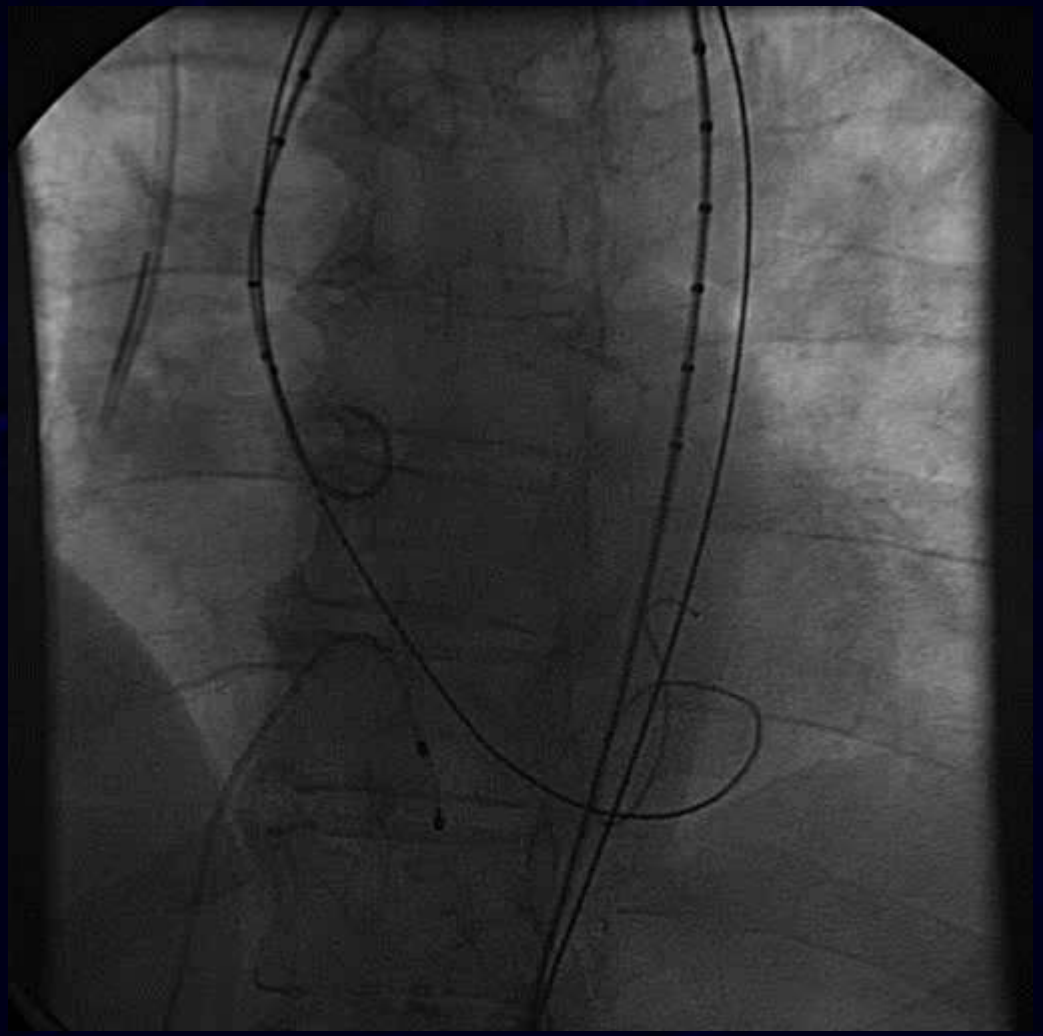


CoreValve Revalving

Transfemoral (18F)

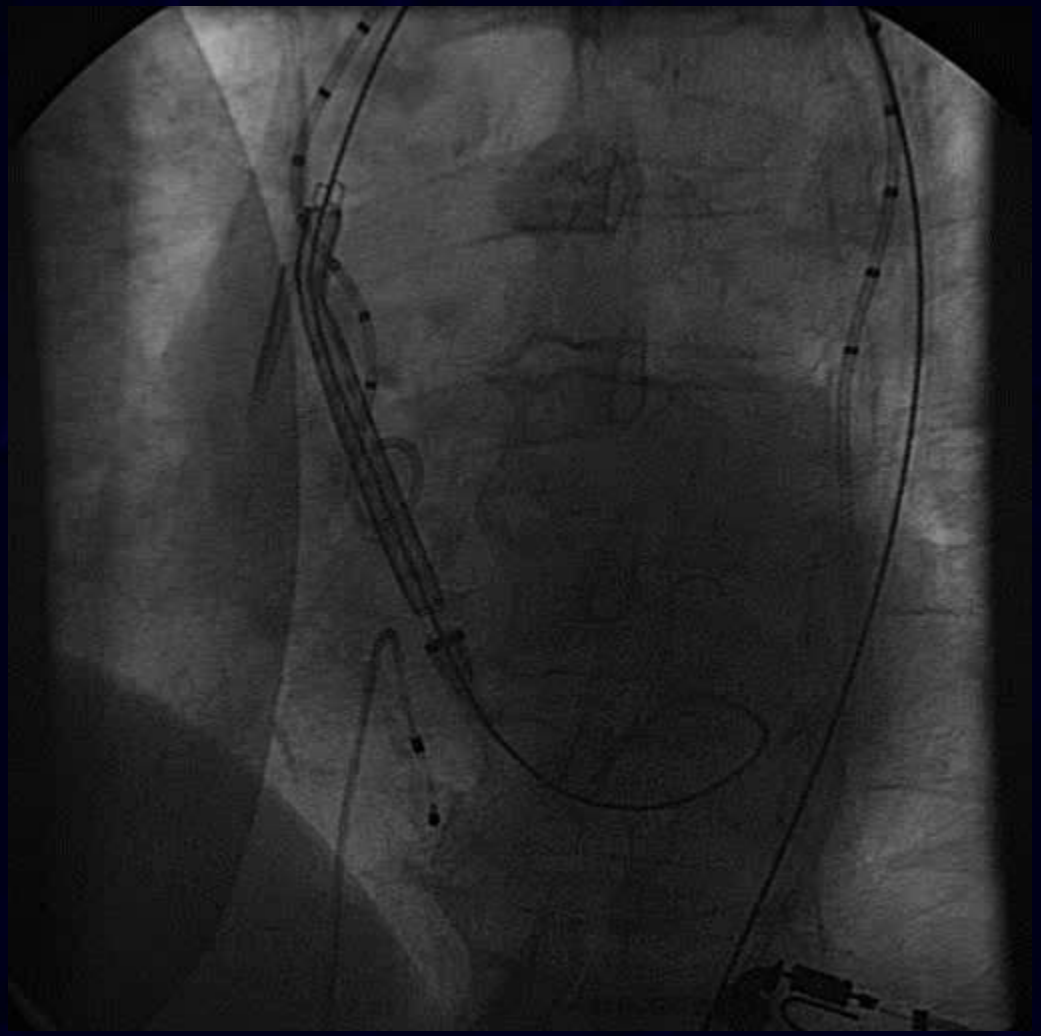
EMO GVM
CENTRO
CUORE COLUMBUS s.r.l.

Montagioli



EMO GVM
CENTRO
CUORE COLUMBUS s.r.l.

Montagioli



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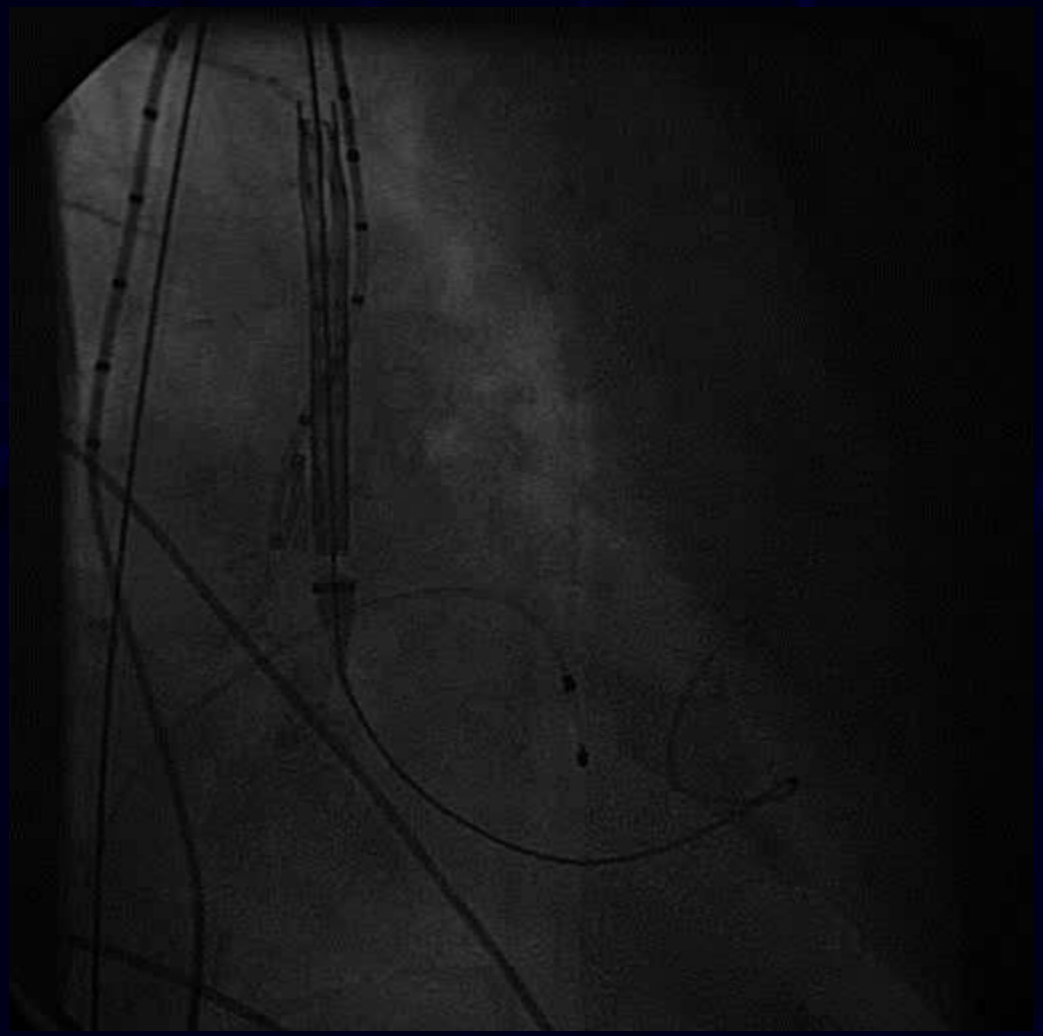

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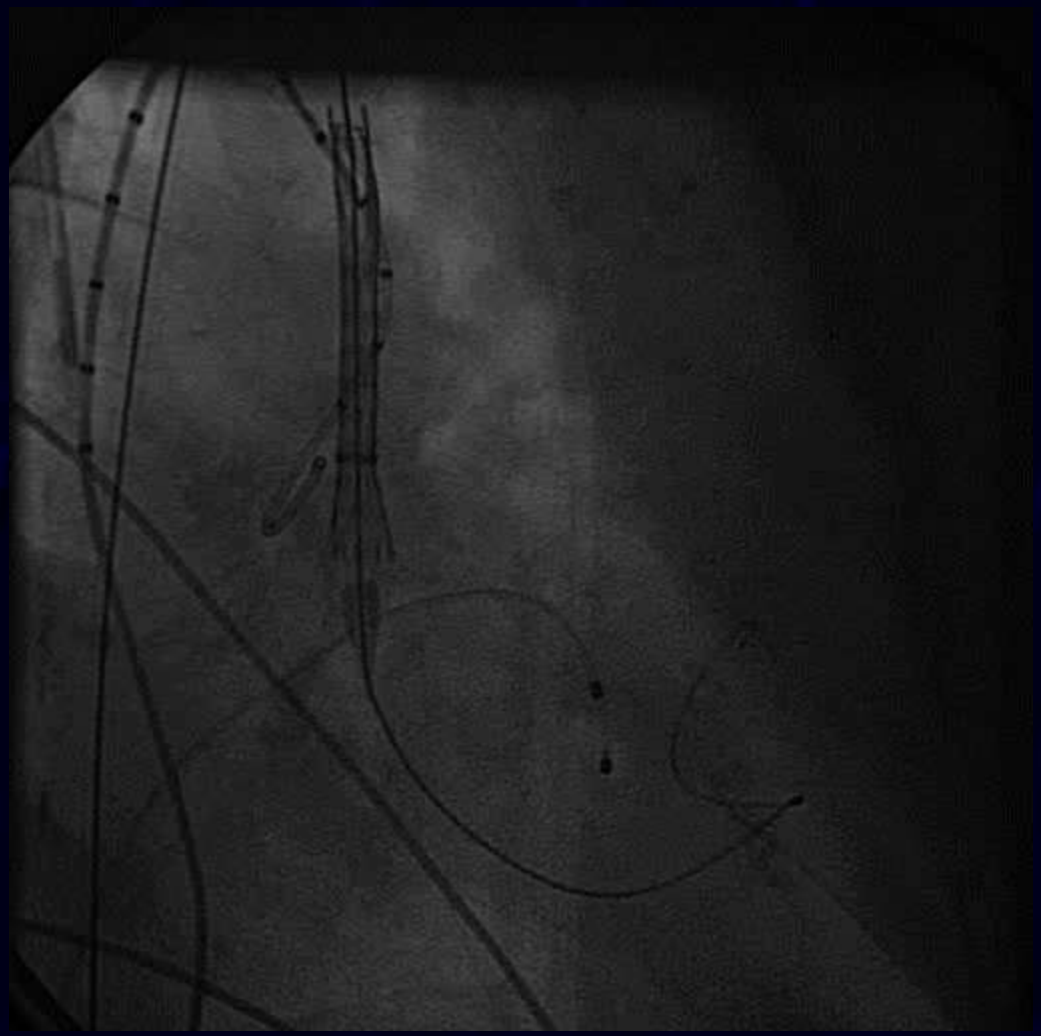

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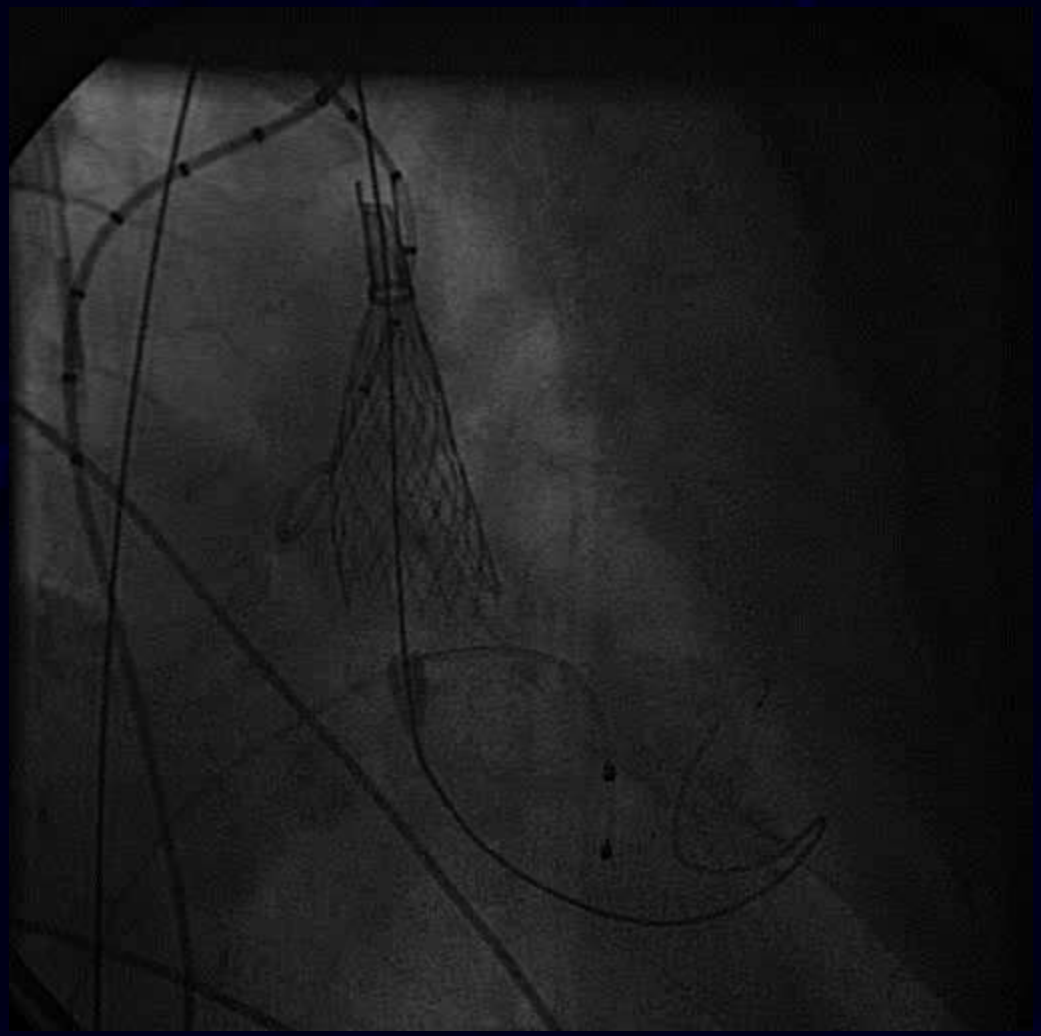

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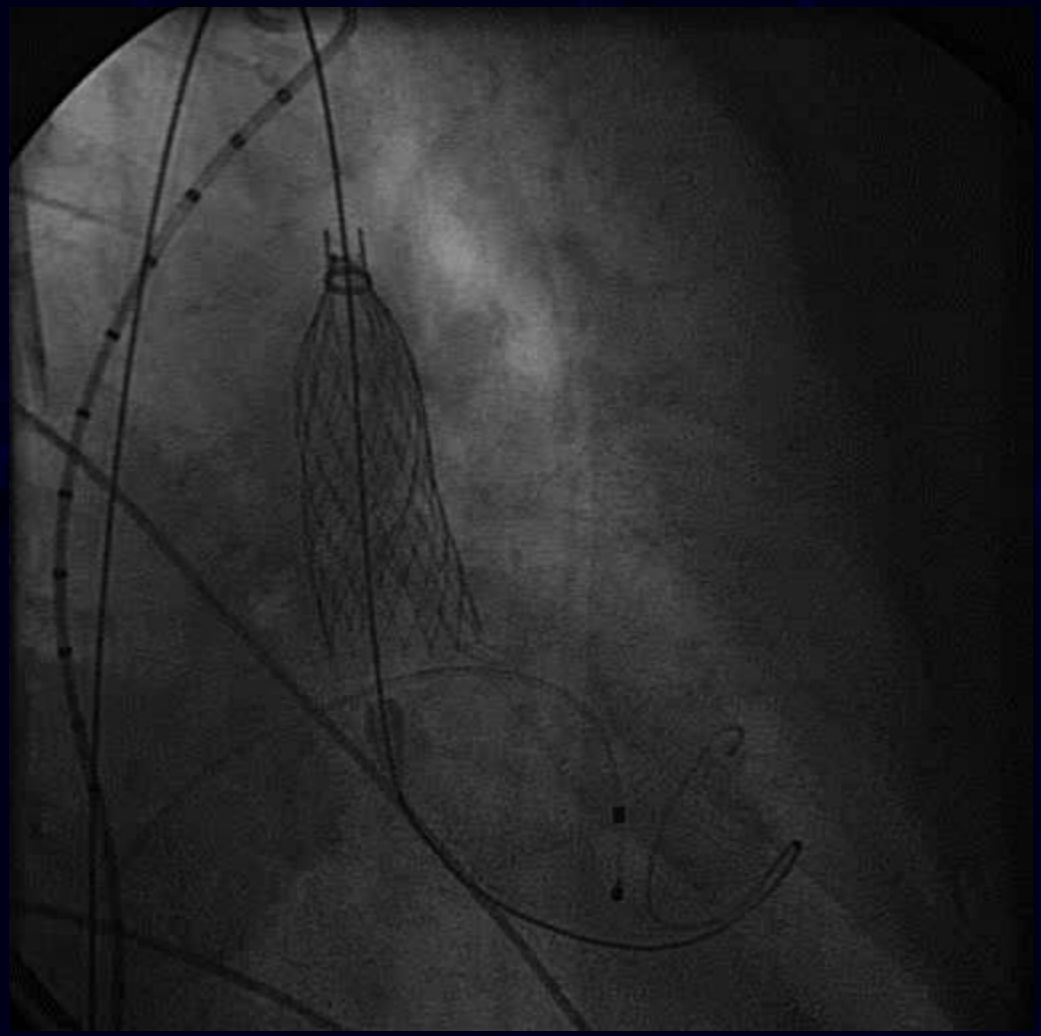

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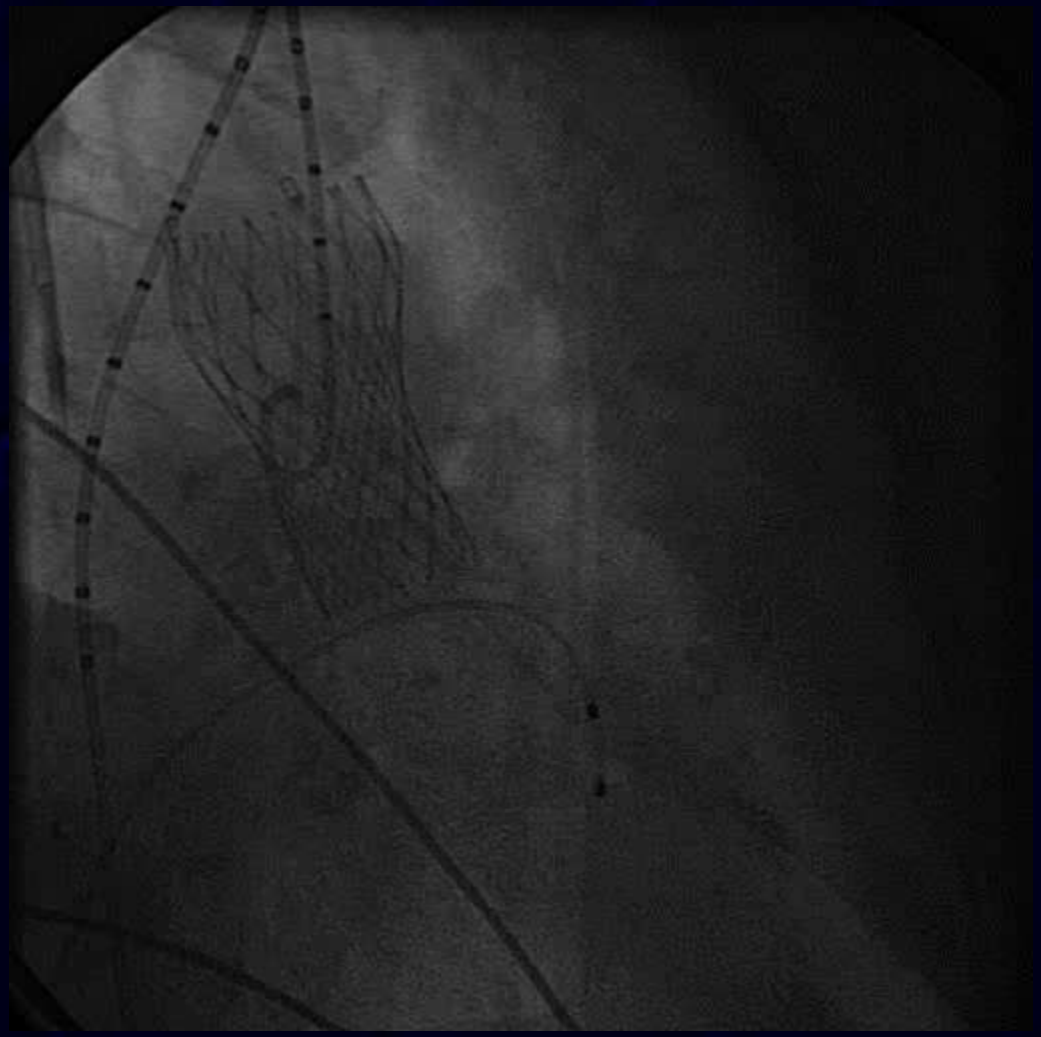
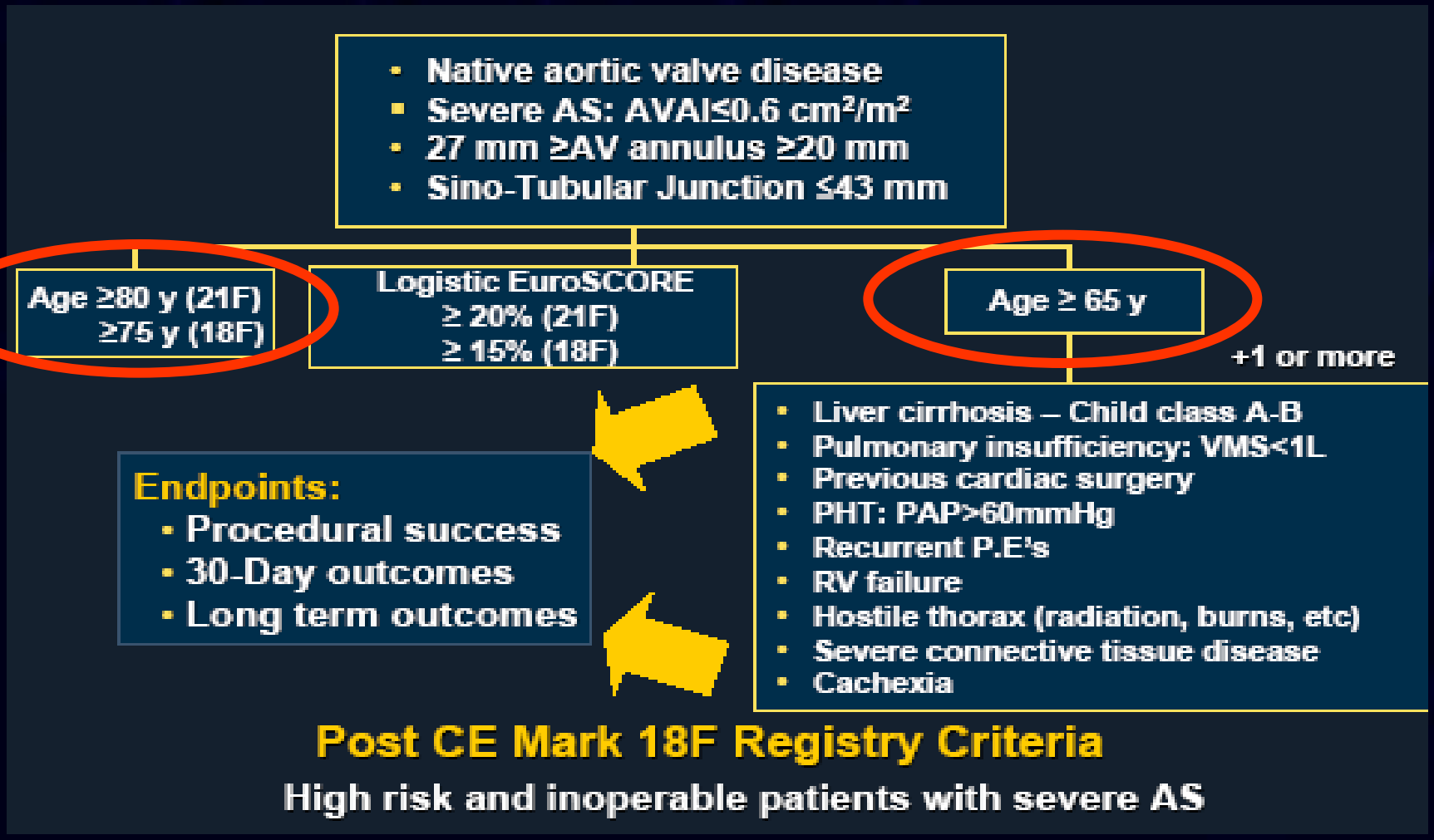


COREVALVE Revalving System

Inclusion Criteria



COREVALVE Revalving System

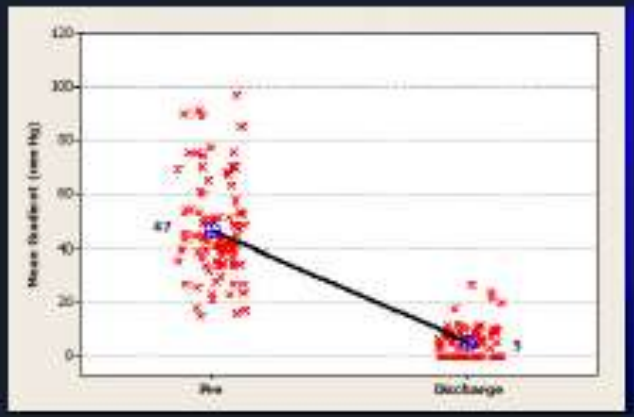
Procedural Results

18F Registry (N=536)	
Procedural Success	520 (97%)
Mean Procedure Time	128 ± 47 Min
Discharged alive & well with CoreValve	504 (94%)

Mean Gradient (mm Hg)

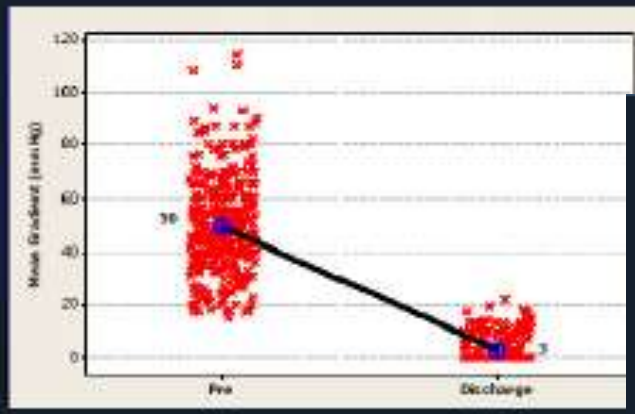
18F S&E (N=112)

Pre: 47.21 ± 17.98 [15-97]
Discharge: 5.07 ± 6.19 [0-27]

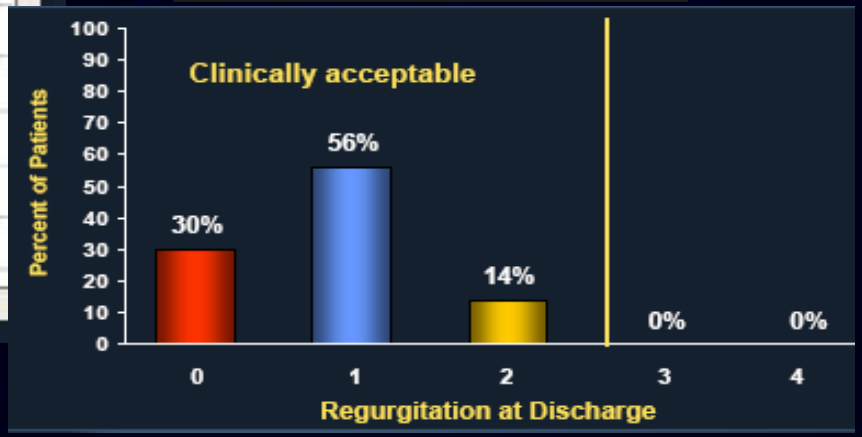


18F Registry (N=536)

Pre: 49.70 ± 17.63 [12-114]
Discharge: 2.71 ± 4.73 [0-27]



AR at Discharge
Post-CE Registry n=536



COREVALVE Revalving System

Procedural Results

	18F S&E (N=112)	18F Registry (N=536)
Procedural Failures	***10 (9%)***	***16 (3%)***
Inability to access vessel	0 (0%)	0 (0%)
Inability to navigate vasculature	0 (0%)	0 (0%)
Inability to cross native vessel	0 (0%)	0 (0%)
Malplacement	6 (5%)	2 (<1%)
Aortic Roof Perforation	1 (<1%)	2 (<1%)
Aortic Dissection	2 (2%)	3 (<1%)
Aortic Vessel Bleeding	4 (4%)	3 (<1%)
LV Perforation, guidewire	1 (<1%)	2 (<1%)
RV Perforation, temp 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

COREVALVE Revalving System

Procedural Results

Complications (0-30 Days)*	18F S&E (N=112)	18F Registry (N=536)
MI*	4 (4%)	4 (<1%)
Aortic Dissection*	3 (3%)	2 (<1%)
Coronary Impairment	2 (2%)	0 (0%)
Acute Vascular Complications	4 (4%)	7 (1%)
Stroke/TIA*	6 (5%)	10 (3%)
Pacemaker	28 (25%)**	48 (9%)
Re-op for valve failure	0 (0%)	8 (1%)

18% in the recent series from Rotterdam
(Piazza et al-JACC Intv 2008)

COREVALVE Revalving System

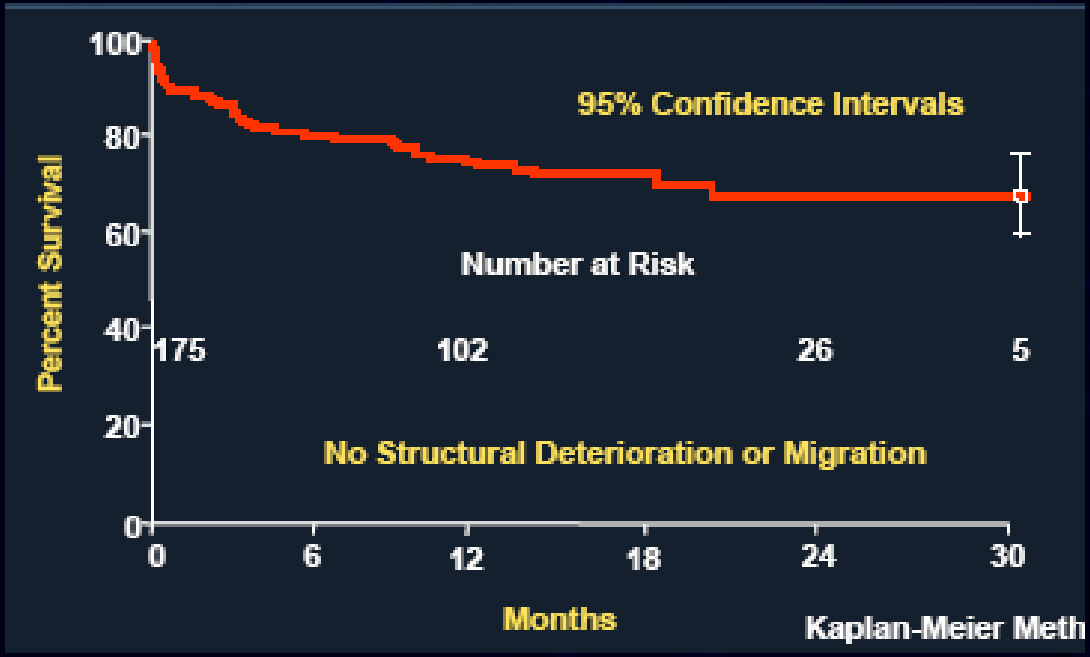
30-Day Outcome

	18F S&E (N=112)	18F Registry (N=536)
Logistic EuroSCORE (%)	24%	25%
All 30-Day Mortality:	15% (17)	8% (44)
Procedure related	11 (10%)	22 (4%)
Non-procedure /Non-valve related	6 (5%)	20 (<4%)
Unknown	0 (0%)	2 (<1%)

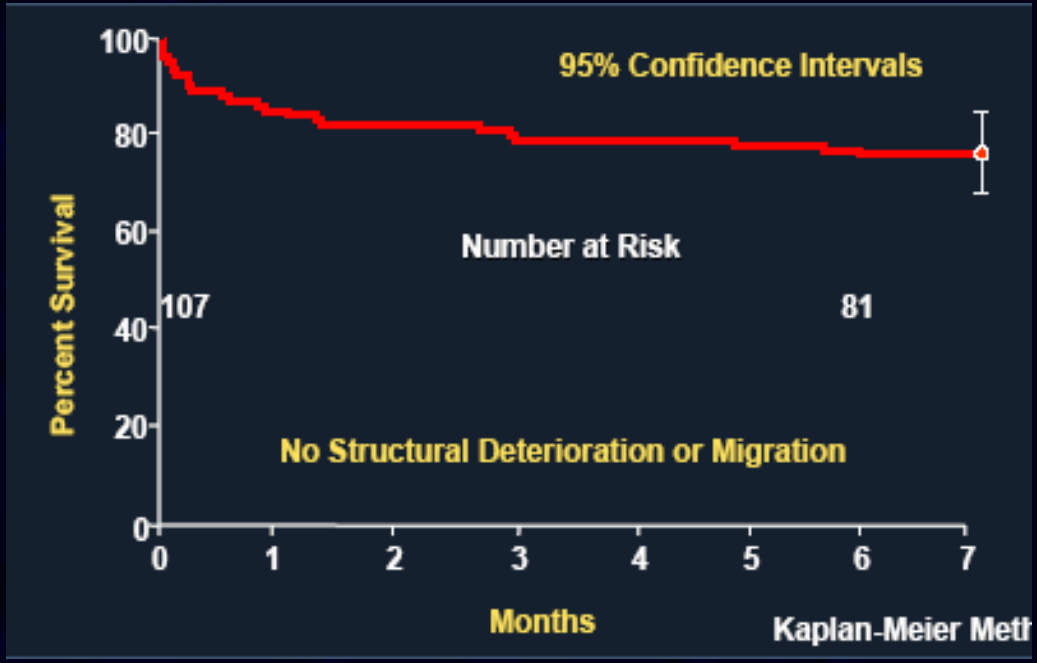
No valve dysfunction
No valve migration

COREVALVE Revalving System
Patient and Valve Follow-up

21F/18F S&E studies
n=175 (30 mths)



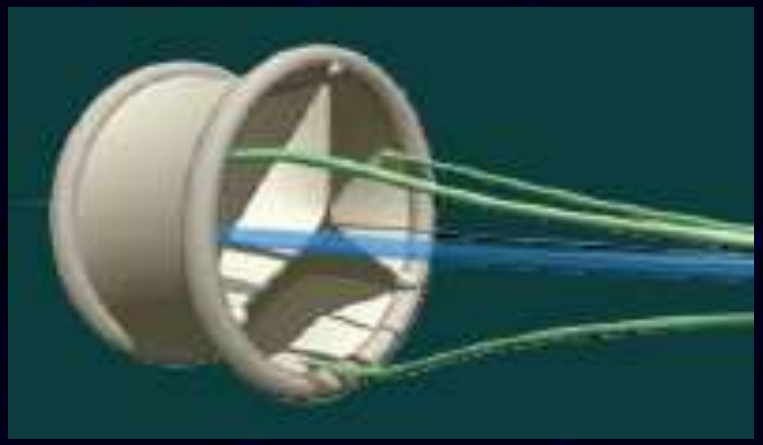
18F Registry
n=107 (7 mths)



Transcatheter Aortic Valve Implantation

Next generation devices

AorTx



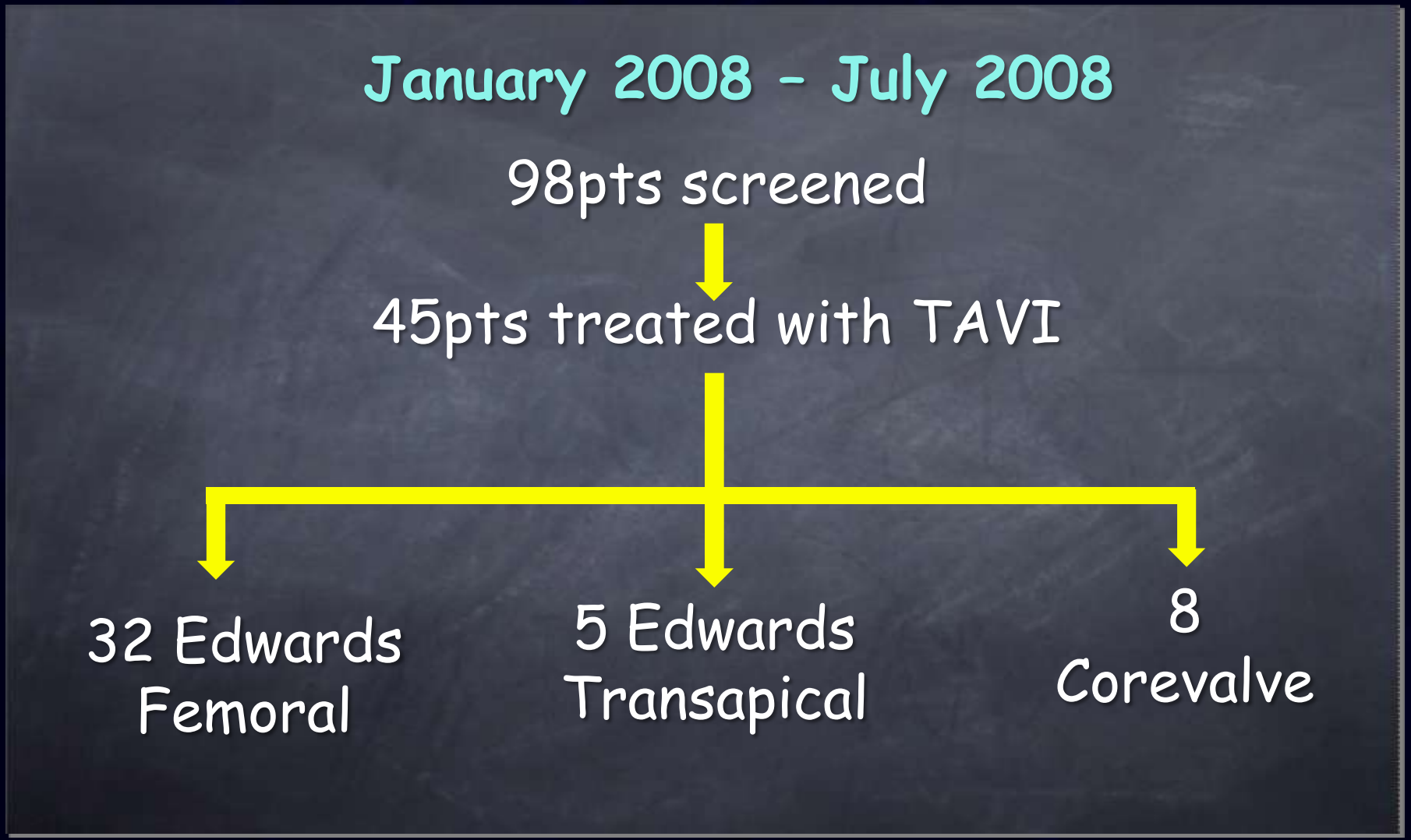
DirectFlow

Sadra

Lower profiles
Repositionable devices
Less paravalvular leaks

? To be confirmed

TAVI at HSR


January 2008 - July 2008
98pts screened
45pts treated with TAVI
32 Edwards Femoral
5 Edwards Transapical
8 Corevalve

TAVI at HSR

98 pts screened

↓

26 pts treated with TAVI

What happened to the other 72 pts?

40%	Medical Therapy
23%	Ao Valvuloplasty
14%	Surgical Ao Implant
14%	Waiting for transfemoral
9%	waiting transapical
→ 13%	Died at 4 months FU

TAVI at HSR

Procedure Outcome

Death	Procedure 0 30 days 2*
Iliac Rupture	3/45 (6%)
Transfusions	13/45 (28%)
CVA	1/45 (2%)
Permanent PM	2/45 (4%)
Prolonged Antibiotic therapy	8/45 (17%)

* 1 multiorgan failure at 58 days - 1 sudden death at 7 days

Conclusions I

- Initially complex, the procedures have become much simpler with fast technological improvements
- Hemodynamic results are good leading to dramatic patient's clinical improvement
- 30-day perivalvular complications are still an issue but decrease with improved screening and experience
- Long-term follow-up are encouraging but would need years (not months) for definitive conclusions
- No THV dysfunction reported so far, but Valve + Platform durability need to be demonstrated

Conclusions II

Ongoing pivotal PARTNER IDE study (Edwards PHV)
will provide the required evidence-based verification that THV implantation is at least comparable to surgery in this high-risk population