北京大学第一医院心内科

Percutaneous Ventricular Restoration （PVR）

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Dept. of Cardiology
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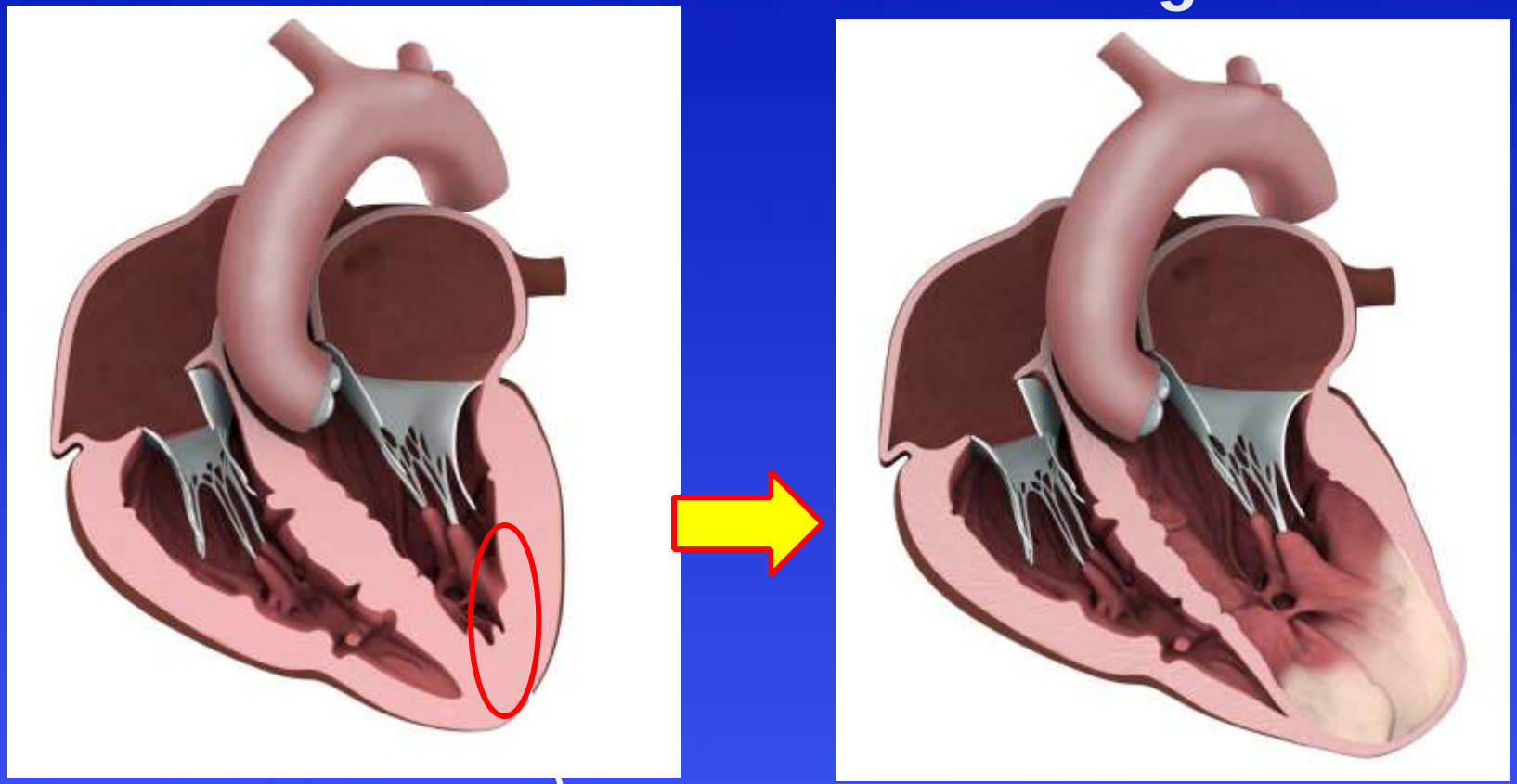
The mechanism of heart failure after myocardial infarction---Remodeling



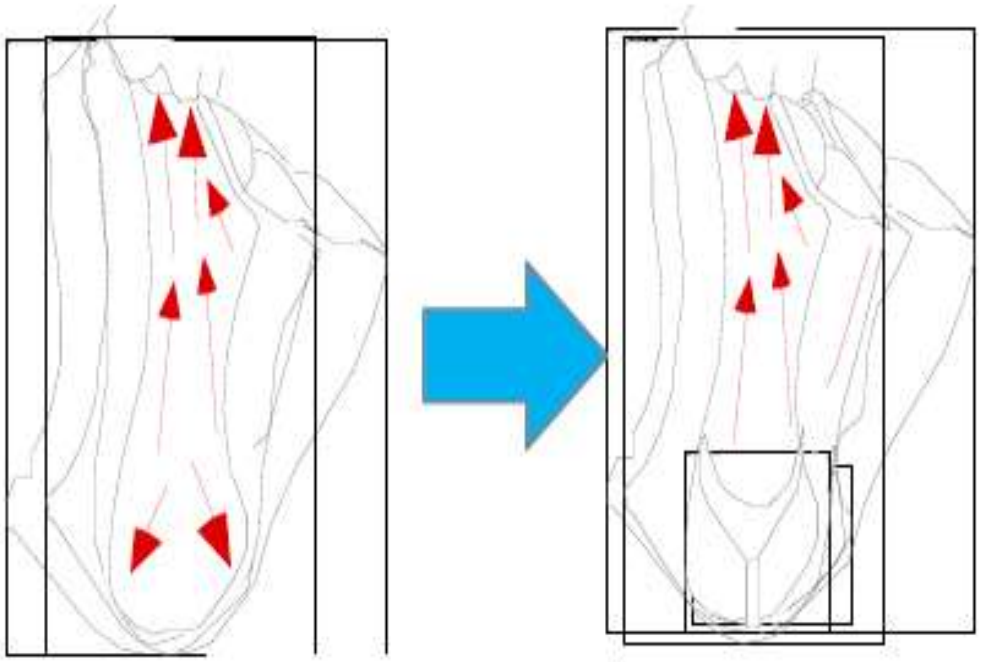
Infarct area which results in a scarred / thin wall initiating **ventricular remodeling** and **dilation.**

Percutaneous Ventricular Restoration

Treatment Goal

Improve heart function by:

- LV Volumes Reduction
- LVED Pressure Reduction
- Restoring LV Conical Shape
- Preserving Torsional Contraction
- Increase LV Apical Ejection
- Minimize risk of scar-related ventricular arrhythmias



Comparison of PVR and SVR

	Parachute®	SVR
Routine Cath Lab Procedure	++	
Need for Conjunctive CABG		++
Targets Cause of Remodeling (scar)	++	++
Reduces LV Volume	++	++
Restores LV Conical Shape	++	+
Reduces LV Wall Stress	++	++
Improves LV Compliance and Diastolic Filling	++	

Current main indications and contraindications

Main indications

- Age >18
- Old anterior MI (>2months)
- LVEF<40%,>15%
- Receiving appropriate medical treatment for heart failure at least 3 months according to current guidelines
- NYHA class II—IV

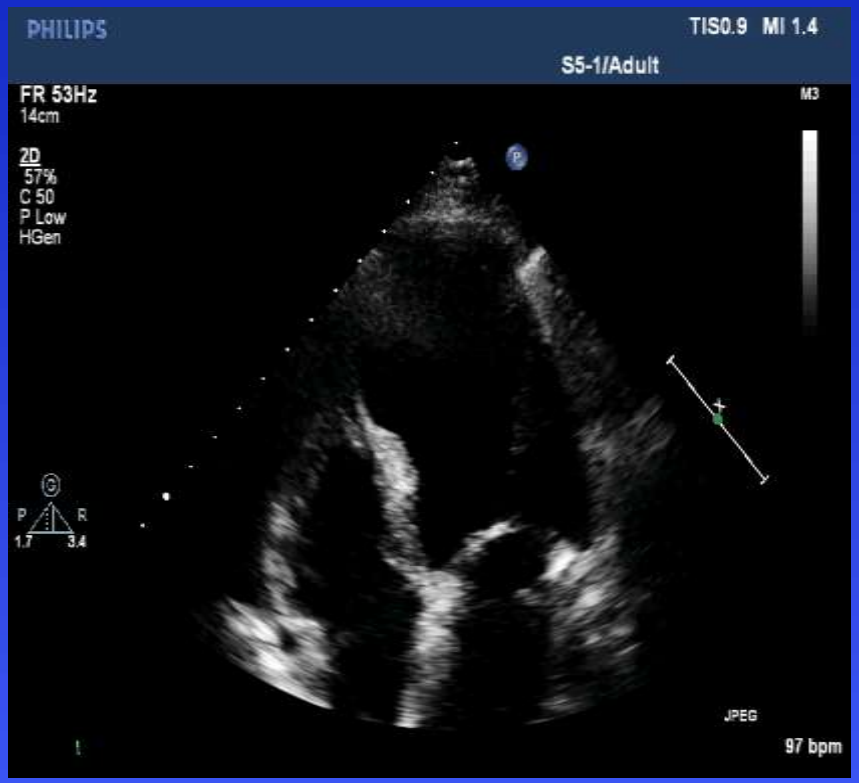
Maint contraindications

- Acute MI within 60 days
- Revascularization therapy (within 60 days)
- CRT within 60 days
- Significant valvular disease
- Other diseases affecting operation

Case Screening

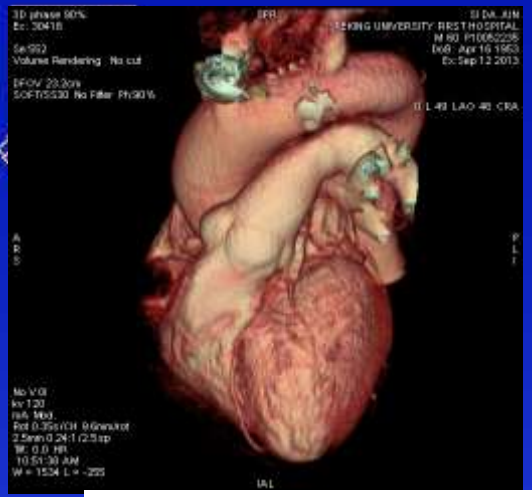
- Clinical: old anterior MI with anterior wall dyskinesis or akinesis and LVEF decreased
- ECHO:TTE
- Heart CT or MRI: the most important

ECHO
core lab review



- Confirm wall motion state
- Presence of any anatomical structure which would interfere with deployment of the PARACHUTE （Such as thrombosis, psudo chordae tendinae）
- LVEF
- Valves condition

CT Scan-Preoperative



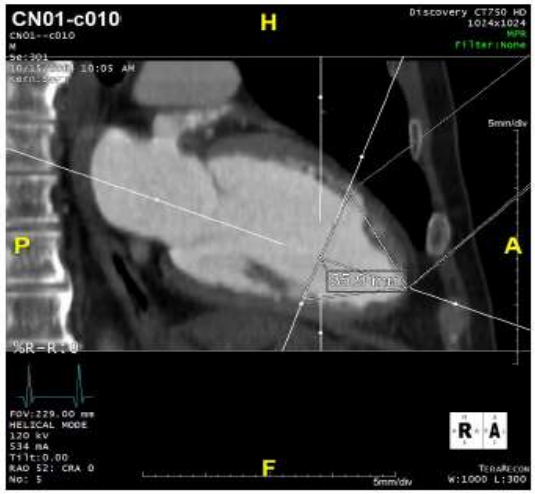
Core Lab Review

- Further confirm LV anatomy
- To determine the PARACHUTE size and guiding catheter/delivery system size
- To determine the release angle
- The most important

Parachute Commercial

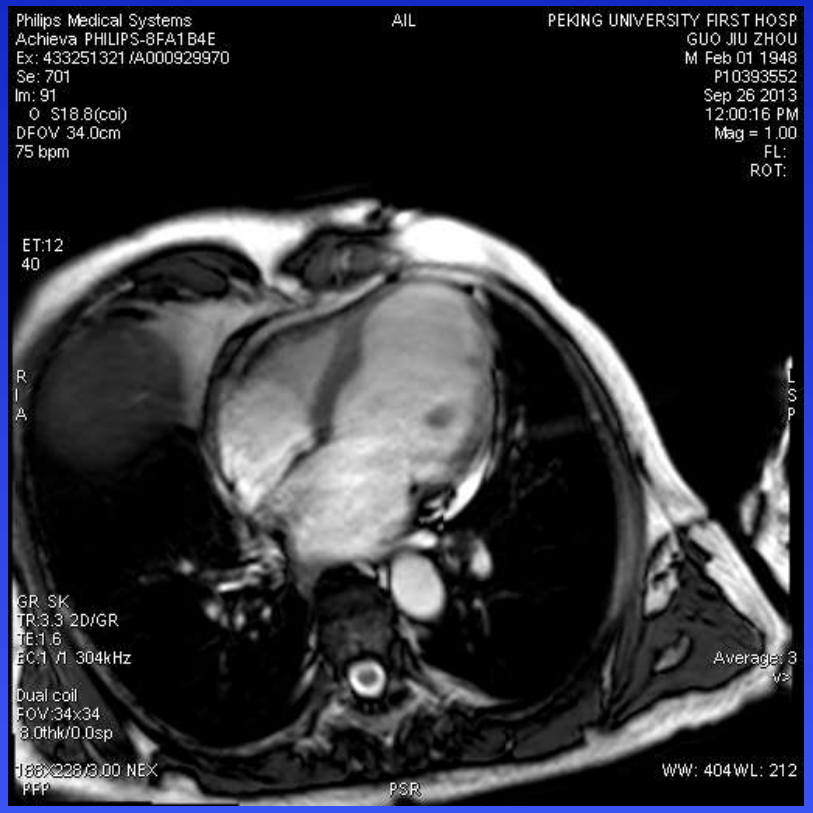
Patient Selection – CTA

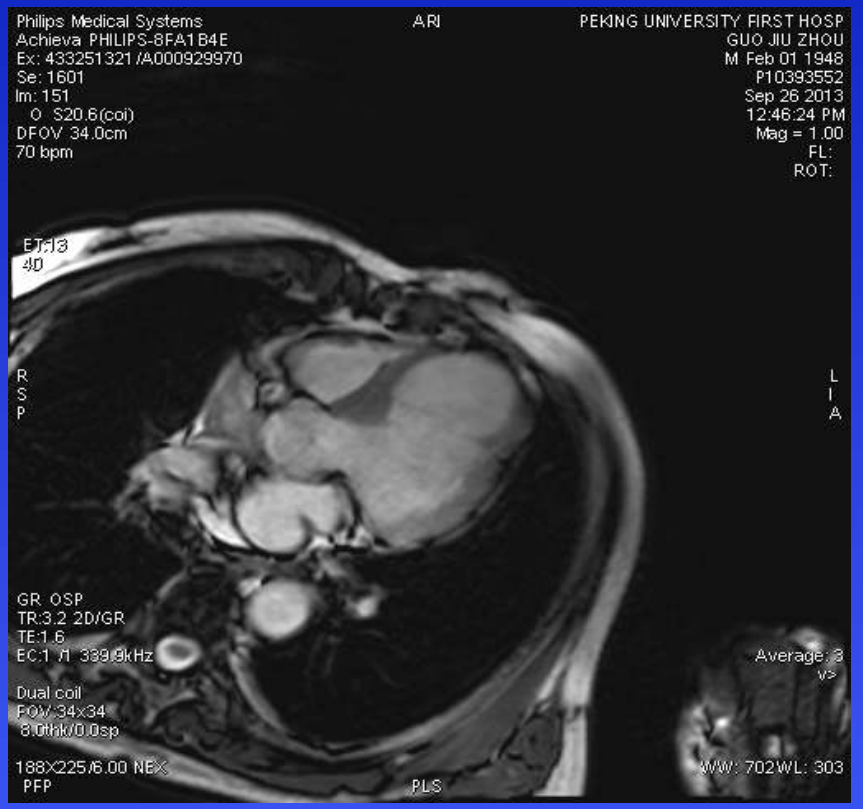
2.3 Other Measurements	
Maximum Diameter Shortening (%)	19
Diameter Shortening Based on Mean Diameters (%)	14
	If >40%, reject the case.
LV Ejection Fraction (%)	33
Best View: (RAO)	52



MR Scan -Preoperative

similar to CT

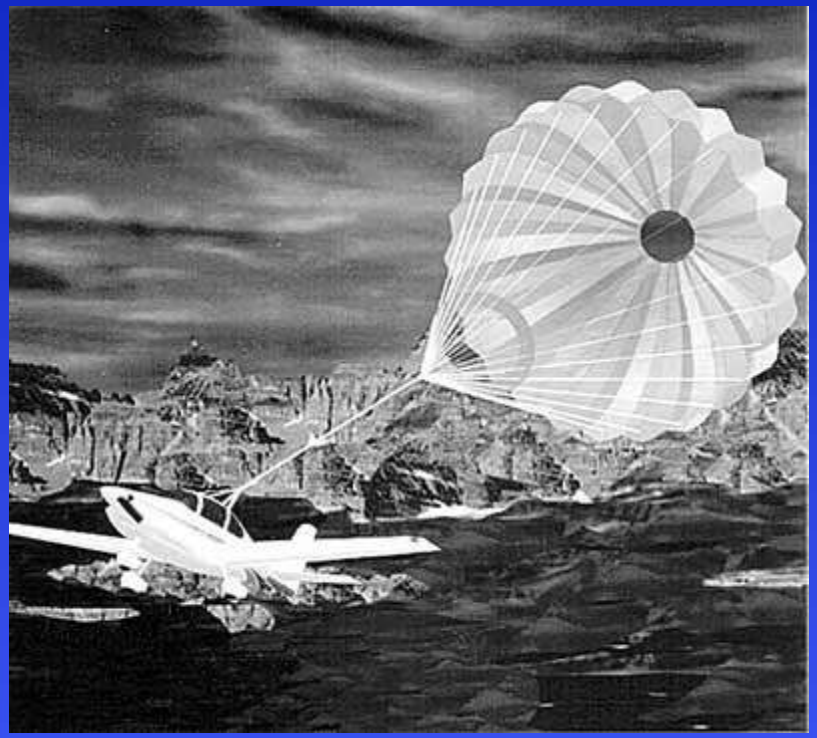




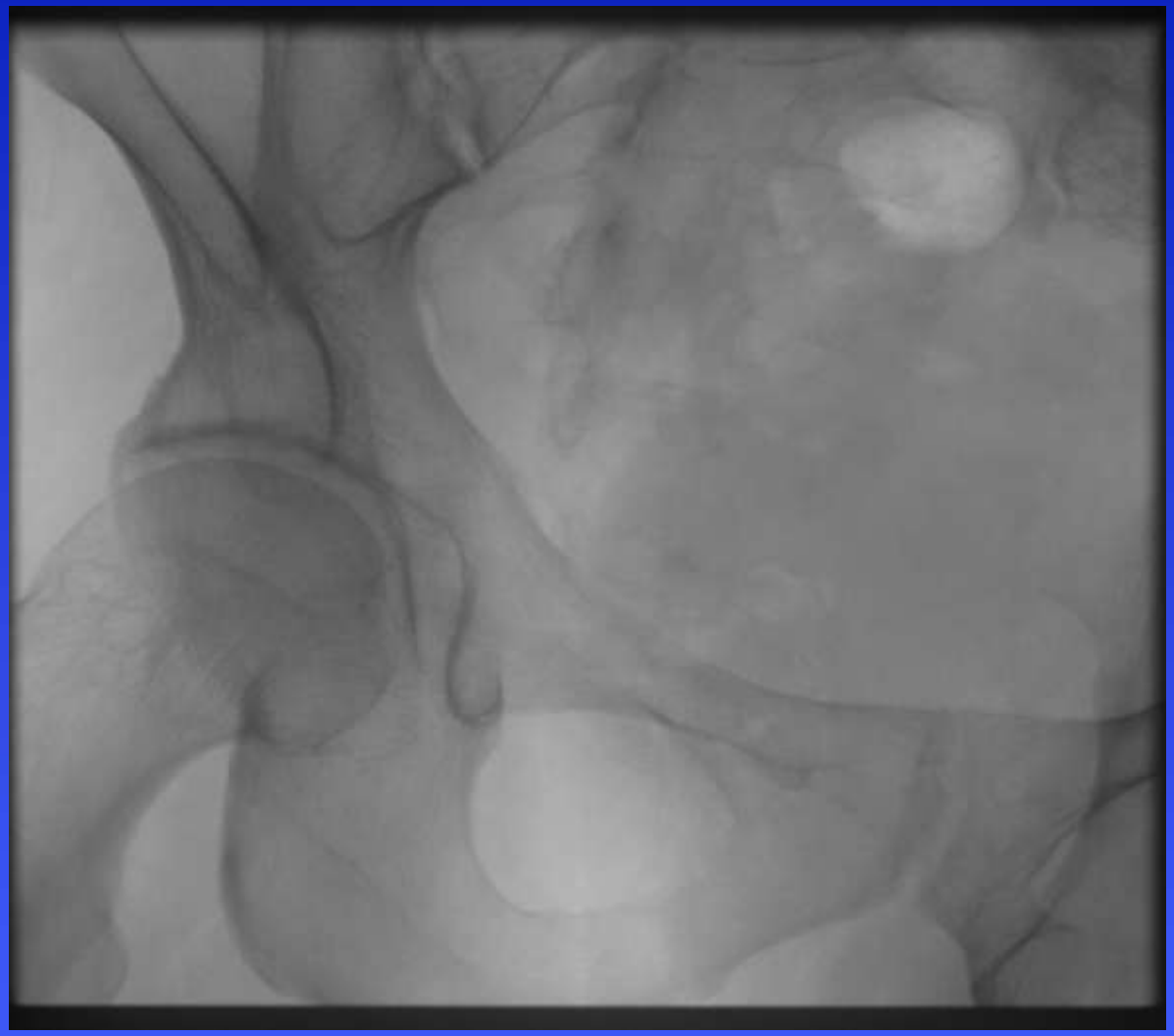
Operation Preparation

- Aspirin：325-300mg Qd for 4 days before the implantation or at least 3 hrs before implantation, then Low-dose aspirin (75-150mg Qd)
- Local anesthesia
- Intraoperative TTE
- Warfarin : give the first dose after 6-8 hrs of implantation , a minimum of 12 months is required

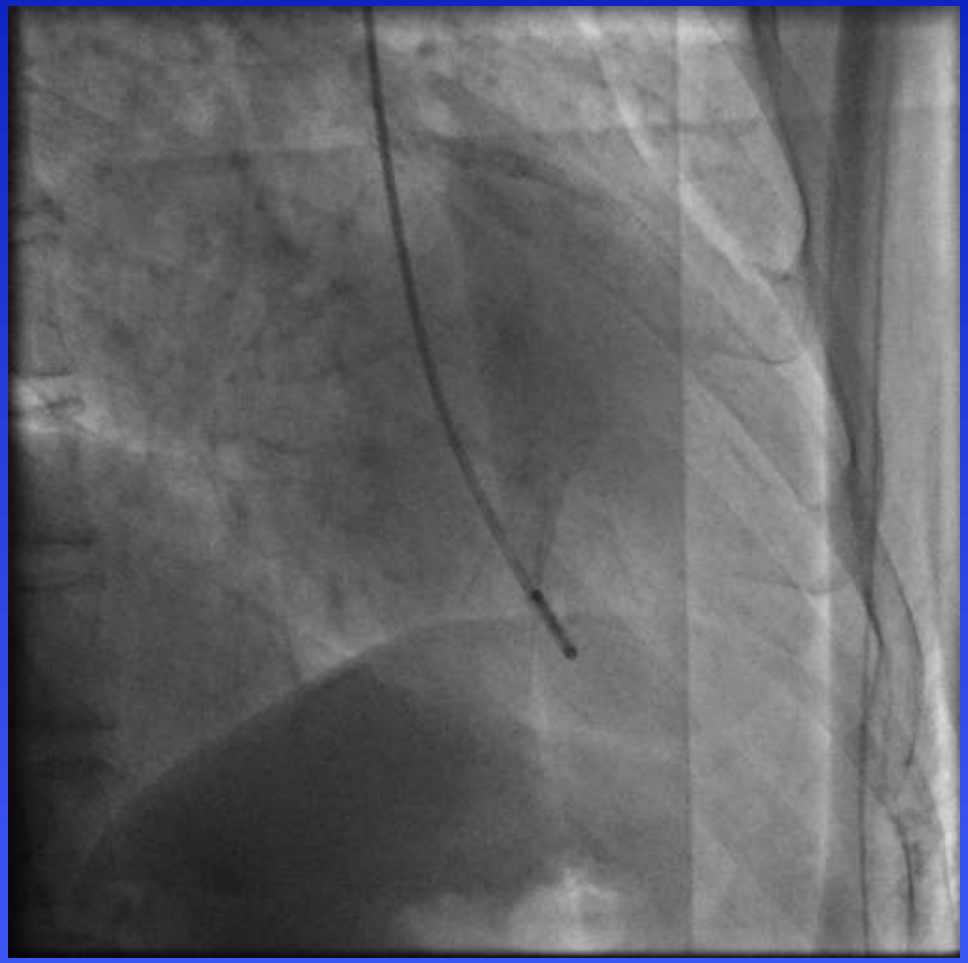
PVR Procedure



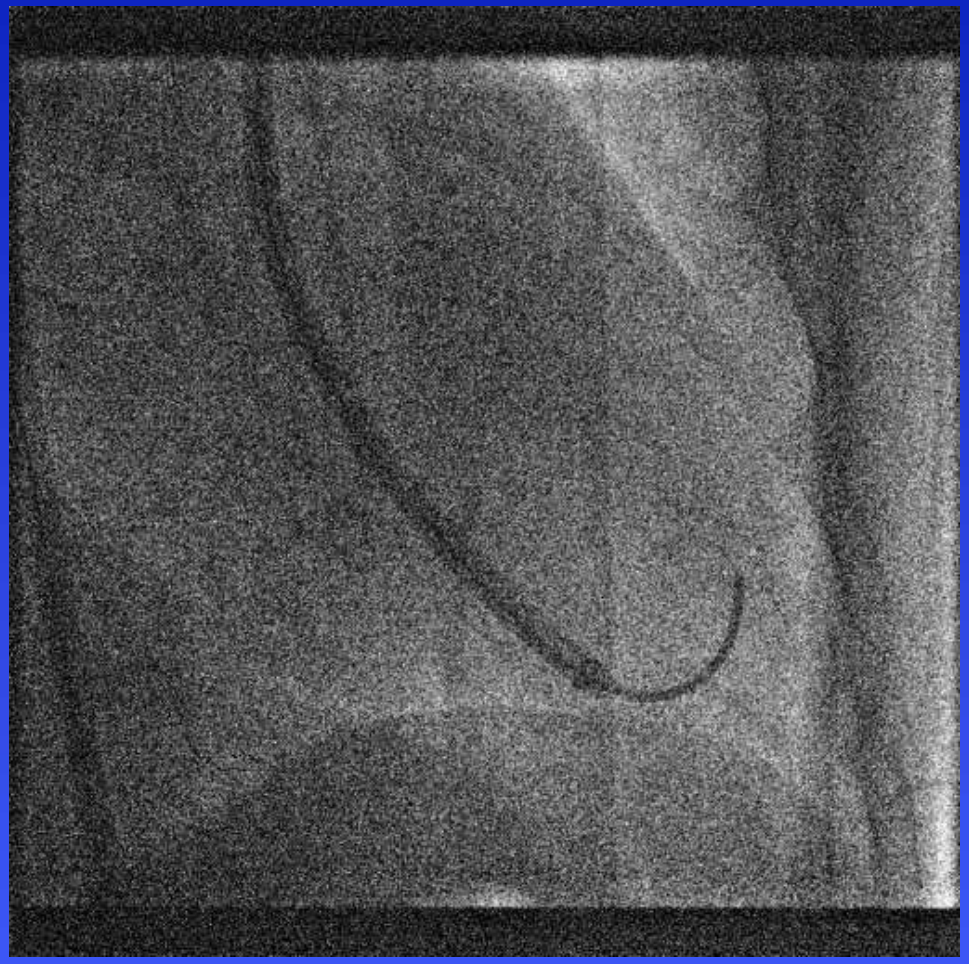
Femoral artery angiography



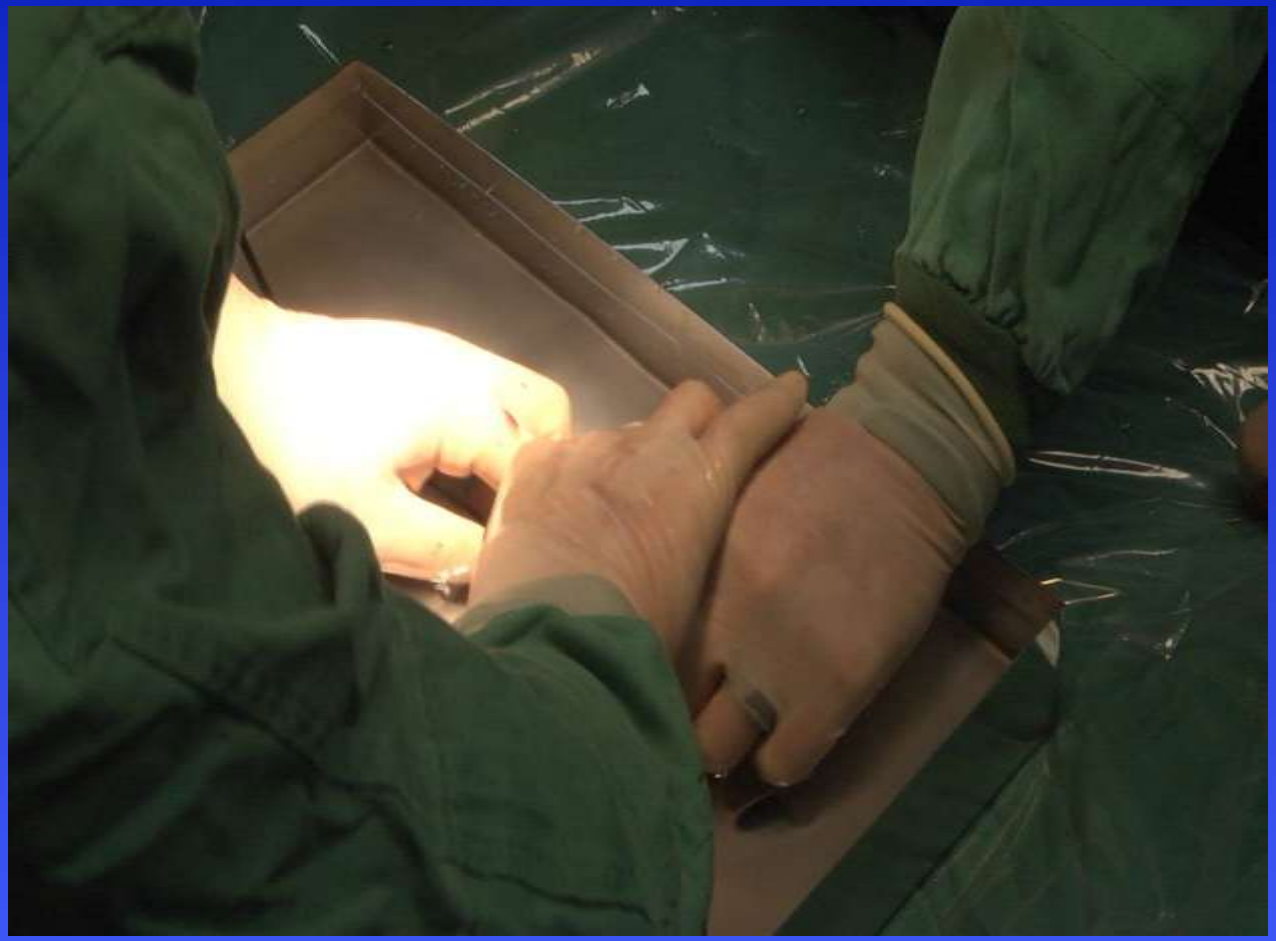
Left ventricular angiography
(RAO, angle by core lab)



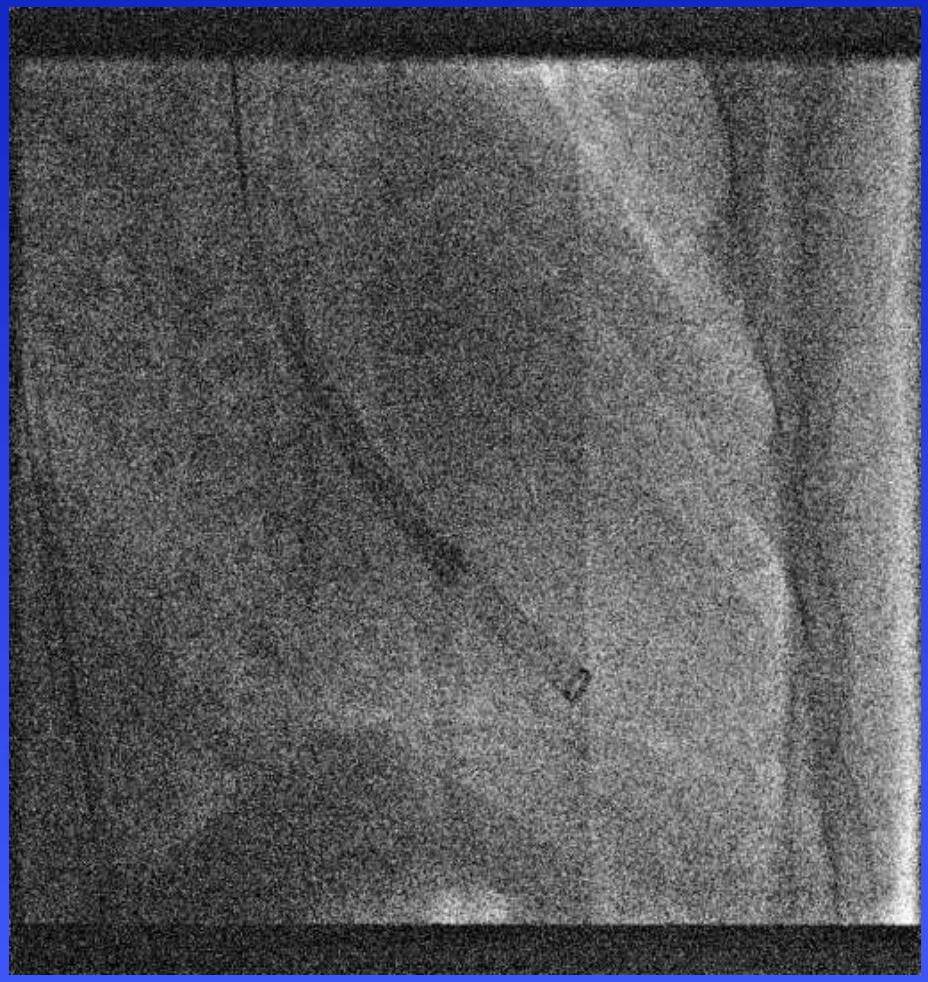
Place the Guide Catheter



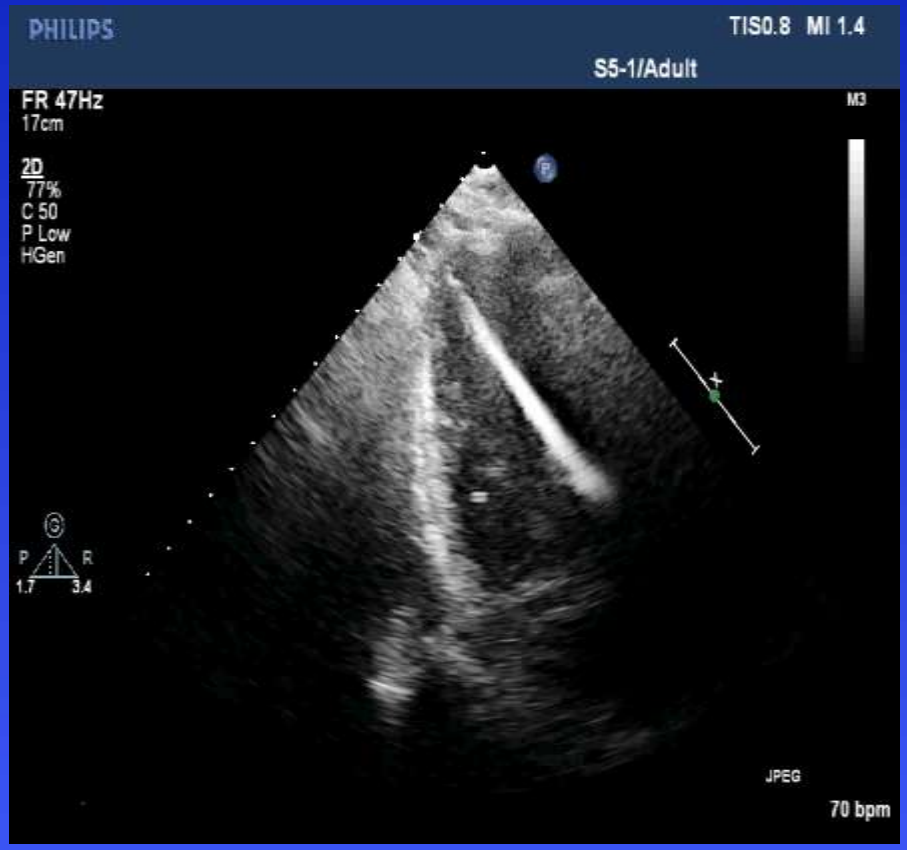
PARACHUTE is submerged in the saline container

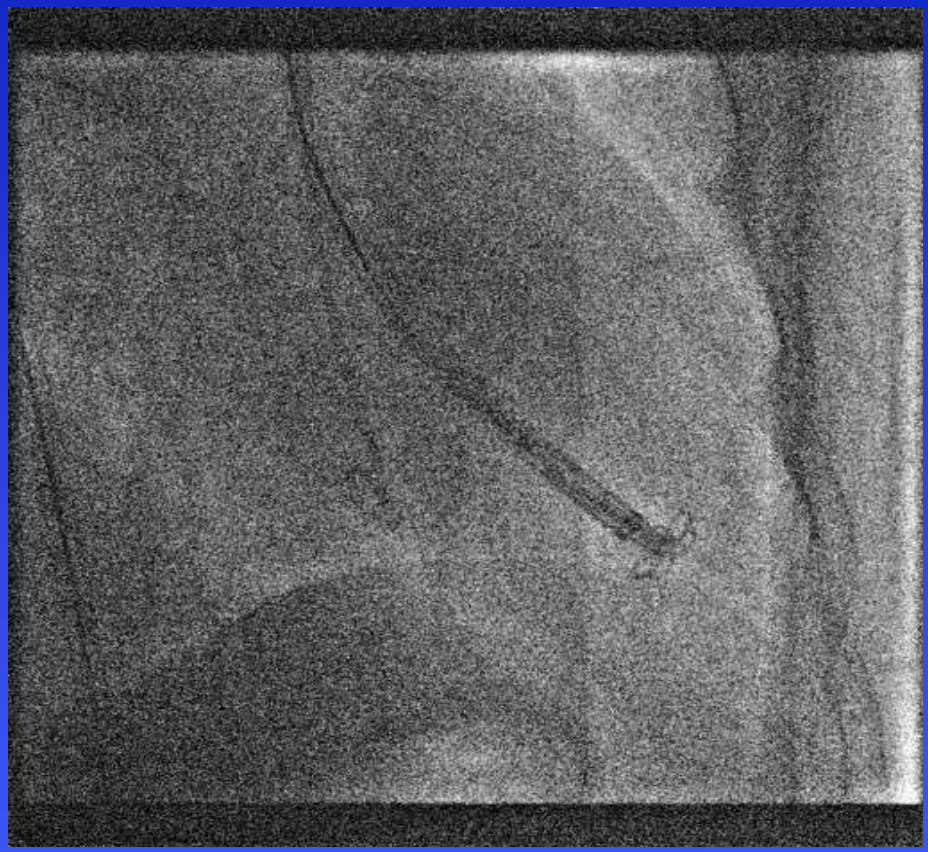


The PARACHUTE is placed to the apex by guide catheter and delivery system

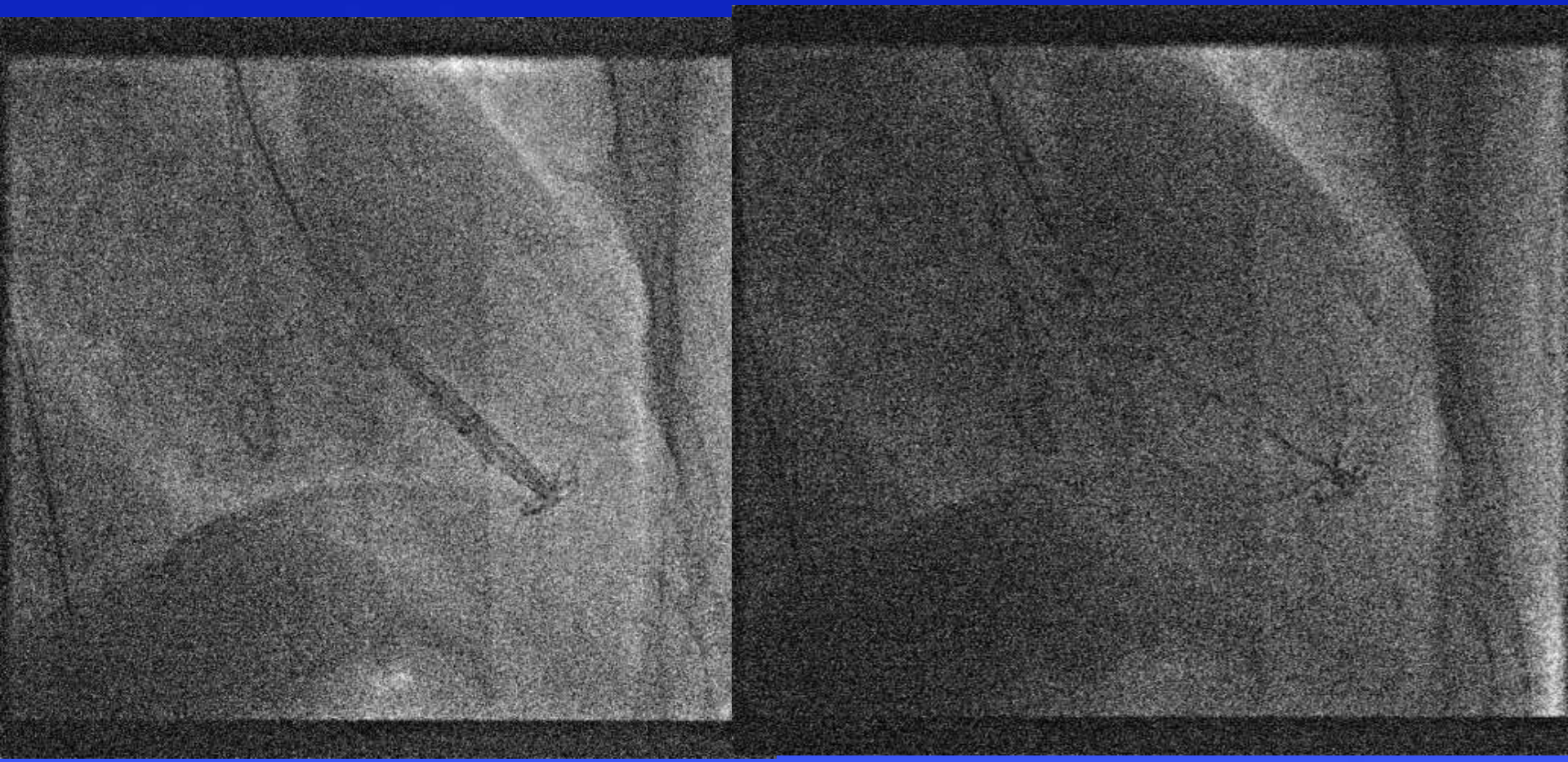


Confirm landing by Echo and LV angiography





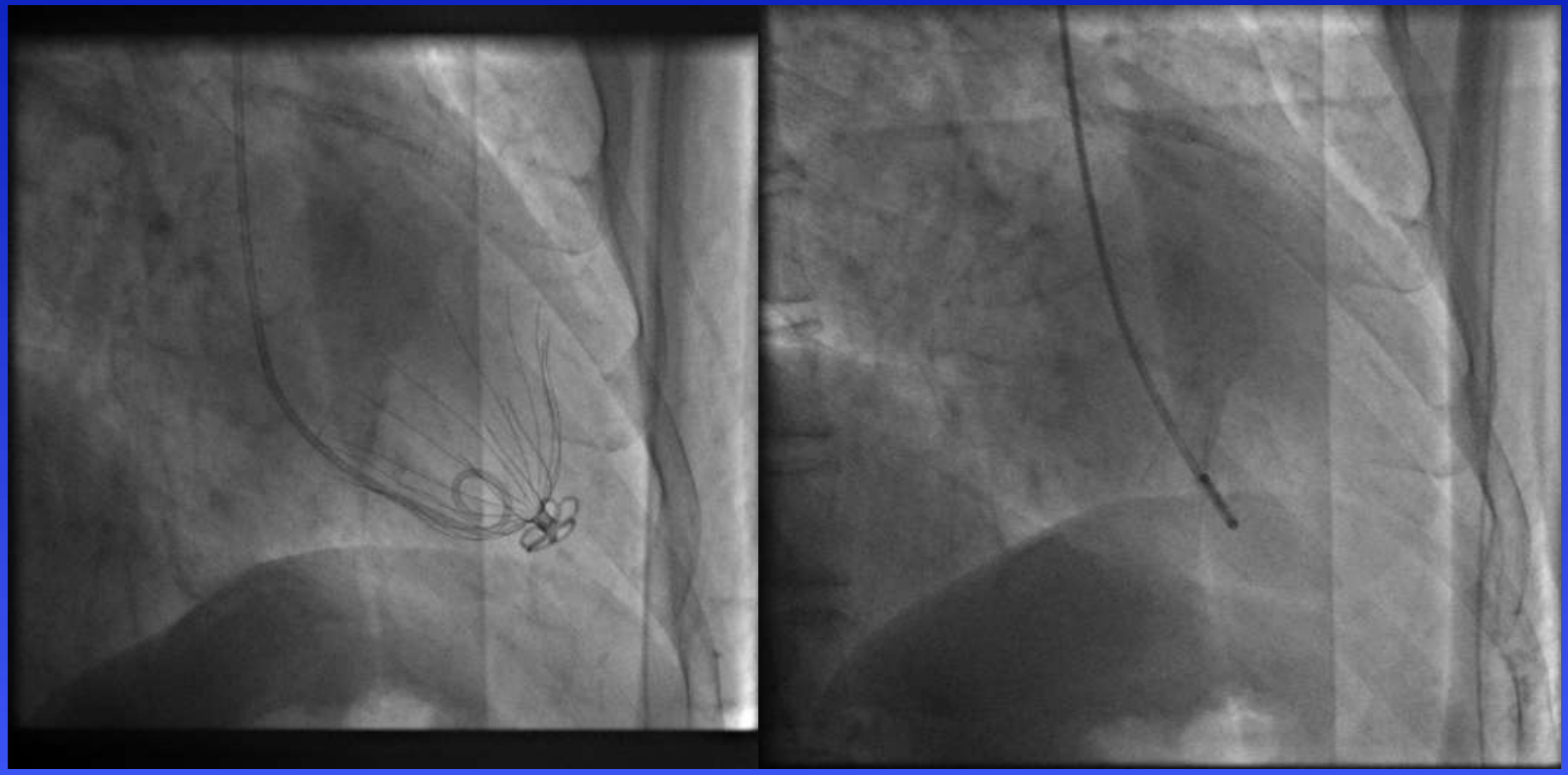
Release PARACHUTE



LV angiography

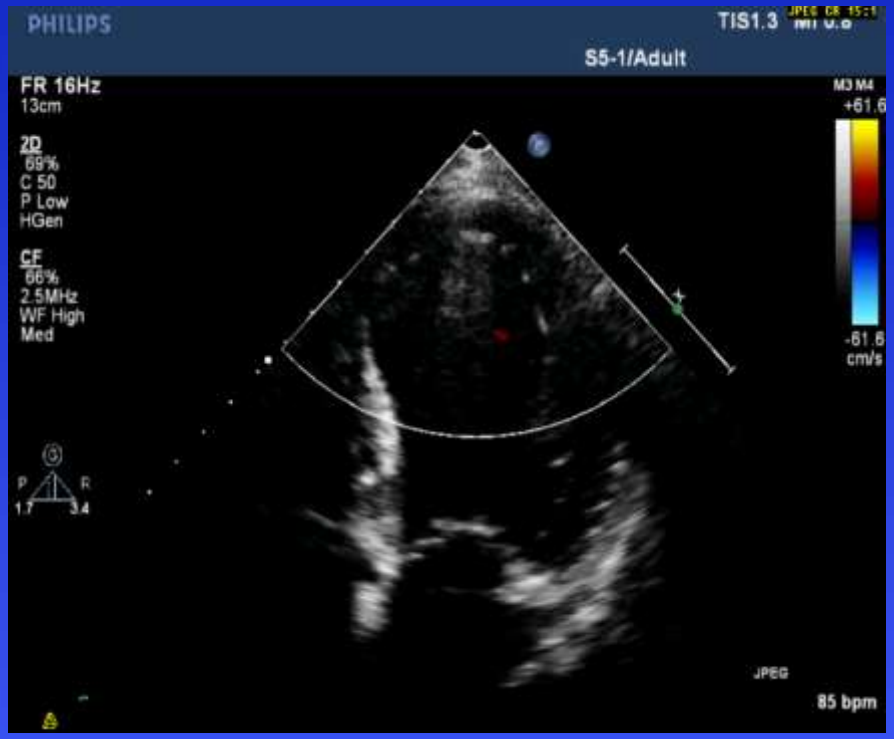
after

before



Follow-up
--- ECHO

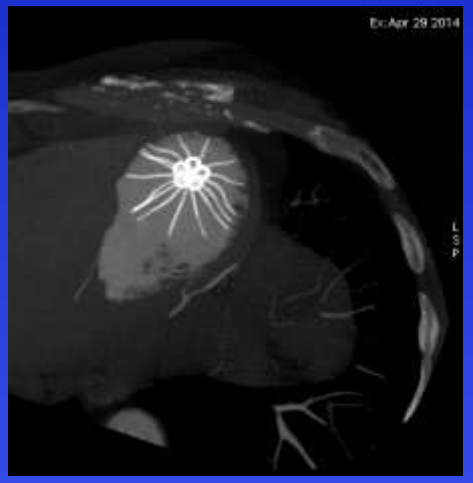
- The cardiac structure and function change after PVR
- Complications (thrombosis, migration)
- Endothelialization



6 months after the procedure, ultrasound showed blood flow signal emerged between device and apex, which indicates endothelialization process has not finished.

Follow-up
--- CT or MRI

- The anatomy change of the heart
- The PARACHUTE configuration
- Evaluation of cardiac function
- Complications
- Endothelialization



Percutaneous LV Restoration Therapy

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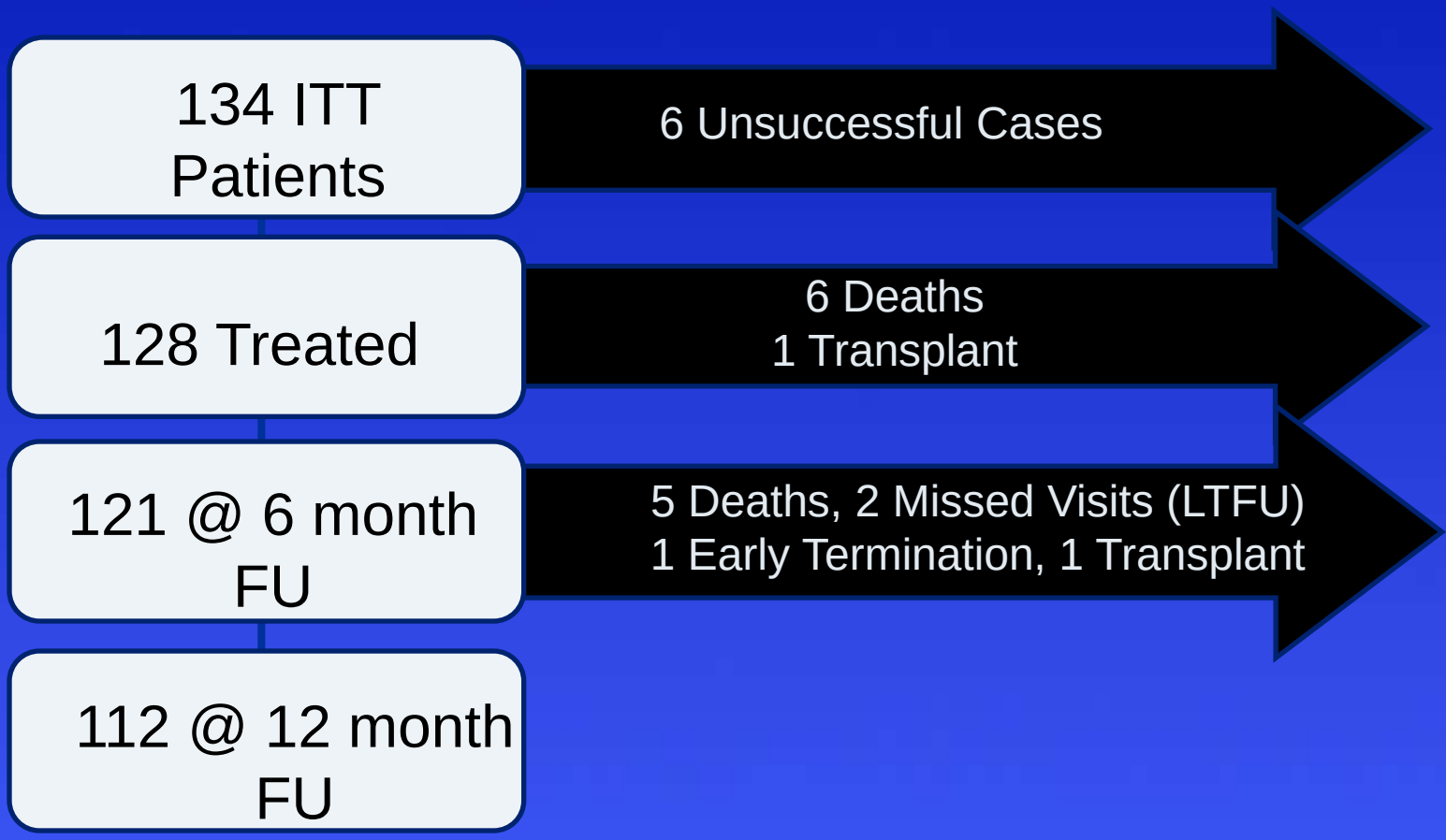
Director of the Cardiac Catheterization Laboratories and Interventional Research

Cardiovascular Institute of the South

Patient Disposition



Baseline Patient Profile, N=134

Demographics	
Age, years	61.2 ± 10.6
Male, %	111/134 (82.8%)
BMI	27.6 ± 3.9
Ischemic Heart Failure, %	100/100 (100%)
NYHA Class	
NYHA I (class III in the last 3M)	1/134 (0.7%)
NYHA II (class III in the last 3M)	55/134 (44.0%)
NYHA III	78/134 (58.2%)
6MWT, m	350.8 ± 109.9

Medical History	
Smoking History, %	95/128 (74.2%)
History of Hypertension, %	29/134 (68.7%)
History of Diabetes, %	52/134 (38.8%)
Prior ICD, %	58/100 (43.3%)
Prior CRT, %	23/134 (17.2%)
Prior PCI, %	103/134 (76.9%)
Prior CABG, %	21/134 (15.7%)
HF Hosp. 12M Before Enrlmt, %	37/118 (31.4%)

Cardiac Medications	
Aspirin, %	100/121 (82.6%)
Anticoagulant, %	41/123 (33.3%)
ACE Inhibitor, %	99/134 (73.9%)
ARB, %	27/134 (20.1%)
Beta Blocker, %	131/134 (97.8%)
Diuretic, %	116/134 (86.6%)
Optimal Medical Therapy[1], %	108/134 (80.6%)

[1]defined as beta blocker + diuretic + (ACE or ARB)

Hemodynamics	
Ejection Fraction, %	28.1 ± 7.6
LV EDVi, ml/m^2	121.8 ± 26.6
LA Vi, ml/m^2	42.1 ± 14.6
LV DD, cm	6.0 ± 0.9
EDP, mmHg	22.9 ± 22.7
Cardiac Index, L/min/m^2	2.4 ± 1.0

Procedure Data, N=134

Treatment Success, %	128/134 (95.5%)
LV Perforation, n	*2*
Device Size	
65mm, %	5/134 (3.7%)
75mm, %	53/134 (39.6%)
85mm, %	53/134 (39.6%)
95mm, %	23/134 (17.2%)
Duration, minutes	90.2 ± 42.5
Fluoroscopy Time, minutes	22.3 ± 27.9

Major Proc. Complications by VARC, %	11/134 (8.2%)
Access Site Bleeding / Haematoma, n	*4*
Aortic Valve Damage, n	*3*
LV Perforation, n	*2*
Mitral Function Damage, n	*1*
Bradycardia (pre-Parachute), n	*1*
Minor Proc. Complications by VARC, %	9/134 (6.7%)

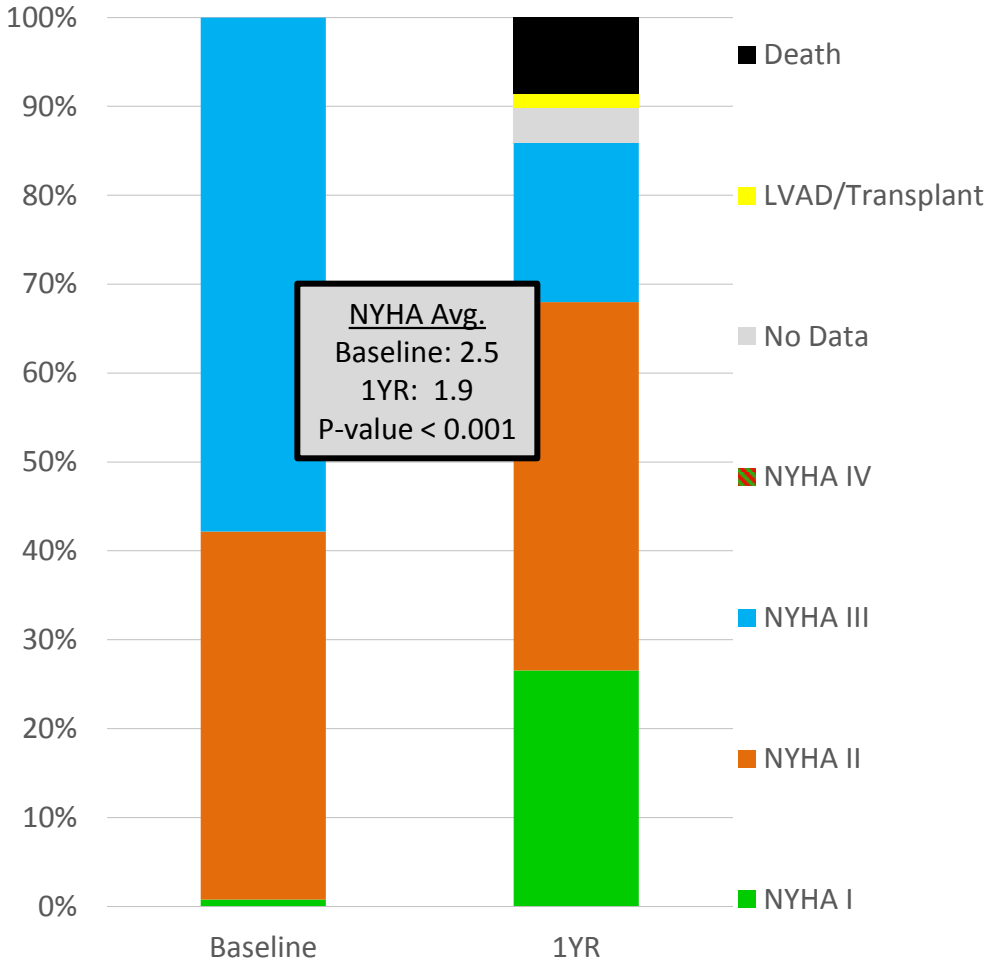
VARC definition citation: Leon et al: Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. EU Heart Journal (2011) 32, 205-217.

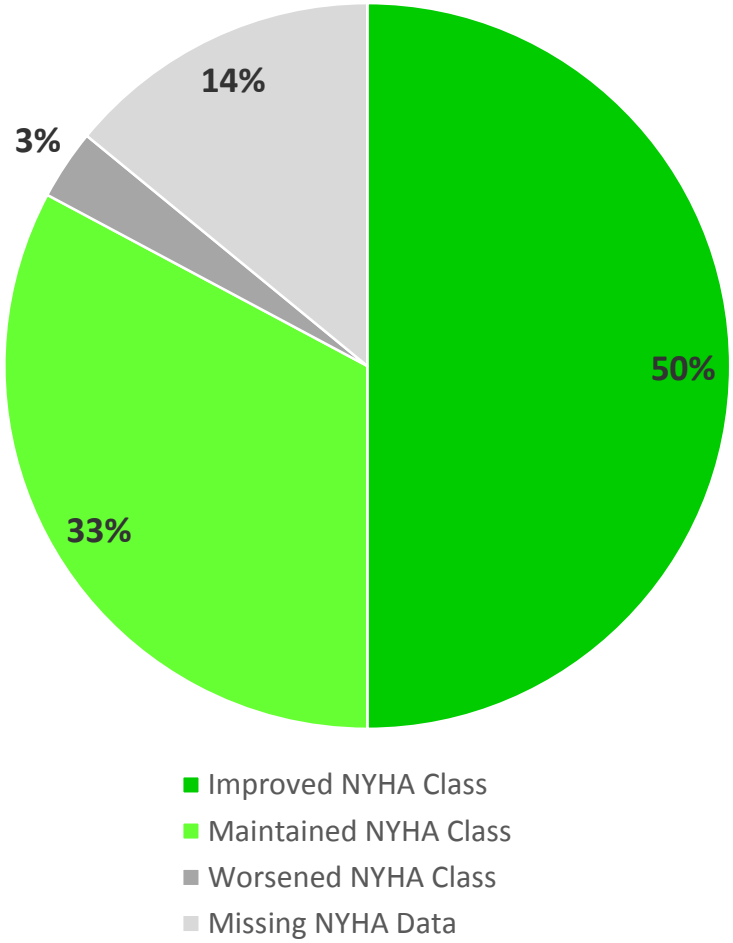
Hemodynamics

	N	Baseline	12 Months	Difference	p-value
Heart Rate & Blood Pressure					
Heart Rate, bpm	111	67.9 ± 13.0	68.0 ± 10.5	0.1 ± 12.5	NS
Systolic, mmHg	110	119.5 ± 16.8	118.2 ± 15.2	-1.3 ± 16.1	NS
Diastolic, mmHg	110	71.8 ± 9.9	72.0 ± 9.8	0.2 ± 11.8	NS
LV Volume					
ESVi, ml/m2	91	86.7 ± 23.7	72.4 ± 23.3	-13.9 ± 26.8	**<.0001**
EDVi, ml/m2	91	120.2 ± 25.5	101.9 ± 26.5	-18.3 ± 25.6	**<.0001**
Systolic Function					
Ejection Fraction, %	91	28.6 ± 7.7	30.5 ± 7.8	1.9 ± 8.7	**<0.05**
Fractional Shortening, %	81	18.9 ± 9.8	20.1 ± 8.5	1.2 ± 10.4	0.3
Contractility Index (Ees), mmHg-m2/ml	90	1.3 ± 0.4	1.6 ± 0.6	0.3 ± 0.5	**<.001**
Stroke Work / EDVi, mmHg	90	26.9 ± 8.9	29.3 ± 8.2	2.4 ± 9.8	**<0.05**
Wall Motion Severity Index	64	2.5 ± 0.3	2.1 ± 0.3	-0.4 ± 0.4	**<0.0001**
Diastolic Function					
LAVi, ml/m2	50	42.5 ± 15.8	38.3 ± 11.2	-4.2 ± 15.1	**0.05**
E-wave Velocity, m/s	77	0.7 ± 0.2	0.8 ± 0.3	0.1 ± 0.2	**0.02**

NYHA Assessment, N=128

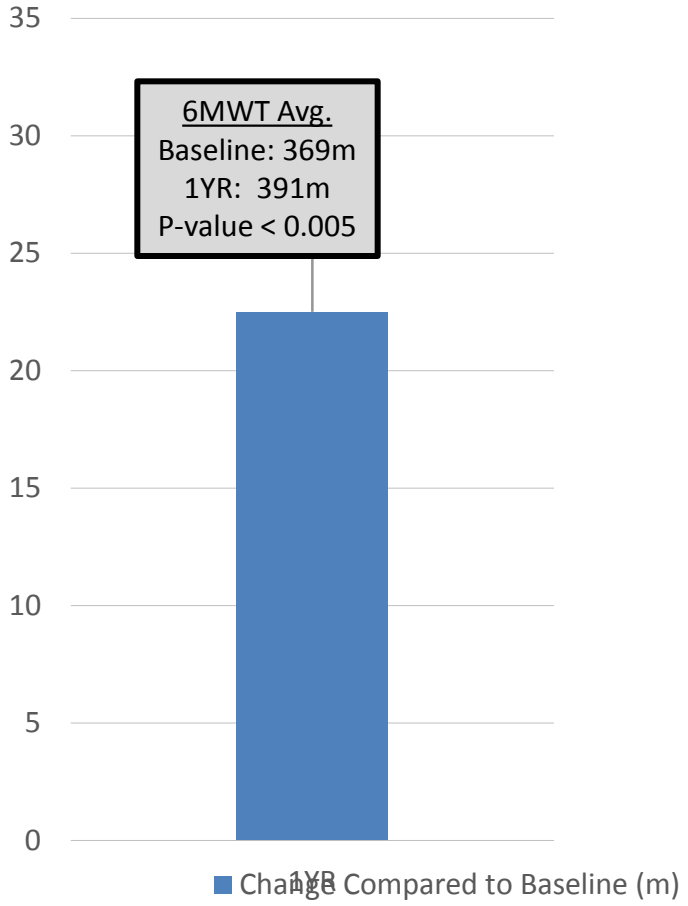
83% of Patients Improved or Maintained at 1Y

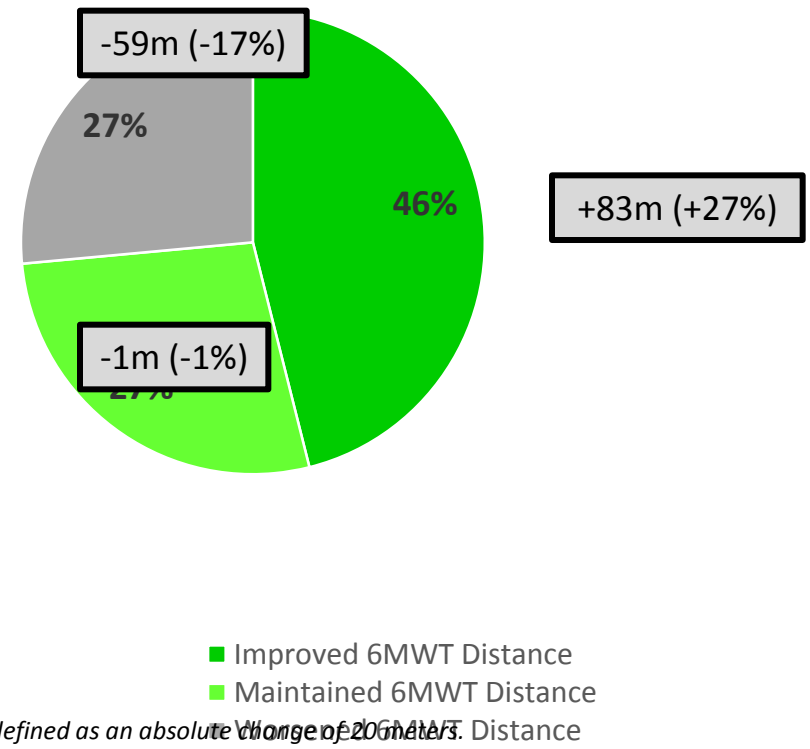




6 Minute Walk Test, N=102

73% of Patients Improved or Maintained at 1Y





Clinically meaningful change in the 6MWT was defined as an absolute change of 20 meters.

Conclusions

- 23.6% Mortality + HF hospitalization rate supports U.S. pivotal trial design
- 8.2% Major Vascular Complications
  - *Less than the observed rates of TAVI (TAVI Meta-Analysis: JACC 2012)*
- Hemodynamic improvements are seen in both systolic and diastolic function
  - *Similar to CRT (MIRACLE: NEJM 2002, MADIT-CRT: JACC 2011)*
- Functional improvement is shown by an increase in the 6MWT and reduction in NYHA class
  - *Similar to CRT (MIRACLE: NEJM 2002)*

PARACHUTE China: Multi-center, prospective single-arm clinical evaluation of the safety and efficacy of the Parachute percutaneous left ventricle partitioning system, Primary Endpoint Results

Runlin Gao, MD

Fu Wai Hospital, Chinese Academy of Medical Sciences

Beijing, China

21 March 2015

Study Organization

- **Principal Investigator** – Prof. Gao Runlin
- **Joint Principal Investigators** – Prof. Huo Yong & Prof. Yang Yuejin
- **Data and Statistics** – Peking University Clinical Research Institute, Prof. Yao Chen
- **CRO** – MediChance Guangzhou Medical Co., LTD
- **CT Core Lab** – Case Western Reserve, Dr. Hiram Bezerra
- **Echo Core Lab** – Yale Cardiovascular Research Group, Dr. Alexandra Lansky and Dr. Lissa Sugeng

PARACHUTE China Trial

- **Aim**
  - Use the Parachute percutaneous left ventricular partitioning system to isolate the dysfunctional part of the left ventricle in patients with symptoms of heart failure due to ischemic heart disease
- **Trial Design**
  - Single-Arm Trial, 7 Centers
  - 30 Consecutive Patients with Symptomatic Ischemic HF
  - Screening with echo (TTE) and cardiac CT or MRI
  - One year anticoagulation post procedure with warfarin and aspirin

PARACHUTE China Trial

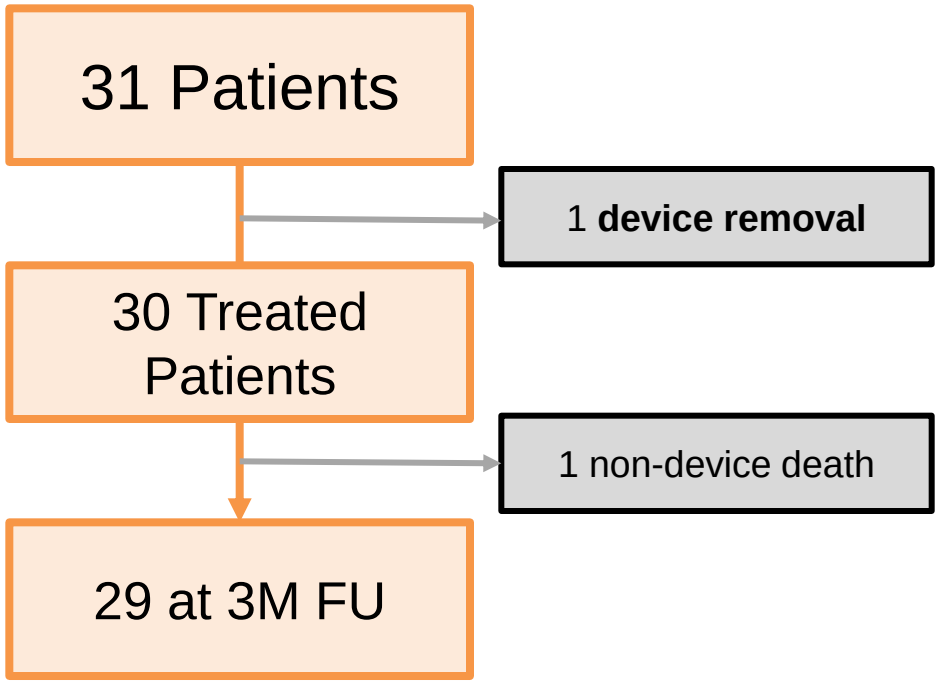
- **Inclusion Criteria**
  - NYHA Class II to Ambulatory IV
  - 18-79 years of age
  - LV wall motion abnormalities (anteroapical akinesis or dyskinesis) secondary to MI
  - LV ejection fraction between 15% and 40%
  - Received appropriate treatment according to ACC/AHA guidelines
  - Signed Ethics Committee approved Informed Consent
- **Exclusion Criteria**
  - Subjects with myocardial ischemia who underwent revascularization or cardiac resynchronization therapy within 60 days of enrollment
  - Valvular stenosis or regurgitation (tricuspid, aortic, or mitral valve) > 2+
  - Recent (within 6 months) cerebrovascular accident (CVA) or transient ischemic attack (TIA)

PARACHUTE China
Endpoints

- Primary endpoint
  - Reduction in left ventricle end systolic volume index (LVESVi) after 3 months compared with baseline.
- Secondary safety endpoint
  - Procedure or Device Related MACE at 3M, where MACE are defined as death from any cause, myocardial infarction, need for elective or urgent cardiac or thoracic aortic surgery or need for use of device or device surgery with a catheter as the basis of interventional therapy, or total renal failure requiring dialysis.
- Secondary efficacy endpoints
  - NYHA improvement at 3M
  - 6MWT improvement at 3M
  - EQ5D improvement at 3M

Patient Enrollment & Disposition

Fu Wai Hospital	9
Peking University First Hospital	6
Shanghai Tenth People's Hospital	6
The 2nd Affiliated Hospital Of Zhejiang University	4
The General Hospital of Shenyang Military Region	3
Zhongshan Hospital Fudan University	2
Shanghai Ruijin Hospital	1
Total	**31**



No Major Inclusion / Exclusion violations

0% Lost to Follow-up

Baseline Patient Profile

Demographics	
Age, years	57.1 ± 10.4
Male, %	29/31 (93.6%)
BMI	25.0 ± 2.2
Ischemic Etiology, %	31/31 (100%)
NYHA Class	
NYHA II	29/31 (93.6%)
NYHA III	2/31 (6.4%)
6MWT, m	479.9 ± 81.4

Medical History	
Smoking History, %	20/31 (64.5%)
History of Hypertension, %	20/31 (64.5%)
History of Diabetes, %	9/31 (29.0%)
Prior ICD, %	0/31 (0.0%)
Prior Pacemaker, %	1/31 (3.2%)
Prior PCI, %	28/31 (90.3%)
Prior CABG, %	0/31 (0.0%)

Hemodynamics	
Ejection Fraction, %	29.8 ± 5.4
LV EDVi, ml/m^2	111.6 ± 26.0
LA Vi, ml/m^2	32.5 ± 8.7
LV DD, cm	5.5 ± 0.6
Cardiac Index, L/min/m^2	2.2 ± 0.6

Procedure Data

Treatment Success, %	**30/31 (96.8%)**
Positioning / Surgical Removal, n	*1*
Device Size	
65mm, %	11/31 (35.5%)
75mm, %	8/31 (25.8%)
85mm, %	5/31 (16.1%)
95mm, %	7/31 (22.6%)

Procedure Complications	**1/31 (3.2%)**
Groin Hematoma, n	*1*
Death, n	*0*
Aortic Valve Injury, n	*0*
LV Injury, n	*0*
Infection, n	*0*
Arrhythmia, n	*0*
TIA / Stroke, n	*0*

Primary Endpoint: LVESVi

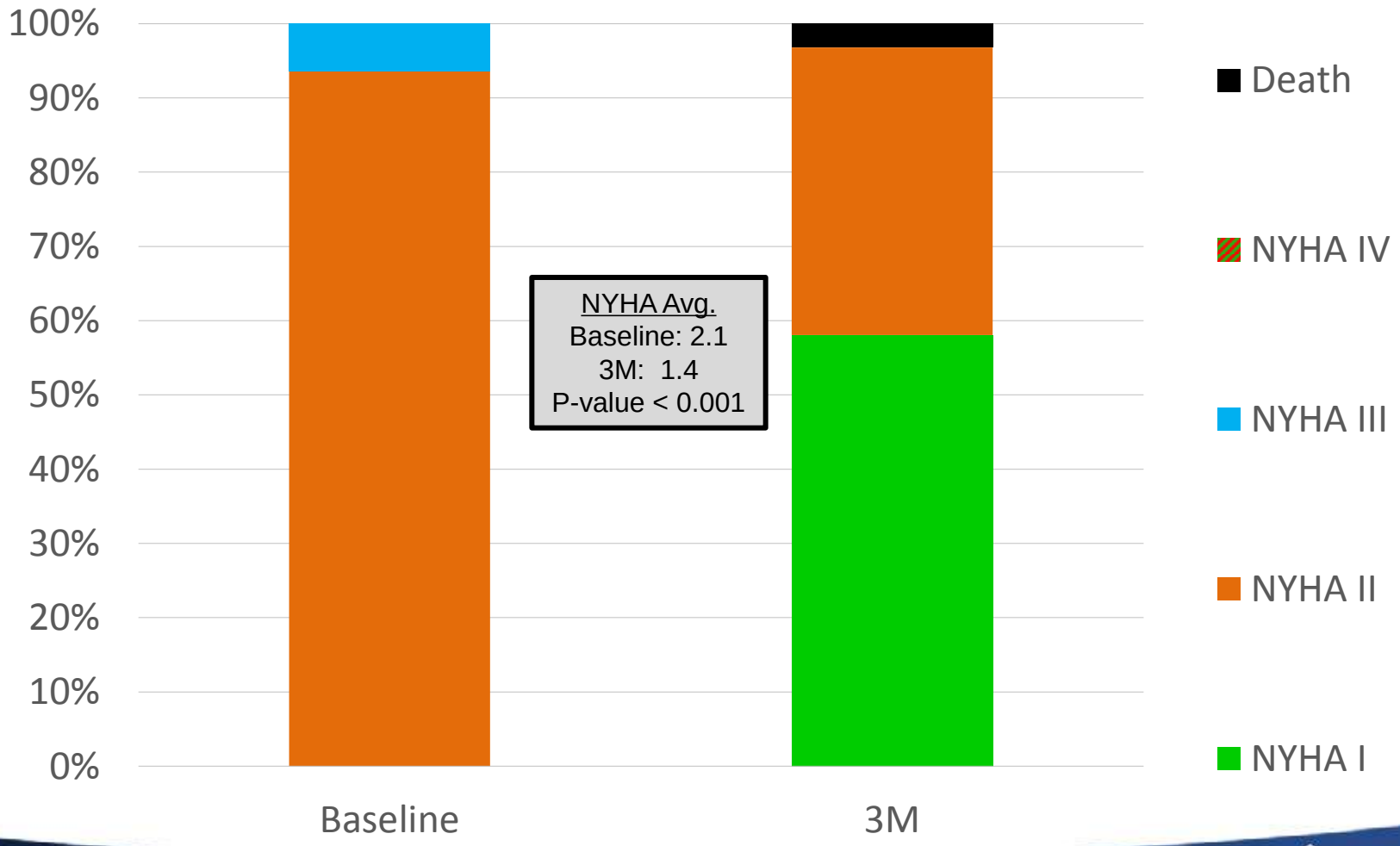
	N	Baseline	3 Months	Difference	p-value
Vitals					
Heart Rate, bpm	29	66.6 ± 10.3	70.4 ± 12.1	3.9 ± 9.1	0.03
Blood Pressure					
Systolic, mmHg	29	121.9 ± 17.5	126.8 ± 14.3	4.9 ± 11.4	0.02
Diastolic, mmHg	29	75.0 ± 10.8	74.2 ± 11.8	-0.7 ± 11.0	NS
LV Volume					
ESVi, ml/m2	28	78.2 ± 20.3	53.4 ± 17.4	-24.7 ± 11.4	**<.0001**
EDVi, ml/m2	28	111.6 ± 26.0	83.0 ± 21.7	-28.6 ± 14.9	**<.0001**
Systolic Function					
Ejection Fraction, %	29	29.8 ± 5.4	36.1 ± 6.8	6.3 ± 6.3	**<.0001**
Fractional Shortening, %	28	18.7 ± 5.7	22.9 ± 7.1	4.3 ± 8.1	**<.01**
Contractility Index (Ees), mmHg-m2/ml	28	1.5 ± 0.5	2.4 ± 0.9	0.9 ± 0.6	**<.0001**
Stroke Work / EDVi, mmHg	28	29.4 ± 5.5	35.9 ± 8.8	6.6 ± 7.9	**<.001**
Wall Motion Severity Index	29	2.6 ± 0.2	2.0 ± 0.3	-0.6 ± 0.4	**<.0001**
Diastolic Function					
LAVi, ml/m2	27	32.5 ± 8.7	32.4 ± 8.4	-0.1 ± 6.9	**NS**

Safety Endpoints

- **Device or Procedure Related MACE** – 3%
  - One device requiring surgical removal
- **Mortality** – 3%
  - One death caused by multiple system organ failure after cerebral hemorrhage
- **Stroke** – 3%
  - One cerebral hemorrhage (non-device/procedure related)

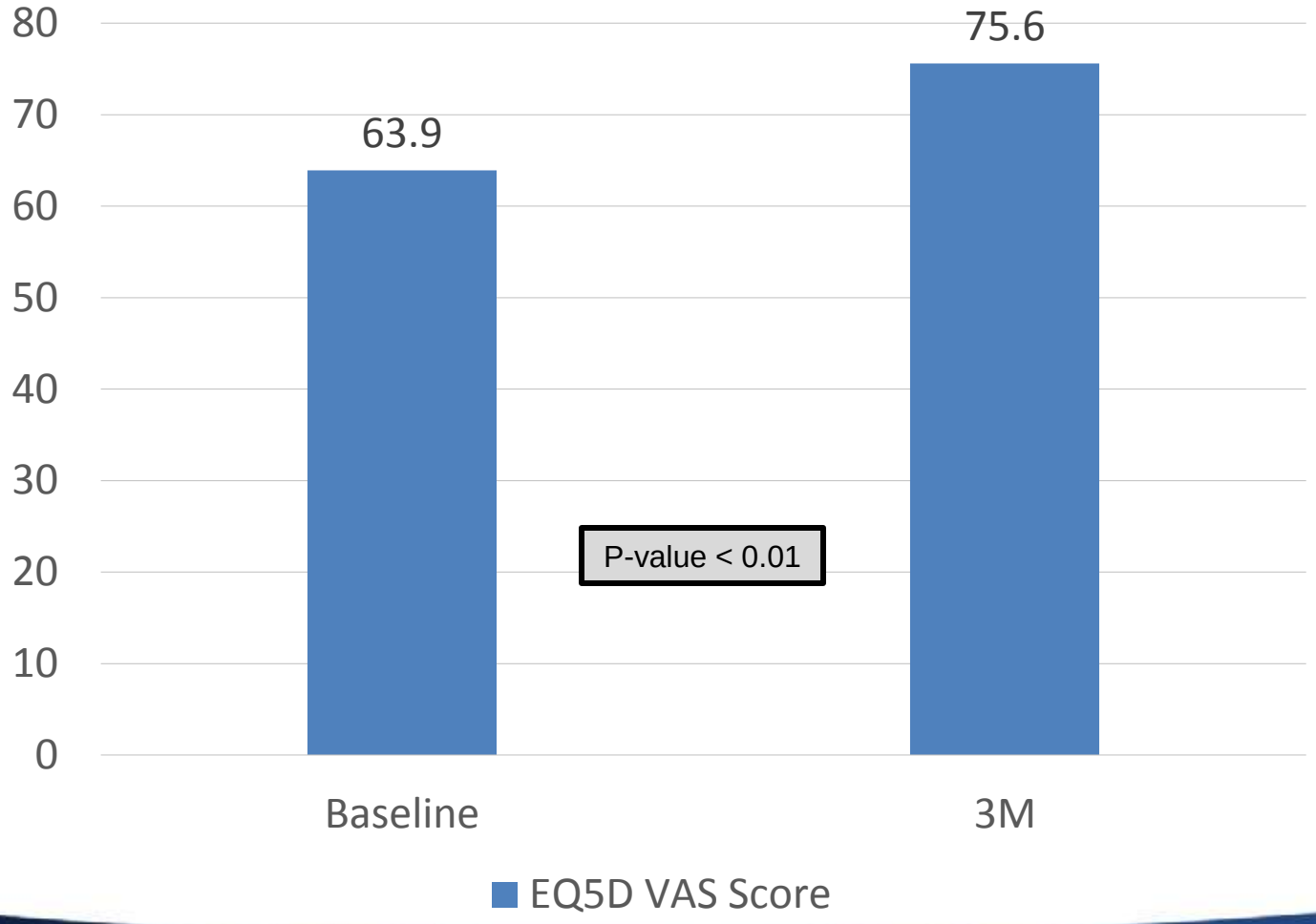
NYHA Assessment

Achieved Secondary Endpoint



Quality of Life – EQ5D

Achieved Secondary Endpoint



6 Minute Walk Test