AP Valve 2018
Seoul, August 10, 2018

The Global Landscape of TAVR Newcomers

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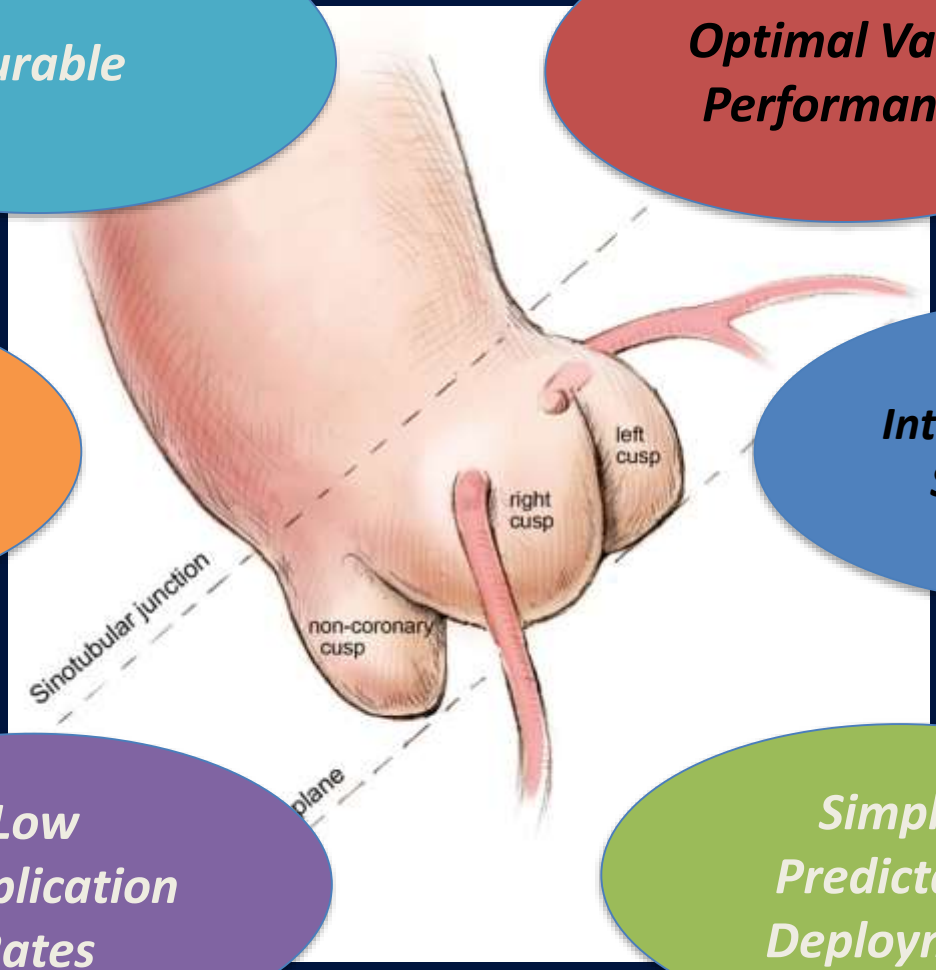
Physician Name	Company/Relationship
Speaker Bureau/Advisory Board:	Medtronic: C, SB, AB, OF LivaNova: C, SB, AB Highlife: AB, SB Boston Scientific: C, SB, AB Millipede: SB, C Pipeline: SB,C
Equity Interest:	InSeal Medical: E, AB, Valtech: E, SB, Claret: E, AB Shockwave: E, AB Valve Medical: E, AB Mitra/Trialign E, AB, SB

Key
G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker's Bureau O – Ownership OF – Other Financial Benefits

The Ideal Transcatheter Aortic Valve



Durable

Optimal Valve Performance

Low Profile for Transfemoral Delivery

Minimal Interference with Surrounding Structures

Low Complication Rates

Simple, Predictable Deployment

TAVR Newcomers

Global Landscape (#25)

- Sapien 3
- Evolut R
- Lo

Current Leaders!

- Jena Valve
- Centera
- Venus A Valve

- J – Valve Ausper
- VitaFlow (Microport)
- Taurus One
- Tri

Future Contenders?

- HLT Meridian
- NVT (Nautilus)
- Xeltis
- Zurich TEHV

TAVR Newcomers

Global Landscape (#25)

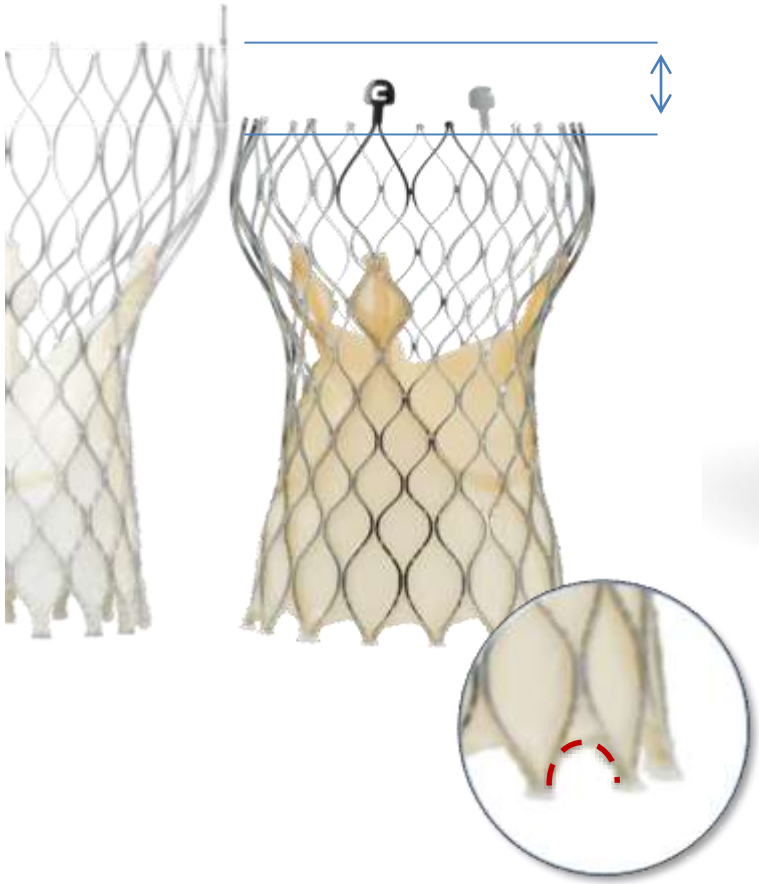
- ***Sapien 3***
- ***Evolut R***

} ***Current Industry Standard***

- **Lotus**
- **Acurate**
- **Portico**
- **Direct Flow**
- **Engager**
- **Jena Valve**
- **Centera**
- **Venus A V**

Current "Standards" for TAVR

MDT Evolut R (PRO)



Edwards Sapien 3

Real-world outcomes in over 12,000 patients have been reported

MVCs	***Pacemakers***
Weighted Average: 2.9%	Weighted Average: 16.3%

MVCs	***Pacemakers***
Weighted Average: 4.8%	Weighted Average: 13.3%

All Stroke	***PVL***
Weighted Average: 2.9%	Weighted Average: 3.7%

All Stroke	***PVL***
Weighted Average: 1.9%	Weighted Average: 2.2%

TAVR Newcomers

Global Landscape (#25)

- Sapien 3
- Evolut
- ***Lotus***
- ***Acurate***
- ***Portico***
- Direct Flow
- Engager
- Jena Valve
- Centera
- Venus A Valve

Next in Line
Increasing Clinical Use

“Next in Line” for TAVR

LOTUS (Edge)

ACURATE neo

PORTICO

"Next in Line" for TAVR

Pacemakers	***Pacemakers***	***Pacemakers***
Weighted Average:	Weighted Average:	Weighted Average:
30.7%	7.8%	17.2%
PVL	***PVL***	***PVL***
Weighted Average:	Weighted Average:	Weighted Average:
0.4%	4.0%	3.8%

TAVR Newcomers

Global Landscape (#25)

- Sapien 3
- Evolut R
- Lotus
- Acurate
- Portico
- *Direct Flow*
- *Engager*
- Jena Valve
- Centera
- Venus

Early or Later Demise

TAVR Newcomers

Global Landscape (#25)

- **Sapien 3**
- **Evolut R**
- **Lotus**
- **Acurate**
- **Portico**
- **Direct Flow**
- **Engager**
- ***Jena Valve***
- ***Centera***
- ***Venus A Valve***

Rebooting and/or Increasing Momentum

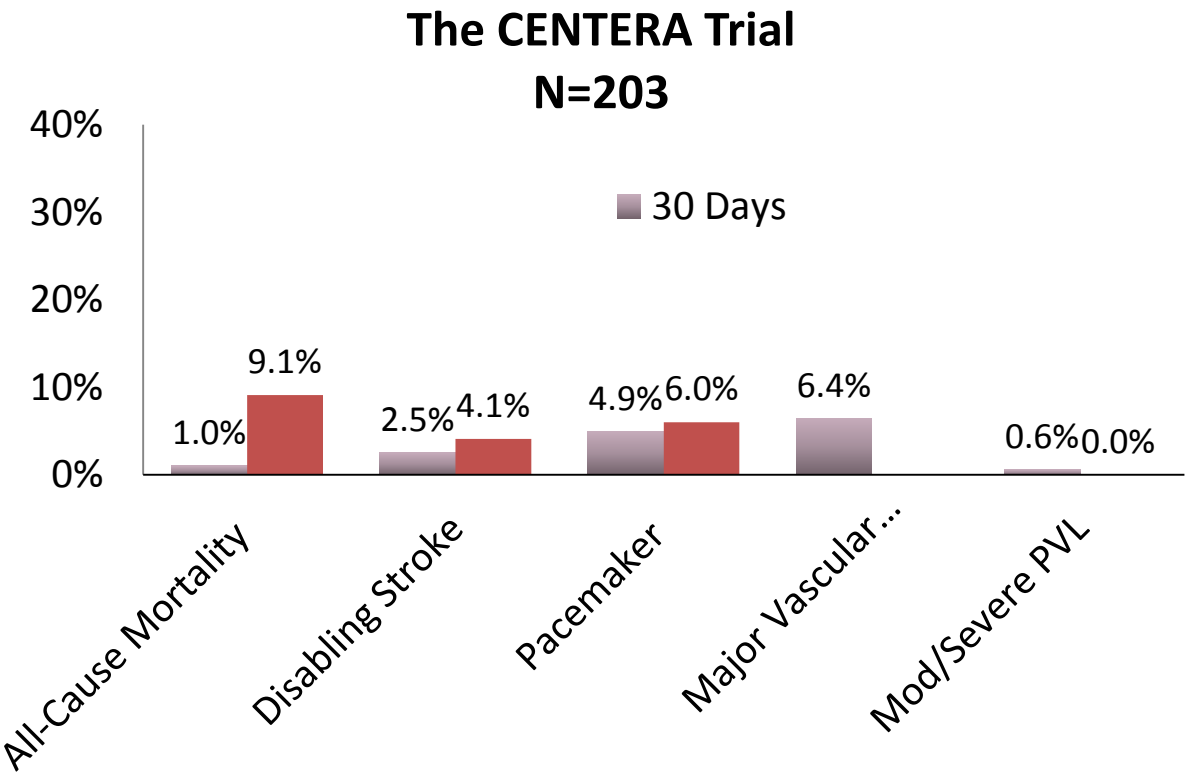
“Rebooting” or Increasing Momentum

JENA Valve

CENTERA

VENUS A Valve

"Rebooting" or Increasing Momentum



TAVR Newcomers

Global Landscape (#25)

All of the Rest!

- J – Valve Ausper
- VitaFlow (Microport)
- Taurus One
- Trinity
- Colibri
- Inovare
- Thubrikar
- Valve Medical
- Triskele
- BioValve (Biotronik)
- MyVal (Meril Lifescience)
- HLT Meridian
- NVT (Nautilus)
- Xeltis
- Zurich TEHV

TAVR Newcomers

Global Landscape (#25)

Pre-clinical

or

Early clinical

- J – Valve Ausper
- VitaFlow (Microport)
- Taurus One
- Trinity
- Colibri
- Inovare
- Thubrikar
- Valve Medical
- Triskele
- BioValve (Biotronik)
- MyVal (Meril Lifescience)
- HLT Meridian
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- Xeltis
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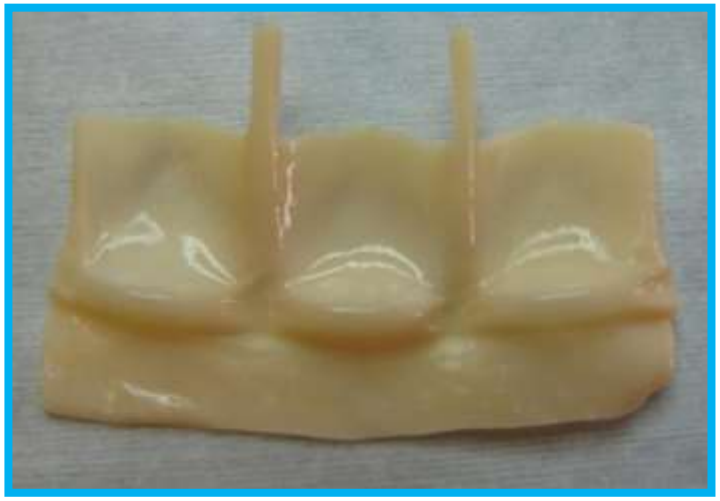
Valve Medical

Valve & System Design



3D valve leaflet

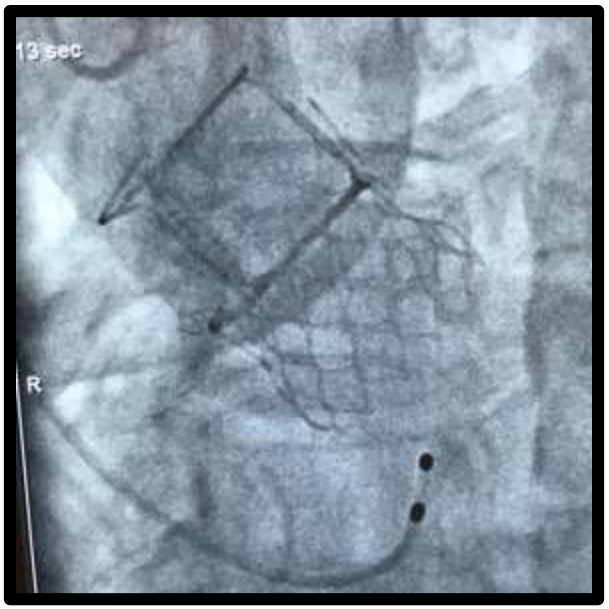
Hydrogel coating

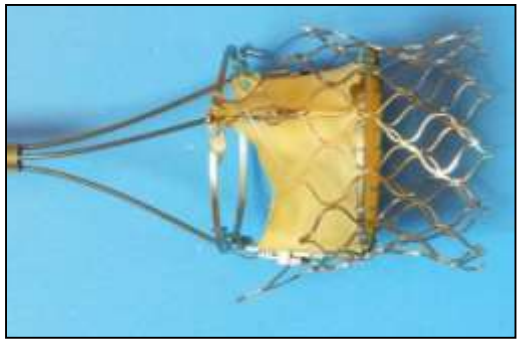
Valve Medical Modular Implant

FIM Case in Sao Paulo (10/09/17)

Grube E, Abizaid A, Leon MBL

Valve Medical TAVR Modular Implant
10/8 French equivalent



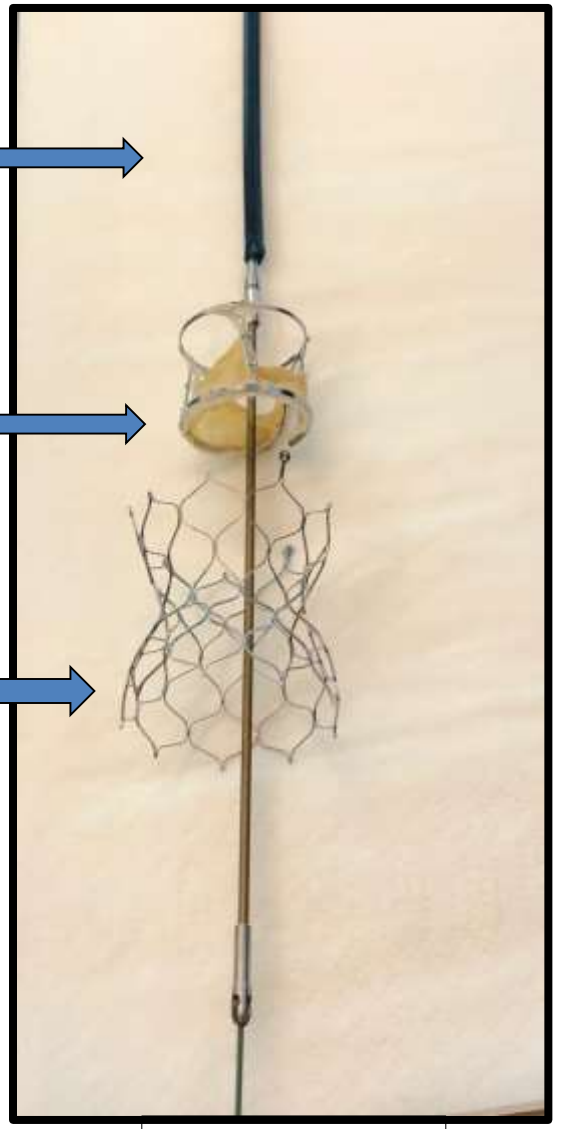


2016

10F/8F Sheath

Valve Module

Frame



2018

TAVR Newcomers

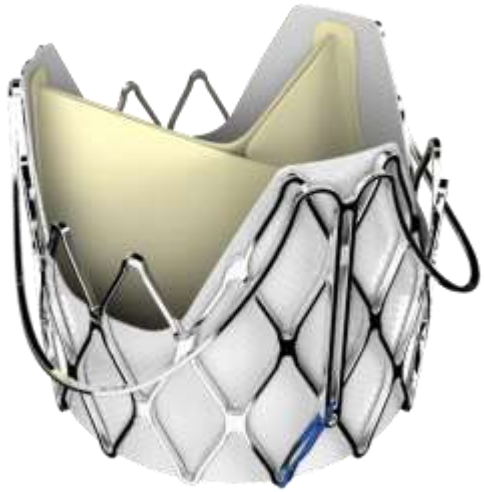
Global Landscape (#25)

International Device Parade

- China
- China
- China
- UK
- U.S.
- Brazil
- U.S.
- Israel
- UK
- Germany
- India
- U.S.
- Germany
- Switzerland
- Switzerland

J - Valve

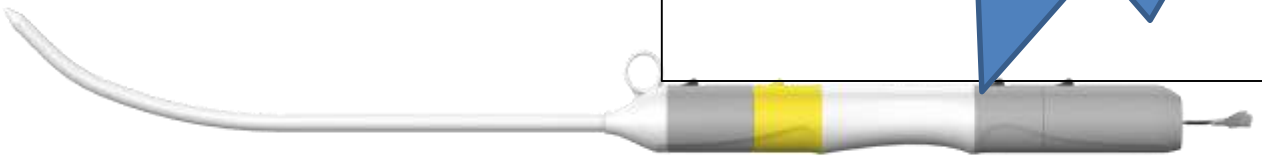
Valve & System Design



J-Valve Ausper

- Porcine pericardial tri-le let valve
- Nitinol short self pa g fra me *for trans-*
- ***Nitinol cle*** ***oper*** ***with nativ*** ***alve-ste*** ***flets***
- 27Fr s atheter with a

CFDA Approved 2017



Microport Shanghai TAVR (VitaFlow)

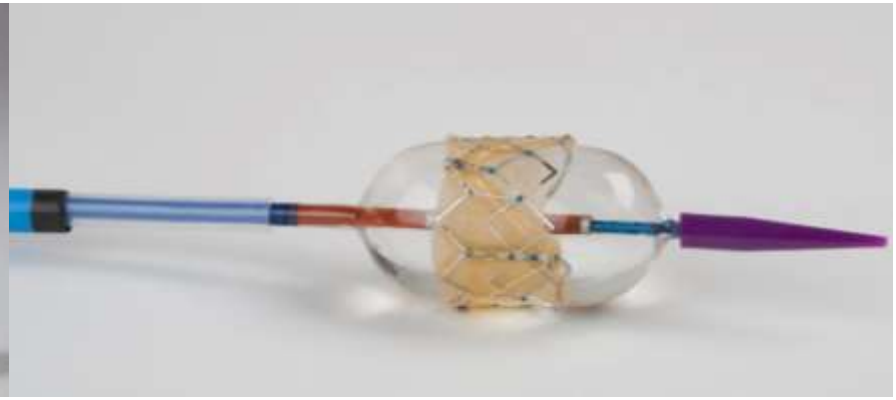
Valve & System Design

VitaFlow

- Bovine pericardial leaflets with anti-calcification treatment
- Multi-level self-expanding nitinol frame (high radial force inflow and open cell outflow for CA access)
- ***18F delivery system (motorized)***
- ***Prolonged (beyond inflow) inner and outer layered double skirt PVL reduction***

Colibri TAVR

Valve & System Design



- ***Thin dry-leaflet tec*** ***continuous surface*** design with few sut ut-of-round anatomies and large EOA (> 2c
- ***Pre-packaged, pre-*** ***ofile, ready-for-use***
- Balloon-expandable ystem
- Valve sizes: 21mm, m

Inovare TAVR

Valve & System Design

Proseal
Synthetic Fibers

- Balloon-expandable CoCr frame design
- ***Single bovine pericardial cut-out***
- Closed resting leaflet position; large EOAs
- Valve sizes 20, 22, 24, 26, 28, 30, and 32 mm diameters
- ***16 Fr expandable sheath for all valve sizes***
- ***Synthetic fibers (Proseal) added to outer frame aspect to interact with the annulus and prevent PVR***

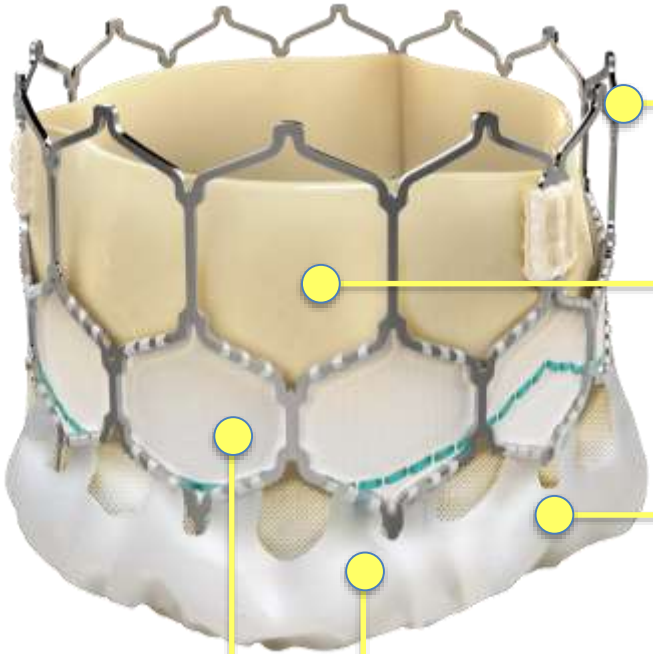
BioValve (Biotronik)

Valve & System Design

- Porcine pericardial tri-leaflet valve
- Nitinol self-expanding frame with high radial force inlet and large cell outlet
- 18 Fr delivery system
- ***Pericardial skirt to reduce PVR***

MyVal (MLS)

Valve & System Design



Hybrid Cell Design Concept

Open cells on upper half to ensure un-jailing of coronary ostia

Closed cells on lower half for high radial strength

Average height 18 mm

Nickel Cobalt alloy frame for high radial strength & RO

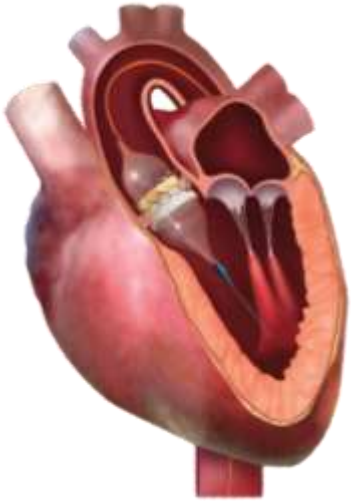
Bovine pericardial leaflets

Tri-axial Pt RO markers
One on each commissure post.
4mm from base

Internal PET sealing cuff for lower profile & puncture resistance

External PET buffing to minimize para-valvular leaks

Ø – 20 mm, 23 mm, 26 mm, 29 mm



MyVal (MLS)

Valve & System Design

14 Fr Distal Entry Profile

Python expandable sheath

Available in 14 Fr & 16 Fr versions

Lubricious, hydrophilic shaft coating

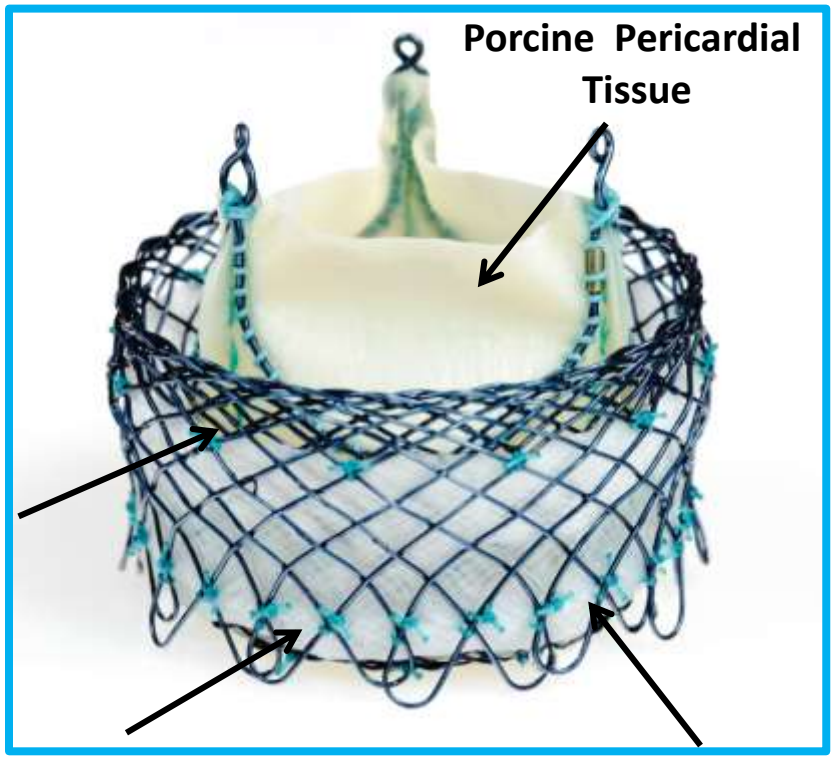
Sheath expands momentarily (like a python swallowing prey) to allow passage of TAVR crimped balloon catheter

MyVal Delivery System in extreme flexion

MyVal TAVR device is crimped directly on the balloon

HLT Meridian TAVR

Valve & System Design



- ***Repositionable and 100% retrievable (after final position)***
- Low profile to avoid coronaries
- Flexible posts to reduce stress on leaflets

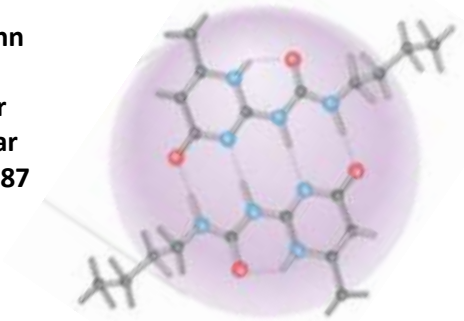
Endogenous tissue restoration:

combining 3 scientific disciplines

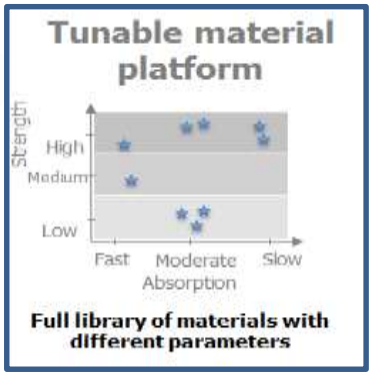
Supramolecular Chemistry

Jean Marie Lehn

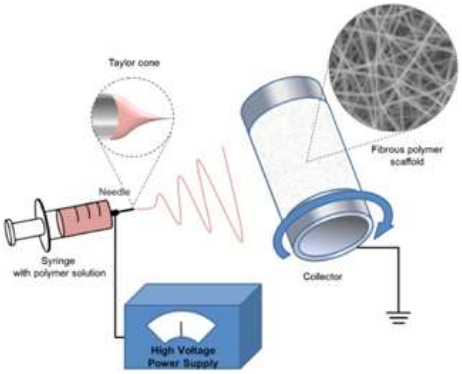
Nobel prize for Supramolecular Chemistry , 1987

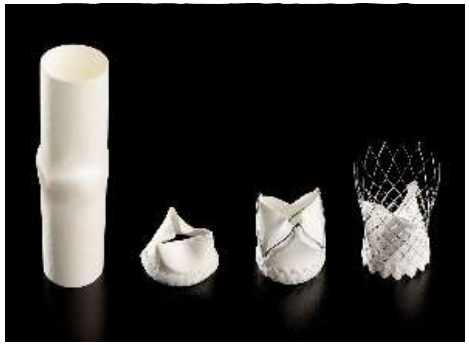


[1]Sijbesma, Science, 1997

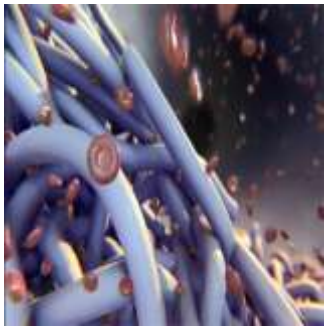


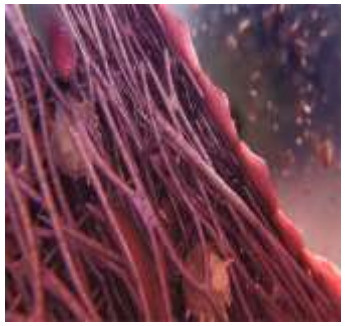
Electrospinning

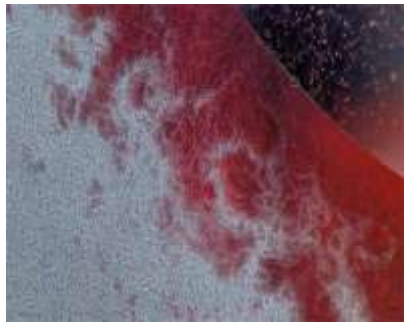




Regenerative Medicine







Xeltis

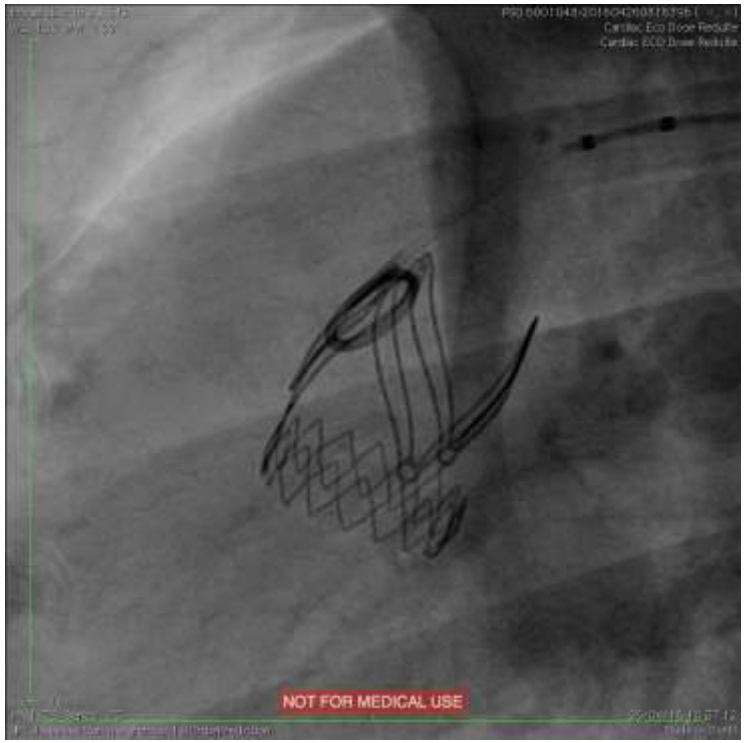
Endogenous Tissue Restoration (ETR)

Valve after bioabsorption

- ***Synthetic matrix made of novel biobsorbable supramolecular polymers*** *using electrospinning techniques*
- *Polymer leaflets mounted on nitinol self-expanding frame*
- ***Regrowth of endogenous tissue coincident with bioabsorption of polymer implant***
- *Natural self-healing anti-inflammatory leaflets*

Xeltis

Endogenous Tissue Restoration (ETR)



Animal implant

- Synthetic matrix made of novel biobsorbable supramolecular polymers using electrospinning techniques
- Polymer leaflets mounted on nitinol self-expanding frame
- Regrowth of endogenous tissue coincident with bioabsorption of polymer implant
- Natural self-healing anti-inflammatory leaflets

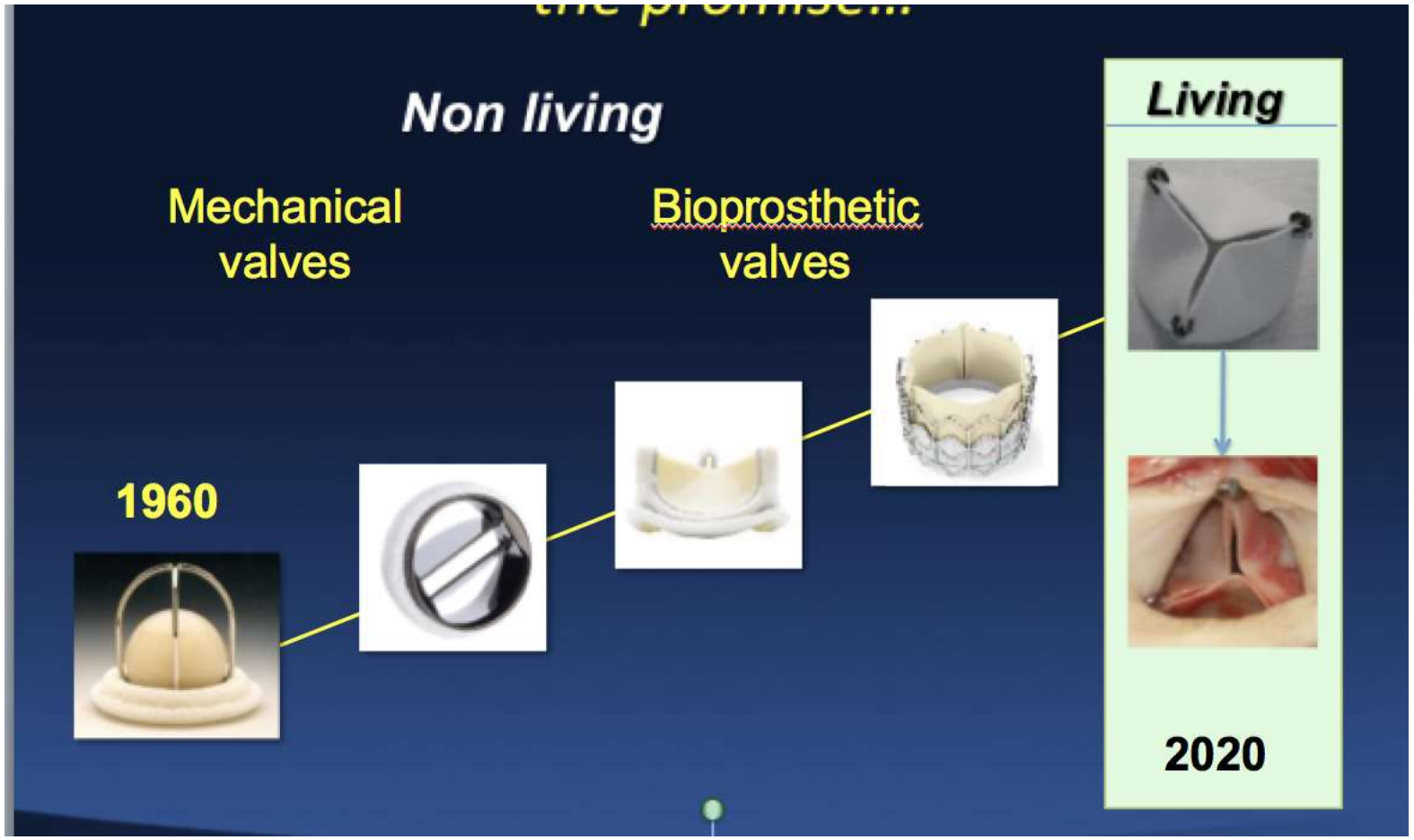
TAVR Newcomers

Caveats to Consider…

- **There is no single "perfect" TAVR system** - *design optimization involves tradeoffs and compromises (e.g. external cuff to reduce PVR adds profile)*
- **Strong subjective opinions regarding features** – *which is more important… PVR prevention, ultra-low profile, low PPM rate, retrievable and repositionable, BE vs. SE, etc.*
- **Significant operator experience necessary to formulate thoughtful impressions** – *difficult to be an expert with more than ~3 TAVR systems*
- **Future TAVR systems should be expected to treat ALL patients with AS** (esp. lower risk and BAV)!

Tissue Engineered Heart Valves

the promise…



One valve for life!

TAVR Newcomers