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Medtronic: CoreValve Evolut R and Engager TAVI System

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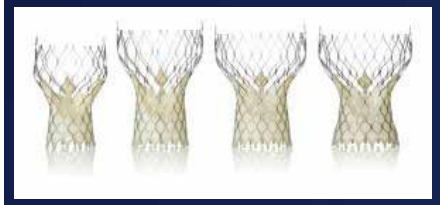
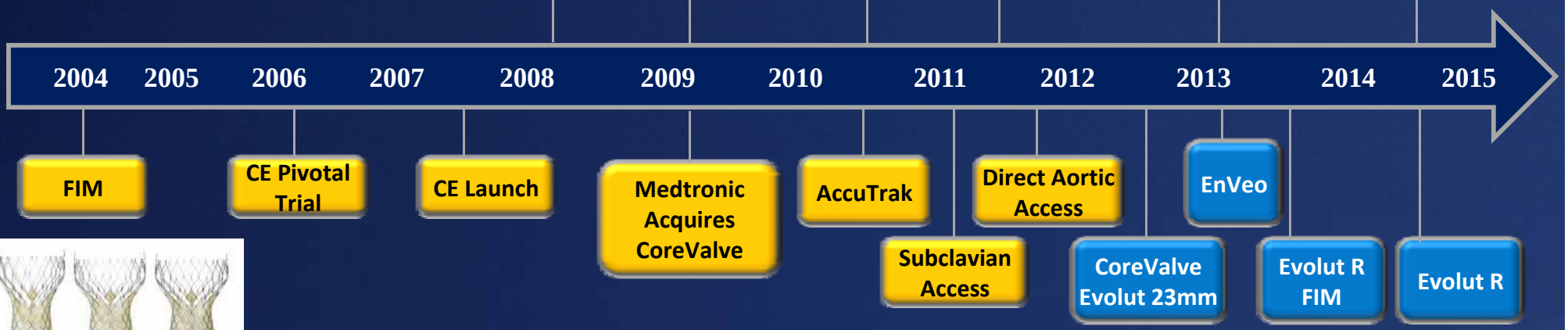
Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Physician Name	Company/Relationship
Eberhard Grube, MD	Medtronic, CoreValve: C, SB, AB, OF Sadra Medical: E, C, SB, AB Direct Flow: C, SB, AB Mitralign: AB, SB, E Boston Scientific: C, SB, AB Biosensors: E, SB, C, AB Cordis: AB Abbott Vascular: AB Capella: SB, C, AB Valtech: E, SB, Claret: SB

Medtronic's Approach to TAVI

- Strategic intent always to offer two complimentary valve platforms
- Multiple valves and multiple access routes needed in order to achieve the best outcome for every TAVI patient
- The right options – valve sizes, access routes – empower heart teams to achieve the best outcomes with every patient



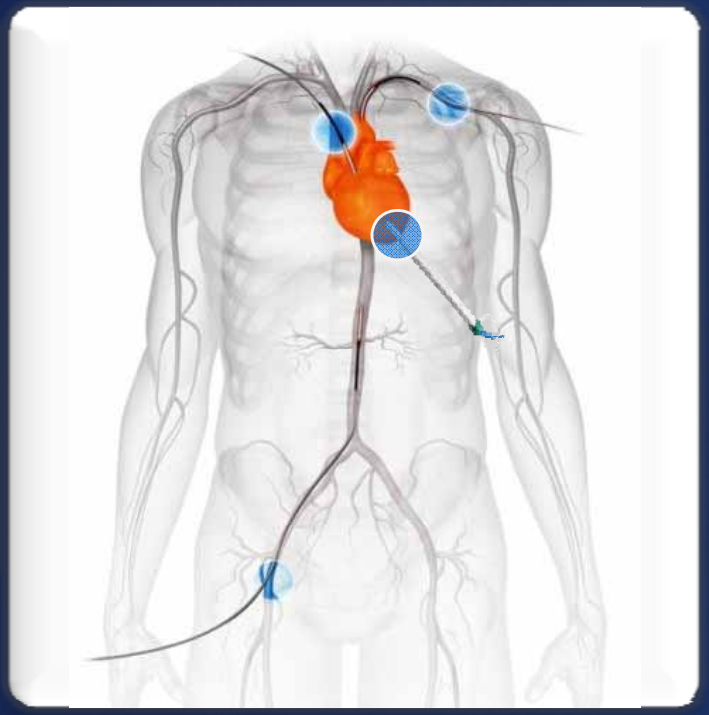


Medtronic's TAVI Portfolio: Common Factors

- Self-expanding, supra-annular valves for every access route
  - Self-expanding frames conform and seal to varying annular shapes
  - Supra-annular valve function facilitates coaptation in non-circular anatomy
  - Repositionability and controlled deployment enable proper positioning

CoreValve® Family

- Transfemoral
- Subclavian
- Direct Aortic

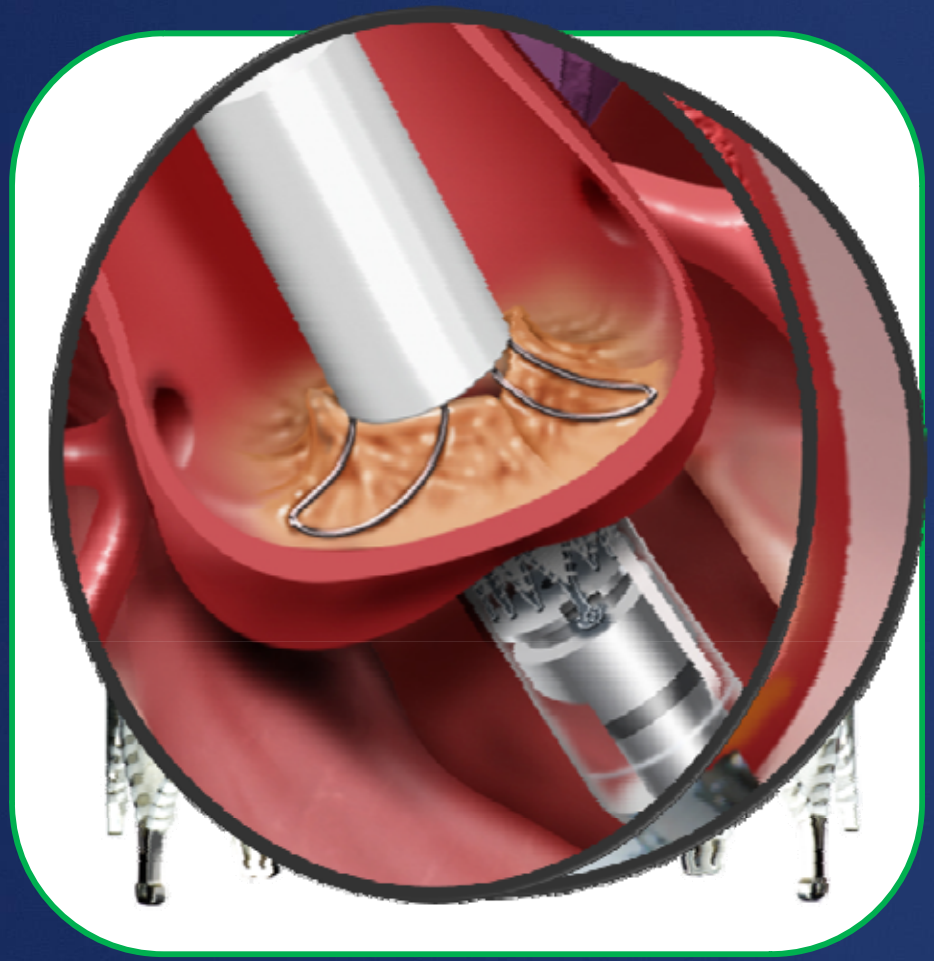


Engager™

- Transapical
- Direct Aortic

Engager Valve Design

- Control arms
- Self-expanding nitinol frame and polyester skirt
- Supra-annular valve function
- Bovine pericardial tissue

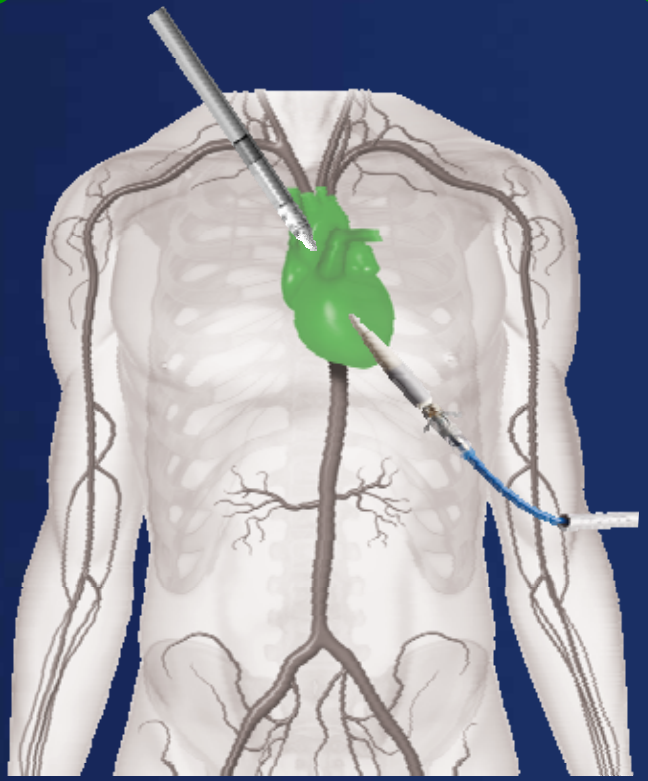


Engager Access Routes

The Engager system is designed to offer both transapical and direct aortic access routes

Direct Aortic

- Multi-center Engager DA Study underway
- Simple three step deployment
- Delivery catheter system with optional stability sheath



Transapical

- CE-Mark approved
- Simple three step deployment
- Integrated introducer sheath

CoreValve Design

Outflow

Supports valve commissures and enables controlled deployment

Low Radial Force

Waist

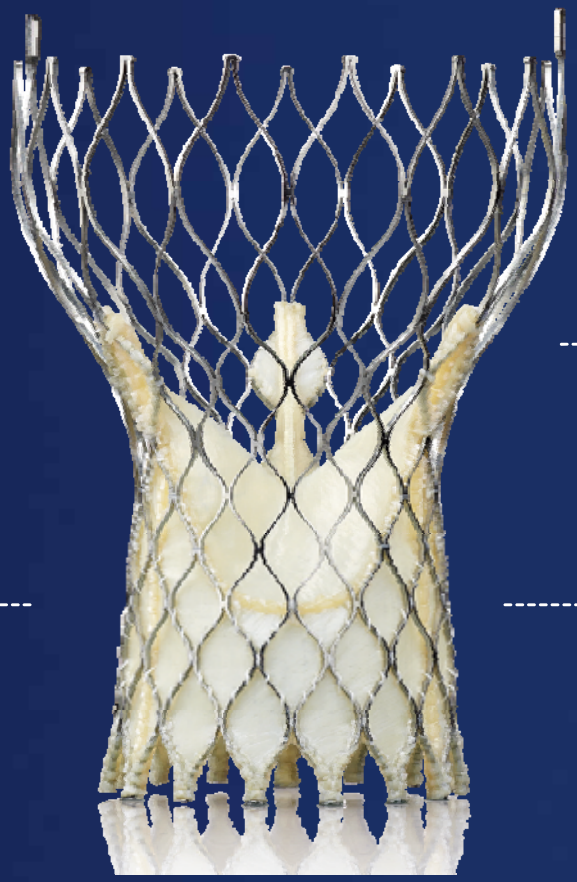
Promotes circularity, supports supra-annular valve

High Hoop Strength

Inflow

Conforms and seals to the annulus

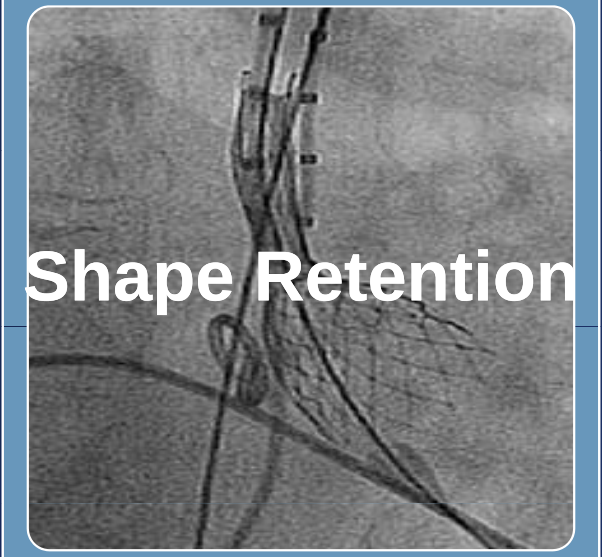
High Radial Force



Nitinol Ideally Suited for Future TAVI

Durable Performance in small package is critical

- Compact design for true low profile delivery



- Self-anchoring
- Controlled retraction for precise delivery and placement
- Maintain valve shape without recoil

- Corrosion resistance
- Low thrombogenicity
- Conformable to patient anatomy
- Fatigue performance

Porcine Pericardium

Optimal TAVI Tissue

Thin

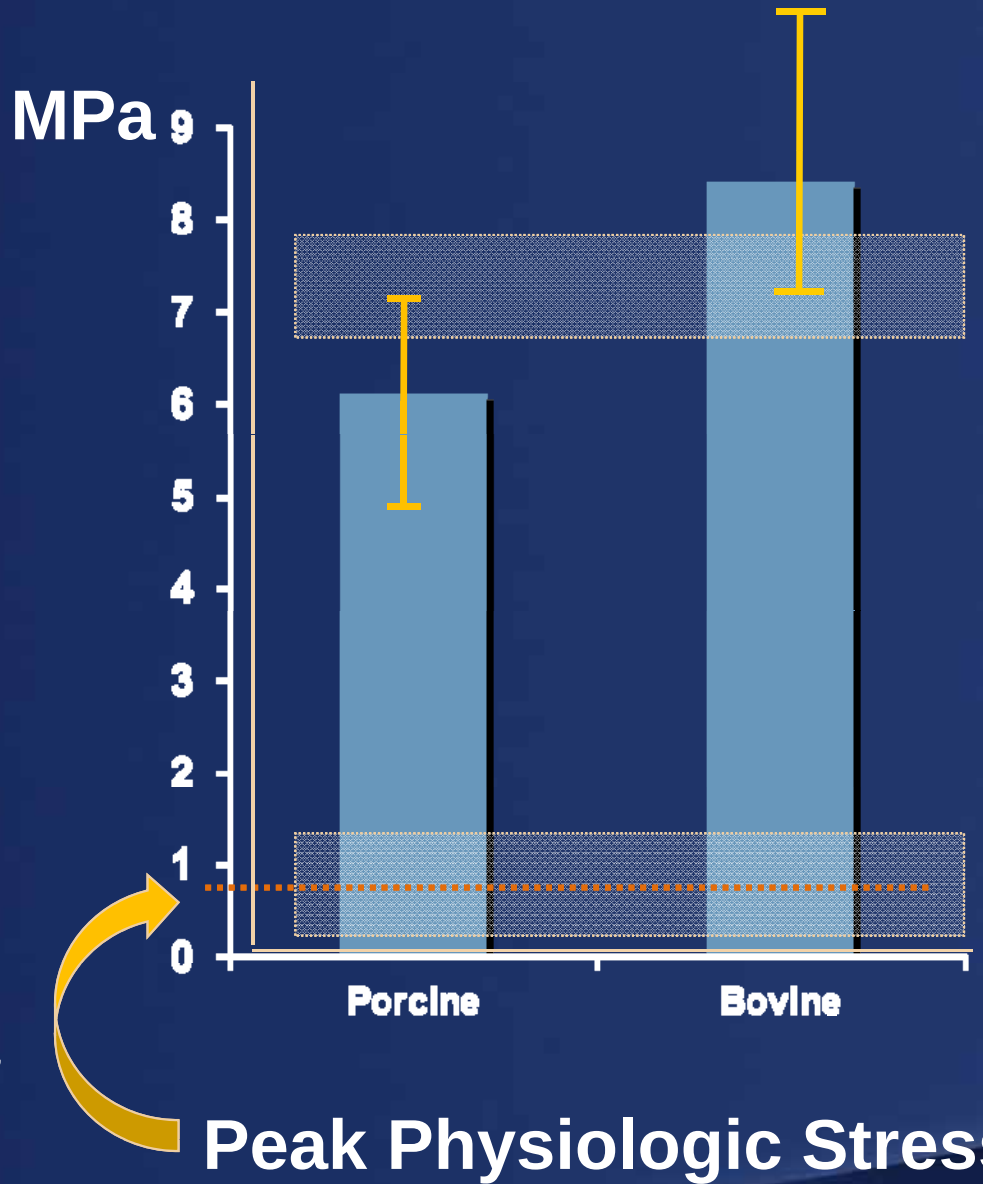
Half the thickness of bovine

Prevents tissue damage during crimping, tracking, and deployment, allowing for low-profile delivery across all valve sizes.[1,2]

Strong

Far exceeds physiologic need

Ultimate tensile strength (UTS) and suture pullout force for porcine and bovine pericardium are not statistically different[1,3] and exceed peak physiologic stresses [4]

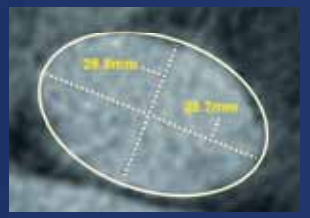


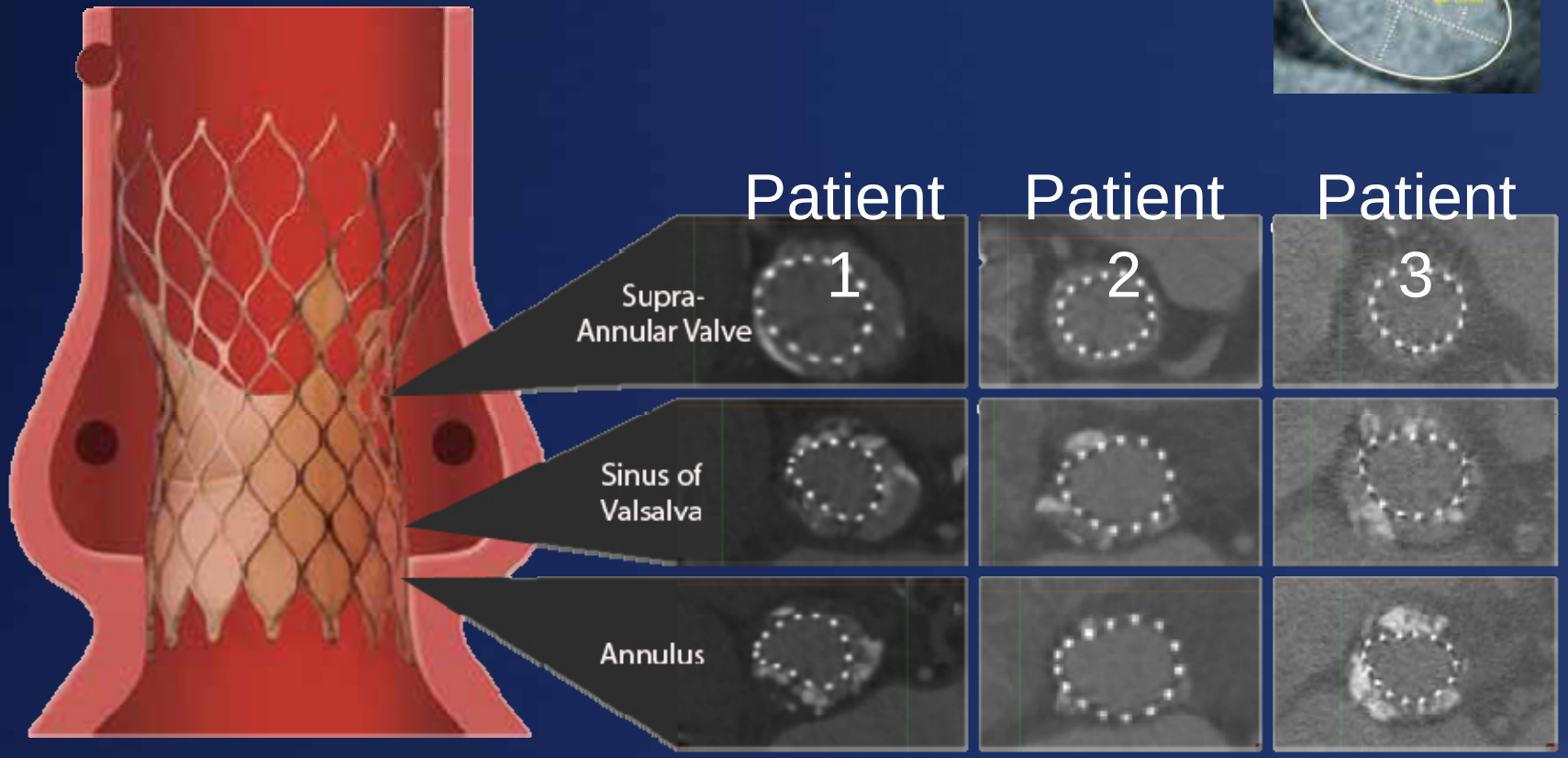
1. Sacks MS. Uniaxial mechanical and structural properties of bovine versus porcine pericardial tissue. Medtronic Engineered Tissue Mechanics Laboratory. University of Pittsburgh, Pittsburgh, PA. January 17, 2008. Data on File.
2. Braga-Vilela AS, Pimentel ER, Marangoni S, Toyama MH, de Campos Vidal B. Extracellular matrix of porcine pericardium: Biochemistry and collagen architecture. *J Membr Biol*. 2008 Jan;221(1):15-25.
3. Garcia Paez JM, Carrera A, Herrero EJ, et al. Influence of the selection of the suture material on the mechanical behavior of a biomaterial to be employed in the construction of implants. Part 2: porcine pericardium. *J Biomater Appl*. 2001;16:68-90.
4. Li, K and Sun, W. "Simulated thin pericardial bioprosthetic valve leaflet deformation under static pressure-only loading conditions: Implications for percutaneous valves" *Ann Biomed Eng*. 2010 Aug;38(8):2690-701.

Supra-Annular Valve Design

Flexible frame conforms to native annulus shape while maintaining the bioprosthesis in a higher position

- This decoupling of the valve from native annulus shape minimizes the impact of ellipticity at the valve level post deployment[1]





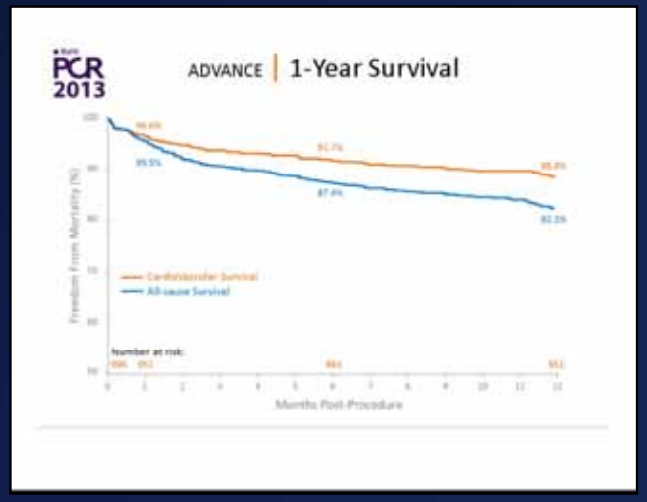
Images courtesy of Drs. de Jaegere and Schultz, Erasmus MC, Rotterdam, The Netherlands

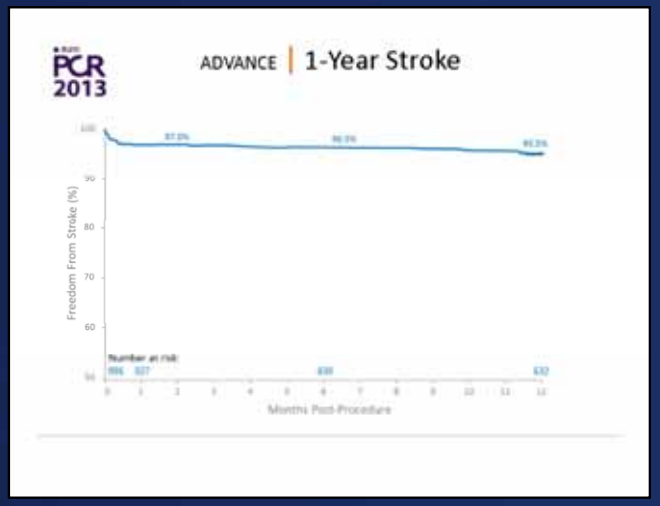
1. Data on file at Medtronic

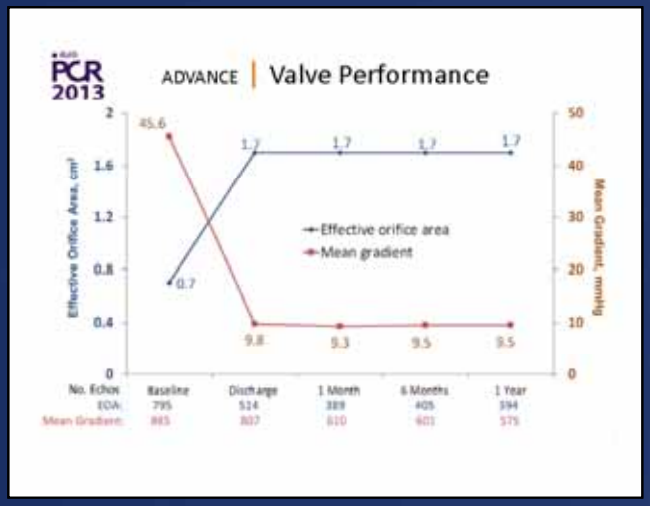
CoreValve Clinical Outcomes

More than 40,000 implants worldwide

- **High procedural success**
  - Low rates of annular rupture, coronary compromise, valve embolism
- **High survival rates**
- **Significant and persistent hemodynamic improvement**



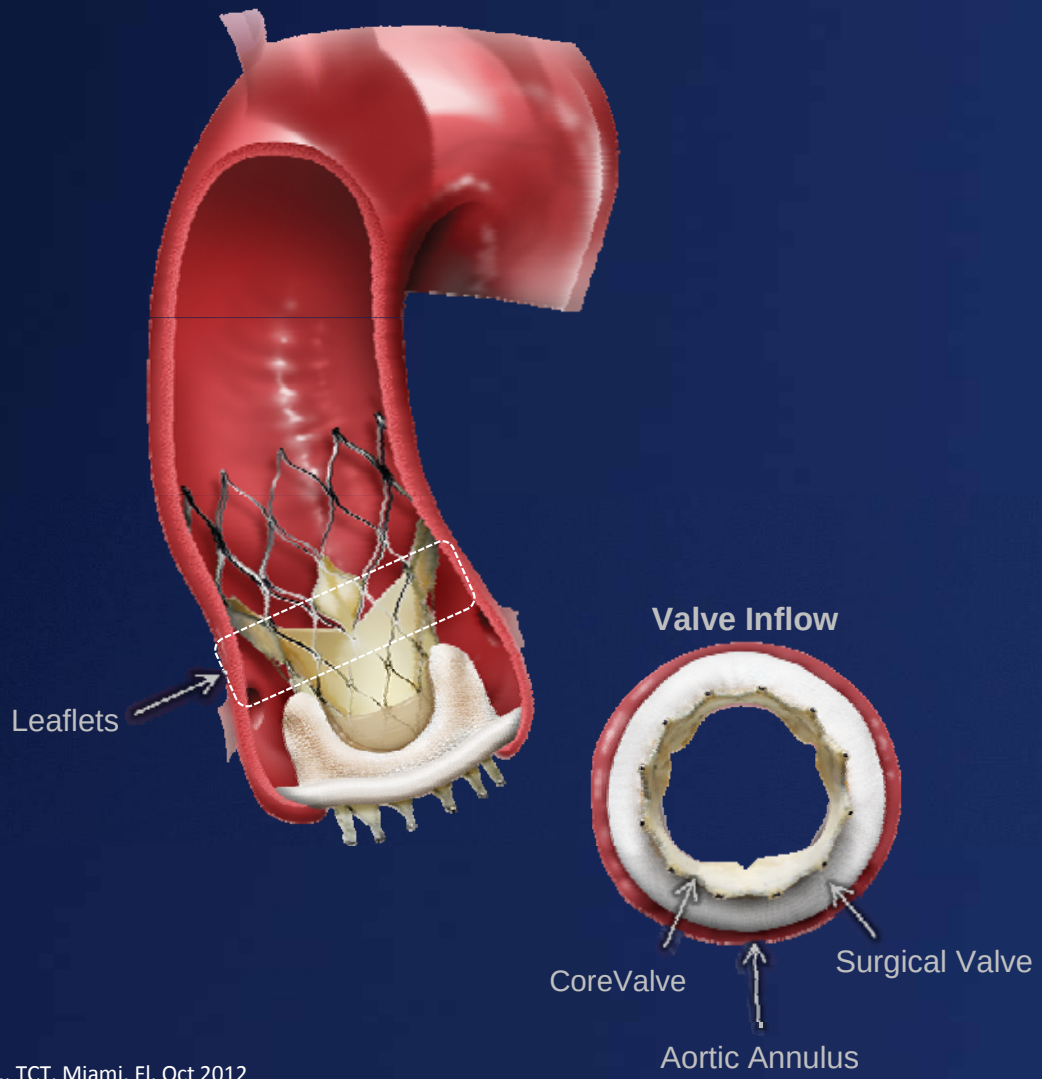




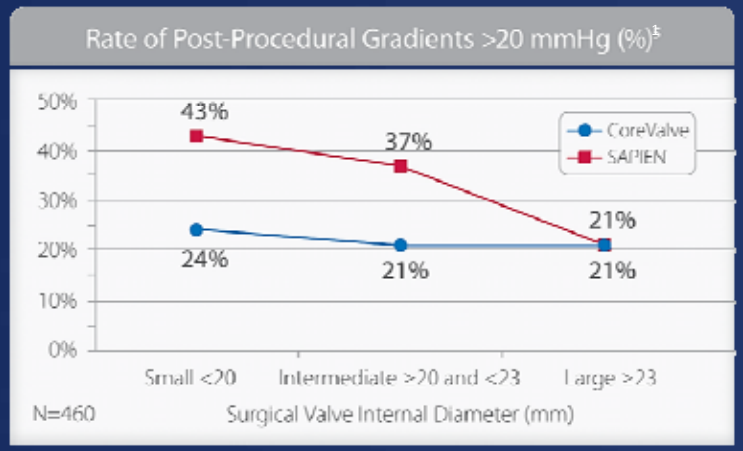
CoreValve ADVANCE, EuroPCR 2013

Use of CoreValve in failed surgical bioprostheses

Supra-annular valve function maximizes blood flow



Low post-procedural gradients



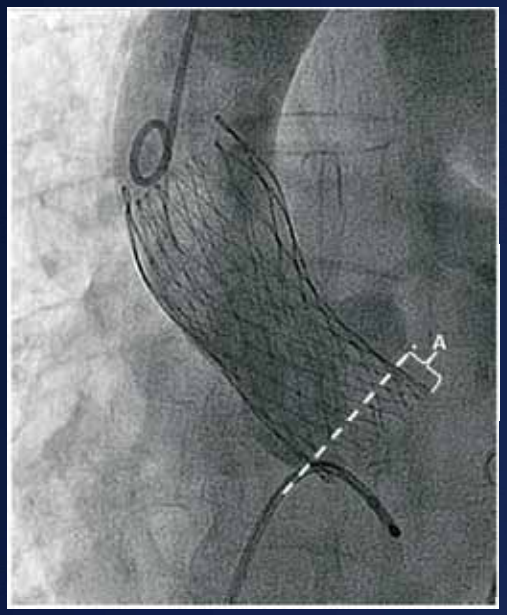
Large potential orifice area

Leaflets sit above the annulus where the frame is least constrained, opening up the valve for greater flow

1. Dvir et al., TCT. Miami, Fl. Oct 2012

Opportunities for Future

1. **Annular sealing**
   Reduces paravalvular leak



(TcheTche, et. al. – EuroIntervention 2012)

2. **Proper positioning**
   Key to achieving superior clinical outcomes, including PVL performance and conduction disturbances

3. **Low OD sheath to femoral artery ratio (SFAR)**
   Reduces major vascular complications

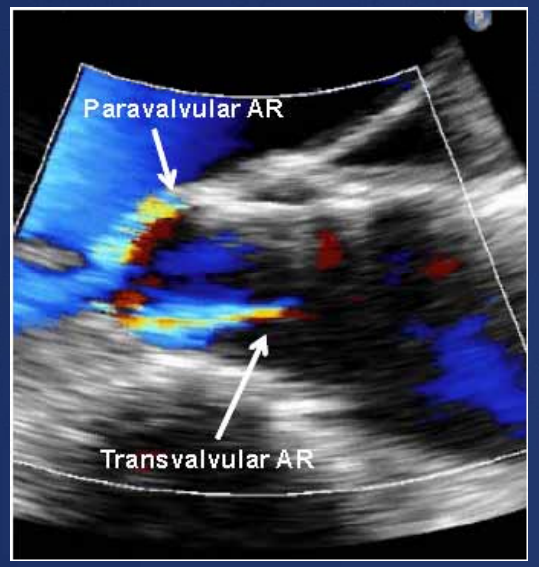
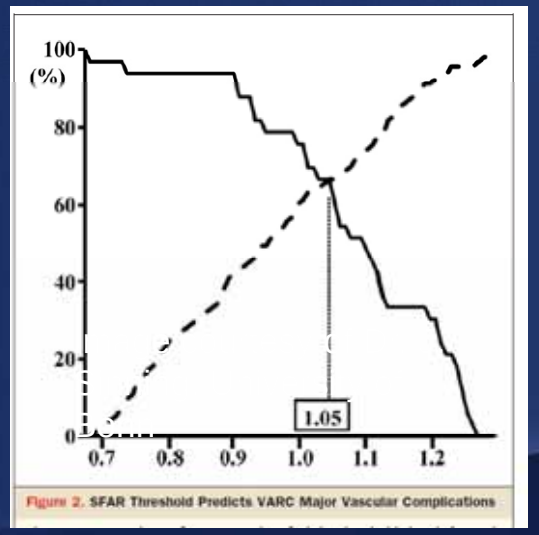


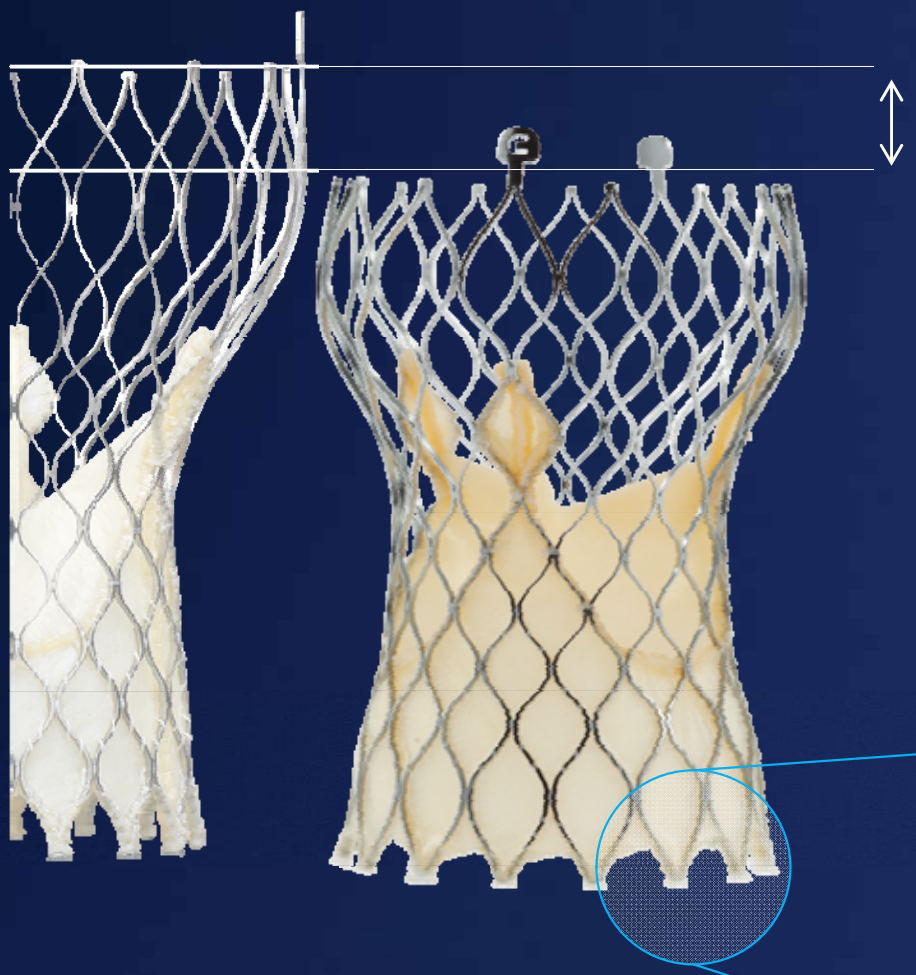
Image courtesy of Dr. J. Sinning, University of Bonn



(Hayashida K., Lefevre T., Chevalier B.; et al. Transfemoral Aortic Valve Implantation; New Criteria to Predict Vascular Complications, J Am Coll Cardiol Intv 4 2011 851-858)

Annular Sealing | Valve Design

Valve Height and Extended Skirt

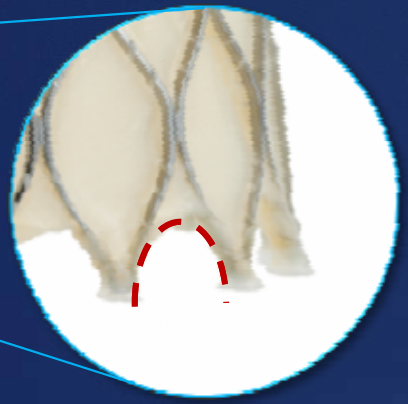


Outflow design

Outflow height reduced by 10% and reshaped for improved fit, especially in angulated anatomy

Extended Skirt

Scalloped skirt creates longer landing plane for better sealing



Annular Sealing | Frame Characteristics

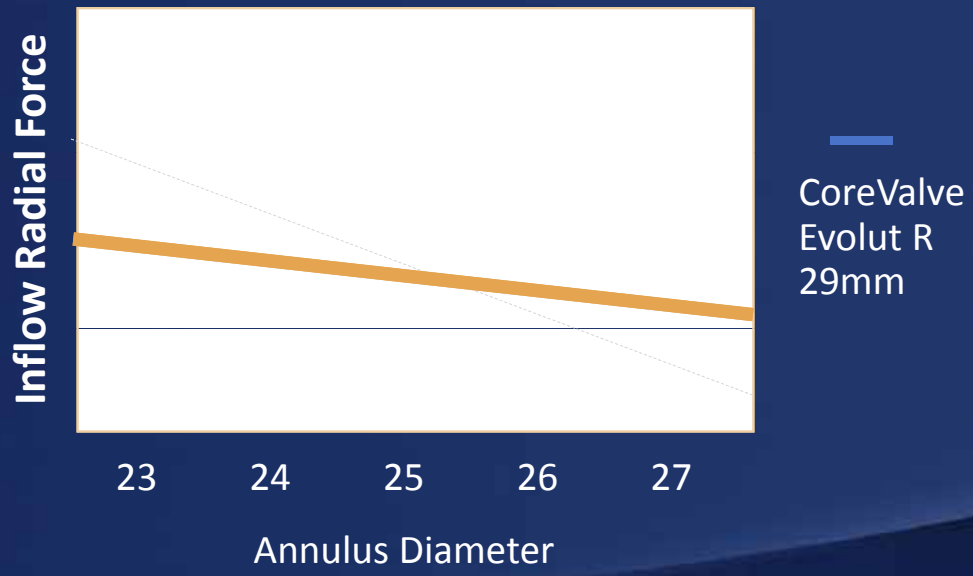
Cell Geometry and Radial Force

Modified cell geometry

Improves conformability in non-circular and calcified annulus while preserving anchoring

Consistent radial force curve across operating zone

Contributes to improved sealing across indicated annulus range



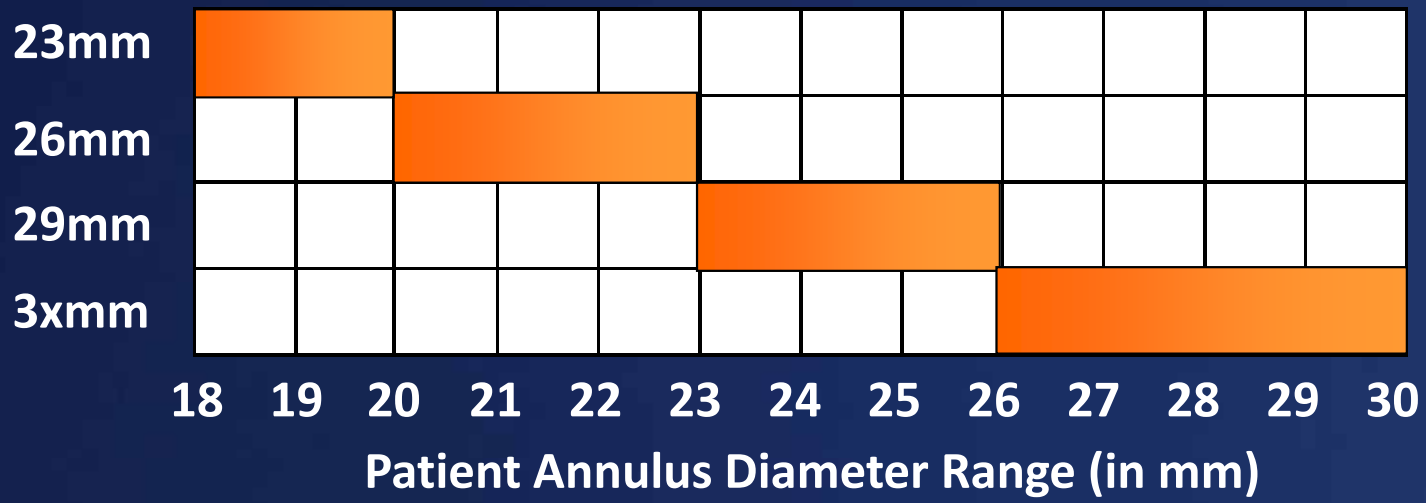
Annular Sealing | Cover Index

Full Range of Valve Sizes

Effect of Cover Index on PVL for CoreValve patients

		Cover Index (%)	
Authors	**# Patients**	**PVL ≥ 2**	**PVL < 2**
Vasa-Nicotera et al. 2012	122	13.5 ± 3.6	16.0 ± 4.4
Gotzmann et al. 2012	198	13.7 ± 6	15.9 ± 6.2
Sinning et al. 2012	146	10.1 ± 6.3	16.0 ± 4.6

Broad Range from 18–30 mm

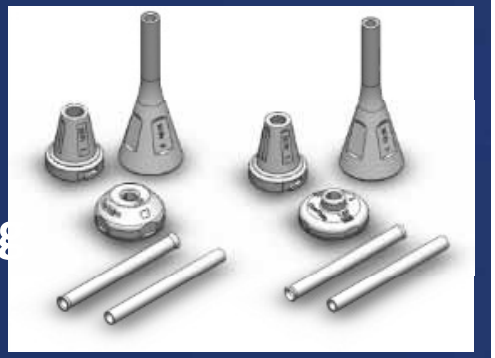


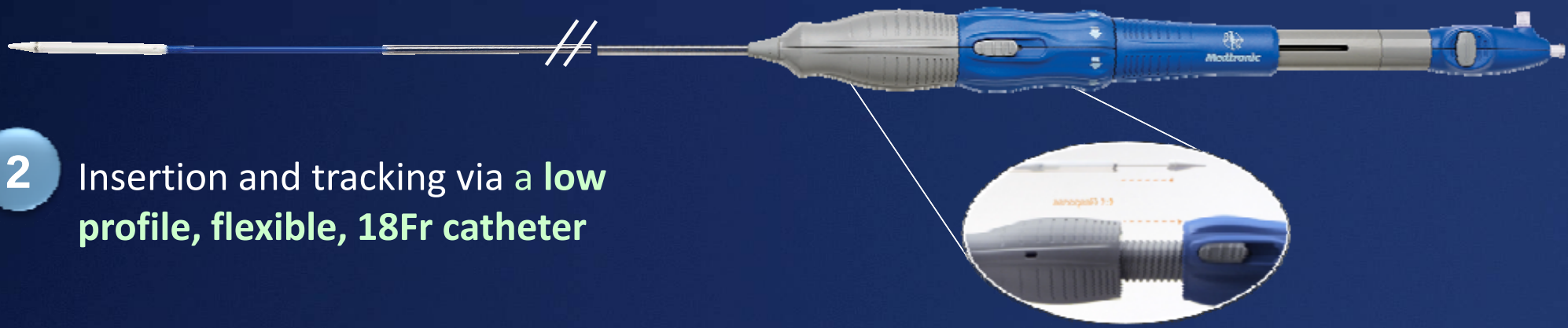
First Time Deployment Accuracy

EnVeo Delivery System

1 **Predictable deployment** through an intuitive handle with 1:1 response and improved valve release

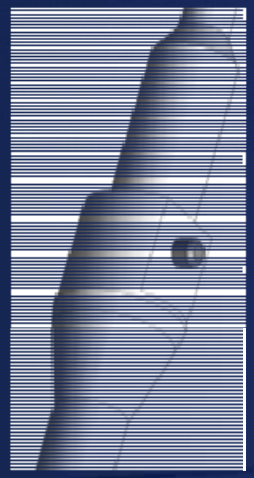
4 Redesigned valve **loading & packaging**





2 Insertion and tracking via a **low profile, flexible, 18Fr catheter**

3 Improved valve **release mechanism**



5 Facilitates delivery with an **optional shorter-length catheter** for subclavian and direct aortic access

Resheathing, Repositioning and Deploying

Cadaver: 29mm CoreValve Evolut R

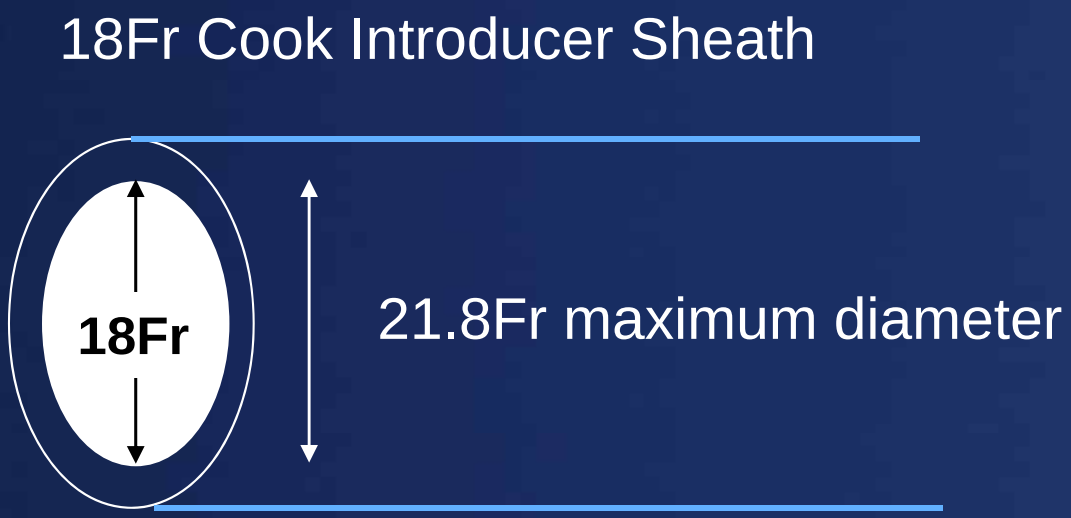
First Time Accuracy

Forced High Implant

Deep Implant

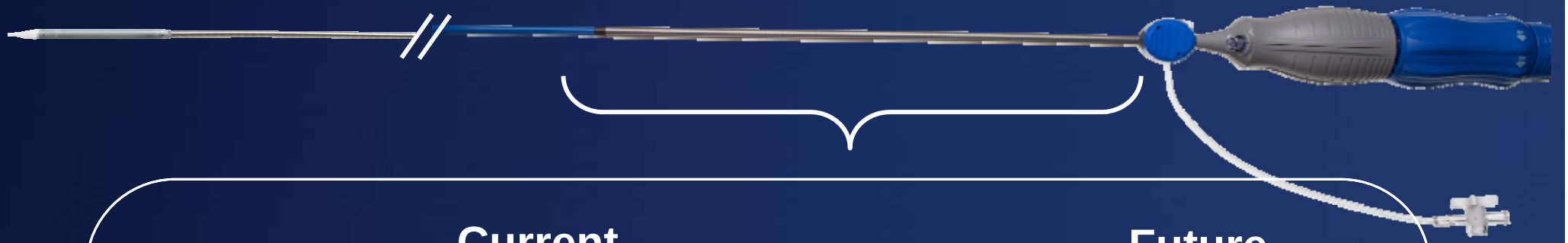
Introducer Sheath Sizing

Recognize inner diameter vs. outer (maximum) diameter measurements



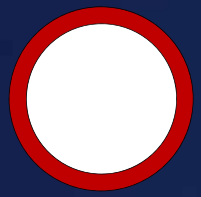
Reduce Vascular Complication Risk

EnVeo R Delivery System with InLine Sheath



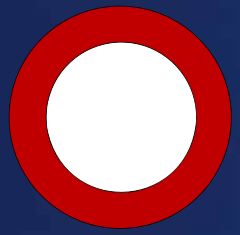
Current

22 FR (OD)



CoreValve w/ 18Fr Cook Sheath

26.7–29.7FR (OD)



Sapien XT w/ Edwards e-Sheath

Future

18 FR (OD)

14 FR Equivalent

CoreValve Evolut R w/ InLine Sheath

Conclusions

- Reducing procedural complications can, ultimately, improve overall TAVI results
  - New technologies to further reduce delivery profile and avoid ventricular damage can contribute to improved TAVI outcomes
- Self-expanding technology provides platform for innovation
- Supra-annular valve provides optimal coaptation
- New delivery systems will enhance positioning necessary for improved TAVI performance
  - First time accuracy is goal, but recapture and repositionable technology provides back-up
- Continued advancement to downsize valve payload can address access challenges