VÝVOJ TECHNOLOGIE TAVI

SPOLEČNOSTI EDWARDS LIFESCIENCES

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Lékařská fakulta UK Hradec Králové

Kardiocentrum Fakultní nemocnice Hradec Králové

Edwards Lifesciences' History: Patient Needs Drive Innovation

- **Replace** the patient's diseased heart valve
  - Mechanical heart valve (1960s)
- **Eliminate** patient's reliance on warfarin
  - Tissue heart valve (1970s)
- **Repair** the patient's native valve
  - Mitral and tricuspid annuloplasty rings (1970s)
- **Improve clinical performance** of tissue valves
  - Bioengineered pericardial heart valves
  - Anti-calcification tissue treatments (1980s)

London, Eng.

DAILY MAIL, Friday, June 17, 1966

SUCCESS! AND A HUG FOR THE SURGEON WHO DID IT

Mother of three gets a new heart

By HUGH McLEAVE
Daily Mail Science Correspondent

MRS. ZIBA VASVI, 27-year-old mother of three children, will wake up in St. Thomas's Hospital, London, today with three man-made valves in her.

The valves were inserted by a combined British and American team in one of the most complicated operations in surgery.

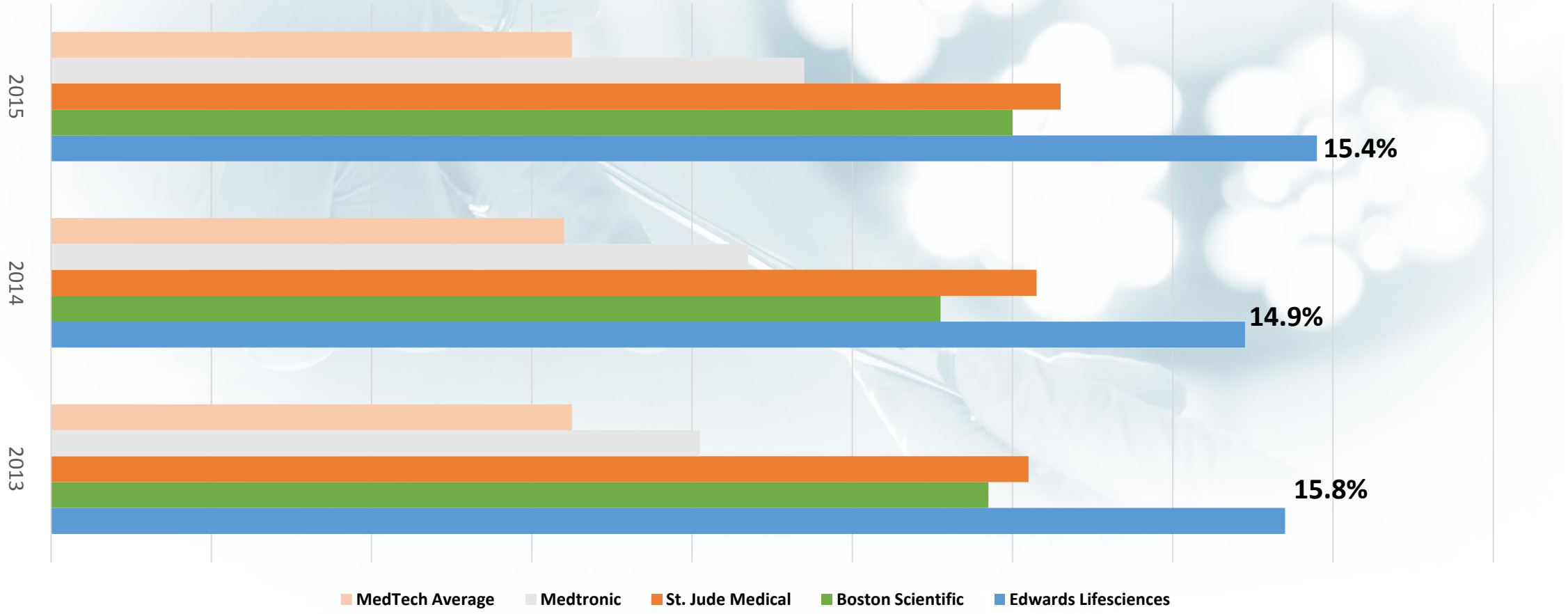
Mrs. Vasvi, a Turkish Cypriot, may notice a clicking sound from the new valves. But gone will be the breathless weariness which kept her housebound and made it impossible for her to climb stairs.

In the seven-hour operation her heart was virtually taken to pieces and put together again.

Medtech average	6.5%	6.4%	6.5%

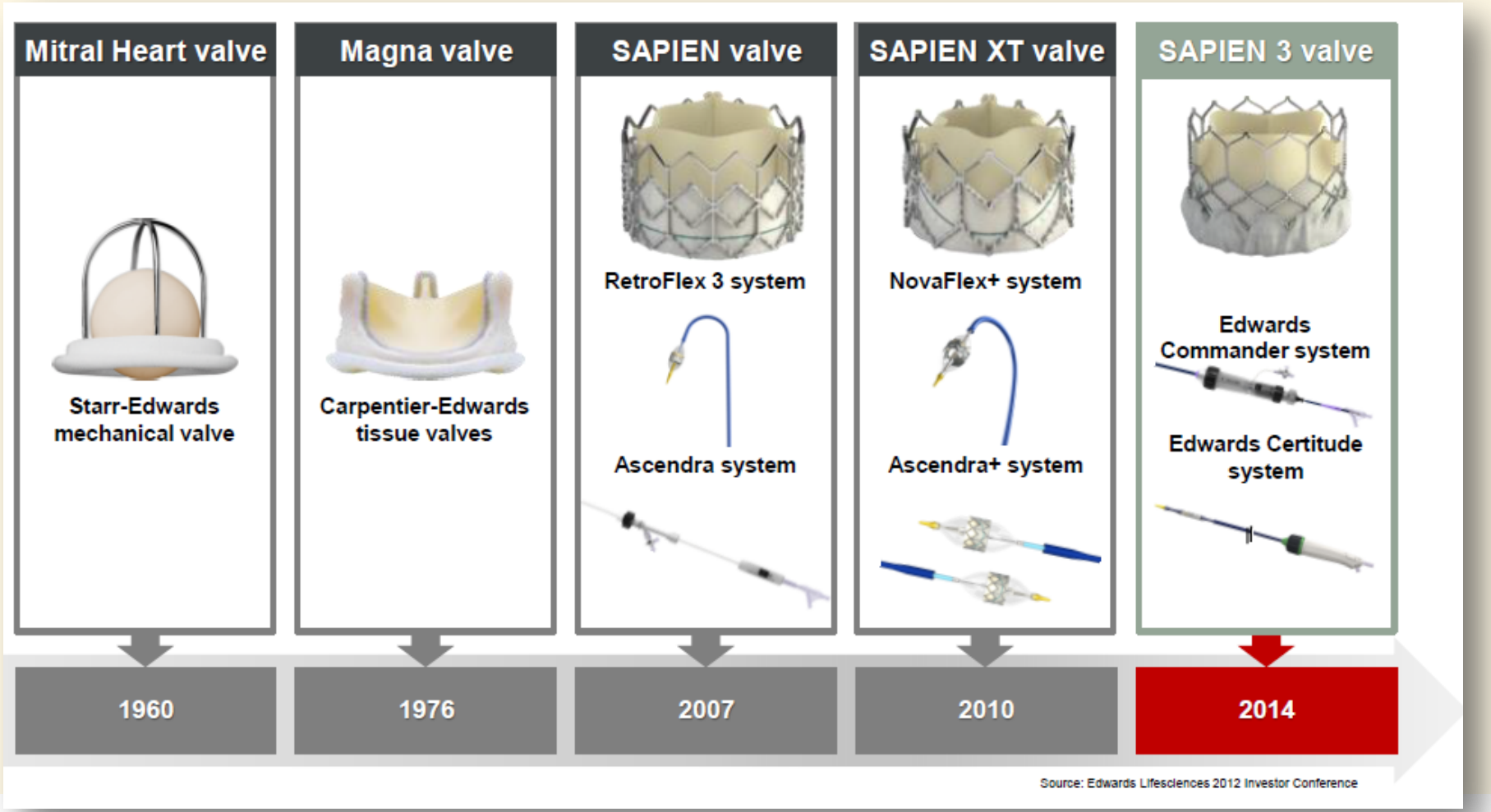
Benchmark of R&D investments (biggest competitors)

Results are stated in terms of R&D expenditures/net sales

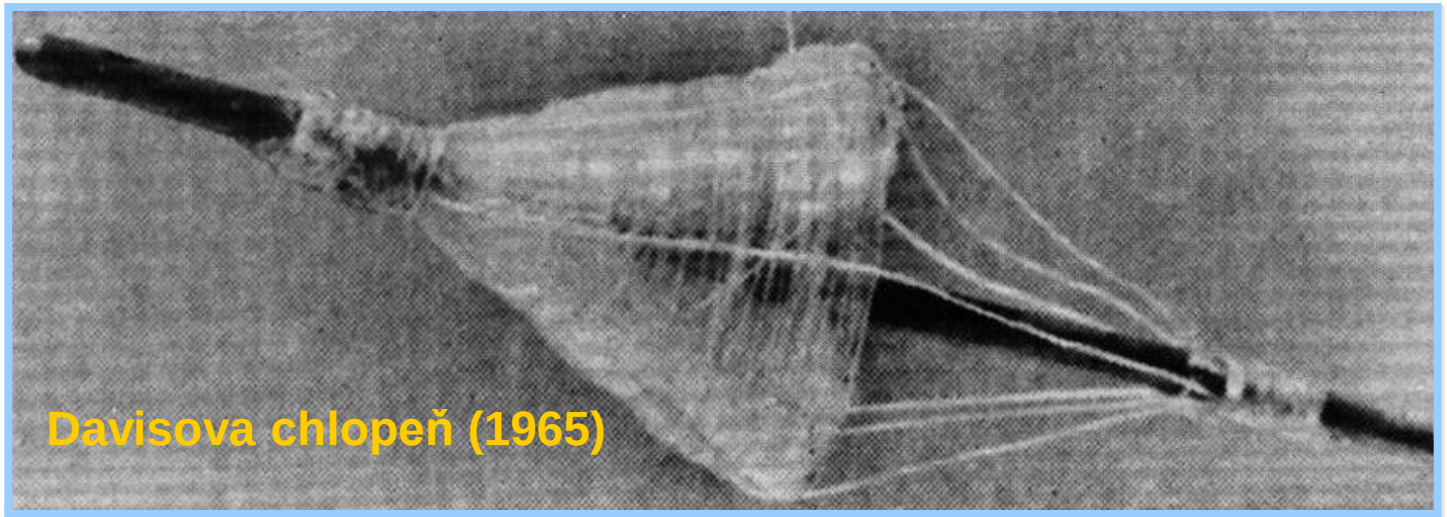


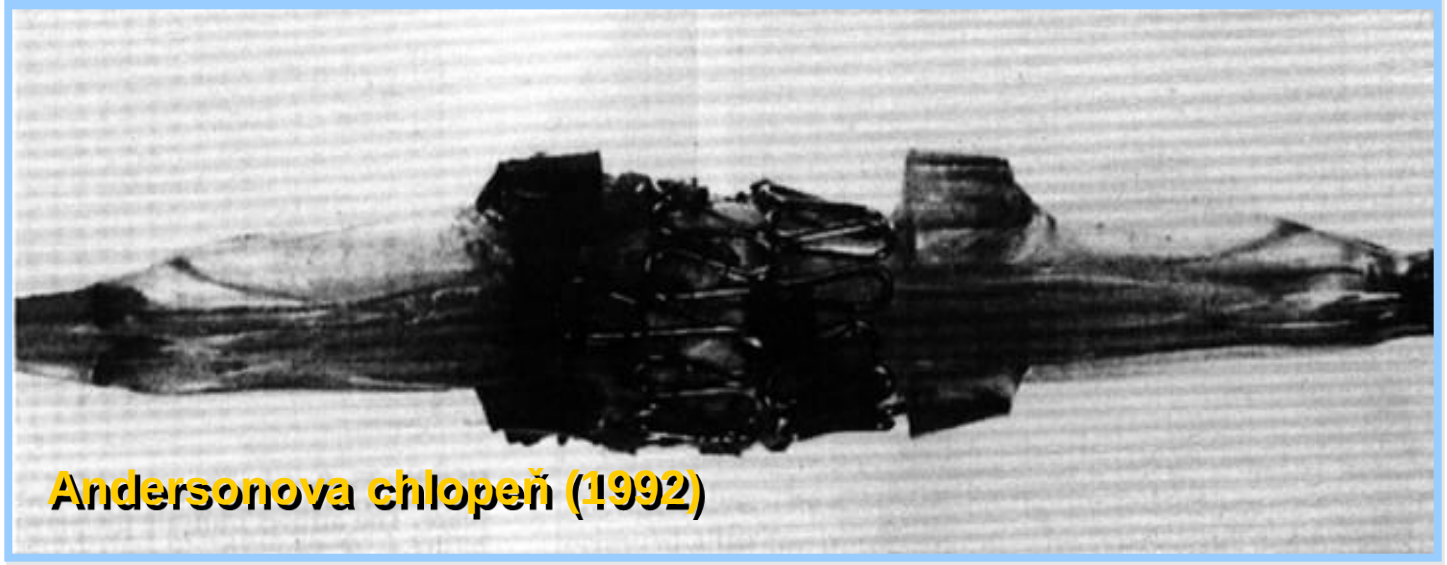
Data gathered from respective annual reports & https://www.statista.com/

With a Robust Transcatheter Valve Pipeline Built on Foundation of Surgical Heart Valve Knowledge



Perkutánní implantace aortální chlopně

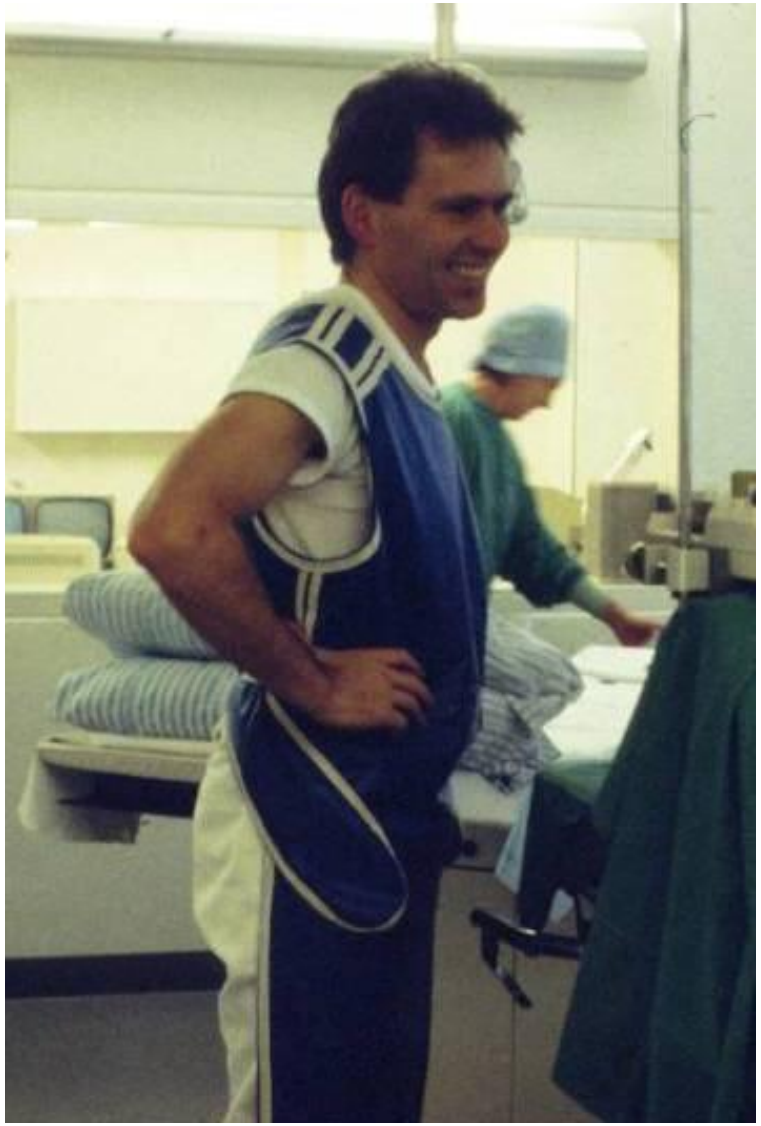




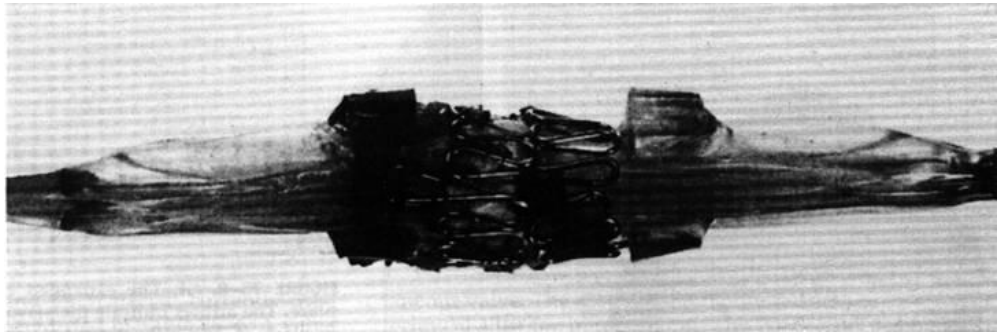
1989: The Journey Begins

Dr. Henning Andersen (May 1, 1989)

Andersen & Colleagues: Balloon-Expandable Aortic Heart Valve



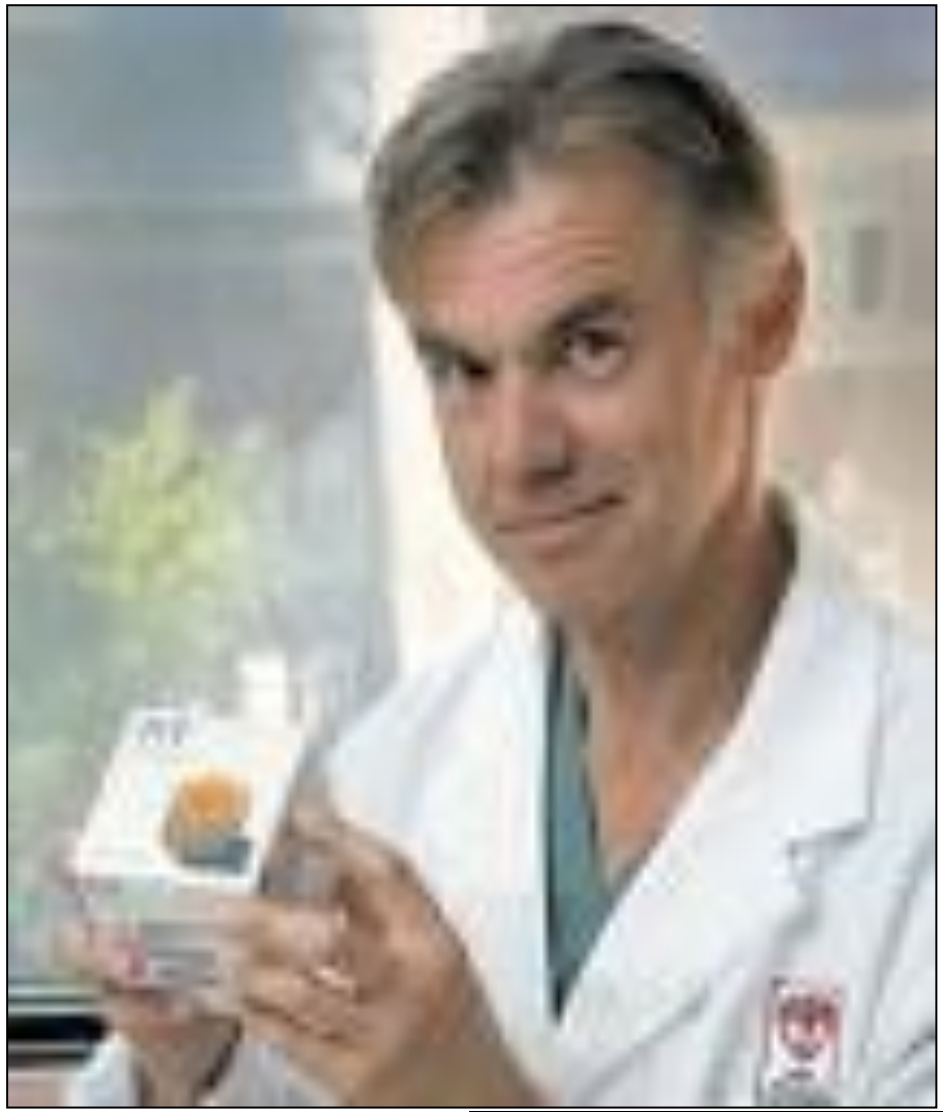
- Porcine aortic valve sutured to a stainless steel frame
- Crimped on a triple balloon catheter: 41F
- IP acquired by Heartport
- No further development




VAIO

1989-1999: Looking for a company interested by the project of “stented valve” for percutaneous treatment of calcific AS

- ***Comments:***
- ***« Interesting idea but not a priority »***
- ***« Totally irrealistic, major technical issues »***
- ***“Definitely impossible to stent a calcific aortic valve”***
- ***“Occlusion of coronary arteries in 100% of cases”***
- ***« Would never be approved by FDA »***
- ***« Surgery covers 100% of the need. No indication»***
- ***« Most stupid project ever heard…»***

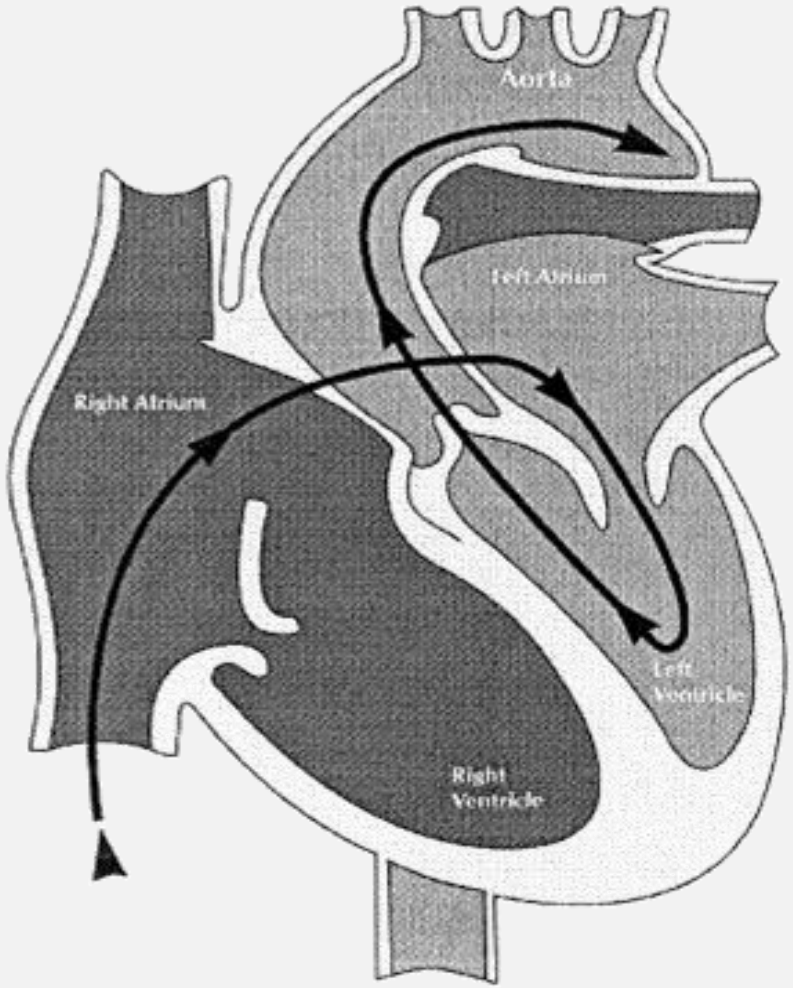


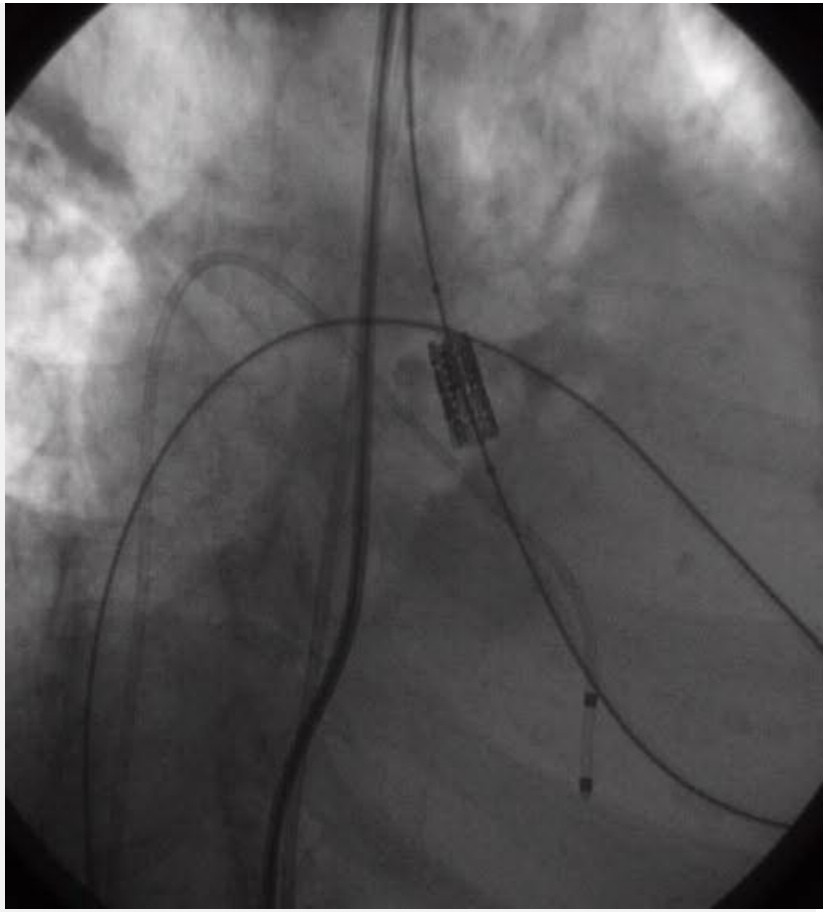
John Webb

- Retrográdní přístup
  (od. 2005)
- Retroflex katétr
- Transapikální přístup

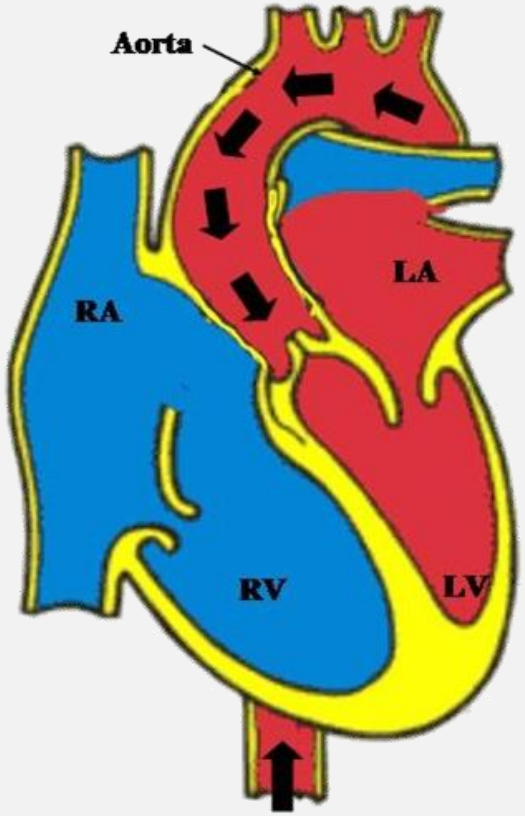
“The antegrade approach is a technically challenging and complex procedure”

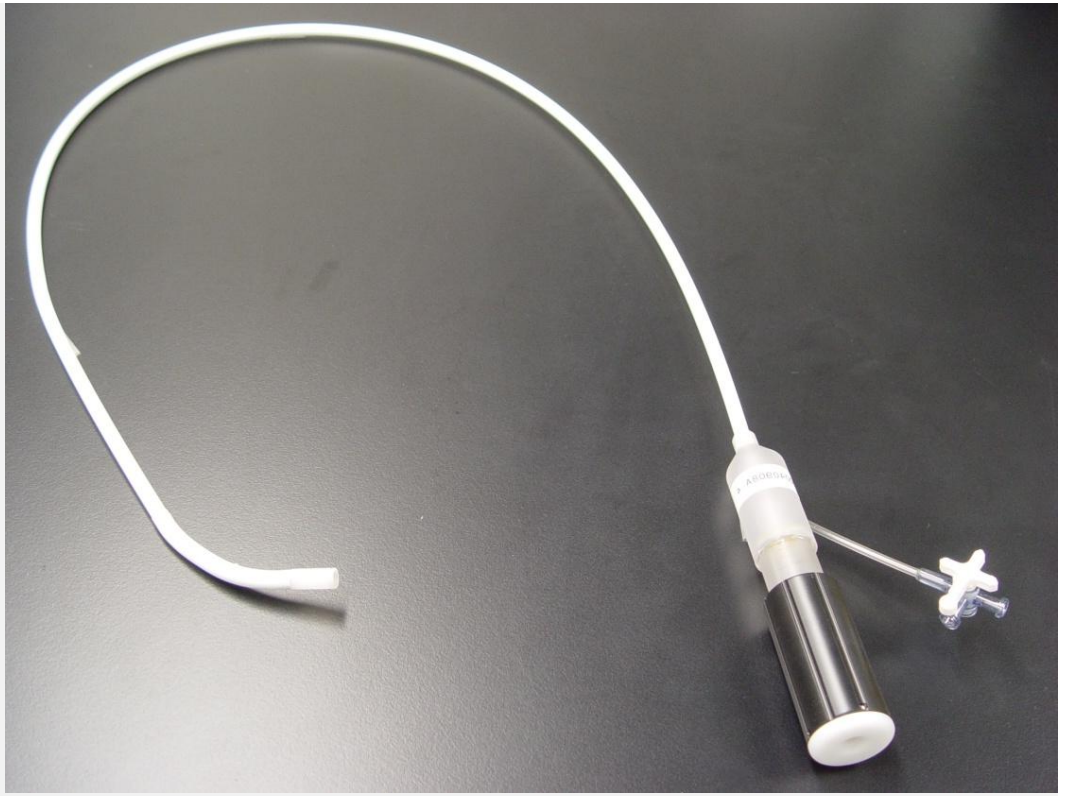
– George Hansel & Bill O’Neill





We Needed A Better Procedure



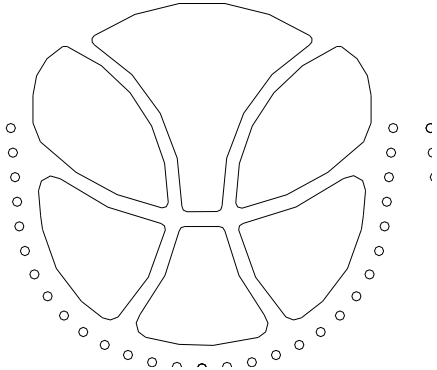


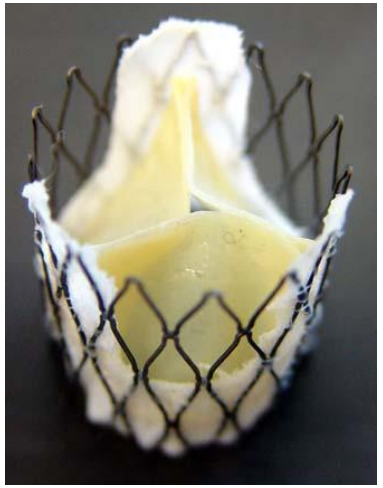
Edwards First Retrograde Catheter

The retrograde procedure changed everything

1999: Edwards Starts THV Program

- *Evaluated three different frame design concepts*
  - Flat sheet design
  - Tube design
  - Crown design





Ironically, as the market leader in Heart Valves, there was no tension with surgeons. … They were convinced this idea would not work

From 2004

1985 — **F.I.M. Balloon Aortic Valvuloplasty**

1987 — Concept of« stented valve », to rule out post-BAV valvular restenosis

1994 — Post-mortem studies of intra-valvular stenting
Sketches of stented valve

1999 — « **Percutaneous Valve Technology** » **(prototypes)**

2000 — **First animal implantation (sheep)**

2000-02 — Large series of animal implantation

2002 — **F.I.M. PHV implantation**

2002-03 — Feasibility Studies (antegrade)

2004 — **Edwards Lifesciences**
Technological improvements

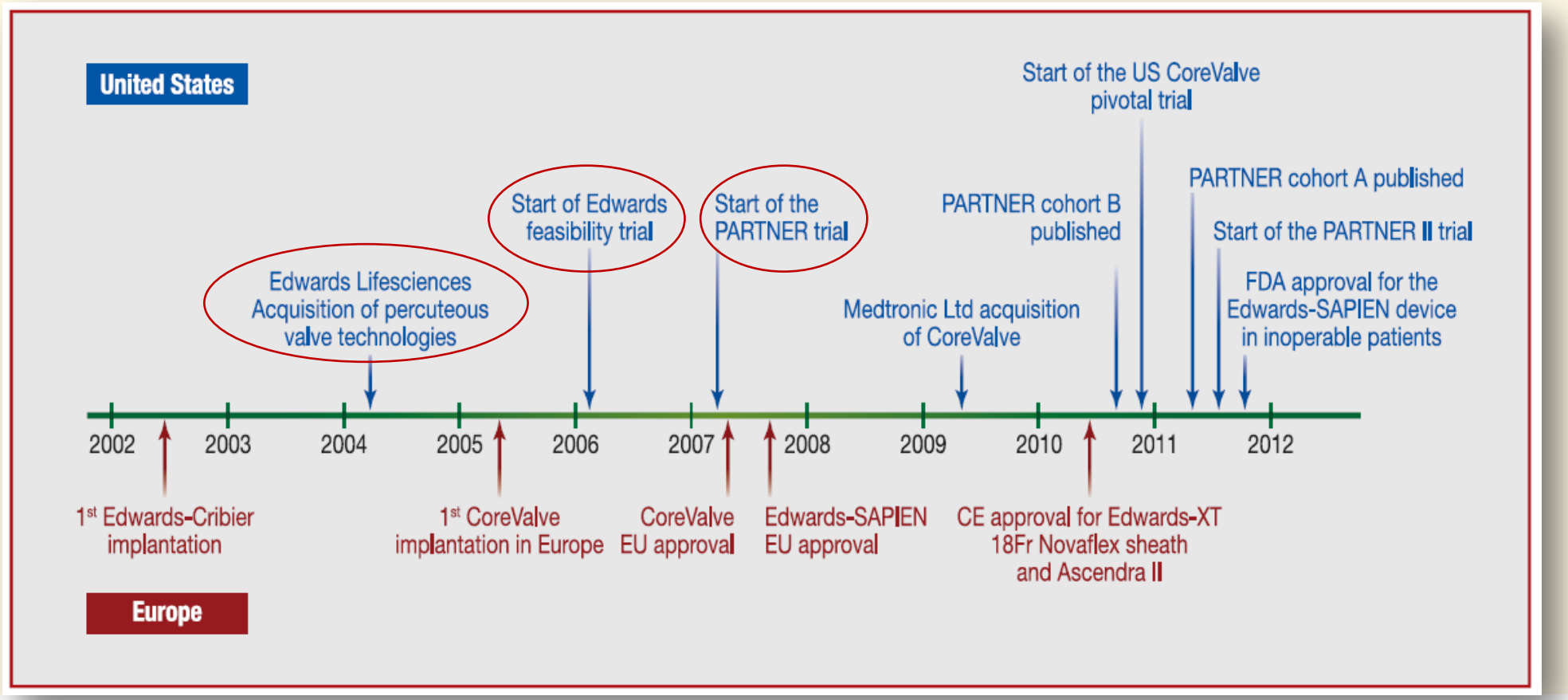
2005-07 — International **TF and TA**
Feasibility Studies

2007 — **CE mark commercialization**

20 years

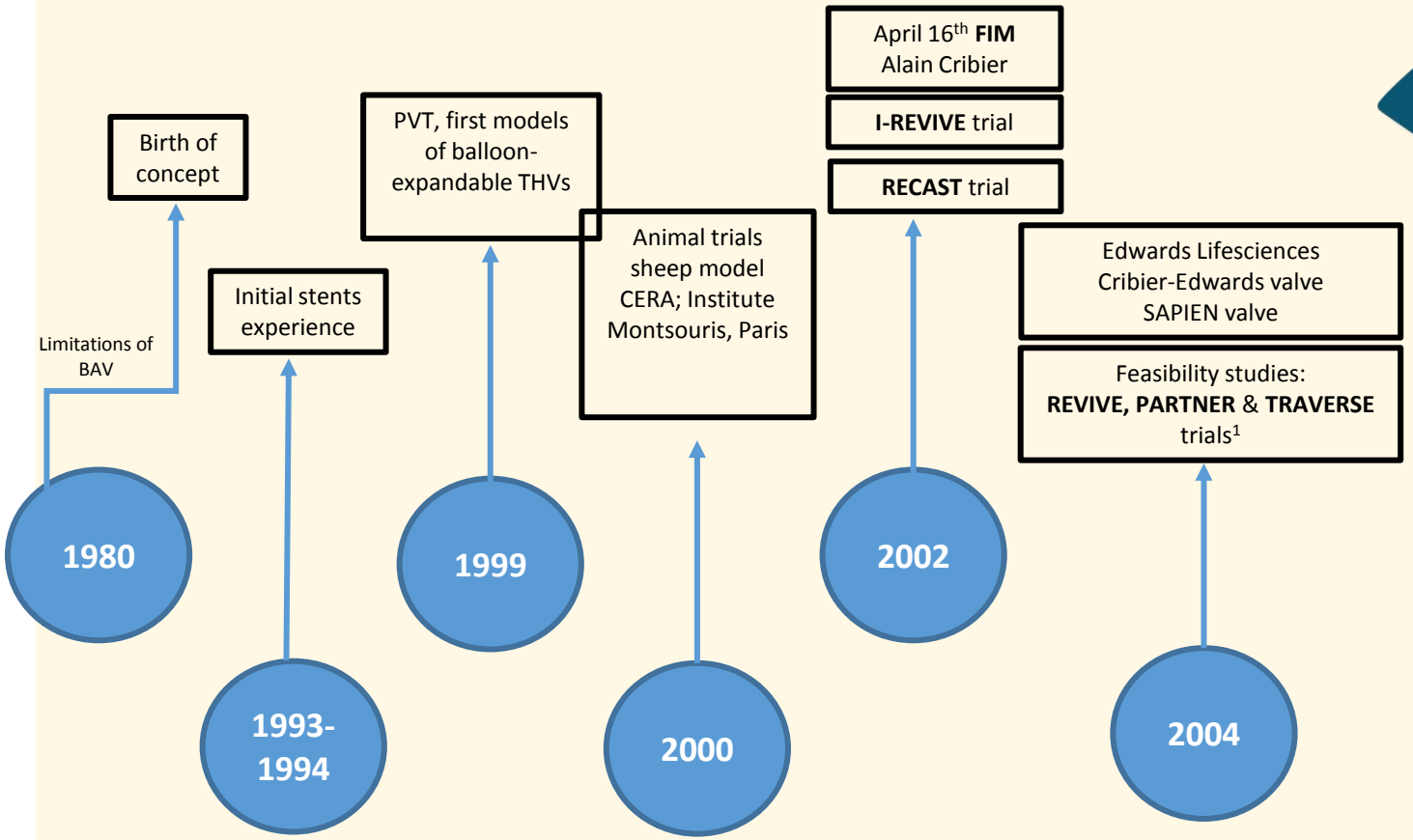
Cribier A.

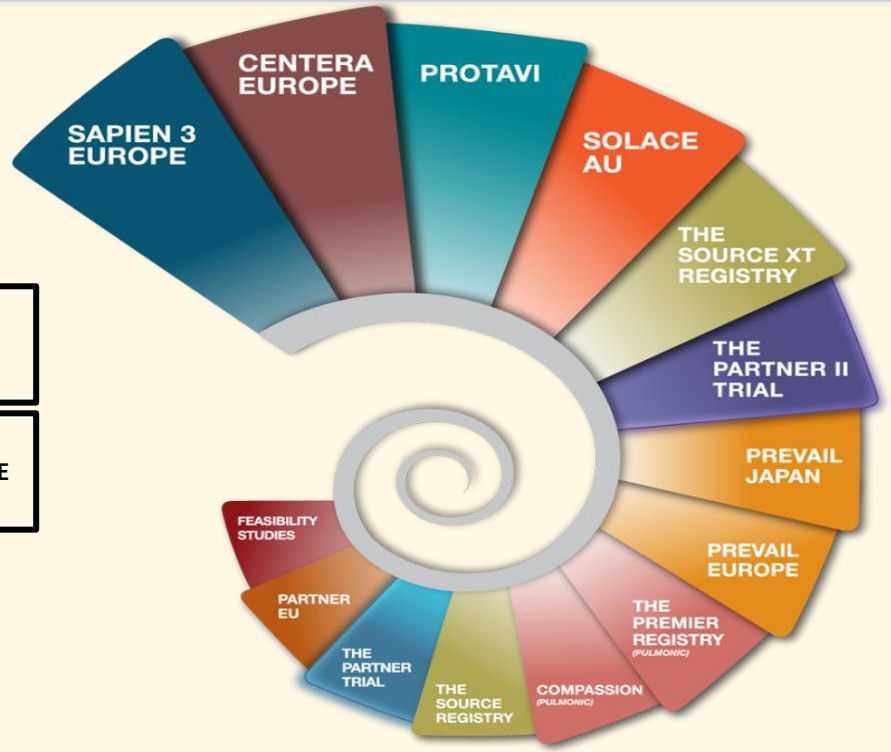
Development



Dvir et al I The development of transcatheter aortic valve replacement in the USA I Archives of Cardiovascular Disease (2012) 105, 160—164

Development of TAVI



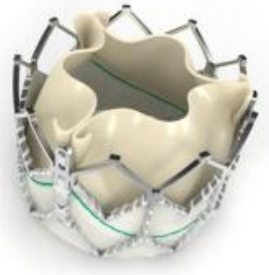
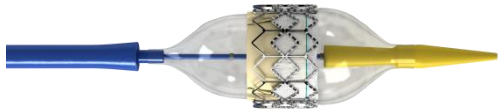
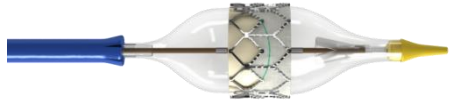


- Edwards SAPIEN transcatheter heart valves are the most widely used transcatheter heart valves worldwide and consistently demonstrate clinical excellence in both trials and real-world experience.
- TAVI has been performed in about 300,000 patients, with an annual compound growth rate of 40%, and is now available in 65 countries around the world2

(1) Cribier et al I Development of transcatheter aortic valve implantation (TAVI): A 20-year odyssey. I Archives of Cardiovascular Disease (2012) 105, 146—152
(2) Cribier et al I Commemorating the 15-year anniversary of TAVI: insights into the early stages of development, from concept to human application, and perspectives I Eurointervention 2017

Edwards Transcatheter Heart Valve Innovation:

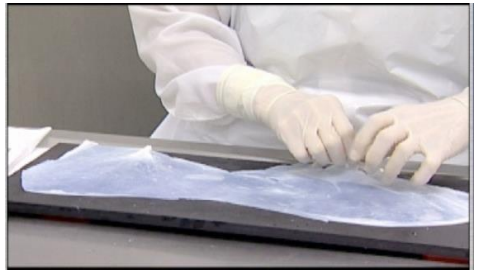
Applying Valve Knowledge and Development of Retrograde DS

2002	2006	2010
Cribier-Edwards THV	**Edwards SAPIEN THV**	**Edwards SAPIEN XT THV**
		
▪ 23 mm Valve ▪ Untreated Equine Tissue	▪ Stainless Steel Frame ▪ Bovine Pericardial Tissue ▪ Carpentier-Edwards ThermaFix Process	▪ **Cobalt-Chromium Frame** ▪ Reduced Crimp Profile ▪ Bovine Pericardial Tissue ▪ Carpentier-Edwards ThermaFix Process
		
▪ Antegrate Approach ▪ Retrograte Prototype Delivery System	▪ Tapered distal tip ▪ 22/24F sheath	▪ Shortened distal tip ▪ 360 degree flex tip ▪ 16/18F eSheath

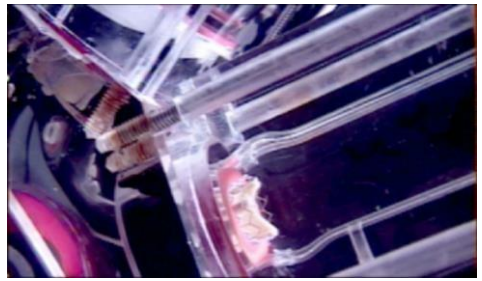
The technology evolution to serve the clinical results

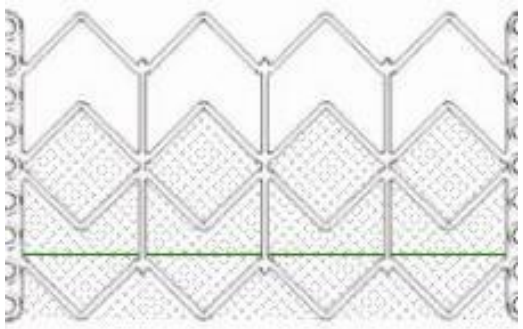
Edwards SAPIEN valve

Pericardial Leaflets with TFX treatment



Only two sizes: 23 and 26 mm





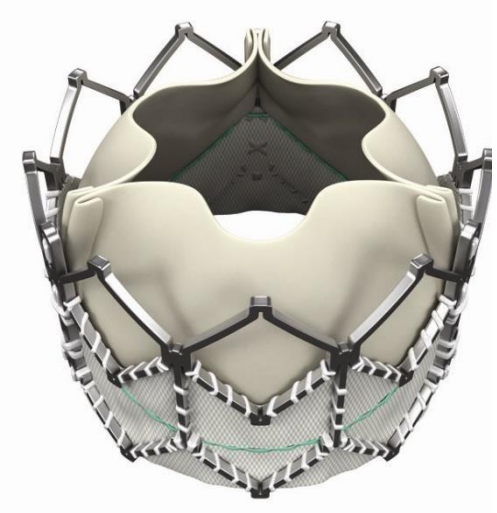
- **Laser Cut Stainless Steel frame designed to resist frame fracture**
  - 316L biomedical grade stainless steel frame
  - Tested to ISO5840:2005 and FDA surgical Heart Valve Guidance
  - Frame fatigue testing simulating 15 years

Edwards SAPIEN Transcatheter Heart Valve is Balloon-Expandable

- Balloon-expandable valves exert consistent radial strength
- The frame on the Edwards SAPIEN valve is made from 316L biomedical grade stainless steel tubing
- ***On balloon crimped***

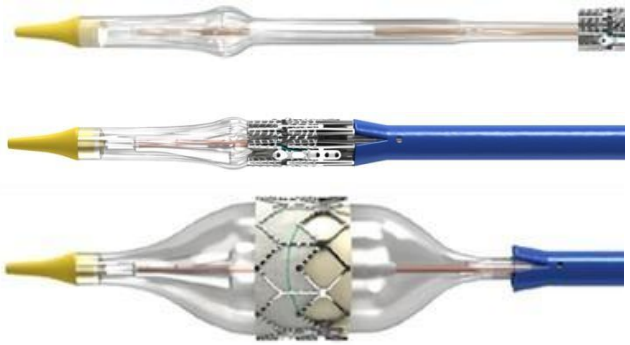
Edwards SAPIEN XT Transcatheter Heart Valve Delivery Systems

Edwards SAPIEN XT THV



Cobalt chromium alloy

NovaFlex Transfemoral Delivery System

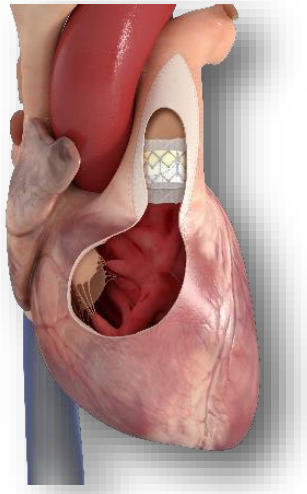


Under balloon crimped

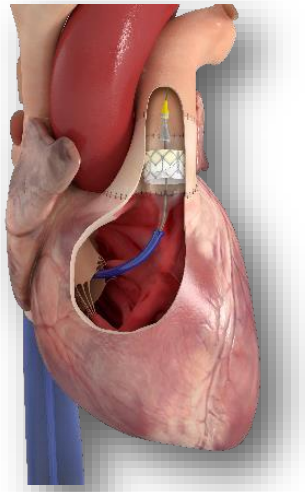
Ascendra2 Transapical Delivery System

The SAPIEN XT valve is approved to treat more patients than ever

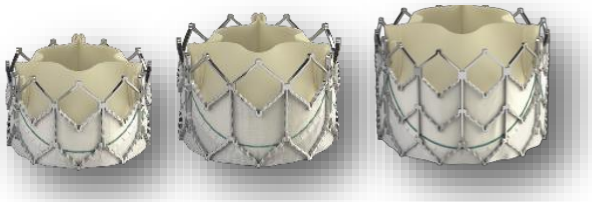
The SAPIEN XT valve is the first transcatheter heart valve approved to treat pre-stented transannular patches, conduits, and surgical valve-in-valve in the pulmonic position



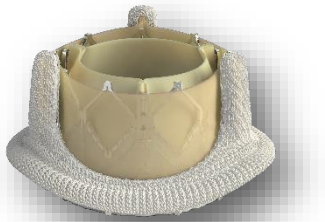
Pre-stented Transannular Patches



Conduits



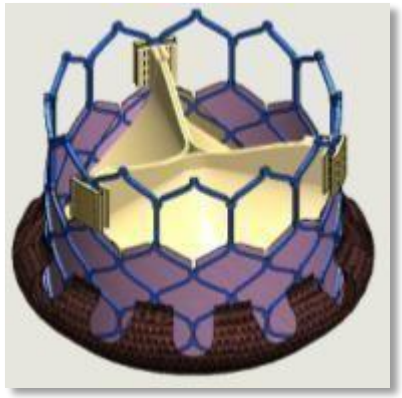
Additional Valve Size
29 mm Approval

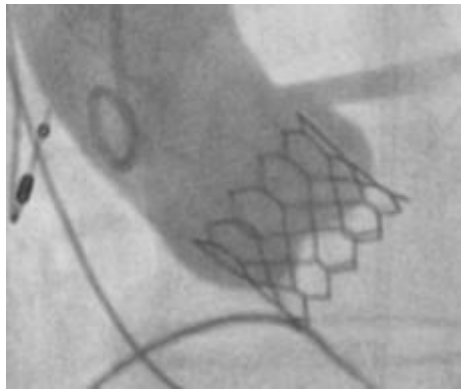


Valve-in-valve In the Pulmonic Position

The SAPIEN 3 Valve System Development Timeline

2010	2011	2012	2013
▪ Concept selection	• Development work for FIM • Delivery systems development • Valve testing • Manufacturing process development	• Refinement of valve and delivery systems and development of additional sizes • Clinical trial preparation	• Clinical trial enrollment and follow-up



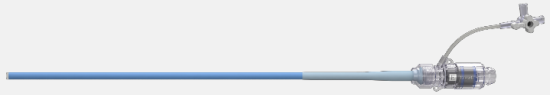


The SAPIEN 3 Valve and the current Delivery systems

SAPIEN 3 valve

Transfemoral Delivery System

Edwards Commander delivery system
14F Certitude Sheath Compatible



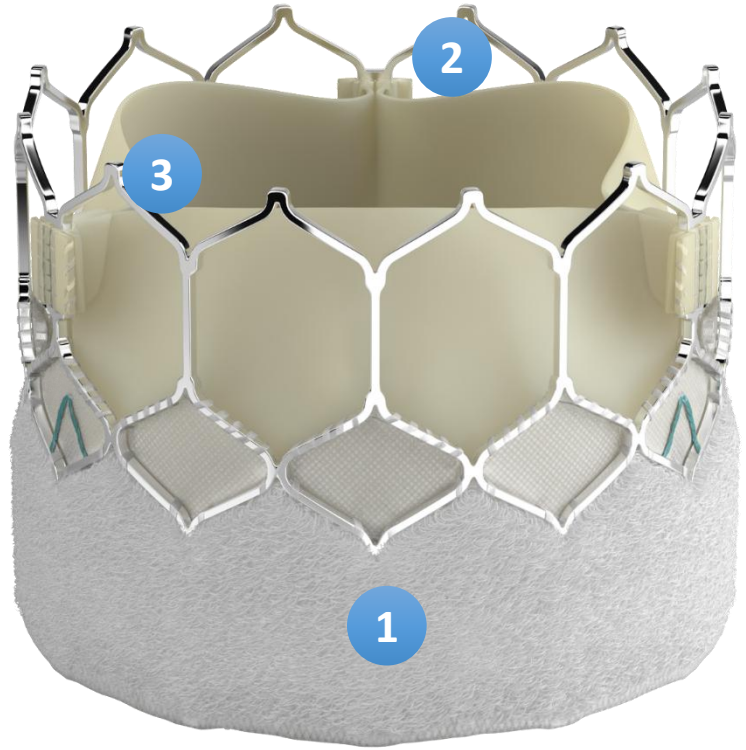
Edwards eSheath

Transapical and Transaortic Delivery System

Edwards Certitude delivery system
18F Certitude Sheath Compatible

Edwards SAPIEN 3 Ultra Transcatheter Heart Valve

featuring a taller, textured PET outer skirt



Taller, Textured PET Outer Skirt 1

- Approximately 40% increased outer skirt height*
- Same inner skirt height*
- Textured PET material
- Similar biocompatible material as the SAPIEN 3 valve

Frame Design 2

- Frame geometry designed for an ultra-low delivery profile with high radial strength for circularity and optimal haemodynamics

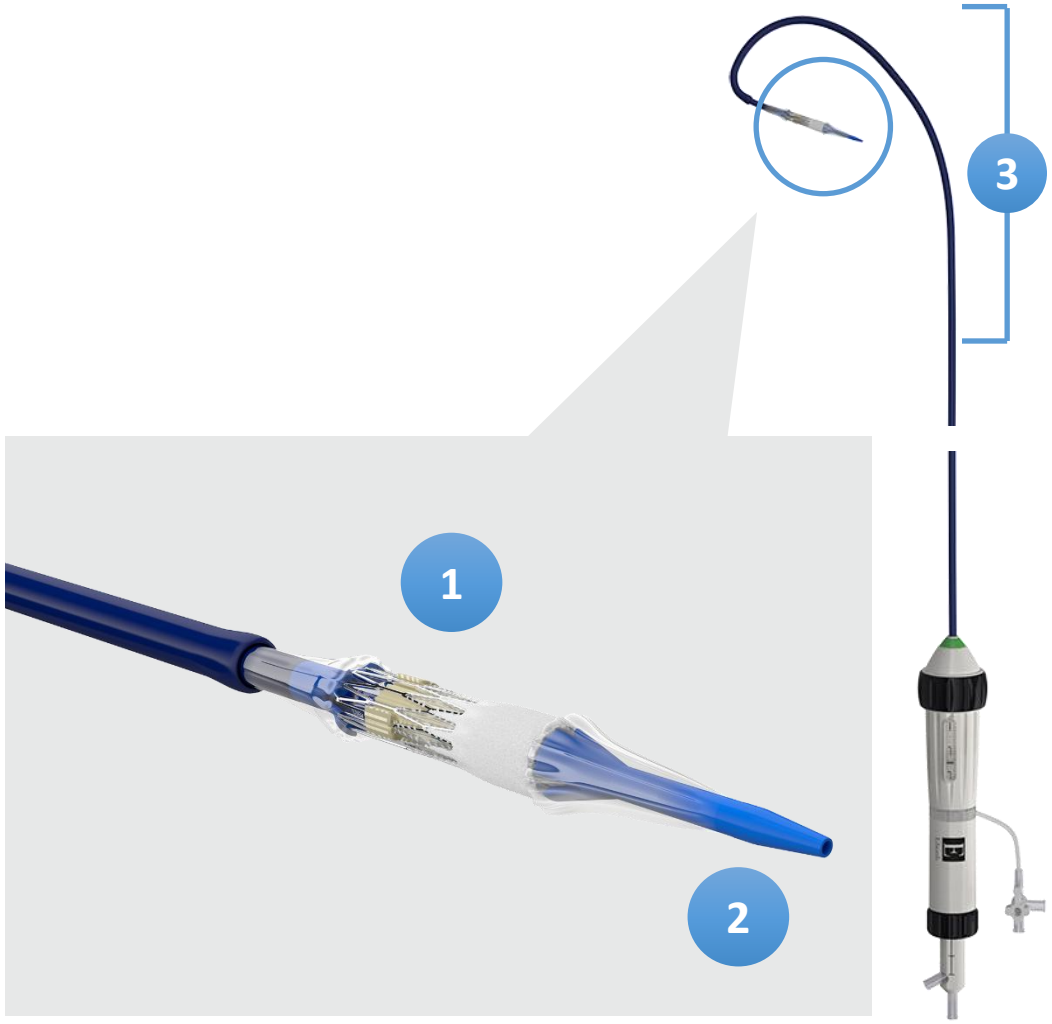
Bovine Pericardial Tissue 3

- Utilises the same bovine pericardial tissue and processes as Edwards surgical valves

** Compared to the SAPIEN 3 valve*

Edwards SAPIEN 3 Ultra Delivery System

Streamlining TAVI procedures



Balloon design

1

- On-balloon valve crimping streamlines the procedure
- Lower crossing profile*
- Eliminates valve alignment and flex catheter retraction steps

Redesigned distal end

2

- Lower crossing profile*
- Smooth tip-to-valve transition
- Short, tapered distal tip

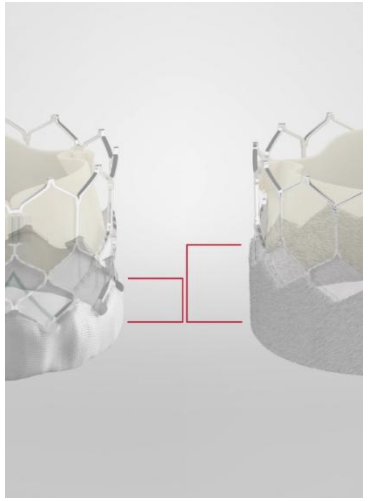
Responsive articulation

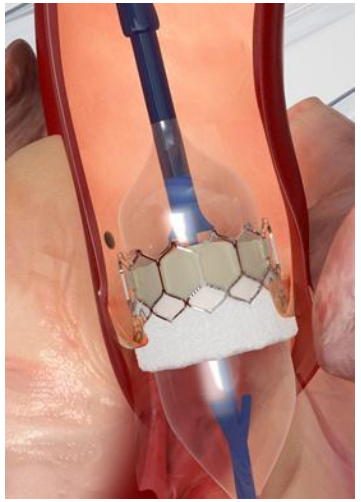
3

- Supports predictable deployment
- Designed for responsive control during tracking and positioning
- Dual articulation with flex indicator

** Compared to the Edwards Commander delivery system*

Edwards SAPIEN 3 Ultra Transcatheter Heart Valve





Increased outer skirt height

- Approximately 40% taller outer skirt*
- Same inner skirt height*

** Compared to the SAPIEN 3 valve*

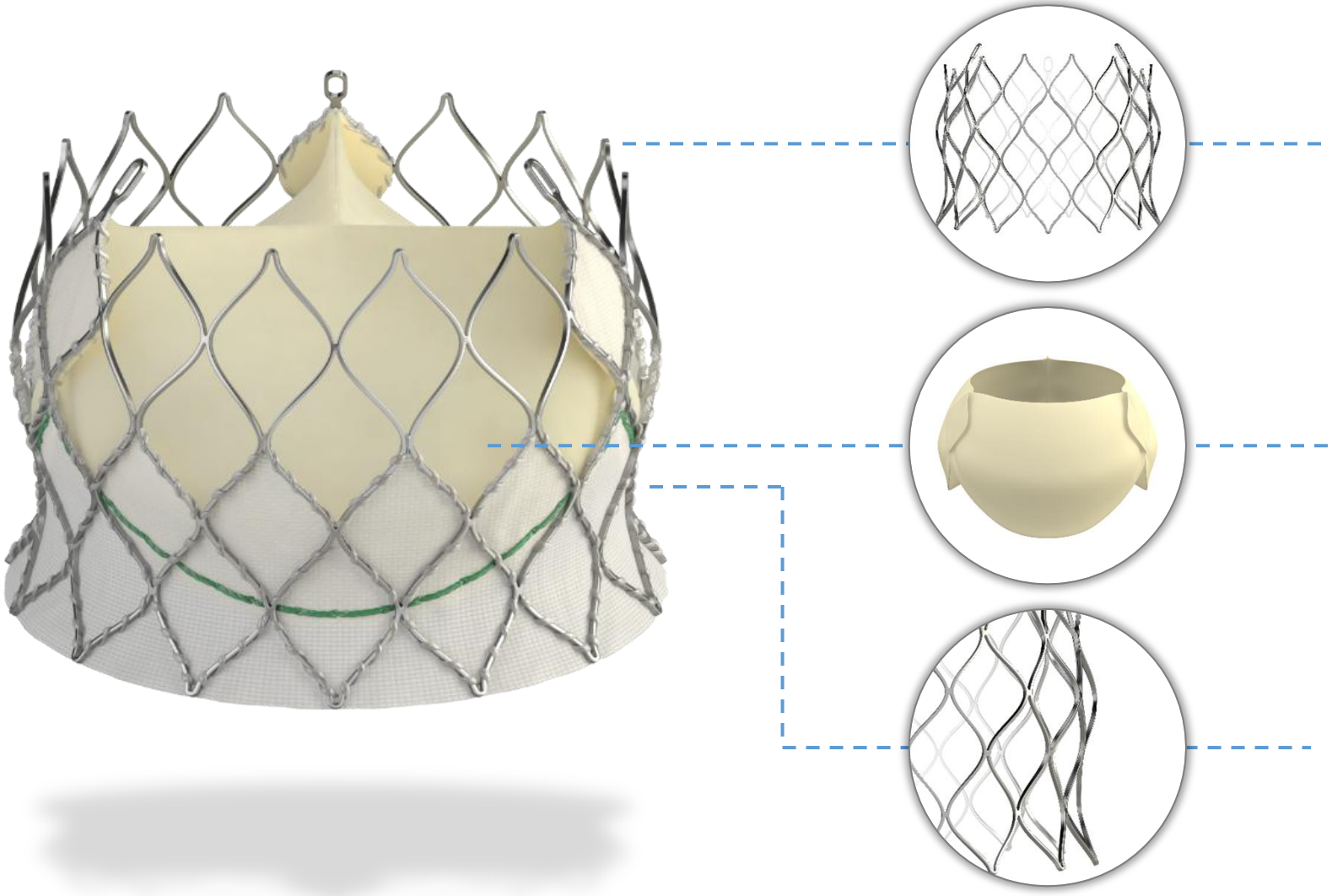
Textured outer skirt

- Textured PET material
- Similar biocompatible material as the SAPIEN 3 valve

Frame and leaflet design

- Cobalt chromium alloy frame for circularity
- Bovine pericardial tissue leaflets
- Leaflet shape optimised for haemodynamics

Edwards CENTERA Transcatheter Heart Valve



Short frame height designed to respect the cardiac anatomy

- Same bovine pericardial tissue as SAPIEN valve family
- **Novel tissue technology** allows the valve to be stored dry

Unique contoured frame geometry designed to anchor and seal within the annulus for low PVL rates

Edwards CENTERA Delivery System

Active articulation aids in tracking over the aortic arch and valve positioning

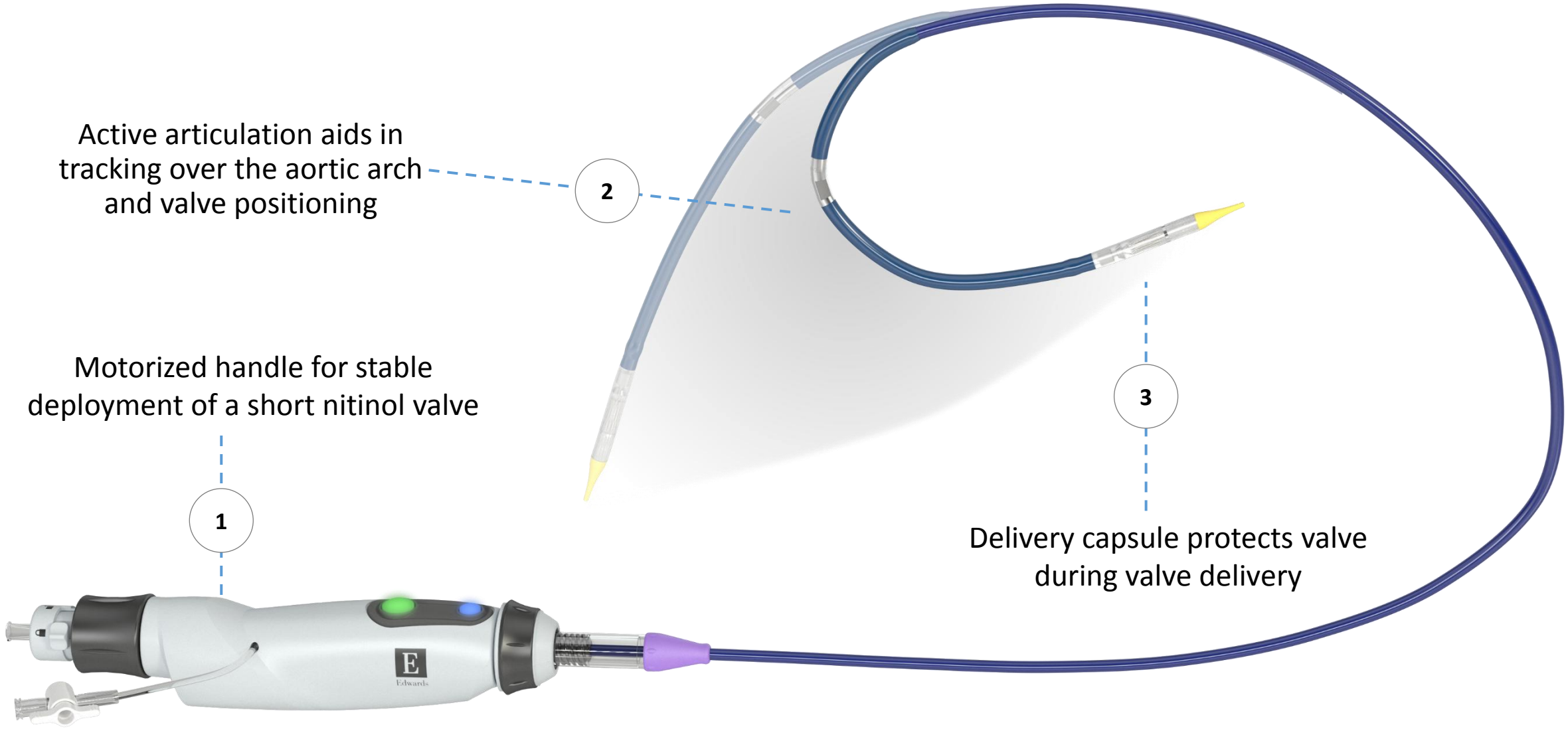
2

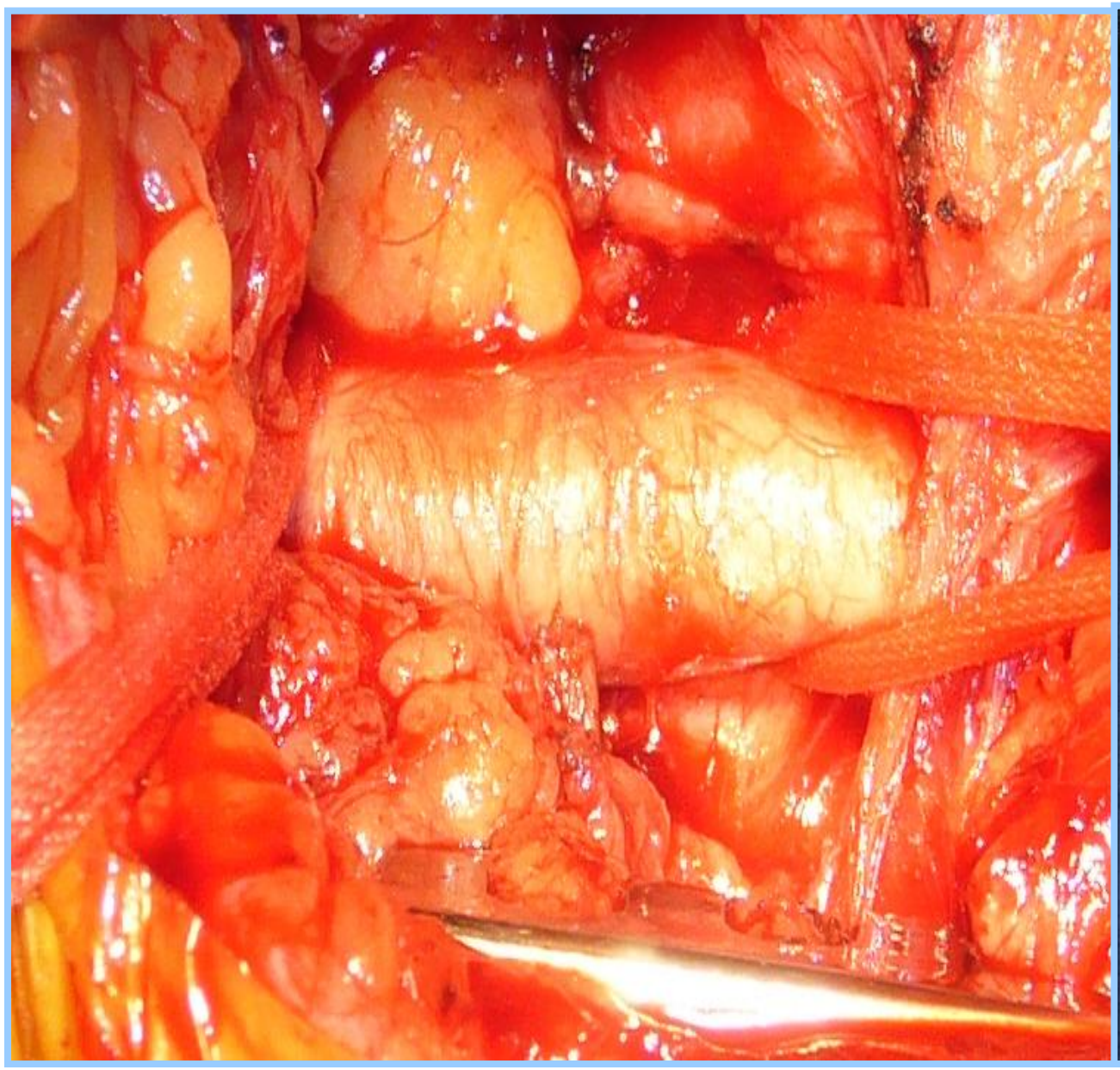
Motorized handle for stable deployment of a short nitinol valve

1

3

Delivery capsule protects valve during valve delivery





22 nebo 24 F
zavaděč

From a standard sheath to the eSheath delivery system

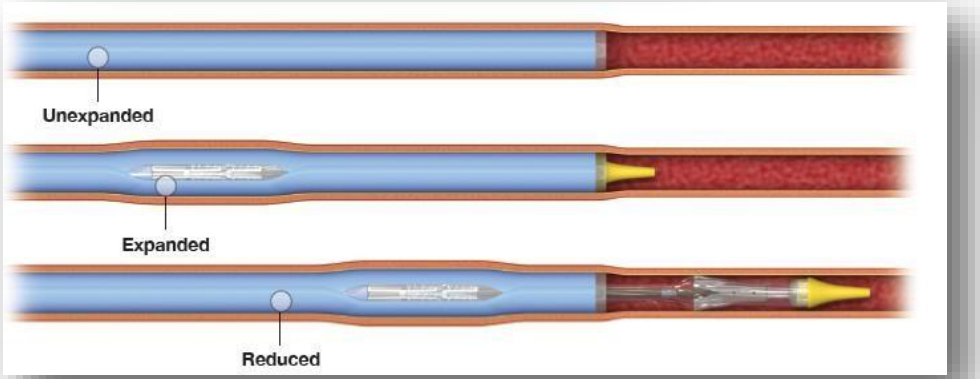
- Designed to reduce vascular trauma

1

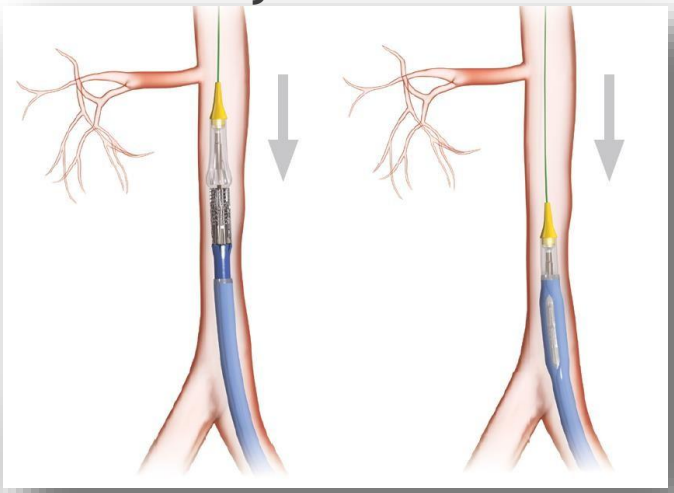
Smaller entry/exit profile

2

The DEM™ offers Transient Expansion

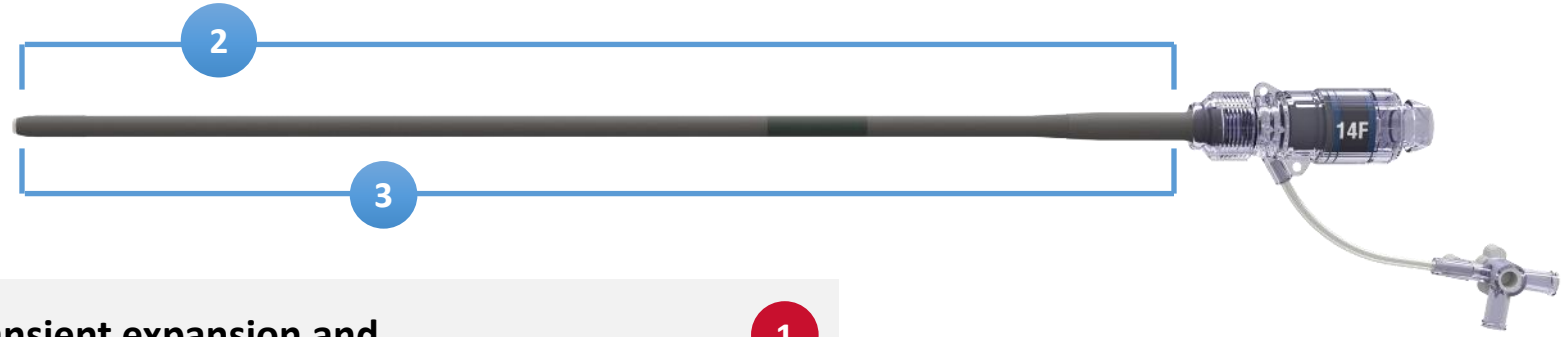


- The DEM™ allows for valve retrievability[1]



Edwards Axela Sheath

Next-generation 14F expandable, seamless sheath



Transient expansion and active contraction 1

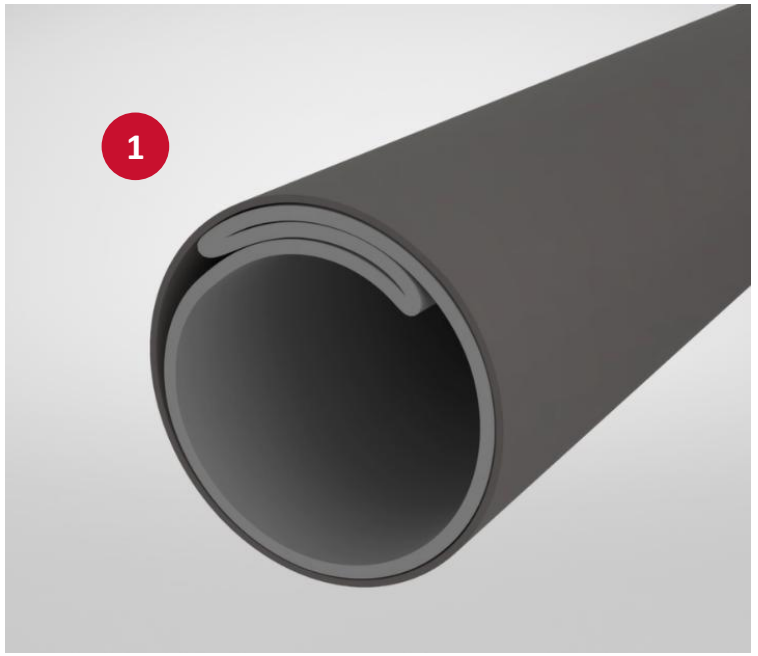
- 14F expandable sheath
- Enables low profile insertion and removal

Seamless sheath 2

- Seamless design maintains optimal haemostasis throughout procedure

Hydrophilic coating 3

- For smooth insertion and tracking



VÝVOJ TECHNOLOGIE TAVI

SPOLEČNOSTI

EDWARDS LIFESCIENCES

Děkuji za pozornost