

Transcatheter Interventional Heart Failure Therapies

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Disclosure Statement of Financial Interest

- I am a full-time employee of the Cardiovascular Research Foundation, which organizes and operates Transcatheter Cardiovascular Therapeutics and which has received educational and research grants from some of the companies developing TMVR devices
- I am a co-founder and co-inventor of Cephea Valve Technologies

Heart Failure is the EPICENTER of Interventional Cardiovascular Therapies

- HF is the 'final common pathway' of ALL CV diseases
 - Prevalence: ~ 4.3% of US population >65 years of age
 - ~70% of CCU admissions and ~50% mortality at 5 years
 - Most costly condition in CV medicine (pharma expenses ~\$30 billion/year)
- HF hemodynamics well suited for analytic differential diagnosis and evidence-based therapy guidance (including AI-based)
- Primary causes easily targeted by catheter-based therapies!

Device-Based Therapies for Heart Failure

Novel HF Devices Approved* in the Past Two Decades

- Cardiac Resynchronization Therapy – August 28, 2001
- **TAVR Prohibitive Risk – November 2011**
- CardioMEMS HF System – May 28, 2014
- Remedē System – October 6, 2017
- **MitraClip (expanded indication) – March 14, 2019**
- OPTIMIZER Smart System – March 21, 2019
- BAROSTIM NEO System – August 16, 2019
- Many more to come!

Percutaneous Treatment of Valvular Heart Disease Beyond TAVR

Natural History of Severe MR in the Real World

1,095 Pts* With 3+/4+ MR and HF Between 2000 And 2008

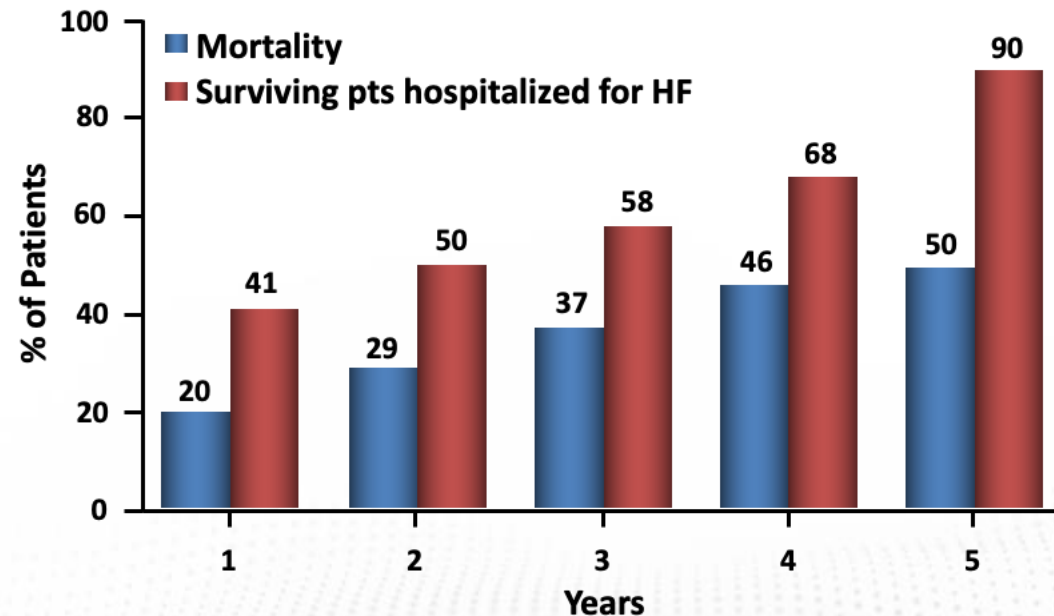
(74% FMR, 21% DMR). Rx Before 10/2011:

DMR Pts (N=226): **84% MV Surgery**, 16% Medical Rx

FMR Pts (N=814): 36% MV Surgery (77% W/CABG), **64% Med Rx**

Un-Operated Pts had Lower LVEF (Mean 27% Vs. 42%, $P<0.0001$ and **Higher STS Score** (Median 5.8 Vs. 4.0, $P<0.001$) Compared With Operated Pts.

Prognosis of
un-operated
pts with
3+/4+ MR
and HF



* Excluded MVA ≤ 2 cm², AR $\geq 2+$, aortic peak velocity ≥ 2.5 m/s, HCM, endocarditis, concomitant AV, Ao or pericardial surgeries, LVAD or OHT.

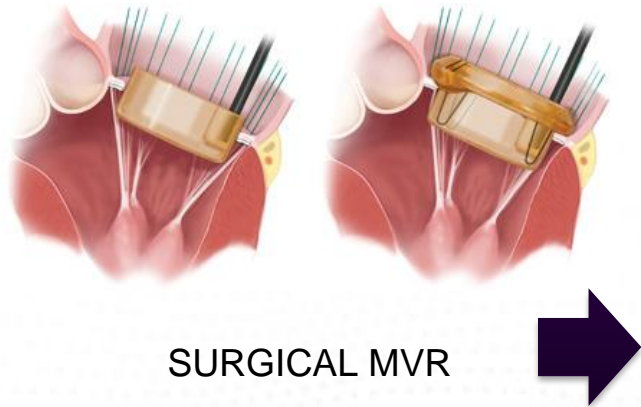
The High-Risk MR Population Represents a Big Opportunity for Catheter-Based Innovation

- The presence of severe MR + HF is highly prevalent in the elderly. This specific patient population is:
 - Frequently rejected from surgery
 - Rejected from MitraClip (MAC and small valve areas)
 - Not represented in surgical clinical trials
 - Frequently re-hospitalized (high financial burden)

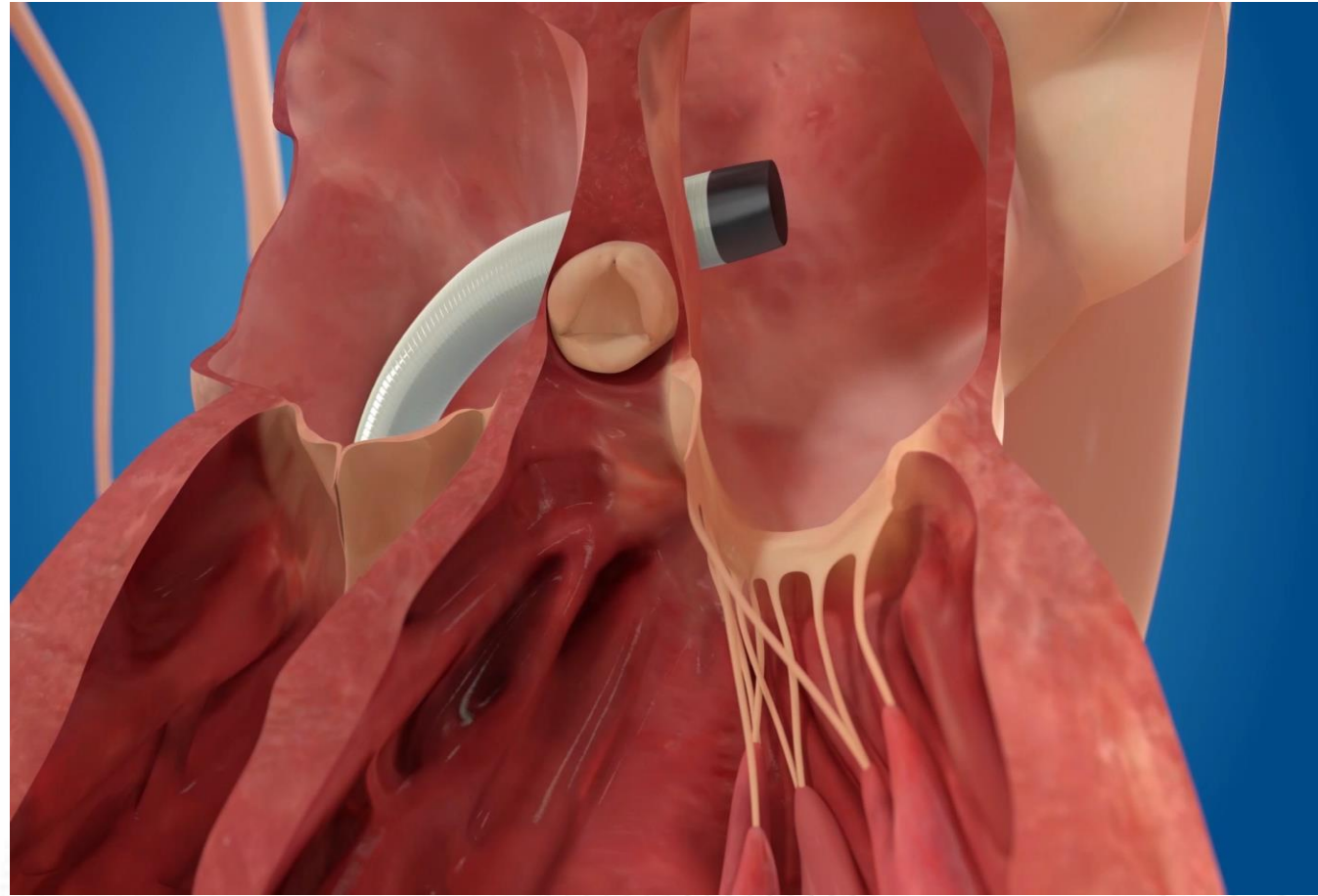
Value Proposition of TMVR Therapies

VALUE PROPOSITION

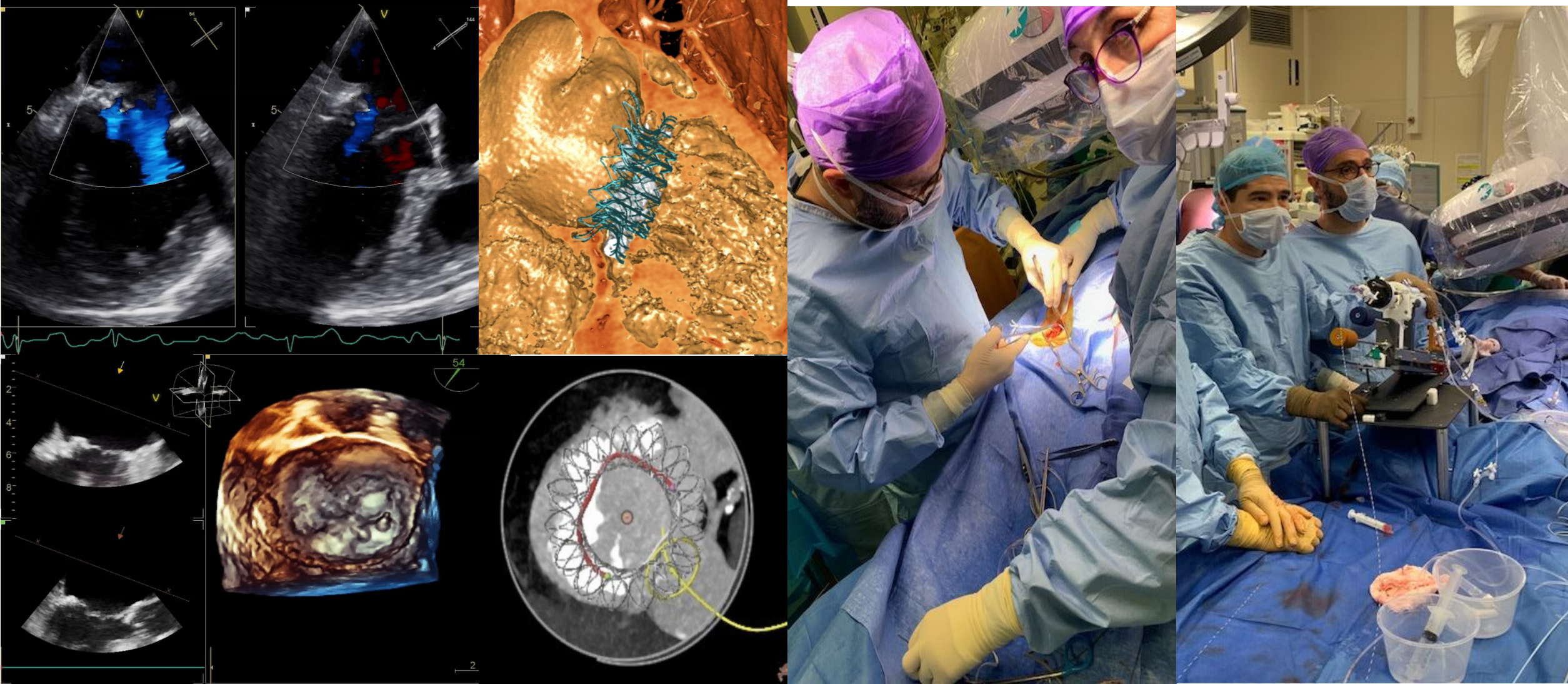
- Ease of implantation
- Agnostic to etiology of MR
- Reliable elimination of MR
- Less recurrence of MR



TRANSITION TO TMVR



Trans-Septal Cephea TMVR System: FIH Implant



Trans-Septal Cephea TMVR System: FIH Implant



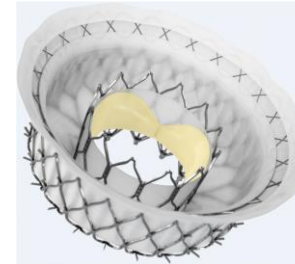
TMVR Devices Under Clinical Evaluation



EVOQUE
Edwards



Sapien M3
Edwards



Intrepid
Medtronic



CardioValve
Venus Medtech



Tendyne
Abbott



CEPHEA
Abbott



AltaValve
4C Medical



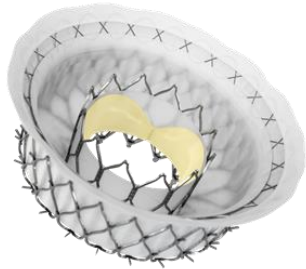
HighLife
HighLife Medical



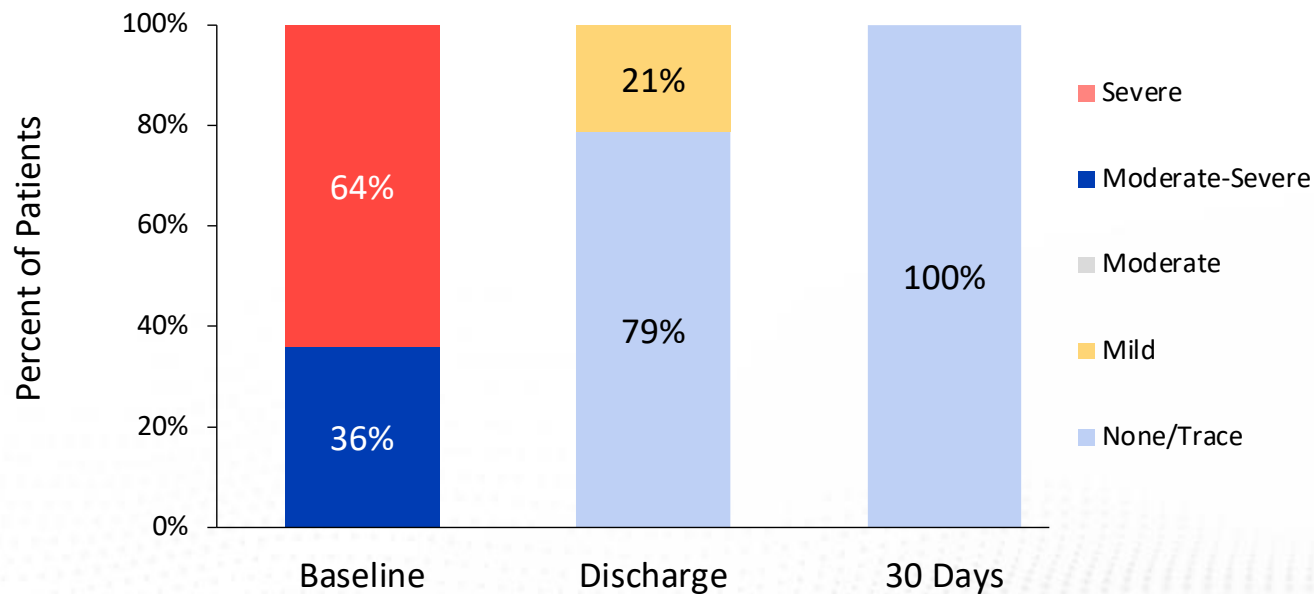
Tiara
Neovasc

Lessons Learned from Clinical Data
Using TMVR Trans-Apical Systems
~1,000 Patients Treated to Date
(Observational Studies)

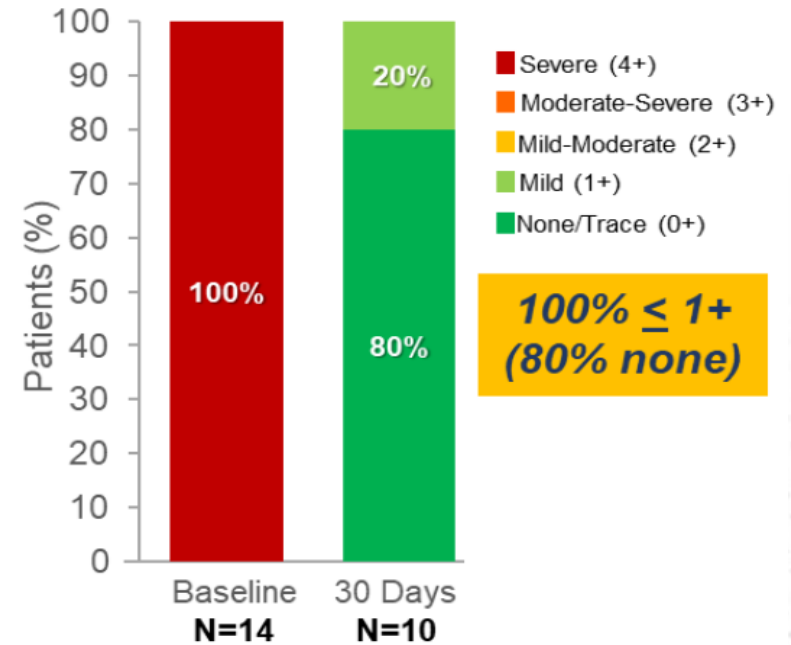
100% MR Reduction <1+ with TMVR Devices



Intrepid



Evoque



Initial Feasibility Study of a New Transcatheter Mitral Prosthesis

The First 100 Patients



PROCEDURAL OUTCOMES (n=100) ¹		ADVERSE EVENTS*	30 DAYS ¹	1 YEAR ¹	2 YEAR ²
Implant success	97%	Any mortality	6%	26%	39%
Technical Success (per MVARC)	96%	Cardiovascular mortality	4%	22%	34%
Implant retrieved/abandoned	3%	Disabling stroke	2%	3%	5%
Retrieved (SAM, LVOT obstruction)	1%	Myocardial infarction	2%	4%	8%
Retrieved (non-orthogonal)	1%	Mitral valve reintervention	1%	4%	5%
Abandoned (pulmonary edema)	1%	Endocarditis	1%	2%	5%
Major apical access complications	1%	New PPM	4%	7%	8%
Procedural mortality	0%	New Onset AF	4%	4%	9%
Procedural stroke	0%	ADVERSE EVENTS*	30 DAYS¹	1 YEAR¹	
Emergency surgery	0%	Device-specific adverse events			
ECMO	0%	Hemolysis	1%	3%	
		Embolization	0%	0%	
		Thrombosis	1%	6%	
		Fracture	0%	0%	

Transcatheter Tricuspid Landscape

Annuloplasty

Trialign



Cardioband



TriCinch



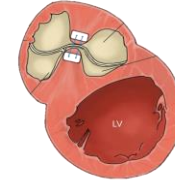
Millipede



MIA



PASTA



DaVinci



Coaptation Enhancement

Edge-to-Edge



TriClip



Pascal



Dragonfly

Mitralix

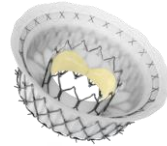


Orthotopic Replacement

Evoque



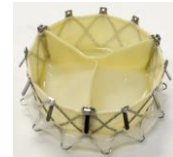
Intrepid



V-Dyne



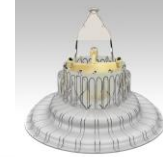
Navigate



Trisol



Lux

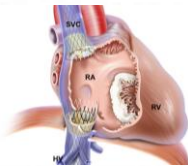


Topaz



Heterotopic Replacement

TricValve



TriCento



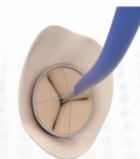
Trillium



Forma



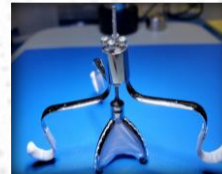
Croi



Coramaze



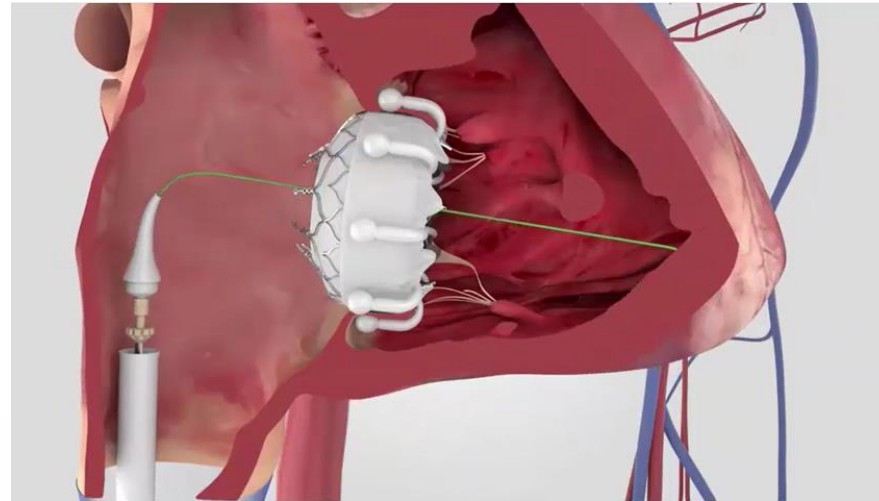
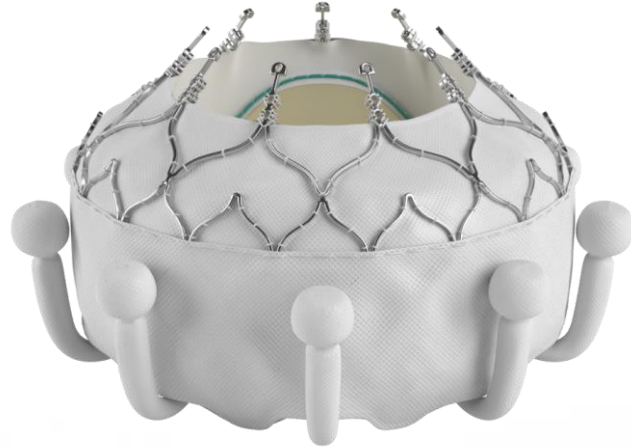
Tri-Flow



Spacers

TTVR in Patients with TR: 6-Month Outcomes from the TRISCEND Study

EVOQUE Tricuspid Valve Replacement System



Anchors compatible with pre-existing leads and respect the native anatomy

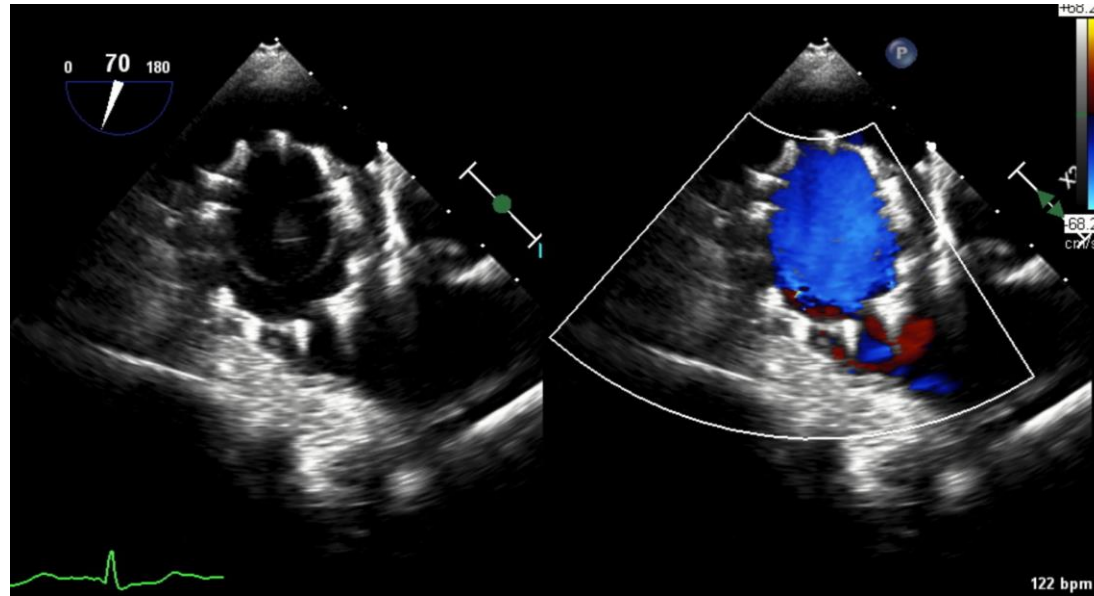
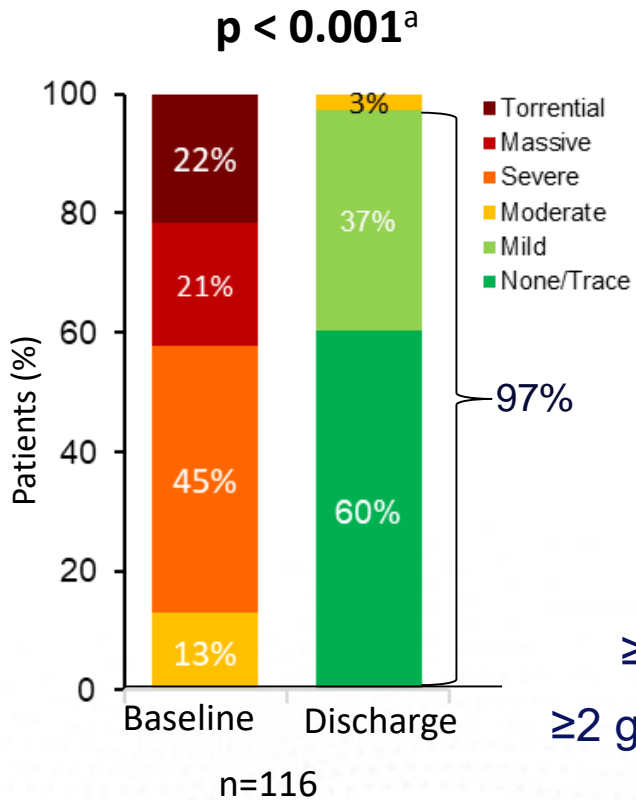
Conforming frame designed to achieve optimal retention force

Multiple sizes offer treatment for a broad range of tricuspid pathologies and anatomies (44, 48, 52 mm)

28F transfemoral delivery system compatible with all valve sizes

TR Severity by Core Lab¹ at 6 Months

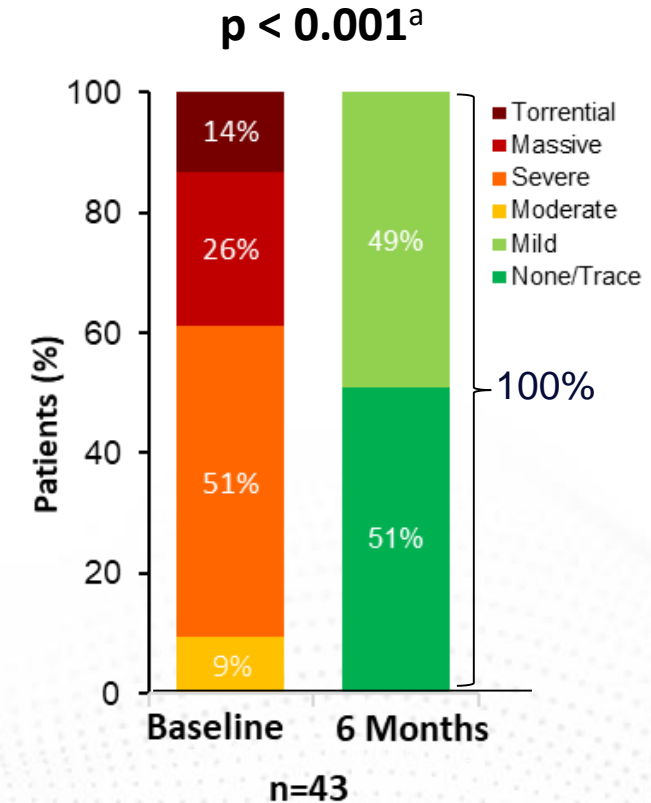
TR Severity at Discharge



No residual TR post implant with EVOQUE valve

≥1 grade reduction in 100% at discharge and 6 months
 ≥2 grade reduction in 95% at discharge and 98% at 6 months

TR Severity at 6 Months

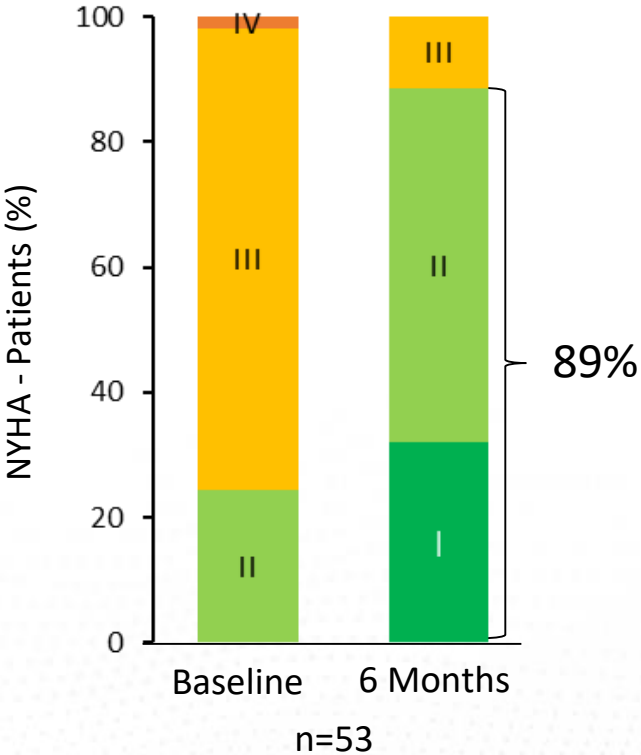


¹Core lab: Baylor, Scott and White Research Institute; ^aWilcoxon signed-rank test. TR, tricuspid regurgitation

Functional and QoL Outcomes at 6 Months

NYHA Class

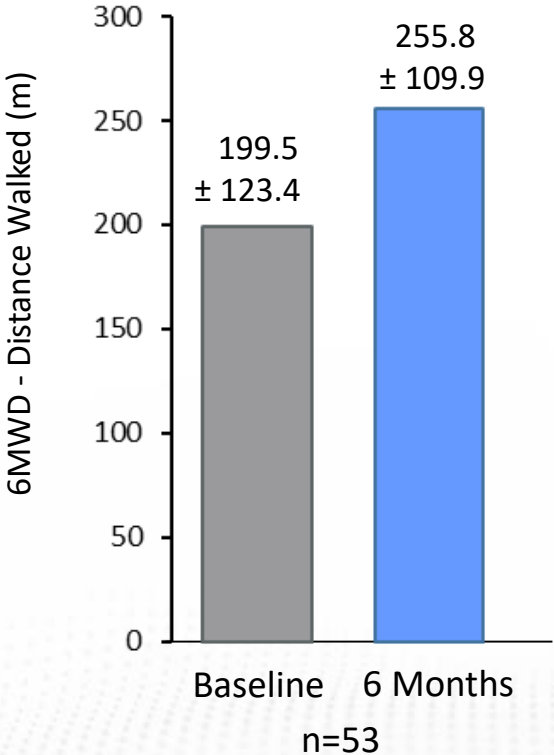
$p < 0.001^a$



6MWD

$p < 0.001^b$

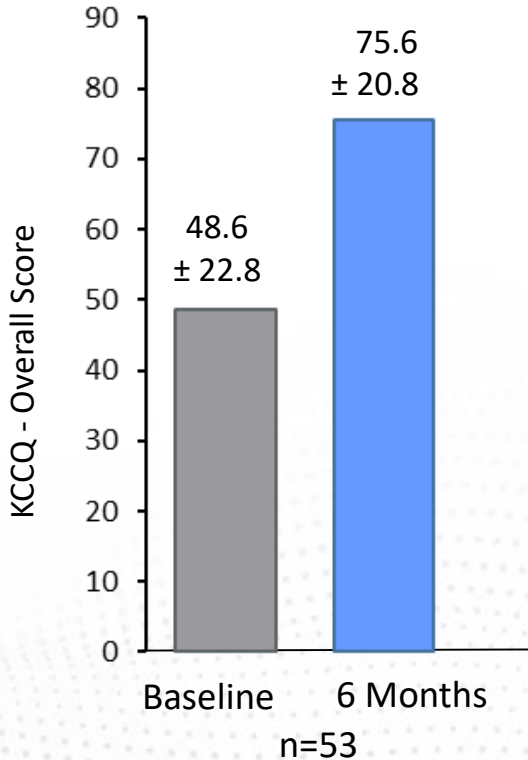
$\Delta=56$ m



KCCQ Score

$p < 0.001^b$

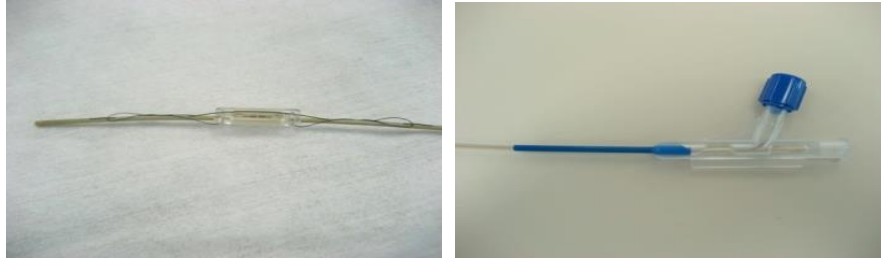
$\Delta=27$ points



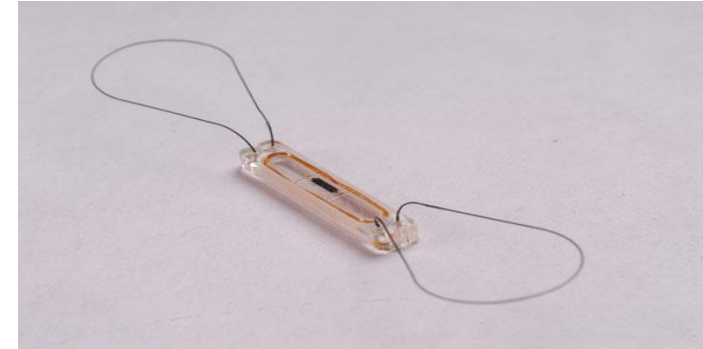
Sensors and Remote Patient Monitoring

Pulmonary Artery Pressure Monitoring System

Catheter-Based Delivery System



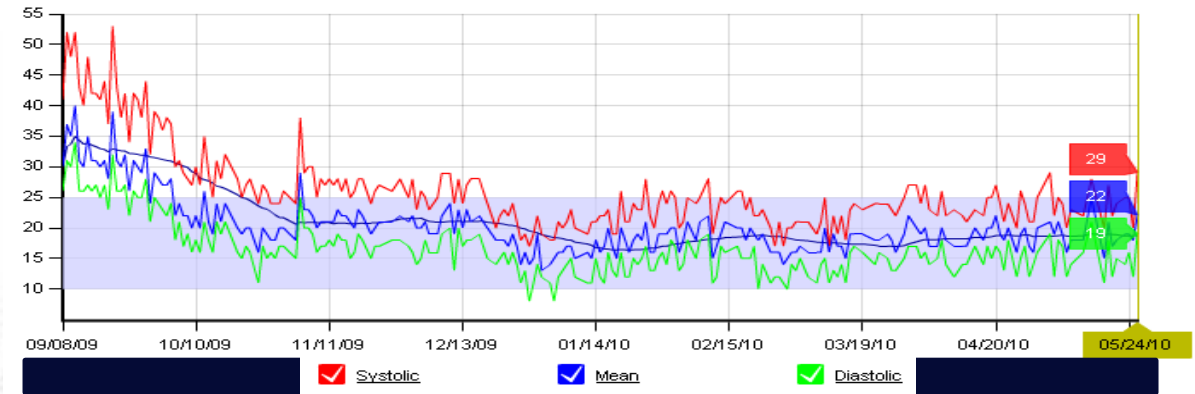
MEMS-Based Pressure Sensor



Home Electronics

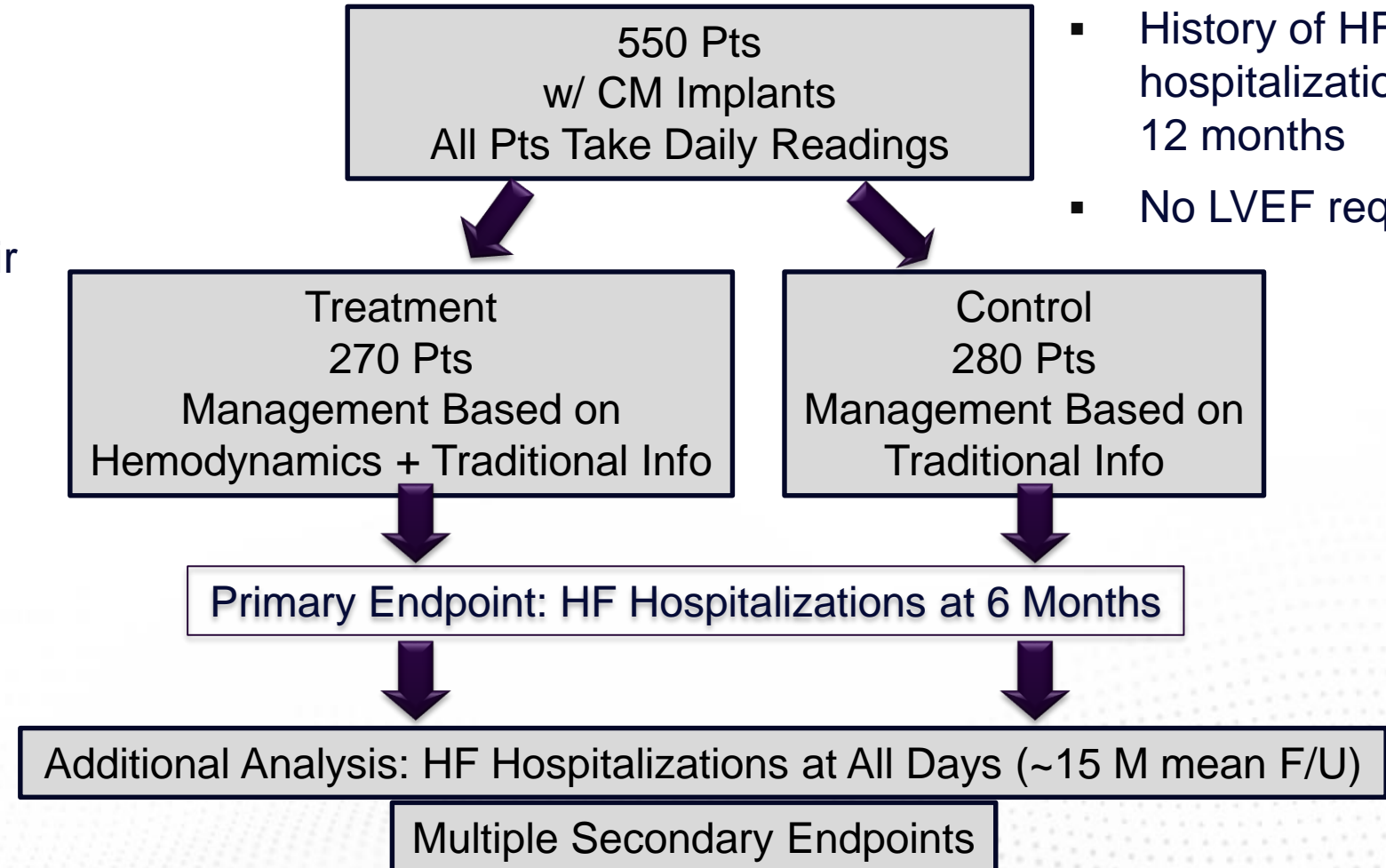


PA Measurement Database



CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients

- Prospective, multi-center, randomized, controlled, single-blind clinical trial
- All subjects followed in their randomized single-blind study assignment until the last patient reached 6 months of follow-up
- Tested the hypothesis that PA pressure-guided heart failure management could lower the rate of heart failure hospitalization



- History of HF hospitalization in past 12 months
- No LVEF requirement

Clinical Outcomes in CHAMPION RCT

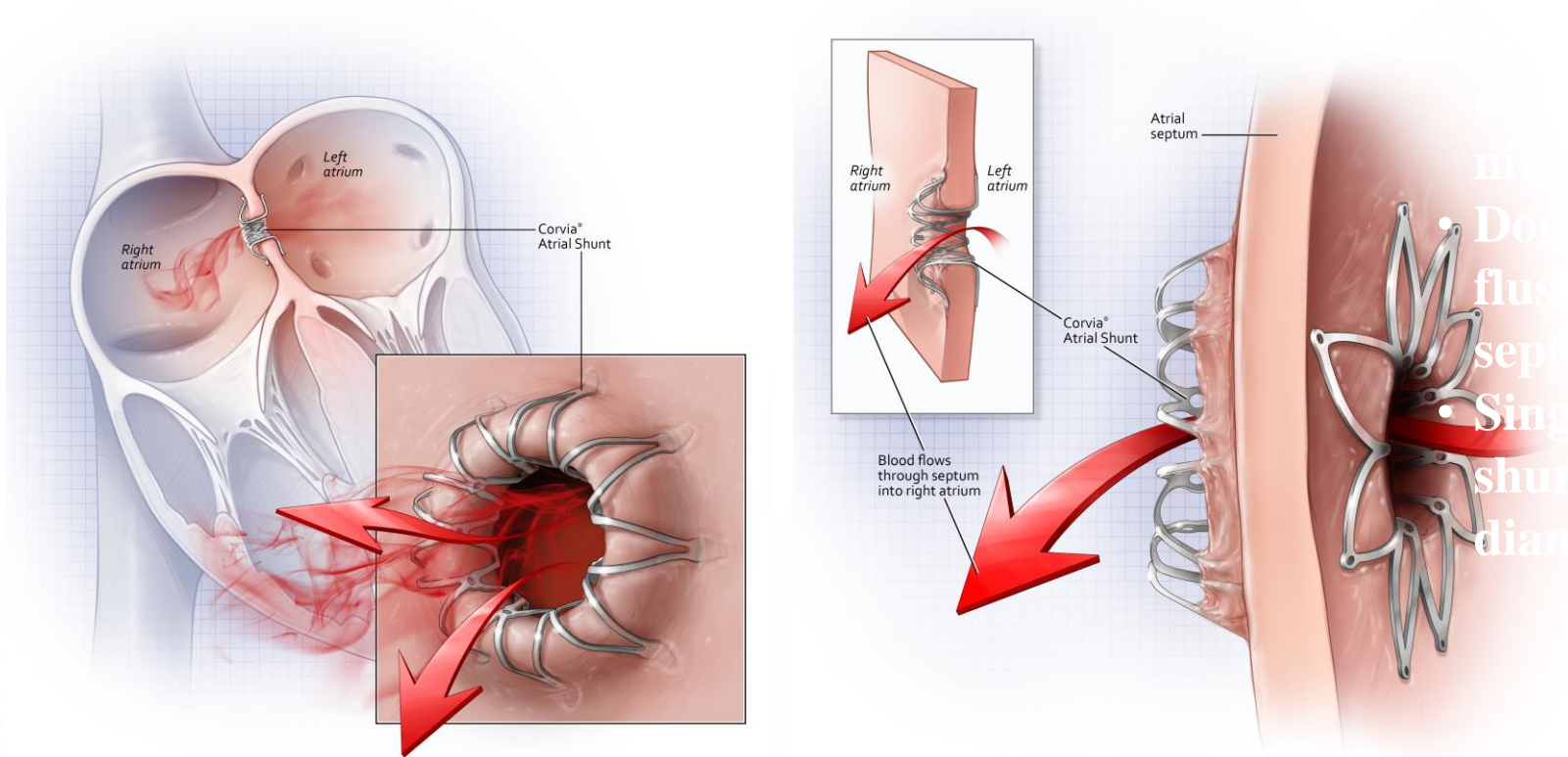
	Treatment (n=270)	Control (n=280)	Absolute Reduction	Relative Reduction	p-value
				HR (CI)	
Heart Failure Hospitalizations	182	279	97	0.67 (0.55 – 0.80)	<0.0001
Death or Heart Failure Hospitalizations	232	343	111	0.69 (0.59 – 0.82)	<0.0001
All Cause Hospitalizations	554	672	118	0.84 (0.75 – 0.95)	0.0032
Death or All Cause Hospitalizations	604	736	132	0.84 (0.76 – 0.94)	0.0017

Results from Andersen Gill model; Hazard Ratio (HR) and 95% Confidence Interval (CI)

Intra-Atrial Shunts and Ventricular Remodeling

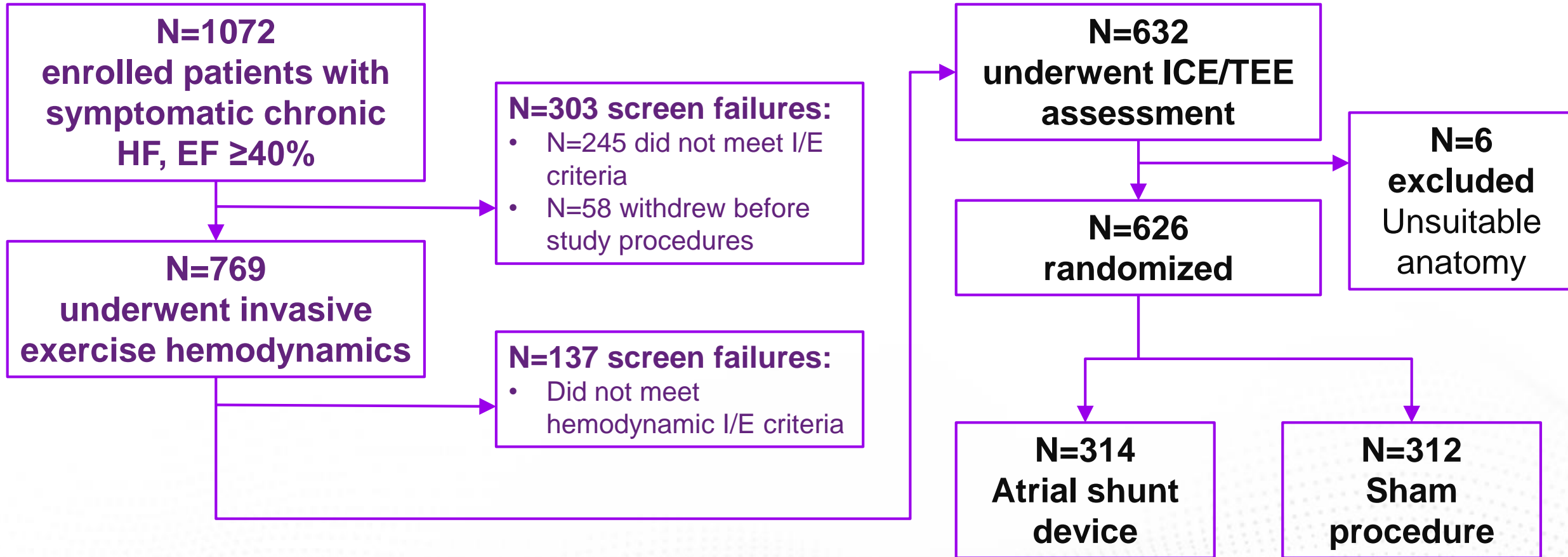
Interventional Heart Failure Therapies

Atrial Shunts: Corvia

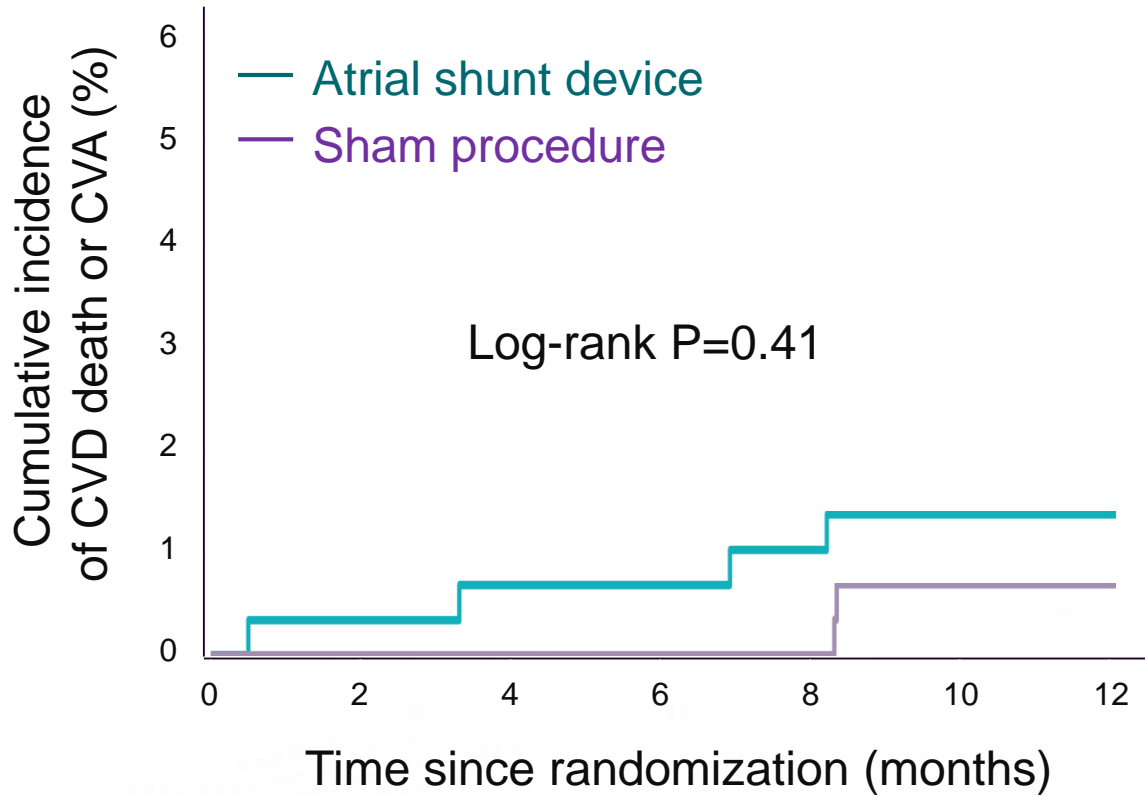


Proposed mode of action: dynamic decompression of overloaded LA chamber by shunting blood from LA → RA (Qp:Qs 1.2-1.3)

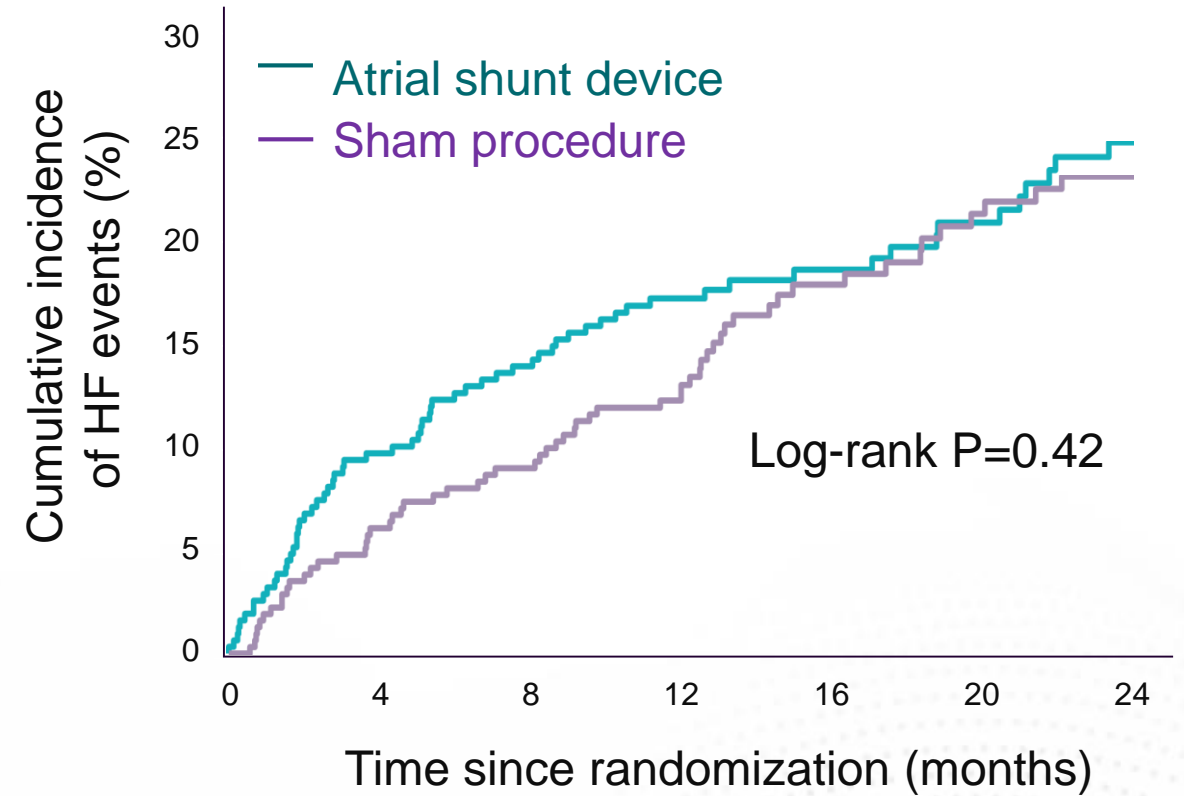
REDUCE LAP-HF II: Study Design



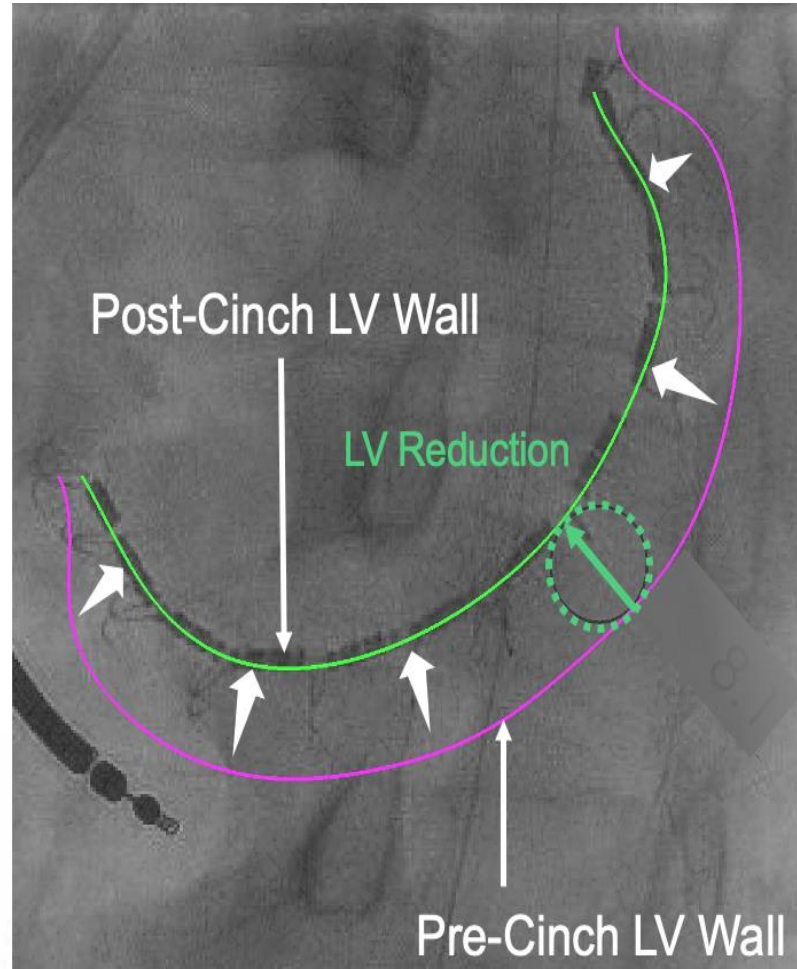
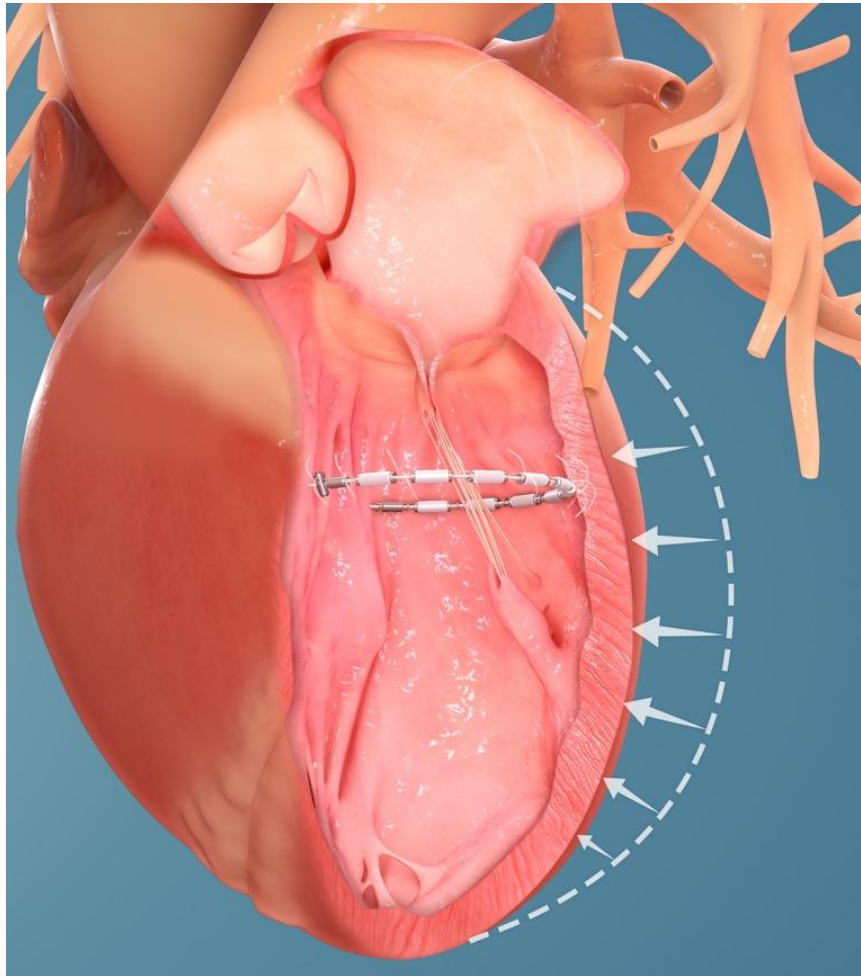
REDUCE LAP-HF II: Primary Endpoint



Finkelstein-Schoenfeld p-value=0.85
Win ratio: 1.0 (95% 0.8-1.2)



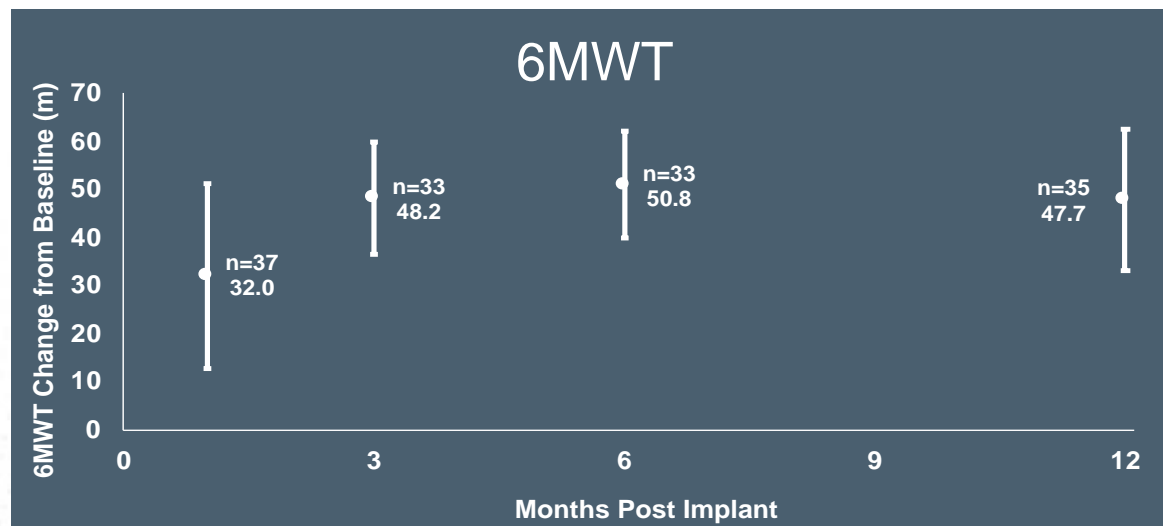
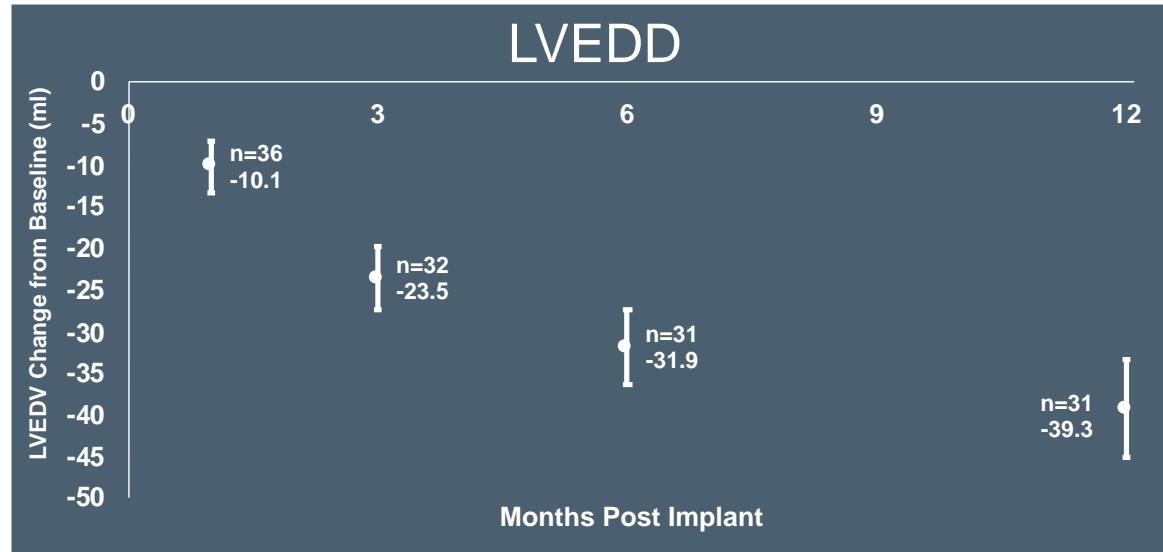
AccuCinch Ventricular Restoration System



Transcatheter, device therapy intended to restore, support and strengthen the dilated left ventricle by reducing LV dimensions and LV wall stress

CORCINCH Studies – HF Group Analysis

41 Subjects
LVEF <40%
MR ≤ 2



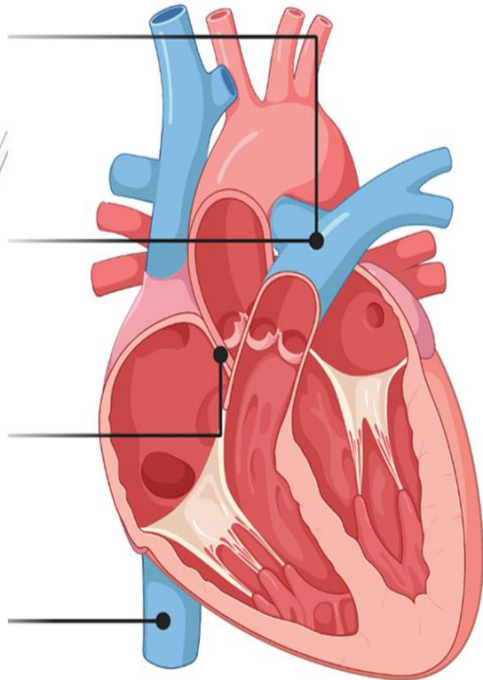
3 US
Early Feasibility Studies (EFS)



1 EU
Safety & Performance

Pipeline of Innovative Technologies and Service Concepts

Multi-Sensor Approach for Heart Failure Management Included in MD2K (NIH)



Created with BioRender.com

Implantable

A SimpleSense, Nanowear



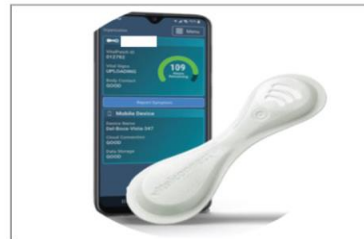
B ReDS, Sensible Medical



C Sensinel, Analog Devices



D Vitalpatch, VitalConnect



E Edema Guard Monitor; iLung, Cardioset



Wearable



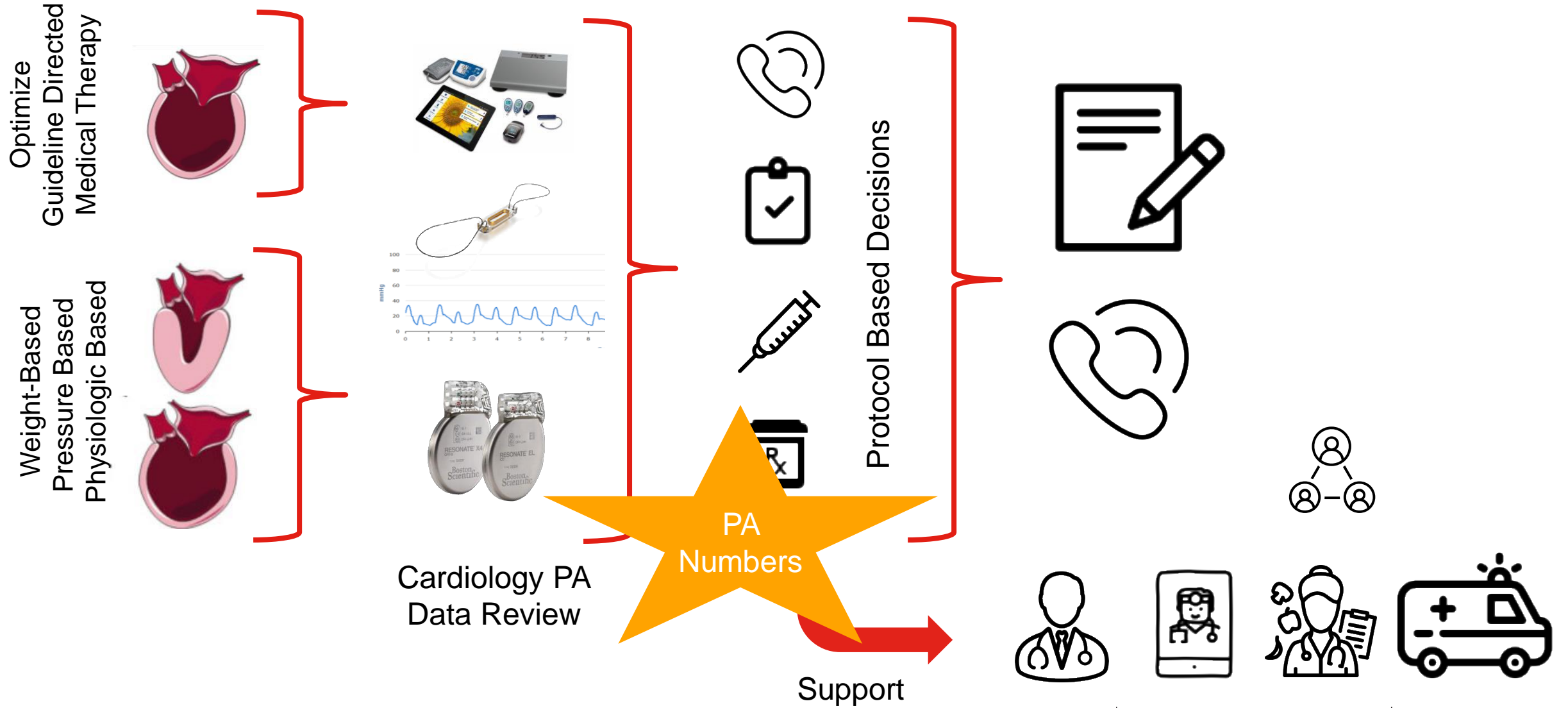
Home Monitors

ORIGINAL ARTICLE

Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation

Marco V. Perez, M.D., Kenneth W. Mahaffey, M.D., Haley Hedlin, Ph.D., John S. Rumsfeld, M.D., Ph.D., Ariadna Garcia, M.S., Todd Ferris, M.D., Vidhya Balasubramanian, M.S., Andrea M. Russo, M.D., Amol Rajmane, M.D., Lauren Cheung, M.D., Grace Hung, M.S., Justin Lee, M.P.H., Peter Kowey, M.D., Nisha Talati, M.B.A., Divya Nag, Santosh E. Gummidi, M.S., Alexis Beatty, M.D., M.A.S., Mellanie True Hills, B.S., Sumbul Desai, M.D., Christopher B. Granger, M.D., Manisha Desai, Ph.D., and Mintu P. Turakhia, M.D., M.A.S., for the Apple Heart Study Investigators*

Development of Centralized Heart Failure Programs

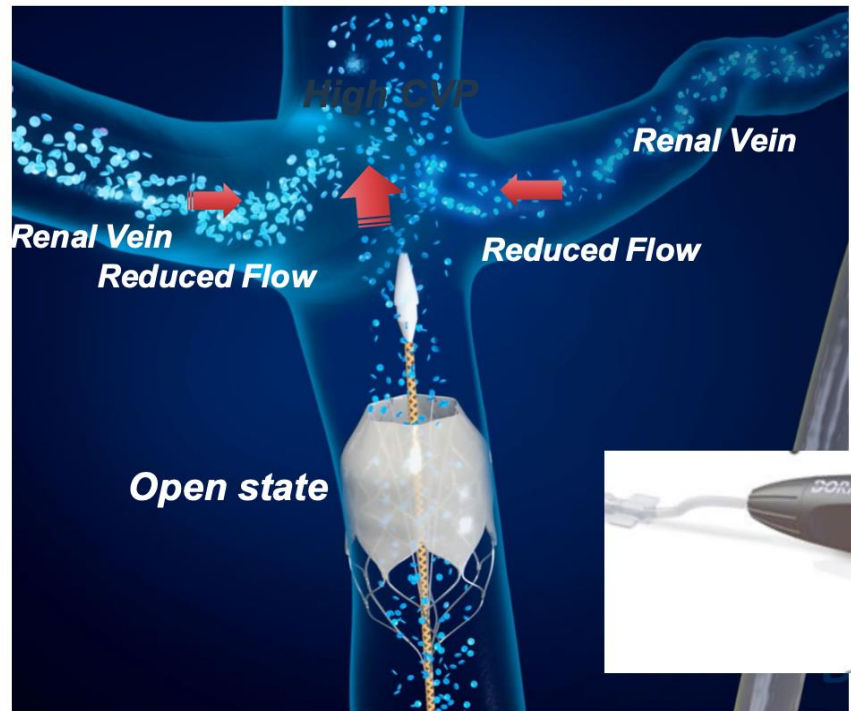


Acute Decompensated Heart Failure – Renal

Revert System – Enhancing Diuresis by Reducing Venous Congestion

Doraya – a temporary partial obstruction of the IVC, below the renal veins.

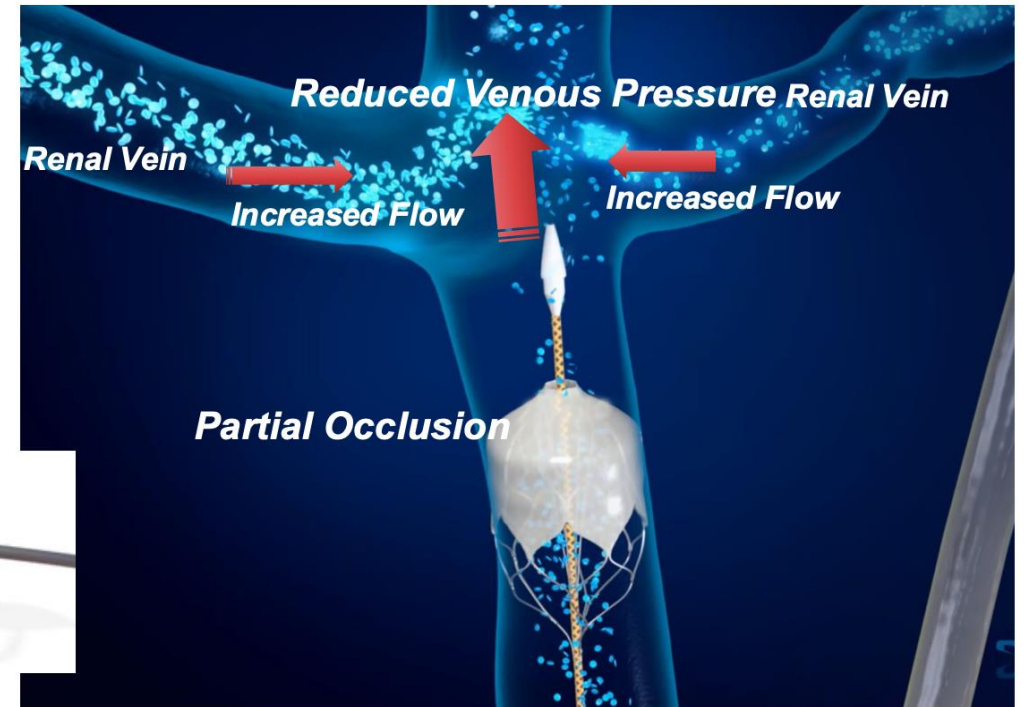
Decreased renal venous pressure resulting in “Pulling” blood from the renal veins outlet



*Normally open,
after deployment*



*Adjustment using an external
handle*

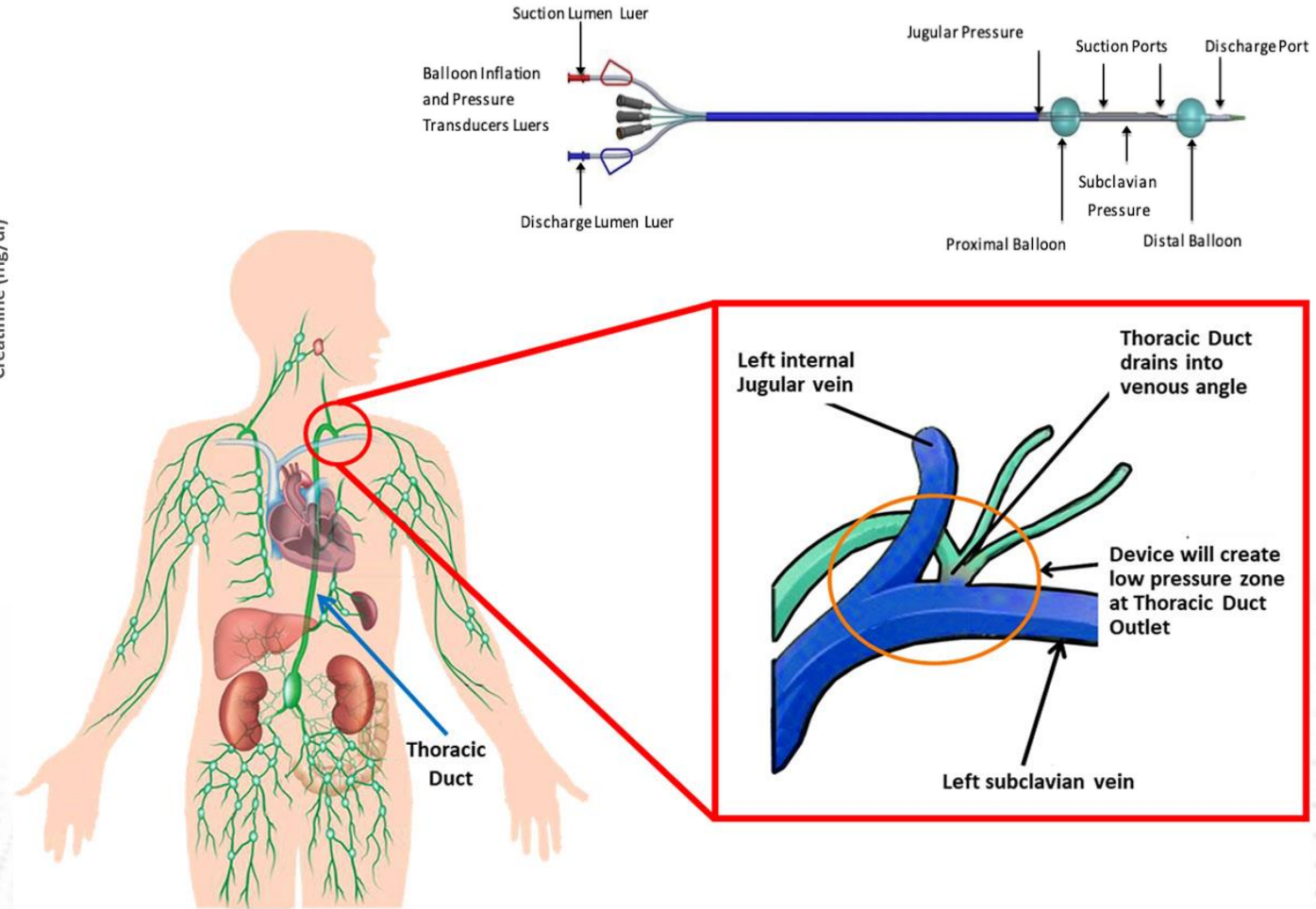


*After adjustment, modulating flow through central
passage, thus effecting hemodynamics*

Acute Decompensated Heart Failure – Interstitial

WhiteSwell System – Transcatheter Decompression of the Thoracic Duct

WhiteSwell Treatment (Tx) Case Example

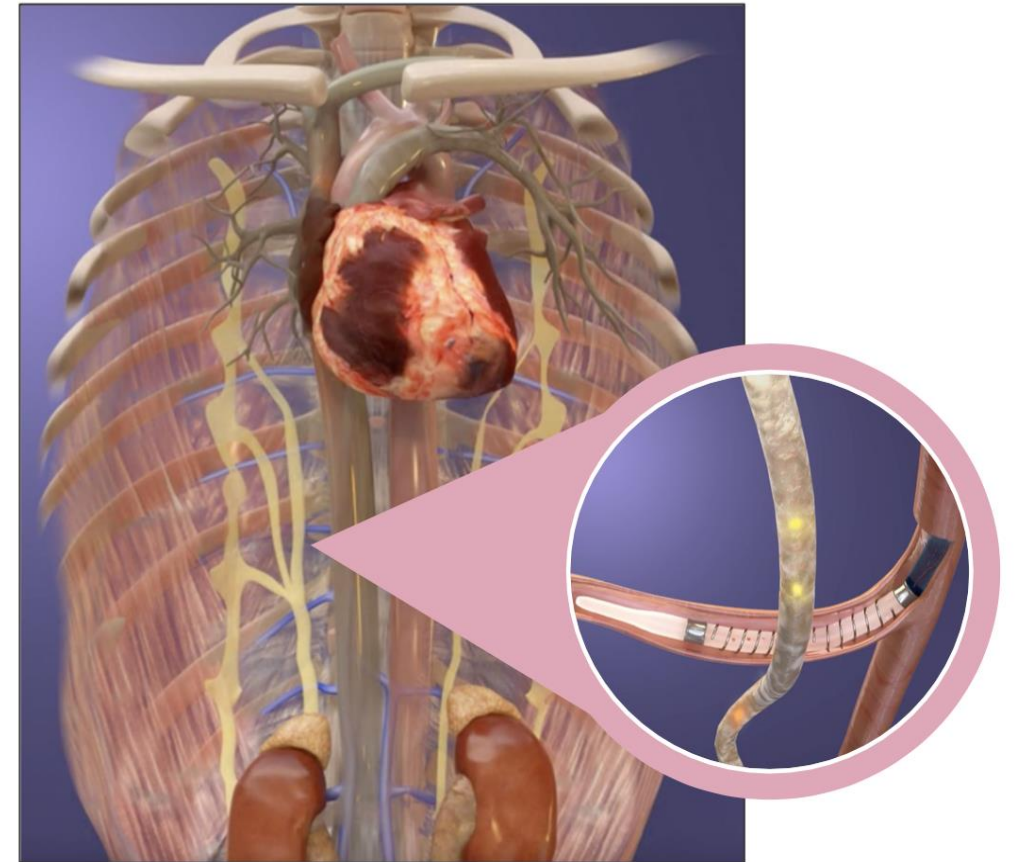


Chronic Decompensated Heart Failure – IV Volume

Axon System – Splanchnic Ablation for Volume Management (SAVM)

New Approach for Treating HFpEF

- ▶ Unilateral ablation of the right greater splanchnic nerve (GSN)
- ▶ Designed to interrupt sympathetic nervous activity to the splanchnic bed, reducing congestion
- ▶ Transvenous femoral, implant-free procedure
- ▶ < 1 hour procedure time (skin-to-skin)
- ▶ Patients typically go home the same day



Conclusions: Interventional Heart Failure

- IC has evolved into distinct sub-specialties in advanced coronary, endovascular and structural heart disease
- The success of the SHD field has been based on the development of new technical skills, evolution of the heart team and commitment to research and training; the HF field provides a similar substrate for growth
- HF is the EPICENTER of cardiovascular medicine, a thoughtful effort to develop interventional HF as a subspecialty is warranted