



# LE FUTUR DU TAVI

**Nicolas DUMONTEIL**  
Cardiologie  
CHU Rangueil, TOULOUSE



# Déclaration de Relations Professionnelles

*J'ai actuellement, ou j'ai eu au cours des deux dernières années, une affiliation ou des intérêts financiers ou intérêts de tout ordre avec une société commerciale ou je reçois une rémunération ou des redevances ou des octrois de recherche d'une société commerciale :*

## Affiliation/Financial Relationship

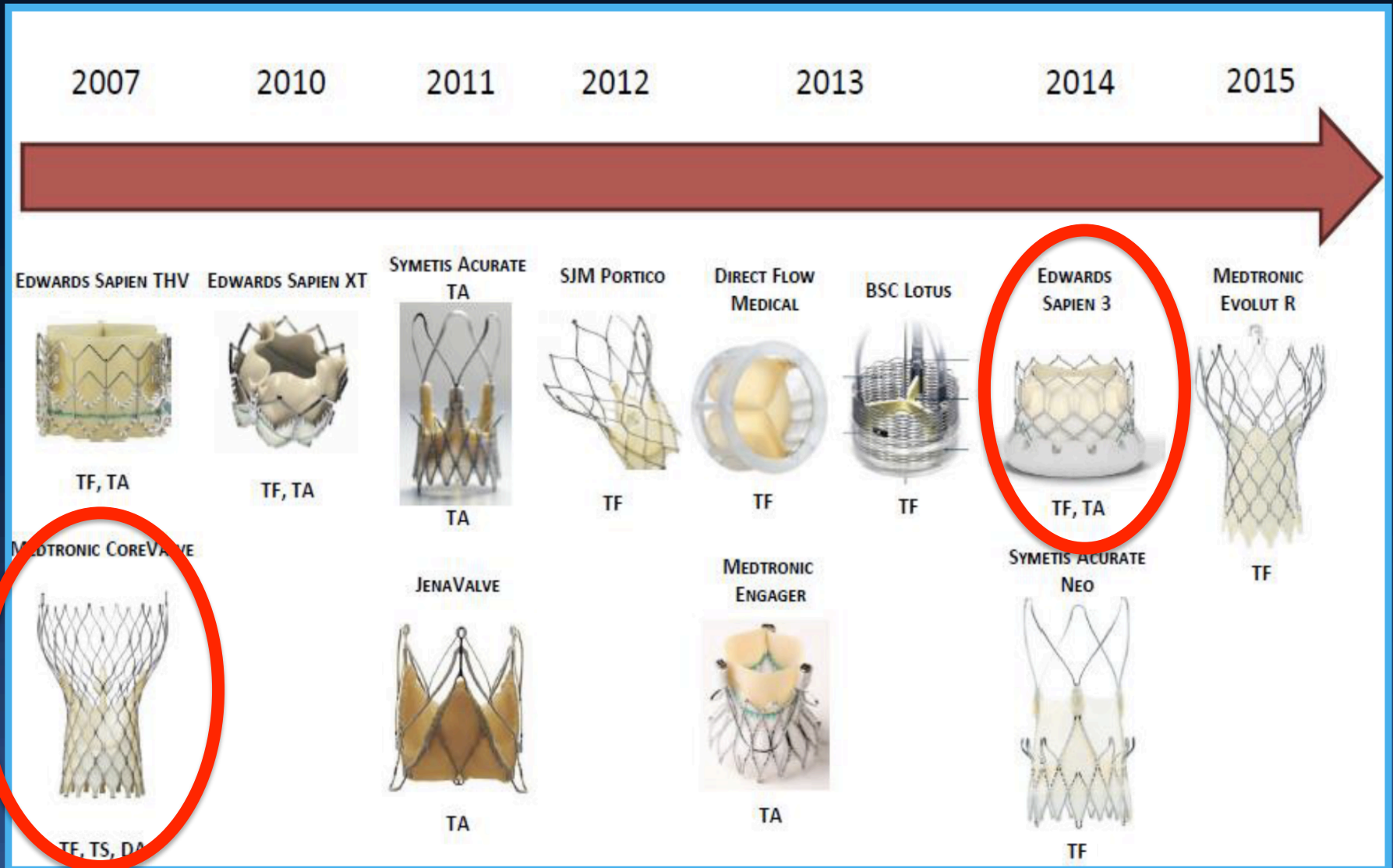
- **Consulting Fees/Proctoring Honoraria**

## Company

- **Edwards LifeSciences**
- **Medtronic**
- **Boston Scientific**
- **Biotronik**
- **Abbott Vascular**

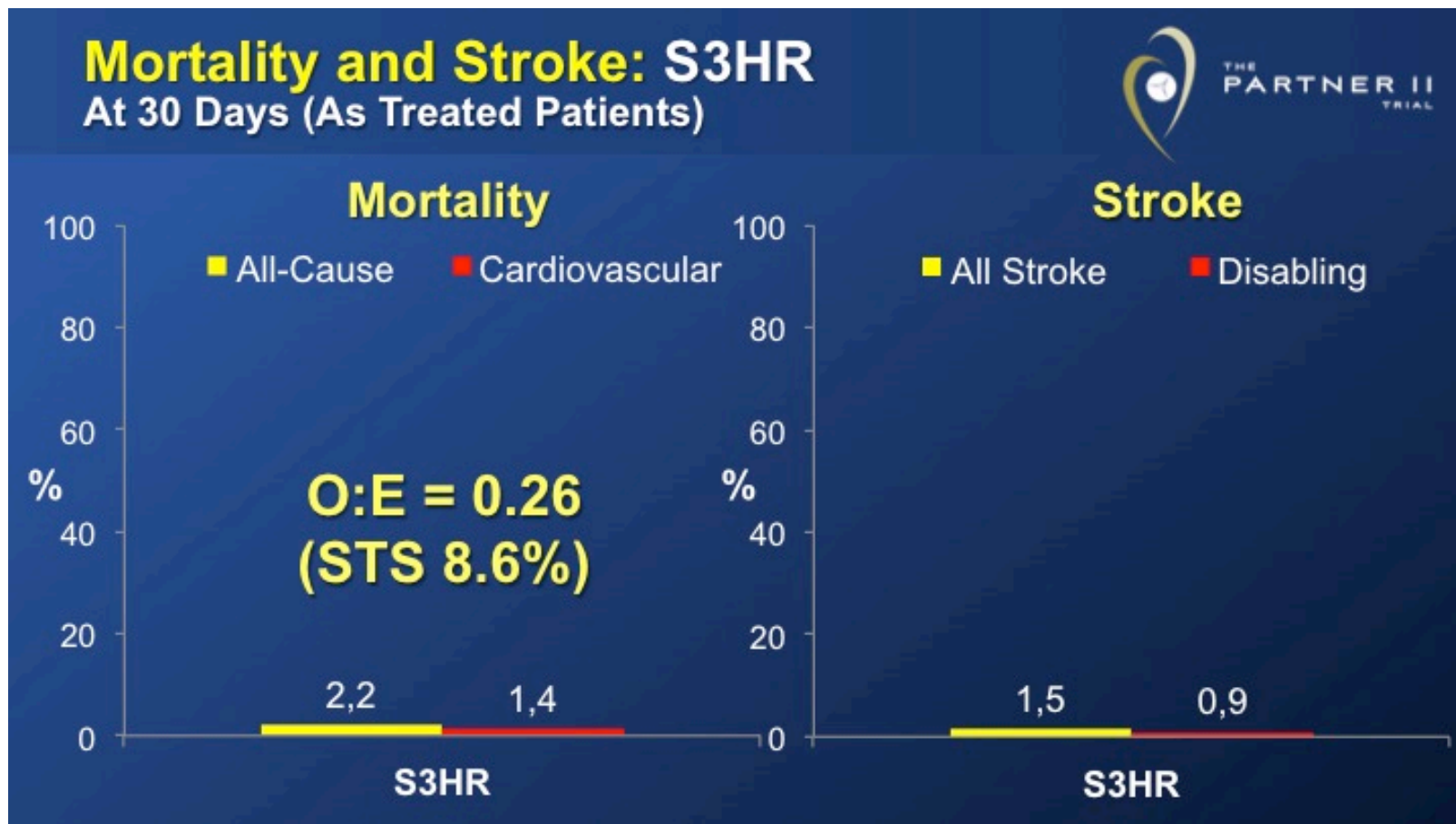
**Où en sommes nous en 2015 ?**

# TAVR Systems with CE-Approval (2007-15)





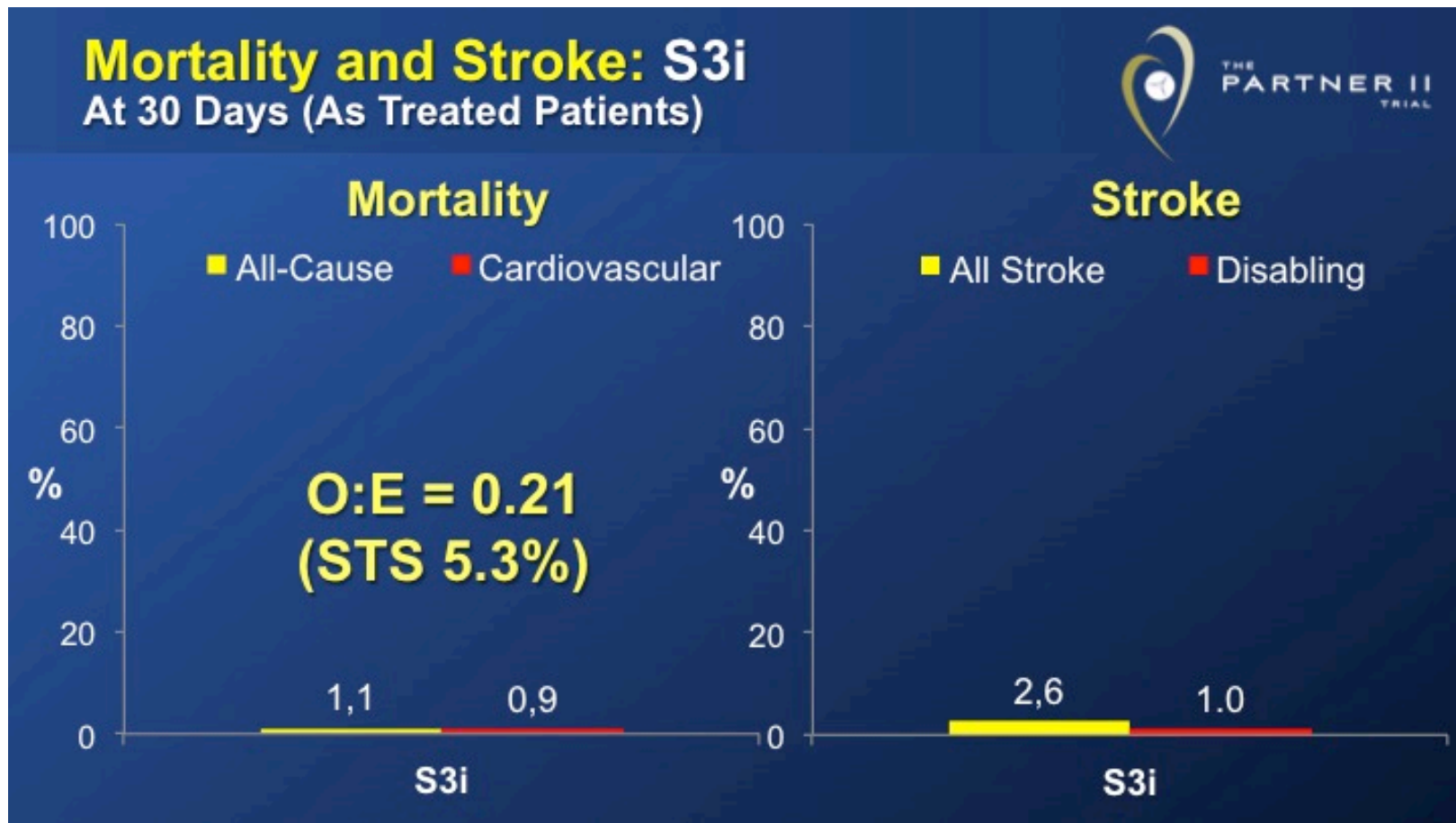
# Où en sommes nous en 2015 ?



**Edwards Sapien 3  
Patients à haut risque**



# Où en sommes nous en 2015 ?



**Edwards Sapien 3**  
**Patients à risque intermédiaire**



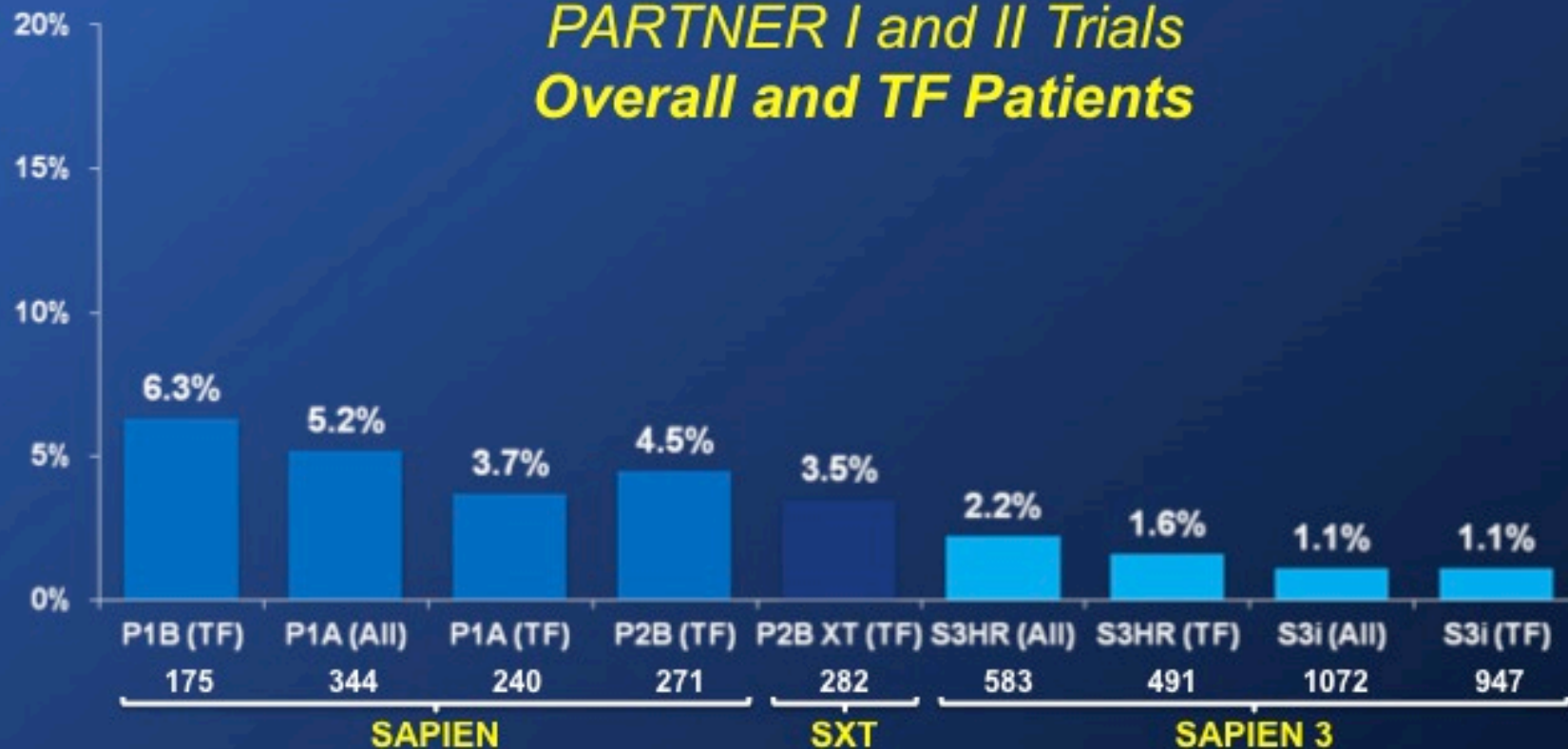
Où en sommes nous en 2015 ?

## All-Cause Mortality at 30 Days

Edwards SAPIEN Valves (As Treated Patients)



*PARTNER I and II Trials  
Overall and TF Patients*





# Où en sommes nous en 2015 ?

## Paravalvular Leak: S3HR & S3i (Valve Implant Patients)







# Où en sommes nous en 2015 ?

## Primary & Key Secondary Endpoints

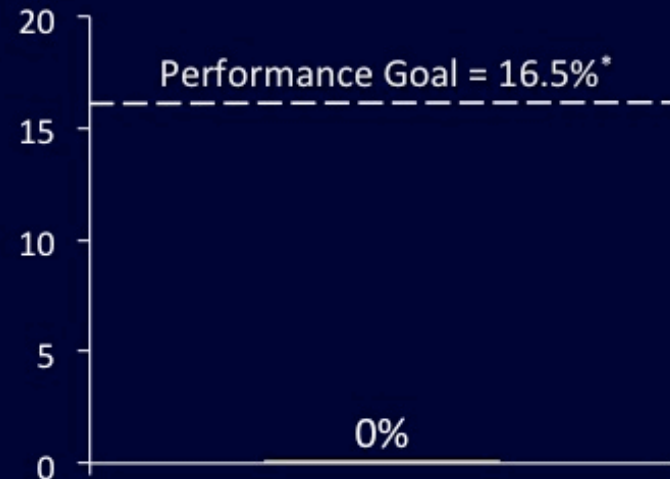
RESPOND

250-Patient Interim Analysis

All-Cause Mortality at  
30 Days



Moderate/Severe Paravalvular  
Regurgitation at Hospital Discharge



**Boston Scientific Lotus  
Utilisation commerciale**

# **Le futur du TAVI**

**Une évolution des indications**

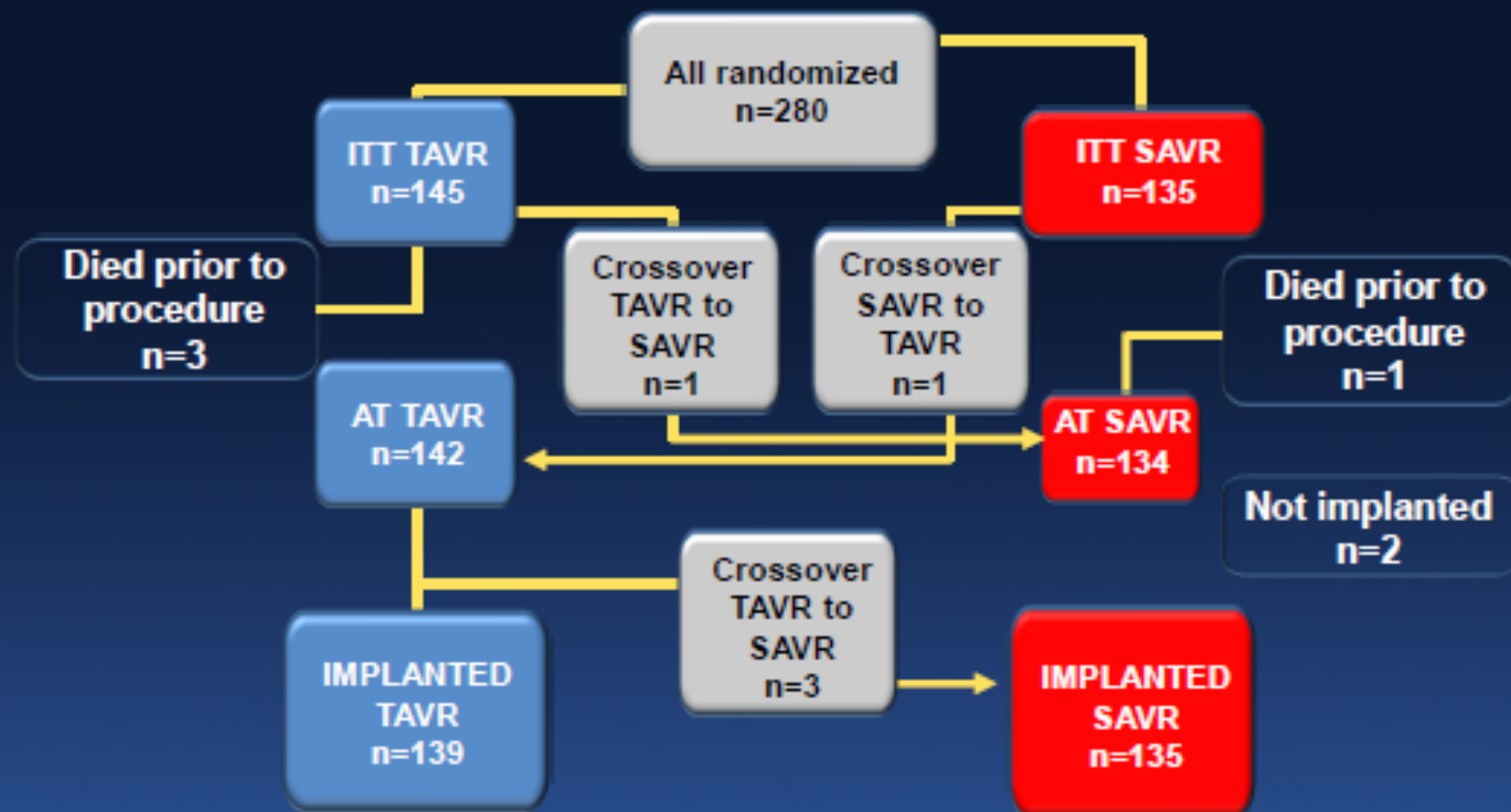
# An All-comers Randomized Clinical Trial Comparing Transcatheter with Surgical Aortic Valve Replacement in Patients with Aortic Valve Stenosis

## *Nordic Aortic Valve Intervention Trial (NOTION)*

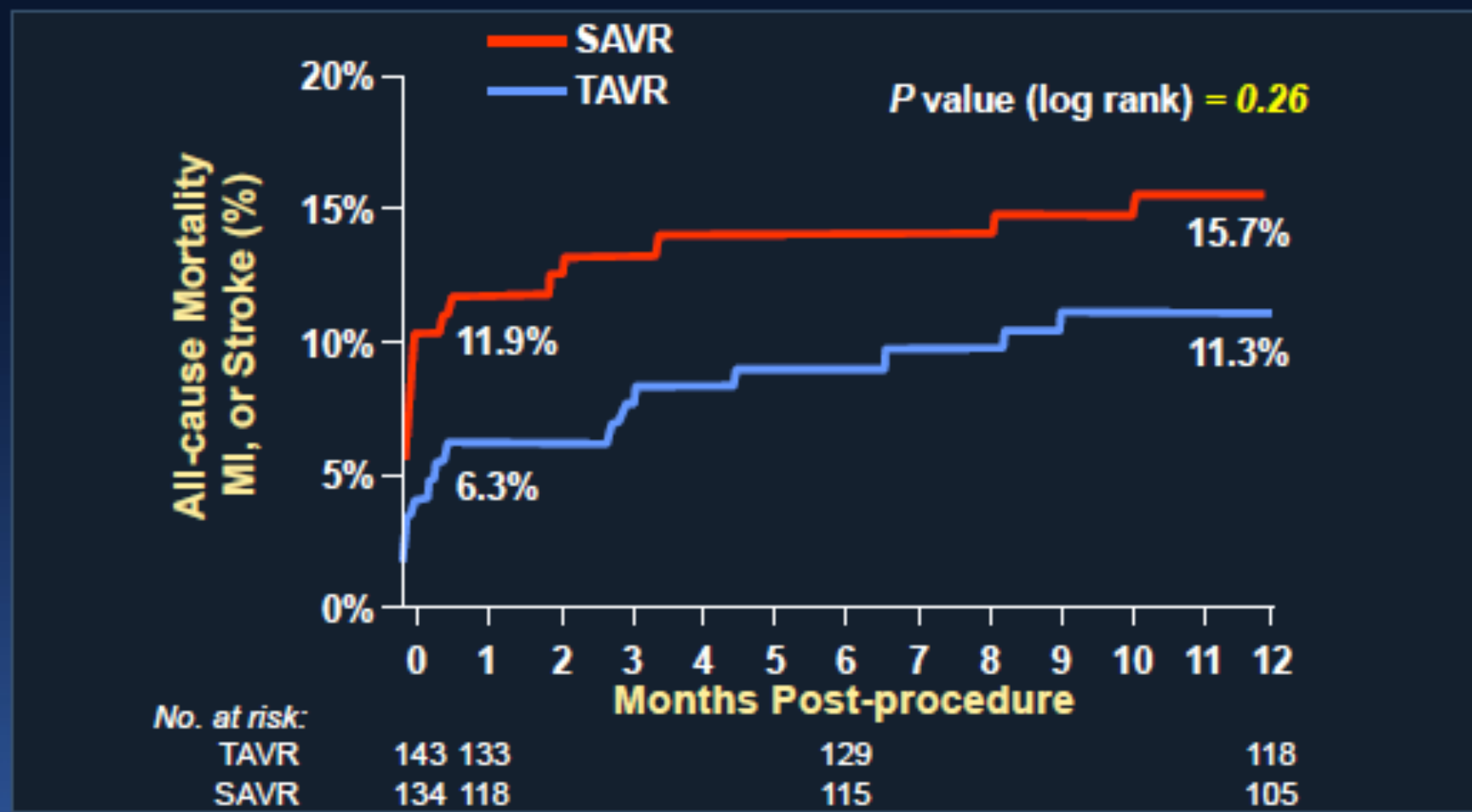
Hans Gustav Hørsted Thyregod, MD

Dep. of Cardiothoracic Surgery, Copenhagen University Hospital, Denmark

# NOTION: Study Flow



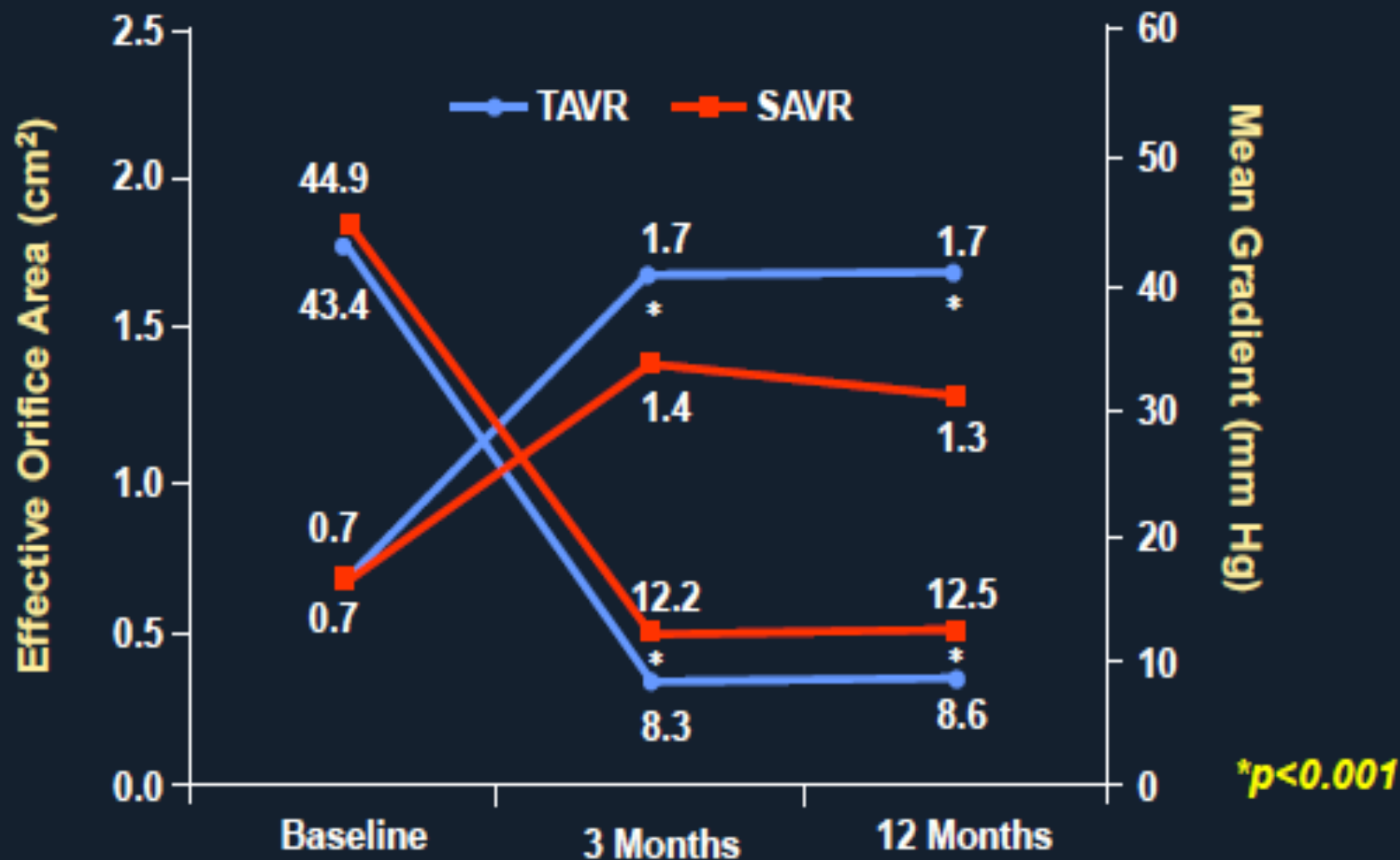
# **NOTION: Death (all-cause), Stroke or MI at 1 Year (as-treated)**



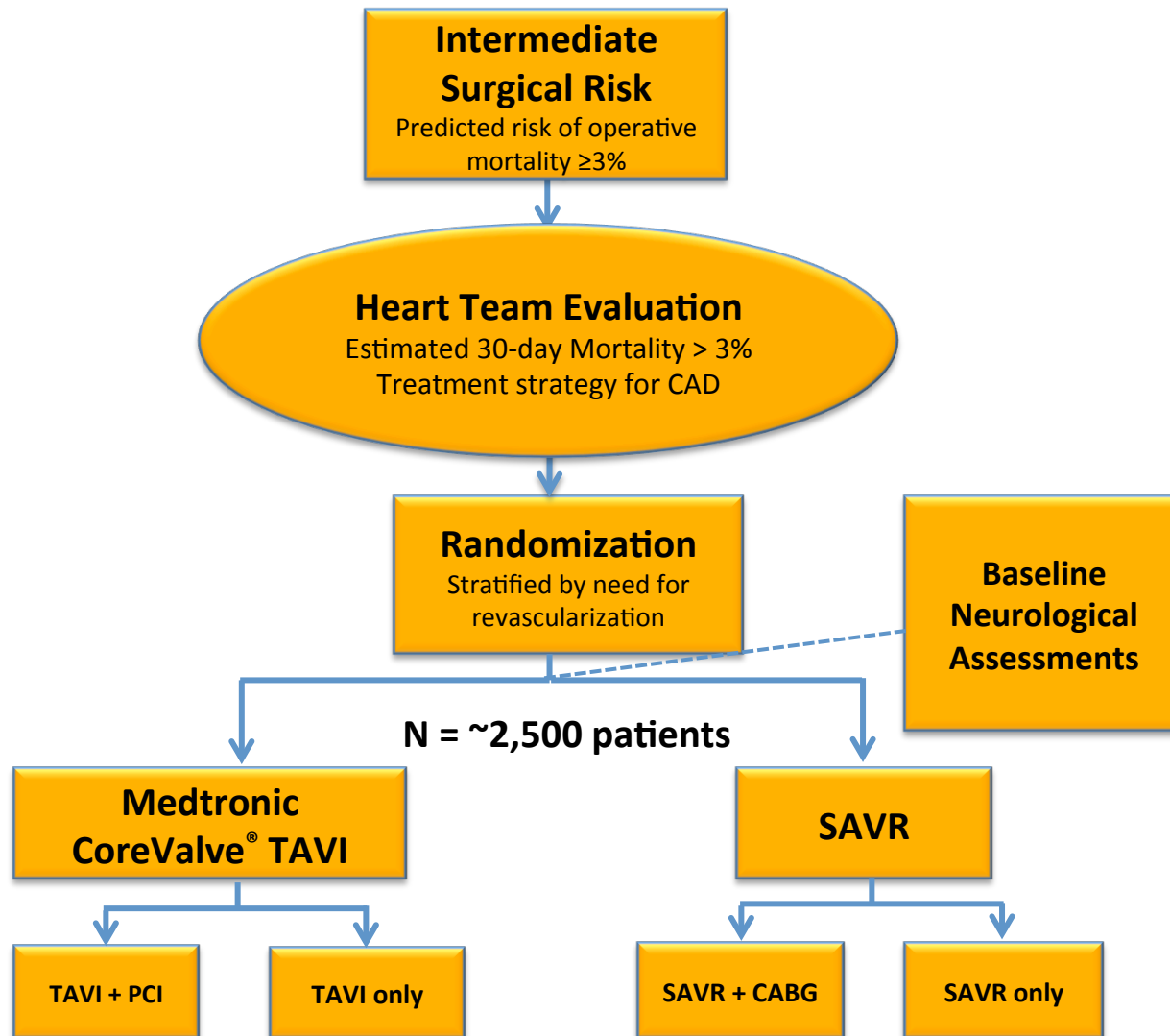
# **NOTION: 2<sup>ry</sup> Outcomes at 30 Days**

Outcome, %	TAVR n=142	SAVR n=134	P value
Death, any cause	2.1	3.7	0.43
Death, cardiovascular	2.1	3.7	0.43
Bleeding, life-threatening+major	11.3	20.9	0.03
Cardiogenic shock	4.2	10.4	0.05
Vascular lesion, major	5.6	1.5	0.10
Acute kidney injury (stage II+III)	0.7	6.7	0.01
Stroke	1.4	3.0	0.37
TIA	1.4	0	0.17
Myocardial infarction	2.8	6.0	0.20
Atrial fibrillation	16.9	57.8	<0.001
Pacemaker	34.1	1.6	<0.001

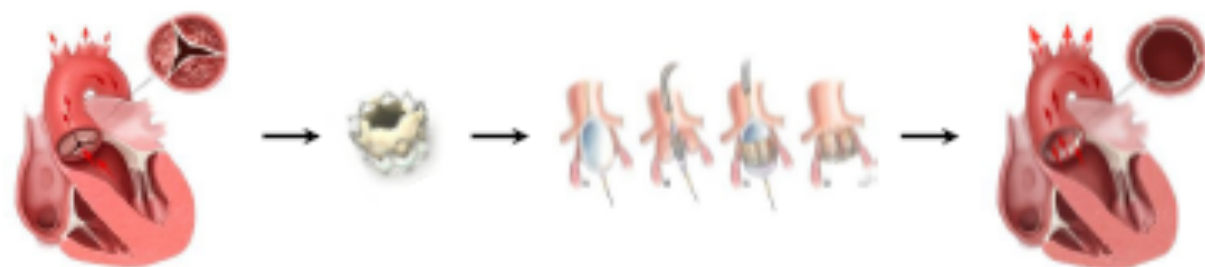
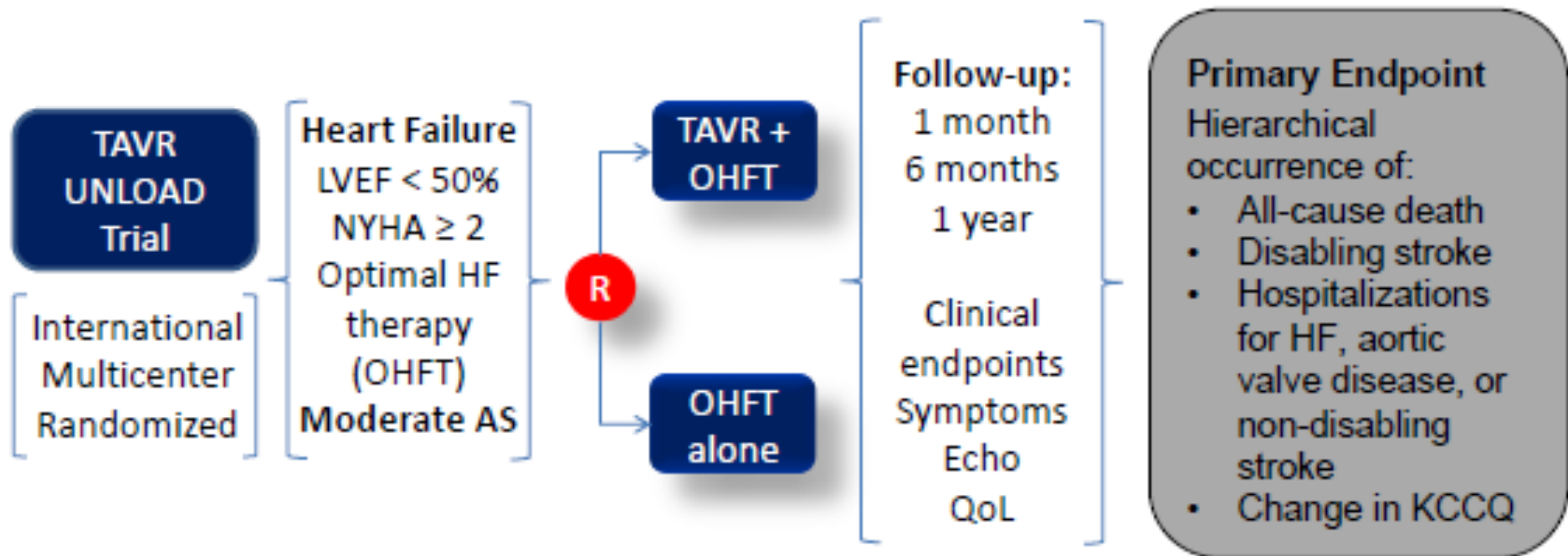
# NOTION: Aortic Valve Performance



# CoreValve<sup>®</sup> SURTAVI Trial Study Design







*Reduced AFTERLOAD  
Improved LV systolic  
and diastolic function*

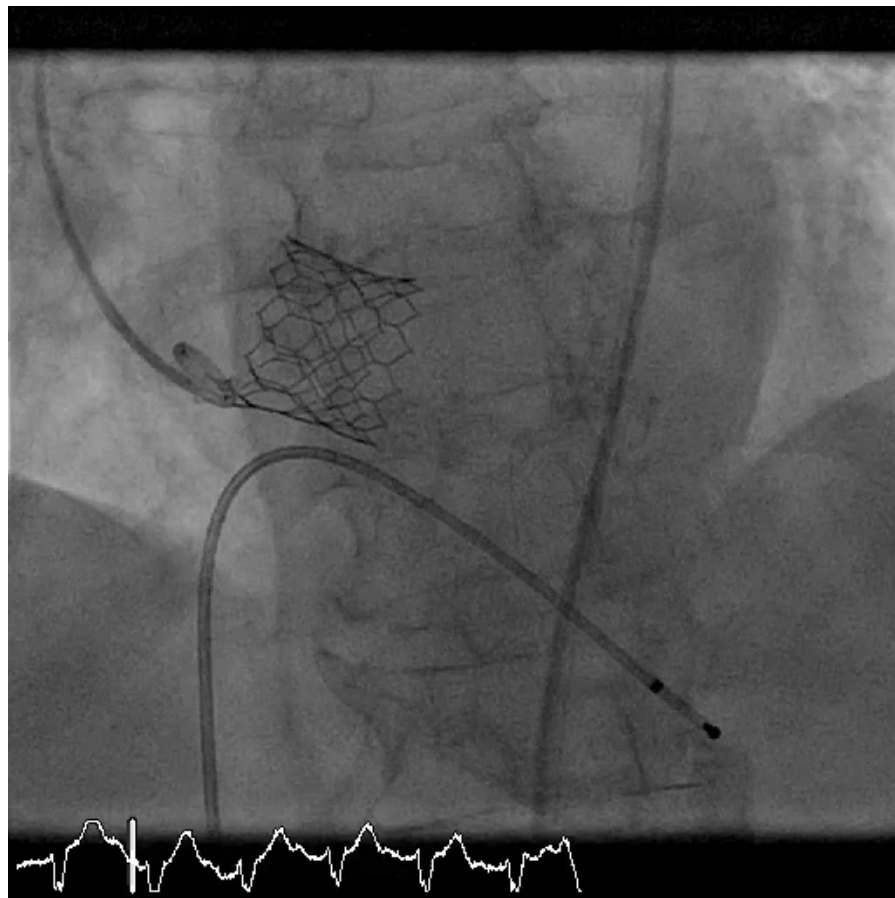
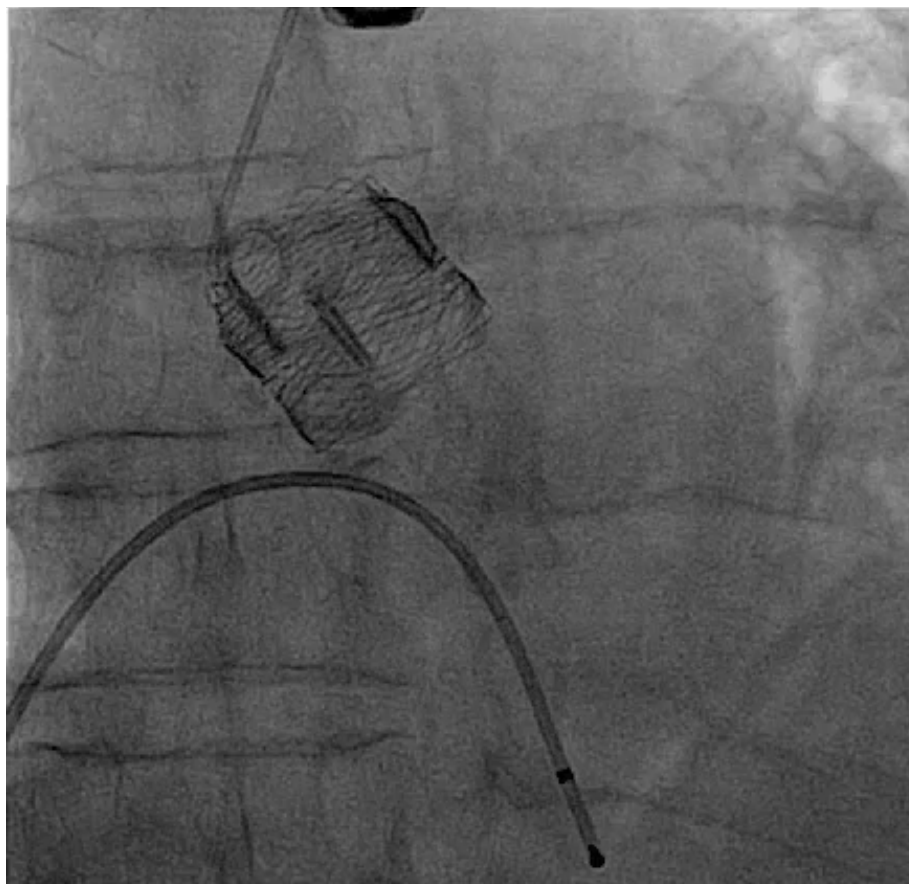
# **Le futur du TAVI**

**La réduction des complications  
actuelles ?**



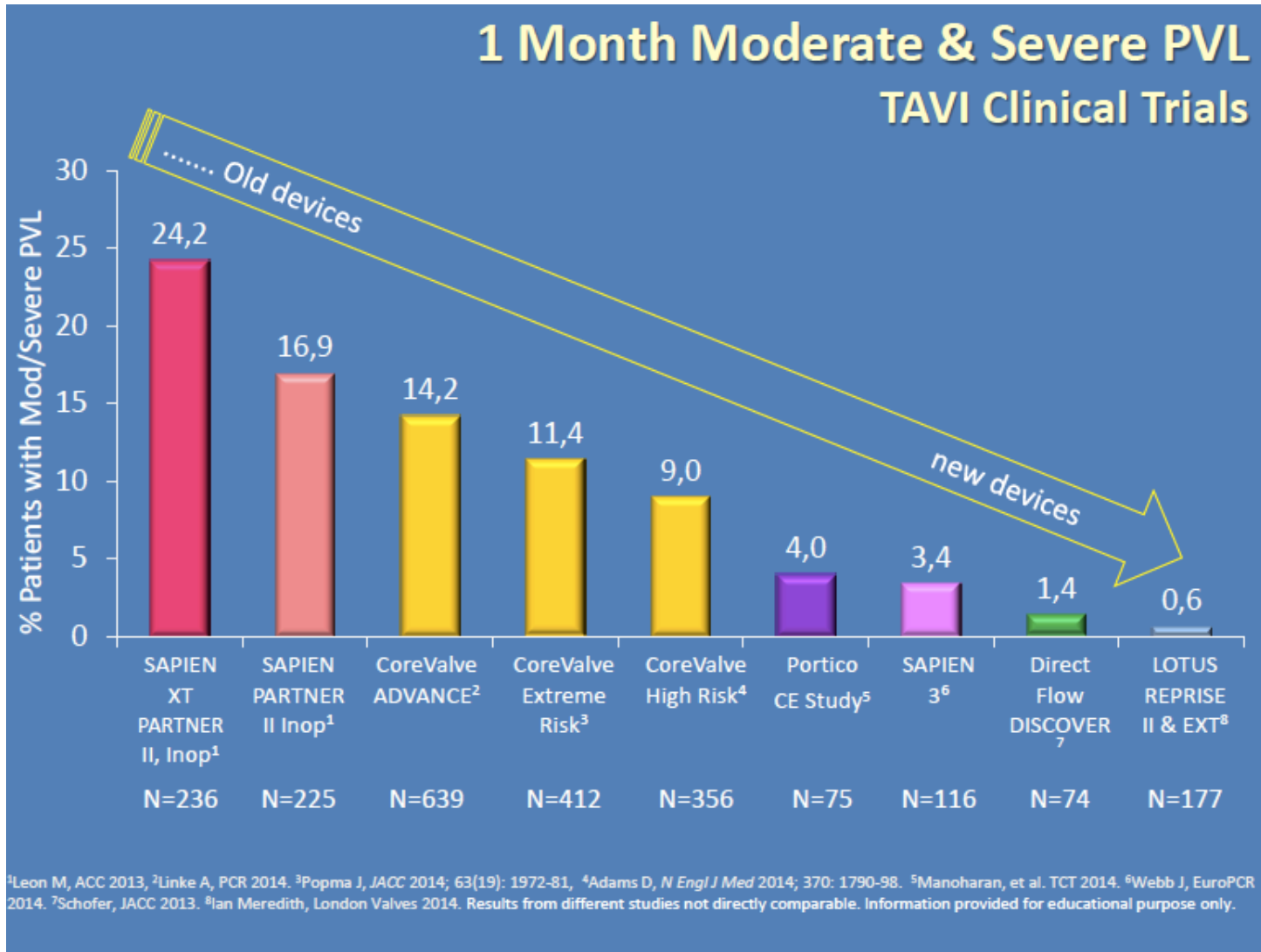
## Les fuites paravalvulaires ?

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# Les fuites paravalvulaires ?

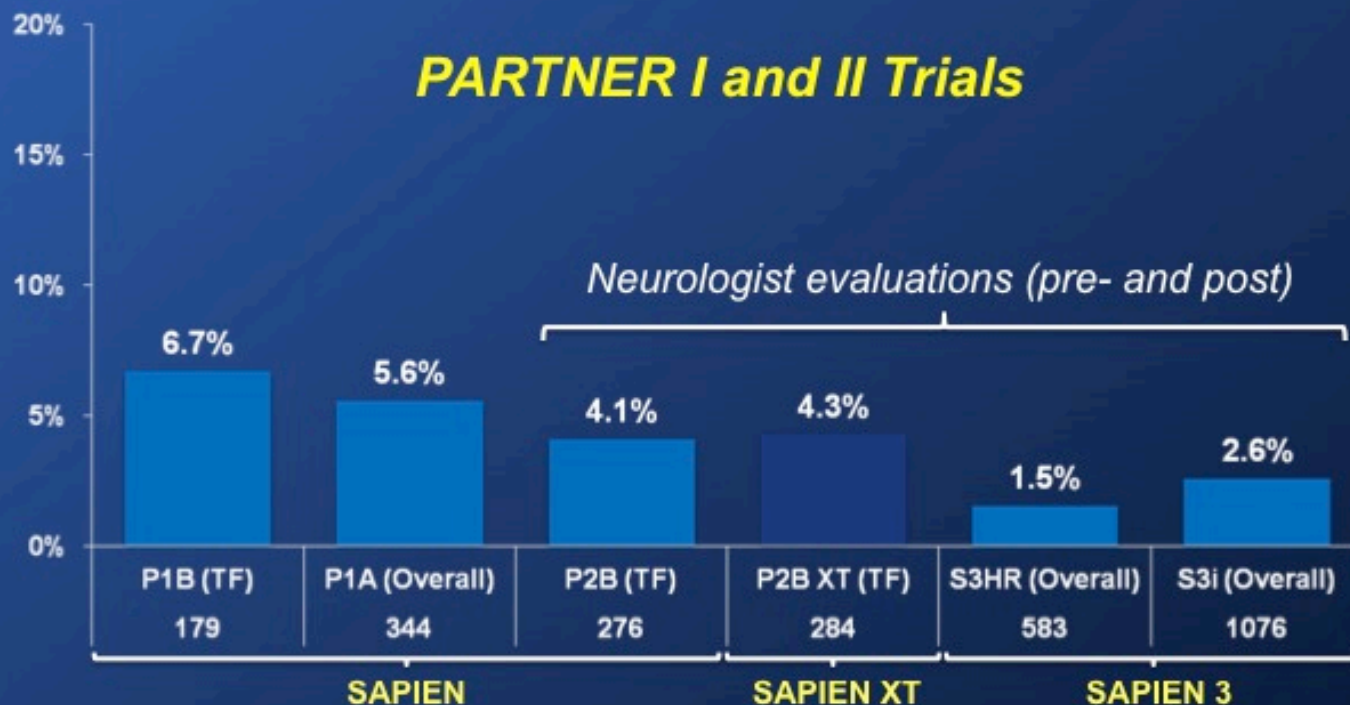




## All Strokes at 30 Days Edwards SAPIEN Valves



### *PARTNER I and II Trials*





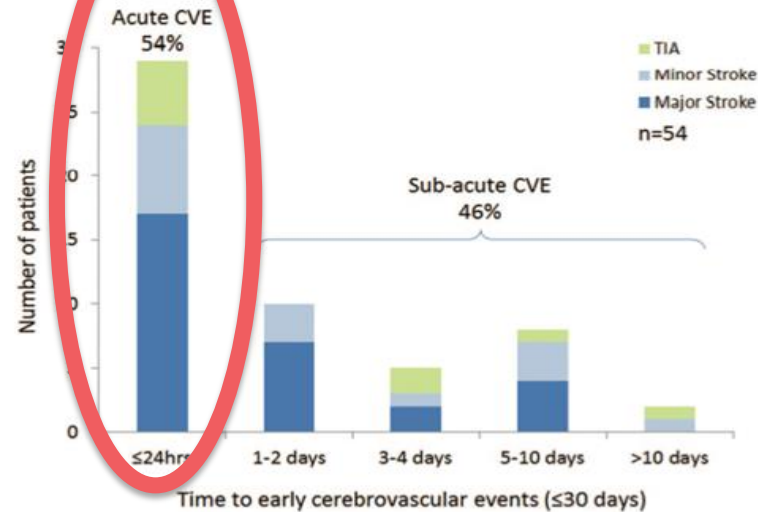
## TAVI & Timing of Cerebral Embolization (TCD)

### Stroke

#### Timing, Predictive Factors, and Prognostic Value of Cerebrovascular Events in a Large Cohort of Patients Undergoing Transcatheter Aortic Valve Implantation

Luis Nombela-Franco, MD; John G. Webb, MD; Peter P. de Jaegere, MD, PhD; Stefan Toggweiler, MD; Rutger-Jan Nuis, MSc; Antonio E. Dager, MD; Ignacio J. Amat-Santos, MD; Anson Cheung, MD; Jian Ye, MD; Ronald K. Binder, MD; Robert M. van der Boon, MSc; Nicolas Van Mieghem, MD; Luis M. Benitez, MD; Sergio Pérez, MD; Javier Lopez, MD, PhD; José A. San Roman, MD, PhD; Daniel Doyle, MD; Robert DeLeonchellière, MD; Marina Urena, MD; Jonathon Leipsic, MD; Eric Dumont, MD; Josep Rodés-Cabau, MD

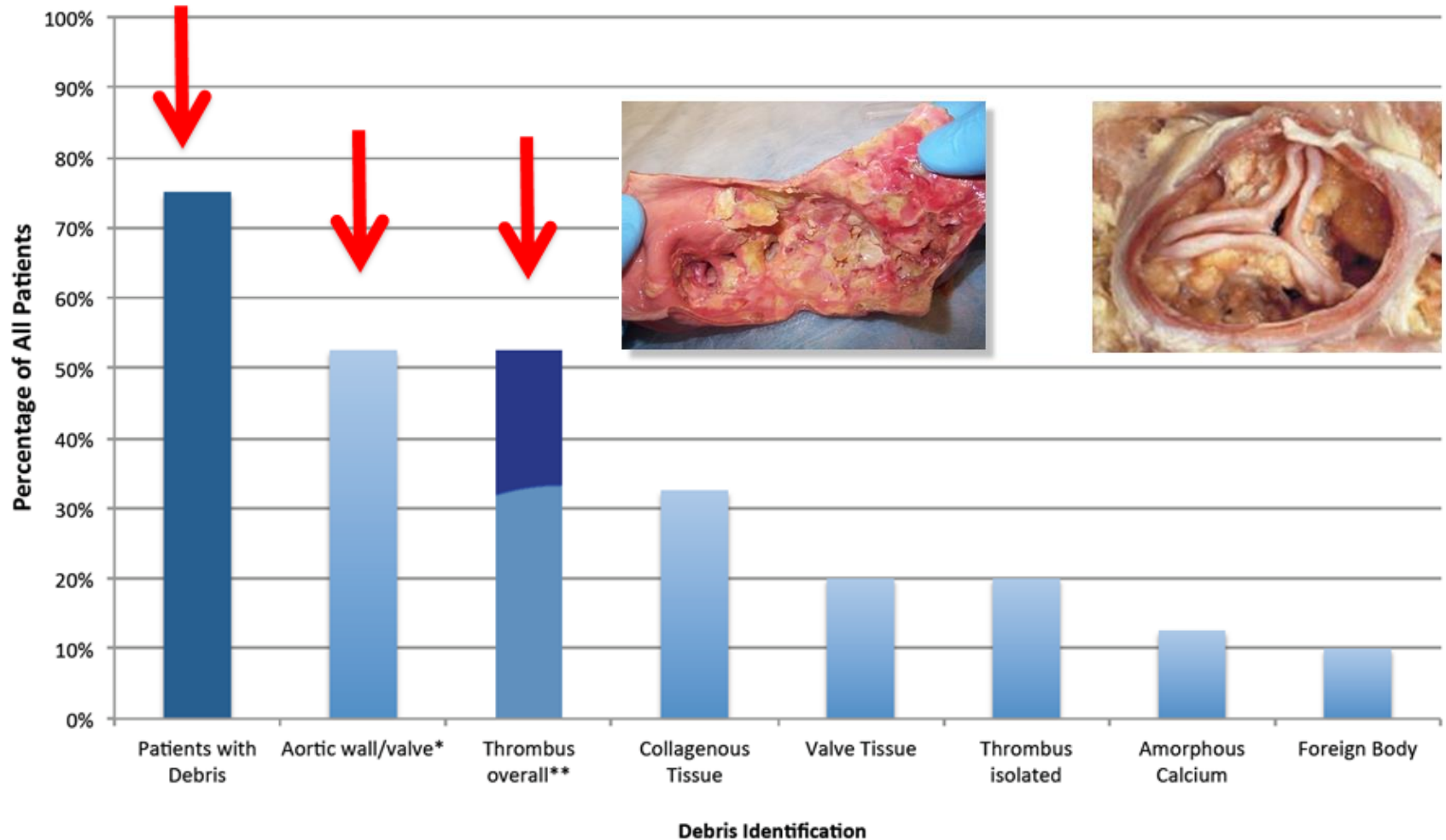
Multi-centre study Cohort  
1061 Patients



Nombela-Franco et al. Circulation 2012;126:3041-53



## TAVI – Debris Pathology (n = 40)



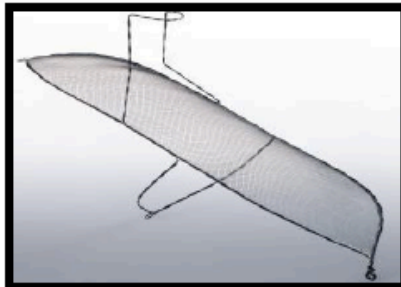
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## Cerebral Embolic Protection

TriGuard™ Cerebral	Embrella™	Claret Sentinel™
Deflector	Deflector	Dual Filter
Femoral Access	Radial Access	Radial Access
9F Sheath (7F Delivery)	6F Shuttle Sheath	6F Radial Sheath
240 micron pore size	100 micron pore size	140 micron pore size
Aortic arch position	Aortic arch position	Brachiocephalic and LCC



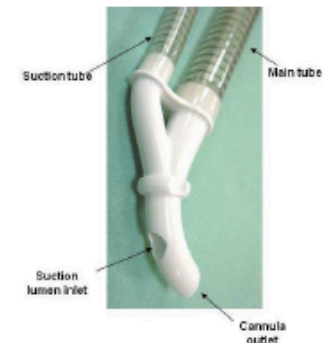
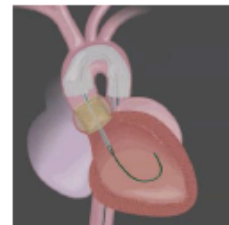
**Embolic debris "deflection" or  
Filtration, "capture & remove"**












## Future Technology

- **Emboline (TAVR) - Aortic arch jacket**
- **Innovative CV Solutions/Emblok™ (TAVR) Similar to Emboline**
- **Gardia (CAS, TAVR) - Filter**
- **Cardioptimus (SAVR, TAVR) – Deflection**
- **Transverse – Deflection**
- **Cardiogard (SAVR) – Aspiration Cannula**





## TAVR Adjunct Pharmacology *Customized Patient-Based Therapy*

BEFORE-	DURING	AFTER
Acetylsalicylic acid (ASA)	<b>UNFRACTIONATED HEPARIN:</b> target ACT $\geq 300''$	ASA + CLOPIDOGREL  Acetylsalicylic acid (ASA) ARTE trial
	Bivalirudin:   <small>Bivalirudin and Acute Valve Intervention Outcomes</small>	Non anti-VKA Oral Anticoagulant $\pm$ ASA:  
	Low Molecular Weight Heparin 	

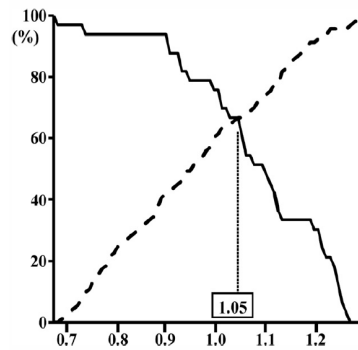
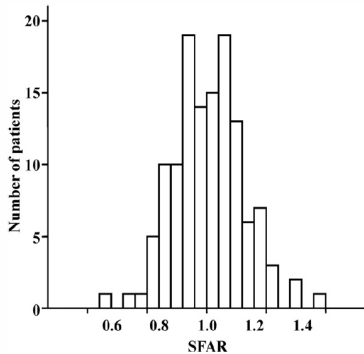


# Les complications vasculaires ?

Events (%)	S3HR+I Overall (n=1659)	Lotus Respond (n=250)
<b>Major Vascular Cpc</b>	<b>5.3</b>	<b>2,4</b>

## ANATOMICAL CRITERIA TO PREDICT VASCULAR COMPLICATIONS

SHEATH TO FEMORAL ARTERY RATIO USING ANGIOGRAPHY (SFAR)

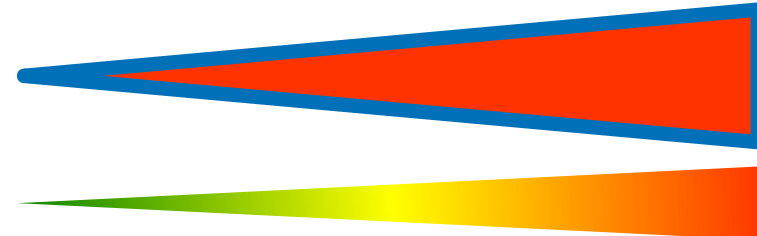


- SFAR 1.0 for calcified arteries
- SFAR 1.10 for non-calcified arteries

PCI	FUTURE?	NEW GENERATION TAVI DEVICES			PREVIOUS GENERATION TAVI DEVICES	
6 Fr	12 Fr	14 Fr	16 Fr	18 Fr	22 Fr	24 Fr
3.1	12.6	17.1	22.3	28.3	42.2	50.2

INNER SHEATH DIAMETER  
AREA (MM<sup>2</sup>)

PROFILE

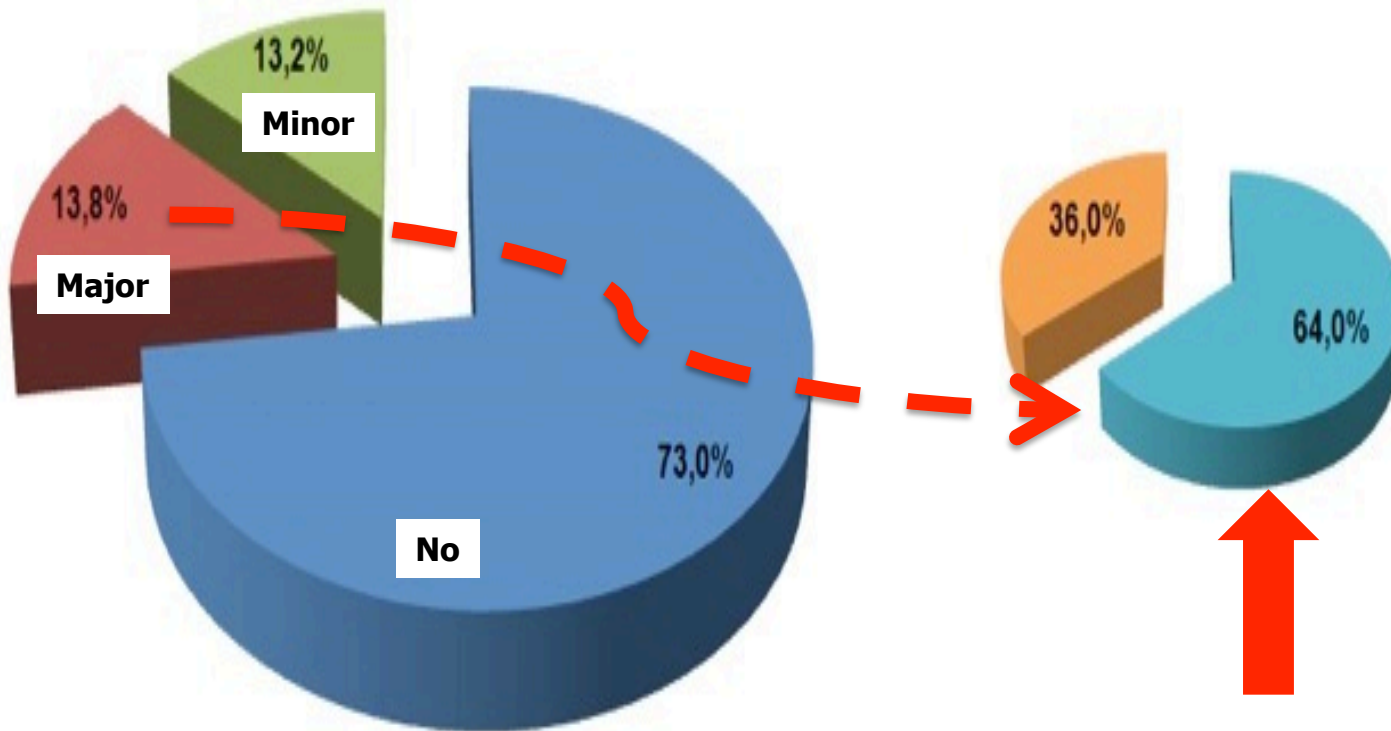


RISK FOR VASCULAR COMPLICATION



# Les complications vasculaires ?




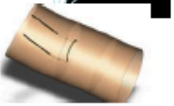
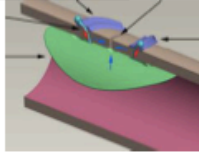
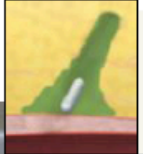
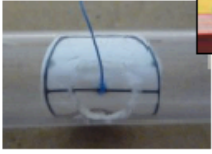

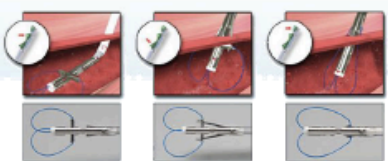
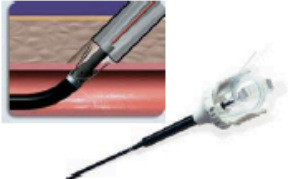


## vascular complications & closure device failure





# Les complications vasculaires ?

## Large Vessel Closure Landscape

Category	Company	Technology
Emerging Suture Based Technologies	Sutura Superstich	
	MediGlobe	
	SpiRx	
	Vasostich	
Emerging Patch or Plug Technologies	Vivasure	
	Access Closure-GRIP	
	InSeal	
	Promed	
Strategic Players	Medtronic, Inc.	
	Abbott Vascular	
	St. Jude Medical	
	Cook/Cardica	

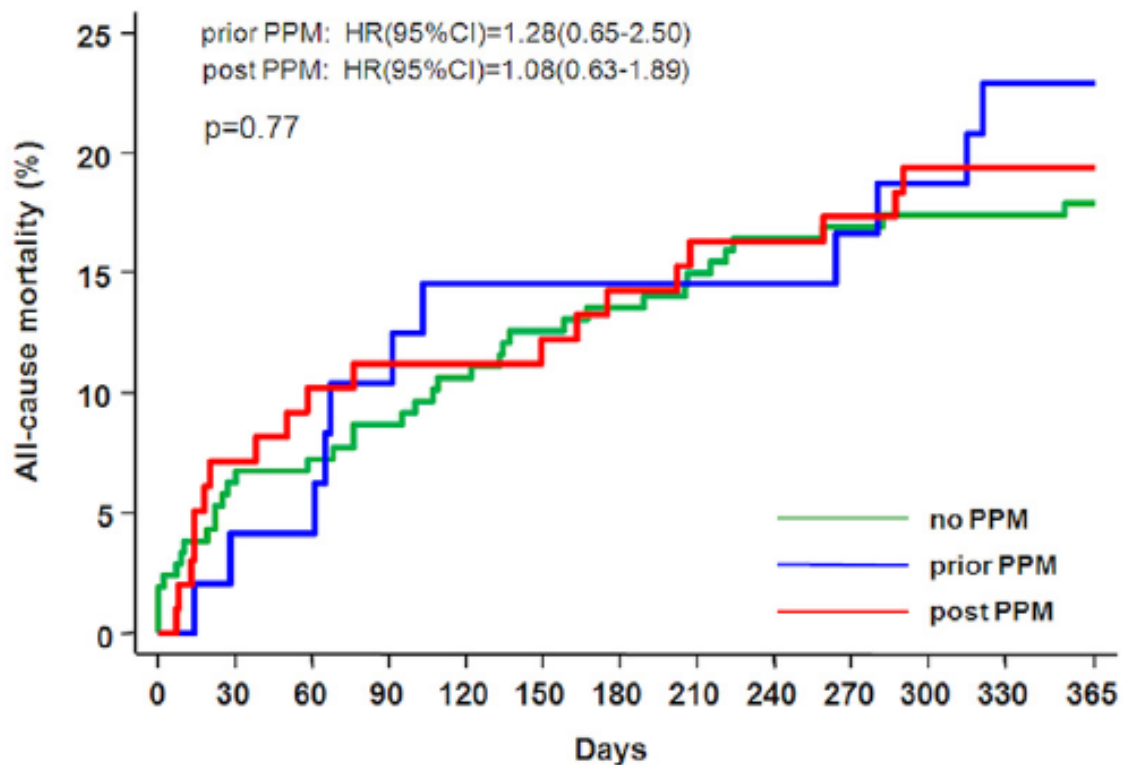


# L'implantation d'un pacemaker ?

Journal of  
© 2012 B  
Published

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xx, No. x, 2012  
735-1097/36.00  
jacc.2012.03.054

Number at risk

no PPM	207	194	191	188	184	180	178	175	172	171	170	170	169
prior PPM	48	46	46	43	41	41	41	41	41	40	39	37	37
post PPM	98	91	88	87	87	86	84	82	82	81	79	79	79



# L'implantation d'un pacemaker ?

## New PPM: Indications & Timing

### 250-Patient Interim Analysis

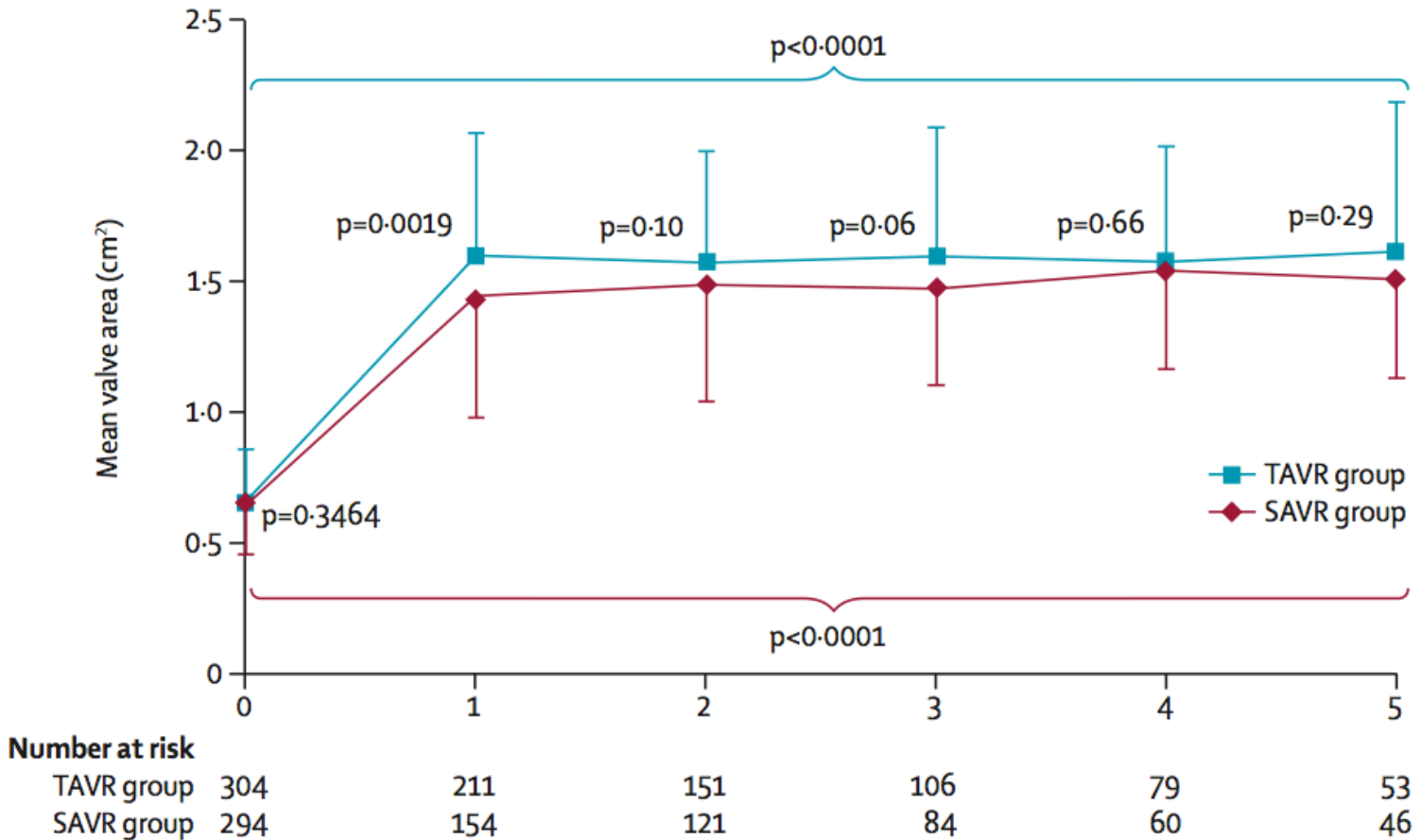
RESPOND 

Indication	N	Indication	N
3 <sup>rd</sup> degree AV block	45 (54.2%)	2 <sup>nd</sup> degree AV block type 1 & LBBB	3 (3.6%)
LBBB & 1 <sup>st</sup> degree AV block	12 (14.5%)	Trifascicular block	1 (1.2%)
New LBBB, symptomatic bradycardia	10 (12.0%)	LBBB, EP study showing severe infranodal disease	1 (1.2%)
Atrial fibrillation & bradycardia	5 (6.0%)	2 <sup>nd</sup> degree AV block type 2	1 (1.2%)
2 <sup>nd</sup> degree AV block type 1, No LBBB	4 (4.8%)	Intermittent sinus arrest	1 (1.2%)

- ➔ Approximately half of pacemaker indications were for indications other than complete heart block
- ➔ Nearly 40% (33/83) of new PPM were implanted on Days 0 to 2
- ➔ Delaying implantation may allow restoration of normal sinus rhythm



# Aortic Valve Area - Durability





**Le futur du TAVI**

**Des innovations ?**

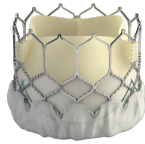
# EDWARDS Pipeline

EMEA

U.S.

Japan

## Today



SAPIEN 3  
23/26/29mm  
20 mm\*

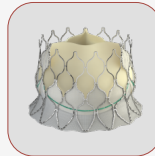


SAPIEN XT  
23/26/29mm

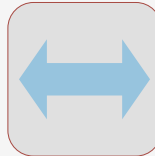


SAPIEN XT  
23/26mm

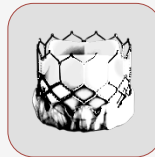
## Future



**CENTERA**



**Expanded Indications**

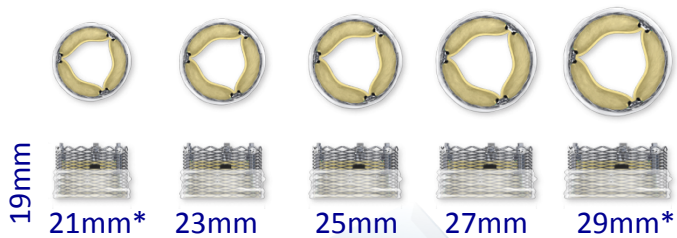


**Next Generation  
Balloon-Expandable**



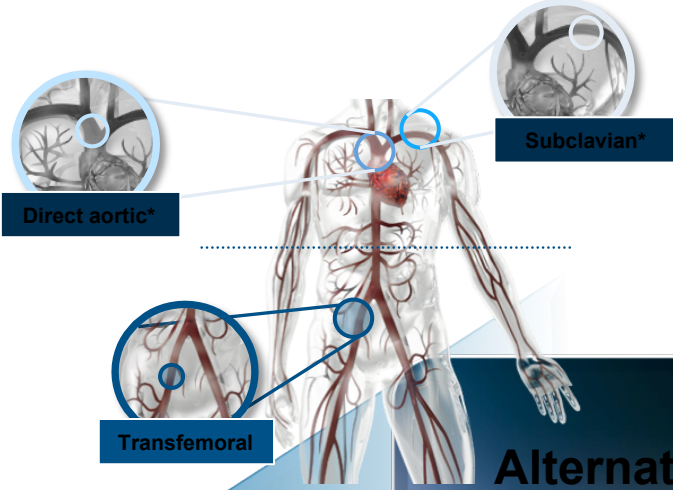
**Next Generation  
Self-Expanding**

# BSC LOTUS Pipeline



**Complete Size Matrix**

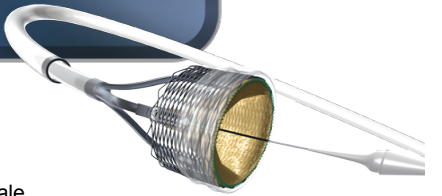
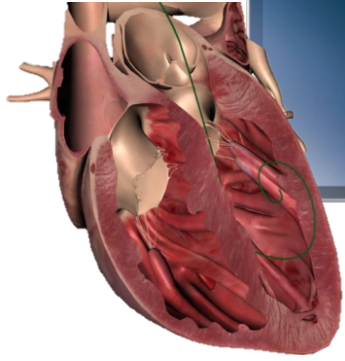
**FUTURE PIPELINE**



**Alternate Access Routes**

**TAVR-Dedicated Wires\***

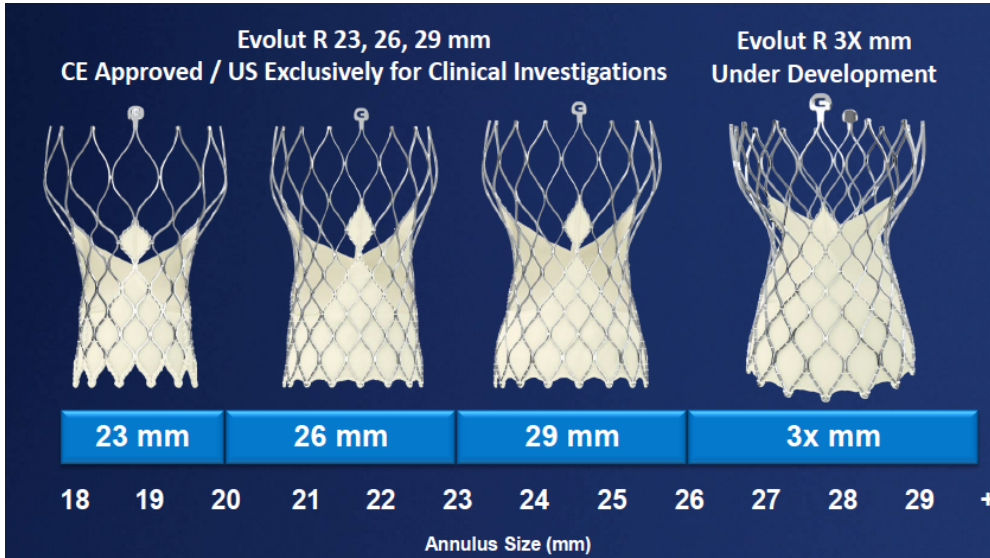
**Enhanced Delivery System\***



\* Future Lotus product portfolio and are only displayed for informational purposes, not available for sale

# Medtronic Pipeline

# Evolut R



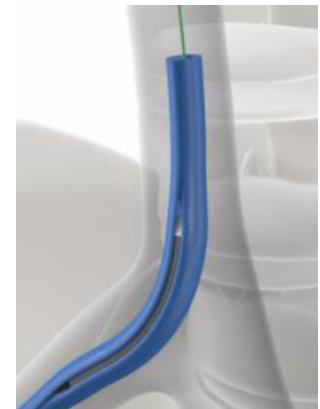
**Confida Profile Adaptive Sheath**  
Expands to 18F ID & self-contracts to 13F ID  
Smaller profile & improved navigation



Capsule  
InLine Sheath  
18Fr Maximum Outer Diameter (4Fr Profile Reduction)

CoreValve®	Evolut™ R
with 18Fr Cook Sheath	with 14Fr-Equivalent InLine™ Sheath
18Fr	18Fr
22 Fr (OD)	True 18Fr (OD)

**Indication Minimum Vessel Diameters ≥ 5.0mm**



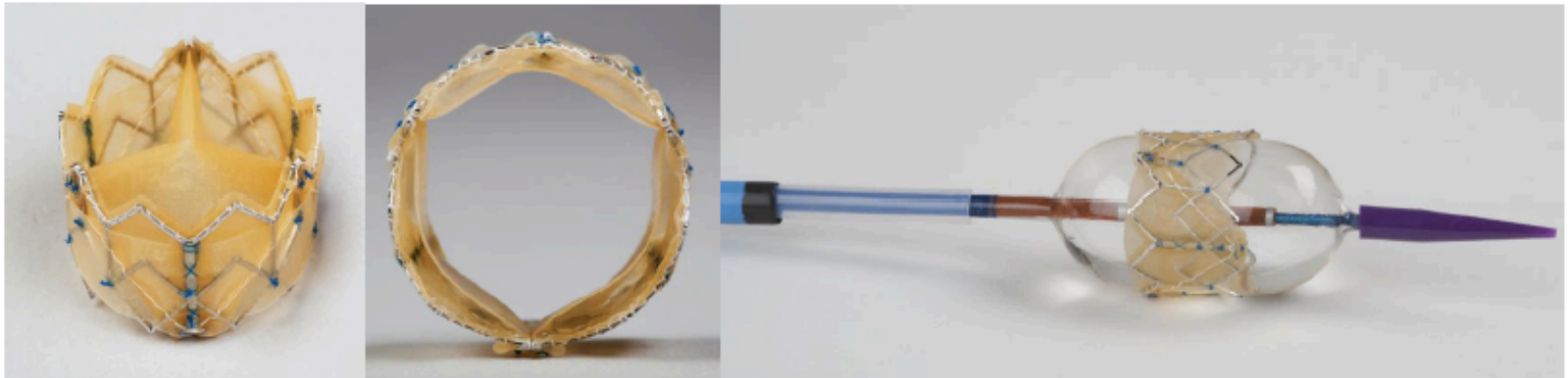
# Upcoming TAVI Devices (#20)

- Sapien 3
- Evolut R
- Symetis
- Direct Flow
- Lotus
- Jena Valve
- Engager
- Portico
- Centera
- Venus A
- Trinity
- Colibri
- Braile
- Thubrikar
- Valve Medical
- Syntheon
- Triskele
- MyVal
- HLT
- Zurich TEHV



# Colibri

## *Valve & System Design*



- Thin dry-leaflet technology; folded continuous surface design with few sutures; adjusts to out-of-round anatomies and large EOA ( $> 2\text{cm}^2$ )
- Pre-packaged, pre-crimped, low profile, ready-for-use
- Balloon-expandable 14 Fr delivery system
- Valve sizes: 21mm, 24mm, and 27mm

# Optimum (Thubrikar)

## *Valve & System Design*

- Single bovine pericardial cut-out used for all three leaflets
- Commissure posts for proper opening and optimal coaptation surface
- Valve design minimizes sutures (no suture holes in moving leaflets) and provides large EOA
- 25mm OD self-expanding Nitinol frame
  - up to 23mm annulus
  - stronger radial force
  - 19-20 mm height
- 20.4 Fr sheathless delivery system



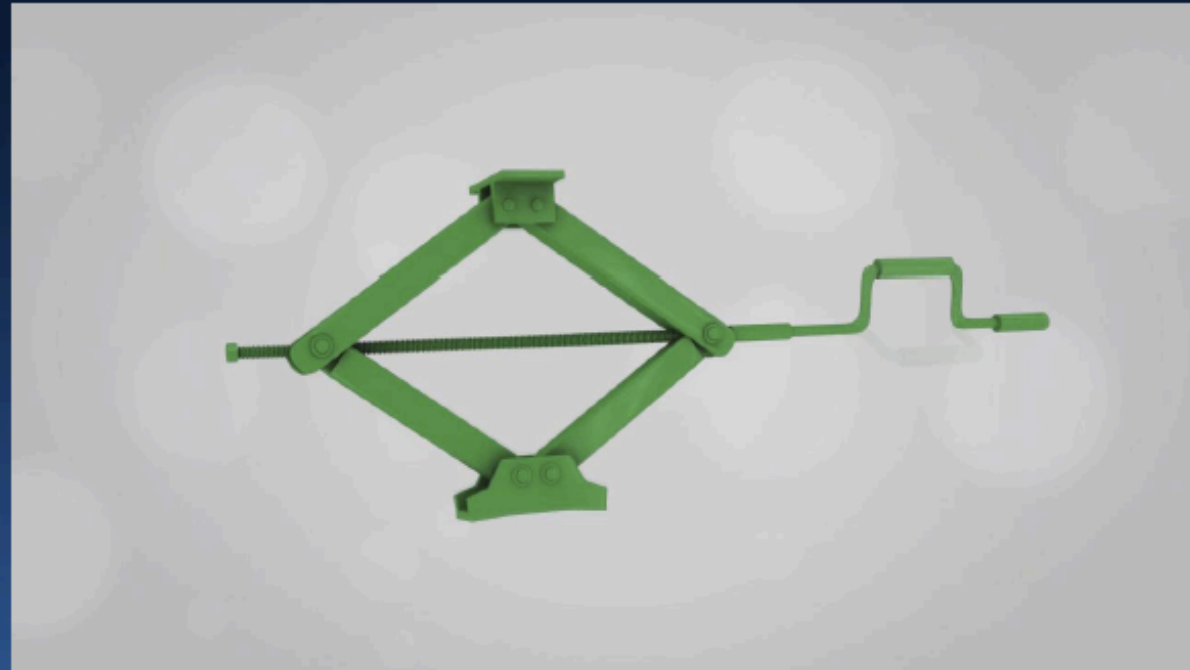
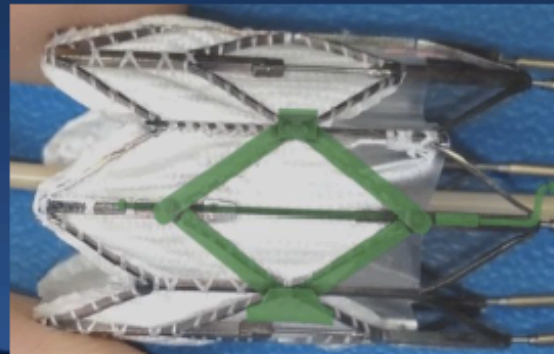
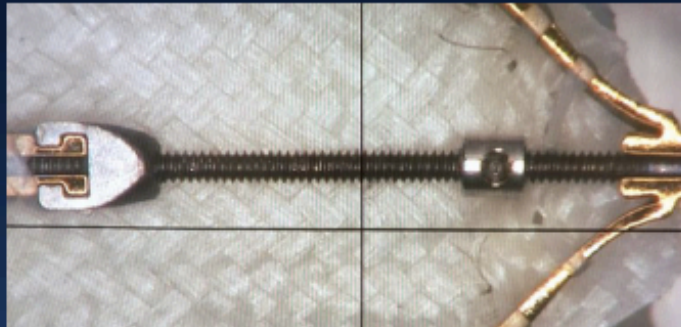
# Syntheon Cardiology Precision Actuated Framework



- **Actuator Driven Expansion**
- **Microprocessor Controlled**
- **Constant Radial Force**
- **Fully Repositionable**
- **Fully Retrievable**
- **Full Verification of Valve Position and Seal Quality**
- **Simple Controls with Feedback**

# Syntheon Cardiology TAVR

- Nitinol Framework
- Micro Screw Actuators
- High Mechanical Advantage
- Exact and Reversible Control
- Continuous Feedback of Diameter and Radial Force
- Accurate Diameter Measurement
- Self-locking Screws Hold Position



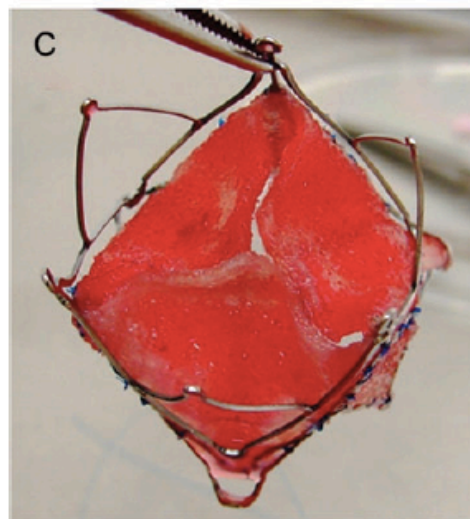
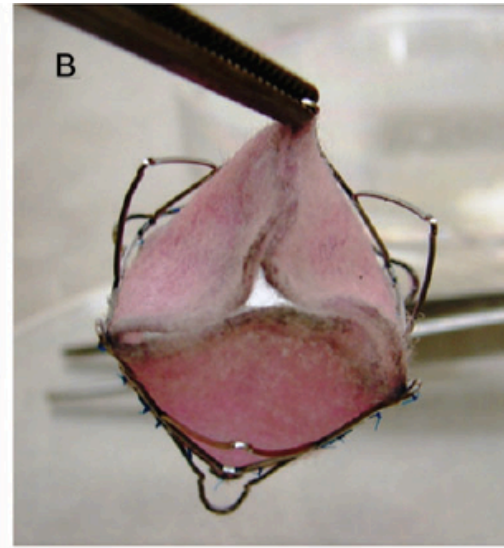
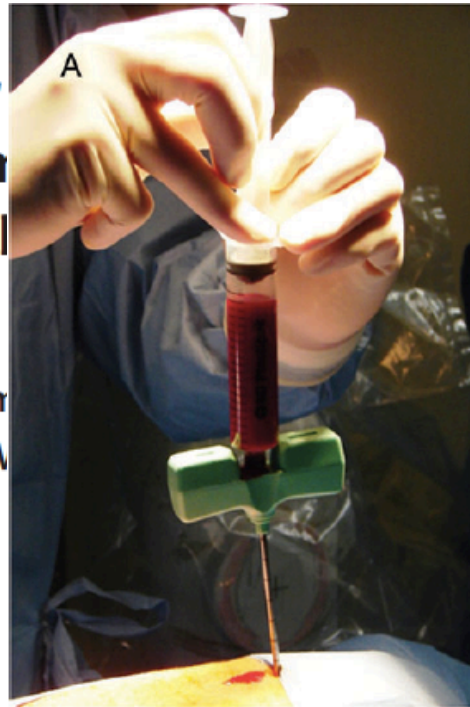
# LEAFLEX Aortic valve Remodeling

- ✓ Mechanical shock waves fracture calcium within valve
- ✓ Increased leaflet compliance: significant, true increase in AVA
- ✓ Trans-femoral 13Fr catheter
- ✓ Non-occlusive: no rapid pacing
- ✓ Device can be used as:
  - ✓ Stand-alone therapy
  - ✓ Bridge to TAVR or SAVR
  - ✓ Preparation for TAVR



# Transcatheter marrow strom technical

Maximilian Y. Emm  
Petra V



# ically oriented, ed heart valves: nsational

Thomas Frauenfelder<sup>a</sup>,  
nfelder<sup>b,c</sup>,



# Conclusion

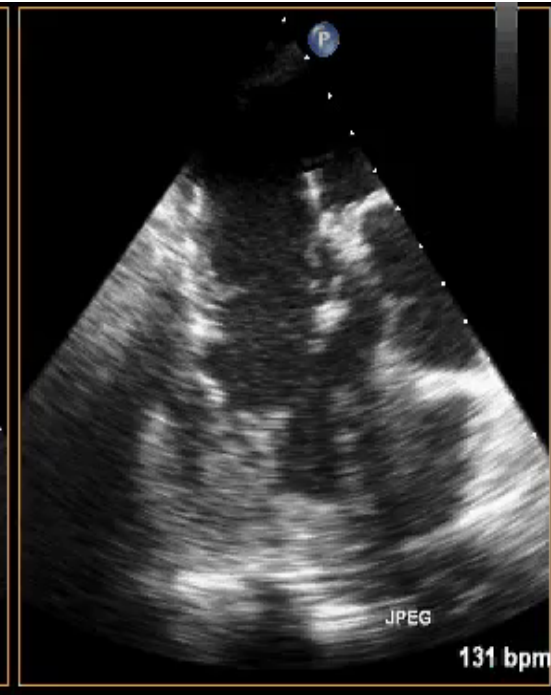
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- Les résultats actuels du TAVI, avec les prothèses de dernière génération démontrent un profil de sécurité/efficacité excellent chez les patients à haut risque (mortalité opératoire < 2 %, AVC majeurs < 2 %, fuites para-valvulaires impactant le pronostic < 2 %, cpc vas majeures 5 %)
- Ces résultats sont encore meilleurs chez les patients à risque intermédiaire.
- Une extension future des indications est inéluctable
- Elle passera bien sur par la validation par des essais cliniques randomisés / chirurgie
- De nombreuses innovations sont en cours de développement, qui, pour certaines amélioreront encore les performances des dispositifs actuels



# Conclusion

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# Où en sommes nous en 2015 ?

**THE ANNALS  
OF THORACIC  
SURGERY**

*Official Journal of The Society of Thoracic Surgeons  
and the Southern Thoracic Surgical Association*

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**JOURNAL CITATION REPORTS 2015  
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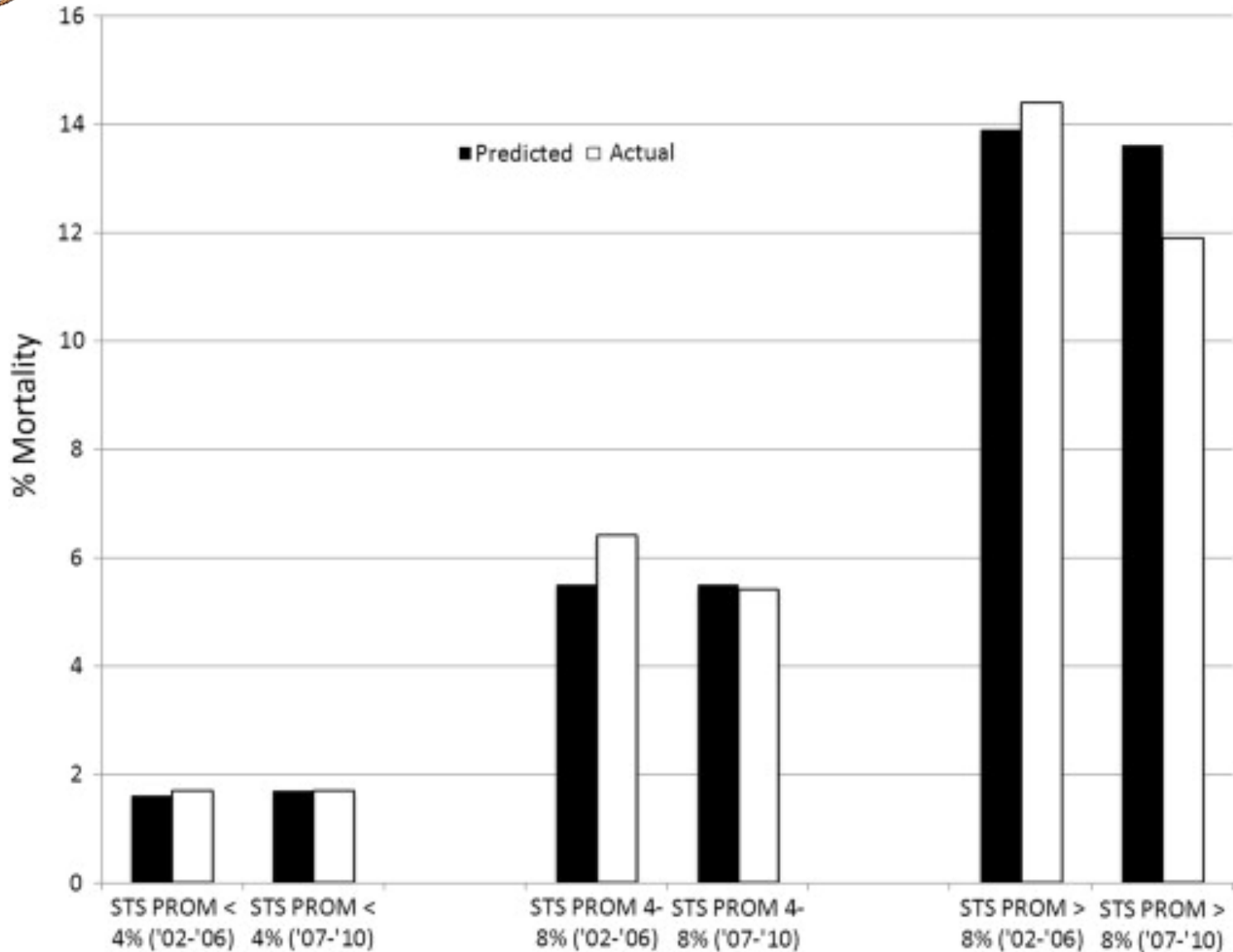
## ***Contemporary Real-World Outcomes of Surgical Aortic Valve Replacement in 141,905 Low-Risk, Intermediate-Risk, and High-Risk Patients***

***Vinod H. Thourani, MD, Rakesh M. Suri, MD, DPhil, Rebecca L. Gunter, MD, Shubin Sheng, PhD, Sean M. O'Brien, PhD, Gorav Ailawadi, MD, Wilson Y. Szeto, MD, Todd M. Dewey, MD, Robert A. Guyton, MD, Joseph E. Bavaria, MD, Vasilis Babaliaros, MD, James S. Gammie, MD, Lars Svensson, MD, PhD, Mathew Williams, MD, Vinay Badhwar, MD, Michael J. Mack, MD***

***The Annals of Thoracic Surgery***  
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# Où en sommes nous en 2015 ?



# DeNOVO Study

## Cardiovascular Surgery

### Stroke After Aortic Valve Surgery Results From a Prospective Cohort

Steven R. Messé, MD; Michael A. Acker, MD; Scott E. Kasner, MD; Molly Fanning, BS;  
Tania Giovannetti, PhD; Sarah J. Ratcliffe, PhD; Michel Bilello, MD, PhD;  
Wilson Y. Szeto, MD; Joseph E. Bavaria, MD; W. Clark Hargrove, III, MD;  
Emile R. Mohler III, MD; Thomas F. Floyd, MD;  
for the Determining Neurologic Outcomes from Valve Operations (DeNOVO) Investigators

**Background**—The incidence and impact of clinical stroke and silent radiographic cerebral infarction complicating open surgical aortic valve replacement (AVR) are poorly characterized.

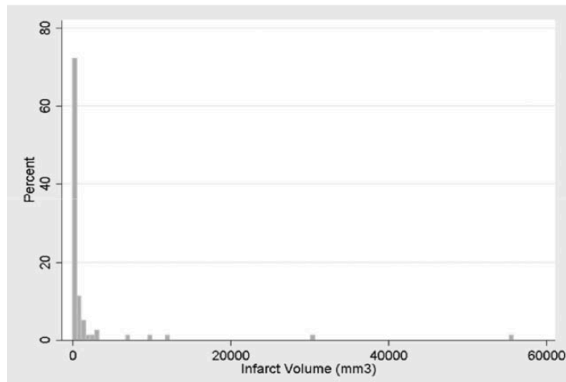
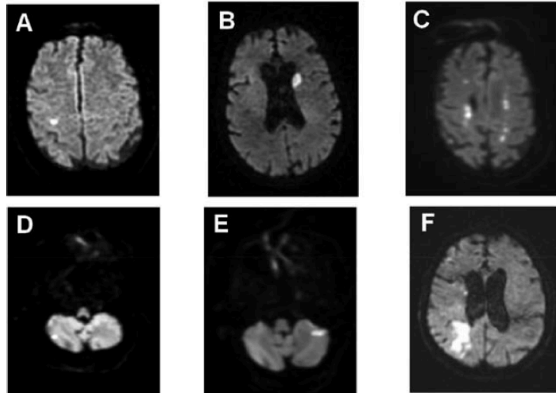
**Methods and Results**—We performed a prospective cohort study of subjects  $\geq 65$  years of age who were undergoing AVR for calcific aortic stenosis. Subjects were evaluated by neurologists preoperatively and postoperatively and underwent postoperative magnetic resonance imaging. Over a 4-year period, 196 subjects were enrolled at 2 sites (mean age,  $75.8 \pm 6.2$  years; 36% women; 6% nonwhite). Clinical strokes were detected in 17%, transient ischemic attack in 2%, and in-hospital mortality was 5%. The frequency of stroke in the Society for Thoracic Surgery database in this cohort was 7%. Most strokes were mild; the median National Institutes of Health Stroke Scale was 3 (interquartile range, 1–9). Clinical stroke was associated with increased length of stay (median, 12 versus 10 days;  $P=0.02$ ). Moderate or severe stroke (National Institutes of Health Stroke Scale  $\geq 10$ ) occurred in 8 (4%) and was strongly associated with in-hospital mortality (38% versus 4%;  $P=0.005$ ). Of the 109 stroke-free subjects with postoperative magnetic resonance imaging, silent infarct was identified in 59 (54%). Silent infarct was not associated with in-hospital mortality or increased length of stay.

**Conclusions**—Clinical stroke after AVR was more common than reported previously, more than double for this same cohort in the Society for Thoracic Surgery database, and silent cerebral infarctions were detected in more than half of the patients undergoing AVR. Clinical stroke complicating AVR is associated with increased length of stay and mortality. (*Circulation*. 2014;129:2253-2261.)

- ✓ Prospective Study in 2 centers in Pennsylvania
- ✓ 196 Patients with SAVR
- ✓ Mean age 75 years, 36% Female
- ✓ Pre- and serial postop assessment by neurologist
- ✓ Brain MRI post SAVR median Day 6

Messe et al. *Circulation* 2014;129:2253-61

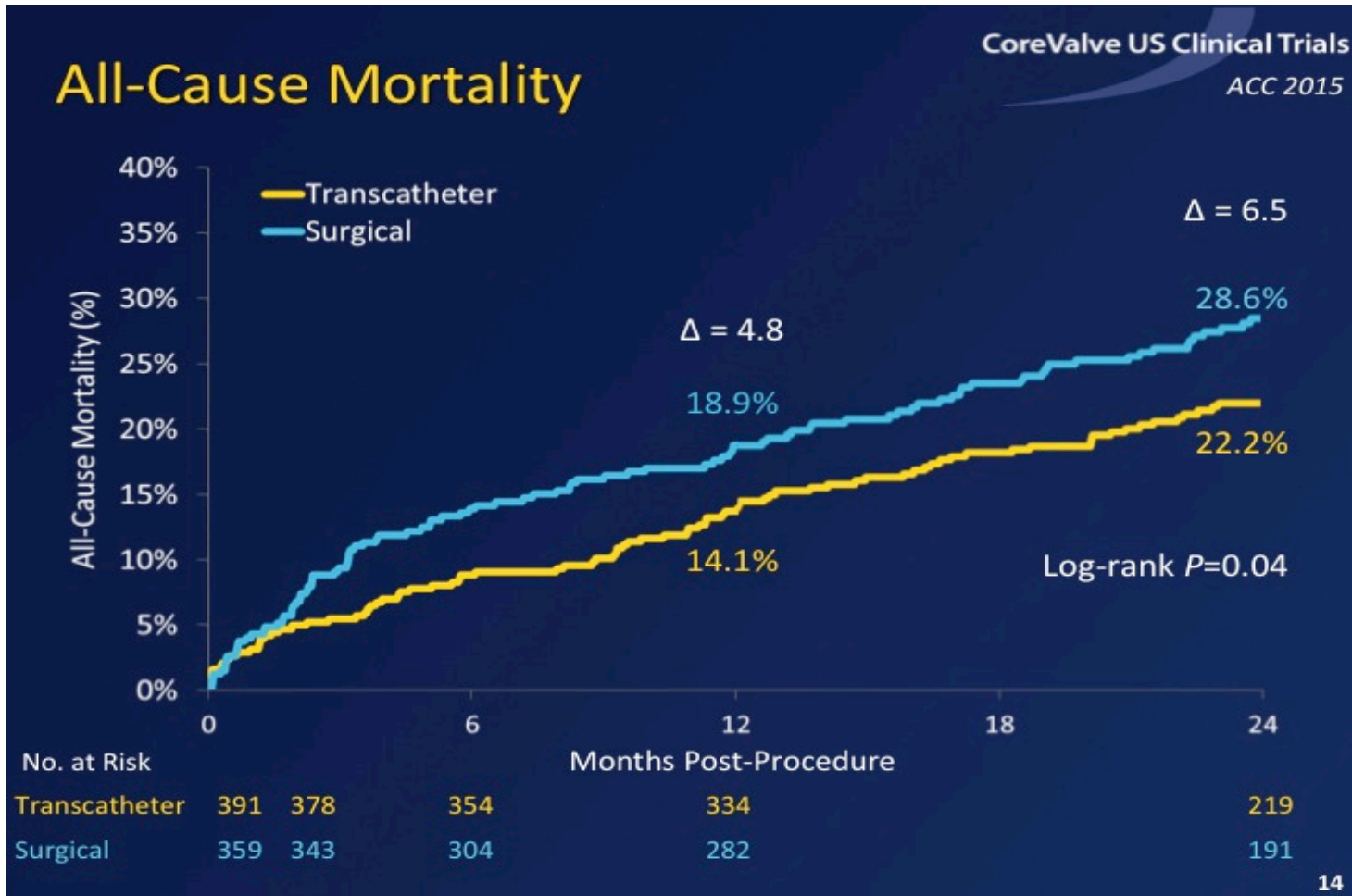
# DeNOVO Study



- ✓ **Clinical Strokes in 17% (median NIHSS 3 = mild)**
  - ✓ 58% on Day 1
  - ✓ Moderate to severe stroke (NIHSS > 10) in 4%
- ✓ **109 patients with no clinical stroke underwent brain MRI**
  - ✓ Silent infarct in 54%!



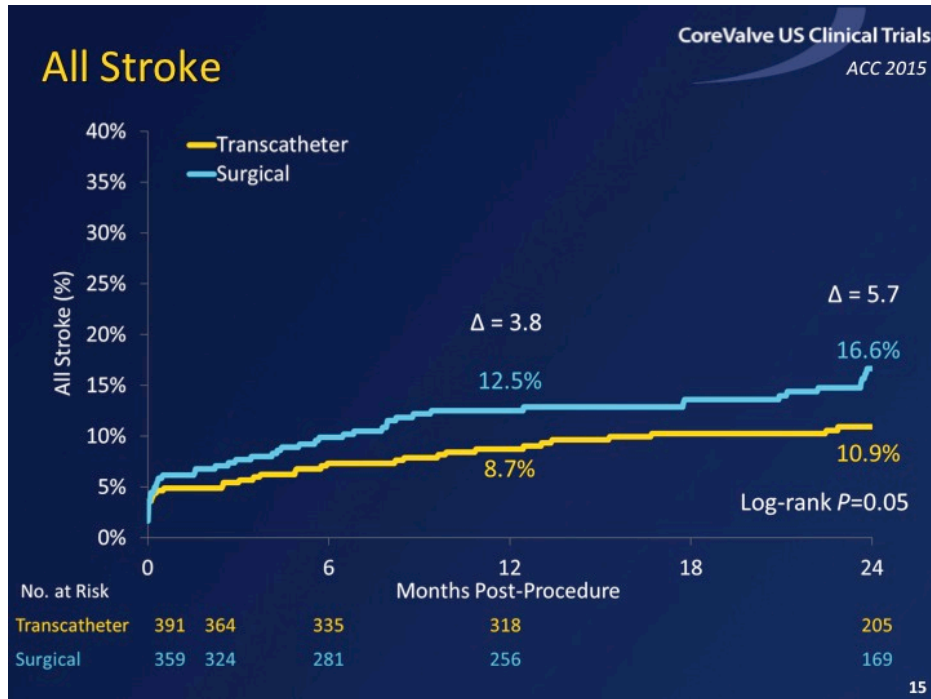
# Où en sommes nous en 2015 ?



**Supériorité TAVI / Chirurgie  
Patients à haut risque**



# Où en sommes nous en 2015 ?

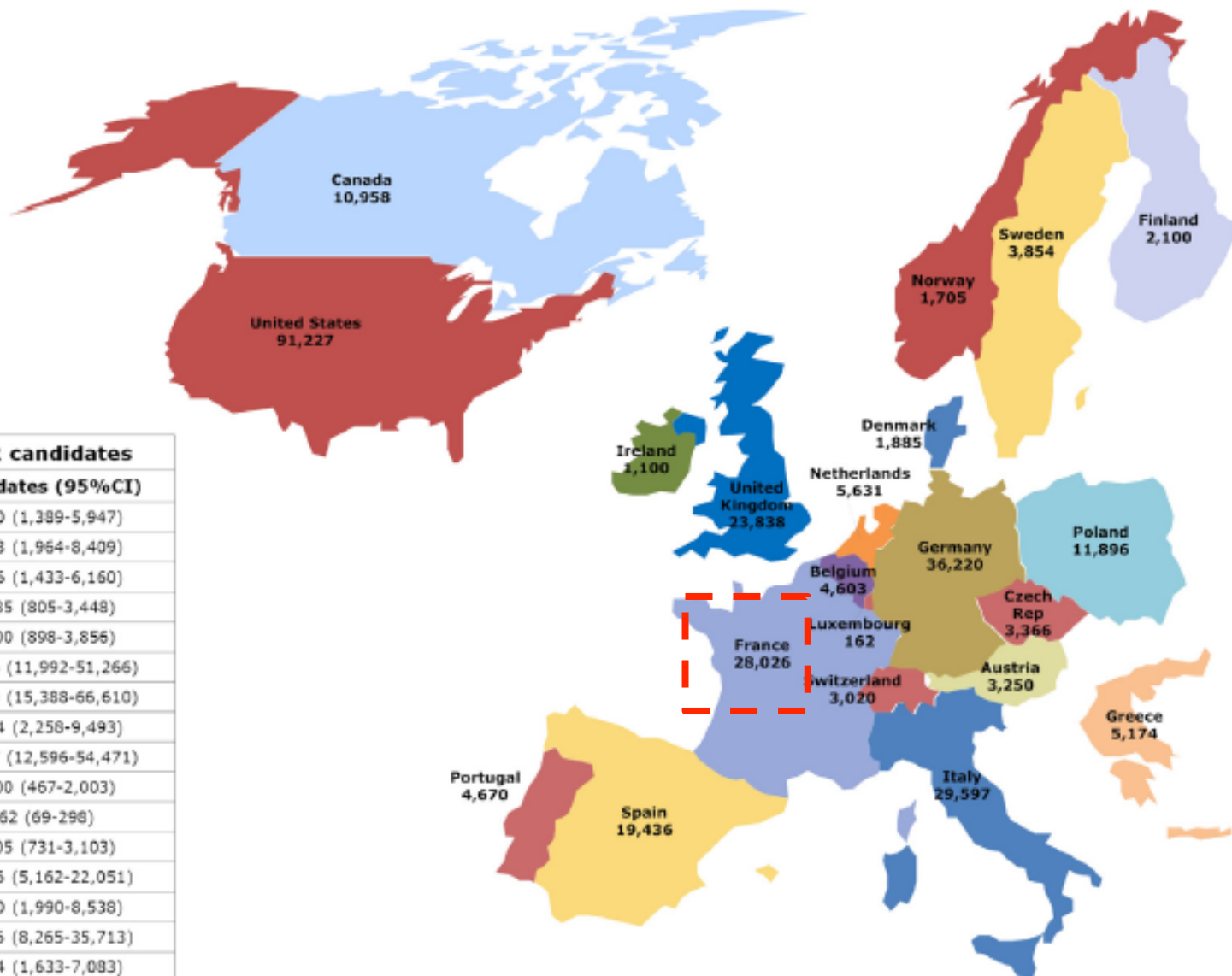


**Other Clinical Endpoints** CoreValve US Clinical Trials ACC 2015

Events*	1 Month			1 Year			2 Years		
	TAVR	SAVR	P	TAVR	SAVR	P	TAVR	SAVR	P
Vascular complications (major)	6.2	1.7	0.002	6.4	2.0	0.003	7.1	2.0	0.001
Pacemaker implant	20.0	7.1	<0.001	22.5	11.6	<0.001	25.8	12.8	<0.001
Bleeding (life threatening or disabling)	13.6	35.1	<0.001	16.5	38.4	<0.001	18.1	39.6	<0.001
New onset or worsening atrial fibrillation	11.7	31.0	<0.001	16.4	33.2	<0.001	19.5	34.9	<0.001
Acute kidney injury	6.2	15.1	<0.001	6.2	15.1	<0.001	6.2	15.1	<0.001

\* Percentages reported are Kaplan-Meier estimates and log-rank P values

**Supériorité TAVI / Chirurgie  
Patients à haut risque**



### Total number of TAVR candidates

Country	Candidates (95%CI)
Austria	3,250 (1,389-5,947)
Belgium	4,603 (1,964-8,409)
Czech Republic	3,336 (1,433-6,160)
Denmark	1,885 (805-3,448)
Finland	2,100 (898-3,856)
France	28,026 (11,992-51,266)
Germany	36,220 (15,388-66,610)
Greece	5,174 (2,258-9,493)
Italy	29,597 (12,596-54,471)
Ireland	1,100 (467-2,003)
Luxembourg	162 (69-298)
Norway	1,705 (731-3,103)
Poland	11,896 (5,162-22,051)
Portugal	4,670 (1,990-8,538)
Spain	19,436 (8,265-35,713)
Sweden	3,854 (1,633-7,083)
Switzerland	3,020 (1,280-5,554)
The Netherlands	5,631 (2,379-10,379)
The United Kingdom	23,838 (10,554-43,461)
<b>Total 19 European countries</b>	<b>189,836 (80,281-347,372)*</b>
The United States	91,227 (38,885-165,875)
Canada	10,958 (4,688-19,995)
<b>Total North America</b>	<b>102,558 (43,612-187,002)*</b>

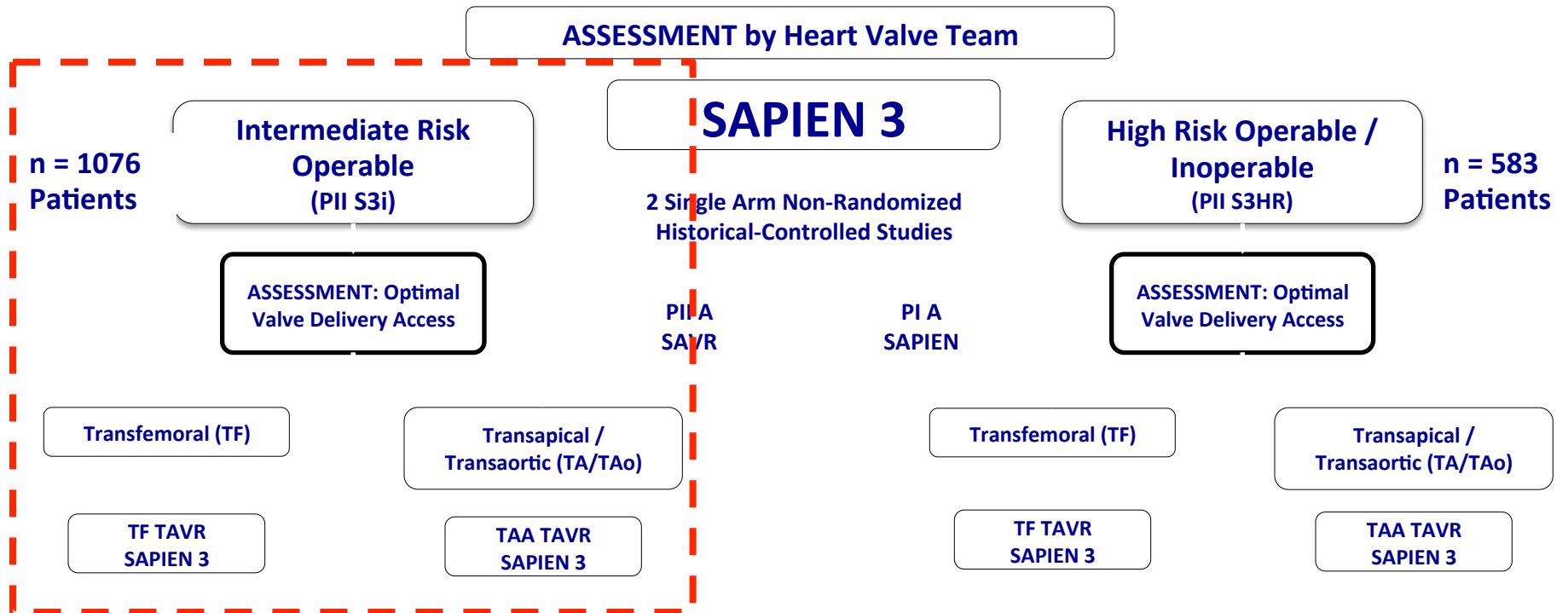
# 2014 AHA/ACC Guideline

Recommendations	COR	LOE
Surgical AVR is recommended in patients who meet an indication for AVR with low or intermediate surgical risk	I	A
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival > 1 year	I	B
TAVR is a <u>reasonable</u> alternative to surgical AVR in patients who meet an indication for AVR (Section 3.4) and who have <u>high surgical risk</u>	IIa	B
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III	B



# PARTNER II S3 Trial

## Symptomatic Severe Aortic Stenosis



# Apica ASC System

European Journal of Cardio-Thoracic Surgery Advance Access published April 5, 2013

European Journal of Cardio-Thoracic Surgery (2013) 1–6  
doi:10.1093/ejcts/ezt198

ORIGINAL ARTICLE

## First-in-man evaluation of the transapical APICA ASC™ access and closure device: the initial 10 patients<sup>†</sup>

Johannes Blumenstein<sup>a\*</sup>, Joerg Kempfert<sup>b</sup>, Arnaud Van Linden<sup>c</sup>, Mani Arsalan<sup>d</sup>, Sina K. Schmidt<sup>e</sup>,  
Helge Mollmann<sup>b</sup>, Won-Keun Kim<sup>a,b</sup>, Vinod Thourani<sup>c</sup> and Thomas Walther<sup>a</sup>

