Interventional Cardiology Transitions to *Structural Heart Disease*

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> 21st CardioVascular Summit **TCTAP**2016 April 26-29, 2016 Coex, Seoul, Korea

20 mins



April 27, 2016



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Martin B. Leon, MD

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

Affiliation / Financial Relationship

• Grant / Research Support

- Consulting Fees / Honoraria
- Shareholder / Equity

Company

Abbott, Boston Scientific, Edwards Lifescience, Medtronic, St. Jude Medical

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Claret, Coherex, Elixir, GDS, Medinol, Mitralign, Valve Medical





IC 2016: An Evolving Landscape

PTCA... The Beginning





The Father of PTCA!



Andreas Gruentzig 1939 - 1985

His dream was the catheter-based percutaneous treatment of vascular disease in alert, awake patients!





Andreas' Tools









Andreas' Results









IC 2016: An Evolving Landscape

New Device Era





The "New Device" Era (1988-1993)







CARDIOVASCULAR RESEARCH FOUNDATION At the heart of innovation

The Palmaz-Schatz Stent







Early Days of Coronary Stents



First Palmaz-Schatz Stent in Human December 31st, 1987





Bare Metal Stents.... the good, the bad, and the ugly!







Drug-Eluting Stents Advanced Biotechnology Platform







First-In-Man study with CYPHER Sao Paulo, FU completed







DES - A Transforming Technology







First Generation DES



Paclitaxel
Drug



Polyolefin derivative Polymer



Express² Stent



Sirolimus



PEVA + PBMA blend



BX Velocity





DES....the good, the bad, and the ugly!







Second Generation DES

Resolute

Xience V*







Zotarolimus Drug BioLinx copolymer Polymer Driver Stent



Everolimus

VDF + HFP copolymer



Vision





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Bioresorbable Vascular Scaffolds (BRS)

DREAMS 1

AMS 1

DREAMS 2

Igaki-Tamai

BVS 1.0

BVS 1.1

Reva gen 1

ReZolve



DESolve

ART

ART18Z (gen 2)

IDEAL BTI

IDEAL Biostent

Amaranth

Xinsorb

ON-AVS





Iqbal J et al. EHJ. 2014;35,:765-76

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IC Perspectives: 1977 - 2016 *A Modern Subspecialty*

- The acceptance of evidence-based medicine (EBM) has distinguished IC as a modern subspecialty, committed to scientific principles and the highest ethical standards of conduct.
- Other factors beyond EBM must also be heavily weighed to optimize clinical decision-making.
- Iterative device development and transformative new therapy solutions are imbedded in the culture of IC.
- Global participation in the assessment of new therapies, physician training, and sharing of educational activities.
- A true subspecialty with formal certification processes!





IC 2016: An Evolving Landscape

Transition to Structural Heart Disease





IC Perspectives: 1977 - 2016 Evolution to Mainstream Therapies

- The less-invasive (non-surgical) use of catheterbased therapies to remotely treat distant disease targets has transformed medicine.
 - Neuro-radiology and neuro-surgery
 - Minimally invasive endoscopic surgery
 - Gastroenterology
 - Orthopedics
 - Oncology
 - Pulmonology (and ENT)
 - Urology and gynecology





IC Perspectives: 1977 - 2016 Evolution to Mainstream Therapies

- The less-invasive (non-surgical) use of catheterbased therapies to remotely treat distant disease targets has transformed medicine.
- A major current effort is to redirect intra-vascular interventional therapies to address "mainstream" cardiovascular and non-cardiovascular disease (e.g. Valve disease, HTN, AF, and HF therapies).
- This requires that the interventionalist become an integrated member of multi-disciplinary teams AND learn new cognitive skills; the transformation from isolated proceduralist to engaged therapist!





IC Perspectives: 1977 - 2016 Important Evolution







TCT Opening 2001



Cardiovascular Research Foundation SHD = structural heart disease

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IC Perspectives: 1977-2016 The STRUCTURAL REVOLUTION

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



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- NewYork-Presbyterian



IC Perspectives: 1977-2016 The STRUCTURAL REVOLUTION

- 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).





WW \$ Cardiology Market Trends



- 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

esearch Foundation





Interventional Cardiology - 2015 Columbia University Medical Center (4,100 interventions)

Interventional Sectors







Structural Heart Interventions - 2015 *Columbia University Medical Center* (850 interventions)

Structural Sectors







Conventional Aortic Valve Surgery



Is there a better way?





April 16, 2002; FIM-TAVR; Rouen, FR







TAVR in 2016: *Milestones*

• TAVR is a "Breakthrough" Technology – Dramatic global growth and universal acceptance with seemingly "unlimited" future potential!





TAVR is Available in More Than 65 Countries Around the World



>250,000 total implants to date





Estimated Global TAVR Growth

Global TAVR Units		
	2019	2025 ~\$5B
February 19, 2016		Goldman Sachs
United States: N Cardiovascular [/ledical Technology: Devices	
		Equity Research
Raising TAVR forecasts; market to reach \$7bn+ by 2025E		
SOURCE: Credit Suisse TAVI Comment –January 8, 2015. ASP assumption for 2024 and 2025 based on analyst model. Revenue split assumption in 2025 is 45% U.S., 35% EU, 10% Japan, 10% ROW		
In the next 10 years TAVD successful increases VAL		

In the next 10 years, TAVR growth will increase X4!





TAVR in 2016: *Milestones*

- TAVR is a "Breakthrough" Technology Dramatic global growth and universal acceptance with seemingly unlimited future potential!
- TAVR growth has been fueled by:
 - the multi-disciplinary heart team
 - commitment to evidence-based medicine
 - rapid technology enhancements
 - striking reduction in complications
 - simplification of the procedure (generalizable)










All-Cause Mortality



All-Cause Mortality or Stroke



37

CoreValve US Clinical Trials

CoreValve US Clinical Trials ACC2016

Valve Hemodynamics*

CoreValve had significantly better valve performance vs SAVR at all follow-ups (P<0.001)



PARTNER THV Evolution



PI - 2007

Edwards SAPIEN™ THV 23 mm and 26 mm **PII - 2010**

Edwards SAPIEN XT ™ THV 23 mm, 26 mm, and 29mm

PII S3 - 2013

Edwards SAPIEN 3™ THV 20 mm, 23 mm, 26 mm, and 29mm

PARTNER enrolled >9,000 patients in FDA studies (including 4 RCTs) with 3 generations of TAVR systems in ~ 7 years!





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



PARTNE



The PARTNER 2A and S3i Trials Study Design



Intermediate Risk Symptomatic Severe Aortic Stenosis



Primary Endpoint: All-Cause Mortality, All Stroke, or Mod/Sev AR at One Year (Non-inferiority Propensity Score Analysis)

Primary Endpoint - Non-inferiority Death, Stroke, or AR ≥ Mod at 1 Year (VI)



Weighted Difference -9.2% Upper 1-sided 95% CI -6.0% Non-Inferiority p-value < 0.001





Primary Non-Inferiority Endpoint Met

Primary Endpoint - Superiority Death, Stroke, or AR ≥ Mod at 1 Year (VI)



Weighted Difference -9.2% Upper 2-sided 95% CI -5.4% Superiority Testing p-value < 0.001



Superiority Achieved

Unadjusted Time-to-Event Analysis All-Cause Mortality and All Stroke (AT)





Paravalvular Regurgitation 3-Class Grading Scheme (VI) $i \in \mathbb{P} \setminus \mathbb{P} \setminus \mathbb{P}$





The PARTNER 2A and S3i Trial Clinical Implications



 The results from the PARTNER 2A randomized trial and the S3i propensity score analysis in > 3,100 intermediate-risk patients with severe aortic stenosis, provide strong evidence that SAPIEN 3 TAVR when compared with surgery <u>improves</u> <u>clinical outcomes and is the preferred therapy!</u>

The PARTNER 2A and S3i Trial The NEJM and Lancet On-line





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter aortic valve replacement versus surgical valve $\rightarrow \mathscr{W}$ replacement in intermediate-risk patients: a propensity score analysis

Vinod H Thourani, Susheel Kodali, Raj R Makkar, Howard C Herrmann, Mathew Williams, Vasilis Babaliaros, Richard Smalling, Scott Lim, S Chris Malaisrie, Samir Kapadia, Wilson Y Szeto, Kevin L Greason, Dean Kereiakes, Gorav Ailawadi, Brian K Whisenant, Chandan Devireddy, Jonathon Leipsic, Rebecca T Hahn, Philippe Pibarot, Neil J Weissman, Wael A Jaber, David J Cohen, Rakesh Suri, E Murat Tuzcu, Lars G Svensson, John G Webb, Jeffrey W Moses, Michael J Mack, D Craig Miller, Craig R Smith, Maria C Alu, Rupa Parvataneni, Ralph B D'Agostino Jr, Martin B Leon

Jonathon Leines, Rob John G Wellt, Jeffrey W Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D.,
 Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D.,
 William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

Expanding Clinical Indications *A TAVR Crossroads?*

- Bioprosthetic valve failure (aortic and mitral)
- Intermediate and low-risk patients
- Low-flow, low-gradient AS
- Bicuspid AV disease
- AS + concomitant disease (CAD, MR, AF)
- Severe asymptomatic AS
- Moderate AS + CHF
- High-risk AR





TAVR: A 10-Year Anniversary



Legion of Honor (2012)





Increasing Prevalence of Valvular Heart Disease in the Elderly



Cardiovascular Research Foundation

Nkomo VT at al. Lancet 2006;368:1005-1011

COLUMBIA UNIVERSITY MEDICAL CENTER NewYork-Presbyterian An Issue of COMPLEXITYAnatomy and ManagementAortic ValveMitral Valve

MR comprises many diseases, some of which aren't even directly associated with mitral valve pathology!

Simple





Adapted from J. Hermiller



Catheter-Based Mitral Valve Repair MitraClip System









~430 patients enrolled at up to 85 US sites

Significant FMR (≥3+ by core lab)

Not appropriate for mitral valve surgery (local heart team)

Specific anatomical criteria

Randomize 1:1





Pls: Michael Mack and Gregg W. Stone Sponsor: Abbott Vascular

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Transcatheter MV Repair: Device Landscape 2015

Edge-to-edge

- MitraClip*
- MitraFlex

Direct annuloplasty and basal ventriculoplasty

- Mitralign Bident*
- GDS Accucinch*
- Valtech Cardioband*
 - MVRx*
 - Valcare*
 - Mitraspan*
 - Quantum Cor (RF)
 - Micardia enCor

Coronary sinus annuloplasty

- Cardiac Dimensions Carillon*
 - Cerclage annuloplasty

MV replacement

- Edwards CardiAQ*
 - Edwards Fortis*
 - Neovasc Tiara*
 - Abbott Tendyne*
- Medtronic Twelve*
 - NCSI Navigate
- Mvalve* Direct Flow
 - Micro Interventional
 - Valtech Cardiovalve
 - ValveXchange
 - HighLife
 - MitrAssist

Cephea • Sinomed

Other approaches MitraSpacer*

- St. Jude leaflet plication*
- Cardiac Implant perc ring

NeoChord*

- Babic chords*
- Valtech Vchordal
- Middle Peak Medical
 - Mardil BACE*
 - Mitralis
 - Millipede

*In patients







Mitral Annuloplasty Systems Under Current development



Cardiac Dimensions Carillon

Indirect annuloplasty Coronary sinus cinching

Mitralign TAMR



 Trans-aortic
 LV implant of 1-3 annular pairs of pledgets

GDS Accucinch



Basal
ventriculoplasty
LV implant of
16-18 anchors

Valtech Cardioband



 Trans-septal
 LA implant of a posterior annulus band (screw fixation)





The TMV<u>R</u> "Wars"



Competitive or Complementary?





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 - Mitraspan*
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 - Micardia enCor

Coronary sinus annuloplasty

- Cardiac Dimensions Carillon*
 - Cerclage annuloplasty

MV replacement

15 new transcatheter MV Replacement Technologies Other approaches

MitraSpacer*

- St. Jude leaflet plication*
- Cardiac Implant perc ring

NeoChord*

- Babic chords*
- Valtech Vchordal
- Middle Peak Medical
 - Mardil BACE*
 - Mitralis
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Transcatheter MV Replacement Devices with Human Implants



CardiAQ



Edwards Fortis



Neovasc Tiara

Tendyne





Twelve





Summary of Clinical Experiences (~85 cases; compassionate use, EU high-risk registries, and U.S. EFS studies)

- Difficult to find patients high screen failure rate due to various anatomic and clinical factors (esp. annulus size and LVOT obstruction); ? optimal patient candidates
- Multi-modality imaging requirements intense CTA important for screening but analysis algorithms in early stage of development; echo <u>necessary</u> for intra-procedural guidance – may be difficult to confirm fixation
- System profile and access concerns (trans-apical may be problematic) – end-stage FMR patients don't tolerate TA approach; current system profiles and stiffness limit TS
- Ultra-sick patients with very low EF do poorly no reserve, little improvement, continued HF, early mortality



Summary of Clinical Experiences (~85 cases; compassionate use, EU high-risk registries, and U.S. EFS studies)

- Precise positioning difficult and device-specific echodependent and few retrieval options
- LVOT obstruction is a definite concern requires careful planning and shallow LV device footprint
- *Excellent MR reduction observed* with correct sizing and positioning, MR is usually eliminated
- PVR uncommon, but still can be problematic unusual cases with PVR but not well tolerated (mainly hemolysis)
- *Device thrombosis is a serious issue* requires careful anti-coagulation for at least several months
- In less sick patients with correct positioning, clinical outcomes have been gratifying!





TMVR: Roadmap for Success

- There is unbridled enthusiasm for continued device growth in the transcatheter mitral space, esp. TMVR - beware "buyer's remorse", reset expectations and anticipate a step-wise incremental growth trajectory during the next decade in response to iterative device refinements and validating clinical trial data.
- Expect many speedbumps and longer gestation times before these TMVR devices are fully realized and they must be integrated with transcatheter repair strategies and surgery!







Cardiovascular Research Foundation

Argarwal et al. Circ Cardiovasc Interv 2009;2:565-73

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Edwards FORMA Repair System Designed to restore leaflet coaptation

FORMA System Consists of:



Spacer

- Positioned into the regurgitant orifice
- Creates a platform for native leaflet coaptation

Rail

- Tracks spacer into position
- Anchored distally and proximally





JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY © 2015 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION PUBLISHED BY ELSEVIER INC.

First-in-Human Transcatheter Tricuspid Valve Repair in a Patient With Severely Regurgitant Tricuspid Valve



Joachim Schofer, MD,* Klaudija Bijuklic, MD,* Claudia Tiburtius, MD,* Lorenz Hansen, MD,* Adam Groothuis, PHD,† Rebecca T. Hahn, MD‡

J Am Coll Cardiol 2015;65:1190–5





Severe Isolated Primary Tricuspid Regurgitation





Trialign - Final 3D TEE Result Baseline



Post-Transcatheter Tricuspid Annuloplasty



NIVERSITY.

LAAC: An Important Structural Therapy Stroke Prevention in AF Patients

• Difficulties with Warfarin use

- Frequent Monitoring
- Difficulty in Compliance (TTR 48-63%)
- Drug / Diet Interactions
- Bleeding Risk (ICH)
- Risks in Elderly (falls, poly-pharmacy)

Autopsy & TEE data implicate LAA

LAA Closure Devices Beneficial









LAAC: An Important Structural Therapy

- Fulfills a growing clinical need stroke prevention in AF patients wo chronic anti-coagulation (esp. high stroke risk/high bleeding risk patients).
- Multi-disciplinary heart team EP/IC operators, neurology, imaging specialists, and cardiologists
- Requires adjunctive imaging (CT/echo) for screening and procedural guidance
- Structural interventional skills necessary
- *Growing EBM validation* = clinical value proposition
- Many familiar issues: economics/reimbursement considerations, market development, competitive pharmacology (NOACs), and many new devices in the future.





Heart Failure Therapies (The next "big breakthrough"?)

- Heart failure is the major driver of mortality, morbidity, and cost in the CV arena, now and in the future!
- Requires a comprehensive multi-disciplinary and multi-factorial approach with greater emphasis on device-based diagnostics and novel therapies.
- The new specialty of *interventional heart failure* will require customized training spanning the range from pharmacotherapy to electrophysiology to advanced mechanical circulatory support and to other new interventional device approaches.





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




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!





Thoratec PHP





Implantable Sensors for CHF





CardioMEMS

- Simple PA artery implant
- Continuously monitors PA pressures (RFpowered, 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







Percutaneous Ventricular Restoration

Treatment Goal

Improve hemodynamics by:

- Partition Scar
- LV Volumes Reduction
- LVED Pressure Reduction
- Restoring LV Conical Shape
- Not preventing Torsional Contraction
- Not causing arrhythmias

Procedural aspects similar to a standard PCI (Duration – 80 min / Flouroscopy time – 20 min)









CircuLite Micro-VAD System



 Inflow cannula transeptal in LA via the subclavian vein and RA by the interventional cardiologist

Outflow graft attached to Subclavian Artery





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



V-wave

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Inter-Atrial Shunt Devices (IASD) (Corvia - HFpEF)





Lancet 387; March 26, 2016



Inter-Atrial Shunt Devices (IASD) (V-Wave - HFrEF)



IC 2016: An Evolving Landscape

Final Thoughts





The Structural Revolution Special Skills and Common Features

- Intensely multi-disciplinary multiple heart team models (e.g. LAAC = EP, IC, imaging, neurology, and clinical cardiology).
- *Multi-modality imaging* for case screening and frequent TEE intra-procedural guidance.
- Access and closure skills TS required and TA often necessary; endovascular experience for transvascular access/closure with large catheters (esp. important for complication management).
- Interventional environment familiarity (cath lab/hybrid OR and catheter/guidewire skills)





3D Imaging - The Path to Holography



Advanced 3D acquisition technologies making high quality volumetric 3D a reality

 Proven clinical value for structural interventions (3DTEE, 3DRA, 3D/4DCT, Electroanatomical maps)

Images: Courtesy of Philips Healthcare

ardiovascular

Research Foundation

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First in Human - Holographic Images

- Real time clinical holographic images
- 16 yo girl with secundum ASD for transcatheter closure





Courtesy of E. Bruckheimer





3D Bioprinting: The Unlimited Potential of Automated Tissue Engineering Processes

Biocompatible Matrix

+ Cells

Cell friendly printing conditions



Patient Scan



Solid Model File

3D-Bioplotter



Printed Valve



Daniel B. Spoon, MD



Interventional Cardiology The Next Decade!

There's never been a better time to be an interventional cardiologist!





Interventional Cardiology The Next Decade!







The Future of IC It's All About the Patients!





