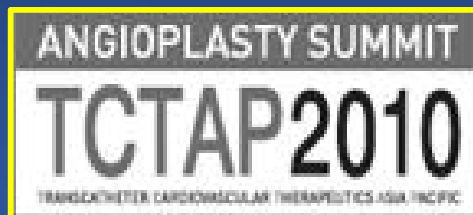


# Status Update and Clinical Impact of Transcatheter Aortic Valve Implantation (TAVI)

***Martin B. Leon, MD***

***Columbia University Medical Center  
Cardiovascular Research Foundation  
New York City***



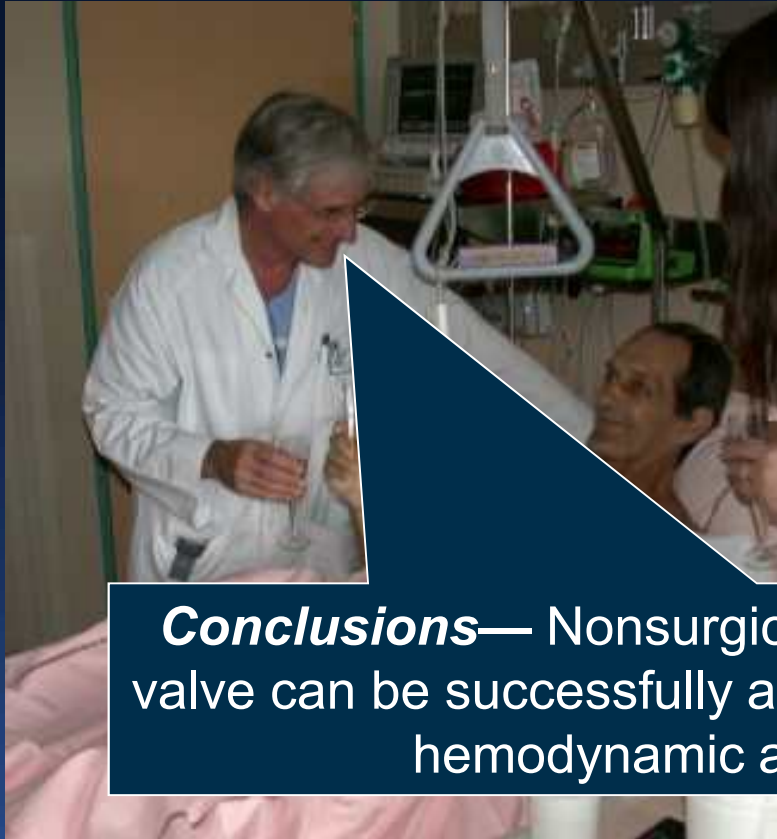
**Presenter Disclosure Information for  
TCTAP 2010; April 27-30, 2010**

***Martin B. Leon, M.D.***

***NON-PAID Consultant:***  
Edwards Lifesciences, Medtronic

# Dr. Alain Cribier

## *First-in-Man PIONEER*



### **Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis**

#### **First Human Case Description**

Alain Cribier, MD; Helene Eltchaninoff, MD; Assaf Bash, PhD; Nicolas Borenstein, MD; Christophe Tron, MD; Fabrice Bauer, MD; Genevieve Derumeaux, MD; Frederic Anselme, MD; François Laborde, MD; Martin B. Leon, MD

**Conclusions**— Nonsurgical implantation of a prosthetic heart valve can be successfully achieved with immediate and midterm hemodynamic and clinical improvement.

**April 16, 2002**

**THV development**  
A long road:  
20 Years  
from concept  
to real world

**CE mark  
commercialization**

**2007**

2005-07

International TF and TA  
Feasibility Studies

2004

Edwards Lifesciences  
Technological improvements

2002-03

**2002**

**April, 2010 – >15,000  
implanted worldwide**

**Animal implantation (sheep)**

1999

« Percutaneous Valve Technology » (prototypes)

1994

Post-mortem studies of intra-valvular stenting  
Sketches of stented valve

1987

Concept of « stented valve », to rule out post-BAV valvular restenosis

**1985**

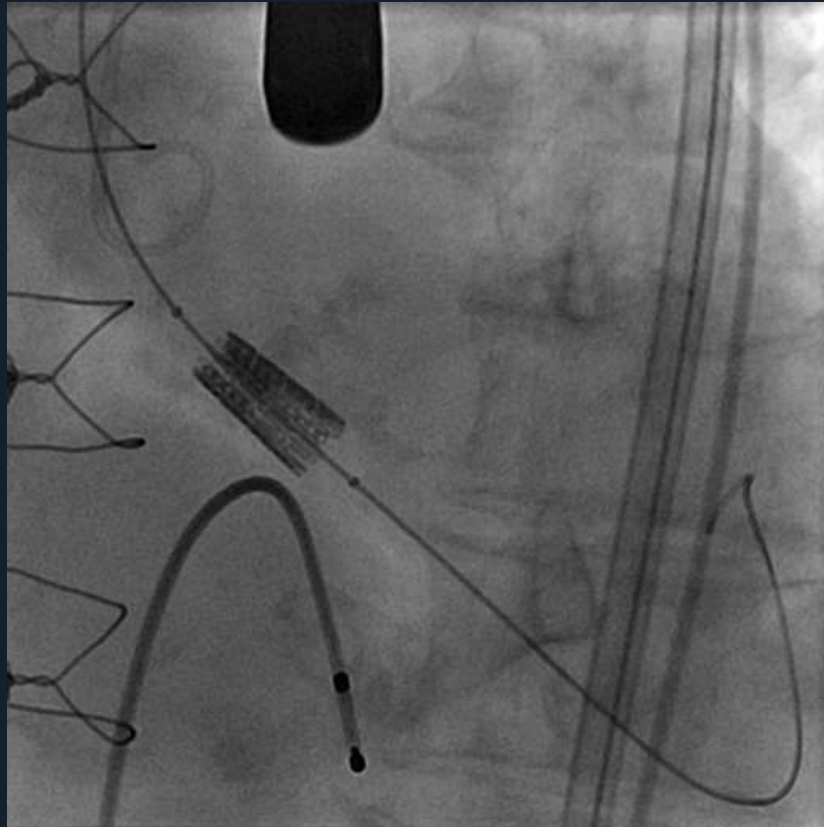
**F.I.M. Balloon Aortic Valvuloplasty**

# TAVI in 2010

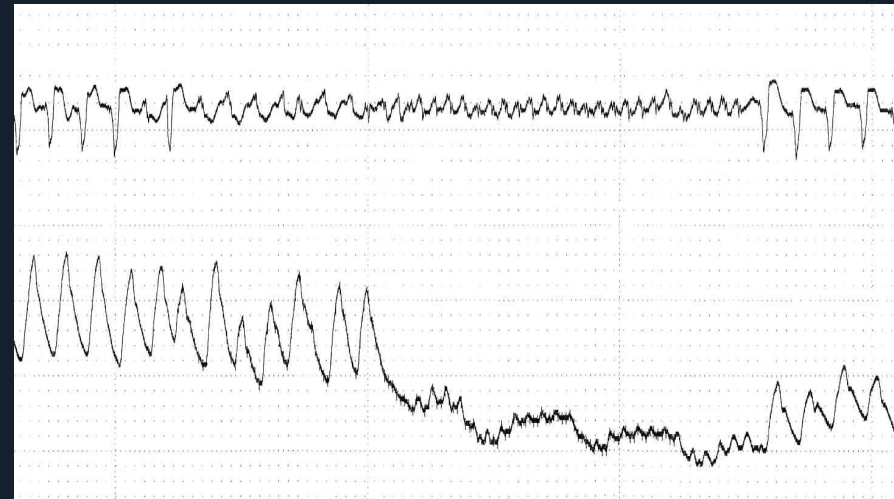
## ***Exciting, “Breakthrough” Technology...Why?***

- ***It's FUN!!!***
  - requires advanced skills, discipline, persistence, and creativity
- ***It's a multi-disciplinary playground***
  - finally a “unifying” procedure which embraces surgical involvement
- ***It's incredibly fulfilling***
  - patient benefits are dramatic
- ***It's an opportunity to transform a therapy for a common disease and redefine patient care!***

# Retrograde Trans-femoral Edwards Aortic Valve Deployment



*Rapid pacing : 220/min*



# TAVI in 2010

## *Lessons Learned...*

**1. *The “high risk” severe AS patients are “under-treated” and are excellent candidates for TAVI procedures***

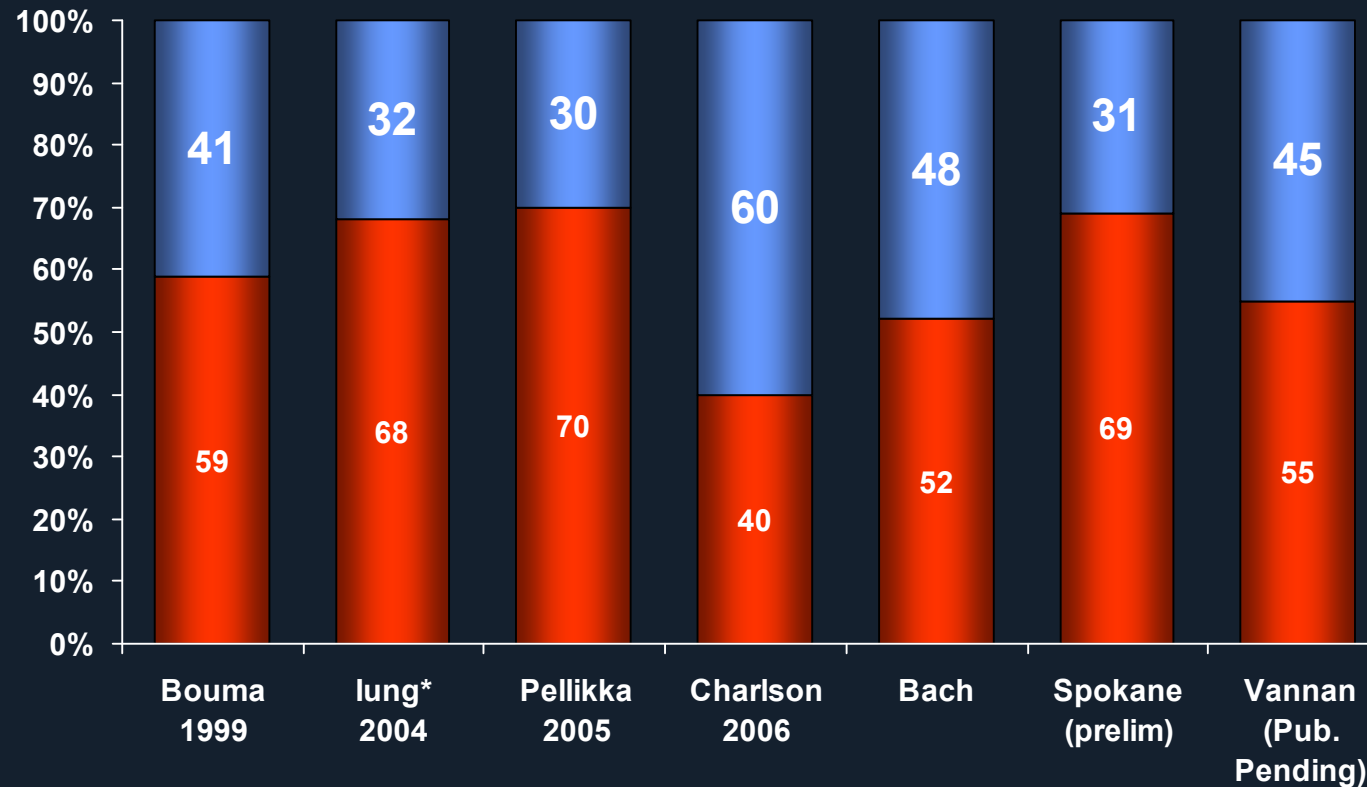
- **Patient screening and case selection for TAVI is demanding and is critical to achieve optimal outcomes**

# At Least 30% of Patients with Severe Symptomatic AS are “Untreated”!

## Severe Symptomatic Aortic Stenosis

Percent of Cardiology Patients Treated

AVR  
No AVR



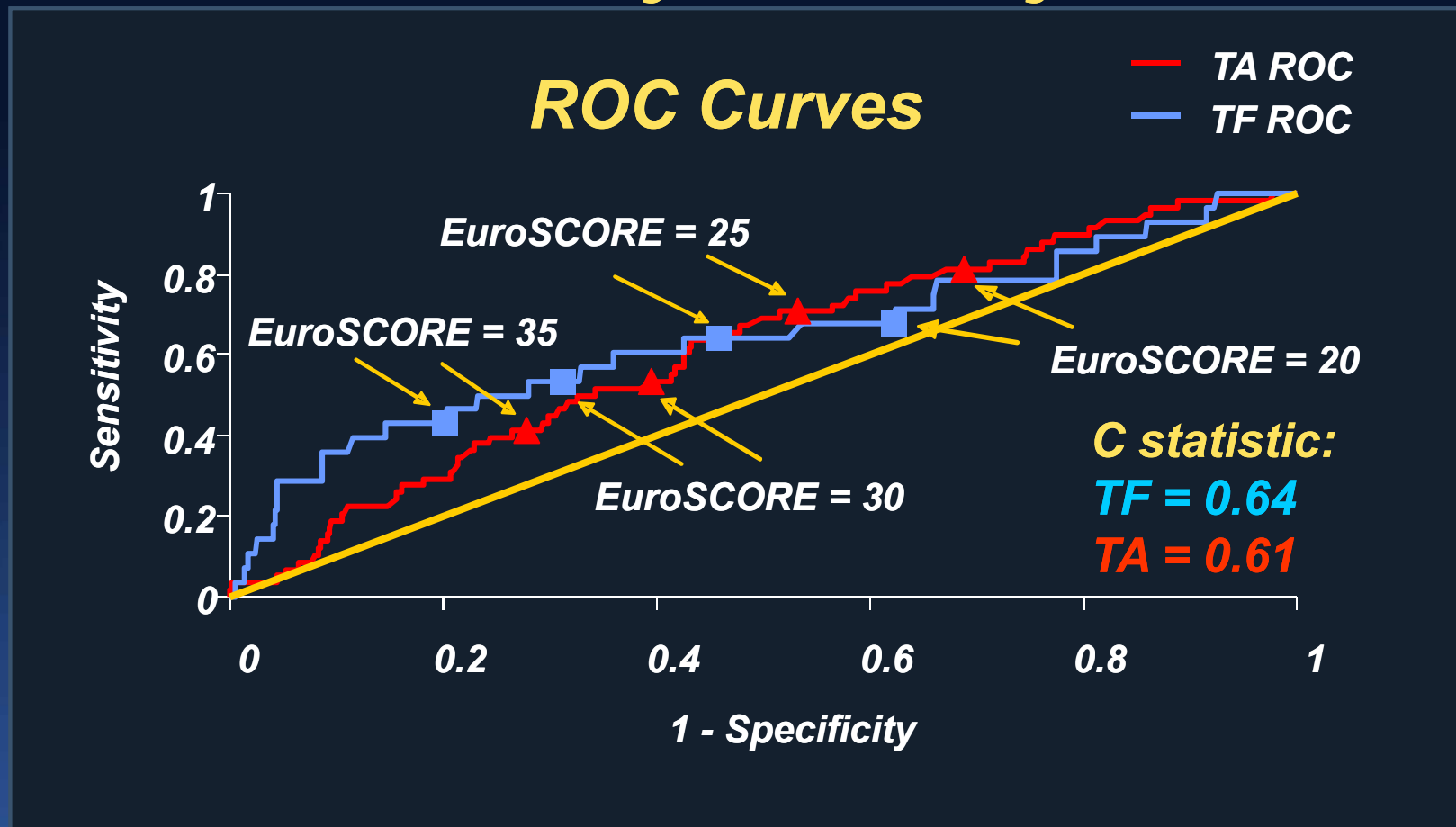
*Under-treatment especially prevalent among patients managed by Primary Care physicians*

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. lung 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 Dis* 2006;15:312-321



# SOURCE Registry

## *EuroSCORE as a Predictor of 30-day Mortality*



# TAVR Patient Selection

## *Includes Careful Frailty Assessment*

*Patient A*



vs.

*Patient B*



***Same age and predicted risk***  
***One passes the “eyeball test” – one does not***

***Frailty is being studied systematically as part of  
the PARTNER U.S. IDE study***

# TAVI in 2010

## *Lessons Learned...*

### ***2. Multiple technology platforms have achieved excellent prosthetic valve hemodynamic results***

- **Both acute and mid-term valve performance has surpassed expectations**
- **Equivalent to surgical valve implants**

# TAVI Technologies

## *Current Generation Devices*



Edwards Lifesciences



Medtronic CoreValve

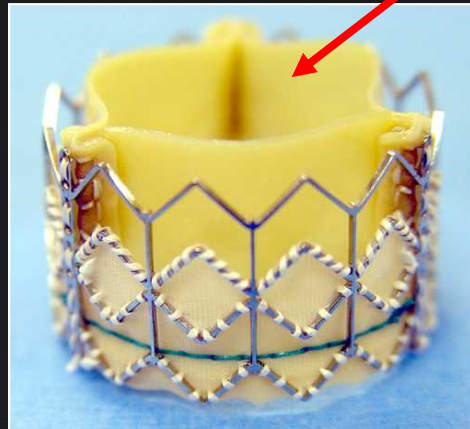
# TAVI Technologies

## *Current Generation Devices*

- **Edwards Aortic Bioprosthesis**
  - Balloon expandable stainless steel bioprosthesis
  - Equine → Bovine pericardial valve
  - Sheathed (RetroFlex) with tip deflection
  - Antegrade, retrograde, or trans-apical approach
- **CoreValve Revalving™ System**
  - Self-expanding nitinol cage bioprosthesis
  - Porcine pericardial valve
  - Sheathed system (low profile = 18 Fr)
  - Retrograde (femoral + subclavian) approach

# The Current Generation

## *Edwards – SAPIEN THV*

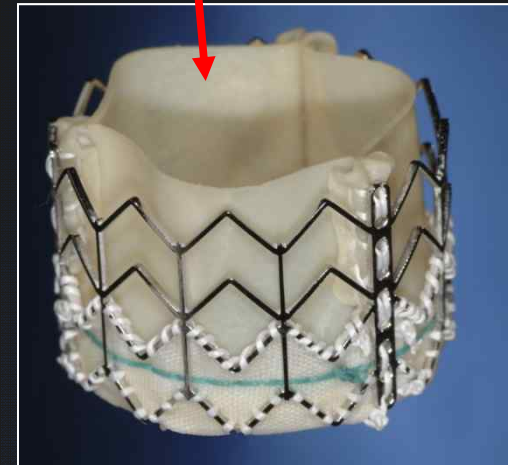


Bovine Tissue  
ThermaFix Treatment  
Pericardial Mapping  
Leaflet Deflection  
Proprietary Processing

New  
Skirt Height

Edwards-SAPIEN THV

Untreated Equine  
Tissue



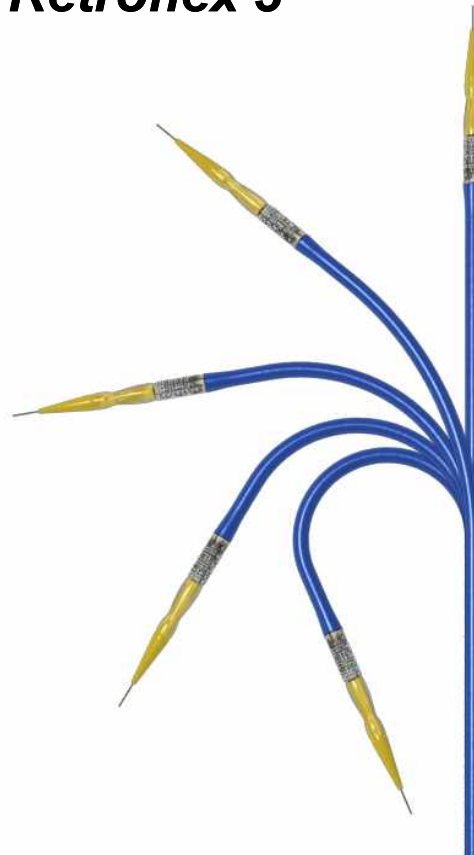
Current  
Skirt Height

Cribier-Edwards THV

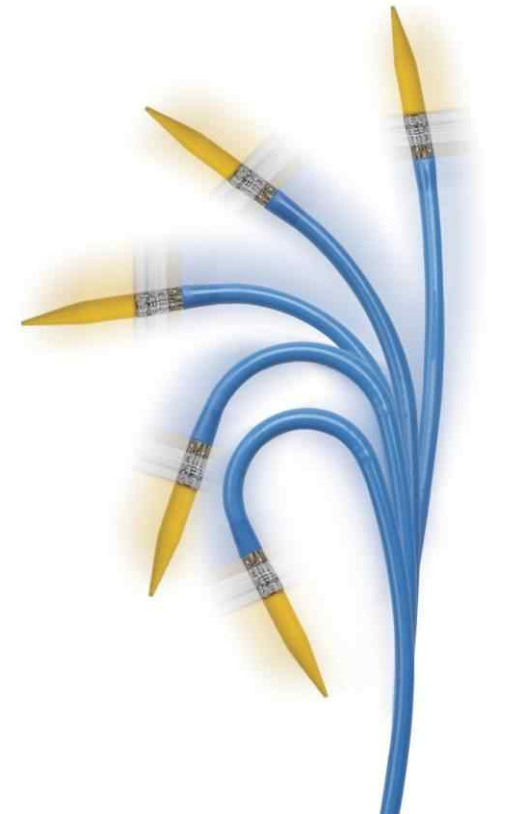
# Edwards *Flex Cath* Delivery System Evolution



***Retroflex 3***



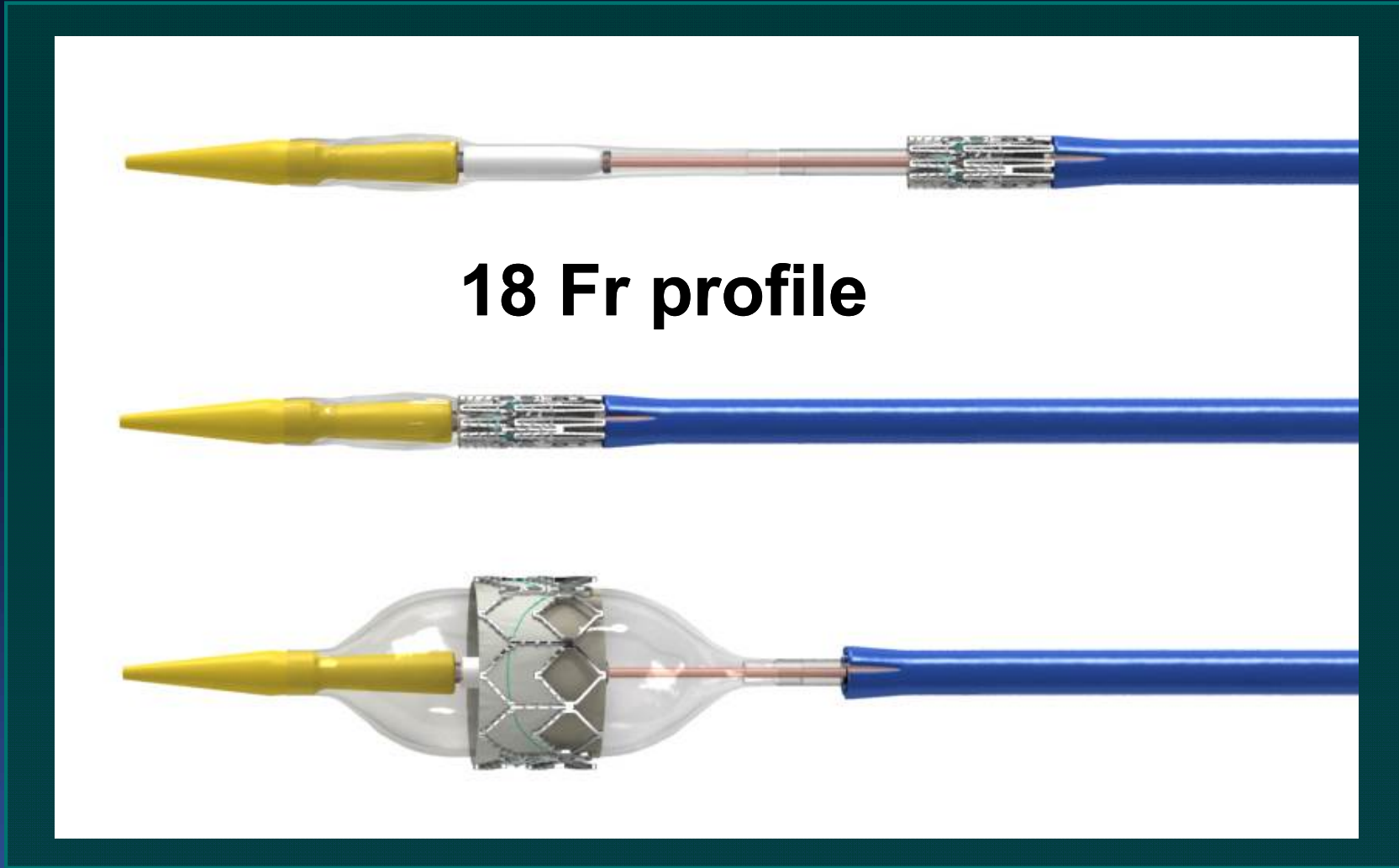
***Retroflex 2***





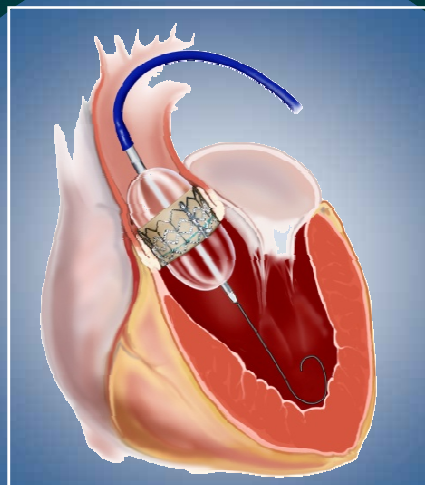
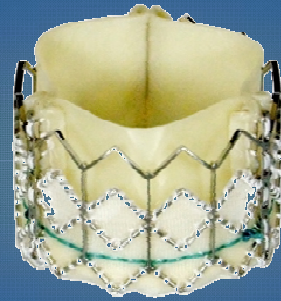


# Sapien XT + NovaFlex Delivery System

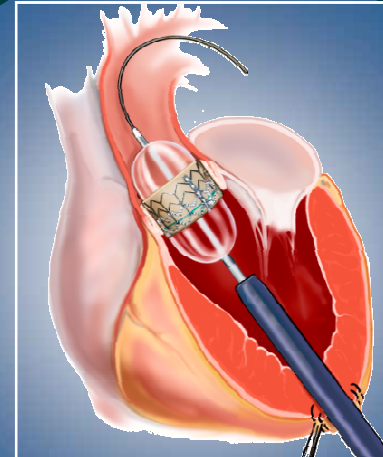


# Transcatheter AVI

## *Transapical Access Route*



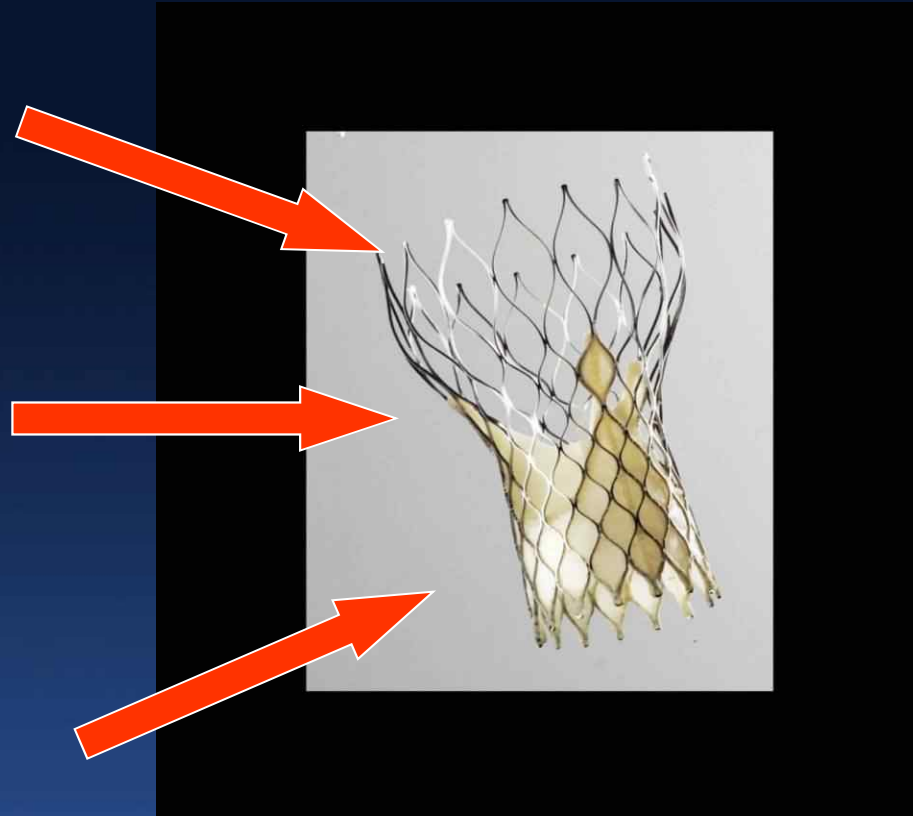
Transfemoral



Transapical

# CoreValve Self-Expanding Bioprosthesis

- **HIGHER PART:** low radial force area axes the system and increases quality of anchoring
- **MIDDLE PART:** functional valve area with three leaflets and constrained to avoid coronaries (convexo-concave) – avoids need for rotational positioning
- **LOWER PART:** high radial force of the frame pushes aside the native calcified leaflets for secure anchoring and avoids recoil and para-valvular leaks



A porcine pericardial tissue valve fixed to the frame with PTFE sutures

# CoreValve **ReValving** System *Delivery Catheter Evolution*

**GEN1**  
**8mm**



**GEN2**  
**7mm**



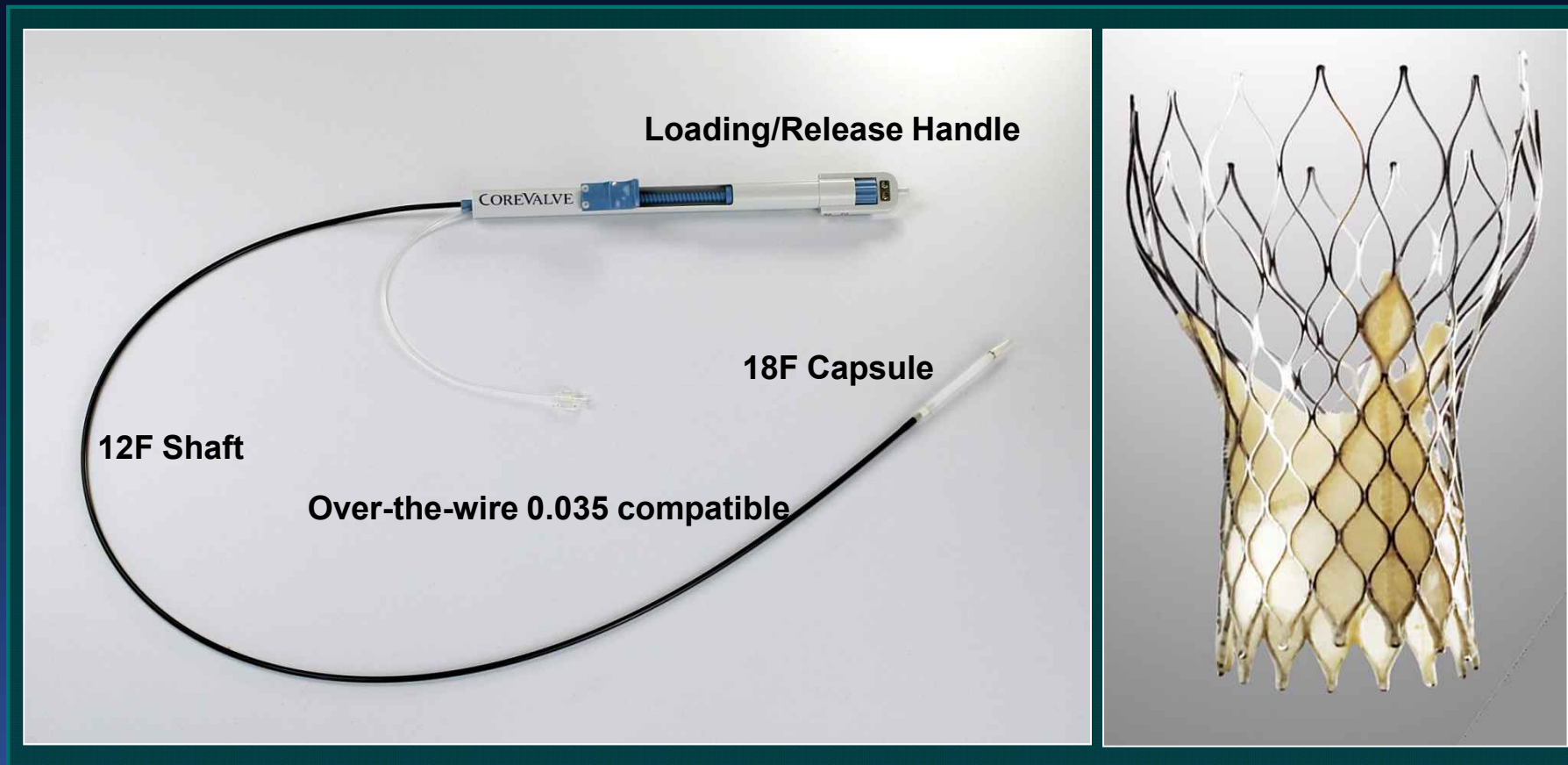
**GEN3**  
**6mm**  
**(18 Fr)**



**12 Fr shaft**

# CoreValve ReValving™ System

## 18 Fr Delivery System





## **CoreValve 2005**

- 24 F 1st Gen CoreValve
- Surgical access and closure
- Cardiopulmonary bypass
- General anesthesia



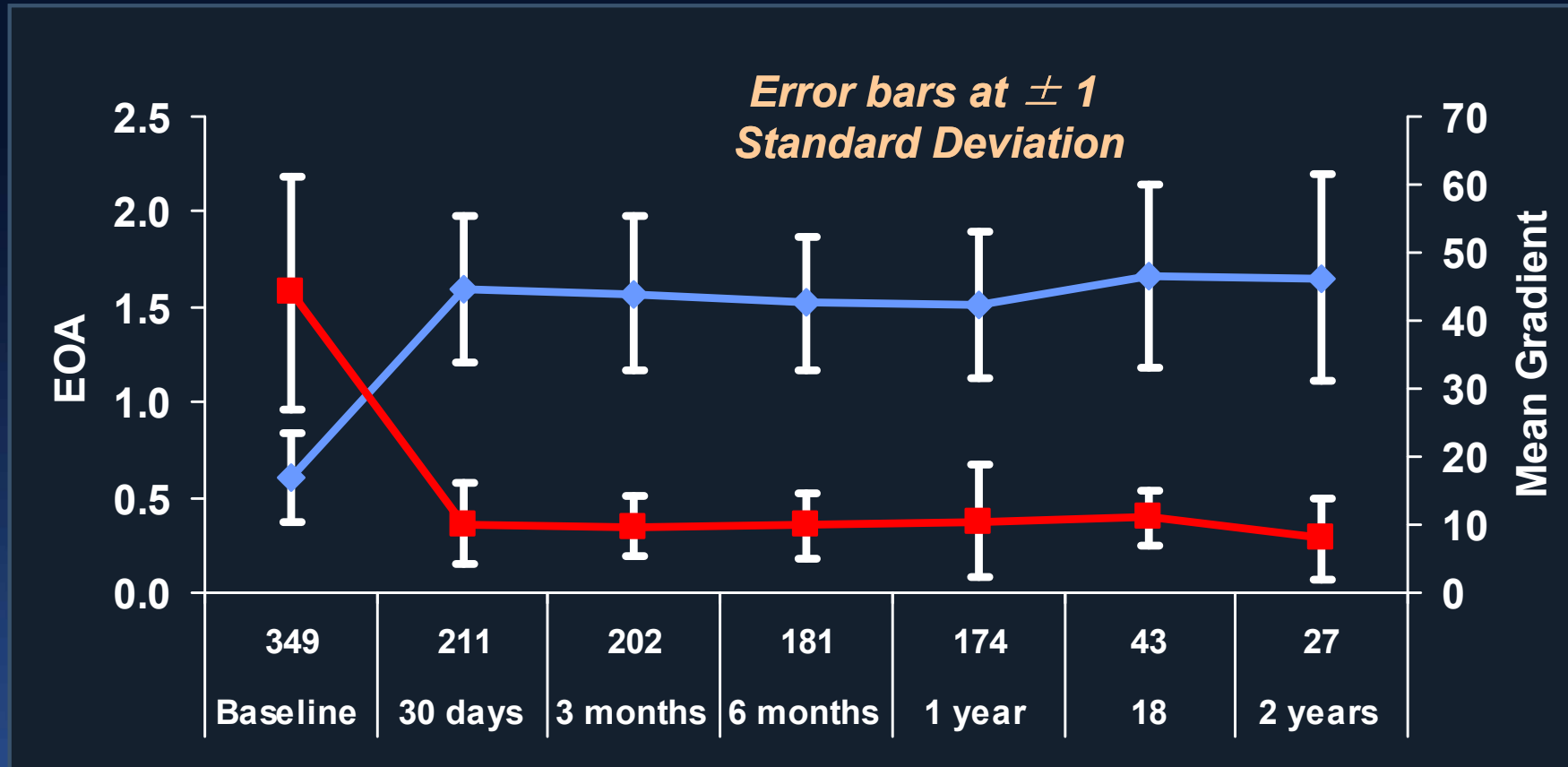
## **CoreValve 2010**

- 18 F 3rd Gen CoreValve
- Percutaneous access and closure
- No hemodynamic support
- Conscious sedation

**PCI – like Procedure!**

# POOLED\* Monitored Edwards TAVI

## Mean Gradients and EOA (Echo)



*\* REVIVE, REVIVAL, TRAVERCE  
and PARTNER EU*

# TAVI in 2010

## *Lessons Learned...*

### ***3. Multiple technology platforms have also achieved acceptable early and mid-term clinical outcomes***

- **Clinical outcomes are improving, perhaps due to better patient selection, device and procedure enhancements, and “learning curve” issues**
- **Clinical benefit is remarkable, sustained, and very fulfilling!**
- **Clinical trial processes require standardization and increased rigor**



# TAVI in 2010

## ***Clinical Data Conundrum...***

- Early clinical trials chaotic, reflecting frequent changes in technology, procedural methods, and data collection processes (small sample sizes and difficult to pool or compare datasets)
- Study endpoints not clarified or standardized (e.g. vascular complications, para-valvular AR)
- Inconsistent use of data coordinating centers, core labs and CECs
- Poor long-term follow-up of essential valve-related endpoints (e.g. FU echoes)
- ***All problems exaggerated due to complexity and acuity of patient population!***

# What is “VARC”?



- “VARC” is the *Valve Academic Research Consortium*, an attempt to harness positive ARC methodologies, but customize the process to the special needs of valvular heart disease therapies
- *GOAL: arrive at consensus on (1) essential endpoints and their definitions and (2) clinical trial methodology.*
- AROs = Cardialysis, CRF, HCRI and DCRI and the Societies represented = AATS, ACC, AHA, EACTS, ESC, SCAI, and STS
- First meeting in SF at TCT on September 19<sup>th</sup> 2009; second meeting in Amsterdam on December 5-6, 2009; manuscript in preparation

# Edwards TAVI Clinical Data Sources

## Edwards

## Other Studies

Transseptal Experience  
(RECAST, I-REVIVE; 36 pts)

**FIRST-in-MAN**

VANCOUVER single center  
(TF=164 pts, TA=86 pts)

REVIVE (OUS, TF)  
TRAVERCE (OUS, TF)  
REVIVAL (US, TF)

**OVERALL TOTAL  
3726 PTS**

US single center  
(TF=11 pts, TA=24 pts)

PARTNER EU (OUS, TF/TA 130 pts)  
SOURCE (OUS, TF/TA, 1123 pts)

**POST  
CE-APPROVAL**

CANADA multi-center (6)  
(TF=167 pts, TA=172 pts)

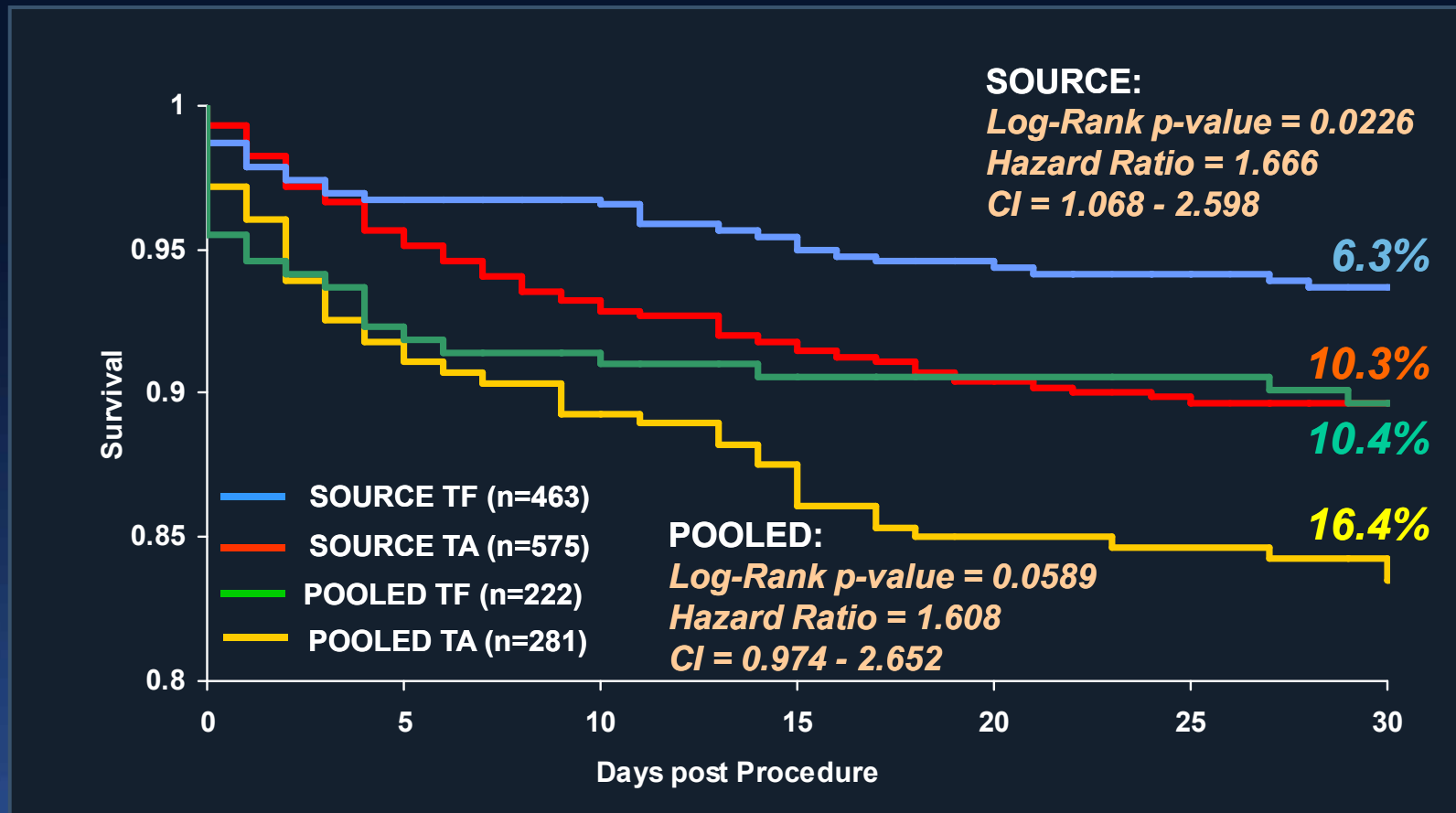
**TOTAL = 664 PTS**

PARTNER FDA  
(US/OUS, TF/TA ~1400 pts)

**PIVOTAL RCT**

**TOTAL = 3062 PTS**

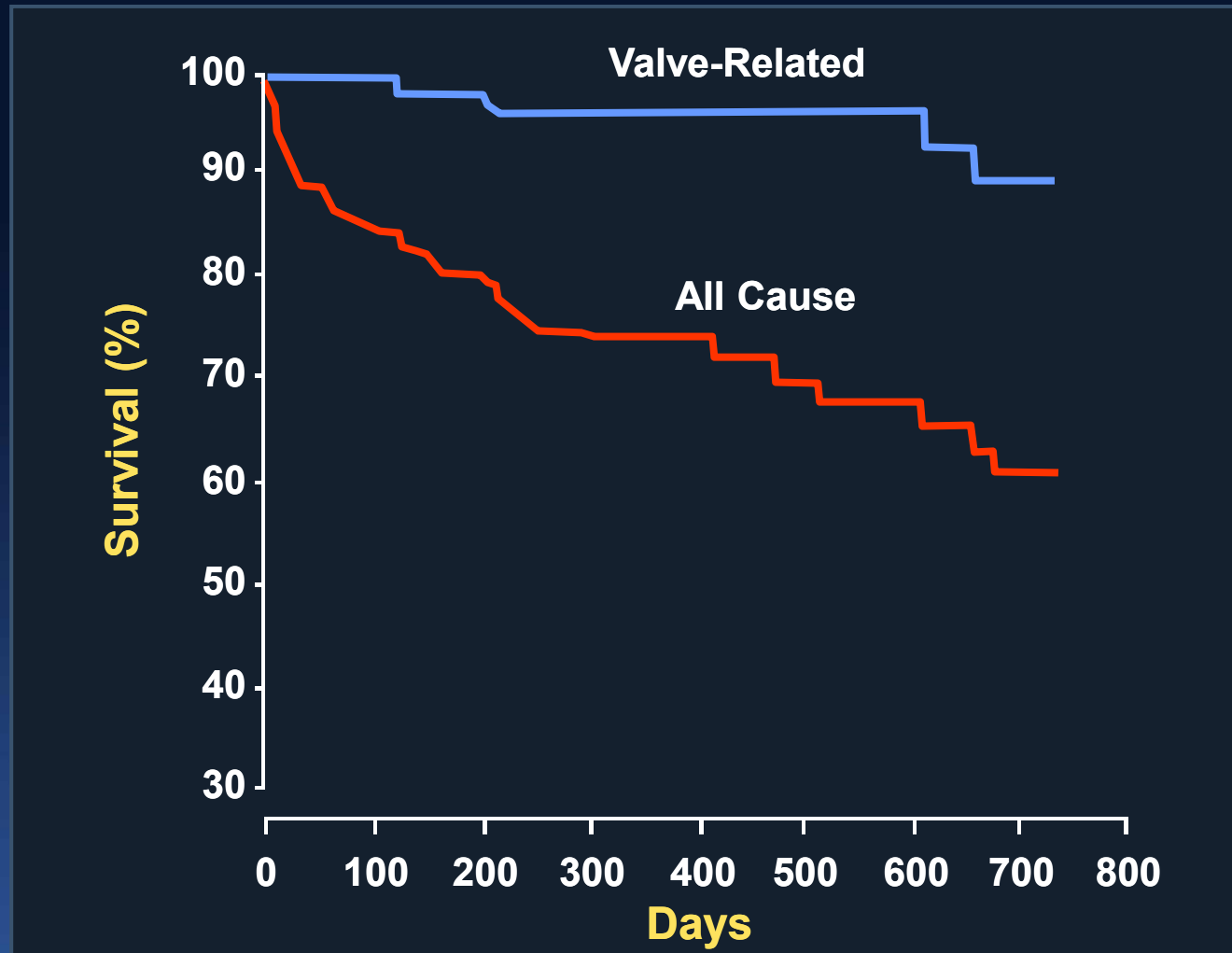
# POOLED\* Monitored Edwards TAVI 30-Day Mortality (vs. SOURCE)



\* **REVIVE, REVIVAL, TRAVERCE  
and PARTNER EU**

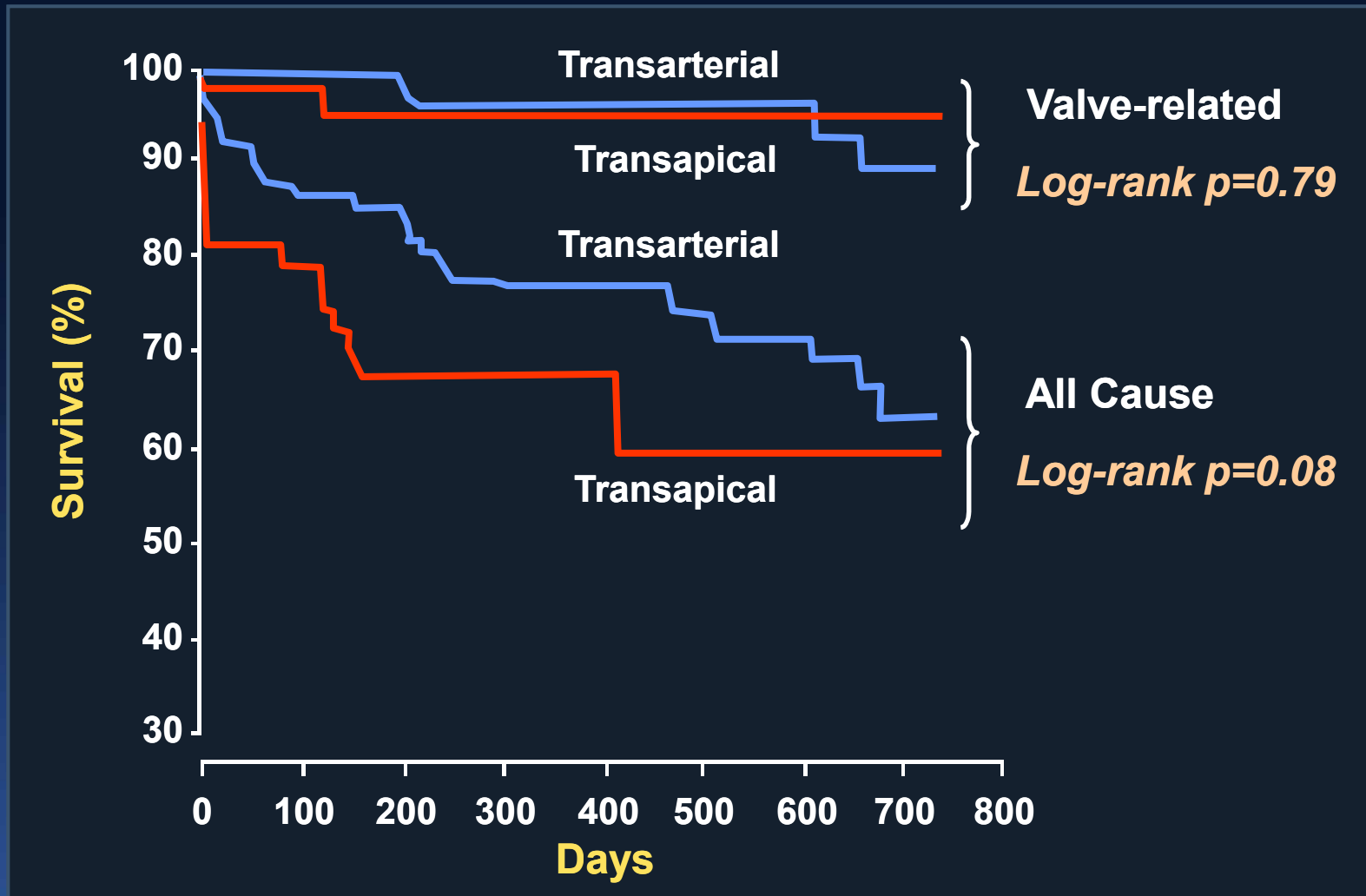
# Vancouver TAVI Experience

## *Survival at 1 Year*



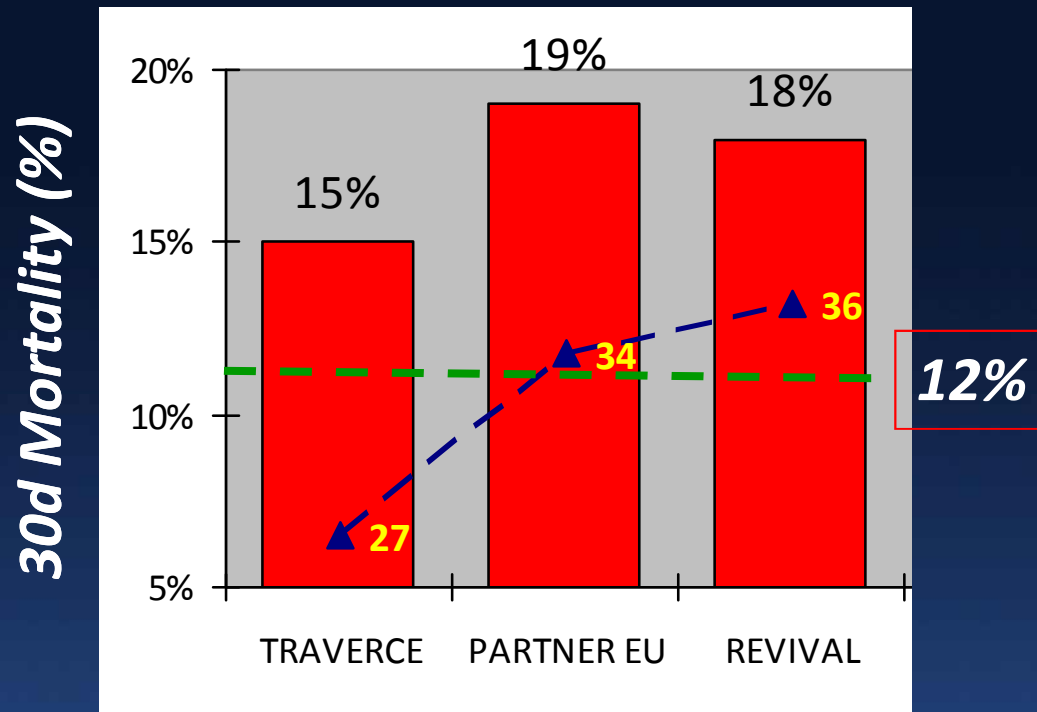
# Vancouver TAVI Experience

## Survival at 1 Year



# TAVI in Evolution

## *Trans-apical*

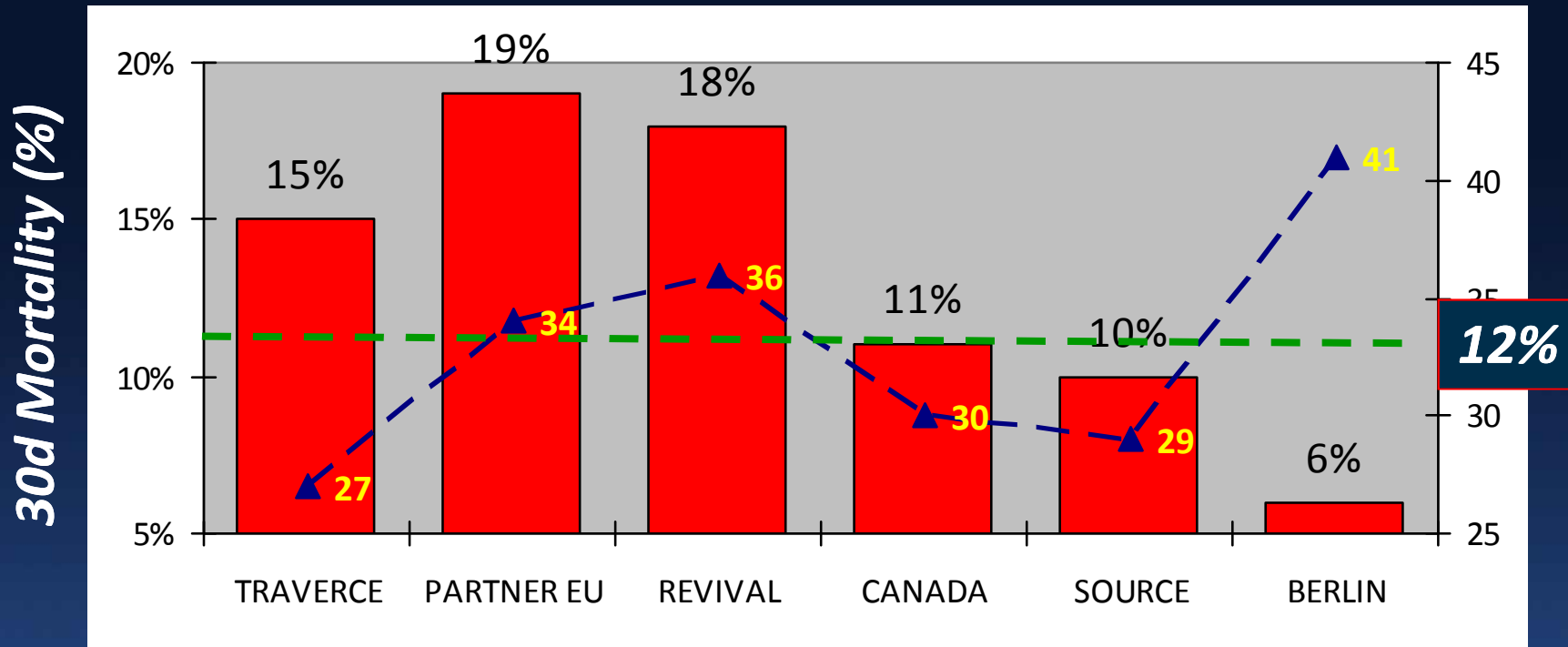


*Clinical Trials*

*Improved short-term outcomes!*

# TAVI in 2010

## *Trans-apical*



*Clinical Trials*

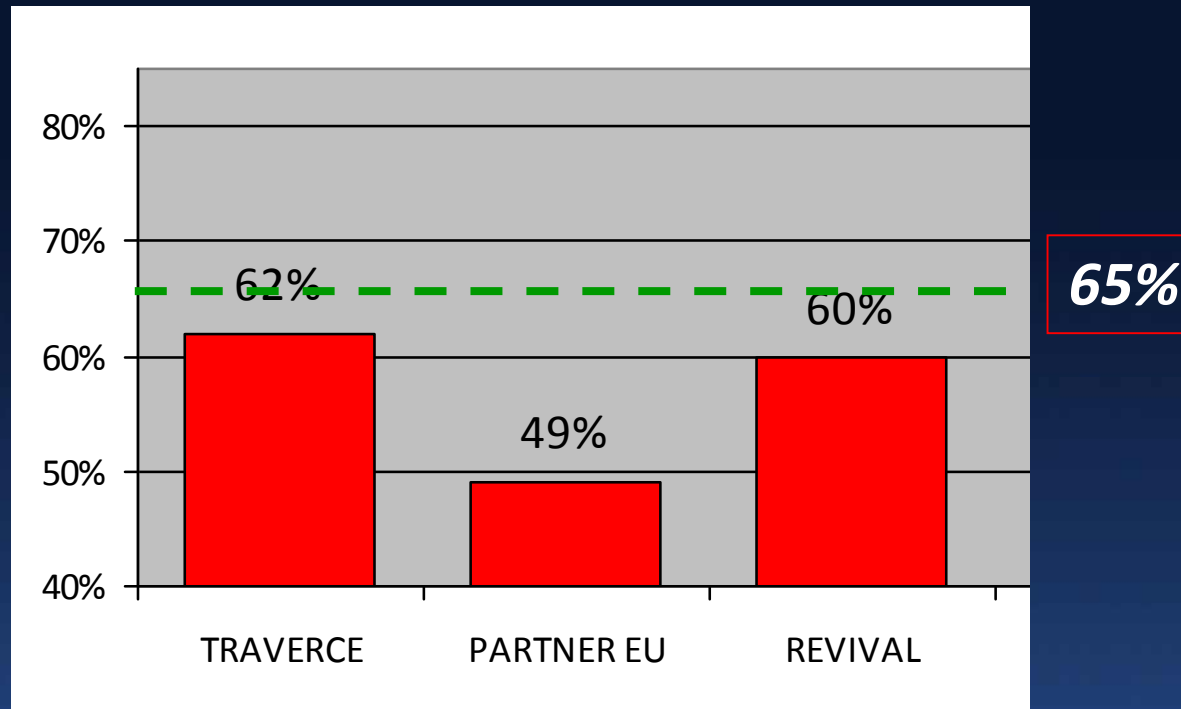
*Improved short-term outcomes!*



# TAVI in 2010

## *Trans-apical*

1-year survival (%)



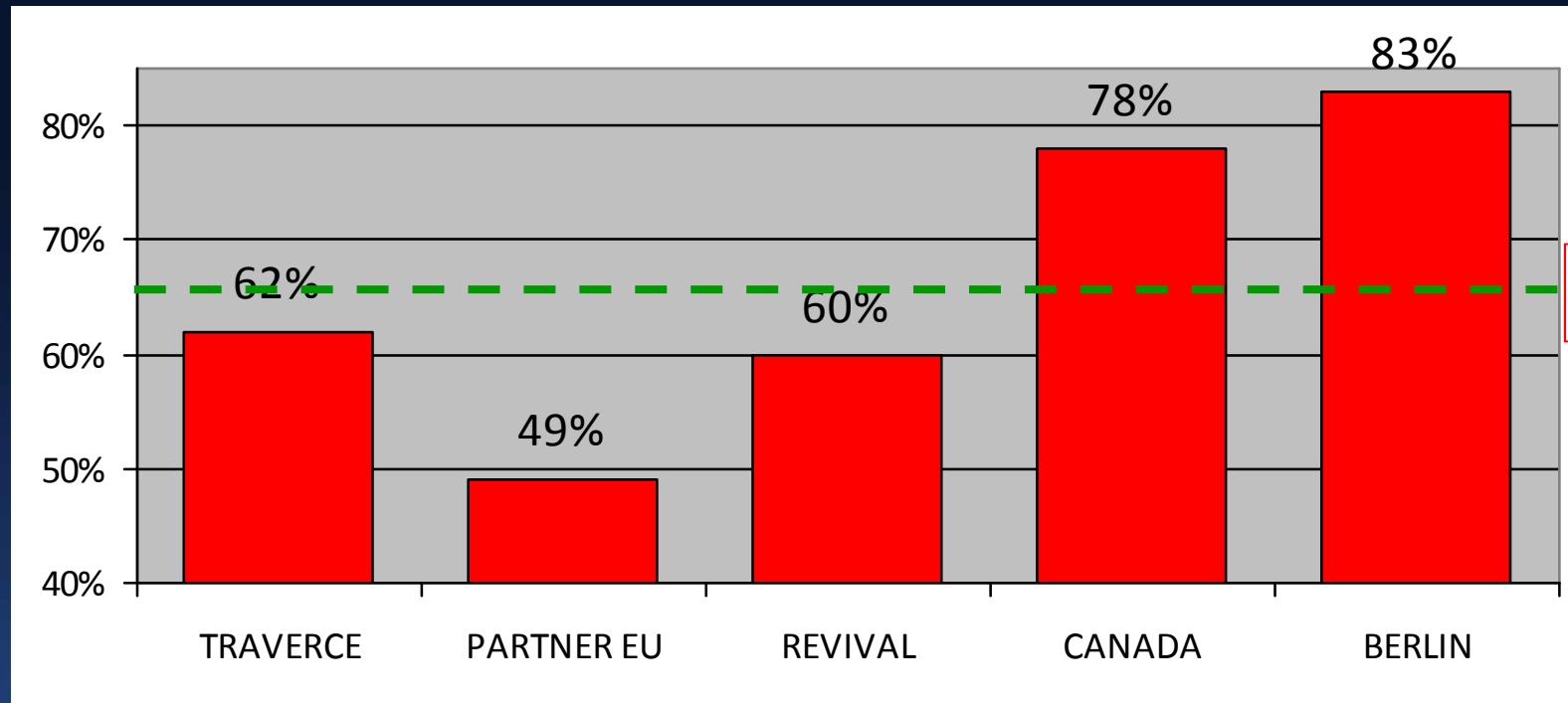
*Clinical Trials*

*Improved one-year outcomes!*

# TAVI in 2010

## *Trans-apical*

1-year survival (%)

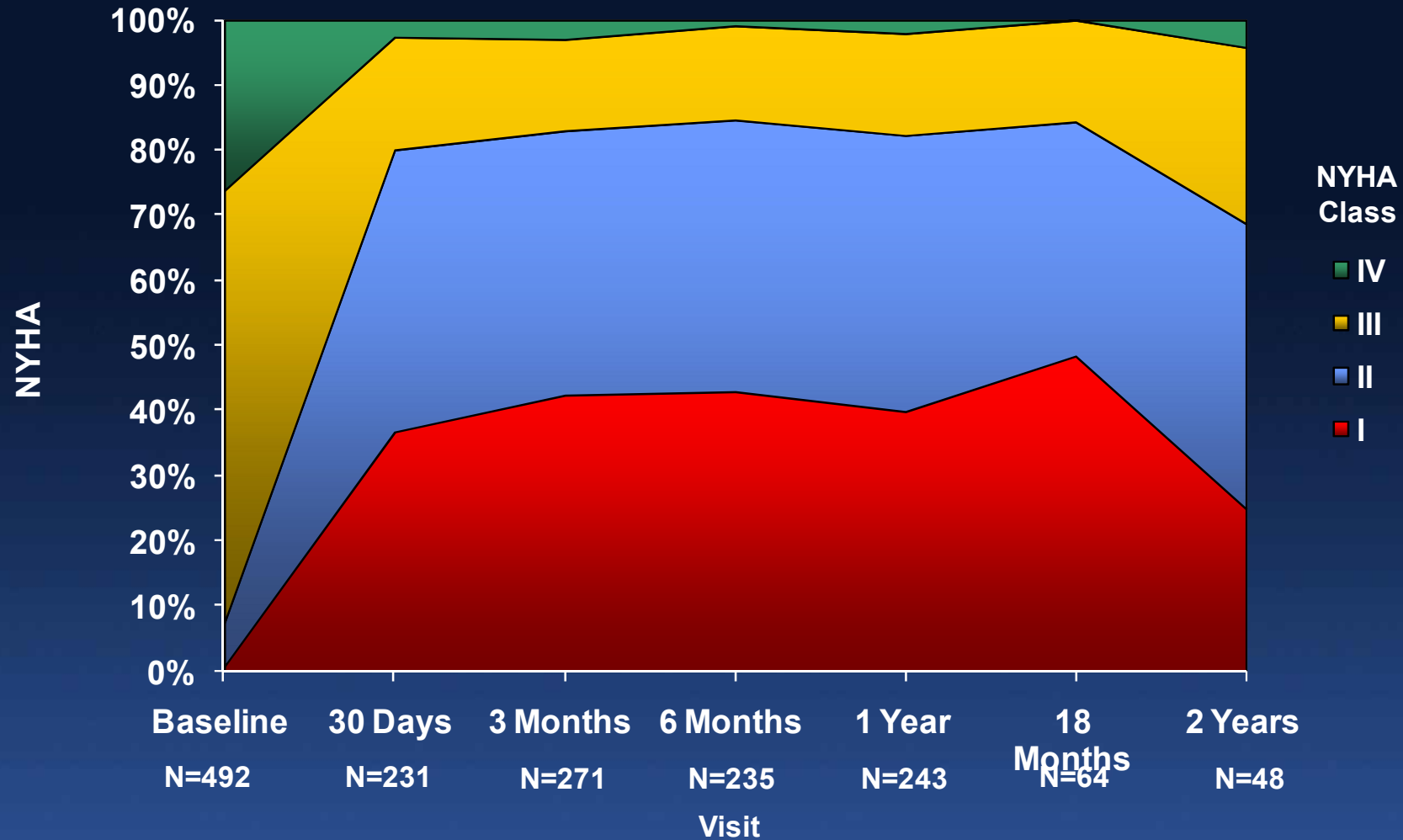


*Clinical Trials*

*Improved one-year outcomes!*

# POOLED\* Monitored Edwards TAVI

## NYHA Class



**\* REVIVE, REVIVAL, TRAVERCE  
and PARTNER EU**

# Vancouver TAVI Learning Experience

First Half	Second Half	Overall
10.9%	4.9%	7.9%

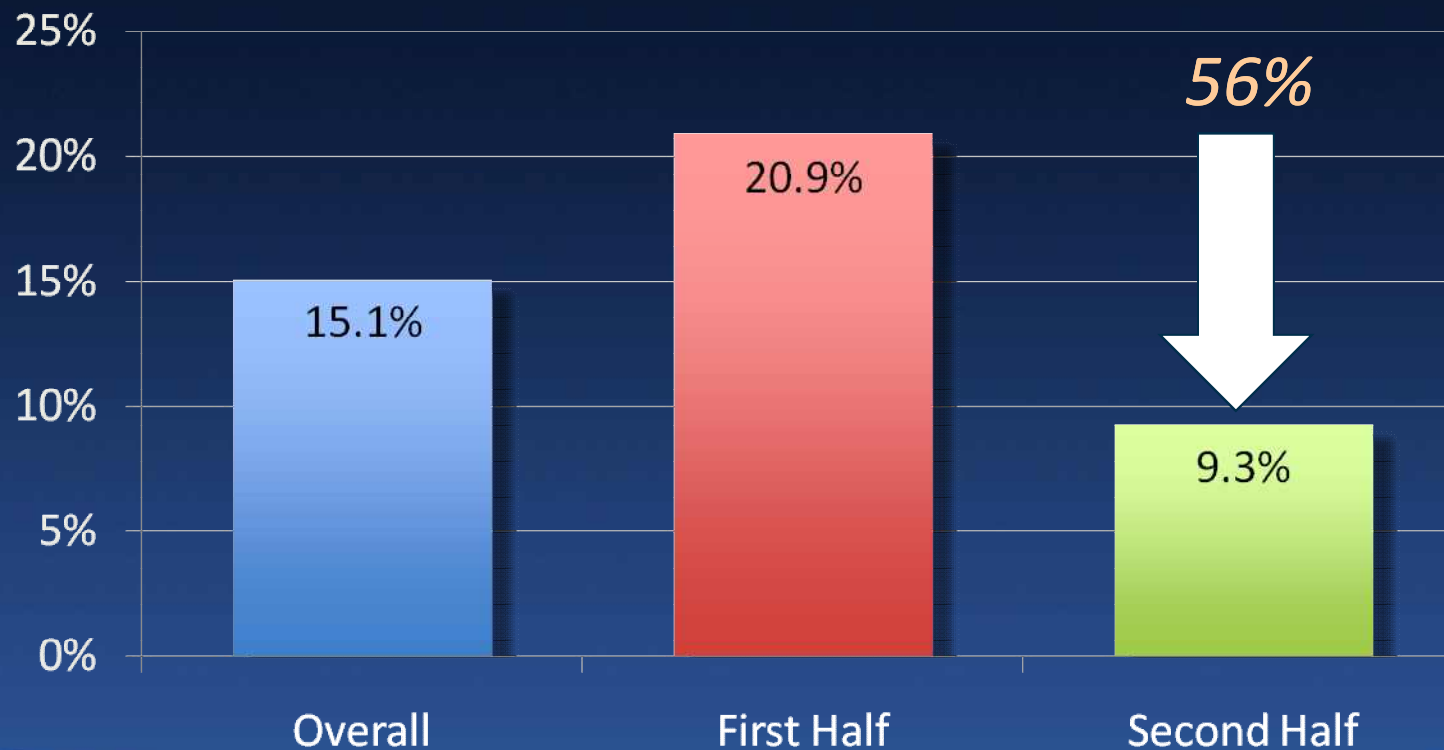
*Mortality @ 30 days – Trans-arterial*



# Vancouver TAVI Learning Experience

First Half	Second Half	Overall
20.9%	9.3%	15.1%

*Mortality @ 30 days – Trans-apical*



# TAVI in 2010

## *Lessons Learned...*

***4. Many TAVI complications have emerged and require further analysis and clarification***

- **Paravalvular AR**
- **Conduction disturbances**
- **Vascular complications**
- **Stroke**
- **Coronary obstruction**

# Edwards TAVI Complications

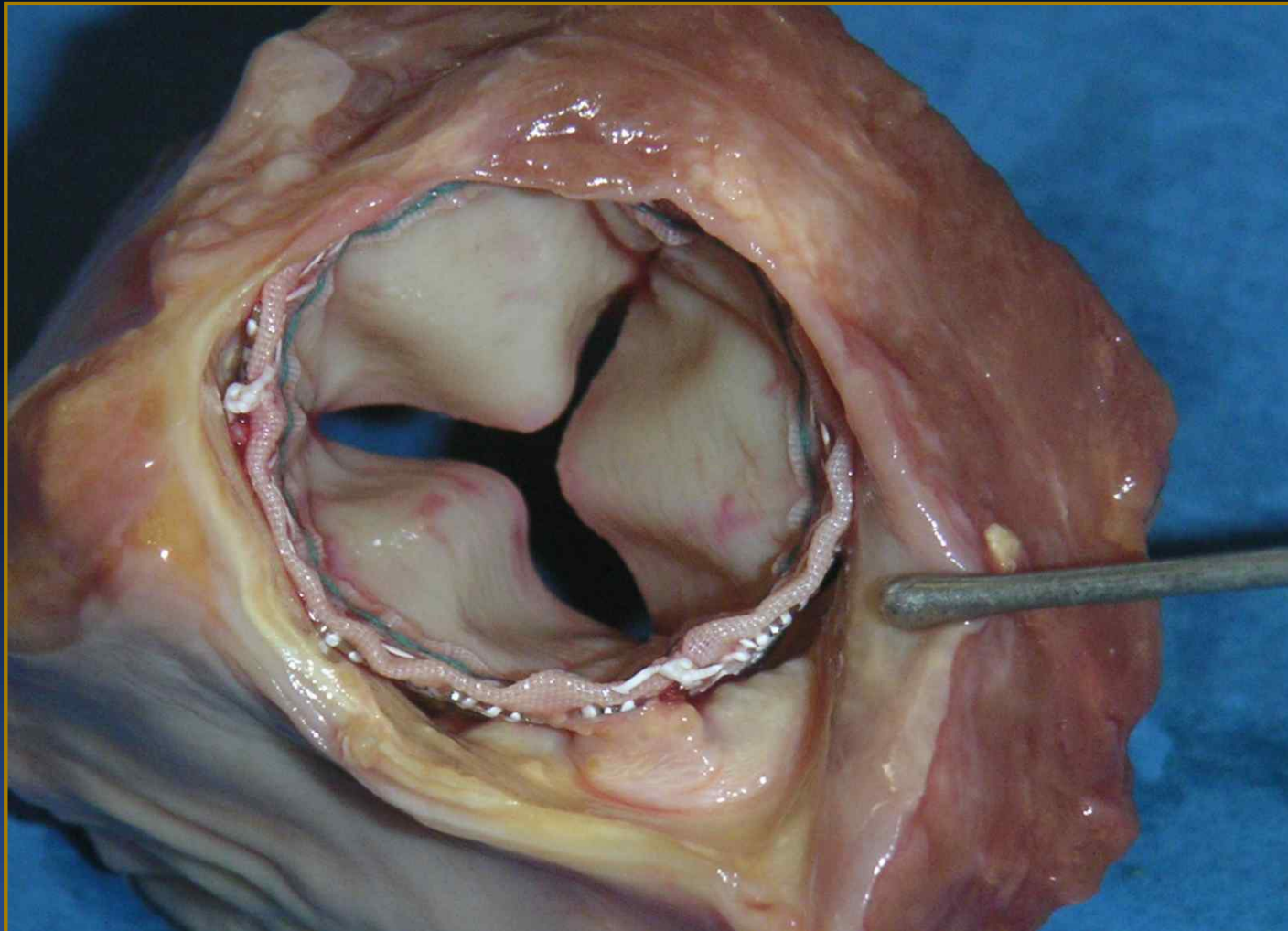
## *Multiple Data Sources (TA and TF)*

	<b>POOLED*</b> <b>(503 pts)</b>	<b>SOURCE</b> <b>(1038 pts)</b>	<b>VANCOUVER</b> <b>(250 pts)</b>	<b>PARIS</b> <b>(75 pts)</b>	<b>CA-Multictr</b> <b>(339 pts)</b>
<b>Vascular (maj)** (%)</b>	<b>18.5</b>	<b>10.6</b>	<b>10.3</b>	<b>11.8</b>	<b>13.1</b>
<b>AR &gt;2+ (%)</b>	<b>10.9</b>	<b>4.7</b>	<b>5.0</b>	<b>5.3</b>	<b>7.7</b>
<b>Stroke (%)</b>	<b>4.0</b>	<b>2.5</b>	<b>3.0</b>	<b>4.0</b>	<b>2.3</b>
<b>New Pacemaker (%)</b>	<b>4.4</b>	<b>7.0</b>	<b>5.5</b>	<b>5.3</b>	<b>4.9</b>
<b>Renal Failure (%)</b>	<b>5.2</b>	<b>8.7</b>	<b>4.2</b>	<b>na</b>	<b>2.6</b>
<b>Coronary Obstr (%)</b>	<b>0.4</b>	<b>0.6</b>	<b>na</b>	<b>0</b>	<b>0</b>

\* REVIVE, REVIVAL, TRAVERCE, PARTNER EU

\*\* TF Only

# Para-valvular Regurgitation

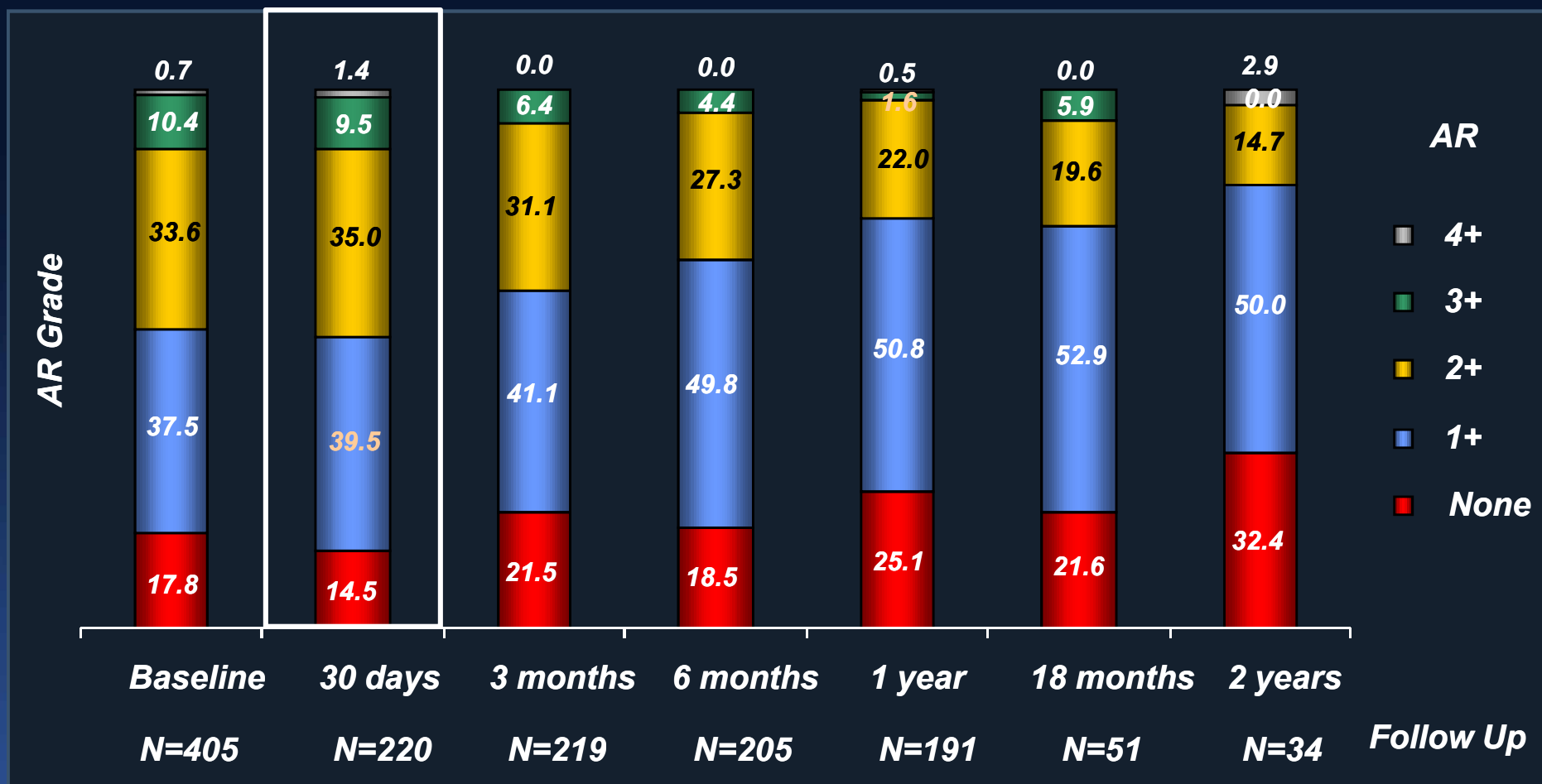


**Patient #5**



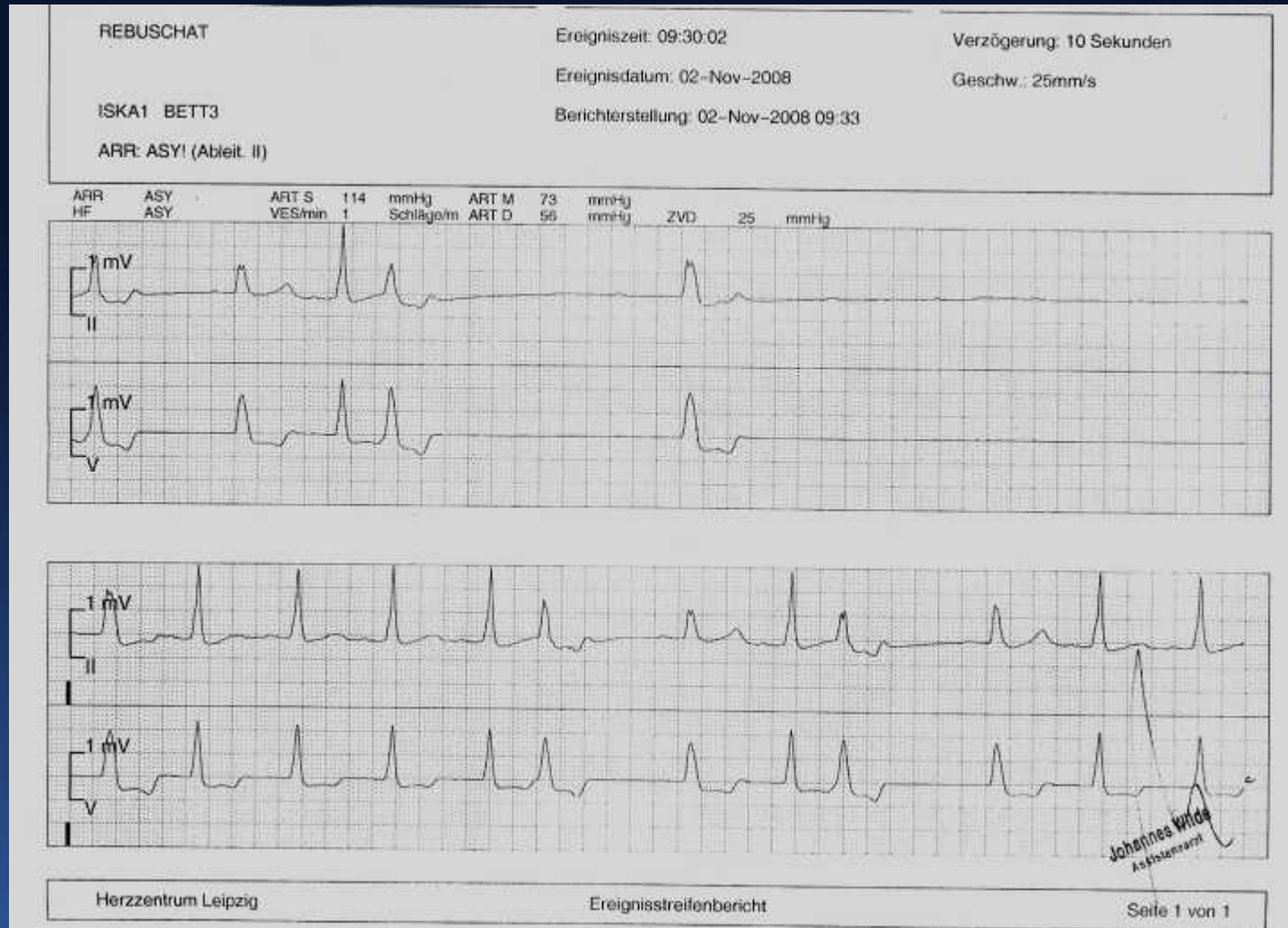
# POOLED\* Monitored Edwards TAVI

## Echo AR Results



\* REVIVE, REVIVAL, TRAVERCE  
and PARTNER EU

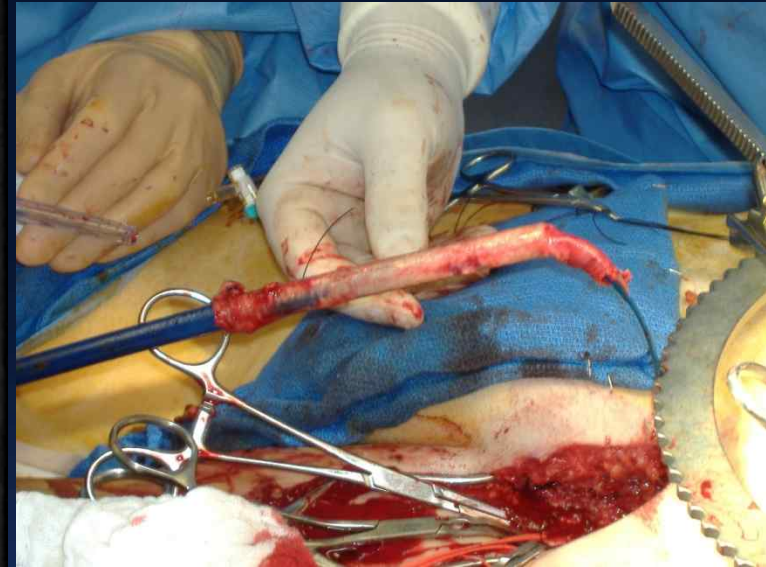
# AV-Block III° Following COREVALVE Implantation



# AV-Block III° Following COREVALVE Implantation



# Iliac Perforation



# TAVI in 2010

## ***Need for embolic protection...***

### **Silent and Apparent Cerebral Ischemia After Percutaneous Transfemoral Aortic Valve Implantation: A Diffusion-Weighted Magnetic Resonance Imaging Study**

Philipp Kahlert, Stephan C. Knipp, Marc Schlamann, Matthias Thielmann, Fadi Al-Rashid, Marcel Weber, Uwe Johansson, Daniel Wendt, Heinz G. Jakob, Michael Forsting, Stefan Sack, Raimund Erbel and Holger Eggebrecht

*Circulation* 2010;121:870-878

- ***32 pts with TAVI; Diffusion-Weighted MRI at baseline, post-procedure, and @ 3 mos***
  - 22 balloon-expandable and 10 self-expanding THV devices
- ***New foci of restricted perfusion in 27/32 pts (84%)***
  - Lesions usually multiple and both hemispheres (embolic)
- ***No impairment of neuro-cognitive function nor clinical neurologic events assoc with MRI defects***
  - 80% of MRI defects resolved at 3 mos imaging study

# Left Main Coronary Occlusion (*VF and SD after implant*)



*High implant, low left coronary ostia,  
long leaflet with bulky calcified nodules*

# TAVI in 2010

## *Lessons Learned...*

### ***5. Long-term durability evaluations of TAVI bioprosthetic valves are still ongoing***

- **Meticulous follow-up necessary including echocardiograms (core lab assessments)**
- **Ultimate value of TAVI will require proof of “near surgical” valve durability**

# TAVI - Durability

**4 year FU specimen**



**Edwards**  
**~8,000 patients**





# Longest reported clinical follow-up (Rouen)

*Mrs S..., 88 yo: > 6 years with THV*



*No valve dysfunction*

*AVA: 1.68 cm<sup>2</sup>, mean gradient: 12 mmHg*

# TAVI in 2010

## *Lessons Learned...*

### ***6. TAVI requires a major milieu adjustment to develop an optimal program***

- Hybrid cath lab - ORs
- Intense clinical care continuum – screening, procedure, post-procedure care, follow-up
- Surgeons and interventionalists **MUST** work closely together (Heart Valve Team)!!!
- Strict training requirements

# Transcatheter AVR

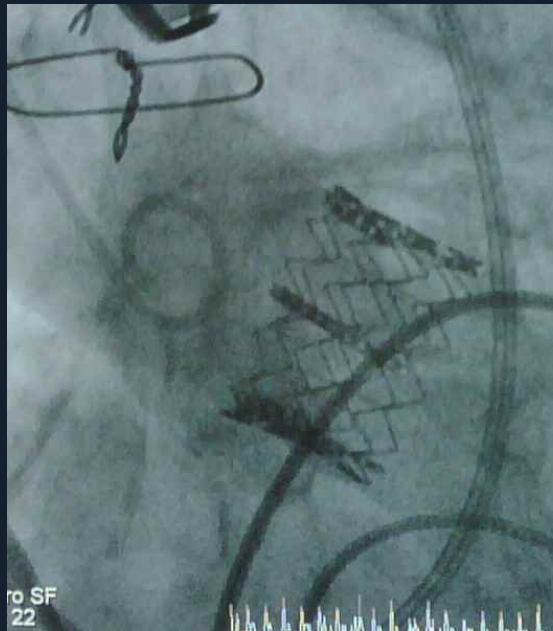
## *Hybrid OR-Cath Lab*



*A unique collaborative experience!*

# Transcatheter AVI

**100<sup>th</sup> TAVI at Columbia...**



**Mat Williams**  
**Susheel Kodali**



# Edwards TAVI Training Program



***Edwards THV  
Training Simulator***

- ***Site preparation and staff training***
- ***Didactic and case review sessions***
- ***Complication planning***
- ***Live case observations***
- ***Patient screening oversight***
- ***Case proctoring***
- ***Critical scrutiny of clinical outcomes***

# Leipzig Training Centre



# Rouen Training Centre



# Nyon Training Centre



# TAVI in 2010

## *Lessons Learned...*

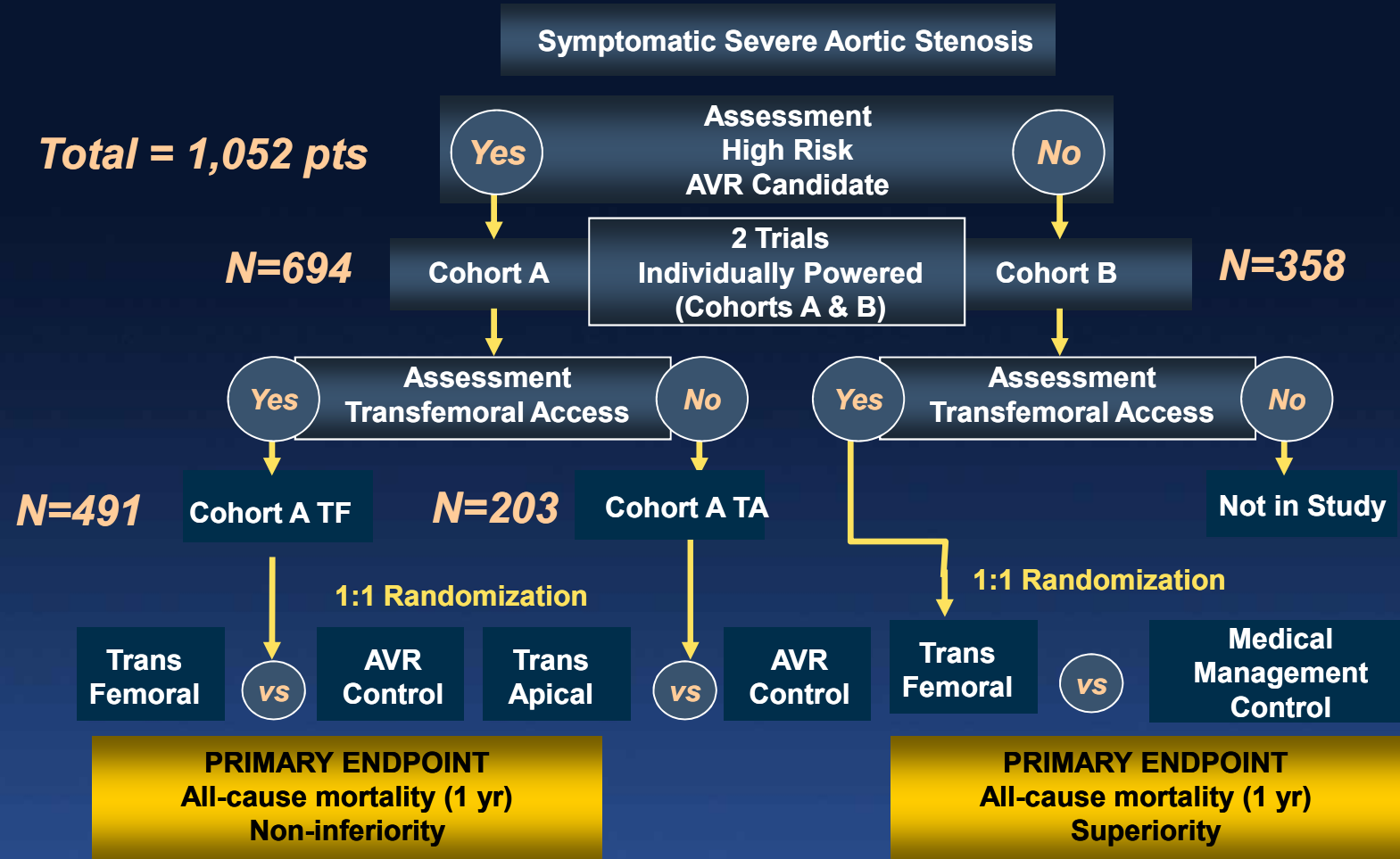
***7. The PARTNER trial should provide valuable insights and (hopefully) will provide the evidence-based medicine justification for future expansion of TAVI!***

- **2 parallel Randomized clinical trials (> 1,500 patients already enrolled)**
- **Rigorous clinical trial methodology**
- **Multi-disciplinary management (surgeon = interventionalist + echo)**



# PARTNER Trial Design

**Fully enrolled:** continued access to both patient cohorts approved by FDA





# PARTNER

## *Baseline Characteristics\**

<b>Variable %</b>	<b>Cohort A-TF (test control)</b>	<b>Cohort A-TA (test control)</b>	<b>Cohort B-TF (test control)</b>
<b>Number of patients</b>	<b>450</b>	<b>182</b>	<b>430</b>
<b>Age (years)</b>	<b>83.6 ± 10.4</b>	<b>82.4 ± 10.8</b>	<b>83.1 ± 8.5</b>
<b>Gender (male)</b>	<b>58.1</b>	<b>57.4</b>	<b>48.7</b>
<b>Diabetes</b>	<b>40.2</b>	<b>41.7</b>	<b>35.4</b>
<b>Hyperlipidemia</b>	<b>79.5</b>	<b>79.3</b>	<b>74.0</b>
<b>Hypertension</b>	<b>90.0</b>	<b>95.4</b>	<b>85.3</b>
<b>Smoking</b>	<b>42.6</b>	<b>56.6</b>	<b>46.9</b>
<b>Prior MI</b>	<b>25.3</b>	<b>31.4</b>	<b>25.2</b>

• *Preliminary snapshot*

• *Outcomes data blinded*

*\*subset of all randomized patients  
in cohort A (TF+TA) and cohort B (incl. CA)*

# PARTNER

## High Risk Co-Morbidities (1)\*

Variable %	Cohort A-TF (test control)	Cohort A-TA (test control)	Cohort B-TF (test control)
Number of patients	450	182	430
Periph Vasc Disease	32.7	<b>56.2</b>	26.8
Hx CHF	97.6	96.6	97.0
NYHA Class III/IV	94.0	91.6	93.2
Prior CABG	59.5	69.8	59.5
Prior PCI	45.7	48.4	37.2
Prior BAV	15.9	15.9	25.6
Severe COPD (O2 dep)	7.1	9.7	<b>23.8</b>

*\*subset of all randomized patients  
in cohort A (TF+TA) and cohort B (incl. CA)*

# PARTNER

## High Risk Co-Morbidities (2)\*

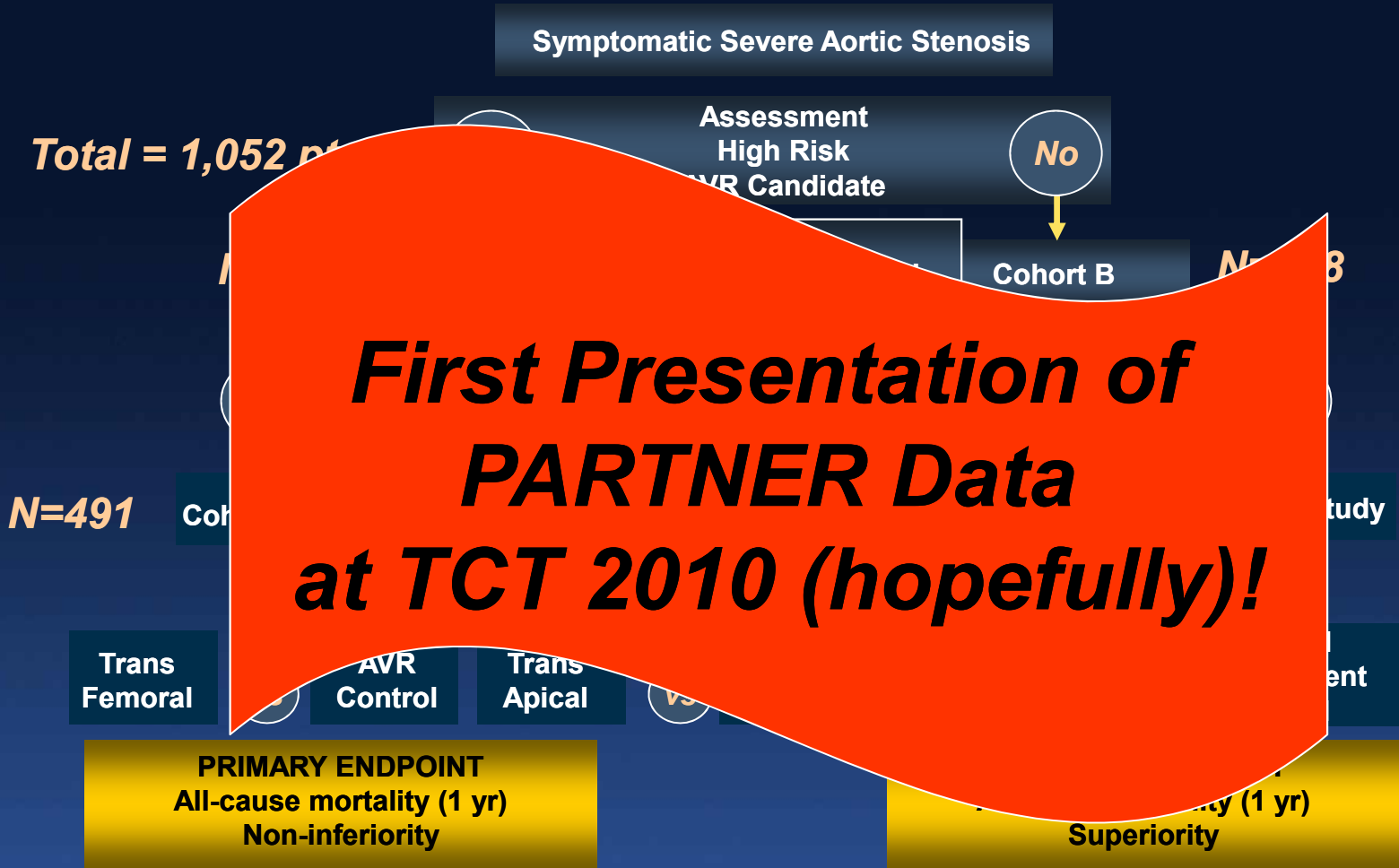
Variable %	Cohort A-TF (test control)	Cohort A-TA (test control)	Cohort B-TF (test control)
Number of patients	450	182	430
CNS Disease	23.0	32.0	26.9
Recent Stroke/TIA	2.5	3.6	2.4
Cirrhosis	2.0	0	2.2
Porcelain aorta	0.4	1.0	15.1
Chest radiation	0.6	1.0	7.8
Chest wall deformity	0	0	6.9
Frailty	18.9	17.6	27.9

*\*subset of all randomized patients  
in cohort A (TF+TA) and cohort B (incl. CA)*



# PARTNER Trial Design

**Fully enrolled:** continued access to both patient cohorts approved by FDA



***First Presentation of  
PARTNER Data  
at TCT 2010 (hopefully)!***

# TAVI in 2010

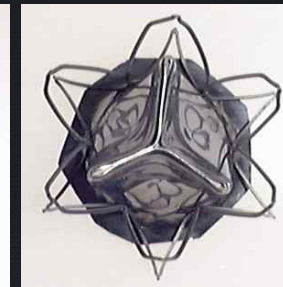
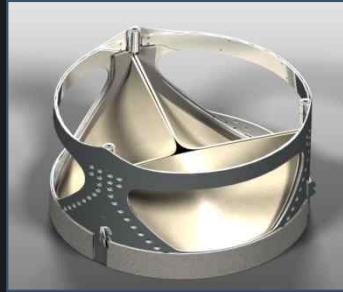
## *Lessons Learned...*

**8. *The future is exciting – TAVI procedure device enhancements (including accessories) and expanded clinical indications!***

- **New valve designs, lower profile systems, cerebral embolic protection, large hole vascular closure**
- **Clinical indications - highest priorities are “medium” or standard risk patients, AS + CAD, and bio-prosthesis valve failure**

# New TAVI Technologies

- Direct Flow
- Sadra
- AorTx
- Jena Valve
- HLT
- ABPS PercValve
- EndoTech
- Ventor Embracer
- Symetis

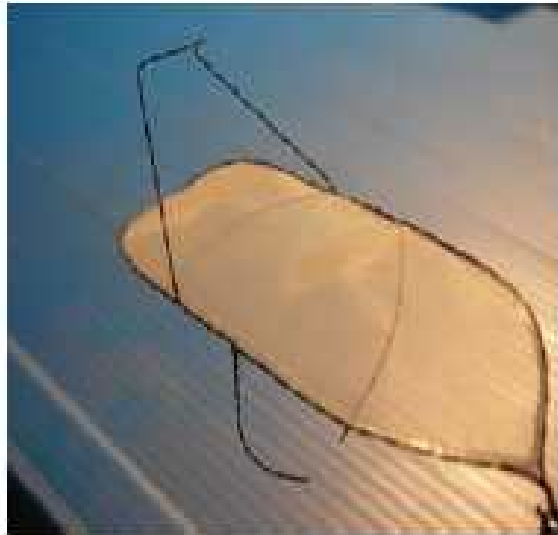


# Embrella: Embolic Protection *(intra-cardiac and valve procedures)*



# TAVI in 2010

## *Cerebral Embolic Protection*



*SMT*



*Embrella*



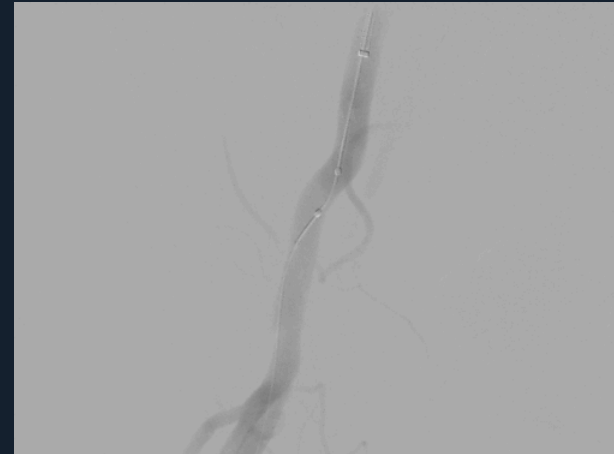
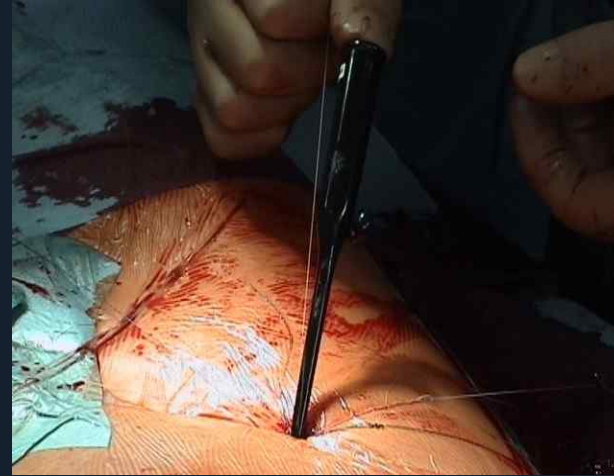
*Claret*

## Deflectors and Filters



# Percutaneous Closure

## *10 Fr Prostar device*



# TAVI in 2010

## *Next Clinical Targets*

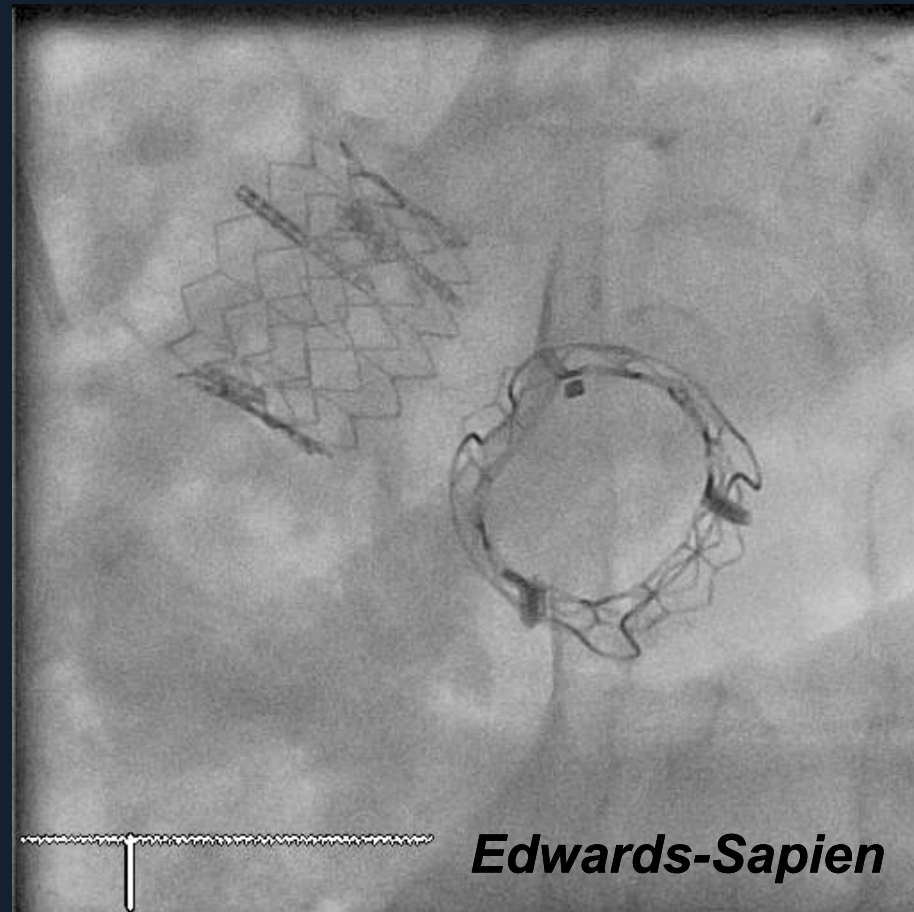
- **Valve-in-valve for bio-prosthetic aortic and mitral valve failure**
- **Lower risk AS patients**
- **Mixed AS and CAD patients**
- **Asymptomatic severe AS**
- **Low flow - low gradient AS – impedance mismatch**
- **Aortic regurgitation**

# Transcatheter AVI

## *Endless Possibilities!*

***Trans-apical  
AVR***

***Trans-apical  
MVR  
(valve-in-valve)***



# TAVI in 2010

## *Lessons Learned*

# Final Thoughts

# TAVI in 2010

## *Final Thoughts...*

- **Clinical “need” for TAVI in “high risk” AS patients is greater than anticipated**
- **TAVI is well beyond “proof of concept” or feasibility – already being integrated into AS clinical Rx paradigms in many parts of the world**
- **Technology and procedure have evolved rapidly and with proper training can be generalized to most clinical environments**
- **Clinical outcomes have stabilized in experienced hands (5-10% mortality at 30 days), with late mortality reflecting underlying co-morbidities**

# TAVI in 2010

## *Final Thoughts...*

- **Undeniable early and sustained clinical benefit**
- **Valve performance has exceeded expectations, BUT need long-term durability data**
- **Multi-specialty “heart valve center” concept will be the model for optimal care**
- **Considerations for the future – further device evolution, improved clinical research methods (“VARC” initiative), judicious extension into lower risk patient categories, and careful cost-effectiveness assessments**

# Transcatheter AVI

## *My Rosey Prophecy*

Surgery – The PAST

***In the next 5-10 years, most patients with severe AS requiring AVR will be treated using transcatheter lesser-invasive modalities!***

TAVR – The Future

FOR MORE INFORMATION, PLEASE VISIT  
[www.tctconference.com](http://www.tctconference.com)



# TCT2010

TRANSCATHETER CARDIOVASCULAR THERAPEUTICS 2010

THE INTERSECTION OF RESEARCH, INNOVATION AND PATIENT CARE

SEPTEMBER 21-25, 2010

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