What is Structural Heart Intervention Today?

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Columbia University Medical Center
Cardiovascular Research Foundation
New York City

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London, United Kingdom
The Heart Team Course
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation / Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Grant / Research Support</td>
<td>Abbott, Boston Scientific, Edwards</td>
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<td>Lifescience, Medtronic</td>
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<tr>
<td>Consulting Fees / Honoraria</td>
<td>Abbott, Boston Scientific</td>
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<tr>
<td>Shareholder / Equity</td>
<td>GDS, Mitralign, Valve Medical</td>
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Background
Coronary Intervention
Endovascular Intervention
Myocardial Preservation
Vulnerable Plaque
Interventional CHD
Interventional EP
Interventional Neuroradiology
Interventional CHF
Interventional Valve Therapy
Intramyocardial Therapeutics
Interventional Therapies

SHD = structural heart disease

TCT Opening 2001

Columbia University Medical Center
New York Presbyterian
• New market segments may exceed PCI market size by 2020
• Emergence of future segments relies on technology and clinical data
• OUS markets will lead and exceed the size of US markets
Modern PCI = Percutaneous Cardiovascular Intervention!
The Modern Era of PCI

Clinical imperatives

New technology

Evidence-based validation
The “modern era” of PCI

“Early” Days

- Devices
- Proceduralist

Modern Era

- Therapies
- Clinician
Definitions & Scope
The Modern Era of PCI

**STRUCTURAL REVOLUTION**

- **Structural Heart Disease is a WASTE BASKET** meant to include all non-vascular procedures utilizing catheter-based technologies!

**Valve**
- BAV/PMC
- TAVR & MitraClip
- New Mitral and Tricuspid therapies
- PVL closure

**Non-Valve**
- Adult Congenital
- LAA/PFO Closure
- HF therapies
- Other…
Structural Heart Disease is a WASTE BASKET meant to include all non-vascular procedures utilizing catheter-based technologies!

Emphasizes the confluence of two fully evolved concepts – non-vascular image-guided therapies (echo and MSCT) and multi-disciplinary heart team strategies (with pre-procedure planning).

Requires significant adjustments in training of interventional operators and treatment milieus (e.g. hybrid cath lab/ORs).
Increasing Prevalence of Valvular Heart Disease in the Elderly

Population-based Studies

Olmsted County, MN

>1 in 10 people >75 years old have mod-severe VHD!

Nkomo VT at al. Lancet 2006;368:1005-1011
Estimated Global TAVR Growth

*This year > 100,000 and by 2025 almost 300,000!*
AS Based on Surgical Experience

2015 Severe Symptomatic AS Patients in the U.S.\(^1\)

AS Including the TAVR Experience

2015 Severe Symptomatic AS Patients in the U.S.¹

AS Patients Undiagnosed and Untreated

2015 Severe Symptomatic AS Patients in the U.S.¹

Mitral Regurgitation in the U.S.

*Disease Prevalence*

Total MR Patients = 4.6 Million

\[\text{MR} \geq 2+\]

44% 41%

2.6 M = DMR (56%)
2.0 M = FMR (44%)

2.0 M = MR \geq 3+

(0.9 M FMR, 1.1 M DMR)

1.9 M > 75 yo

Surgical Candidates* (54%)

1.6 M DMR, 0.9M FMR

* based upon “guidelines”

Mitral Regurgitation in the U.S.

**Disease Prevalence**

- **Total MR Patients (MR ≥2+)**: 4,600K
  - **Severe, MR≥3+**: 2,000K
  - **High-risk, MR≥3+**: 965K
  - **Annual incidence, MR≥3+**: 290K
  - **Annual MV surgery (3%)**: 55K

2016 MR Statistics

Large and Growing Clinical Unmet Need
Tricuspid Regurgitation
Currently Undertreated by Surgery

EU-22
Prevalence = 4,700,000
Incidence = 331,000
13,000

USA
Prevalence = 2,500,000
Incidence = 217,000
10,000

Patients w/ Moderate or Severe TR
Annual TR Surgeries

* Copyright 2017, Dymedex Consulting, Minneapolis, MN
(over 200 papers reviewed)
LAA Closure Devices

An Expanding Landscape

Watchman

Amulet

WaveCrest
PFO Closure (Amplatzer)

History of the RESPECT Trial

- 1st Enrollment occurred in 2003
- Final Enrollment occurred in 2011
- First Presentation – TCT Main Arena LBCT, October 2012
- NEJM – Concurrent publication October 2012
- Second Presentation – TCT Main Arena LBCT, October 2015
- Positive FDA Panel Vote 11 to 5 on Benefit/Risk, May 2016
- FDA Requests Final Updated Data Analysis, June 2016
- Third Presentation – TCT Main Arena – First Report Tuesday, Nov. 1 12:15 PM
- FDA Approval Pending

Primary Endpoint Analysis – As Treated Cohort
72.7% risk reduction of stroke in favor of device

Event-free Probability

Time to Event (years)
Heart Failure Therapies
(The next “big breakthrough”?)

- Mechanical circulatory support
- Sensors to monitor therapy
- LV remodeling devices
- Contractility modulation
- Micro-VADs (interventional)
- Inter-atrial shunt implants
- Stem cell therapies
- Digital health initiatives
Advanced catheter-based hemodynamic support devices are under-utilized and will be a mainstay of acute HF, shock therapy, and protected PCI in the future!
Implantable Sensors for CHF

- **CardioMEMS**
- Simple PA artery implant
- Continuously monitors PA pressures (RF-powered, no battery)
- PA measurements by patients from home transmitted to a secure database and available to the physician for therapy changes

- **CHAMPION trial**
- Evaluate the safety and efficacy of the HF Pressure Measurement System in reducing heart failure (HF) related hospitalizations
- **550 randomized pts with HF**
  - 30% reduction in hosp at 6 mos
  - 38% reduction in hops over entire randomized period
Inter-Atrial Shunt Devices (IASD)  

*(Corvia and V-wave)*

- High LA pressures (LAp) and pulmonary congestion are the common link in both HFrf and HFpf.
- Transcatheter implant to create permanent interatrial shunt to decompress the elevated Lap without reducing CO.
Inter-Atrial Shunt Devices (IASD)

(Corvia - HFpEF)

A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial

Gerd Hosenfuß, Chris Hayward, Dan Burkhoff, Frank E Silvestry, Scott McKenzie, Finn Gustafsson, Filip Malek, Jan Van der Heyden, Irene Lang, Mark C Petrie, John G F Cleland, Martin Leon, David M Kaye, on behalf of the REDUCE LAP-HF study investigators

Lancet 387; March 26, 2016
Inter-Atrial Shunt Devices (IASD)

*(V-Wave - HFrEF)*

Unidirectional left-to-right interatrial shunting for treatment of patients with heart failure with reduced ejection fraction: a safety and proof-of-principle cohort study.

Lancet 387; March 26, 2016
Interventional Cardiology - 2016

Columbia University Medical Center
(4,100 interventions)

Interventional Sectors

- Coronary: 68%
- Structural: 22%
- Endovascular: 10%
Structural Heart Interventions - 2016

Columbia University Medical Center
(850 interventions)

Structural Sectors

- TAVR/BAV: 65%
- Adult Congenital: 19%
- Mitral/Tricuspid: 9%
- LAAC: 7%
Multi-disciplinary heart team with dedicated expertise in critical areas and sufficient infrastructure to optimize clinical care pathways

- structured clinics, patient care conferences, and pre/post-treatment clinical care and FU
- “full-time” physicians = cardiology, intervention, surgery, anesthesia, and imaging
- “consultants” = HF, neurology, geriatrics, etc.
- hospital nursing and hospital admin support to manage logistics and financial considerations
Structural Heart Team Collaborators

500th TAVR at Columbia...

Mat Williams
Susheel Kodali
• **Multi-modality imaging** with dedicated experts, although the entire operating team must have requisite interpretation skills

  ✓ imaging is necessary for diagnosis, pre-procedure planning, intra-procedure guidance, and long-term follow-up

  ✓ required = Echo - 2D/3D and TEE, advanced CTA and analysis workstations, angiography and DSA

  ✓ optional (nice to have) = CMR and co-registration software (CT – fluoro, echo – fluoro)
Structural Heart Interventions 2017

**Novel Imaging Systems**

Multi-modality Imaging is the RULE!

![Diagram showing imaging modalities]

- Patient Follow-up
- Patient Screening, Procedural Planning
- Intra-procedural Guidance

- Angio
- CTA
- TTE
- TEE + 3D
Training and Environment - dedicated training programs and tutorials for structural techniques (e.g. TEE, TS puncture, vascular access and management), new devices and novel procedures; modified interventional milieu to accommodate structural needs

- structural fellowships, programs and centers
- the concept of interventional echocardiography
- commitment to “hybrid” cath lab-OR or structural cath labs with anesthesia and imaging capabilities
A Dedicated TAVR Milieu

Hybrid Cath Lab/OR

Cath Lab Multi-Disciplinary Collaboration OR
A Dedicated TAVR Milieu

Hybrid Cath Lab/OR

A unique collaborative experience!
Clinical Research Capabilities with dedicated staff and infrastructure to screen, enroll, and execute with proficiency all stages of clinical trials

- key elements are IRB, contracting, and clinical research team fully aligned and supported by the hospital and institution
- involves early feasibility trials, pivotal clinical trials (incl. RCTs), and post-approval registries to comply with national standards and/or reimbursement requirements
Pipeline of TAVR Trials across the spectrum of aortic stenosis

Investigational devices
- **Edwards** Sapien/Sapien XT/S3
- **Medtronic** CoreValve/Evolut R
- **Boston** Lotus
- **Direct Flow Medical** Direct Flow
- **Abbott Vascular** Portico
- **Symetis** Acurate Neo
- Any available TAVR system

23 Studies!
Clinical Trial Pathways

**Preclinical**
- Preliminary testing of safety and side effects

**Phase I**
- Additional testing of efficacy and safety in larger sample size

**Phase II**
- Pivotal studies to compare efficacy and safety against comparator

**Phase III**
- Post-market studies to monitor safety and efficacy in real world

**Phase IV**
- Bench testing

**Clinical Trial Pathways**

Cardiovascular Research Foundation
Clinical Trial Pathways

**Bench Testing**
- Preclinical: Preliminary testing of safety and side effects
- Phase I: Additional testing of efficacy and safety in larger sample size
- Phase II: Pivotal studies to compare efficacy and safety against comparator
- Phase III: Post-market studies to monitor safety and efficacy in real world
- Phase IV: Clinical trial pathways
Final Thoughts
Final Thoughts...

- **Structural heart disease (SHD) is a new, dynamic, and clinically important sub-specialty which has sparked excitement and growth in the modern era of PCI.**

- The requirements include a dedicated multi-disciplinary team, specialized imaging expertise, continuous training exercises, specific cath lab and OR capabilities, and a commitment to clinical research (evidence-based medicine).

- TAVR has already achieved significant success as the “poster child” of SHD.
Soon to follow will be mitral/tricuspid disease and LAA/PFO closure.

An interesting recent development has been the realization that “combination therapies” are frequently required to manage complex SHD scenarios (e.g. TAVR + mitral + LAAC or combo mitral therapies or combo mitral/TV therapies).

Finally, an important future vision is to explore and conquer the impact of interventional device therapy in patients with various heart failure syndromes.
tct2017 takes you to the heart of Denver
October 29--November 2, 2017 • Colorado Convention Center
Denver, Colorado
Structural Heart: The Journal of the Heart Team is the new journal emphasizing the importance of the Heart Team in diagnosing and treating diseases of the heart valves, myocardium, and great vessels, as well as congenital heart disease.

Topics covered include:
• Diagnostic techniques
• Percutaneous interventional procedures
• Cardiovascular surgery
• Drug treatment
• Findings from the laboratory
• Clinical trials

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