Update on Percutaneous Mitral Valve Therapy

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Disclosures

Consultant

Abbott Vascular, Tendyne, Bracco

Research Grants

Abbott Vascular, Medtronic, Baxter, Aastrom

Echo Core Lab Contracts

Guided Delivery Systems, Valtech Cardio

Agenda

- Percutaneous Approaches
  - Annuloplasty, Edge-to-Edge
- MitraClip
  - Anatomic criteria/patient selection
  - Echo procedural guidance
  - EVEREST II Randomized Trial
  - High Risk Registry Data
  - Proposed label/indication (FDA panel 3/20/2013)
- Transcatheter Mitral Valve Replacement

Transcatheter Approaches to Mitral Valve Repair

- Annuloplasty
  - Coronary Sinus Approach
  - LA approach
  - LV approach
- Edge to Edge (Alfieri)
  - MitraClip (FDA approval anticipated soon)
  - Suture
- Transcatheter Mitral Valve Replacement

Primary vs Secondary MR

- Primary MR
  - Abnormal leaflets, most commonly MVP
  - “Valve makes the heart sick”
  - Surgical valve repair is gold standard
- Secondary (functional)
  - Leaflets are normal or nearly so
  - MR is caused by LV dilation/dysfunction
  - It is not clear if MR repair is beneficial or not
  - Surgery is Class IIB LOE C (except during CABG)

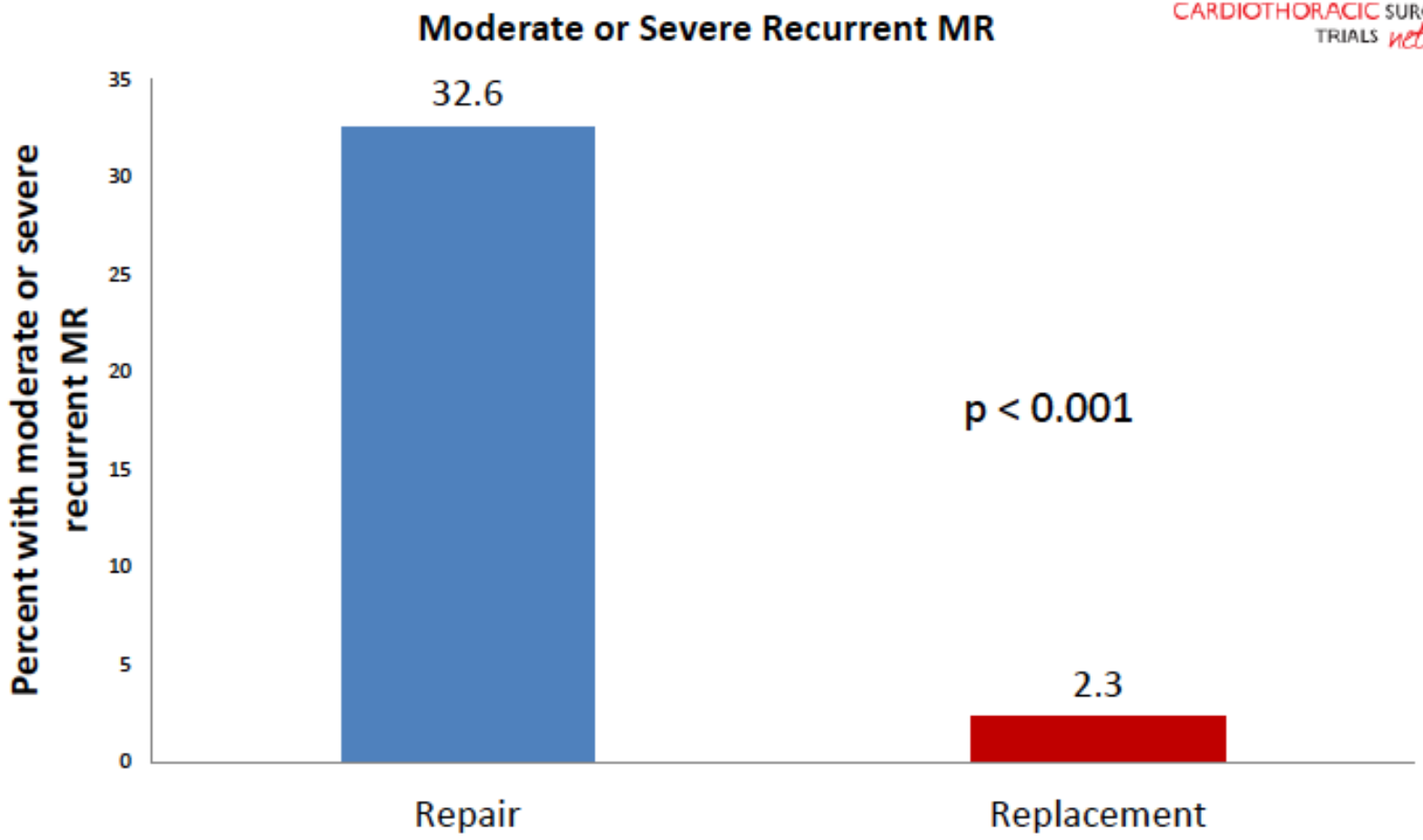
Annuloplasty Rings

Note the various size, shape, configuration, materials

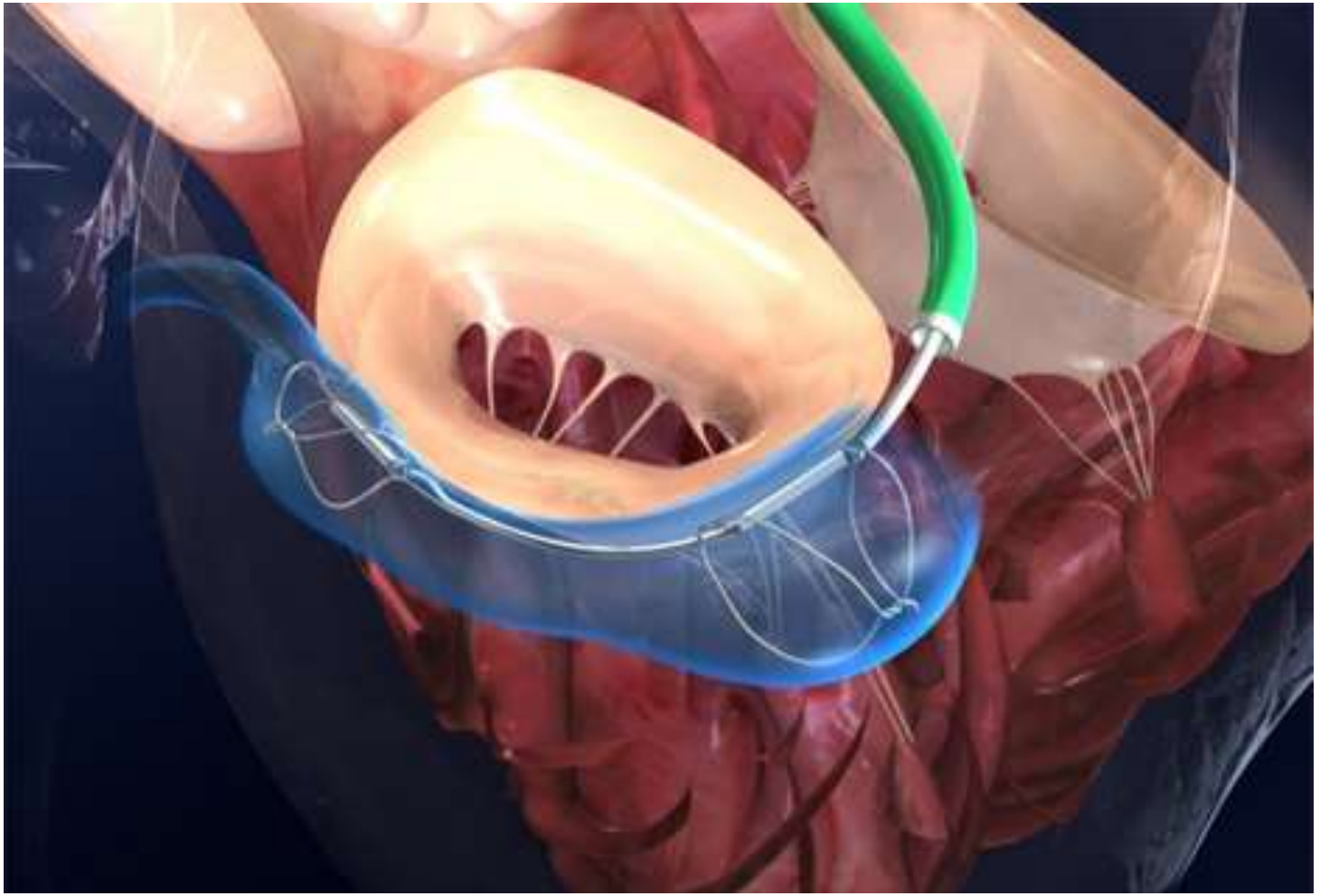
Courtesy of D. Craig Miller, MD

Recurrent MR at 1 year

CTSN
CARDIOTHORACIC SURGICAL TRIALS network



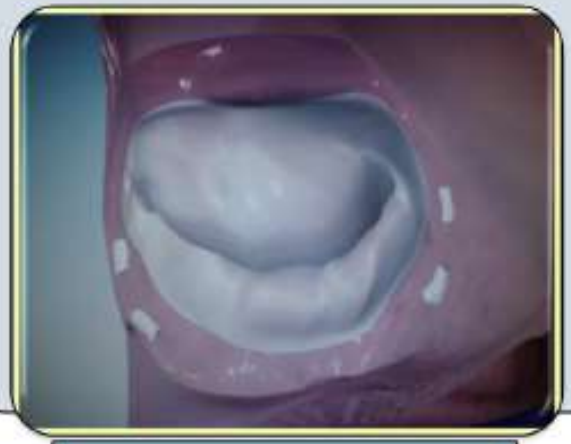
Carillon Device



Problems with CS Approach

- Coronary sinus is often superior to annulus
- Coronary sinus often overlies LCx artery, which can lead to acute MI
- Coronary sinus does not allow for complete ring annuloplasty
- Indirect mitral annuloplasty via coronary sinus is not a viable approach – it is dead!

Transcatheter Direct Annuloplasty



Mitralign

Bident

- Arterial access
- Transannular cinching

GDS

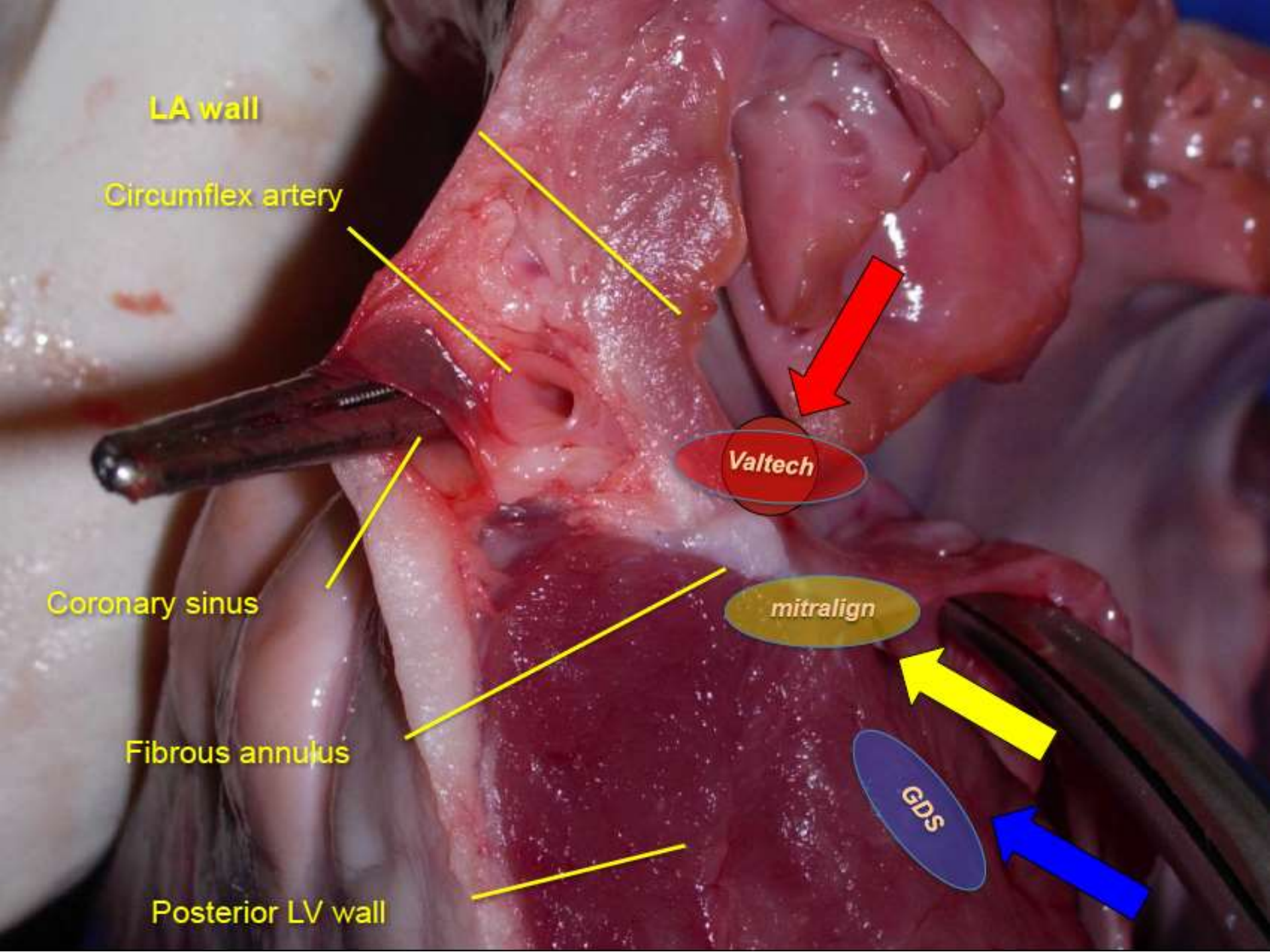
Accucinch

- Arterial access
- Subannular cinching

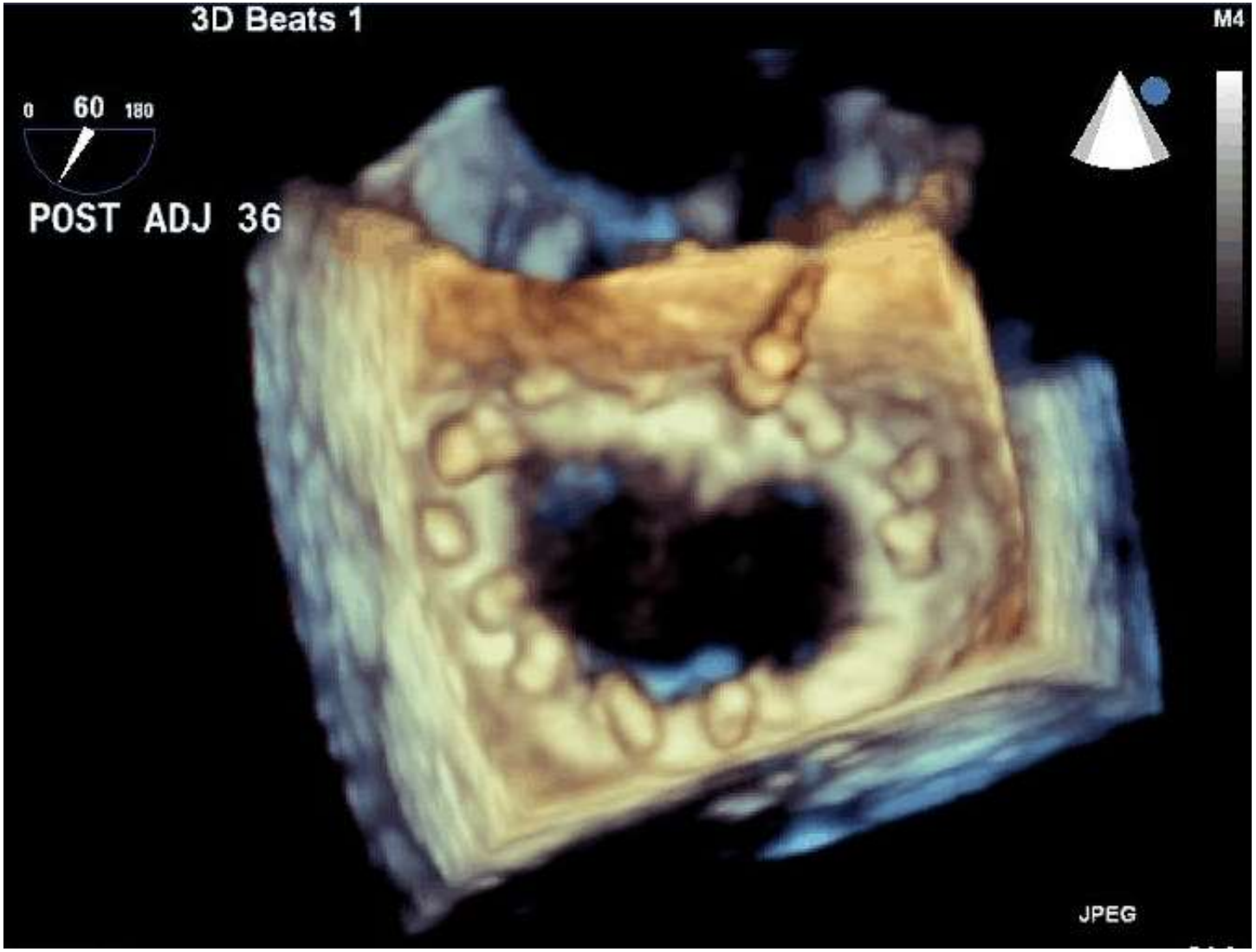
Valtech

Cardioband

- Venous access
- Annular fixation

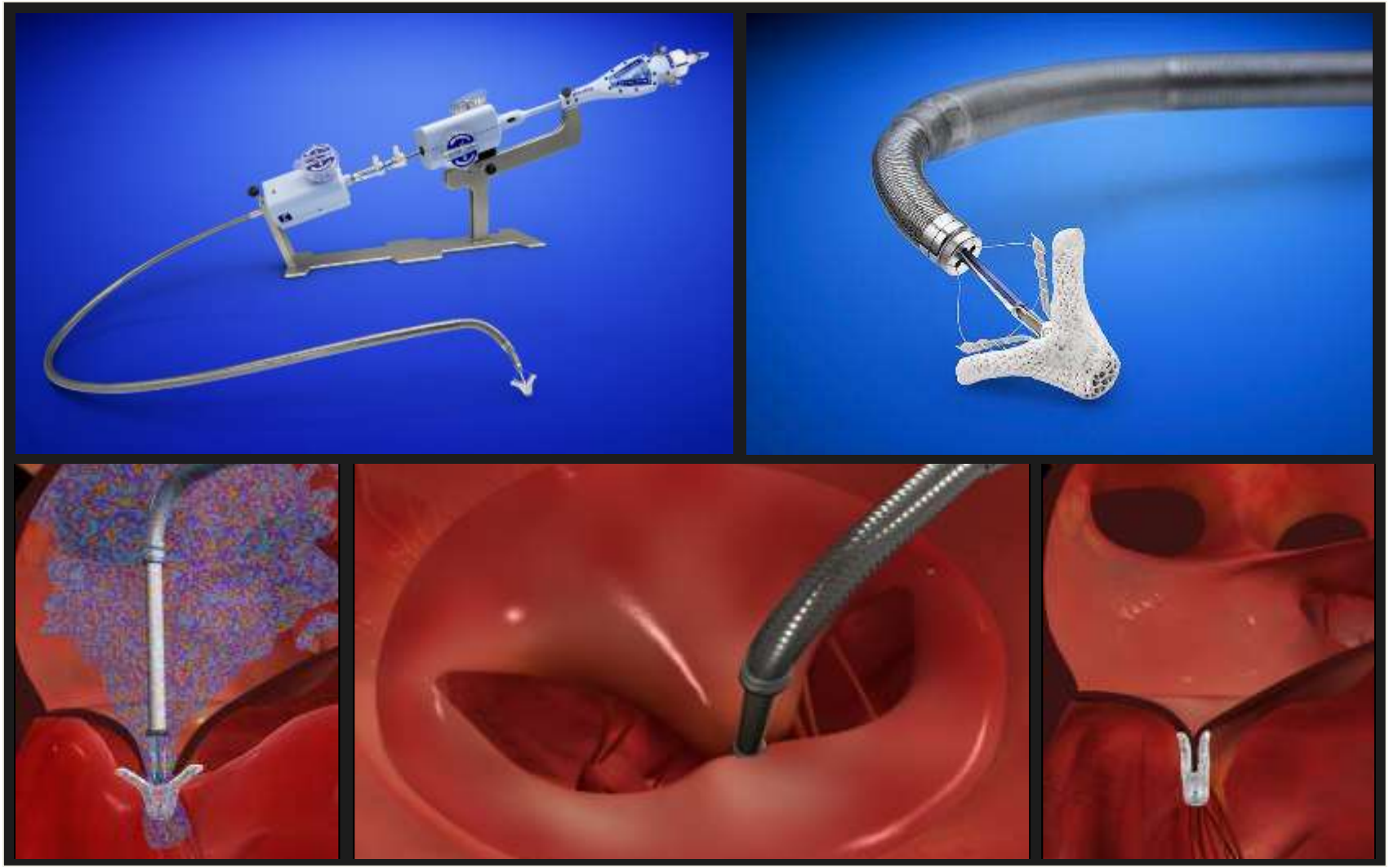

LA wall
Circumflex artery
Valtech
Coronary sinus
mitralign
Fibrous annulus
GDS
Posterior LV wall

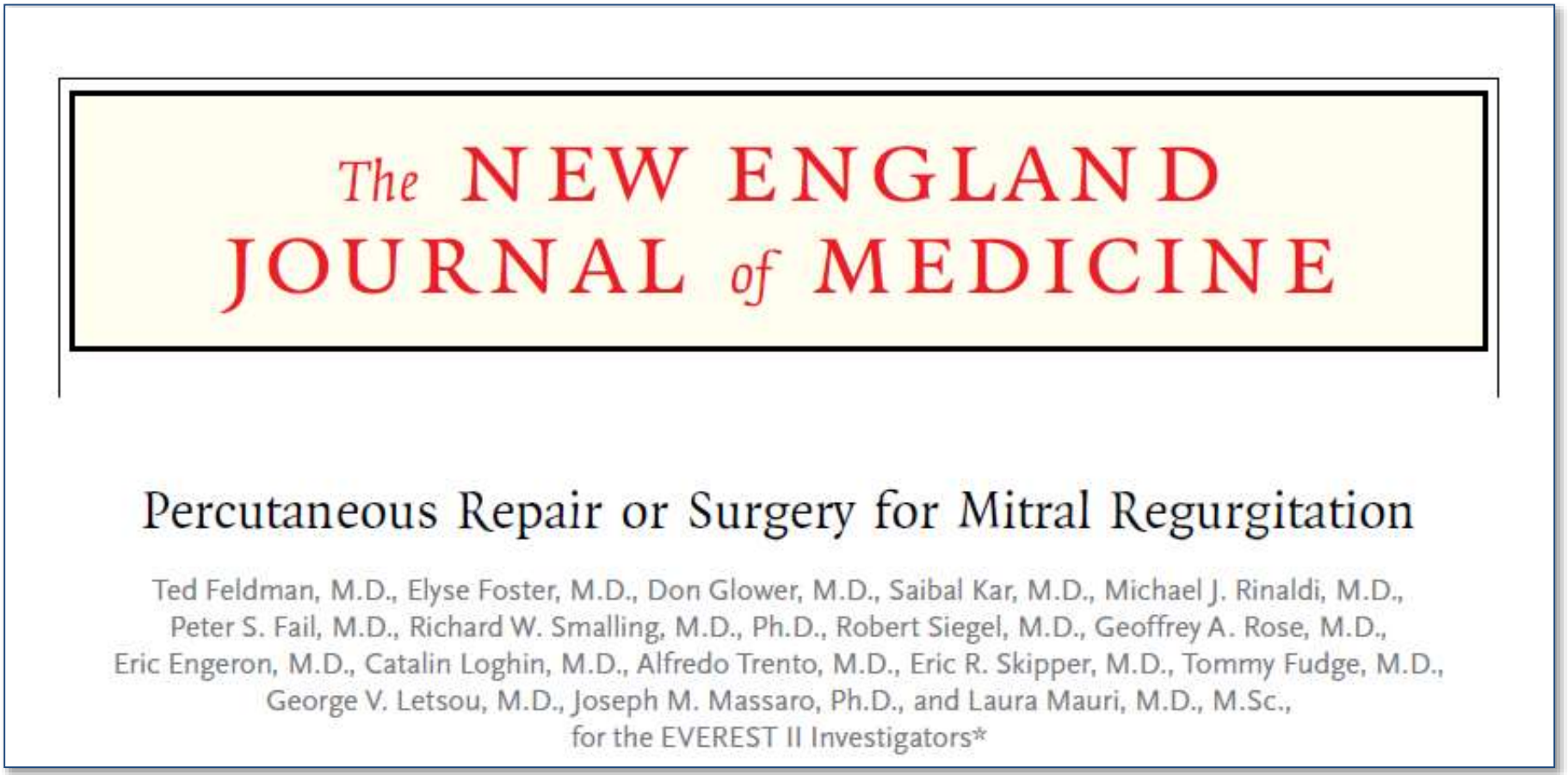
Cardioband Human Implant



Transcatheter Mitral Valve Repair

MitraClip® System





Surgery was superior to MitraClip in MR reduction;

MitraClip was safer than surgery due to lower risk of transfusion.

MitraClip® Therapy

Worldwide Clinical Experience

- Over 18,000 patients have been treated with the MitraClip device worldwide
  - Nearly 2,000 patients have been enrolled in prospective clinical trials worldwide
- A majority of patients are considered high risk for mitral valve surgery

MitraClip Approved October 24, 2013

Indication for Use:

"The MitraClip Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation."

Definition of Prohibitive Risk

- "Prohibitive risk" is due to the presence of one or more of the following documented surgical risk factors:
  - 30-day STS predicted operative mortality risk score of
    - ≥8% for patients deemed likely to undergo MV replacement or
    - ≥6% for patients deemed likely to undergo MV repair
  - Porcelain aorta or extensively calcified ascending aorta
  - Frailty (assessed by in-person cardiac surgeon consultation)
  - Hostile chest
  - Severe liver disease / cirrhosis (MELD Score > 12)
  - Severe pulmonary hypertension (systolic pulmonary artery pressure >2/3 systemic pressure)
  - Unusual extenuating circumstance, such as
    - Right ventricular dysfunction with severe tricuspid regurgitation
    - Chemotherapy for malignancy
    - Major bleeding diathesis
    - Immobility
    - AIDS
    - Severe dementia
    - High risk of aspiration
    - Internal mammary artery (IMA) at high risk of injury, etc.

Prohibitive Risk DMR Cohort Overview

- 141 high risk DMR patients enrolled consecutively in US clinical trials with 1-year follow-up identified
- Risk factors reviewed by 3 physicians
  - 2 cardiothoracic surgeons (Drs. Mack and McCarthy);
  - 1 cardiologist (Dr. Grayburn)
  - 127 patients identified that met Prohibitive Risk definition
  - Outcomes analyzed and provided to FDA

Improved Functional Status and Quality of Life in Prohibitive Surgical Risk Patients With Degenerative Mitral Regurgitation After Transcatheter Mitral Valve Repair

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ABSTRACT

BACKGROUND Surgical mitral valve repair (SMVR) remains the gold standard for severe degenerative mitral regurgitation (DMR). However, the results with transcatheter mitral valve repair (TMVR) in prohibitive-risk DMR patients have not been previously reported.

OBJECTIVES This study aimed to evaluate treatment of mitral regurgitation (MR) in patients with severe DMR at prohibitive surgical risk undergoing TMVR.

METHODS A prohibitive-risk DMR cohort was identified by a multidisciplinary heart team that retrospectively evaluated high-risk DMR patients enrolled in the EVEREST (Endovascular Valve Edge-to-Edge Repair Study) II studies.

RESULTS A total of 141 high-risk DMR patients were consecutively enrolled; 127 of these patients were retrospectively identified as meeting the definition of *prohibitive risk* and had 1-year follow-up (median: 1.47 years) available. Patients were elderly (mean age: 82.4 years), severely symptomatic (87% New York Heart Association class III/IV), and at prohibitive surgical risk (STS score: 13.2 ± 7.3%). TMVR (MitraClip) was successfully performed in 95.3%; hospital stay was 2.9 ± 3.1 days. Major adverse events at 30 days included death in 6.3%, myocardial infarction in 0.8%, and stroke in 2.4%. Through 1 year, there were a total of 30 deaths (23.6%), with no survival difference between patients discharged with MR ≤1+ or MR 2+. At 1 year, the majority of surviving patients (82.9%) remained MR ≤2+ at 1 year, and 86.9% were in New York Heart Association functional class I or II. Left ventricular end-diastolic volume decreased (from 125.1 ± 40.1 ml to 108.5 ± 37.9 ml; $p < 0.0001$ [$n = 69$ survivors with paired data]). SF-36 quality-of-life scores improved and hospitalizations for heart failure were reduced in patients whose MR was reduced.

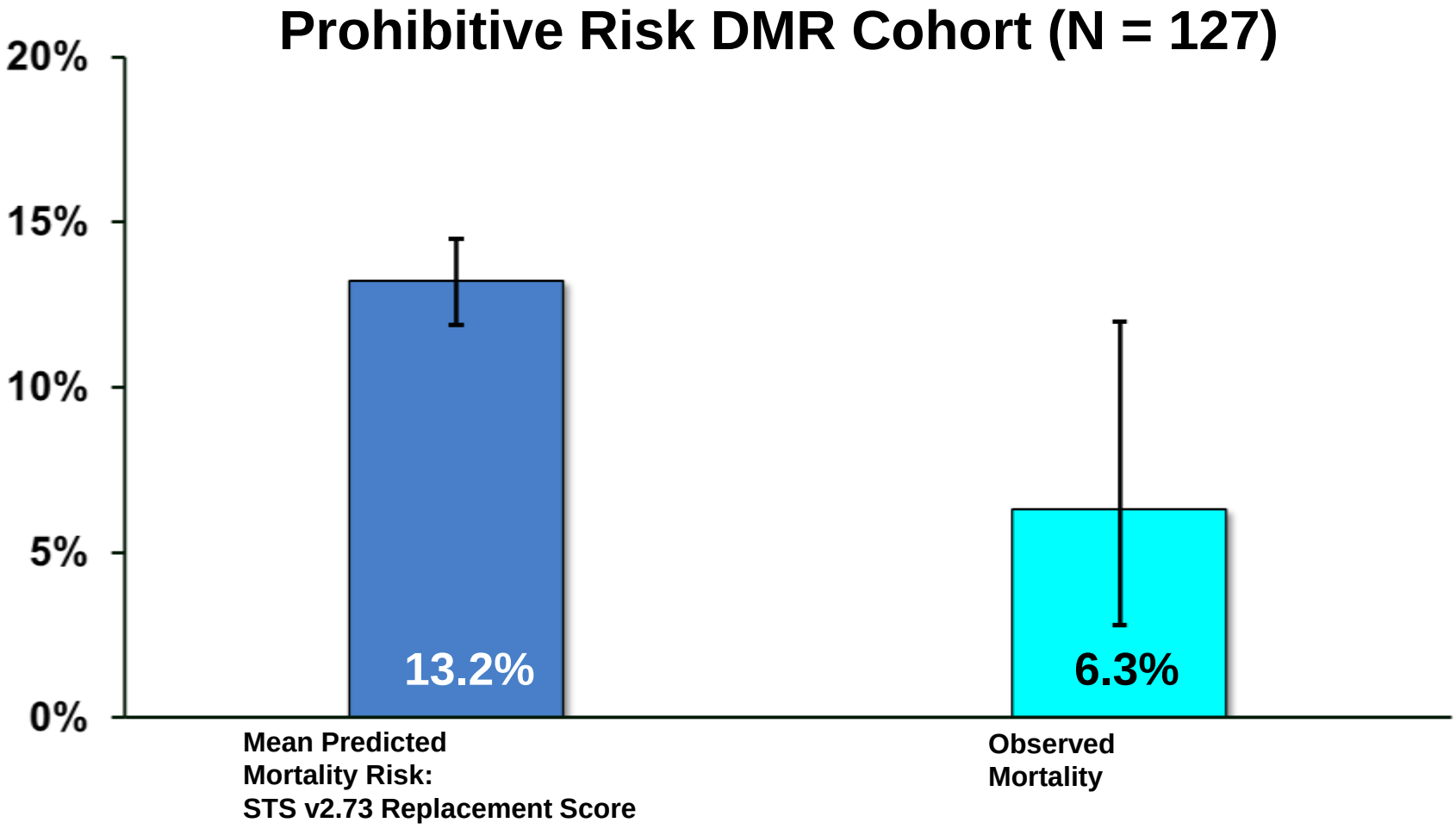
CONCLUSIONS TMVR in prohibitive surgical risk patients is associated with safety and good clinical outcomes, including decreases in rehospitalization, functional improvements, and favorable ventricular remodeling, at 1 year. (Real World Expanded Multi-center Study of the MitraClip System [REALISM]; NCT01931956)
(J Am Coll Cardiol 2014;64:182–92)

Baseline Demographics and Comorbidities

Characteristic	Prohibitive Risk DMR N = 127
Age (mean ± SD)	82 ± 9 years
Patients over 75 years of age	84%
Male Gender	55%
Coronary Artery Disease	73%
Prior Myocardial Infarction	24%
Previous Cardiovascular Surgery	48%
Atrial Fibrillation History	71%
Prior Stroke	10%
Diabetes	30%
Moderate to Severe Renal Disease	28%
Chronic Obstructive Pulmonary Disease	32%
NYHA Functional Class III or IV	87%
STS Mortality Risk (mean ± SD) [v2.73, replacement]	13.2 ± 7.3%

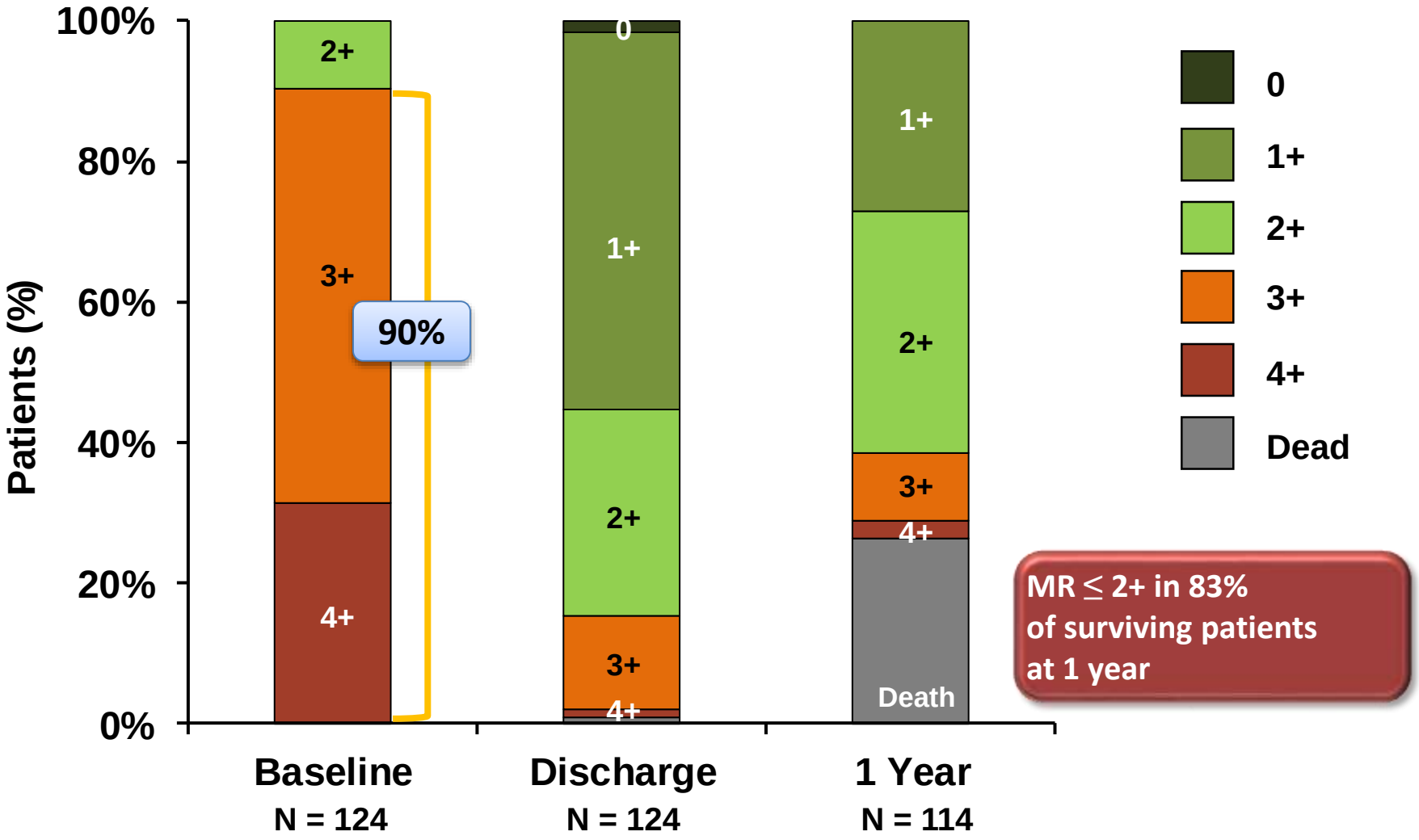
Lim DS, et al, JACC 2014

30-Day Observed Mortality Lower than Predicted



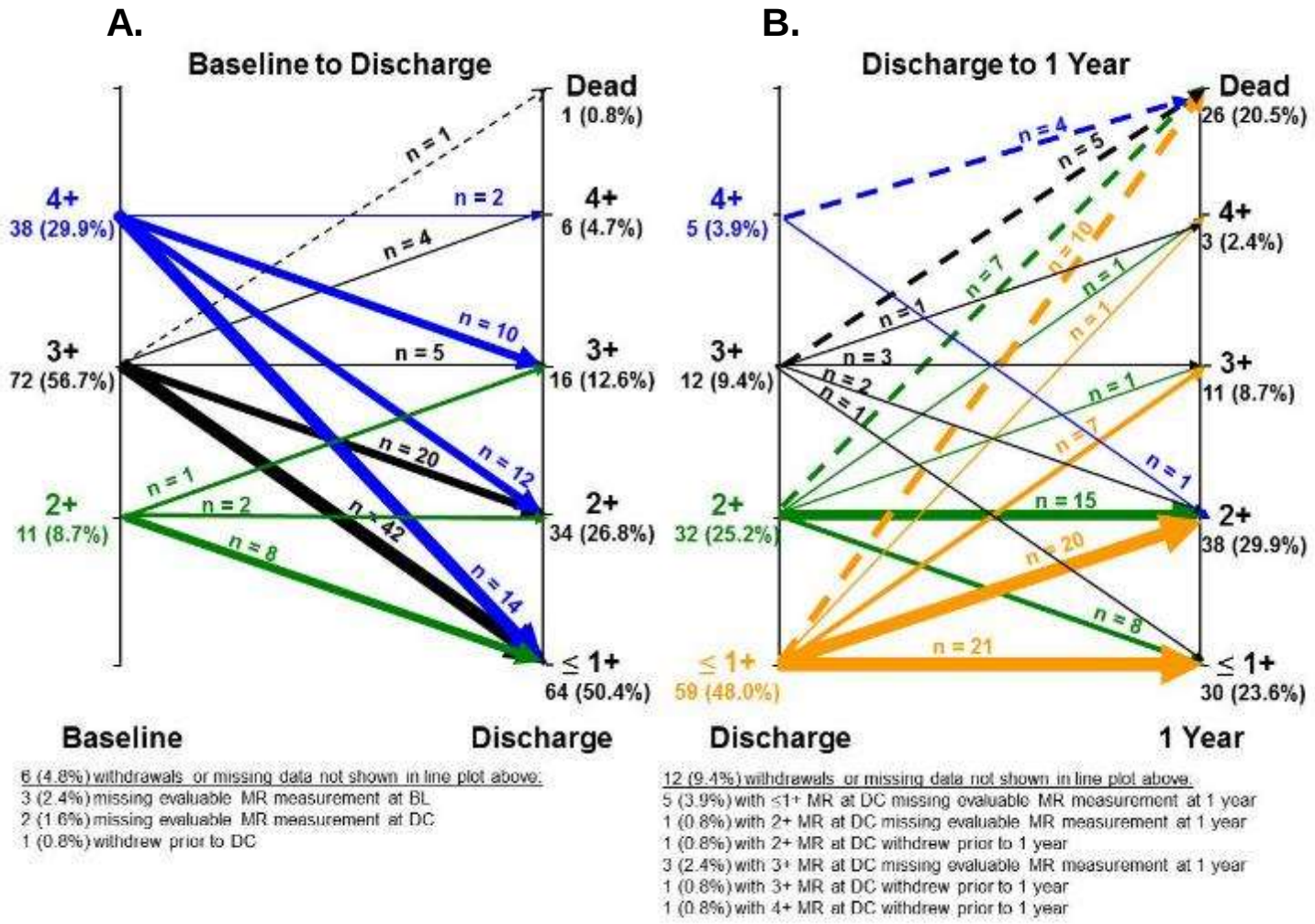
Lim DS, et al, JACC 2014

Reduction of Mitral Regurgitation Grade



Lim DS, et al, JACC 2014

MR Reduction (Detailed)



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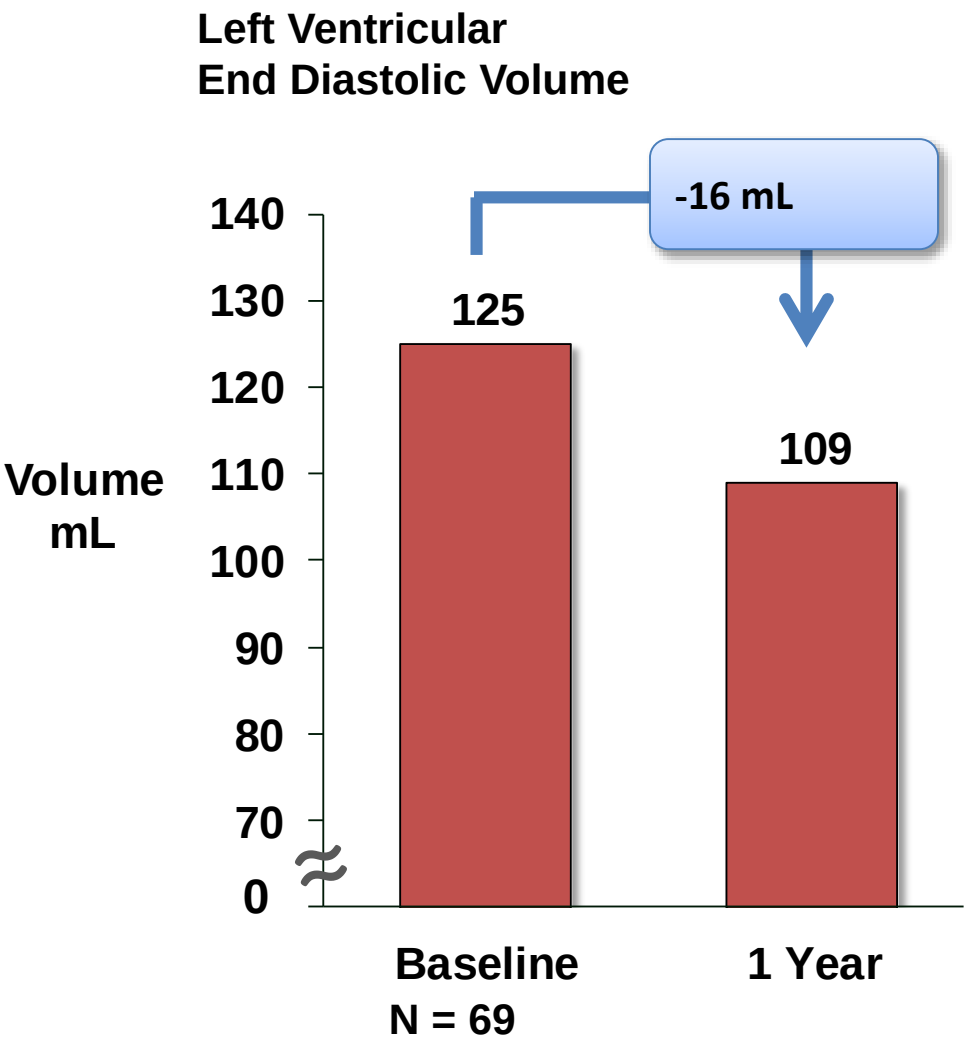
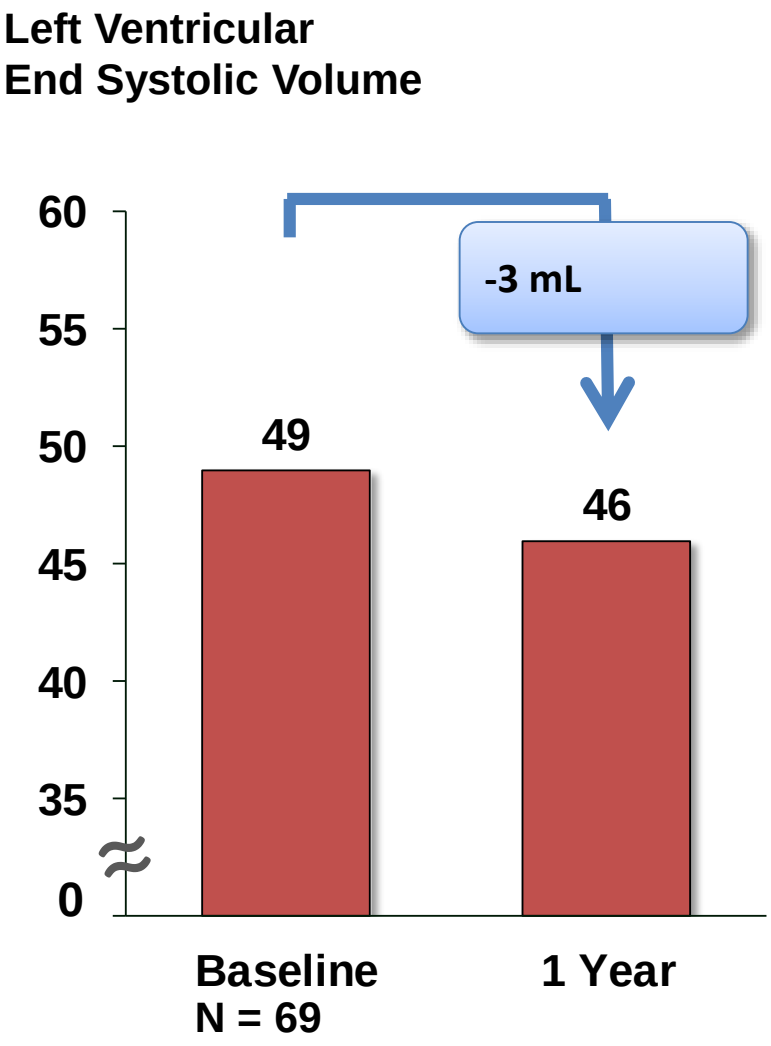
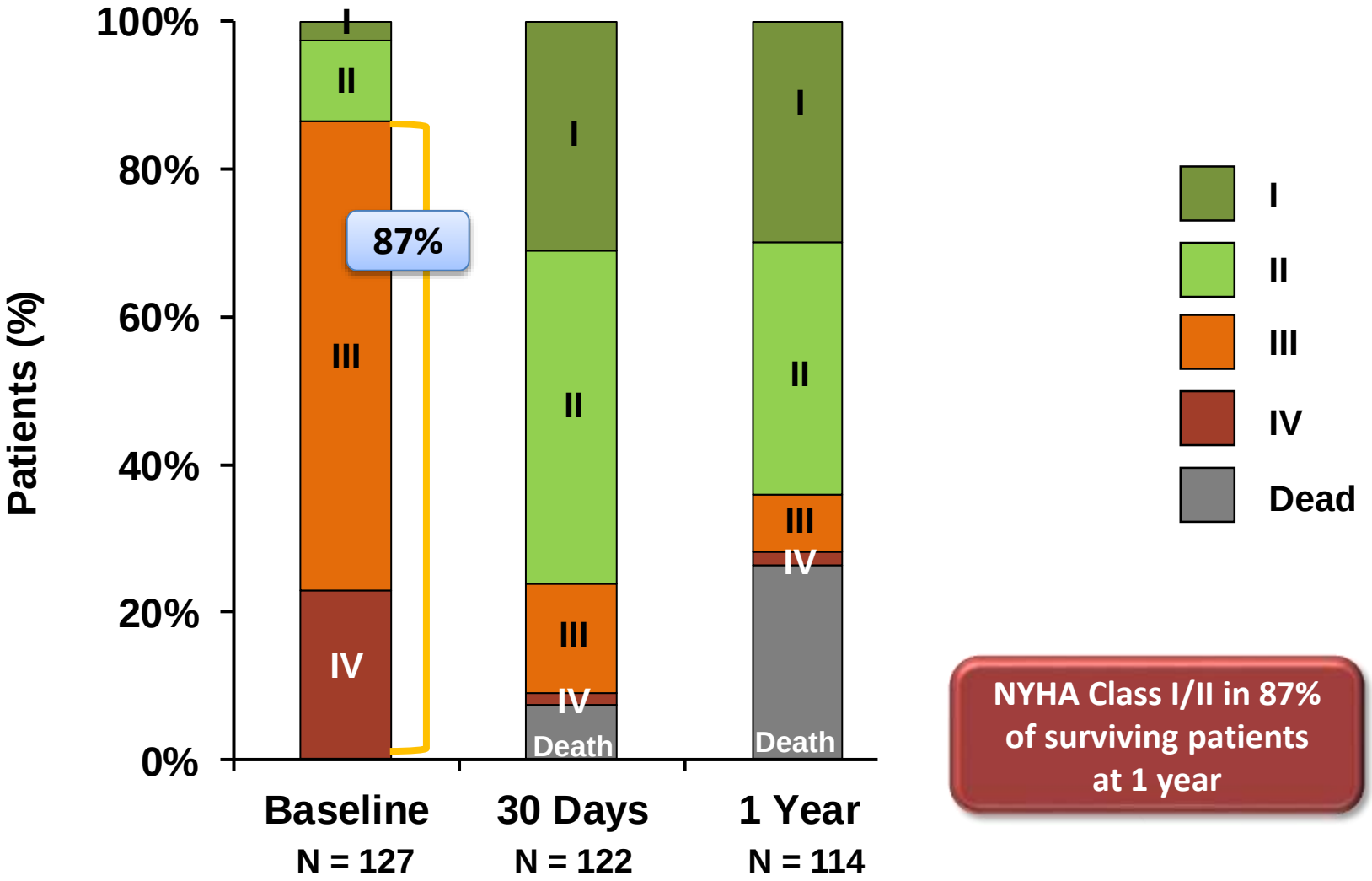
Reduction in Left Ventricular Volumes





Lim DS, et al, JACC 2014

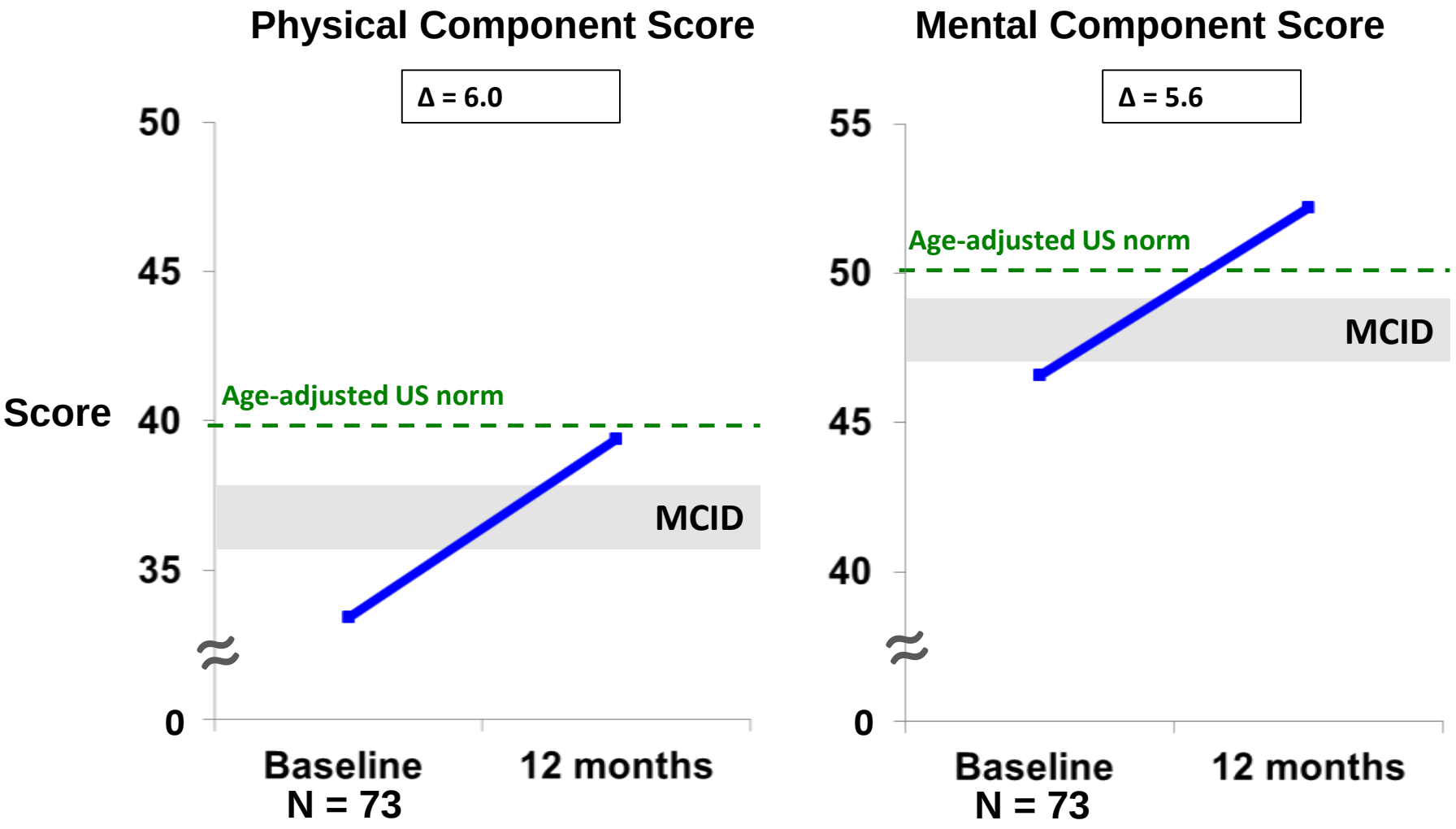
Improvement in NYHA Functional Class



Lim DS, et al, JACC 2014

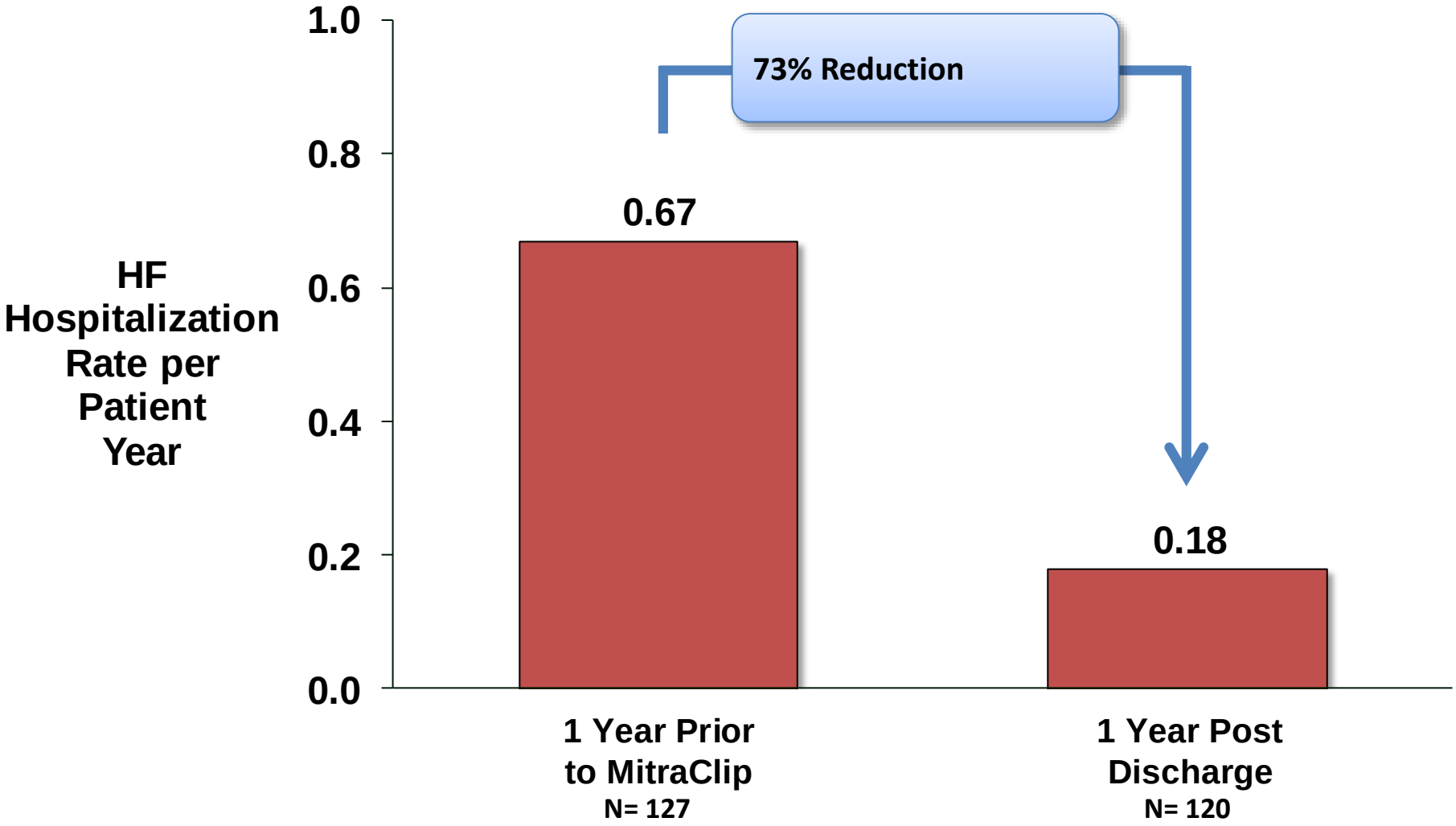
Improvement in SF-36 Quality of Life at 1 Year

Paired Analysis



Lim DS, et al, JACC 2014

Reduction in Heart Failure Hospitalization



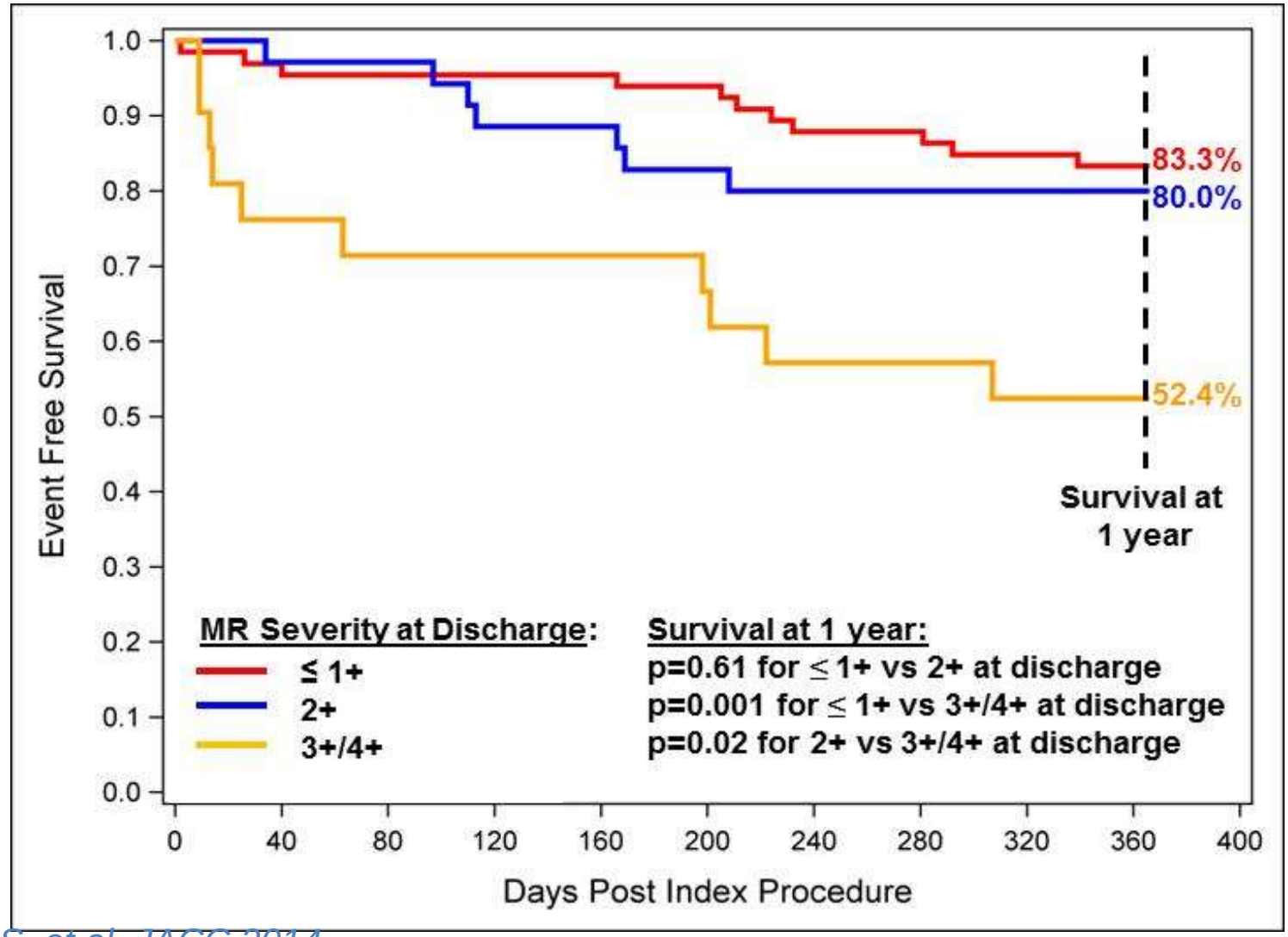
Lim DS, et al, JACC 2014

CEC-Adjudicated Safety Events

	Prohibitive Risk DMR N = 127			
	30 Days		1 Year	
Event (Non-Hierarchical)	n	%	n	%
Death	8	**6.3%**	30	**23.6%**
Myocardial Infarction	1	**0.8%**	1	**0.8%**
Non-elective CV Surgery for AEs	1	**0.8%**	1	**0.8%**
Stroke	3	**2.4%**	3	**2.4%**
New onset of permanent AF	0	**0**	0	**0**
Renal Failure	2	**1.6%**	5	**3.9%**
Ventilation > 48 hours	4	**3.1%**	6	**4.7%**
GI complication requiring surgery	1	**0.8%**	3	**2.4%**

Lim DS, et al, JACC 2014

Survival by MR at Discharge



Lim DS, et al, JACC 2014

Commercial Experience US

1,167 cases done since approval

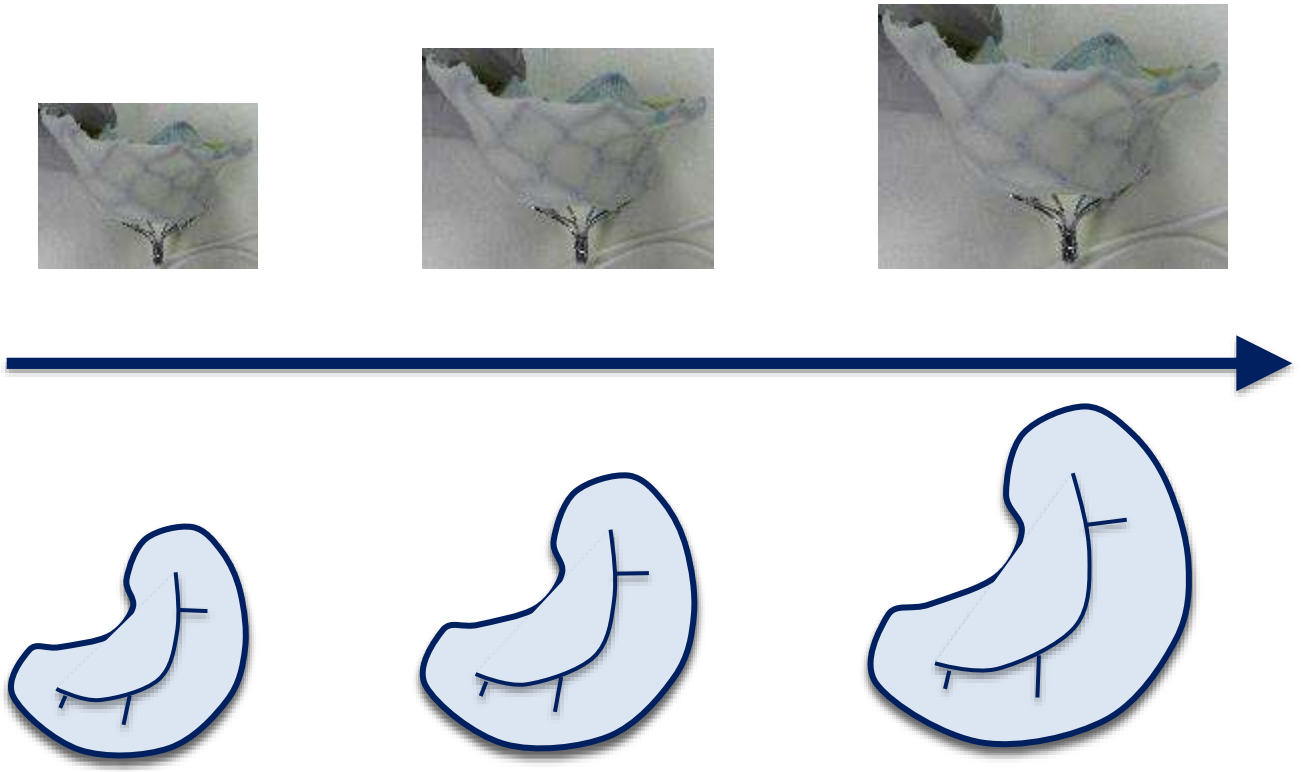
Data to be presented at ACC in San Diego March 2015

Tendyne Trans-apical Mitral Valve

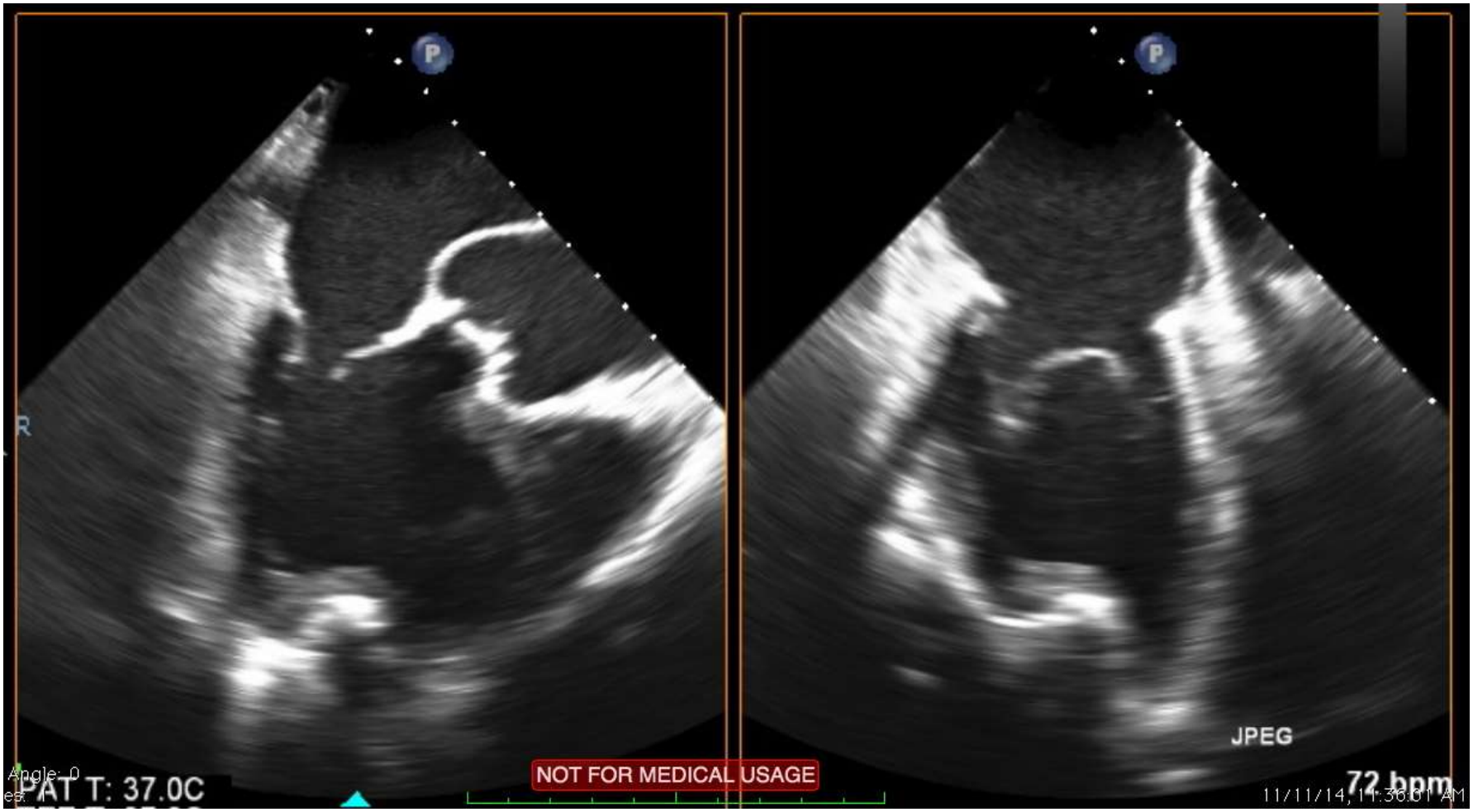
Self-expanding tri-leaflet porcine pericardium 29 mm bioprosthesis with orifice area > 3 cm^2

- Left ventricular apical tether
- Leaflet indifferent
- Multiple device sizes
- Simple, controlled deployment
- Fully **retrievable** and **repositionable**

Tendyne Valve Offers Multiple Sizes

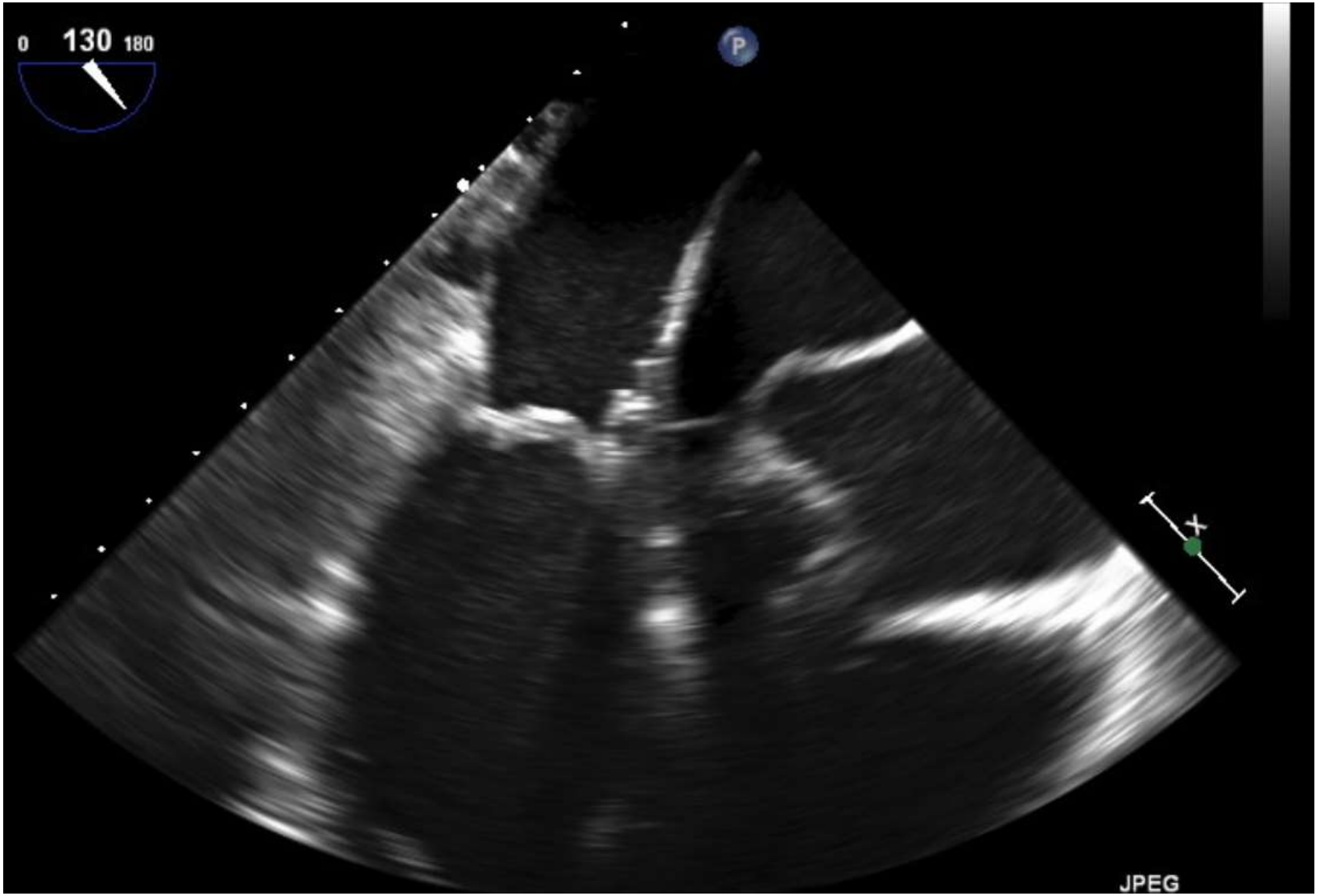


Finger at LV Apex



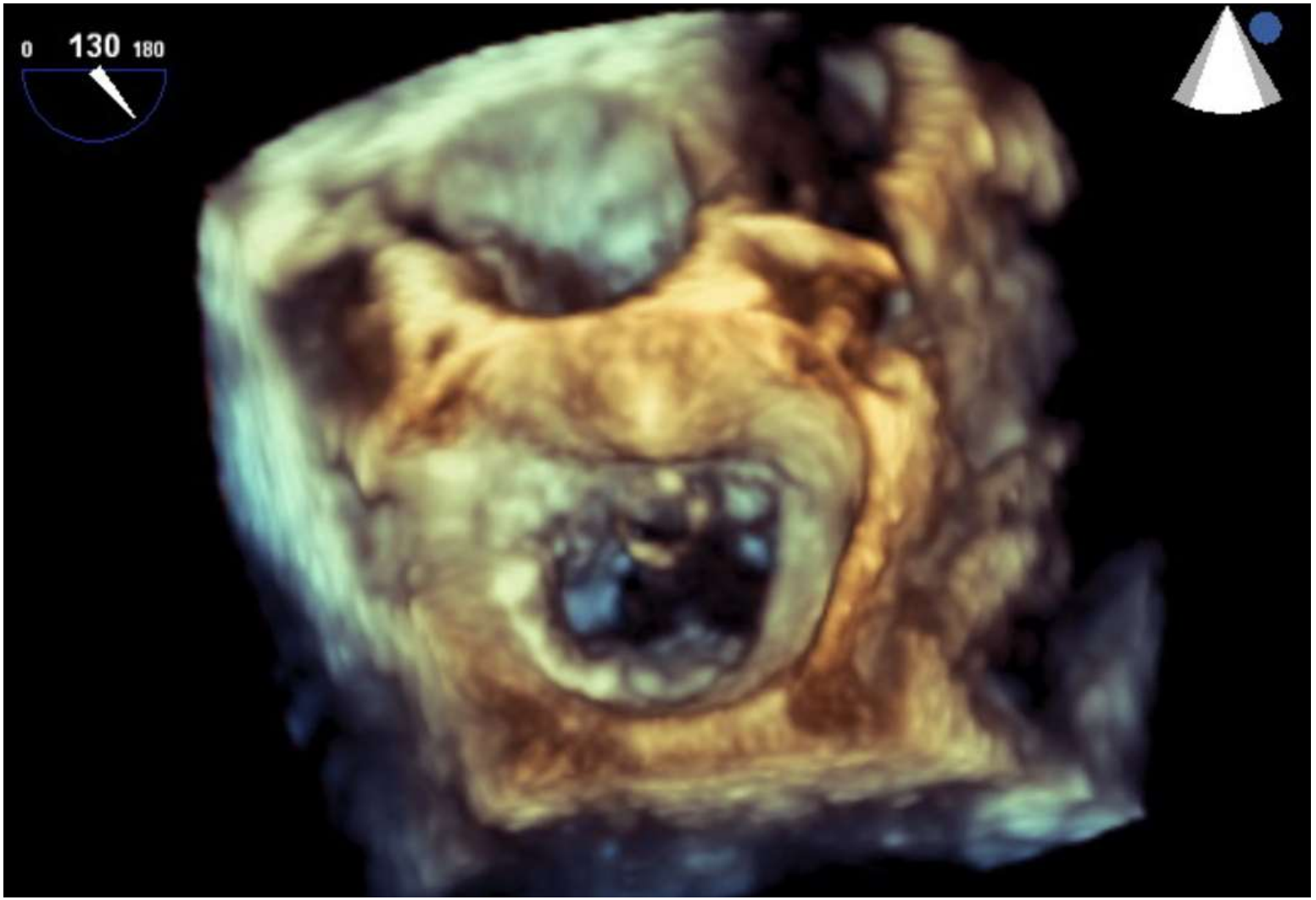
Images courtesy of N. Moat, A. Duncan, Royal Brompton

Wire in LUPV – Sheath to LA



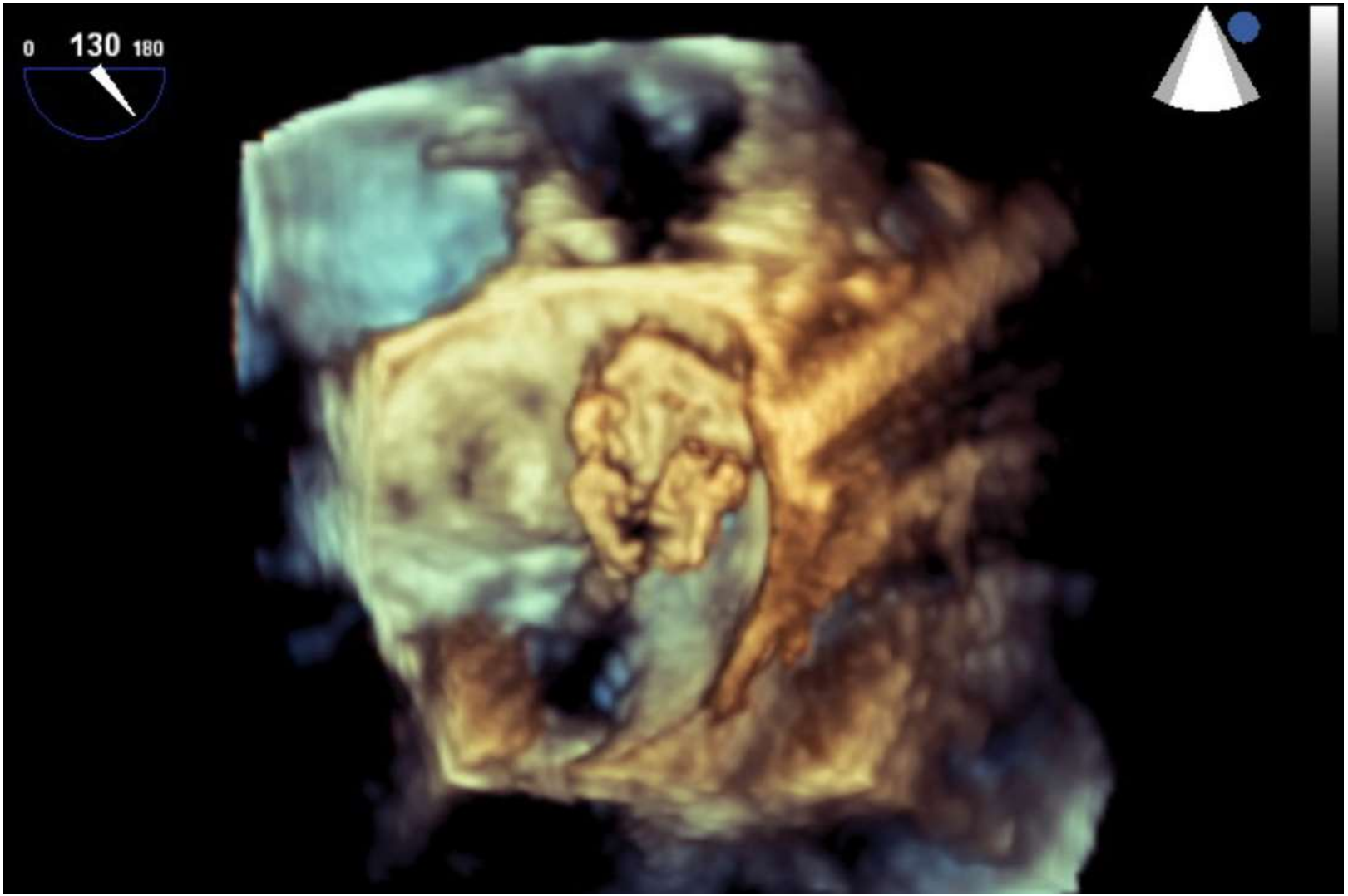
Images courtesy of N. Moat, A. Duncan, Royal Brompton

Sheath in LA



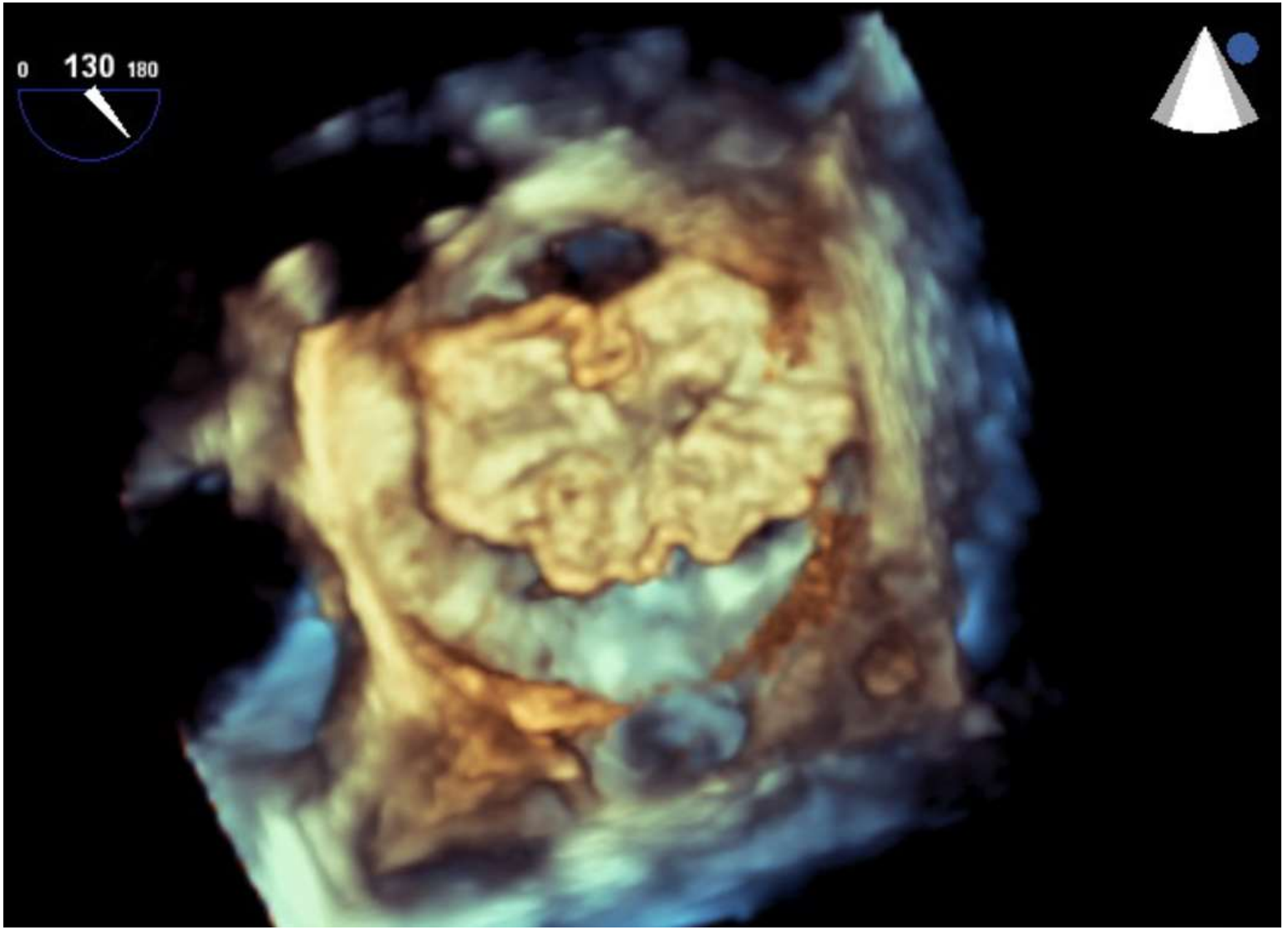
Images courtesy of N. Moat, A. Duncan, Royal Brompton

Device into LA



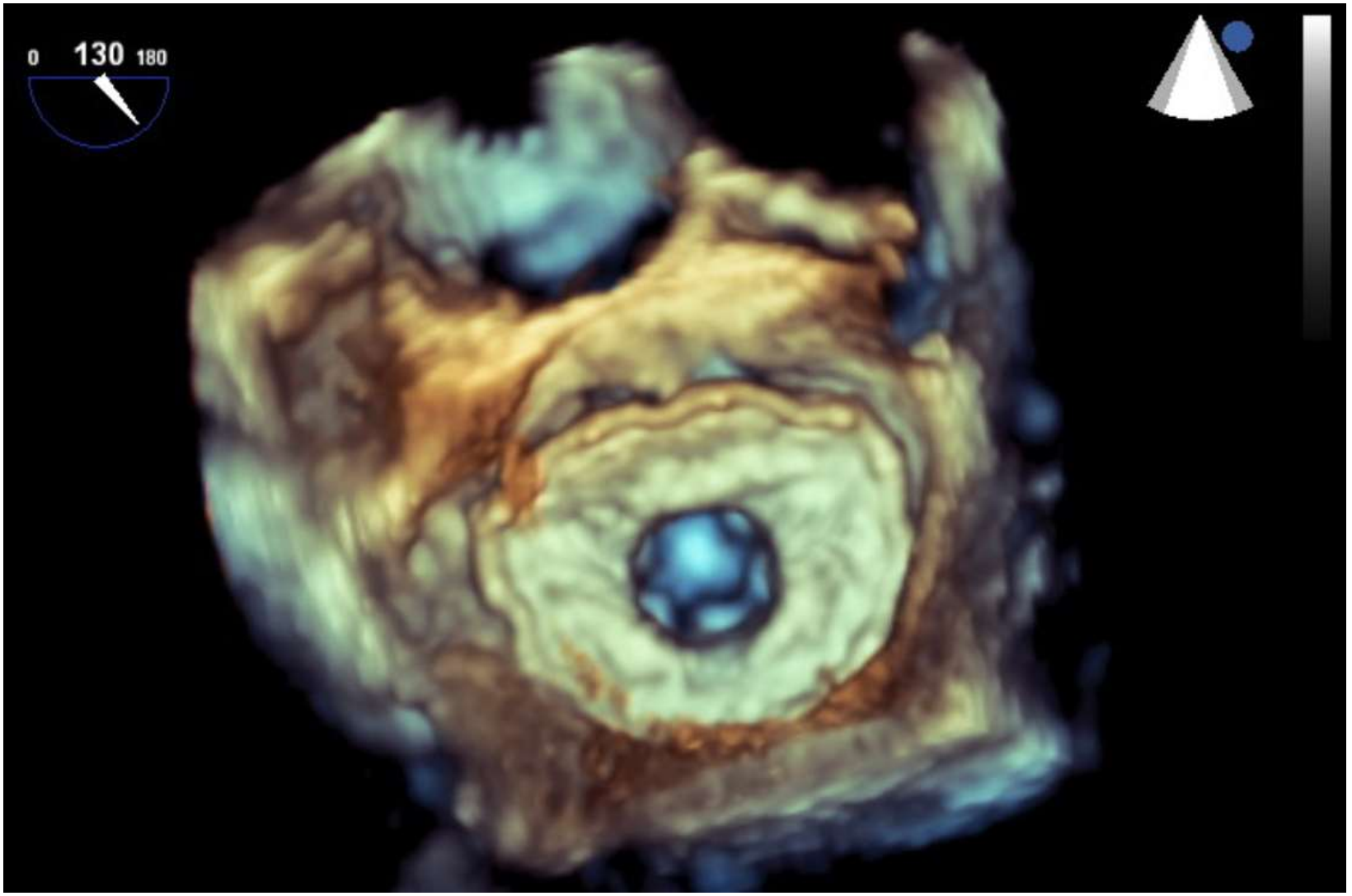
Images courtesy of N. Moat, A. Duncan, Royal Brompton

Device Rotated to Curtain



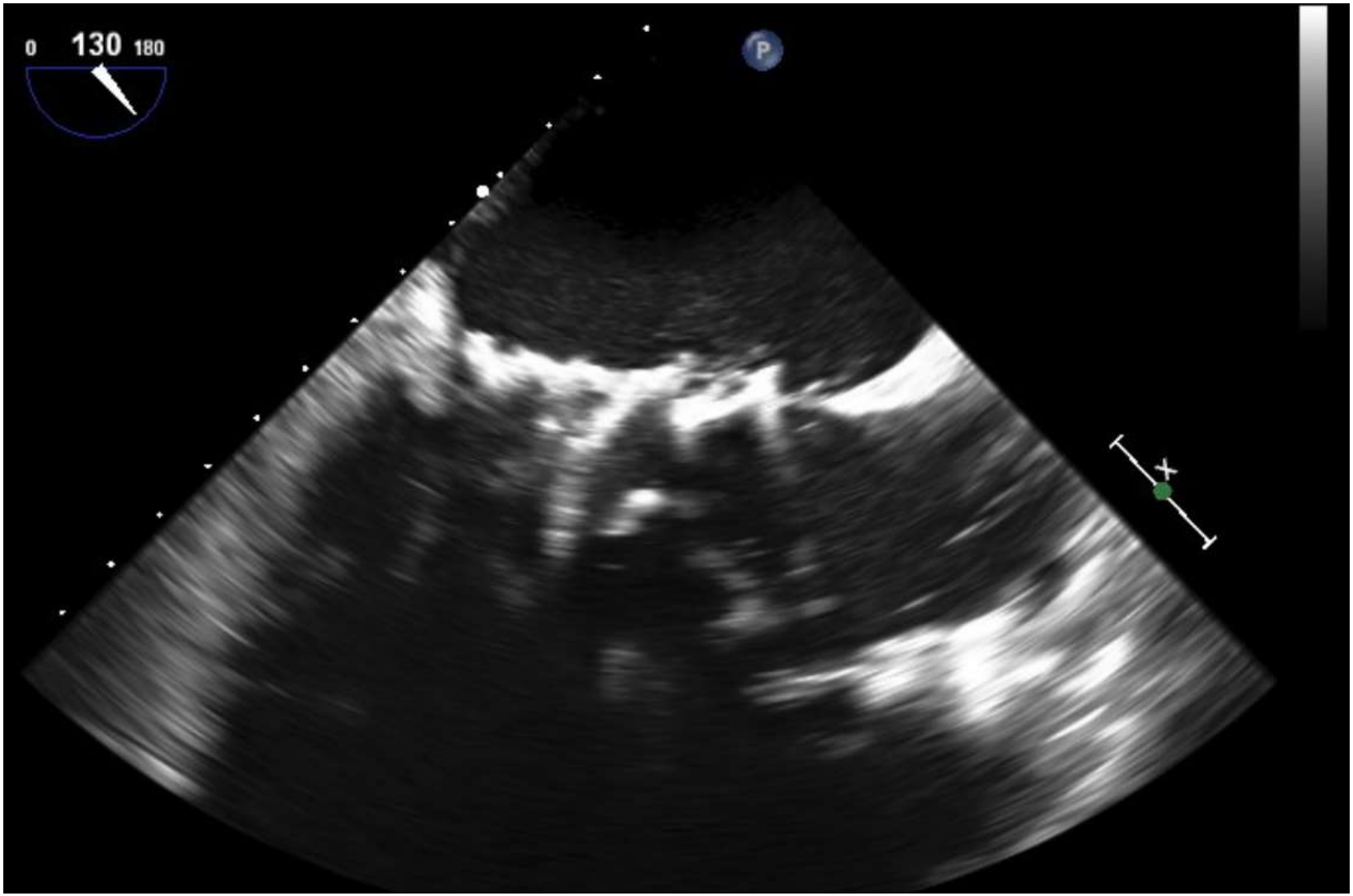
Images courtesy of N. Moat, A. Duncan, Royal Brompton

Device 3D EnFace View



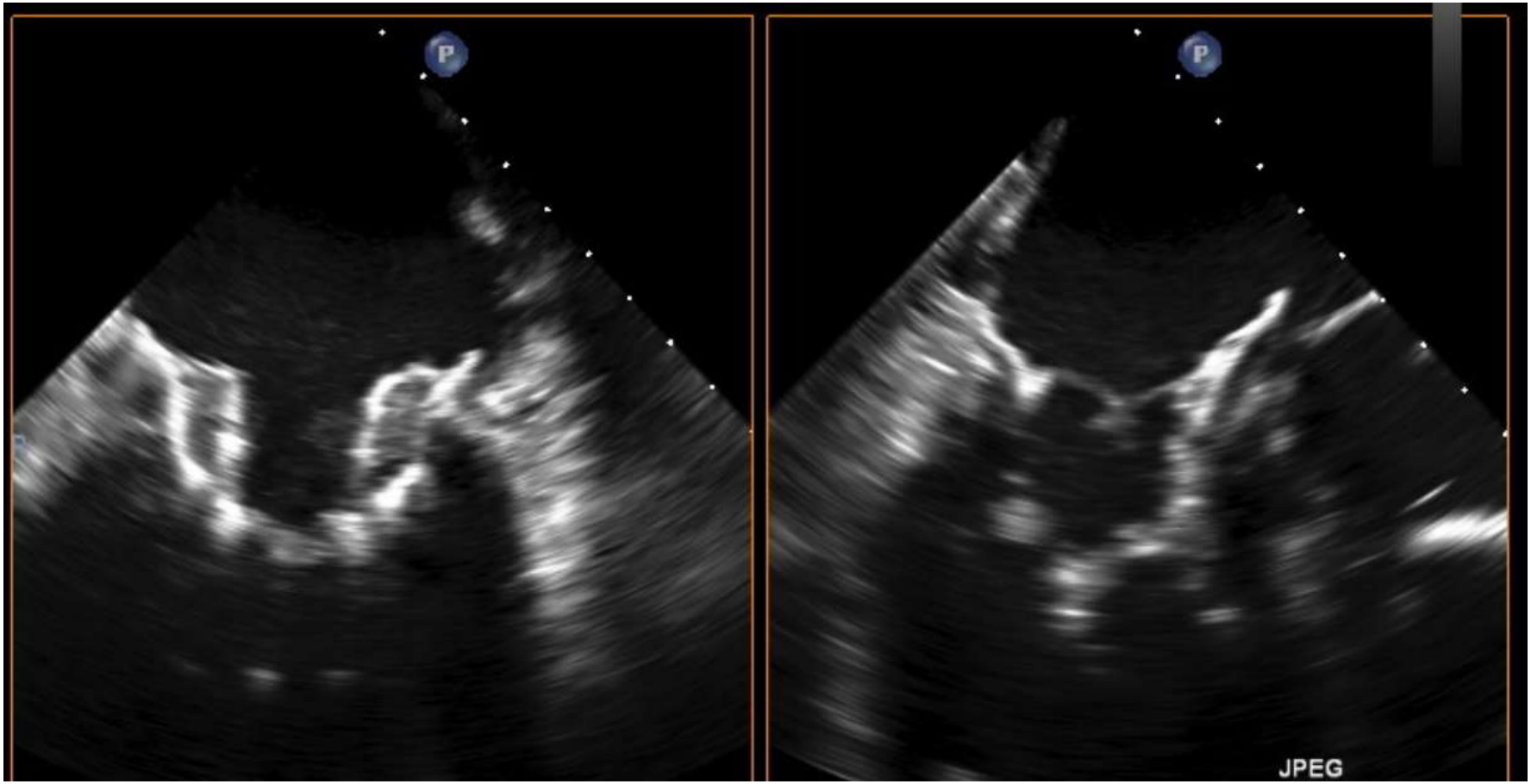
Images courtesy of N. Moat, A. Duncan, Royal Brompton

Device in Annulus LAX View



Images courtesy of N. Moat, A. Duncan, Royal Brompton

Device Deployed



Images courtesy of N. Moat, A. Duncan, Royal Brompton

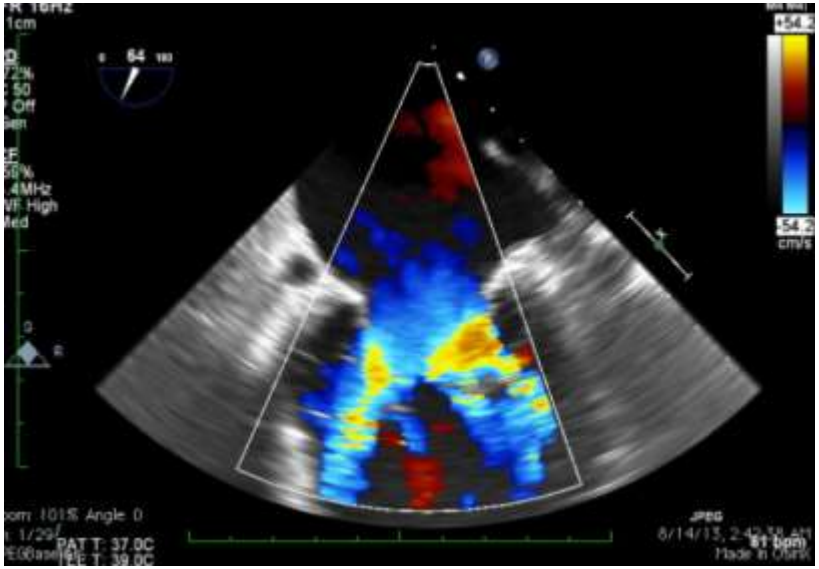
Tendyne Chronic Implantation

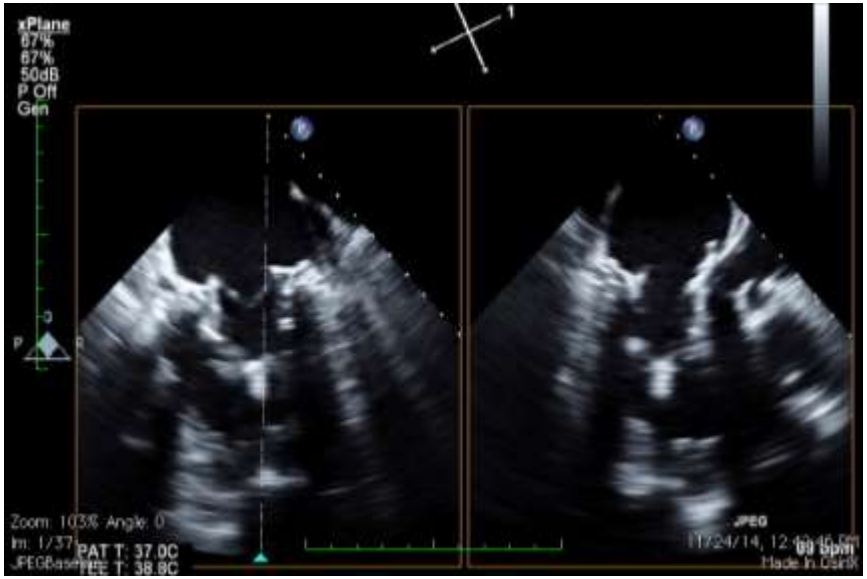
Tendyne Announces Successful First Human Implants of the Tendyne Transcatheter Mitral Valve Implant (TMVI)

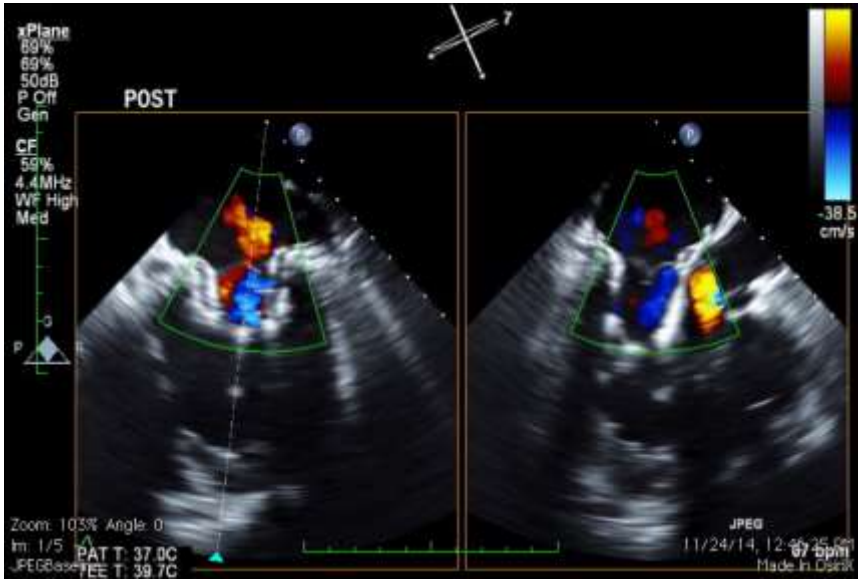
ROSEVILLE, Minn., Dec. 2, 2014 /PRNewswire/ -- Tendyne Holdings, Inc. ("Tendyne"), a privately held clinical stage medical device company, announced today that the Tendyne Transcatheter Mitral Valve system has been successfully implanted in three patients. Mr. Neil Moat, a leading expert in mitral valve surgery and TAVI, performed the procedures at the Royal Brompton Hospital in London, England under a compassionate use protocol in October and early November. The patients had severe mitral regurgitation that was eliminated after the procedure was performed via a trans-apical approach without cardio-pulmonary bypass (known as a trans-catheter mitral valve implantation, or TMVI).

- Begun October 2014
- 4 patients treated, all have been discharged from hospital to their own homes
- Results under review for publication and presentation at future international meeting.

Tendyne Chronic Implant 2014







Patient

- 75 y.o. Male
- Mod/Severe FMR
- Prior CABG, Moderately depressed LV Function
- Chronic Pulmonary Disease

TMVR: Current State

- Fortis
- NeoVasc Tiara
- CardiaQ
- Tendyne
- Medtronic
- Others