From PVT into Contemporary Edwards Sapien Valves

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PVT to Sapien

Why Did We Do It?
Which therapy – AVR, nothing?

92 yo man with critical AS...

- severe COPD
- creat 2.8
- previous CABG (patent LIMA)
- EF 30%
- Class IV CHF
- STS 15.5%
At Least 30% of Patients with Severe Symptomatic AS are “Untreated”!

Severe Symptomatic Aortic Stenosis
Percent of Cardiology Patients Treated

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

Reasons for non-treatment: 1. elderly, 2. co-morbidities, 3. patient refusal

- Bouma 1999: 41%
- Lung* 2004: 32%
- Pellikka 2005: 30%
- Charlson 2006: 40%
- Bach 2009: 52%
- Spokane (prelim): 31%
- Vannan (Pub. Pending): 55%

AVR: Red
No AVR: Blue
PVT to Sapien

Pre-Clinical Development
The Andersen Stent-Valve (1989)
The Andersen Stent-Valve (1992)
Alain Cribier Sketches (1990)

1 2 3

Systole

Diastole

1. Catheter + valve + sheath across the valve
2. Sheath withdrawal
3. Balloon inflation
4. Balloon deflation
5. Catheter withdrawal Valve in place

FOUNDERS

Martin Leon
Alain Cribier
Santon Rowe
Stan Rabinovich

Partner: ARAN Research & Development Ltd.
Percutaneous Valve Technologies (PVT)

*Early Prototypes*

- Different valve configurations
- Different leaflet materials, designs and attachment means.
- Extensive hydrodynamic testing

PVT designed the testing equipment and crimping tools
PVT 2000-2002: The Sheep Era

CERA (Centre d’Experimentation et de Recherche Appliquée)
Institut Monsouris, Paris, France
PVT - Cadaver Heart Study at AFIP
PVT to Sapien

The First Case in Rouen
I have a fascinating case that I would like to discuss with you!

57 y/o  
EF 10%  
BP 60 mmHg with vasopressors  
Intra-LV thrombus  
Transeptal BAV performed  
Valve implantation, transseptal approach!

What do you think?

Imminent death
Externalization of wire
Highest risk !..

You have my complete support to move ahead with the first PVT clinical placement in this desperately ill man.

Snaring the stiff wire is a good idea
IABP?

High likelihood of failure but... it just might work and save his life!

Best operator in the world!
Antegrade Approach: Guidewire Position in LV
Valve Positioning
April 16, 2002; FIM-TAVI, Transseptal
April 16, 2002; FIM-TAVI, Transseptal
April 16, 2002; FIM-TAVI, Transseptal

15 min Post-TAVI
Conclusions—Nonsurgical implantation of a prosthetic heart valve can be successfully achieved with immediate and midterm hemodynamic and clinical improvement.
PVT to Sapien

Early Clinical Speedbumps
Dr. Alain Cribier
First-in-Man PIONEER

April 16, 2002

OK, What Now?

15 min post-TAVR
TAVR - The Early Skeptics

- Strokes
- Aortic rupture
- Coronary occlusion
- Mitral valve injury
- Valve instability – embolization
- Para-valvular regurgitation
- Vascular complications
- Valve durability
- Technical challenges insurmountable

This is a crazy project that will fail!
The “Early Days” of TAVR

Equine Pericardial Valve

Single size 23mm

Paravalvular AR > Grade 2 in 25%


RECAST: 20 patients Dec 2003 – April 2005

24F Sheath in Femoral vein
Collaboration across the seas....

Drs. John Webb and Alain Cribier
**Retrograde** Trans-femoral Cribier-Edwards Aortic Valve Deployment

Rapid pacing: 200/min
The Heart Team - A Deal with the Devil?

Transapical case

Leipzig 2004

M. Mack

F. Mohr
2004: Edwards Lifesciences Acquires PVT

New Valve, New Delivery Systems, New Approaches

Transfemoral

Transapical

Cribier-Edwards, 23mm

Edwards SAPIEN 23mm, 26mm

J. Webb

F. Mohr

M. Mack

T. Walther

Treated tri-leaflet Bovine Pericardial Valve

Stainless steel stent
PVT to Sapien

The Road to Sapien
TAVR in 2017: Growth Drivers

- TAVR growth has been fueled by:
  - the multi-disciplinary heart team
  - rapid technology enhancement
  - commitment to evidence-based medicine
  - striking reduction in complications
  - simplification of the procedure
The Current Generation

*Edwards – SAPIEN THV*

- Bovine Tissue
- ThermaFix Treatment
- Pericardial Mapping
- Leaflet Deflection
- Proprietary Processing

New Skirt Height

Untreated Equine Tissue

Current Skirt Height

Edwards-SAPIEN THV

Cribier-Edwards THV
Edwards Sapien XT THV

Cobalt Frame & New Leaflet Geometry

Leaflet Matching & ThermaFix

Partially Closed Design

Sapien XT

Tissue Attachment

Finite Element Analysis
## Edwards Balloon Expandable Valve Platforms

<table>
<thead>
<tr>
<th>SAPIEN Valve</th>
<th>SAPIEN XT Valve</th>
<th>SAPIEN 3 Valve</th>
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</thead>
<tbody>
<tr>
<td><strong>Stainless steel frame</strong></td>
<td><strong>Cobalt chromium frame</strong></td>
<td><strong>Cobalt chromium frame</strong></td>
</tr>
<tr>
<td><strong>Bovine pericardial tissue</strong></td>
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<tr>
<td><strong>Low frame height</strong></td>
<td><strong>Lower profile: 16-20F</strong></td>
<td><strong>Lower profile: 14/16F</strong></td>
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<tr>
<td><strong>Multiple access approaches</strong></td>
<td><strong>Complete range of sizes: 20, 23, 26, 29 mm</strong></td>
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<tr>
<td><strong>Sizes: 23, 26 mm</strong></td>
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**Images:**
- Edwards Balloon Expandable Valve Platforms
  - SAPIEN Valve
  - SAPIEN XT Valve
  - SAPIEN 3 Valve
Bovine pericardial tissue
- Scalloped leaflet shape
- CE ThermaFix* process is intended to minimize the risk of calcification

Frame design
- Enhanced frame geometry for low delivery profile
- High radial strength for circularity

Low frame height
- Respects the cardiac anatomy

Outer skirt
- PET outer skirt designed to reduce paravalvular leak

Inner Skirt
- Polyethylene terephthalate (PET)
Edwards *Flex Cath*
Delivery System Evolution

Retroflex 3

Retroflex 2
Sapien XT + NovaFlex Delivery System

18 Fr profile
SAPIEN 3 Commander Delivery System
Distinguishing Features

- Improved coaxial alignment
- Accurate positioning

### SAPIEN 3 Valve Size

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<th>SAPIEN 3 Valve Size</th>
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<th>23 mm</th>
<th>26 mm</th>
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<tr>
<td>Expandable Sheath</td>
<td>14F</td>
<td>14F</td>
<td>14F</td>
<td>16F</td>
</tr>
<tr>
<td>Minimum Access Vessel Diameter</td>
<td>5.5 mm</td>
<td>5.5 mm</td>
<td>5.5 mm</td>
<td>6.0 mm</td>
</tr>
</tbody>
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Evolution of Balloon-Expandable Transcatheter Valves

- Cribier-Edwards 2002
- SAPIEN 2006
- SAPIEN XT 2009
- SAPIEN 3 2013

Sheath compatibility for a 23 mm valve
PARTNER THV Evolution

PARTNER enrolled >9,000 patients in FDA studies (including 4 RCTs) with 3 generations of TAVR systems in ~ 7 years!
Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheater aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis

Baseline Patient Characteristics
S3HR Patients (n=583 at 29 sites)

Average STS = **8.6%** (Median 8.4%)

Average Age = **82.6 yrs**

- Male 58%
- Female 42%

- TF, 84%
- TA, 10%
- T Ao, 6%

N = 583

Bar graph showing distribution of implant size:
- 1.9% for 20 mm
- 34.3% for 23 mm
- 38.9% for 26 mm
- 24.9% for 29 mm
Mortality and Stroke: S3HR
At 30 Days (As Treated Patients)

Mortality

- All-Cause
- Cardiovascular

O:E = 0.26
(STS 8.6%)

Stroke

- All Stroke
- Disabling

2.2
1.4

1.5
0.9

S3HR

S3HR
Baseline Patient Characteristics
S3i Patients (n=1076 at 51 sites)

Average STS = 5.3% (Median 5.2%)
Average Age = 81.9 yrs

N = 1076

TF, 89%
TA, 7%
TAo, 4%

Male 62%
Female 38%

4.1% 32.2% 43.7% 20.0%
20 mm 23 mm 26 mm 29 mm
Mortality and Stroke: S3i
At 30 Days (As Treated Patients)

Mortality

- All-Cause
- Cardiovascular

O:E = 0.21
(STS 5.3%)

Stroke

- All Stroke
- Disabling

S3i

1.1
0.9

2.6
1.0
All-Cause Mortality at 30 Days
Edwards SAPIEN Valves (As Treated)

PARTNER 1 and 2 Trials
(Overall and TF Patients)
Strokes (All) at 30 Days
Edwards SAPIEN Valves

PARTNER 1 and 2 Trials
(Overall and TF Patients)

Neurologist evaluations (pre- and post)
PARTNER I and II Trials
Overall and TF Patients

- SAPIEN
  - P1B (TF): 12.0%
  - P1A (Overall): 11.5%
  - P2B (TF): 16.9%

- SAPIEN XT
  - P2B XT (TF): 24.2%

- SAPIEN 3
  - S3HR (Overall): 2.9%
  - S3i (Overall): 4.2%
Same Day Discharge after Transcatheter Aortic Valve Replacement: Are We There yet?

Philippe Généreux, M.D., Philippe Demers, M.D., and Frédéric Poulin, M.D.

Early discharge after transcatheter aortic valve replacement (TAVR) has been increasingly reported, and is now becoming routinely performed in experienced TAVR centers. However, to the best of our knowledge, no case has been described where a patient was safely discharged on the same the day of the procedure. This report will present the case of a patient who underwent a successful transfemoral TAVR and was safely discharged home the same day. Specific requirements and criteria are proposed to ensure the safety of this approach. © 2015 Wiley Periodicals, Inc.

Key words: TAVR; TAVI; discharge
PVT to Sapien

A Breakthrough Technology
What is a Breakthrough Technology?

• Address an unmet clinical need; penetrate an important area of clinical medicine which is not well served by current therapies

• Innovative concept and/or novel device, drug, or diagnostic technology

• Must be validated by rigorous evidence-based medicine clinical research

• Must be “generalizable” to the practicing medical community (sufficiently user-friendly)

• Rarely, elevates beyond subspecialty medicine and resonates as a significant socio-medical cultural advance (the “X” factor)