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Heart Failure Devices

Peter Eckman MD, FACC, FHFSA, FAHA

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Disclosures

- Abbott – Honoraria (prior)
- **Alleviant – support to institution/trial**
- **Ancora (Accucinch) – Eligibility committee for CORCINCH-HF trial**
- BrioHealth Solutions - Honoraria
- **CVRx (Baroreceptor activation therapy) – Consulting**
- Daxor – Advisory board
- **Edwards Lifesciences – Support to institution/trial**
- Medtronic – Eligibility committee for TTVR trial

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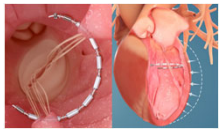
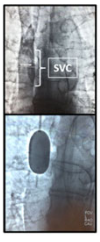
Topics

- Atrial shunts

- LV remodeling



- Baroreceptor activation therapy



- Preload reduction in cardiogenic shock

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HFpEF – Lutembacher syndrome

- Hallmark is effort intolerance
- Profound/brisk increase in LA pressure during exercise
- Lutembacher syndrome (1916)
  - Combination of mitral stenosis and secundum ASD
  - Originally described 1750 by Johann Friedrich Meckel, Sr.

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Interatrial Shunting in Heart Failure: Why It Should Work

- Patients with mitral valve stenosis and an atrial septal defect (ASD) have fewer symptoms than patients with an intact septum[1]
- Closure of ASDs in patients with unrecognized left ventricular dysfunction results in elevated LAP and pulmonary edema[2]
- Pre-clinical animal studies demonstrate hemodynamic, echocardiographic, and survival benefits with interatrial shunting[3]
- First-in-human / clinical pilot studies support the safety, feasibility, and potential effectiveness of interatrial shunting in heart failure[4-10]

1. Lutembacher R. Arch Mal Coeur 1916
2. Ewert P, et al. Catheter Cardiovasc Interv 2001
3. Eigler N, et al. Structural Heart 2017
4. Søndergaard L, et al. Eur Heart J 2014
5. Hasenfuß, et al. Lancet 2016
6. Feldman et al. Circulation 2017
7. Del Trigo M, et al. Lancet 2016
8. Rodés-Cabau J, et al. JACC Intv 2018
9. Paitazoglou C, et al. EuroInterv 2019
10. Guimmarães L, et al. EuroInterv 2020

CRF THT W Abraham from THT 2024

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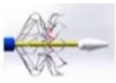
Shunt devices in human trials

Device/ procedure	Corvia	V-Wave	Occlutech	Edwards	Alleviant	NoYA	InterShunt
							
Type	Implant	Implant	Implant	Implant	Procedure	Procedure	Procedure
Description	Nitinol stent	Nitinol/PTFE hourglass	Nitinol braid with central orifice	Tubular nitinol device with retention arms	Coring catheter	RF catheter	Cutting catheter
Shunt flow	LA → RA	LA → RA	LA → RA	LA → CS	LA → RA	LA → RA	LA → RA
Shunt size	8 mm	5.1 mm	4, 6, 8, 10 mm	7 mm	6 mm	4-12 mm	6 mm
Development stage	Pivotal RCT complete, follow-up confirmatory RCT in responder subgroup ongoing	Pivotal RCT enrollment complete, follow-up ongoing	Pivotal RCT enrollment ongoing	Phase 2 feasibility / mechanistic RCT ongoing	Pivotal RCT enrollment ongoing	Open-label trial ongoing	Small pilot studies in humans

Summary from William Gray, MD (Lankenau)

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Background: REDUCE LAP-HF II Trial

- Pivotal, phase 3, international, multicenter, sham-controlled RCT of Corvia Atrial Shunt Device in patients with HF and LVEF ≥40%
  - NYHA II-IV, GDMT, age ≥40, LVEF ≥40%, preserved RV fn
  - Ex RHC with peak exercise PCWP ≥25mmHg, L-R gradient >5mmHg
- Primary outcome: hierarchical composite (win ratio)
  - CV death, non-fatal ischemic CVA, HF events, KCCQ summary score
- N=626 randomized 1:1 to shunt (n=314) vs. sham (n=312)
- Overall trial was **neutral** (win ratio = 1.0 [95% CI 0.8-1.2])

CRF THT Kaye, 2024

Shah SJ, et al. Lancet 2022

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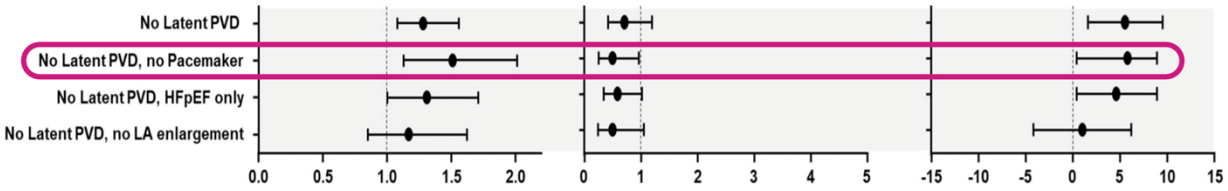
REDUCE LAP-HF II Responder Subgroup

- Post hoc, pre-specified analysis:
  - Large subgroup: 50% of randomized patients (n=313)
  - Peak exercise PVR <1.74 WU + no pacemaker/ICD
  - After 12 months of follow-up: Beneficial treatment response



Responder Group
(shunt vs. sham)

↑ *Win ratio = 1.43 (p=0.009)*

↓ *HF events (IRR 0.49, P=0.035)*

↑ *KCCQ (+5.9 points; =0.01)*

CRF THT Kaye, 2024

Borlaug BA...Shah SJ. Circulation 2022

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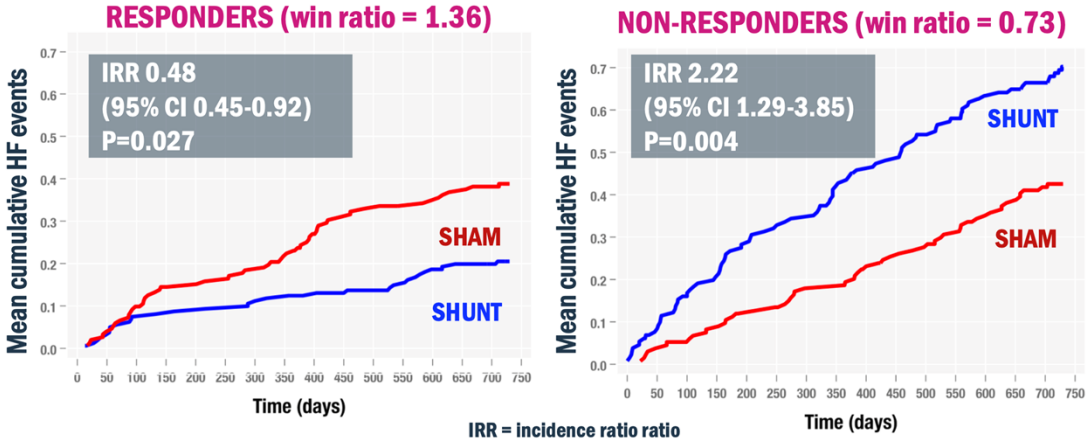
HF events by shunt responder status

- 24-month recurrent HF events analysis



IRR = incidence ratio ratio

CRF THT Kaye, 2024

Gustafsson F...Shah SJ. ESC-HFA 2023

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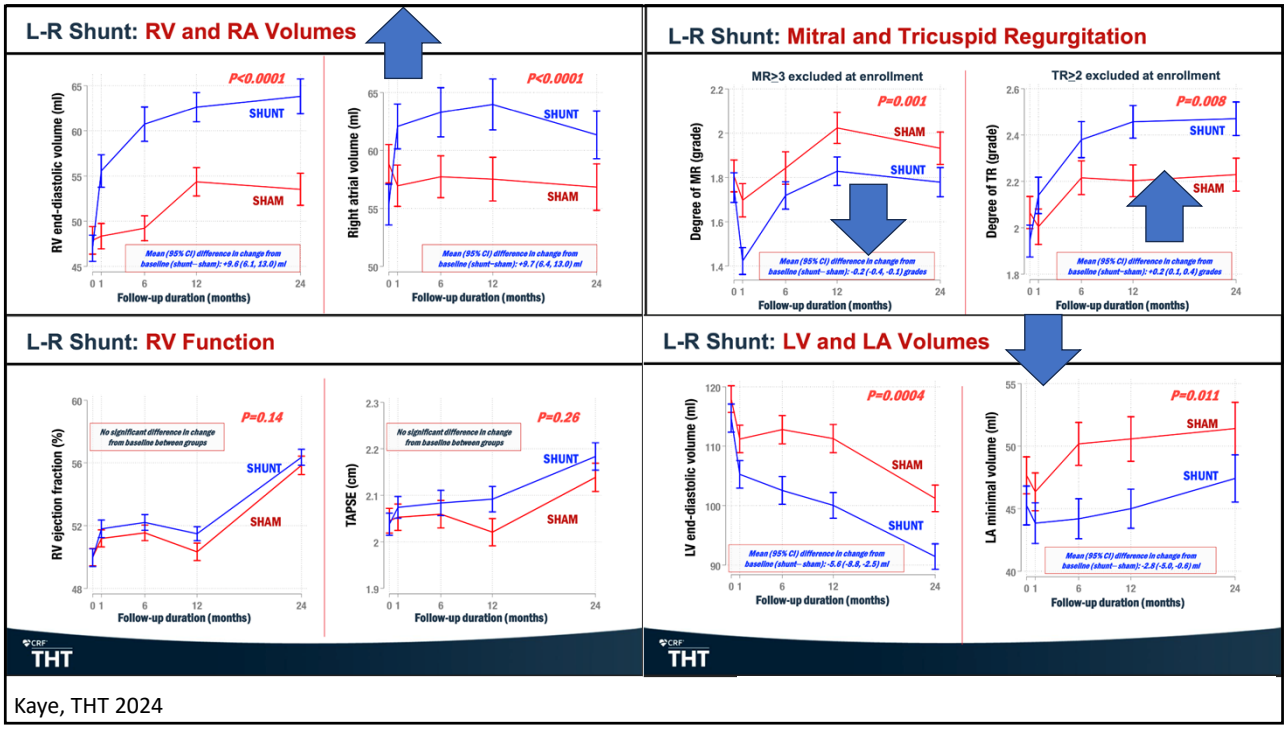

Kaye, THT 2024

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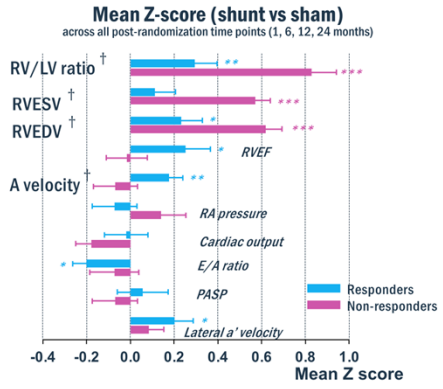
Responder Status: Serial Echocardiographic Changes



- ***4 echo parameter treatment effects were significantly different between responders vs. non-responders*** ($P_{interaction}$ <0.05):
  - **Lower RV/LV volume ratio**
  - **Lower RVESV, RVEDV**
  - **Higher transmitral A velocity**

RESPONDER-HF (NCT05425459)***: Ongoing RCT of Corvia Atrial Shunt in Responder Gp: NYHA II-IV, LVEF≥40%, GDMT, ExPVR<1.75, No Pacemaker***

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*P<0.05 vs. sham, **P<0.01 vs. sham, ***P<0.001 vs. sham. † Interaction P<0.05

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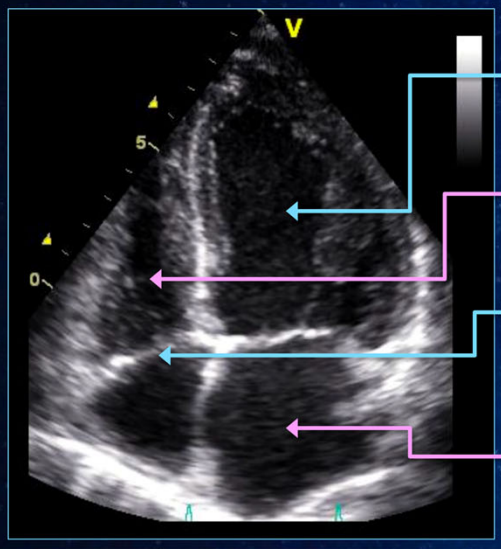
Effects of IASD on the heart



LV and LA get smaller: Avoid HCM, avoid low output states

RV and RA get bigger: Avoid vulnerable RV, overt RV failure, RA failure

Tricuspid annulus will dilate: Avoid moderate or greater TR

Blood needs to get back to left heart: Avoid pulmonary vascular disease, tricuspid/pulmonary valve obstruction

Shah S at THT 2024

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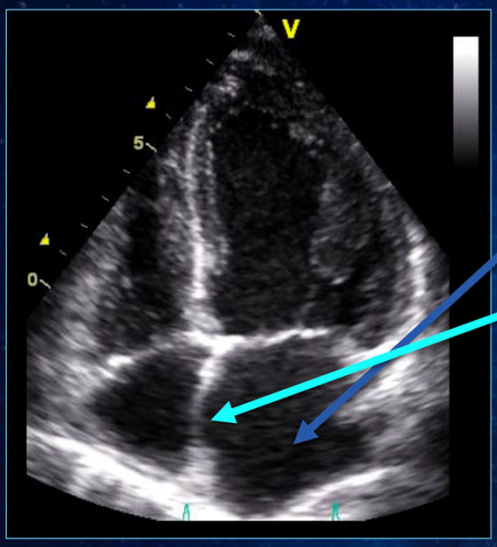
Echo evaluation for optimal candidate



Left atrial enlargement (LA size > RA size)

Interatrial septum bows from left to right

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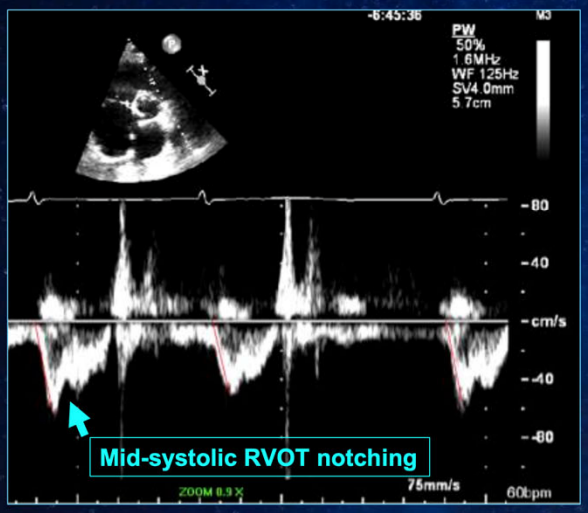
Echo evaluation for optimal candidate



RVOT notching on PW Doppler is associated with high PVR: unlikely to benefit from interatrial shunting!

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ALLAY-HF

Safety and Efficacy of the Alleviant System for No-Implant Interatrial Shunt Creation in Patients with Chronic Heart Failure

Figure 2. Alleviant Catheter (Distal Assembly)

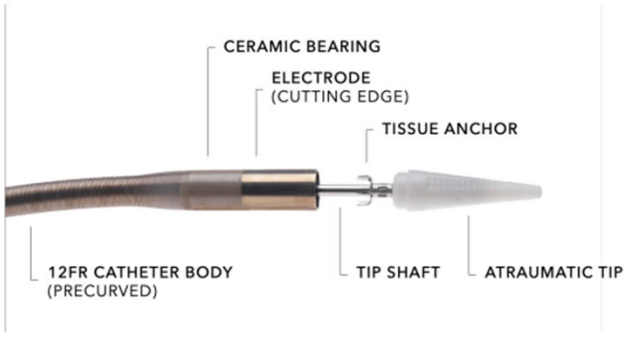
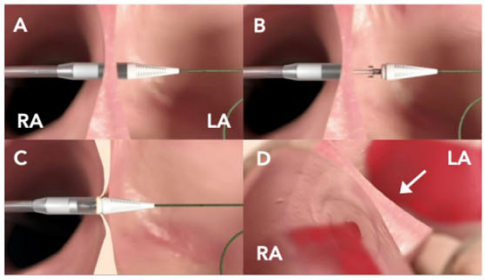


Figure 6. Alleviant System (Procedure Overview)

A – Catheter is advanced over guidewire into LA; B – Device tip is opened and slowly retracted under image guidance until electrode resides in RA; C – A short pulse of RF energy is applied to cut target tissue; D – Guidewire and catheter (with excised tissue) are withdrawn, leaving a durable passageway to permit LA-to-RA shunt flow (arrow).



ALLEVIANT

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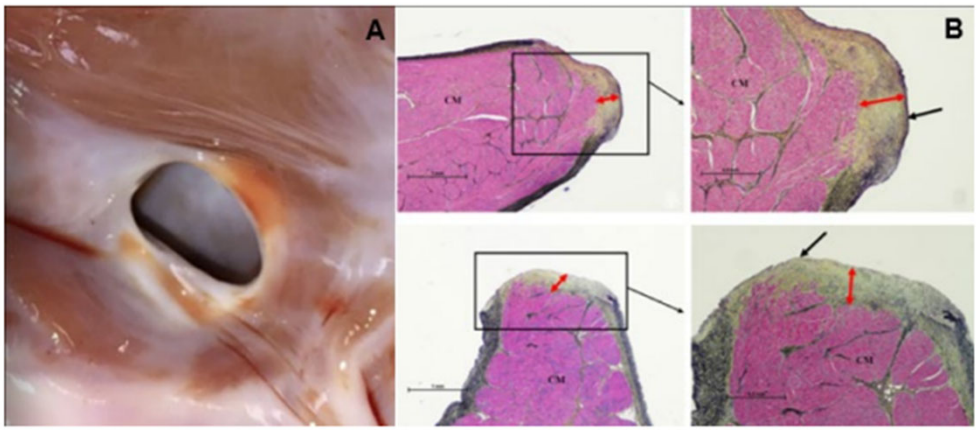
Figure 9. Representative Images from GLP Study

(A – Gross Shunt at 60 Days; B – Photomicrographs of Shunt Margin Sections at 60 Days



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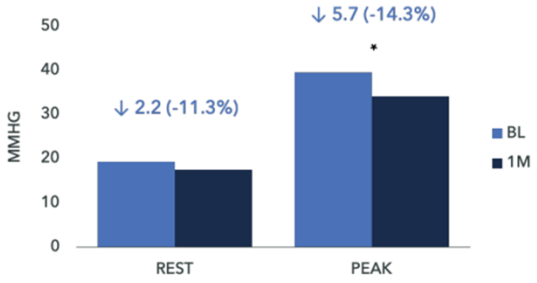
Preliminary Data (EFS)

- N=32, 20F, mean age 67, mean BMI 35.4
- Technical success in 100% with mean size 7.1 ± 0.8 mm
- No major CV AEs, 10 SAE's in 6/32, none deemed device or procedure related (1 died d/t COVID, 1 died d/t breast cancer, 3 HF hospitalization with IV diuretics)

Figure 7. PCWP at Baseline and 1 Month



Rest: P=0.108 (95% CI -0.5-4.9)
*Peak: *P=0.007 (95% CI 1.7-9.6)*
PCWP measured at BL and 1M only.
P values from paired t-test.
Data represents n=26 patients across both timepoints.

Table 12. Listing of Serious Adverse Events Reported in ALLEVIATE HF-1 and HF-2

Event Description	Device Relationship	Procedure Relationship
General – Other Brief loss of consciousness, probable vasovagal event	Unlikely Related	Unlikely Related
General – Other Type 2 MI	Unlikely Related	Unlikely Related
Respiratory – Dyspnea or Respiratory Distress	Unlikely Related	Unlikely Related
General – Cardiac Angina or Chest Pain	Not Related	Not Related
General Cardiac – Arrhythmia	Unlikely Related	Unlikely Related
Cardiac disorders – Cardiac Failure	Unlikely Related	Unlikely Related
Death	Not Related	Not Related

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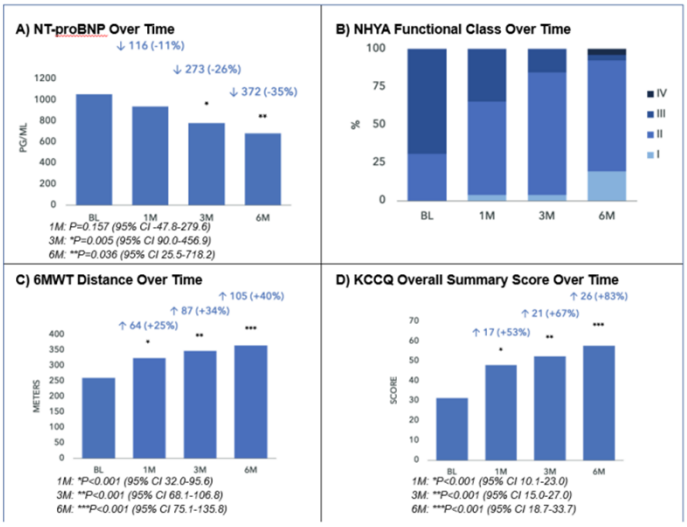
Secondary Effectiveness (6 mos)

- Mean NTproBNP:
  - 1050 ± 908 to 682 ± 502
- 69% improvement in NYHA functional class
- Mean 6MW
  - 260 ± 64 to 366 ±75
- KCCQ Overall
  - 31 ± 14 to 58 ± 18

Figure 8. Secondary Effectiveness Endpoints



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ALLAY-HF

Enrollment underway…

Name	Safety and Efficacy of the Alleviant System for No-Implant Interatrial Shunt Creation in Pts with Chronic HF
Design	Multicenter, randomized, double-blinded, adaptive, sham-controlled
Size	400 - 700 patients (adaptive/Bayesian)
Patient Population	HFpEF and HFmrEF, identified with exercise hemodynamics
Primary Endpoint (Composite, Hierarchical)	• Time to CV mortality • HF events • KCCQ
Key Inclusion	• Symptomatic HFpEF/HFmrEF (LVEF ≥ 40%) • NYHA Class II, III or ambulatory IV • Elevated PCW during exercise RHC (≥ 25 mmHg) • Exercise PVR < 1.8 WU • Ongoing stable guideline-directed medical therapy
Key Exclusion	• Advanced HF • Presence of a pacemaker • Evidence of right heart dysfunction

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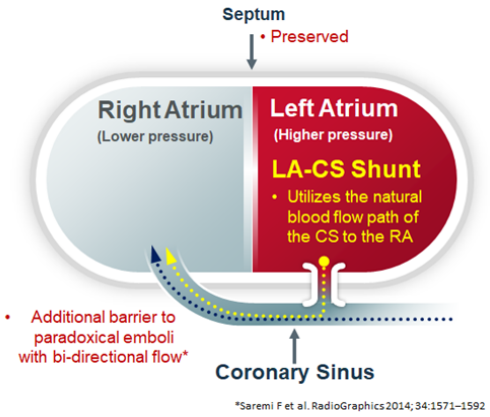
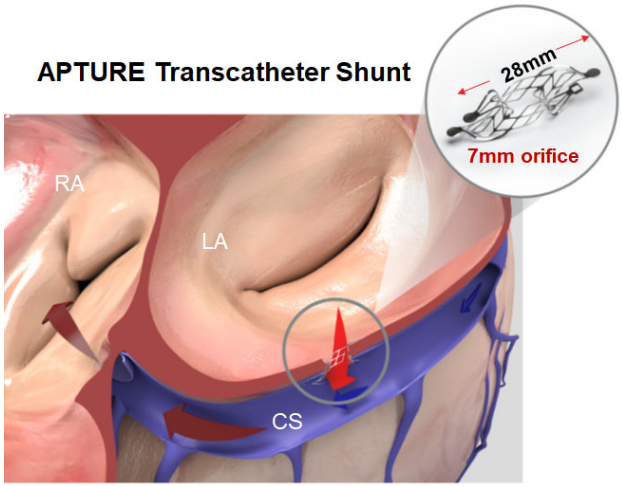
Left atrium to coronary sinus shunting
An alternative approach to chronic left atrial decompression





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ALT FLOW early feasibility study design
A prospective, multi-center, single-arm study

Objective: To evaluate initial clinical safety, device functionality, and effectiveness of the APTURE transcatheter shunt system

Key Inclusion Criteria

- **Chronic Symptomatic HF, NYHA Class II-IV, AND**
  - HF event requiring IV Lasix in prior 12 months, OR
  - Elevated BNP (> 50pg/ml; 150pg/ml for AF) or NT-pro BNP (>150pg/ml; 450pg/ml for AF) in prior 6 months
- **Stable GDMT for HF and co-morbidities**
- **PCWP > 15mmHg at rest with LAP > RAP by 5mmHg, OR PCWP > 25mmHg during supine ergometer exercise stress test with LAP > RAP by 10mmHg.**
- **Site PVR < 5 WU**

Key Exclusion Criteria

- **Severe HF**
  - Hemodynamic instability or inotrope infusion within 6 months
  - Stage D HF or on transplant waiting list
  - LVEF < 20%
- **Significant untreated coronary, carotid or valvular disease** (e.g., MR > 3+ or TR > 2+, AS > moderate)
- **CRT initiation, MI or Stroke within 6 months**
- **Serum Creatinine > 2.5mg/dl or eGFR > 25ml/min/1.73m²**
- **6MWT < 50m or > 450m**
- **HOCM or infiltrative cardiomyopathy**
- **More than mild RV dysfunction**

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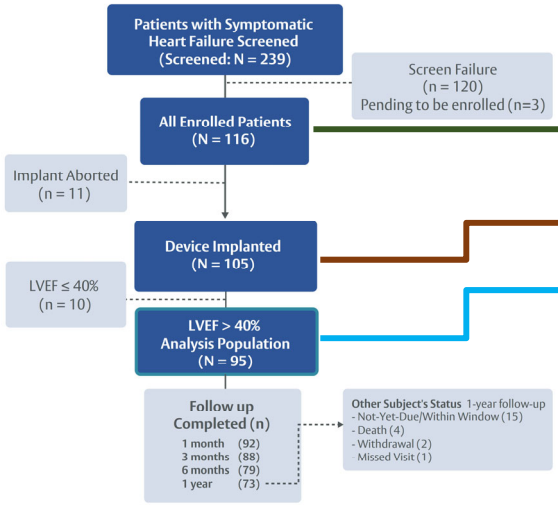
ALT-FLOW EFS
Patient flow and endpoints



Pre-Specified Endpoint Assessments

All Enrolled Patients (N=116):
- Performance outcomes
- MACCRE and Reintervention (30d)

Device Implanted Patients (N=105)
- Shunt patency at one year

Analysis Population (N=95):
- All implanted patients with LVEF > 40%
- Outcomes Assessment up to 1-year for total population and subgroups
  - Clinical
  - Hemodynamic
  - Functional
  - Quality of Life

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30-day safety endpoint: all enrolled patients
MACCRE* plus reintervention

Safety Endpoint	Total Cohort N=116
MACCRE or Reintervention	2.6% (3/116)
Acute Myocardial Infarction	0.0% (0/116)
Stent Occlusion/Thrombosis	0.0% (0/116)
Stroke/TIA	0.9% (1/116)
AKI Stage 3	0.0% (0/116)
Death	0.0% (0/116)
Reintervention	2.6% (3/116)

Successful shunt implantation achieved in 90.5%

(All Enrolled Patients: 105/116)

Shunt patency per Echocardiography CoreLab 100% at one year

(Device Implanted patients: 105/105)

3 Patients with 4 Events:
- (1) Embolization with surgical retrieval, with (2) post-surgical stroke
- (3) Surgical reintervention for tamponade and CS repair
- (4) Percutaneous Drainage of tamponade and CS covered stent

Categorical measures - % (n/N or n/n).

*MACCRE – major adverse cardiac, cerebrovascular and renal events, TIA – transient ischemic attack, AKI – acute kidney injury.

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Baseline patient characteristics
Analysis population

	Total N=95
Age (yrs)	71 ± 9
Male	51%
BMI (kg/m²)	33 ± 8
Hypertension	87%
Atrial Fib/Flutter	59%
COPD	48%
CKD	36%
Prior CABG / PCI	31%
Prior MI	23%
Pacemaker / ICD	14%
CRT	6%
Prior Stroke / TIA	10%
NYHA Class II	7%
NYHA Class III	93%
Primary HFH within 1 yr	38%

	Total N=95
LVEF (%)	62 ± 8
RAVI (mm)	29 ± 12
RVDD (mm)	39 ± 6
RVFAC (%)	48 ± 6
TAPSE (mm)	20 ± 4
KCCQ-OSS	38 ± 18
6MWT (m)	248 ± 101
BNP (pg/ml)	128 ± 113
NT-pro BNP (pg/ml)	899 ± 1047
CHA_2DS_2VASc	4.4 ± 1.3
Loop Diuretic	93%
ACEI / ARNI / ARB	57%
Beta Blocker	70%
MRA	42%
SGLT2i	27%

Continuous measures - mean ± SD.

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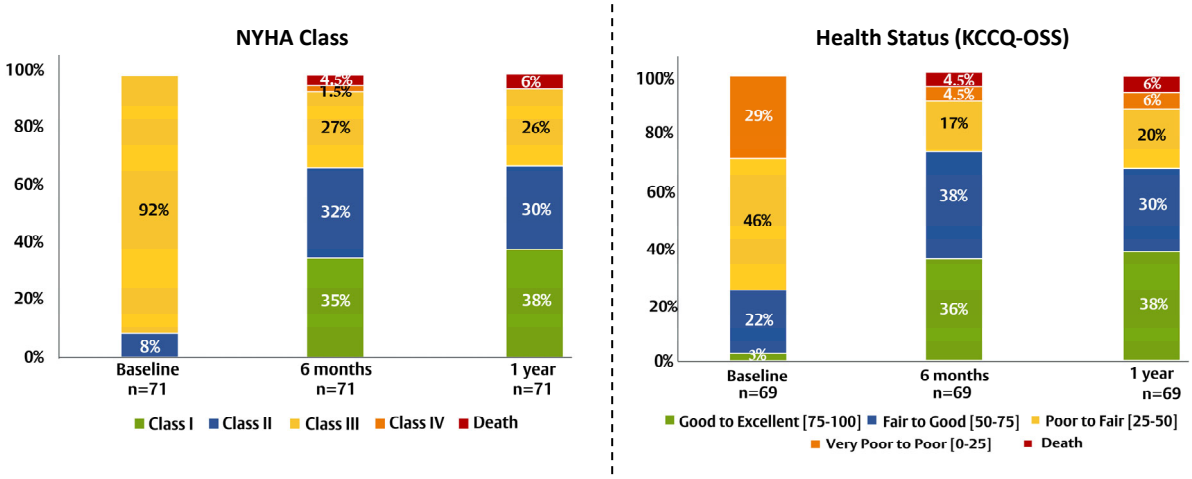
NYHA functional class and health status
Paired changes from baseline – analysis population



NYHA = New York Heart Association; Health Status category base on Quartile of KCCQ-OSS Score (0-100).

CAUTION: Investigational device. Limited by Federal (or USA) law to investigational use.

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Baseline hemodynamics
Analysis population – core lab data

Resting	Total Cohort N=95	PVR ≤ 2 n=69	PVR > 2 n=24	p-value PVR ≤ 2 vs. PVR > 2
PCWP	20.1 ± 8.25 (93)	19.8 ± 8.11 (69)	20.9 ± 8.77 (24)	0.59
RAP	9.6 ± 4.69 (95)	9.2 ± 4.67 (69)	10.5 ± 4.87 (24)	0.26
PASP	44.2 ± 15.60 (94)	39.3 ± 11.68 (69)	57.8 ± 17.71 (24)	<0.0001
Mean PA	28.1 ± 9.68 (94)	25.6 ± 7.79 (69)	35.6 ± 11.05 (24)	<0.001
PVR (Site)	2.1 ± 0.94 (94)	1.8 ± 0.79 (68)	3.0 ± 0.72 (24)	<0.0001
Cardiac Index (Thermodilution)	2.5 ± 0.51 (95)	2.6 ± 0.51 (69)	2.2 ± 0.48 (24)	0.01
20W Exercise				
PCWP	35.1 ± 8.41 (84)	35.1 ± 8.24 (62)	35.2 ± 9.08 (22)	0.96
RAP	18.7 ± 7.08 (89)	18.0 ± 6.19 (65)	21.0 ± 9.27 (22)	0.16
PASP	71.3 ± 17.81 (80)	67.6 ± 14.57 (57)	81.4 ± 21.89 (22)	0.01
Mean PA	46.6 ± 10.71 (79)	44.8 ± 8.73 (56)	51.7 ± 13.66 (22)	0.04

Continuous measures - mean ± SD (n).

*DOI: 10.1183/13993003.00879-2022

Presence or absence of Pulmonary Vascular Disease (PVD) at rest defined using ESC/ERS 2022* criteria.

Baseline resting PVR > 2 WU

PVD at rest

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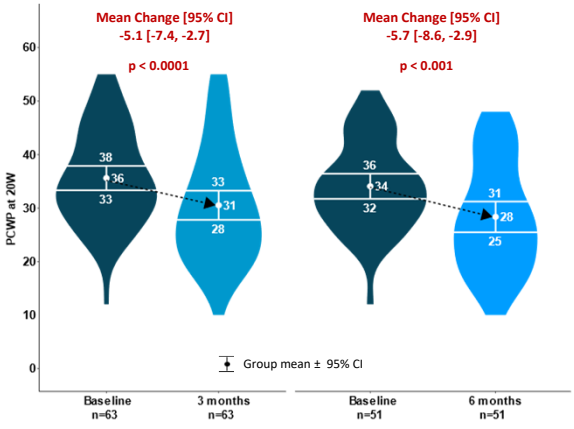
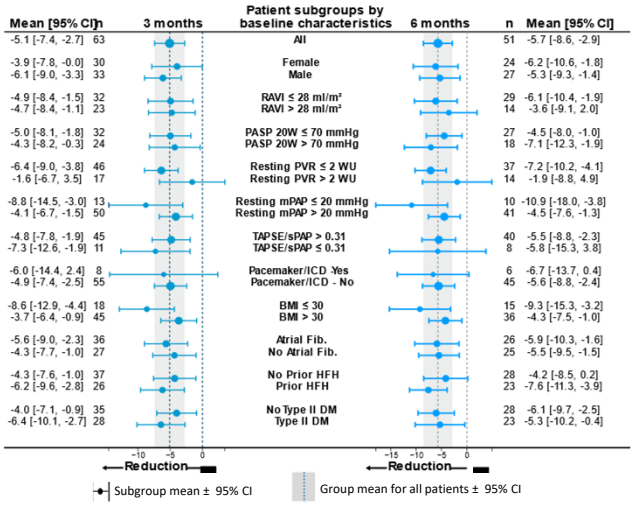
PCWP at 20 watts exercise (PCWP 20W)
Paired comparisons vs. baseline – analysis population





All values in mmHg.

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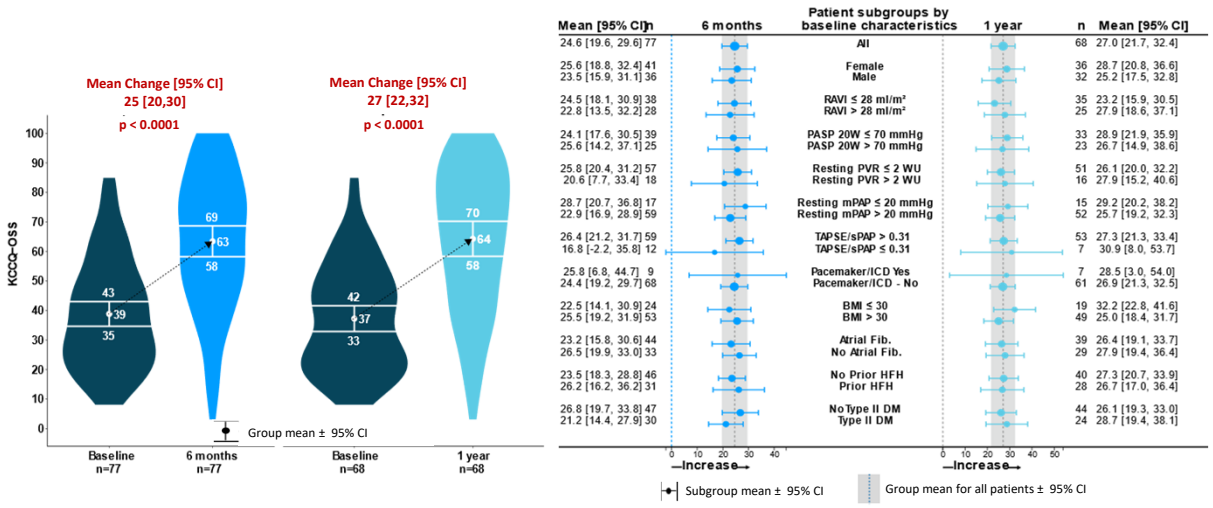
KCCQ-Overall summary score (KCCQ-OSS)
Paired comparisons vs. baseline – analysis population



KCCQ 23-item questionnaire used.

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ALT-FLOW Early Feasibility Study - Conclusions

In patients with chronic symptomatic HF and elevated PCWP at rest and/or exercise with an LVEF > 40%, the APTURE transcatheter shunt demonstrated:

- High implant success rate with low 30-day MACCRE or reintervention,
- Clinically meaningful improvements in HF symptoms and overall health status at one year,
- Significant and durable reductions in PCWP at 20-W exercise through 6 months,
- Overall consistency in favorable responses for changes from baseline in exercise PCWP and KCCQ-OSS among multiple analyzed subgroups, and
- No evidence of adverse effects on right heart volumes, hemodynamics, function, or RV-PA coupling.

Presented at THT 2024 (Zahr F on behalf of ALT FLOW study team)

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Trial Comparison

	ALLAY	ALT-FLOW 2
Pacing/Leads	No leads allowed	RV ok, none in CS
PVR	Resting excludes PVR >3.5 PVR < 1.8 at 25W exercise	Excludes > 5
Cost	Covered	CMS approval Private payors likely to refuse due to randomization
RHC	Screening	Baseline and 6-month exercise RHC
Requires diuretic	Yes, stable 2 weeks	No, but stable for 4 weeks
Resting RHC requirements	RAP <15 PCWP > RAP	PCWP > RAP by 5

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Please consider…

- Is this an option for a persistently symptomatic HFpEF patient?
- Would an exercise RHC be helpful clinically?
- Measure LVEDP
- Does echo suggest high left – and normal right-sided filling pressures?

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LV Remodeling Therapy Comparisons

	Enalapril	Carvedilol	CRT	MV Repair	MV Replace	MitraClip
	CONSESUS et al Konstam et al. 1 year	Doughty et al Packer et al 1 Year	Abraham et al 6 months	Acker et al. N Eng J Med 370 1 year		Mitra-fr 1 year
Δ EF%	+4	+5	+3.6	0	0	-3
Δ ESV (mL)	-13	-32	-25.6	-7	-5	+1
Mortality (% risk reduction)	31%	65%	10%	Not Evaluated	Not Evaluated	No Effect
Death or HF Hosp	50%	27%	18%	Not Evaluated	Not Evaluated	No Effect

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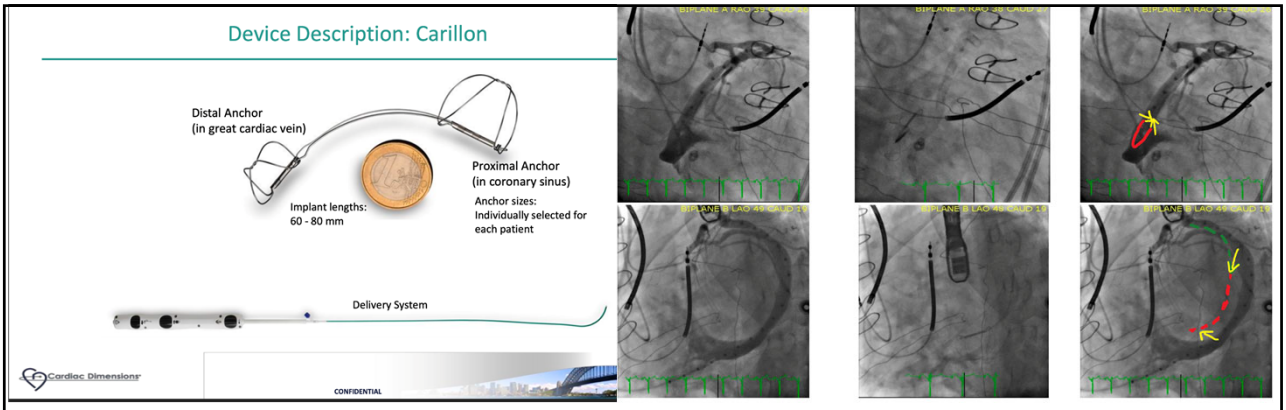
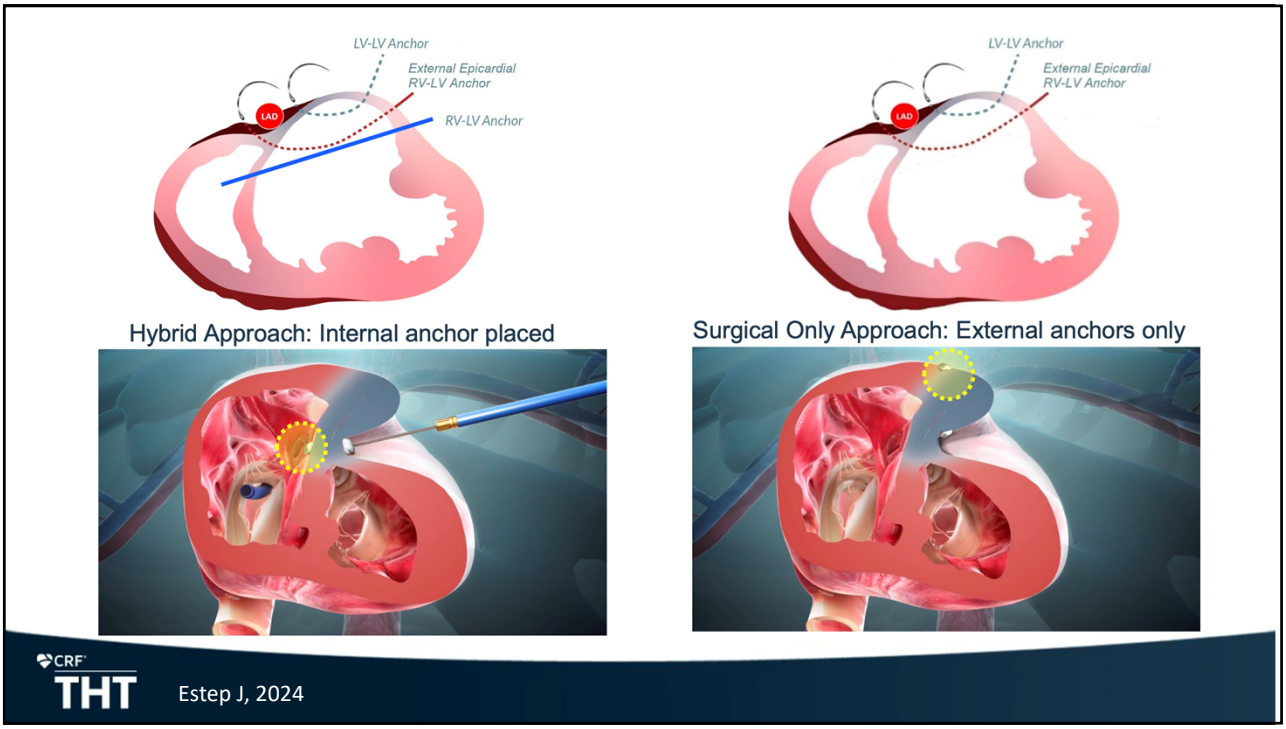


- **18 patients randomized**
- **5 additional have completed screening**
- **80 total consented**
- **49 sites active**
- **11 sites being activated**

Kapadia S, THT 2024

34



35

ALIVE Trial: Baseline and Follow-Up Left Ventricular End-Systolic Volume Index Results

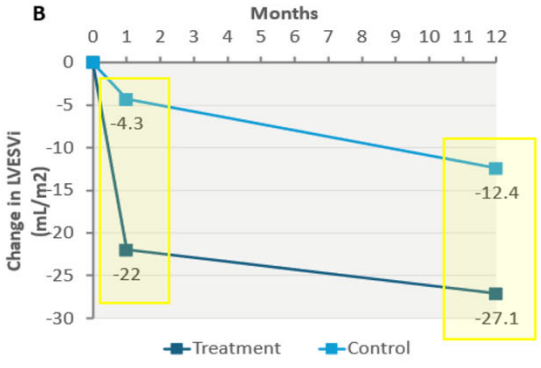
A

ITT Population (N=127)

	Test N=84		Control N=42		
Visit Interval	**LVESV index (mL/m²)**	**Change from Baseline**	**LVESV index (mL/m²)**	**Change from Baseline**	**P Value***
Baseline	96.7 ± 36.2 (84) (44, 226) 88 [72, 112]	--	89.0 ± 33.6 (41) (33, 178) 86 [62, 117]	--	0.23
1-Month Follow-up	75.3 ± 31.4 (69) (22, 192) 71 [52, 94]	-22.0 ± 25.8 (69) (-126, 22) -20 [-37, -3]	84.8 ± 35.5 (34) (23, 190) 75 [64, 113]	-4.3 ± 17.7 (34) (-53, 30) -4 [-14, 10]	0.0005
1-Year Follow-up	69.7 ± 28.8 (64) (20, 170) 65 [51, 80]	-27.1 ± 28.4 (64) (-133, 40) -24 [-46, -8]	69.1 ± 27.4 (34) (31, 123) 65 [47, 87]	-12.4 ± 24.9 (34) (-77, 45) -13 [-21, 2]	0.01

Data presented as mean ± std (n); (min, max); median [25th percentile, 75th percentile].
Based on Core Lab data for subjects with available measurements.
*For follow-up comparison of the change inLVESVi (delta from baseline).

B



CRF THT Estep J, 2024

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ALIVE Trial: Primary Safety End Point

Endpoint Result (Pass if Upper Confidence Bound < 40.5%)	Total Events (N)	Revivent + OMT Patients (%) N=84	One-Sided 97.5% Upper Confidence Bound
Composite MAE at 30 days	**30**	**15 (17.9%)**	**27.7%**
All-Cause Death[1]	3	3 (3.6%)	
Placement of Mechanical Support Device Intra- or Post-op[2]	10	8 (9.5%)	
Emergent Cardiac Surgery	7	7 (8.3%)	
Prolonged Mechanical Ventilation[3]	9	8 (9.5%)	
Renal Failure	3	3 (3.6%)	
Clinically Important Stroke (Rankin Score of 4 or higher)	0	0 (0.0%)	

***Post hoc*: Composite MAE at 30 days**
Device (Surgical only LV-LV approach) 3/23 (**13%**)
Device (Hybrid RV-LV approach) 12/60 (**20%**)

The primary 30-day safety endpoint **was met** (MAE 15/84 (17.9%); one-sided 97.5% upper confidence limit 27.7%; p<0.0001).

CRF THT Estep J, 2024

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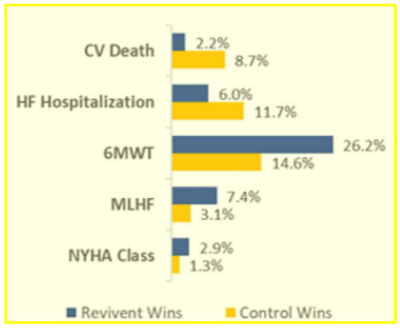
ALIVE Trial: Primary Composite Efficacy Endpoint Results

A



B

Composite Efficacy Endpoint	Number of Patients REVIVENT	CONTROL	Win ratio	P-value
All Patients	**83**	**42**	**1.13**	0.320

Anchor Configuration	Number of Patients REVIVENT	CONTROL	Win ratio	P-value
LV-LV vs. Control	23	42	1.32	0.182
RV-LV vs. Control	60	42	1.06	0.393

The primary 12-month hierarchal composite efficacy endpoint **was not met** (win ratio 1.13; p=0.32)

CRF THT Estep J, 2024

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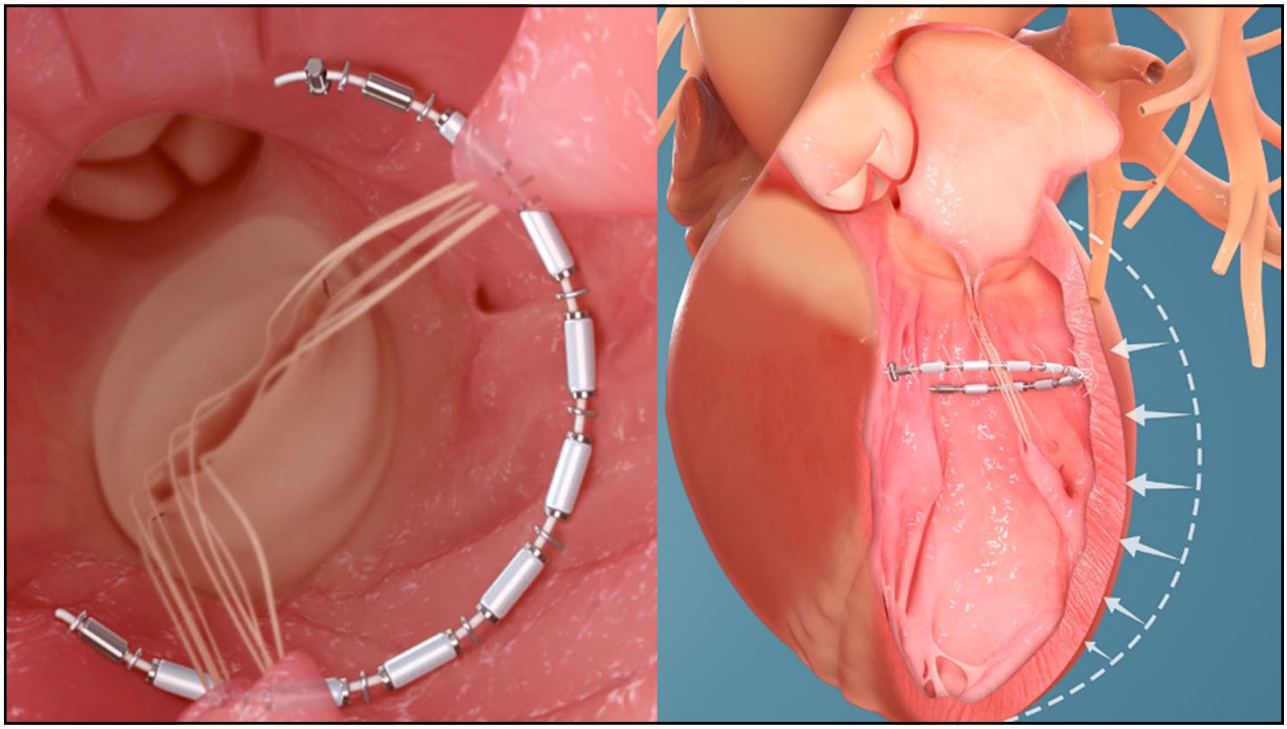
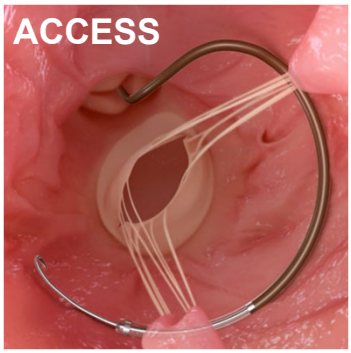


39

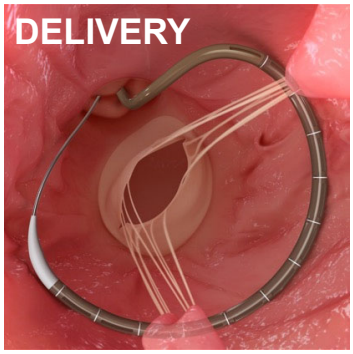
40

The AccuCinch System Procedure in 3 Steps



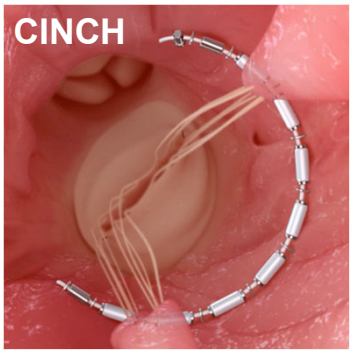
LV ACCESS USING THE ACCUCINCH **GUIDE** CATHETER

LV FREE WALL GUIDEWIRE PLACEMENT WITH THE ACCUCINCH **NAVCATH**



ADVANCEMENT OF THE ACCUCINCH **TRACCATH**

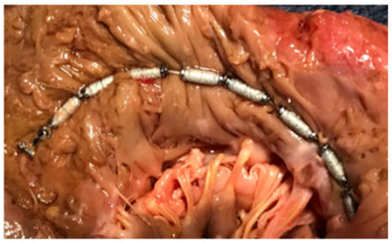
DELIVERY OF THE ACCUCINCH IMPLANT



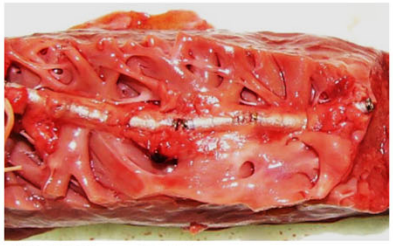
COMPLETION OF THE ACCUCINCH PROCEDURE BY **CINCHING** AND ACUTELY REDUCING THE SIZE OF THE LEFT VENTRICLE

41

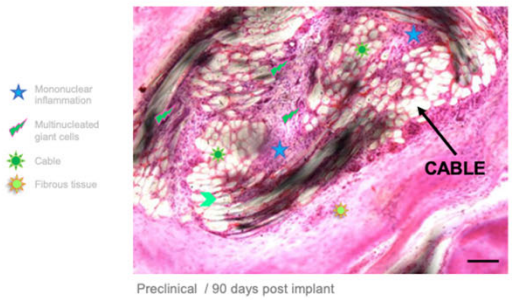
Acute Implantation → LV Wall Integration



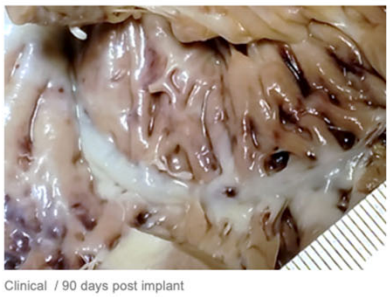
Cadaver / Immediately post implant



Clinical / 10 days post implant



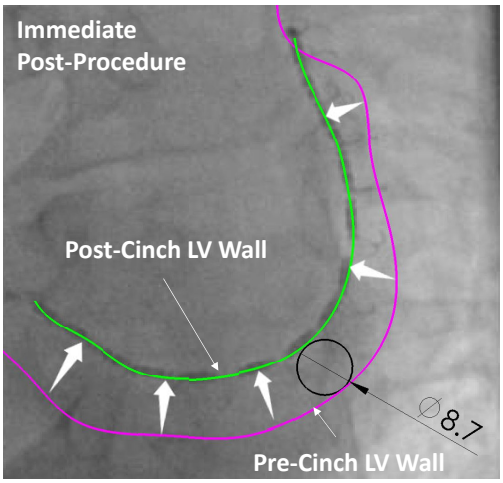
Preclinical / 90 days post implant

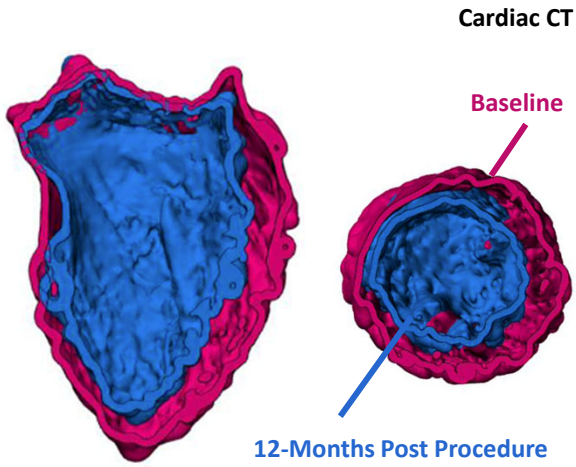


Clinical / 90 days post implant

42

Acute LV Reduction → Biological Reverse Remodeling



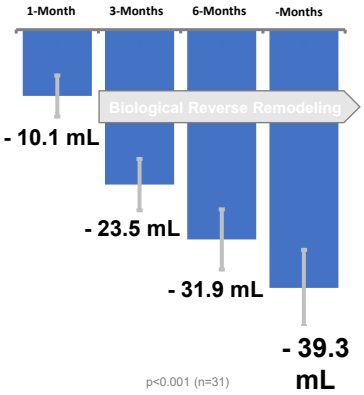


4631-320-319
CT - End Systole

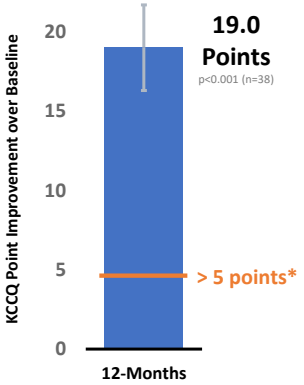
43

Improvement in LV Volume, QoL & Exercise Capacity

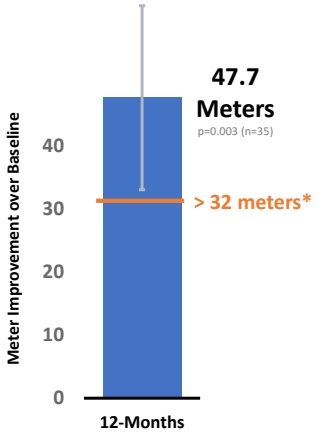
Significant, Progressive Left Ventricle Volume Reduction (LVEDV)



Clinically Significant Improvement in Quality of Life (KCCQ)



Clinically Significant Improvement in Exercise Capacity (6MWT)

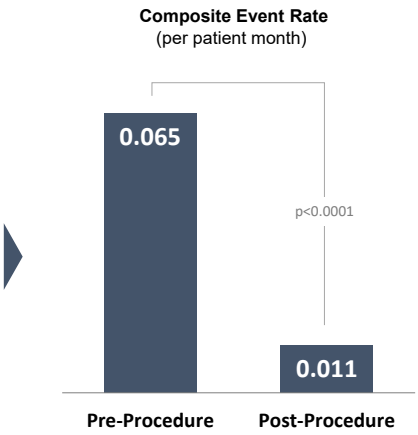


*Thresholds of clinical significance
Mean ± SE; Jorde, U. & Hamid, N. / TVT 2022

44

Improvement in Events Post-Procedure

Events (n=41 Subjects)	12 Mo. Pre-Procedure	12 Mo. Post-Procedure
Death	n/a	1
Heart Transplant	n/a	0
LVAD	n/a	1
HF Hospitalization	**32**	**3**
Total	**32 Events** in 21 Subjects	**5 Events** in 3 Subjects



Jorde, U. / TVT 2022

45

The CORCINCH-HF Study / IDE Pivotal Trial (NCT04331769)

DESIGN: Prospective, randomized, open-label, multi-center clinical safety and efficacy investigation in patients with symptomatic HFrEF

RANDOMIZATION: 1:1 - Treatment with the AccuCinch System plus GDMT or GDMT alone

ENROLLMENT: 400 randomized subjects at up to 80 centers, globally

ENDPOINTS: Safety & efficacy evaluated when 250 subjects reach 6-mo follow-up, and when 400 subjects reach 12-mo follow-up

KEY ELIGIBILITY CRITERIA

- **LVEF**: 20-40%
- **NYHA**:
  - II with HF hosp. in the past 12 mo.
  - III
  - IV ambulatory
- **LVEDD**: ≥ 55 mm
- **MR**: ≤ 2+

Study Leadership

Chairman:
Martin Leon, MD

Co-Principal Investigators:
Mark Reisman, MD
Ulrich Jorde, MD

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CORCINCH-HF Study Eligibility Guide

HFrEF
LVEF ≤ 40

- ARNI (or ACEi/ARB)
- SGLT2i
- MRA
- Beta-Blocker

Maximally Tolerated Dose

+ additional Rx and/or ICD when indicated

→ Persistent Symptoms

→ **NSR**
QRS >150ms
LBBB — CRT → Persistent Symptoms

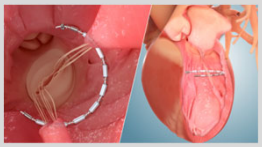
+/-

→ **MR ≥ 3+** — TEER → Persistent Symptoms

CORCINCH-HF Study
AccuCinch Ventricular Restoration System

Adult HFrEF patients who **remain symptomatic** despite GDMT:

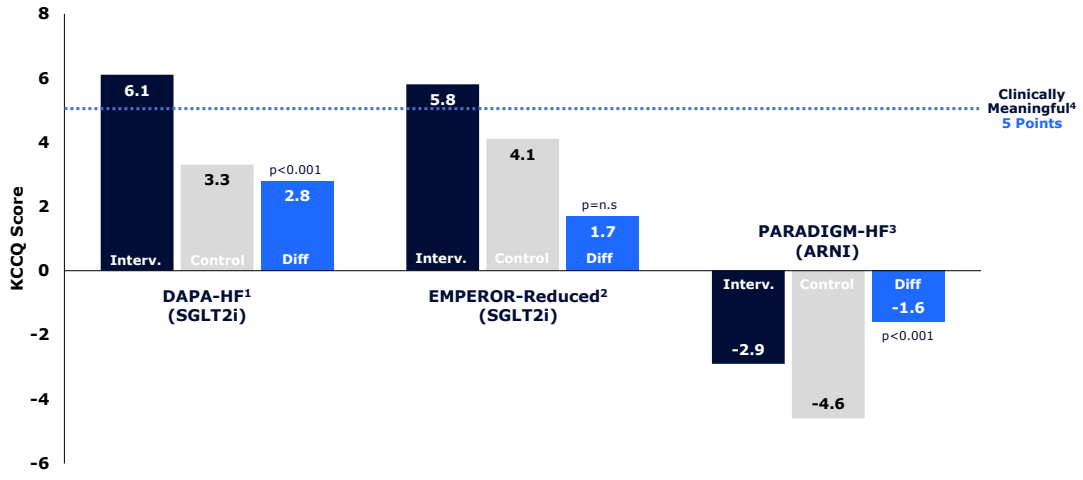
LVEF 20 - 40%
NYHA II w/Hosp, III, IV amb
LVEDD ≥ 55 mm
MR ≤ 2+



Refer to the CORCINCH-HF Protocol for the complete list of inclusion / exclusion criteria

47

GDMT produces modest improvements in QOL

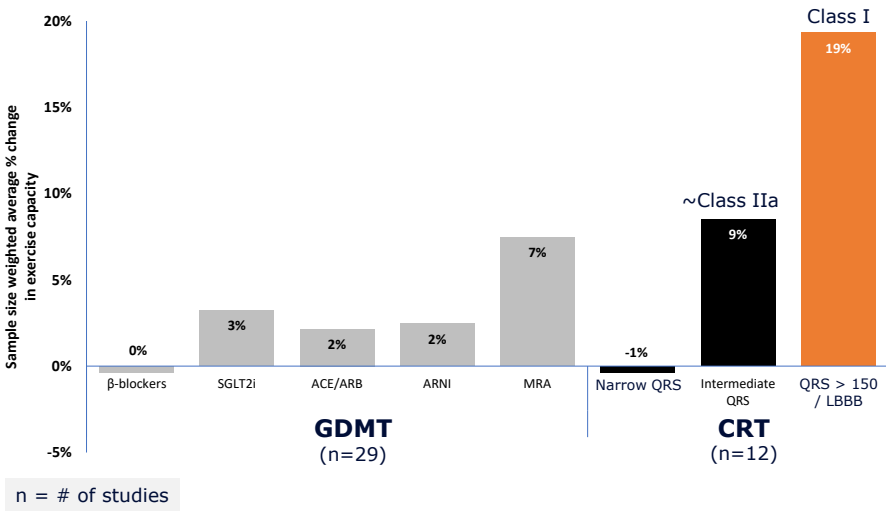


48

1. McMurray JJV et al. N Engl J Med 2019;381:1995-2008; 2. Packer M et al. N Engl J Med 2020;383:1413-24; 3. McMurray JJV et al. N Engl J Med 2014;371:993-1004; 4. Butler J et al, Butler J et al. J Am Coll Cardiol HF. 2022 Sep, 10 (9) 651–661

48

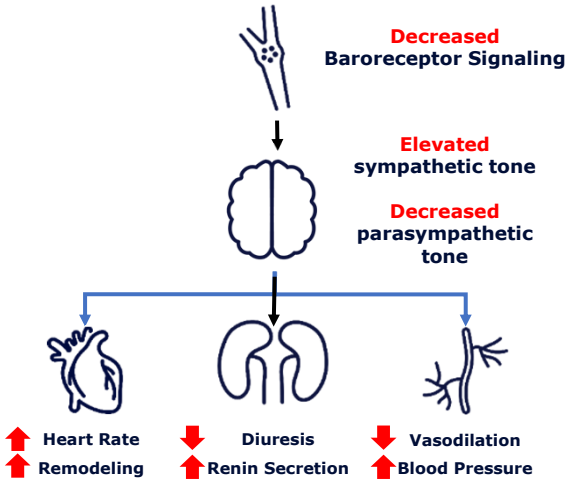
GDMT produces modest improvements in exercise capacity



49 Adapted from Lewis G et al, Developments in Exercise Capacity Assessment in Heart Failure Clinical Trials and the Rationale for the Design of METEORIC-HF. Circ Heart Fail. 2022 May; 15(5):510-524

49

Autonomic nervous system in heart failure



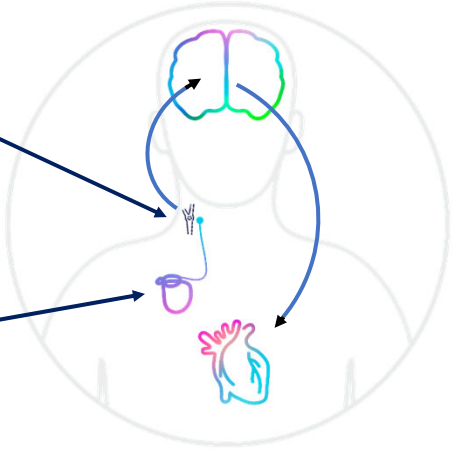
50 1. Creager MA, Creager SJ. J Am Coll Cardiol. 1994;23(2):401-5

50

Baroreceptor activation therapy (BAT) elements

Designed to deliver electrical stimulation to carotid baroreceptors to increase baroreceptor signaling

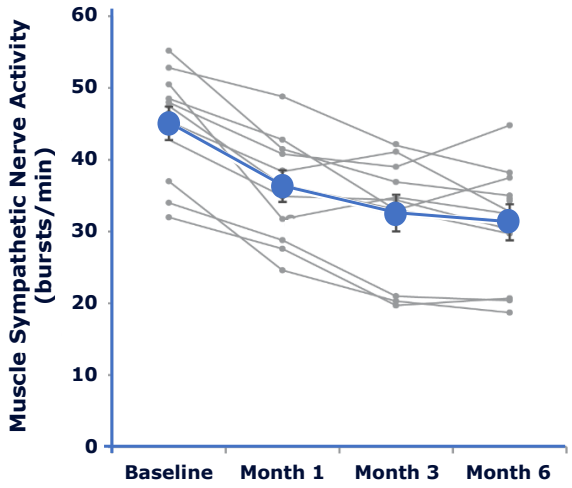
Implantable Pulse Generator (IPG) & Carotid Sinus Lead

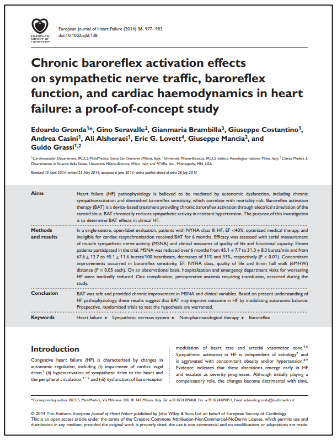


51

51

BAT decreases sympathetic tone[1]





Chronic baroreflex activation effects on sympathetic nerve traffic, baroreflex function, and cardiac haemodynamics in heart failure: a proof-of-concept study

Edoardo Gronda[1*], Gino Seravalle[2], Gianmaria Brambilla[2], Giuseppe Costantino[1], Andrea Casini[1], Ali Alsheraei[1], Eric G. Lovett[4], Giuseppe Mancia[2], and Guido Grassi[1,3]

Study Details
- N = 11 patients
- Single center
- NYHA III , EF < 40%
- GDMT
- Barostim delivered for 6m

52

1. Gronda, E, et al. European Journal of Heart Failure 16.9 (2014): 977-983

52

BeAT-HF Inclusion/Exclusion Criteria

Key Inclusion/Exclusion Criteria

- NYHA Functional Class III
- Left ventricular ejection fraction ≤35%
- Six-minute hall walk distance: 150-400m
- Elevated NT-proBNP or previous HF hospitalization
- Stable optimal medical therapy ≥4 weeks
- CRT-eligible subjects are excluded

- No restriction on AF, QRS width or concomitant devices

53

1. Zile MR, et al. J Am Coll Cardiol. 2020;76(1):1-13

53

BeAT-HF baseline demographics

	Barostim (n=163)	Control (n=160)
Demographics		
Age at Screening (years)	63 ± 11	63 ± 10
Gender (Female)	28 (17.2%)	35 (21.9%)
Race (Caucasian)	120 (73.6%)	116 (72.5%)
Heart failure and physical status		
SBP (mmHg)	120 ± 16	121 ± 16
DBP (mmHg)	74 ± 10	73 ± 10
HR (bpm)	75 ± 10	75 ± 11
BMI (kg/m2)	31 ± 5	31 ± 5
eGFR	62.5 ± 16.3	61.1 ± 18.9
NYHA: Class III	155 (95.1%)	151 (94.4%)
LVEF (%)	27 ± 6	28 ± 6
6 Minute Walk (m)	314 ± 66	300 ± 71
QOL	53 ± 24	51 ± 24
NT-proBNP (pg/mL)	736 (474, 1057)	704 (442, 1044)
LBBB	4 (2.5%)	2 (1.3%)
>=1 HF Hospitalization	66 (40.5%)	79 (49.4%)
Number of HF Hospitalizations	0.6 ± 0.9	0.7 ± 0.8

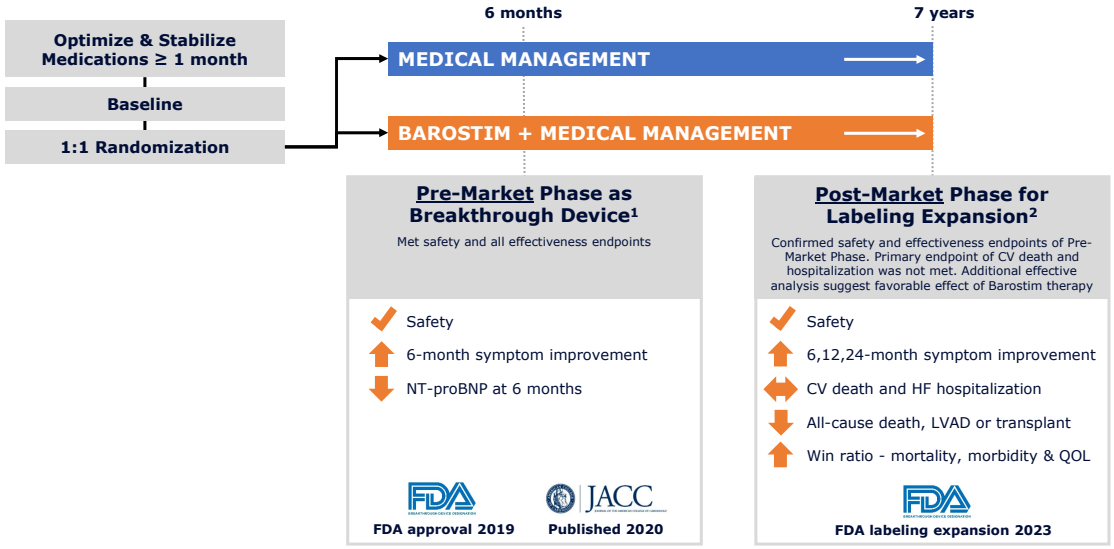
	Barostim (n=163)	Control (n=160)
Co-Morbidities		
Coronary Artery Disease	104 (63.8%)	107 (66.9%)
Atrial Fibrillation	53 (32.5%)	66 (41.3%)
Stroke or TIA	29 (17.8%)	37 (23.1%)
Chronic Kidney Disease	45 (27.6%)	43 (26.9%)
Type II Diabetes	74 (45.4%)	80 (50.0%)
Heart failure treatment		
Number of Meds	4.0 ± 1.3	4.1 ± 1.5
ACE-I / ARB / ARNI	143 (88%)	129 (81%)
ARNI	57 (35%)	43 (27%)
Beta-Blocker	152 (93%)	147 (92%)
MRA	74 (45%)	64 (40%)
Diuretic	138 (85%)	139 (87%)
Ivabradine	4 (2.5%)	9 (5.6%)
ICD	125 (77%)	127 (79%)

54

1. Instructions for Use 900133-001 Rev. D available at www.cvrx.com/ifu

54

BeAT-HF two-phase trial design



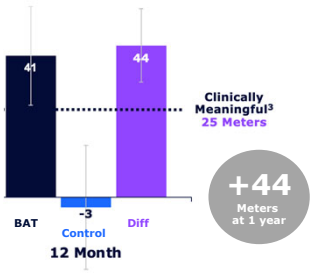
55

1. Zile MR, et al. J Am Coll Cardiol. 2020;76(1):1-13 2. Instructions for Use 900133-001 Rev. D available at www.cvrx.com/ifu

55

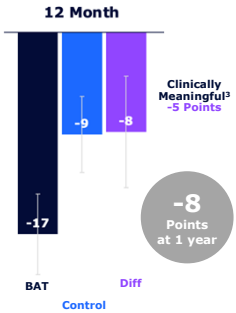
BeAT-HF symptom improvement at 12 months[1]

Exercise capacity (6MHW)



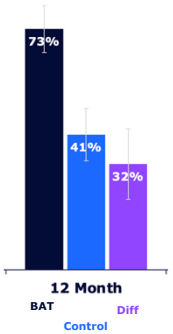
CRT trial results at 6 months		
CONTAK CD³	NYHA III or IV LVEF ≤ 35% QRS > 120ms	39
MIRACLE⁴	NYHA III or IV LVEF ≤ 35% QRS > 130ms	29

Quality of life (MLWHF)



CRT trial results at 6 months		
CONTAK CD³	NYHA III or IV LVEF ≤ 35% QRS > 120ms	-11
MIRACLE⁴	NYHA III or IV LVEF ≤ 35% QRS > 130ms	-9

NYHA class

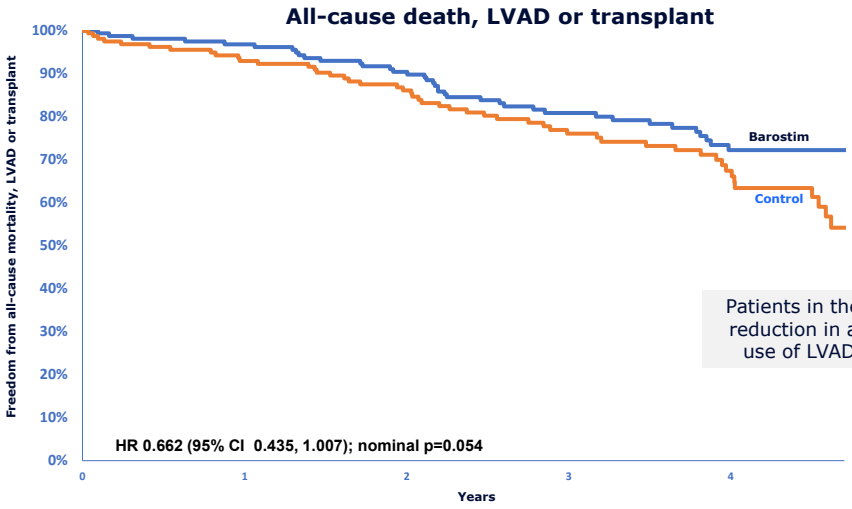


CRT trial results at 6 months		
CONTAK CD³	NYHA III or IV LVEF ≤ 35% QRS > 120ms	20%
MIRACLE⁴	NYHA III LVEF ≤ 35% QRS > 130ms	30%

*Data from different studies and different patient populations may not be directly comparable
1. Instructions for Use 900133-001 Rev. D available at www.cvrx.com/ifu. 2. Zile M, Presented at THT 2023, March 21, 2023. 3. Gremeaux V, et al. Arch Phys Med Rehabil. 2011;92(4):611
4. Higgins SL, et al. J Am Coll Cardiol 2003;42:1454 –1459. 5. Abraham WT, et al. N Engl J Med 2002;346:1845–1853.

56

Reduction in all-cause death, LVAD or transplant



-34%
Relative reduction

Patients in the BAT arm had a 34% reduction in all-cause death or the use of LVAD or heart transplant

57

1. Instructions for Use 900133-001 Rev. D available at www.cvrx.com/ifu & Zile M, Presented at THT 2023, March 21, 2023

BeAT-HF safety

MANCE-Free Rate[1]

97%
MANCE-Free Rate

6-month MANCE (System or Procedure-Related)[1]

Event	Barostim Subjects (N=159) Number of Events	Number of Subjects	Event Rate
CV Death	0	0	0.0%
Stroke	1	1	0.6%
Cardiac Arrest	0	0	0.0%
Acute MI	0	0	0.0%
Acute Decompensated HF	1	1	0.6%
Hypertensive Crisis	0	0	0.0%
Severe Complication of HF Treatment	0	0	0.0%
Systemic and Pulmonary Thromboembolism	0	0	0.0%
Infection Requiring Explant	2	2	1.3%
Cranial Nerve Damage	0	0	0.0%
Non-Elective Major Restorative Procedures	1	1	0.6%
Total	**5**	**5**	**3.1%**

58

1. Instructions for Use 900133-001 Rev. D available at www.cvrx.com/ifu,
MANCE - Major Adverse Neurological and Cardiovascular Events includes all events that occur within 6 months of implant

BeAT-HF: Serious cardiovascular events at 6 months

Potential Reduction in Serious Cardiovascular Events[1]

Cardiovascular Event	Barostim (n=125)		Control (n=134)		Relative Reduction
	Number of Events	Event Rate*	Number of Events	Event Rate*	
Cardiac Arrhythmias/ Cardiac Arrests	8	0.054	18	0.109	50%
MI/Angina	5	0.034	10	0.060	44%
Hypotension/ Syncope	2	0.014	6	0.036	63%
Total	**15**	**0.101**	**34**	**0.206**	**51%**

* Events per patient-year of follow-up

p-value=0.023
Not a powered endpoint

59 1. Zile MR, et al. J Am Coll Cardiol 2020;76:1-13; 2. Zile MR, et al. J Am Coll Cardiol 2020; Supplemental Appendix Table 13
MANCE - Major Adverse Neurological and Cardiovascular Events includes all events that occur within 6 months of implant

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Sample BAT Titration Schedule

Titration over 2-3 months →

	@ Implant	Week 2	Week 4	Week 6	Week 8
Typical device amplitude	1mA	2mA	4mA	6mA	8mA
Drug titration	Δ Diuretic	Δ Diuretic	Δ Diuretic	Δ Diuretic	Δ Diuretic ± NH Blockade
Assessment	-	-	-	-	6MHW NT-proBNP

60 Device and drug titration is physician-directed

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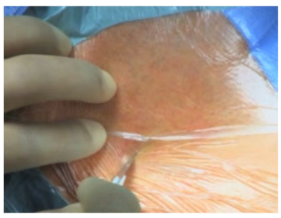
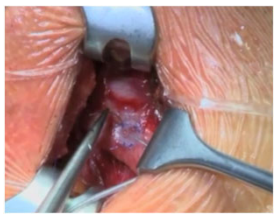
BAT Implant

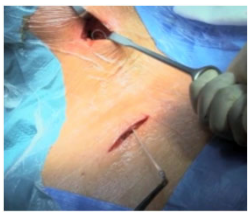
Small Incision in Neck



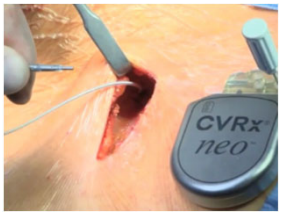
Electrode sutured to Carotid Artery



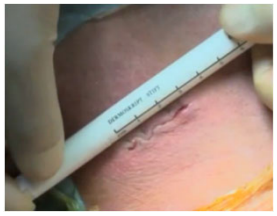
Lead tunneled to pectoral pocket



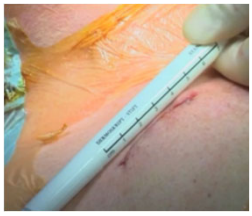
Lead connected to device and placed in pocket



Incision in neck closed



Pocket incision closed



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MHI Experience To Date

- 4 implants, another ~3 approved and pending
- Must have proBNP <1600
- High rate of payors refusing coverage
- I want to acknowledge Dr. Haglund for spearheading, Dr. Jim for implanting, and HF nurses (Emily Bernstein RN and Ruwayda Mohamed RN) for extensive efforts to organize process and program and Stephanie Garrison for PA support

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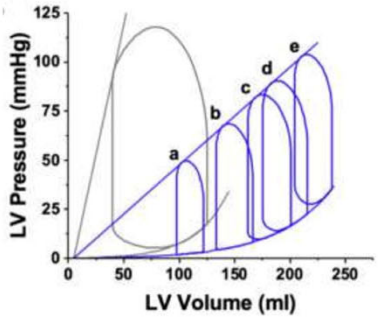
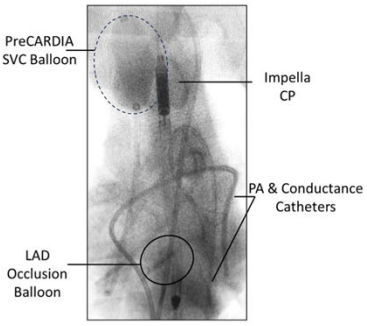
MCS: Innovative Technologies for Cardiogenic Shock

Optimizing MCS with **M**echanical **C**ardiac **P**reload **R**eduction

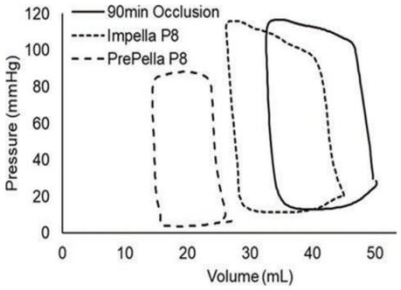
Reducing Preload



Impella + SVC Occlusion



Pre-Pella Unloading



CRF THT

Kapur and Sunagawa et al Circ HF 2024; Kapur and Burkhoff et al ASAIO 2024

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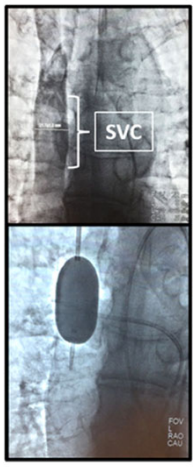
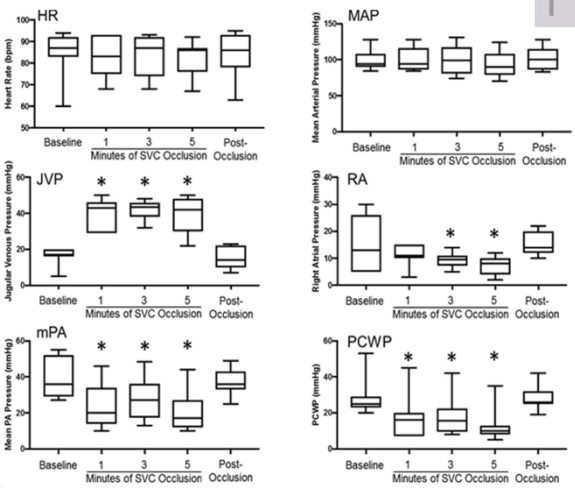
Intermittent SVC Occlusion

preCARDIA





Kapur NK et al, *Catheter Cardiovasc Interv* 2019

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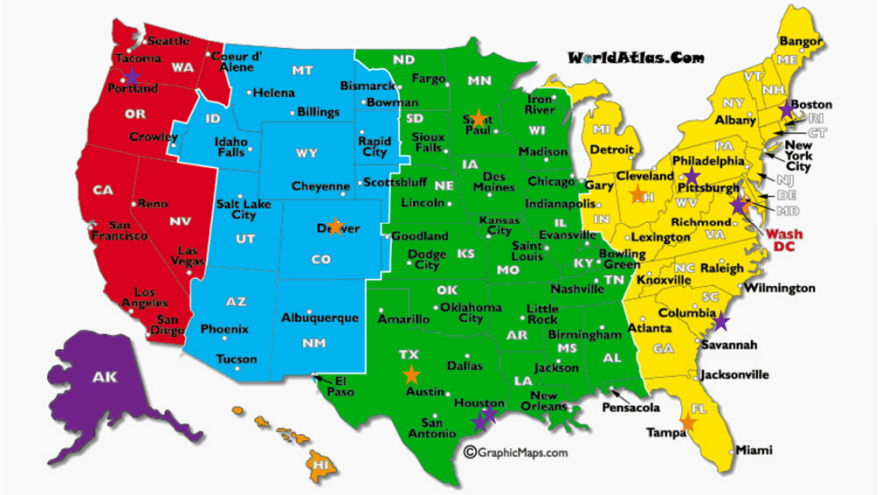
preCARDIA Site Locations

Time Zones: Red = Pacific; Blue = Mountain; Green = Central; Yellow = Eastern



Current Sites: ★

1. Tufts – **Michael Kiernan**; Boston, MA
2. MUSC – **Ryan Tedford**; Charleston, SC
3. Houston Methodist – **Rayan Yousefzai**; Houston, TX
4. Providence – **Jacob Abraham**; Portland, OR
5. Allegheny General Hosp. – **Manreet Kanwar**; Pittsburg, PA
6. Baylor Scott & White – **Jamie Hernandez**; Temple, TX
7. Inova – **Shashank Desai**; Falls Church, VA

Site in Start Up (completed SQV): ★

1. Medstar – **Farooq Sheikh**; Washington, D.C.
2. OhioHealth – **Anupam Basuray;** Columbus, OH
3. **MHI - David Miranda**
4. Baylor College of Medicine – **Ajith Nair**; Houston, TX
5. Tampa General Hospital – **Debbie Rinde-Hoffman and Iona Dumitru;** Tampa, FL
6. Colorado Heart and Vascular – **Nima Aghili**; Lakewood, CO

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SVC Occlusion in Subjects With Acute Decompensated Heart Failure (VENUS-HF)

ClinicalTrials.gov ID NCT03836079

Sponsor Abiomed Inc.

Outcome Measures

Change History	See all versions of this study
Primary (Current) ICMJE (Submitted: 2023-05-30)	• Freedom from Major Adverse Events through 90 days post-discharge. [Time Frame: 90 days post-discharge] ◦ MAE is defined as death, myocardial infarction, major thromboembolic event, vascular damage requiring surgical intervention, hemorrhagic stroke or prolongation of heart failure- related hospitalization attributable to the preCARDIA device or procedure.
Primary (Original) ICMJE (Submitted: 2019-02-07)	• Freedom from Major Adverse Events through 30 days. [Time Frame: 30 days] ◦ MAE is defined as death, myocardial infarction, major thromboembolic event, vascular damage requiring surgical intervention, hemorrhagic stroke or prolongation of heart failure- related hospitalization attributable to the preCARDIA device or procedure.

Inclusion Criteria:

- NYHA Class III-IV heart failure
- Subjects with inadequate diuresis
- Stage C-D systolic heart failure

Exclusion Criteria:

- Active myocardial ischemia or acute coronary syndrome (ACS)
- Severe aortic or mitral valve insufficiency
- Severe peripheral vascular disease

Site Initiation Visit TOMORROW!

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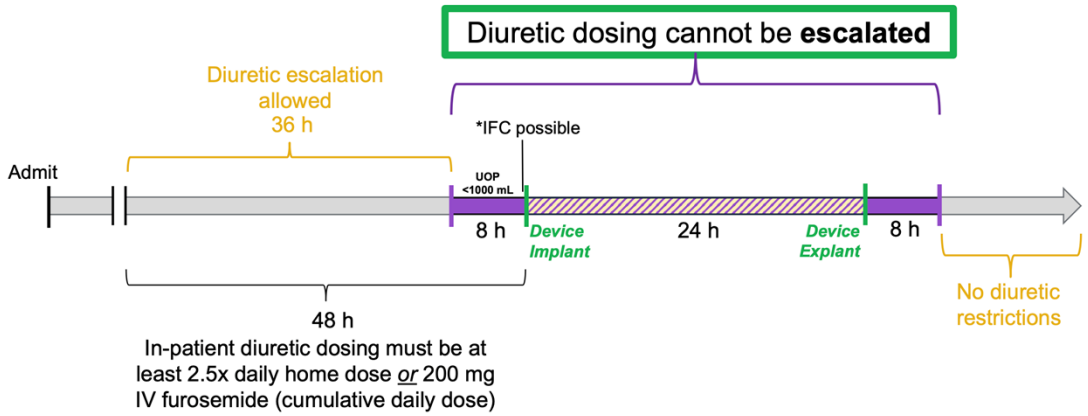
DIURETIC PROTOCOLIZATION
(IDEALIZED FLOW)



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Thank you!

Allina Health MINNEAPOLIS HEART INSTITUTE

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