

**Good news and a challenge
for cardiac surgeons:
Can we definitively repair
ischemic MR?**

Robert A. Levine, M.D.

**Israel Working Groups in Echocardiography
and Cardiothoracic Surgery**

Ischemic Mitral Regurgitation

Definition and mechanism

Good news about prognosis

**Good news and a challenge for
repair**

Ischemic Mitral Regurgitation

Definition and mechanism

Good news about prognosis

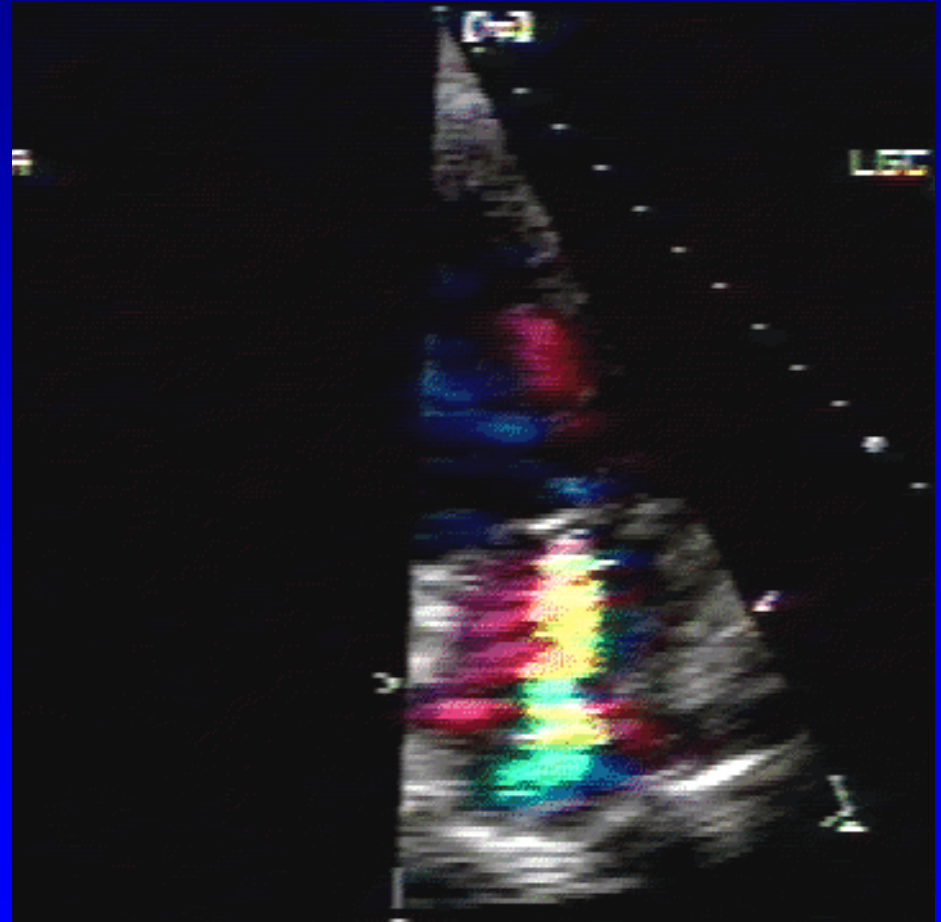
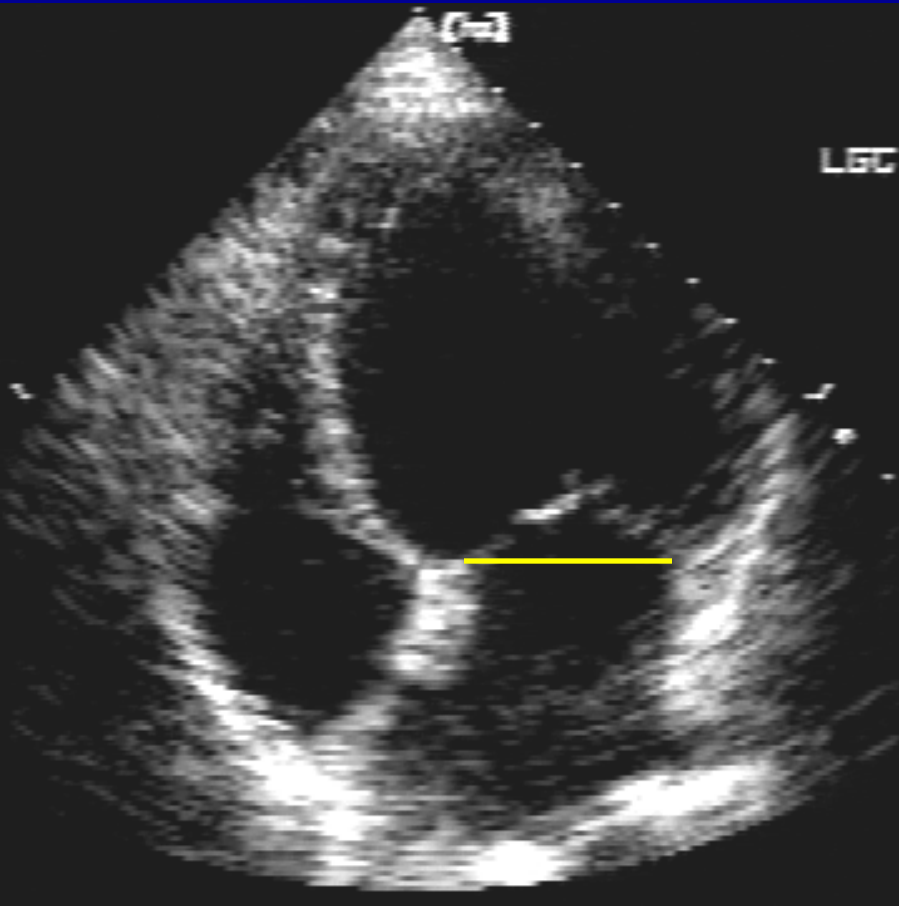
**Good news and a challenge for
repair**

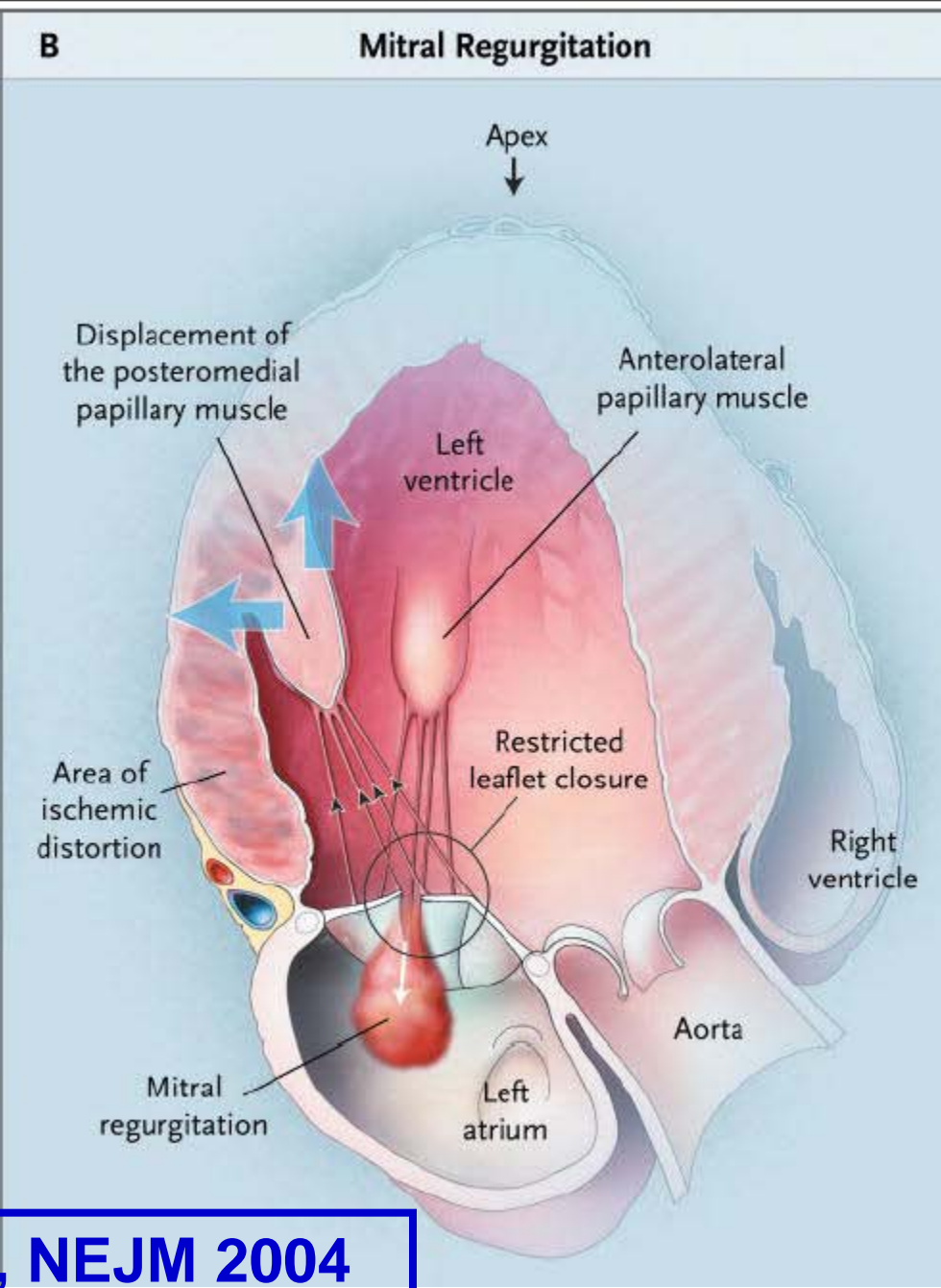
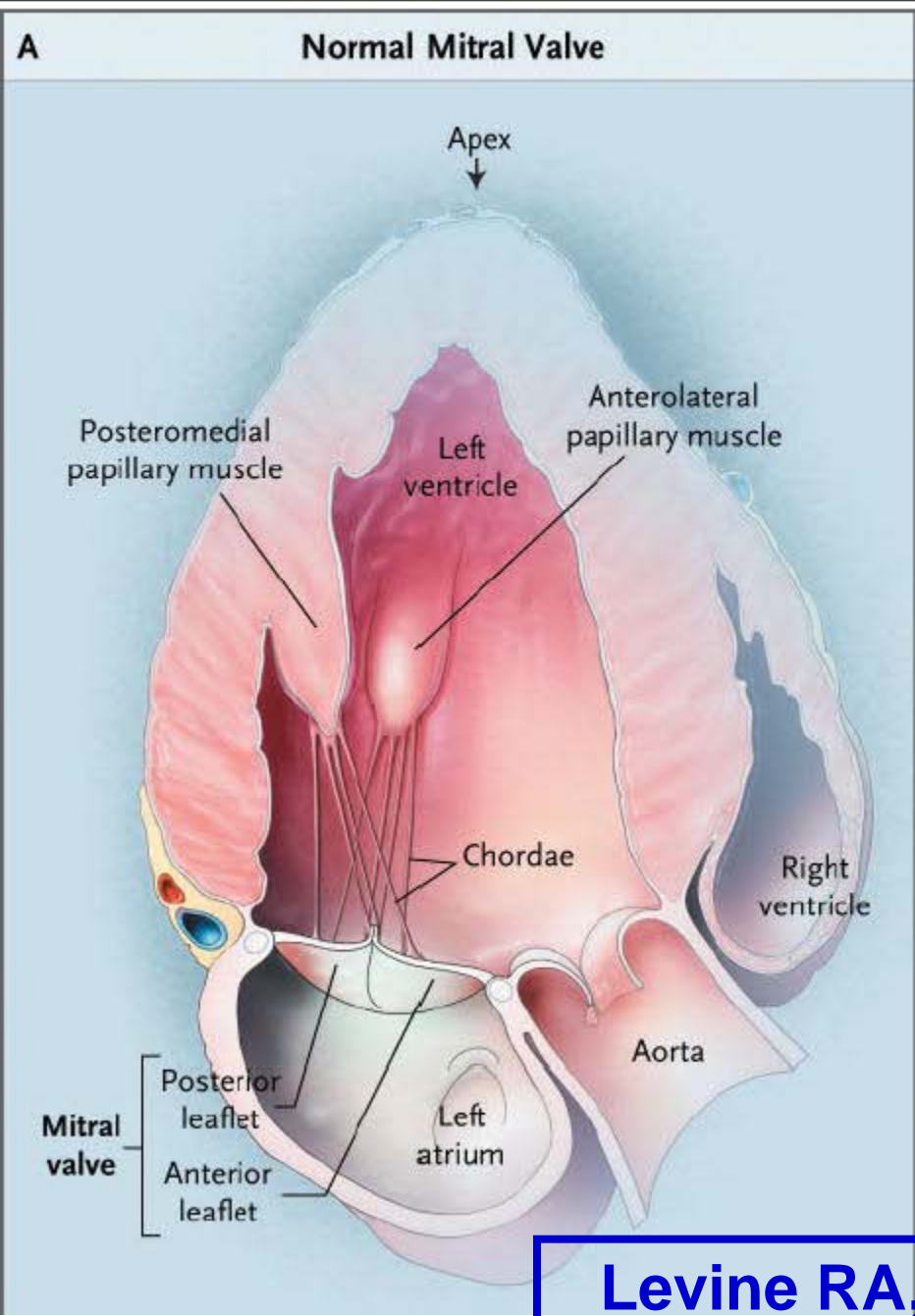
ISCHEMIC MITRAL REGURGITATION

- **Predominantly postinfarction MR caused ultimately by ischemia.**
- **Functional MR: Normal leaflets, abnormal function.**

Incomplete mitral leaflet closure

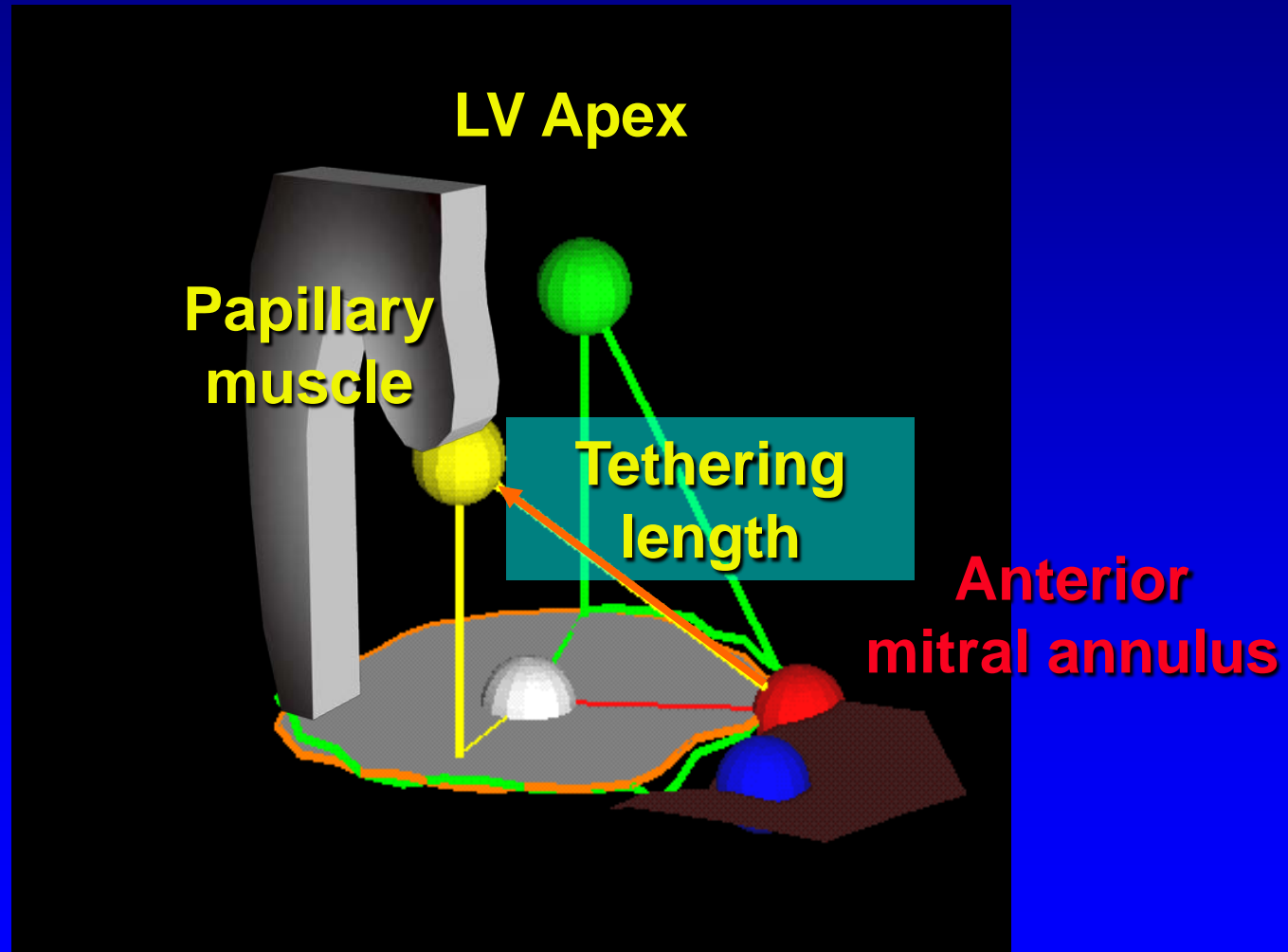
Apical displacement of the mitral leaflets





Levine RA, NEJM 2004

Tethering Distances Between Papillary Muscles and Anterior Mitral Annulus



2D tethering length: Yiu and Sarano

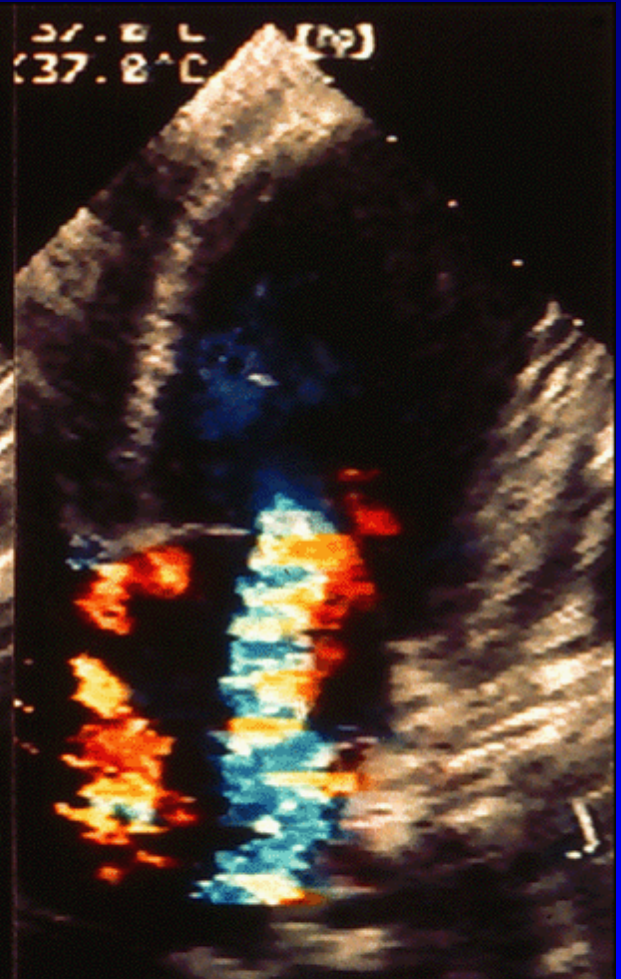
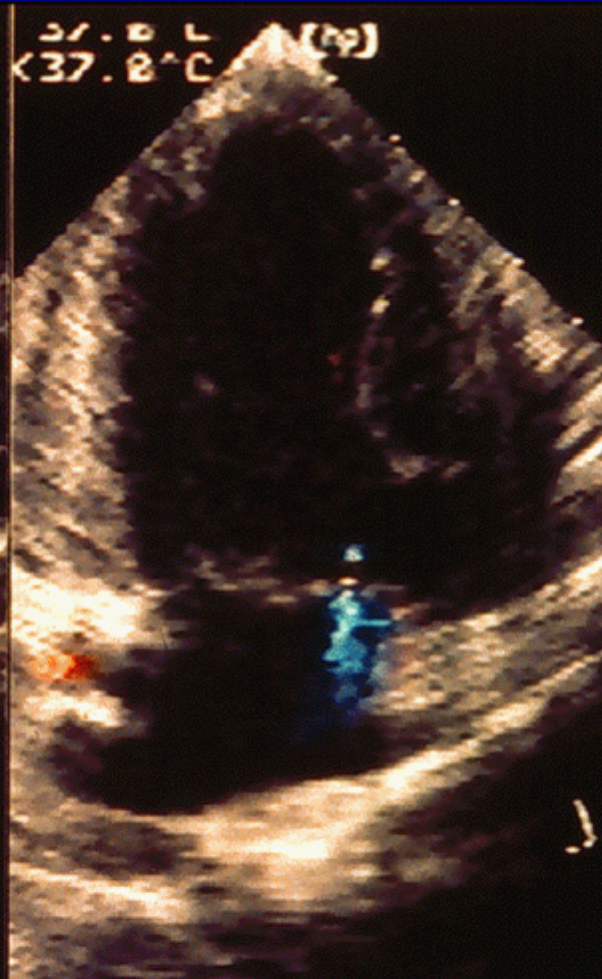
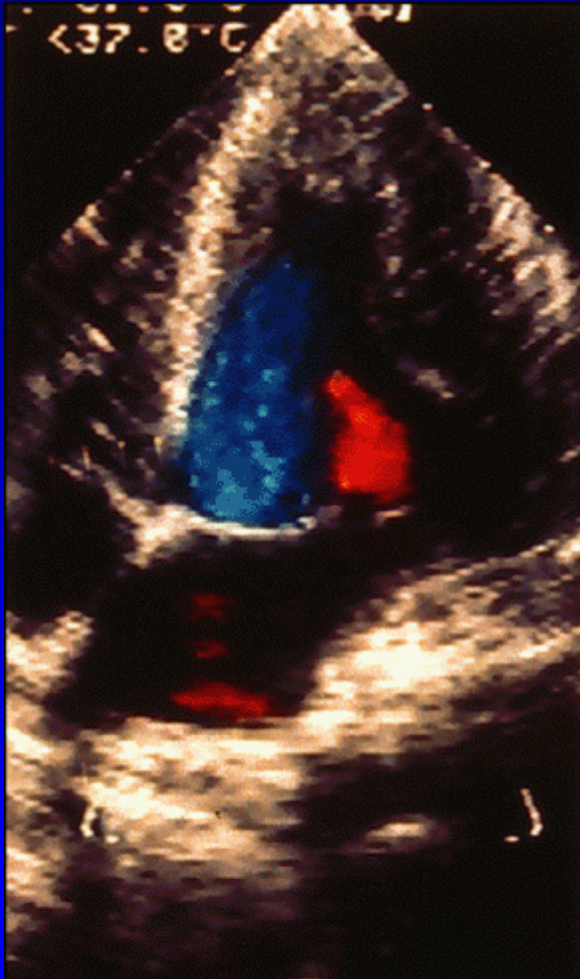
EHUD SCHWAMMENTHAL

**Chaim Sheba Medical Center,
Tel Ha-shomer, Israel**

Baseline

**LV dysfunction
- dilation**

**LV dysfunction
+ dilation**



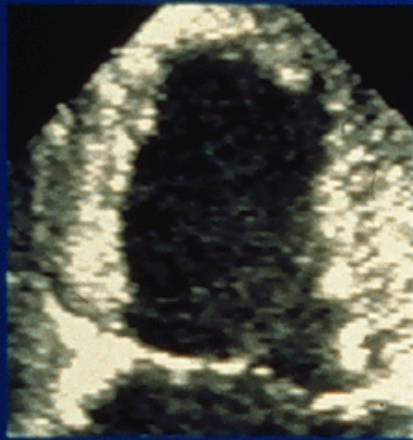
**YUTAKA OTSUJI Circ. 2007
MARK HANDSCHUMACHER
EHUD SCHWAMMENTHAL**

NOAH LIEL-COHEN

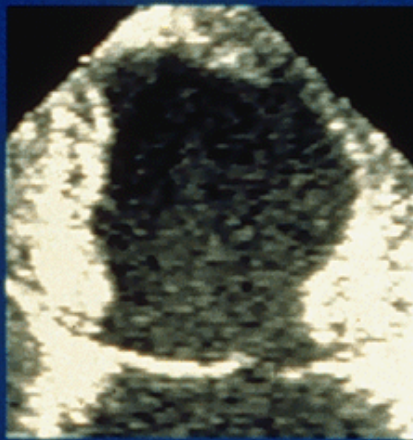
**Soroka Medical Center,
Ben-Gurion University,
Beer Sheva, Israel**

SEGMENTAL DYSFUNCTION: Progression of MR

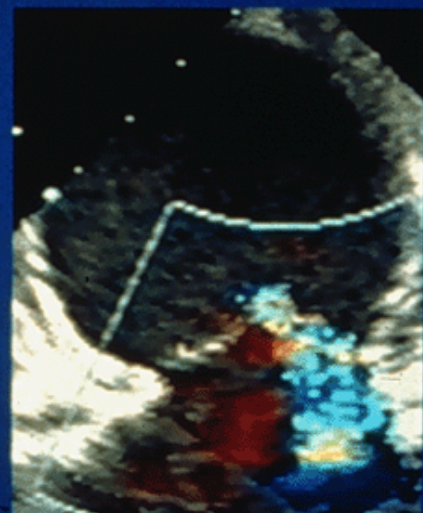
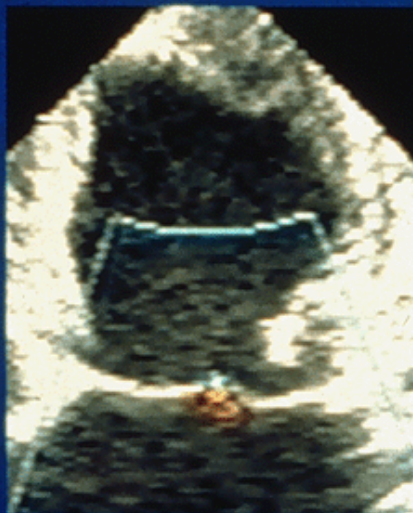
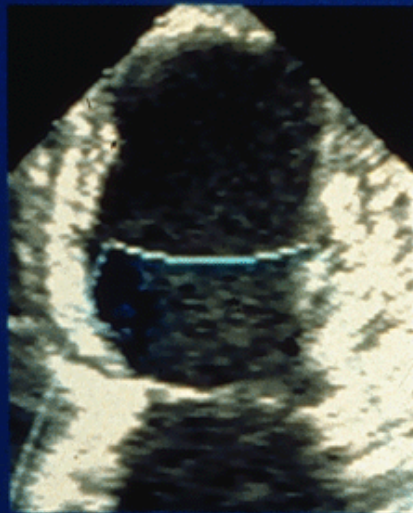
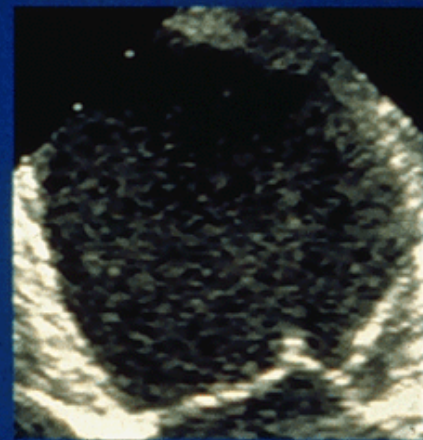
Baseline



Acute MI



Chronic MI



NOAH LIEL-COHEN, YUTAKA OTSUJI

**Primacy of tethering: No MR if low
EF but no dilatation in patients**

DAN GILON

**Hadassah University Hospital
Hebrew University
Jerusalem, Israel**

Primacy of tethering: TR and tethering geometry in patients

**ALIK SAGIE
and MOTI VATURI**

**Rabin Medical Center, Petach
Tikvah, Israel**

CHAIM YOSEFY

**Barzilai Medical Center,
Ben-Gurion University,
Ashkelon, Israel**

Circulation 2010

MI: 1.0 TIS: 1.1

S3

03 NOV 10

09:59:46

2/0/C/M2/A

MGH # 7

MGH

CA 0482690

0482690

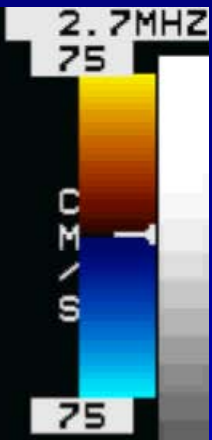
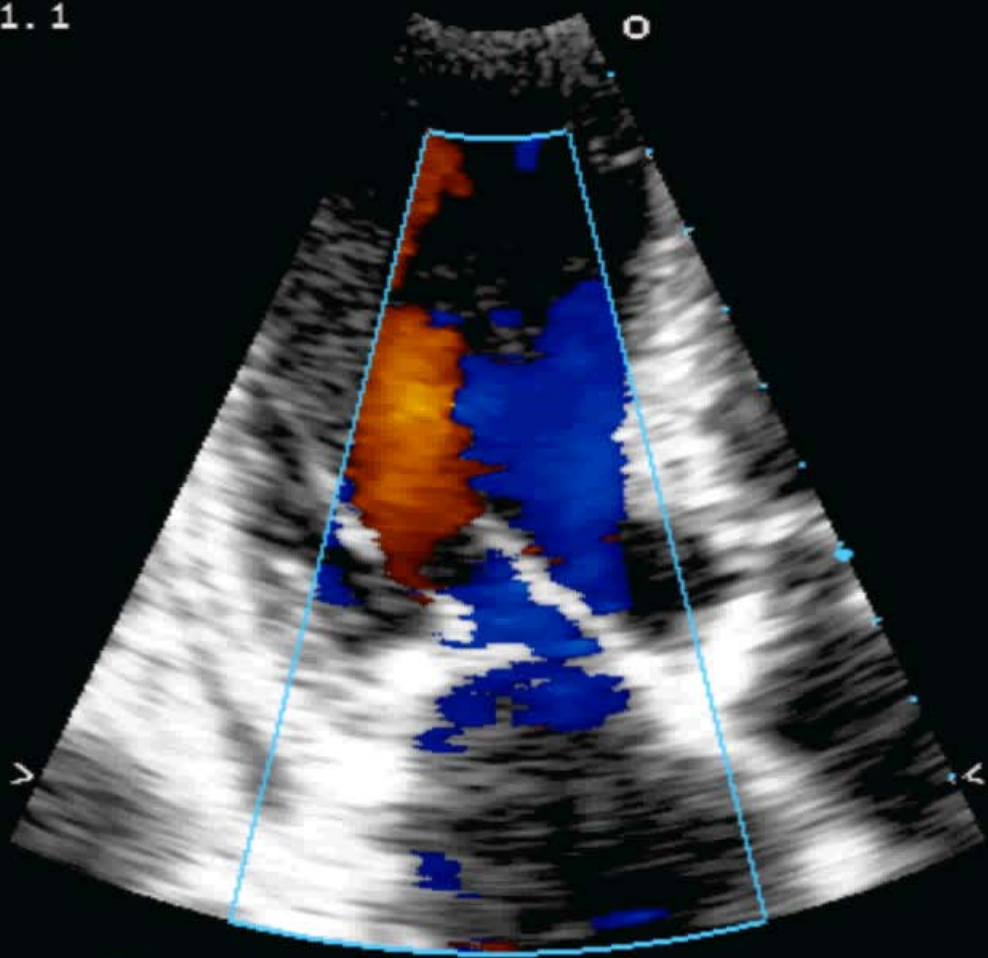
GAIN 62

COMP 37

75BPM

14CM

25HZ



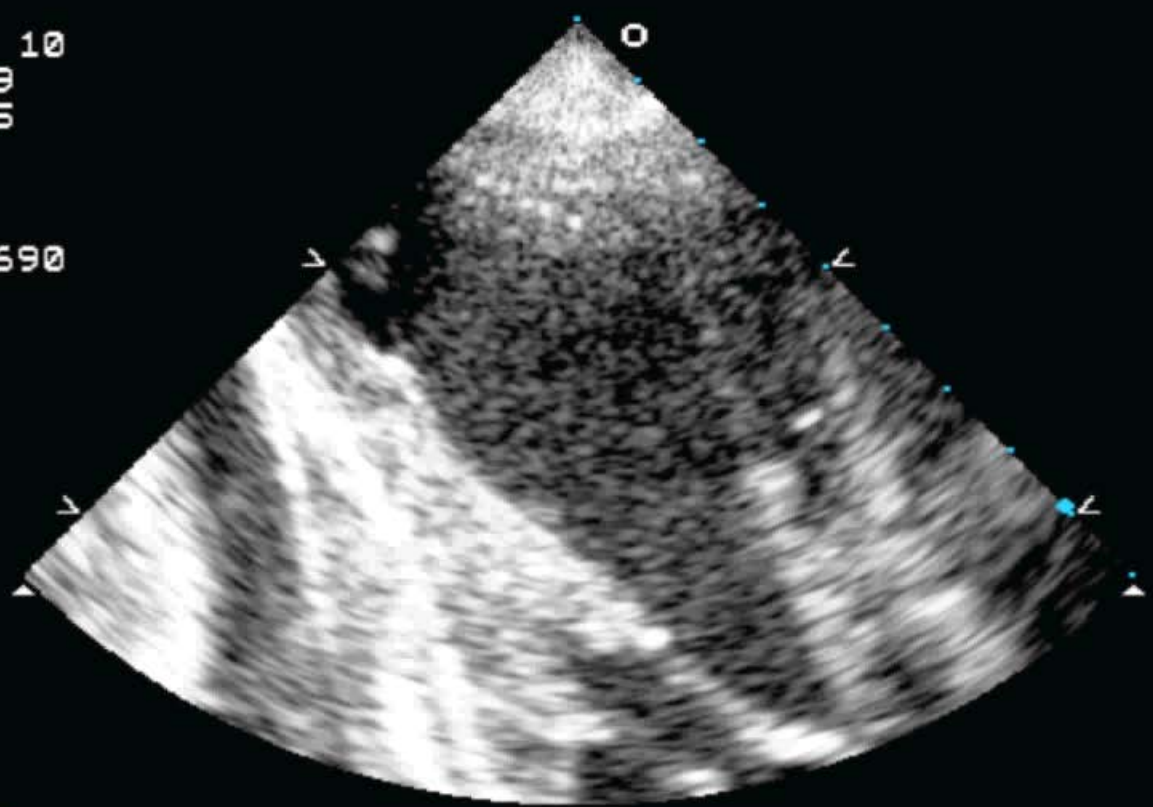
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CA 0482690

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GAIN 62
COMP 37
73BPM

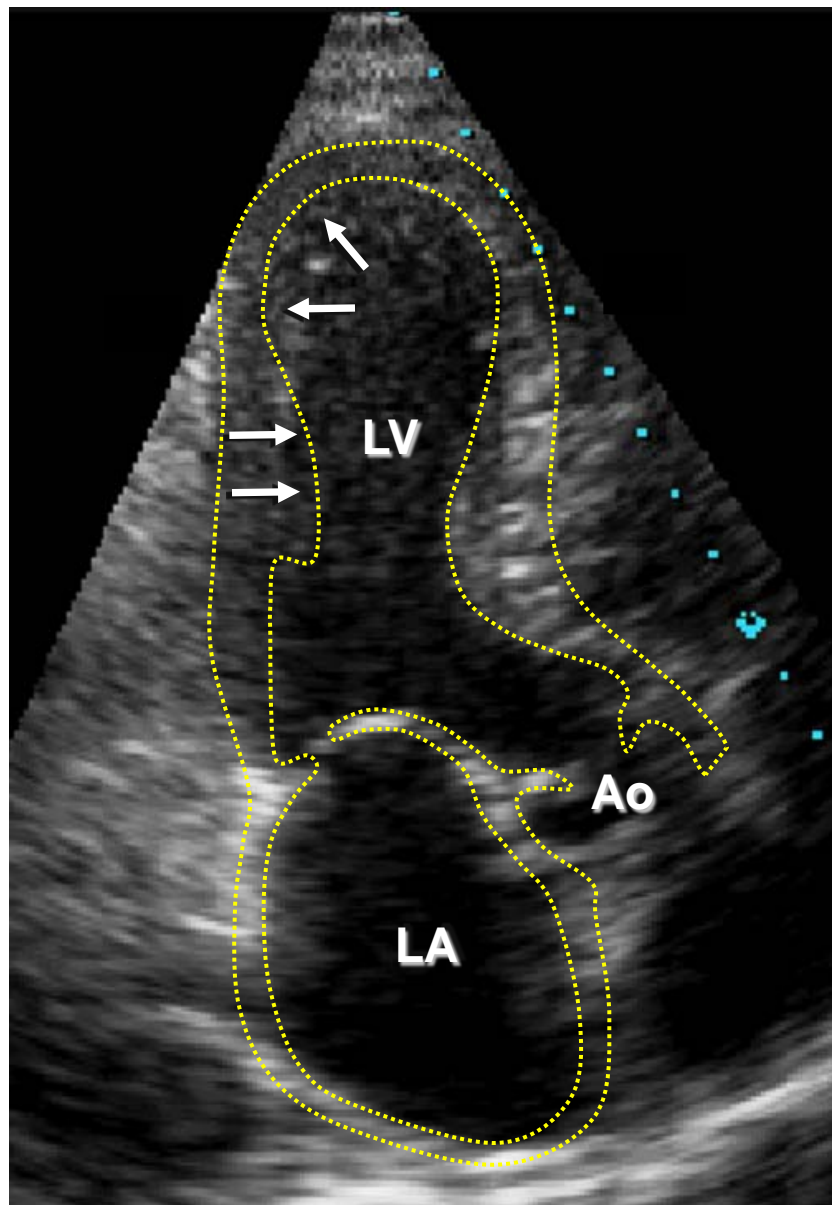
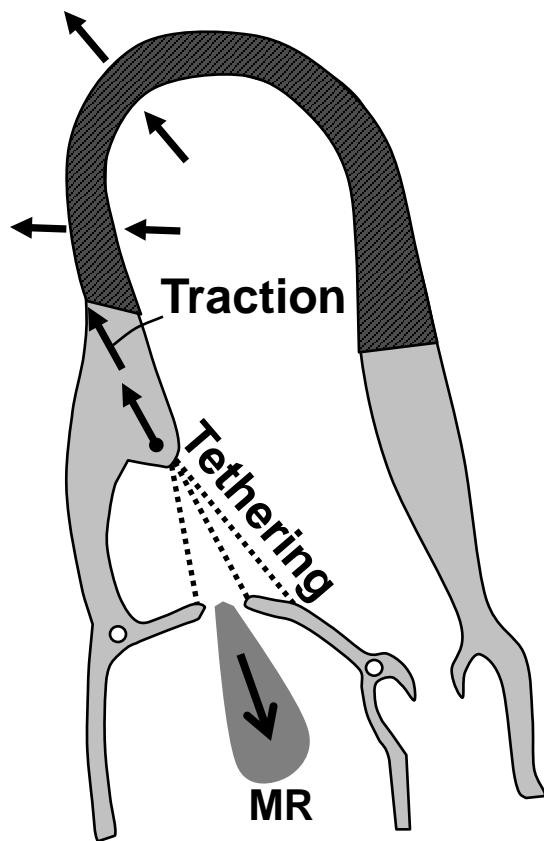
9CM
40HZ



P \triangle T \oplus
1.6 3.2



Patient with Apical MI and MR



Ischemic Mitral Regurgitation

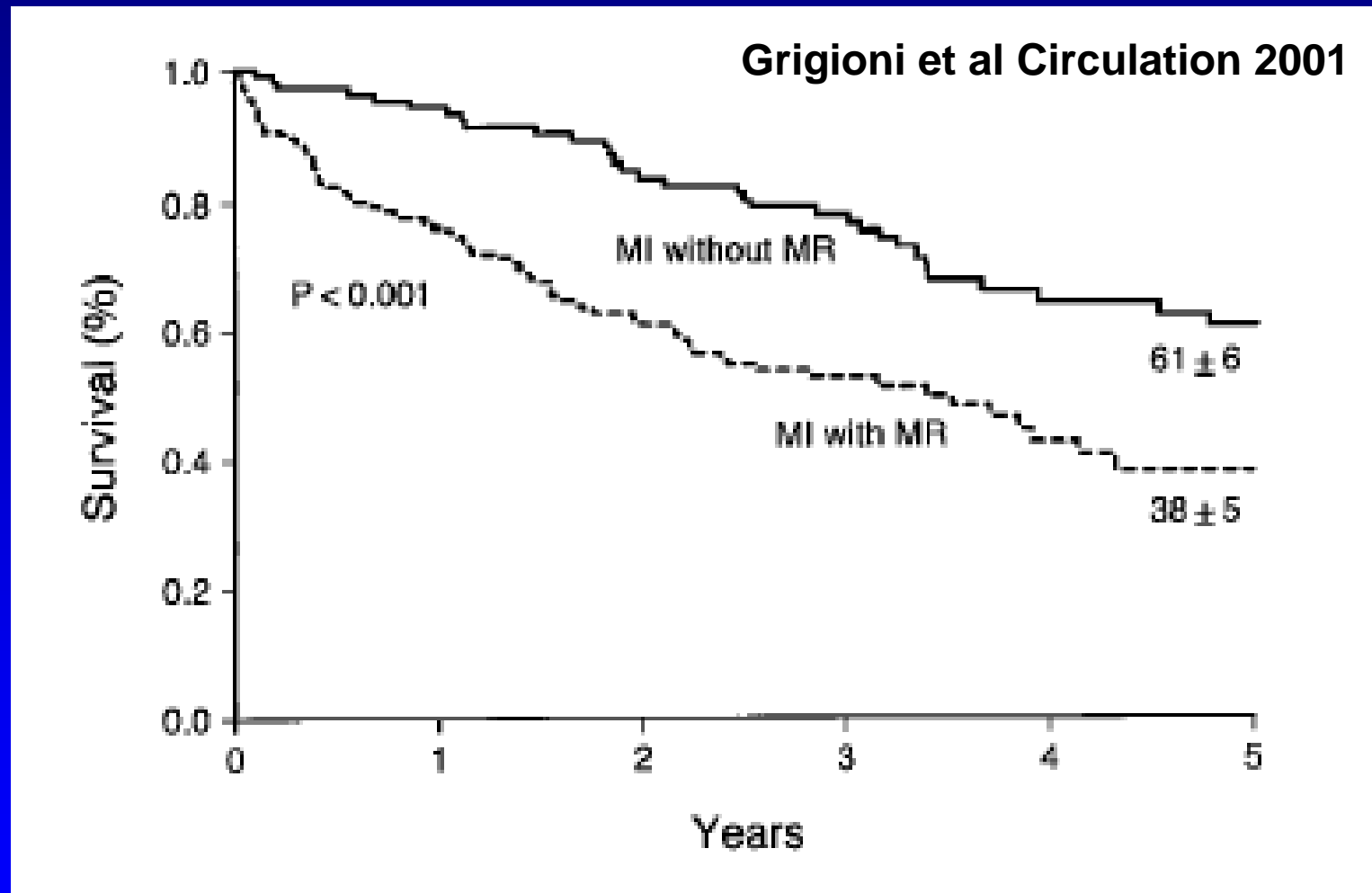
Definition and mechanism

Good news about prognosis

**Good news and a challenge for
repair**

MAURICE SARANO

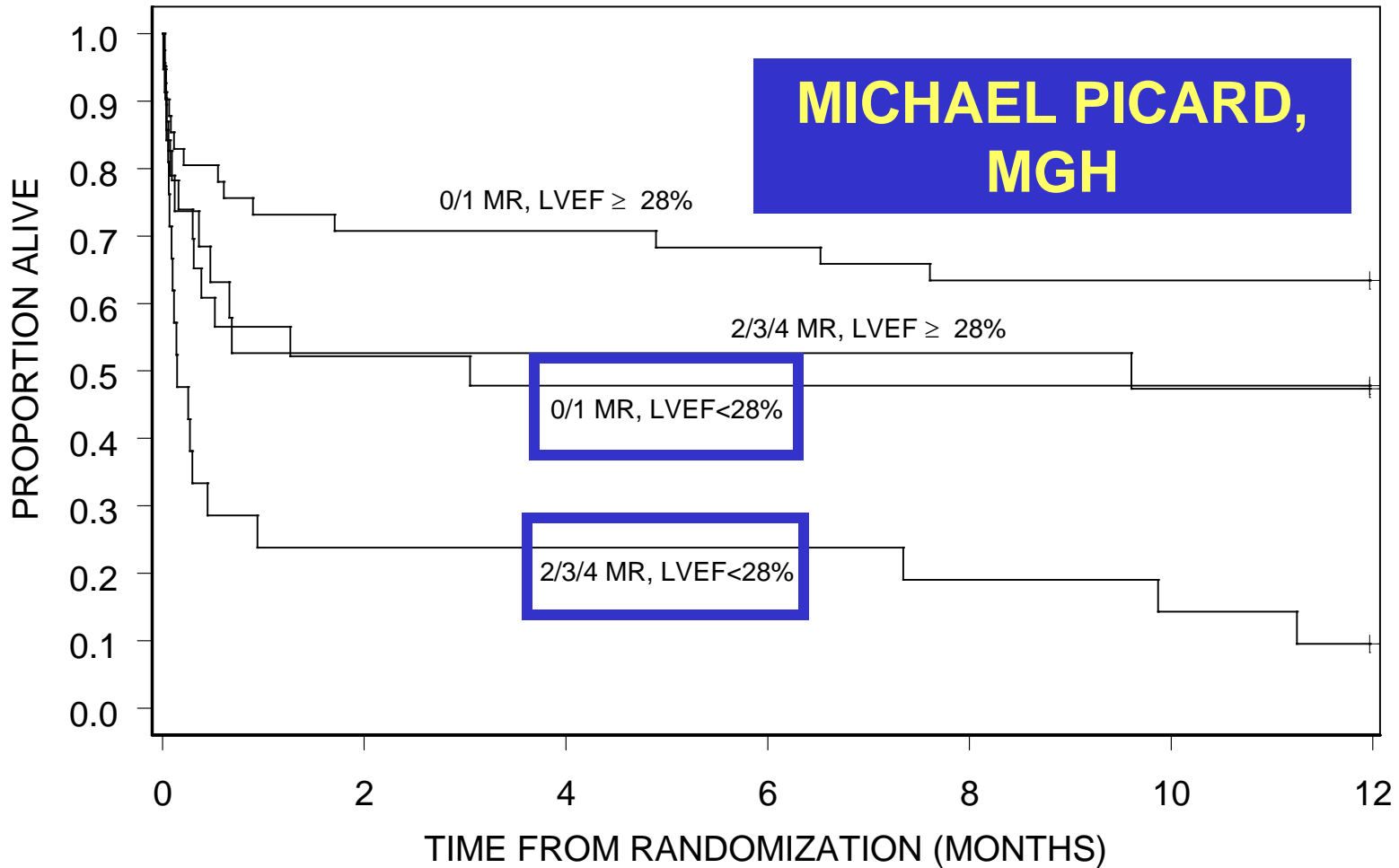
Mayo Clinic, Minnesota



MR decreases survival post infarction

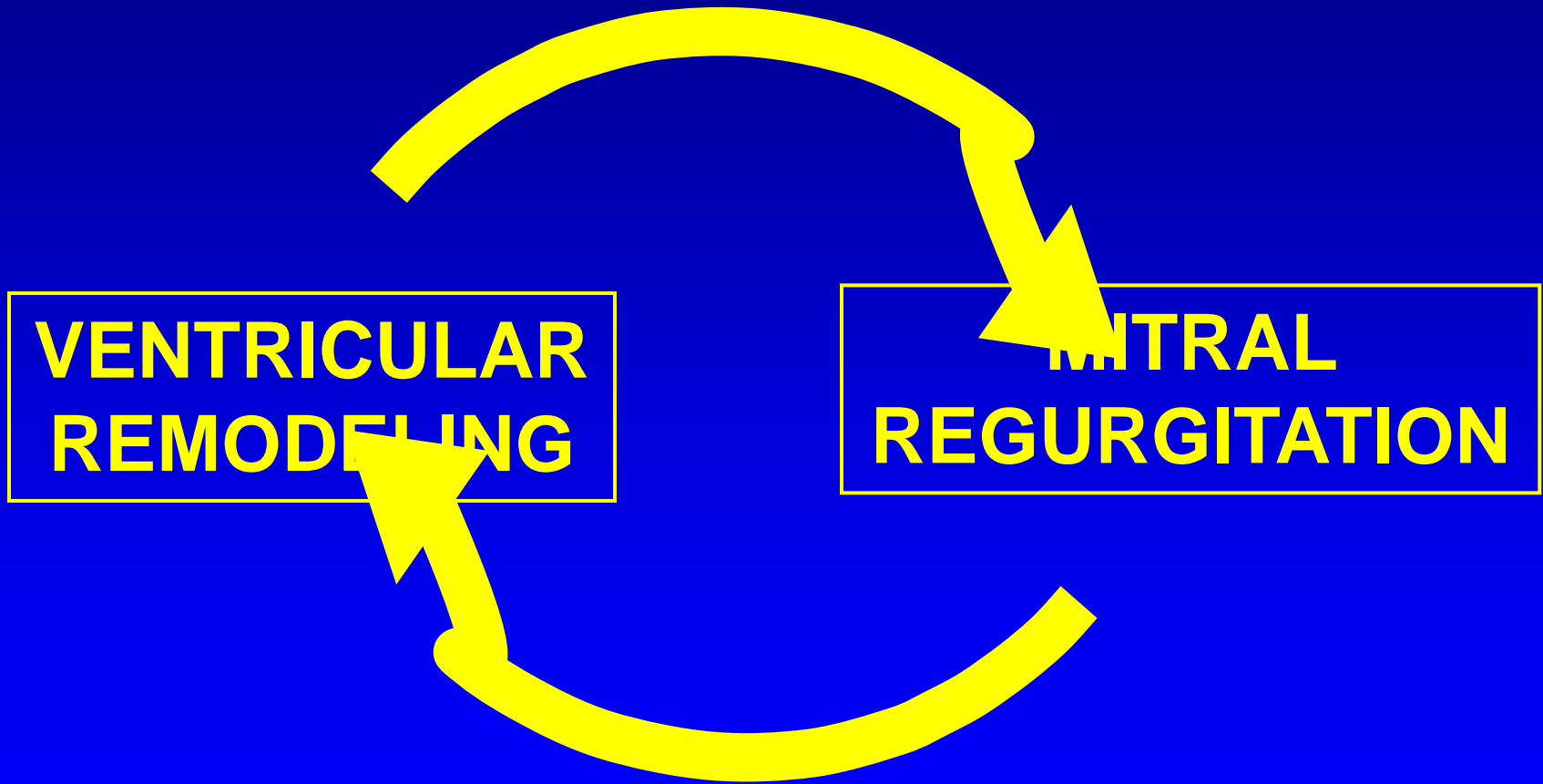


SHOCK Trial: Kaplan-Meier survival based on independent effects of MR and LVEF



Circulation 2003;107:279-284

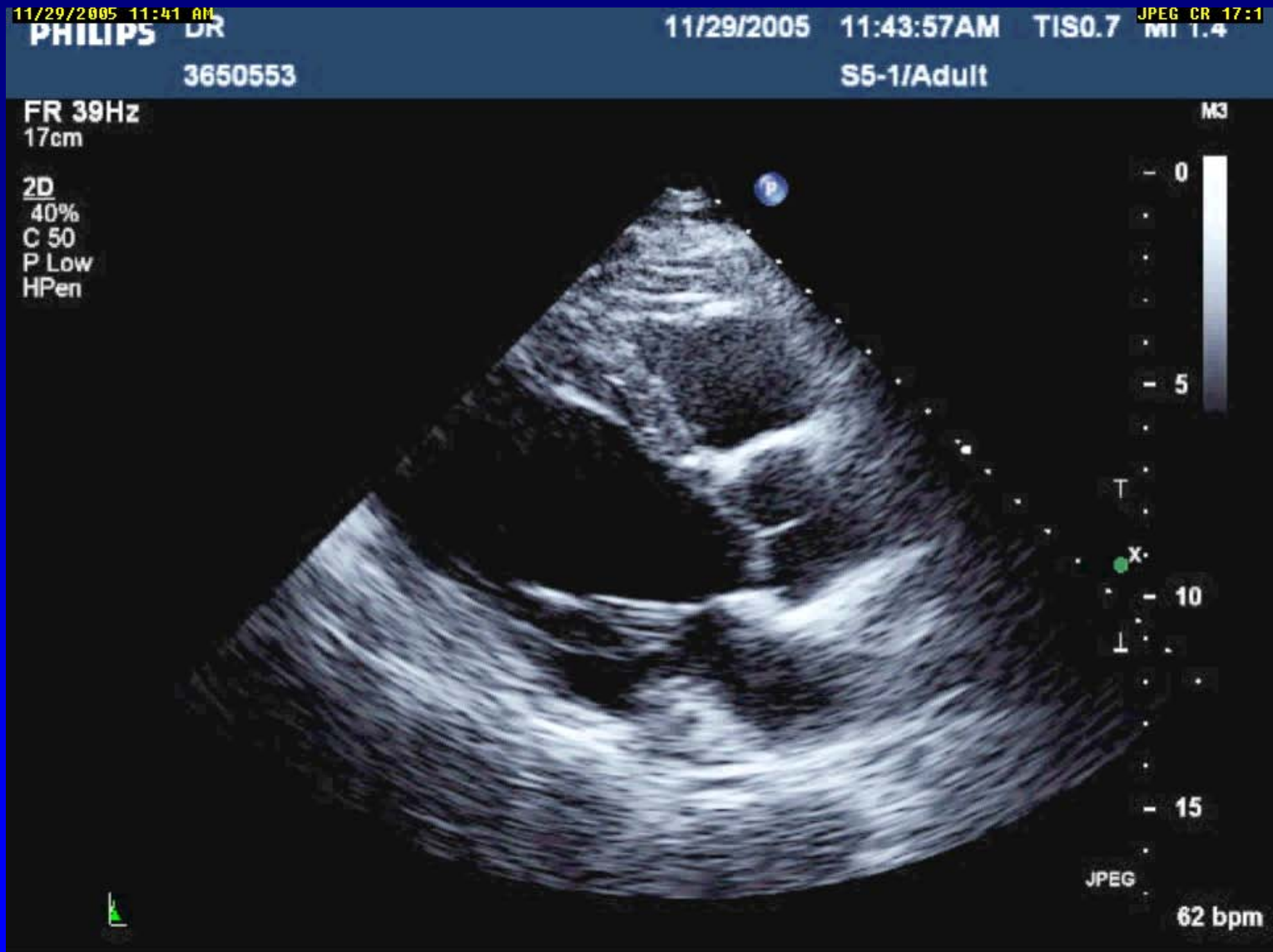
REMODELING AND MR: A VICIOUS CYCLE



Case 1: Why repair ischemic MR?

- 72 year-old man**
- Long history of CAD, old inferior MI**
- Gradually increasing exertional dyspnea over 5 years, no new MI**

2005



2010



2005

11/29/2005 11:41 AM

PHILIPS DR

11/29/2005

11:46:52AM

TIS2.3

JPEG CR 20:1

MI 1.2

3650553

S5-1/Adult

FR 22Hz
17cm

2D
38%
C 50
P Low
HPen
CF
67%
2.5MHz
WF High
Med

M3 M1
+63.9

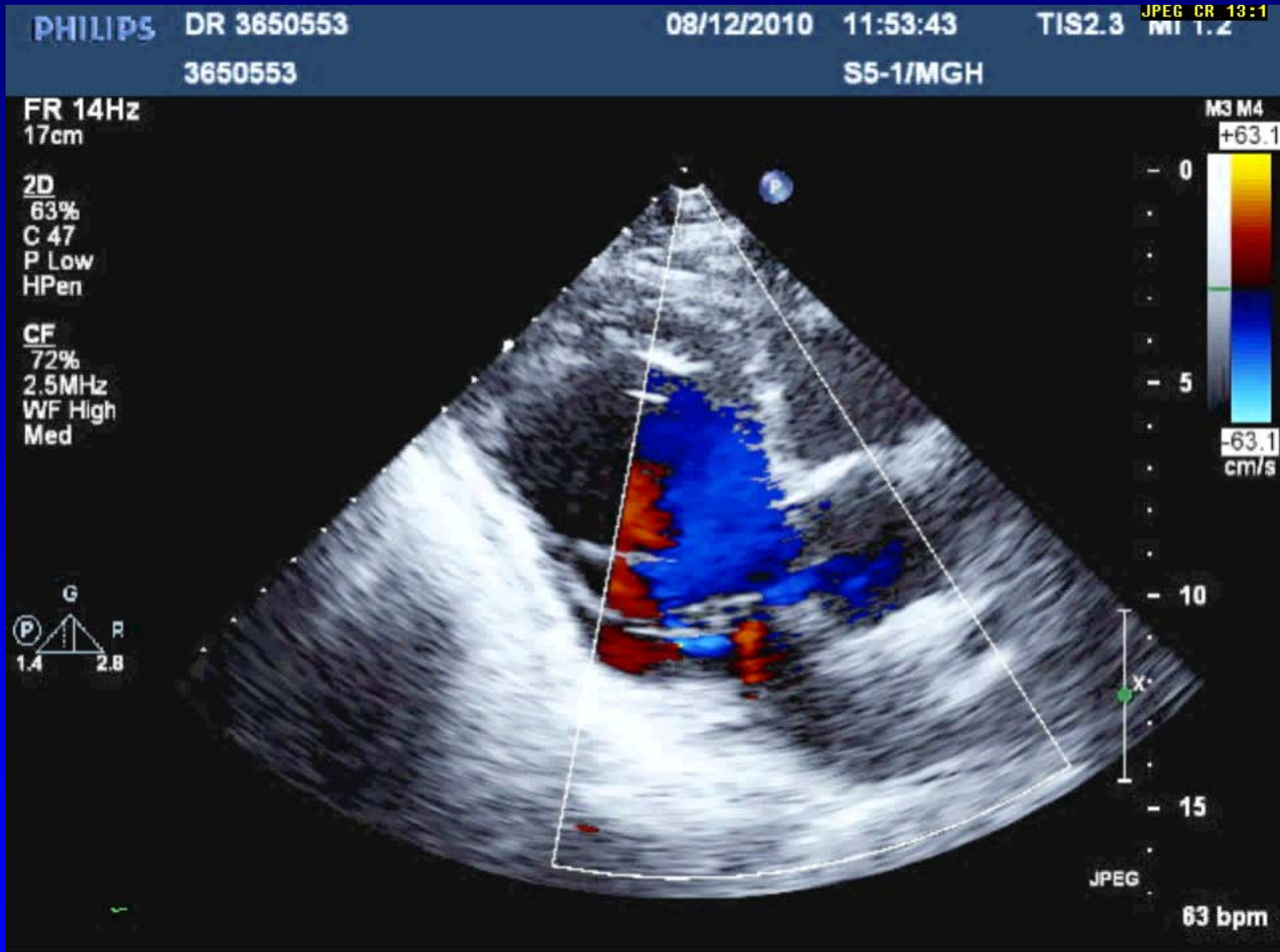


T
x
10
15

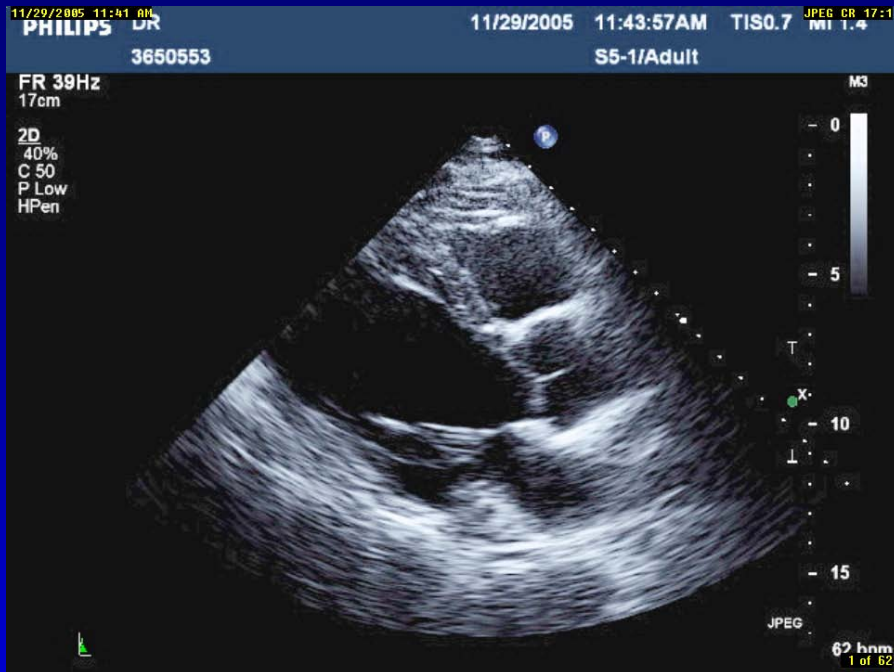
JPEG

63 bpm

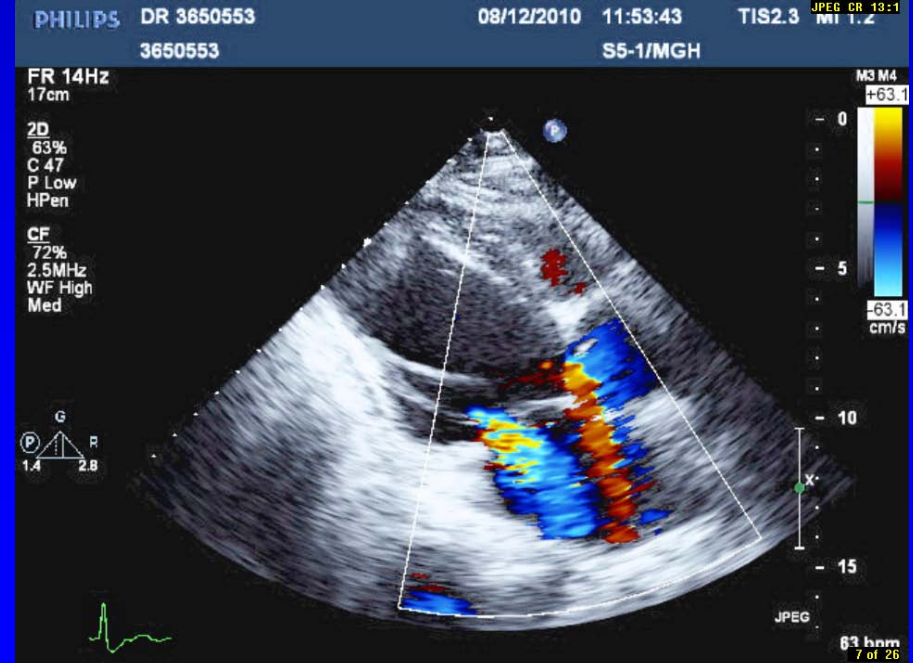
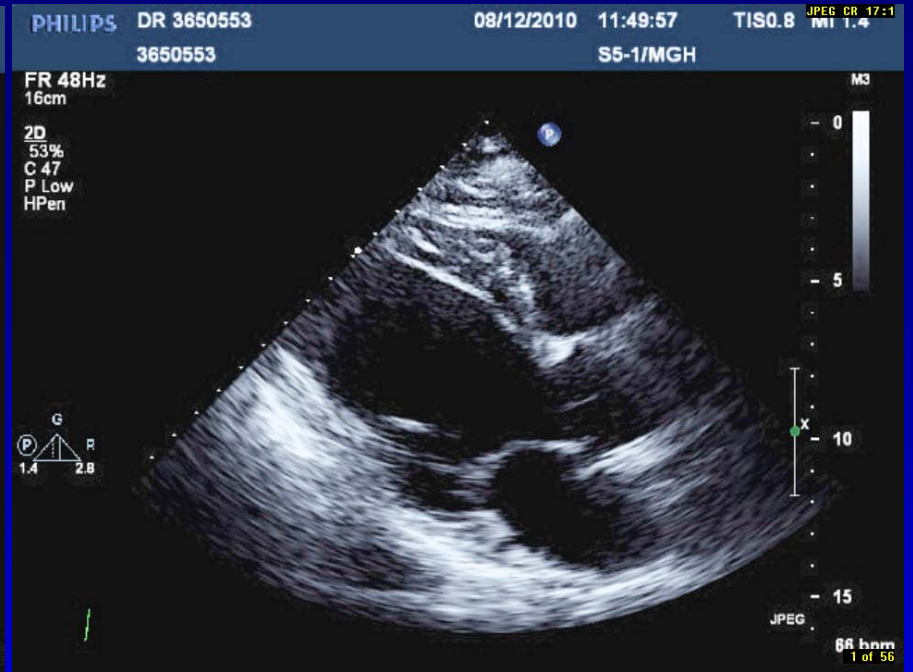
2010



2005



2010



LV remodeling (dilatation and dysfunction) occurs independent of new MIs

MR creates more MR as the LV remodels

**How can we separate the
effects of MR and MI?**

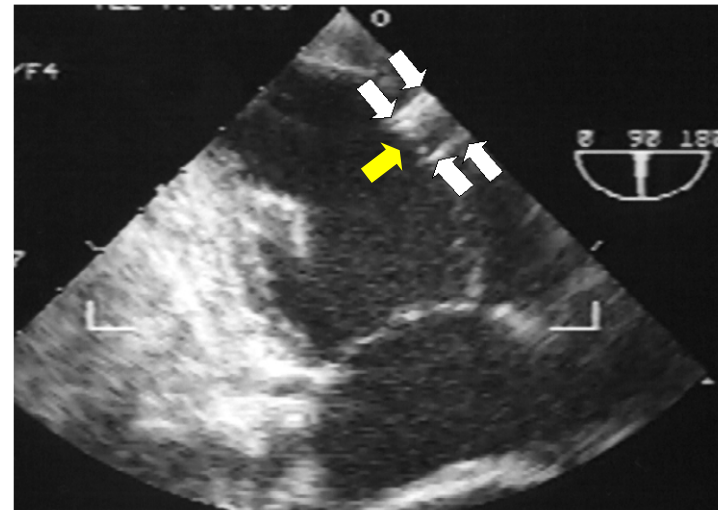
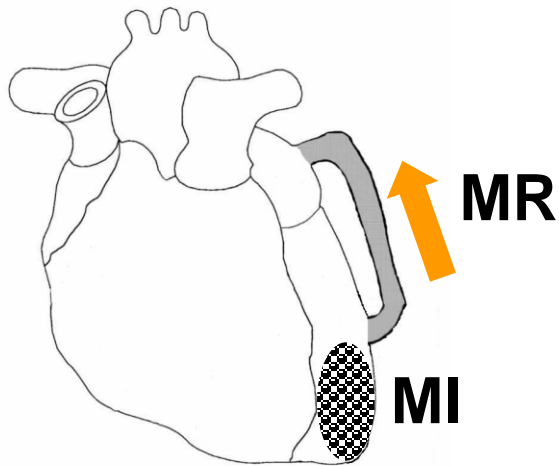
RONEN BEERI

ROGER HAJJAR

Circulation 2007; JACC 2008

**Hadassah University Hospital
Massachusetts General Hospital**

INDEPENDENT MR AND MI: APICAL MI AND LV-TO-LA SHUNT



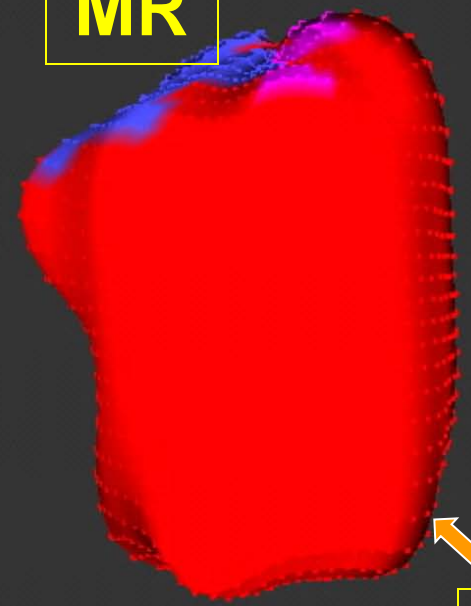
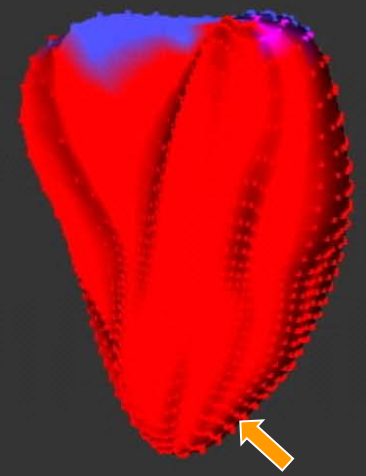
No MR

MR

Diastole

A

C



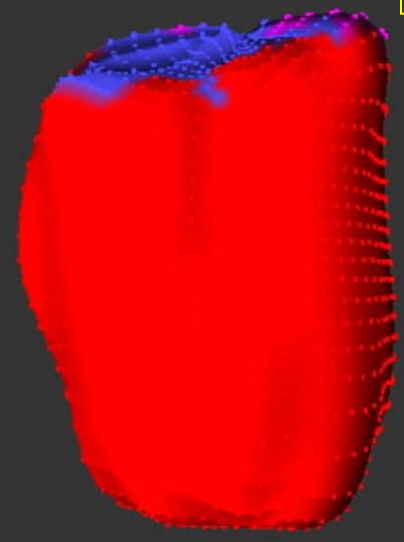
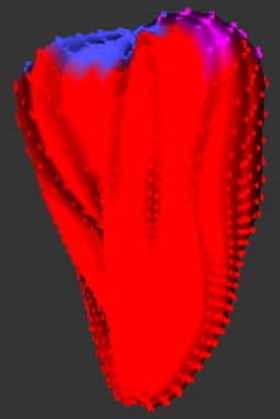
MI

MI

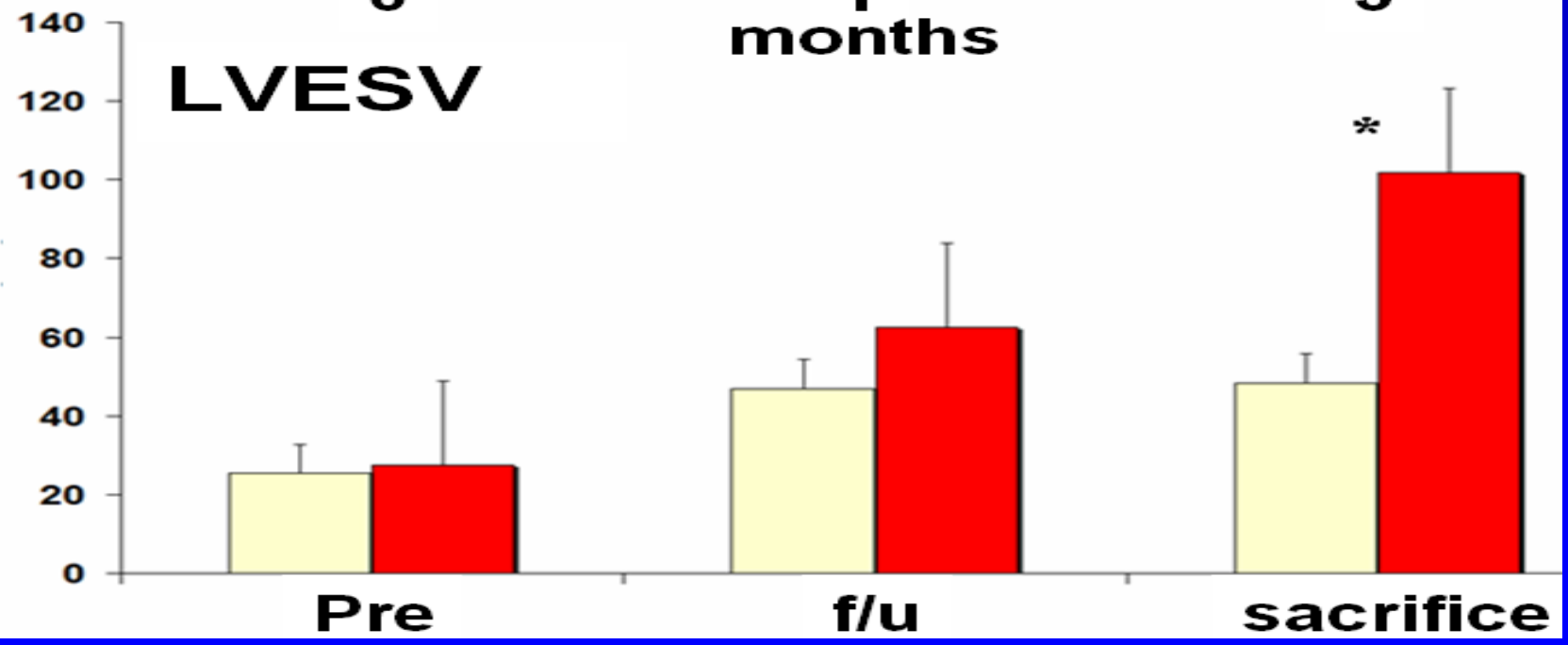
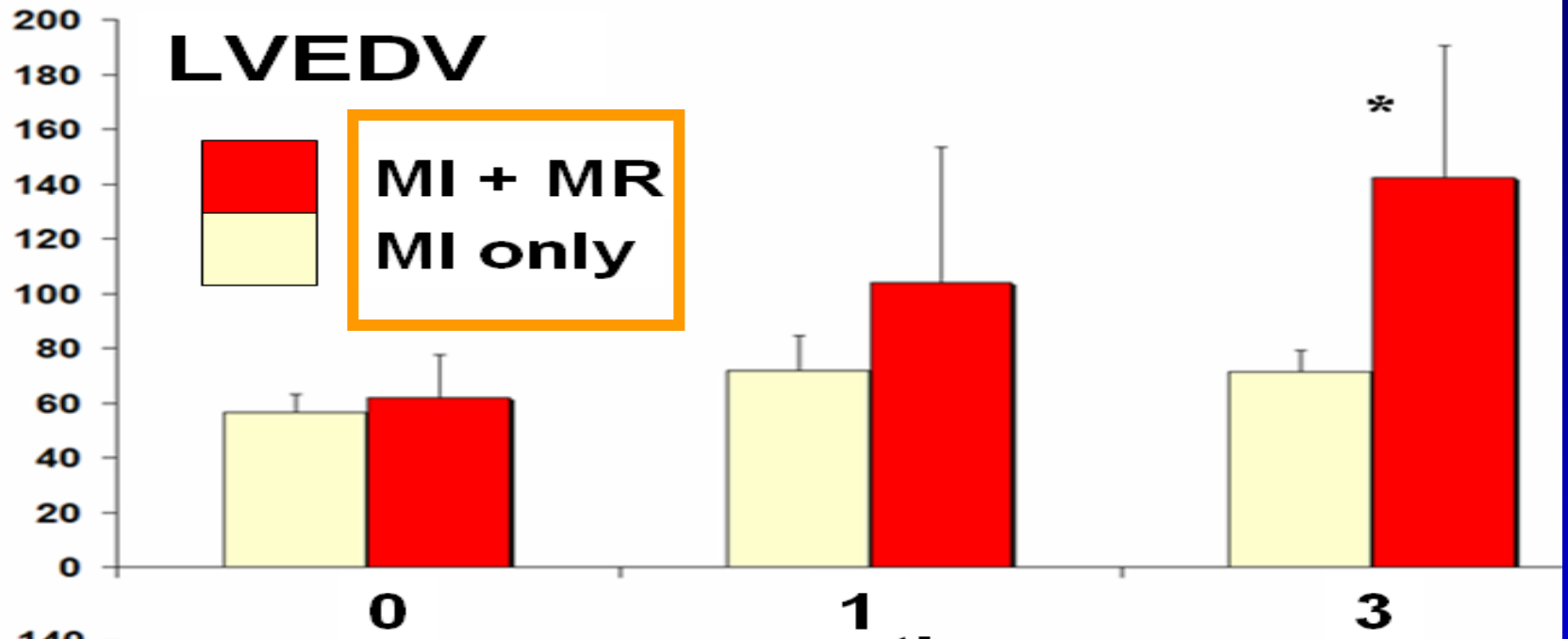
Systole

B

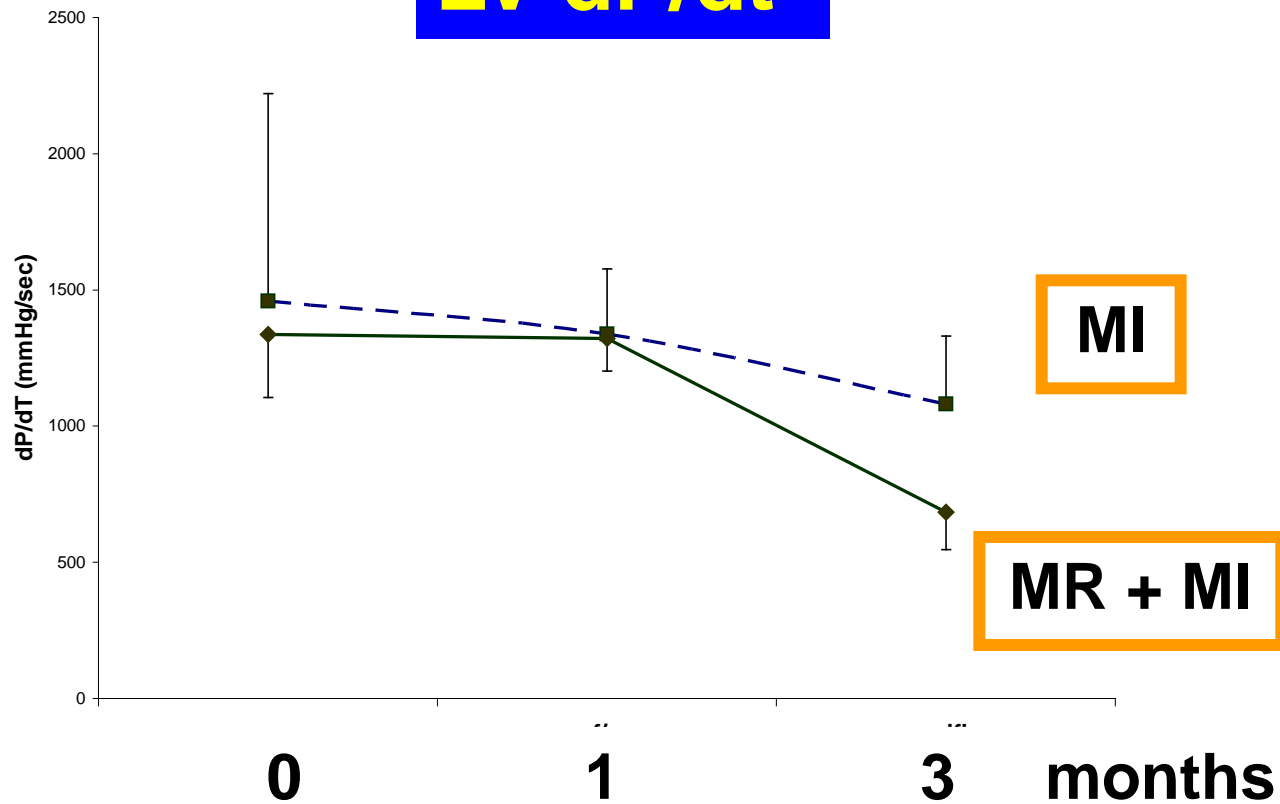
D



Ronen Beerli

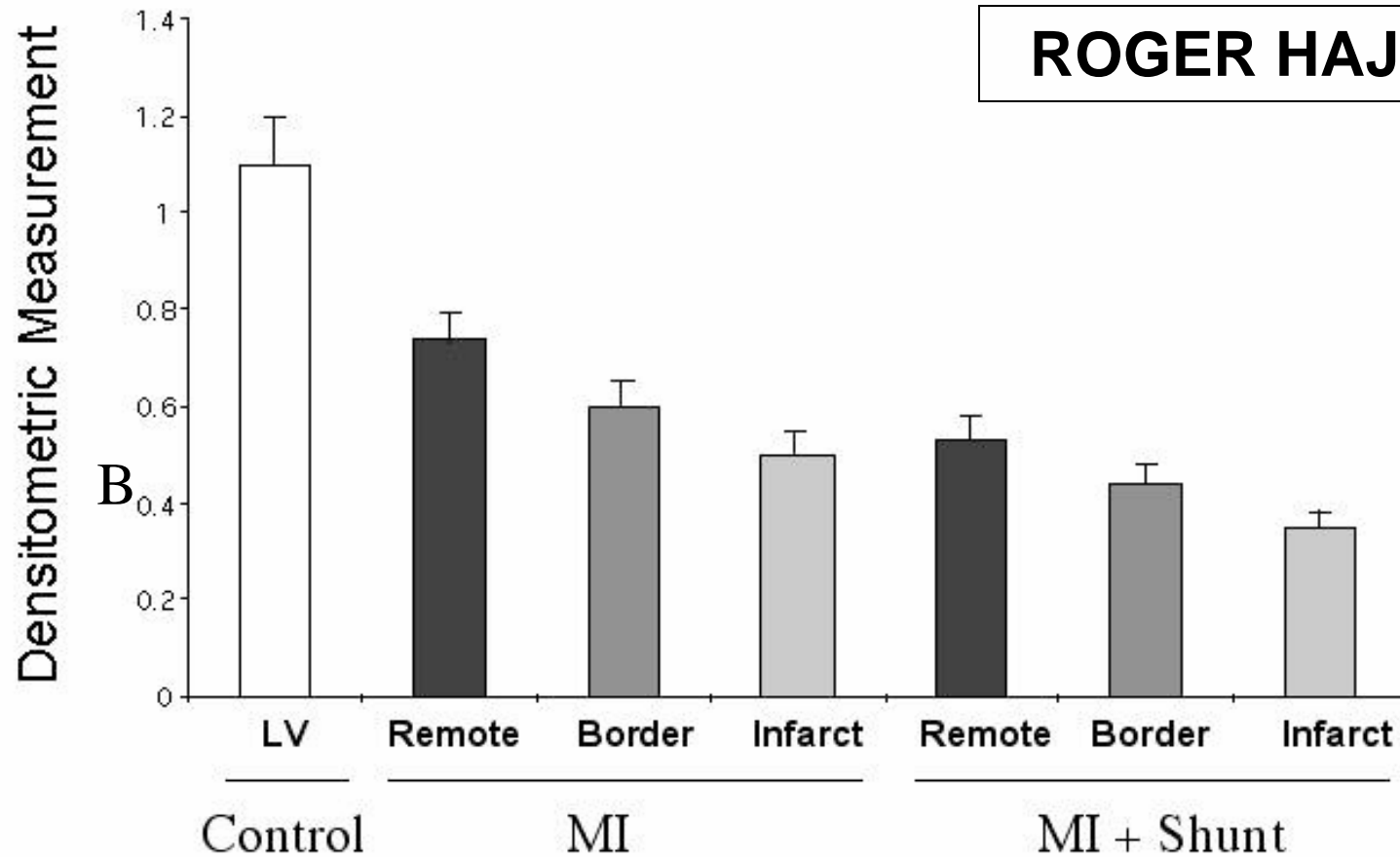


LV dP/dt



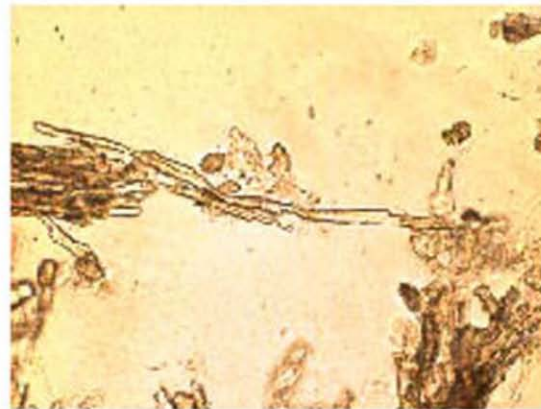
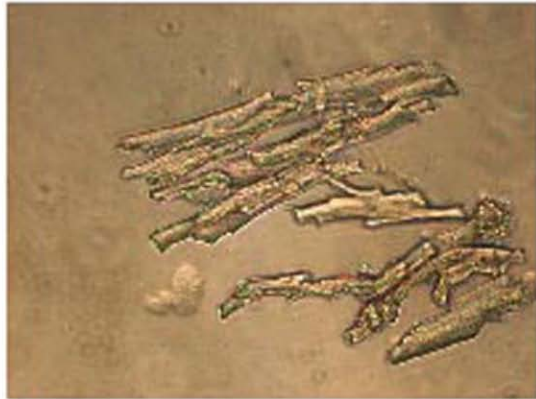
Densitometric Measurements of SERCA2a in various Models

A



B

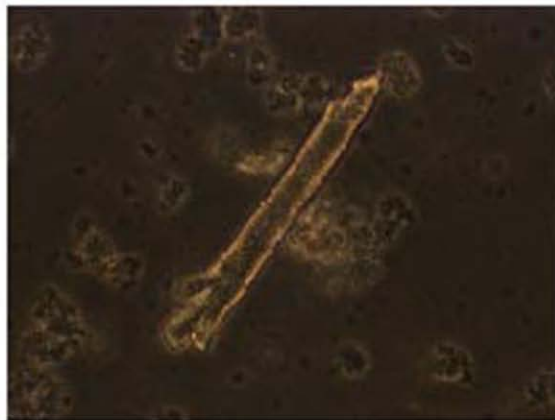
ALTERED CELL SIZE AND SHAPE



A. Abnormal cells

20 μ

FEDERICA DEL MONTE

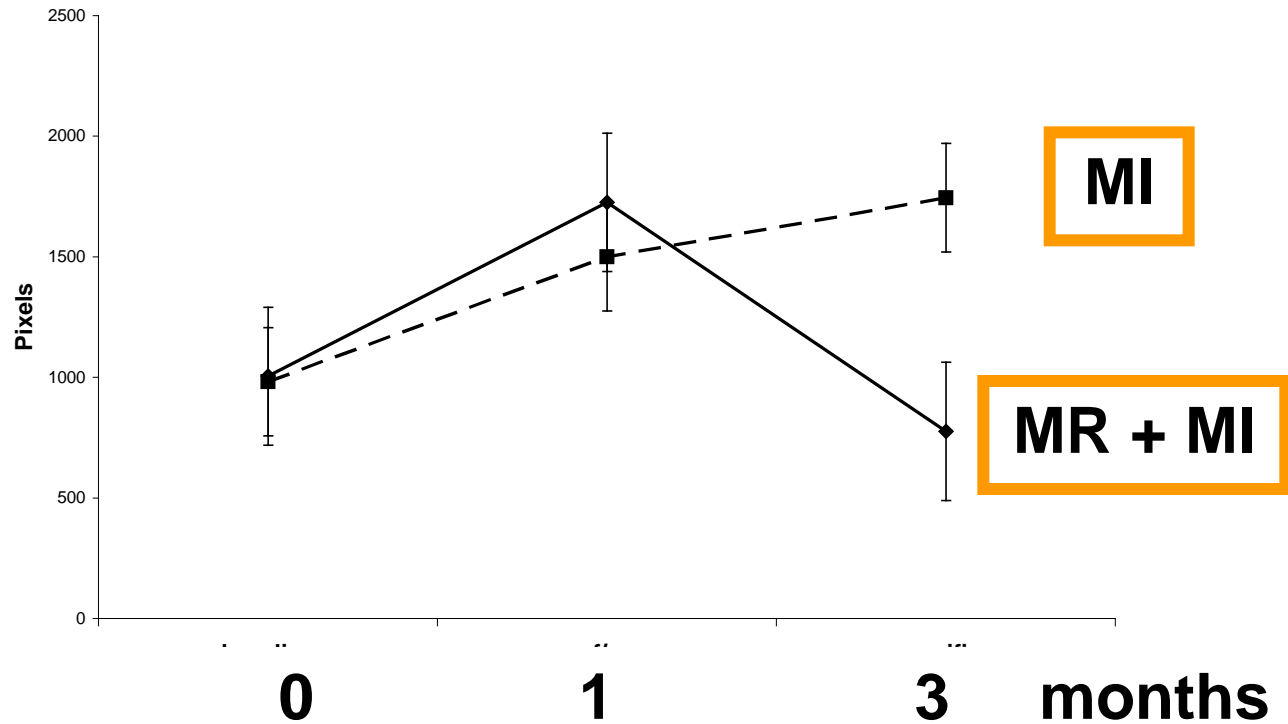


B. Normal Cells

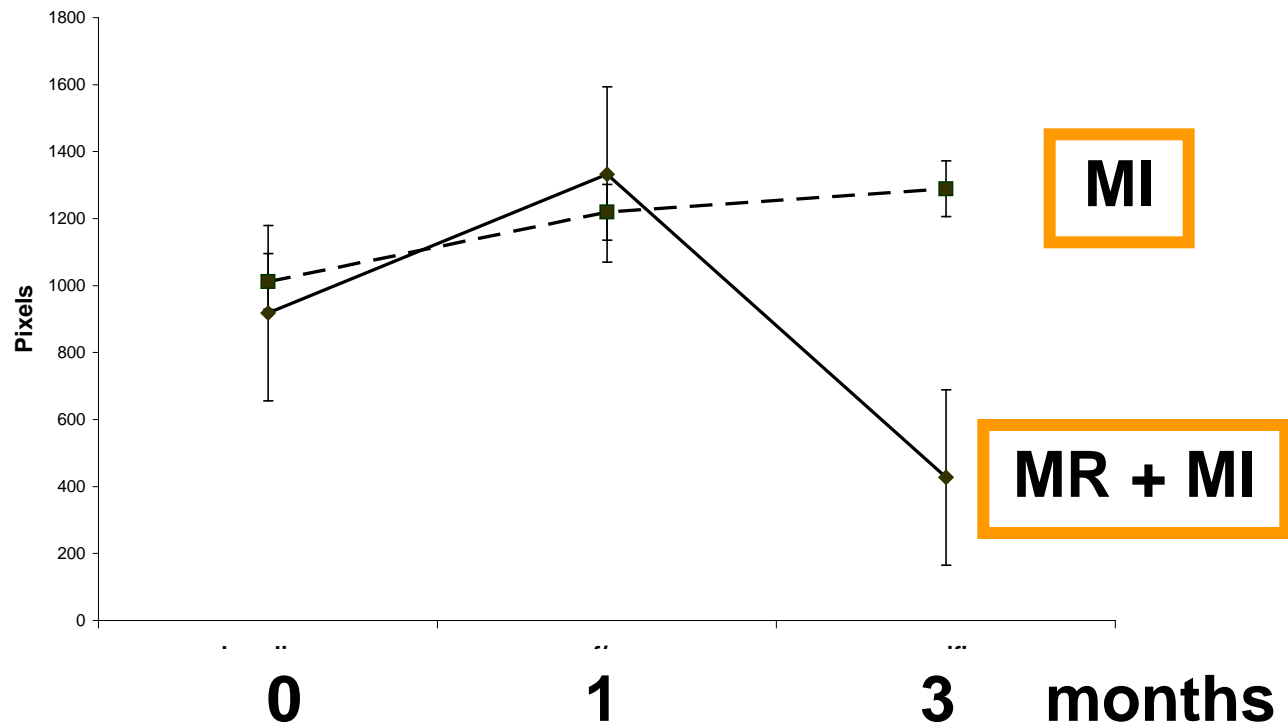
20 μ

gp130: Pro-hypertrophic signal

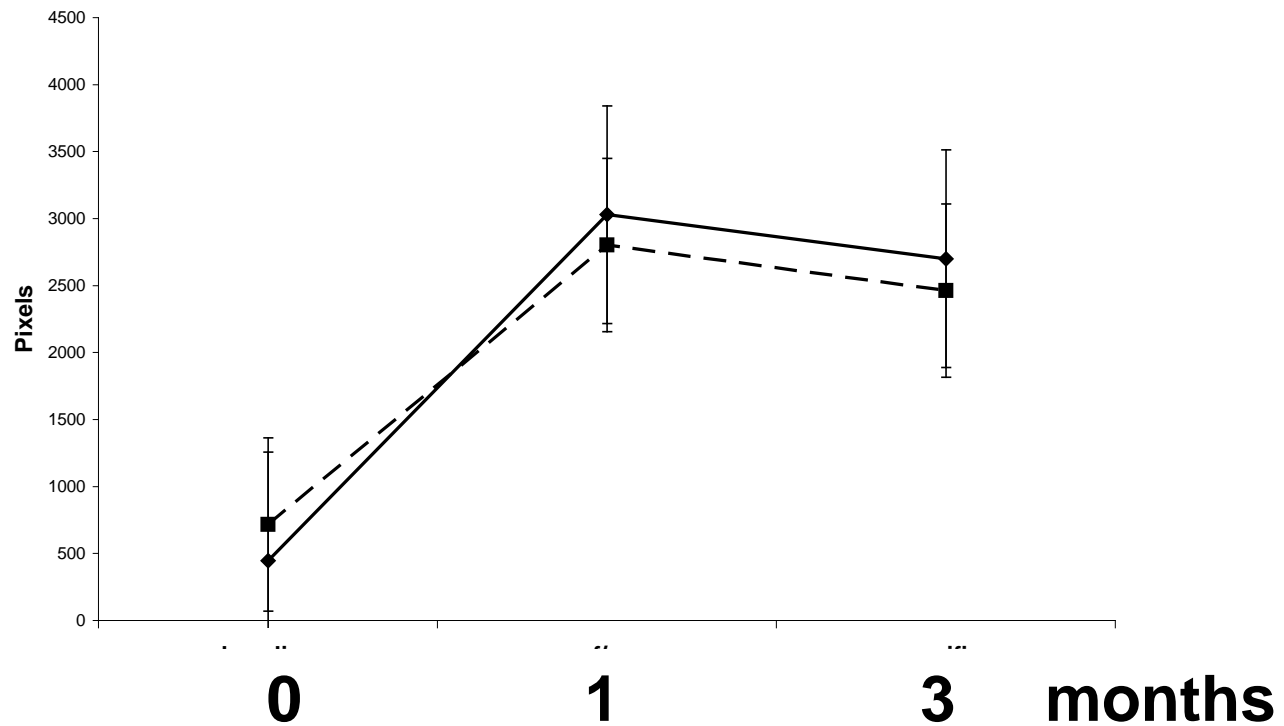
gp130



Akt: Anti-apoptotic signal

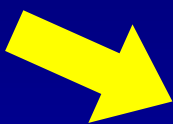


Caspase 3: central to apoptosis

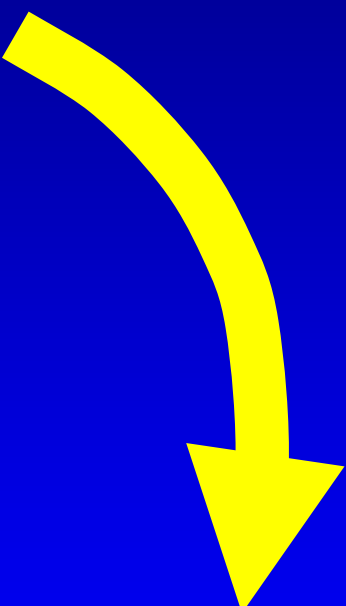


REMODELING: A VICIOUS CYCLE

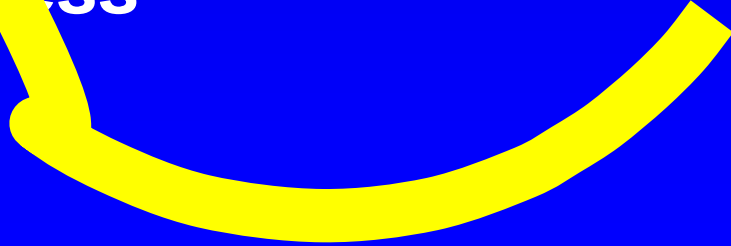
ISCHEMIA



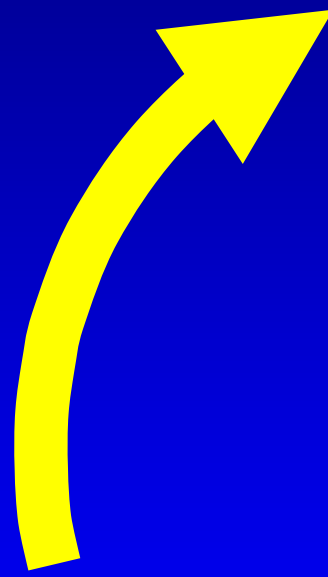
**Decreased
contractile
function**



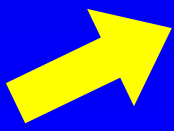
LV dilation



**Increased
wall stress**

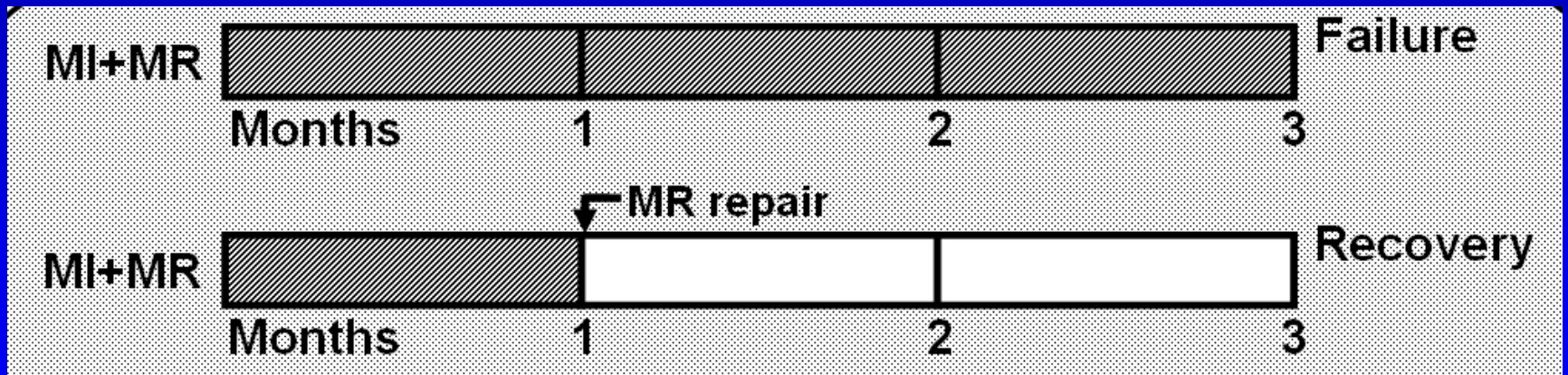


MR

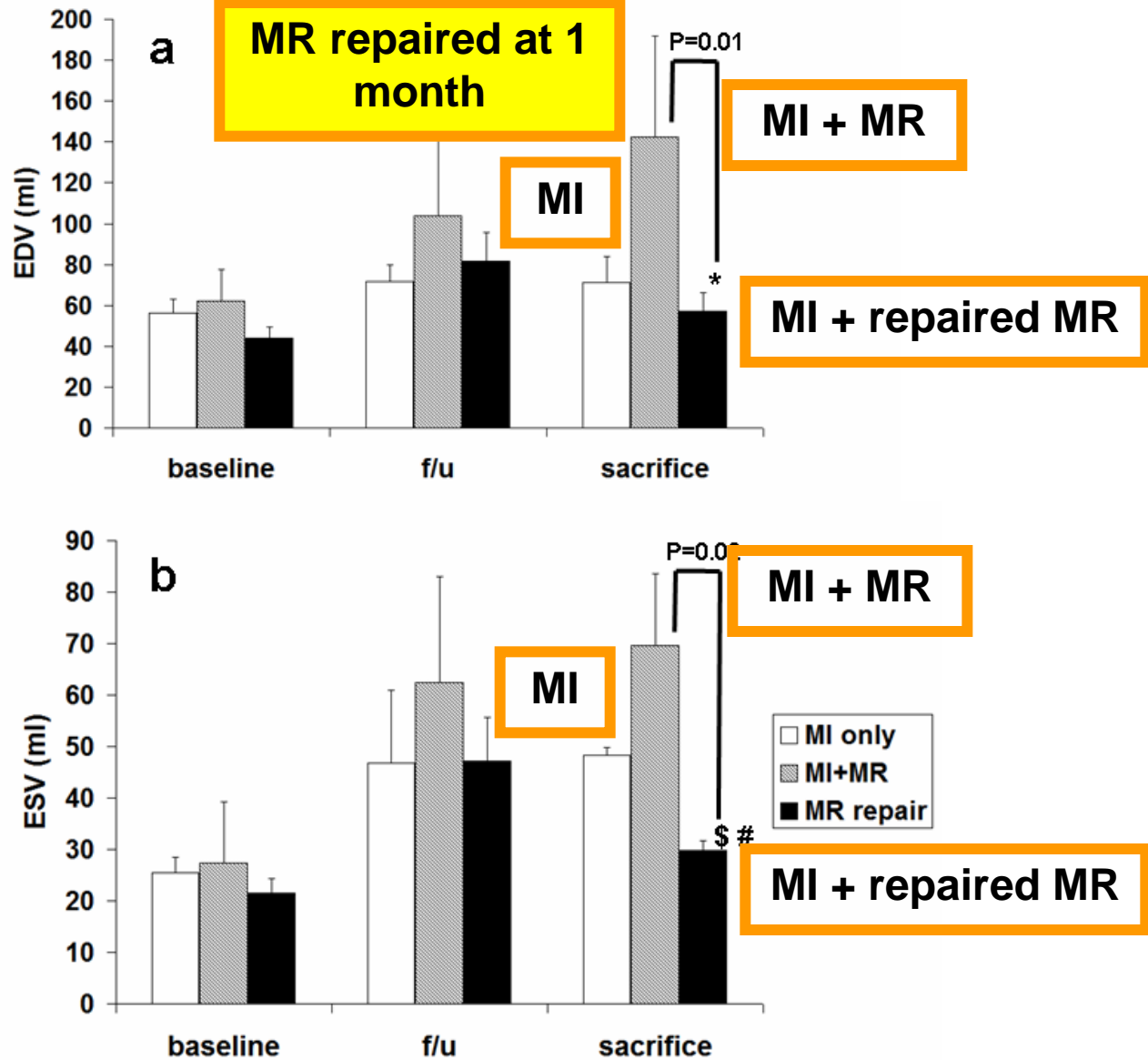


- Failed hypertrophy
- Decreased contractility
- Apoptosis
- Matrix remodeling

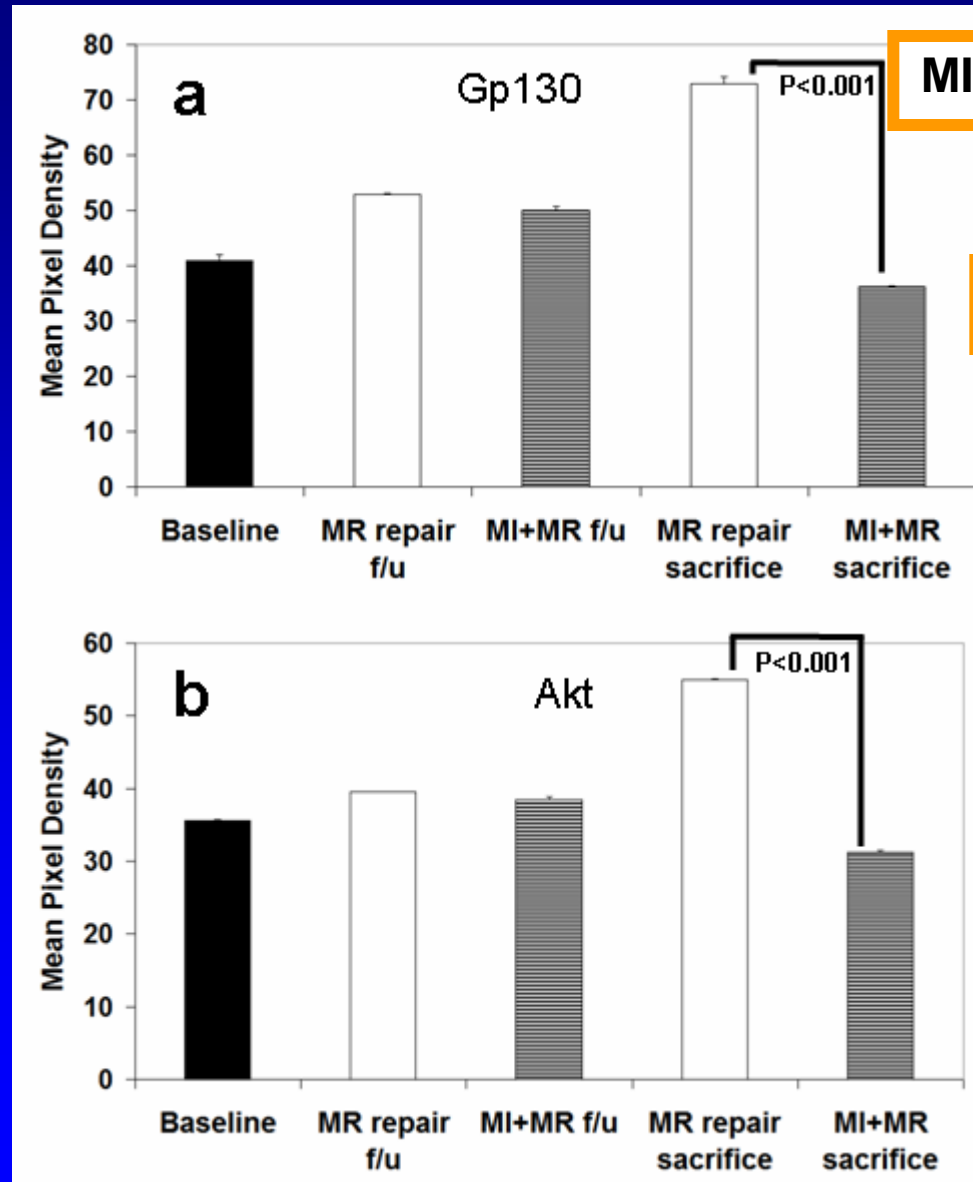
CAN THIS REMODELING BE REVERSED BY MR REPAIR?



IT CAN BE REVERSED BY EARLY REPAIR



REVERSE REMODELING “MOMENTUM”



MI + repaired MR

MI + MR

INTERRUPTING THE VICIOUS CYCLE

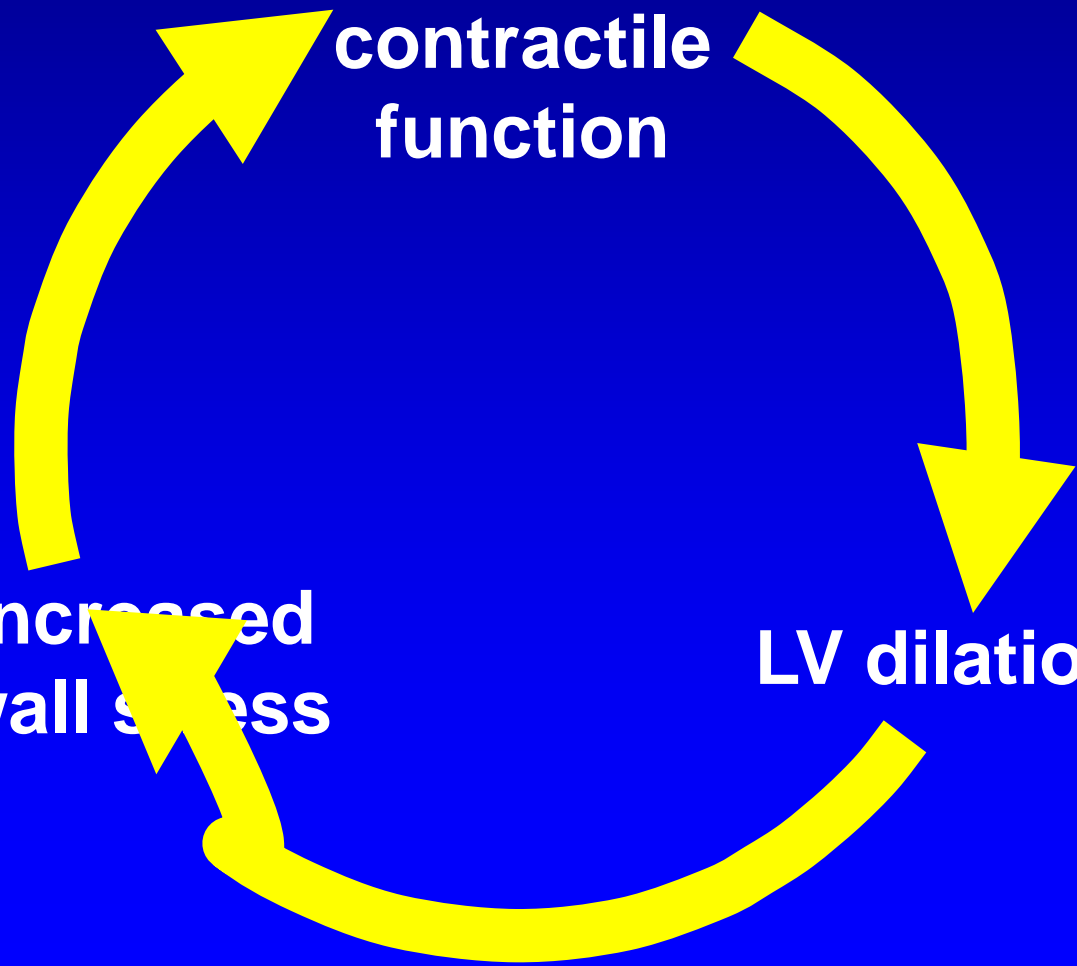
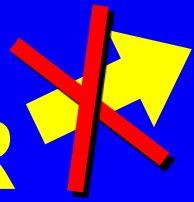
ISCHEMIA →

**Decreased
contractile
function**

LV dilation

**Increased
wall stress**

MR

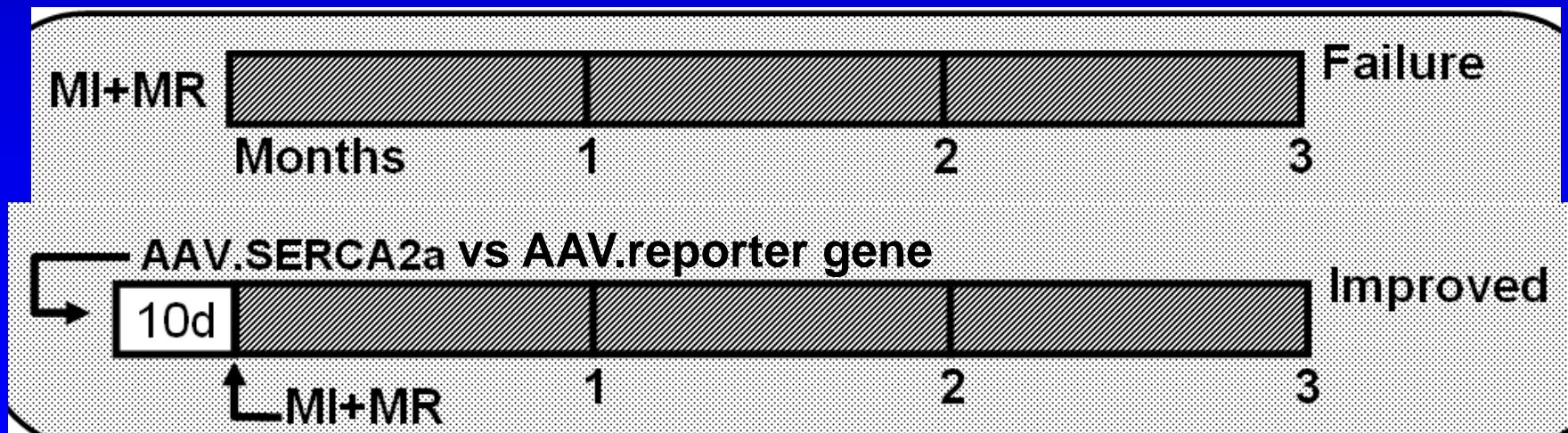


INTERRUPTING THE VICIOUS CYCLE

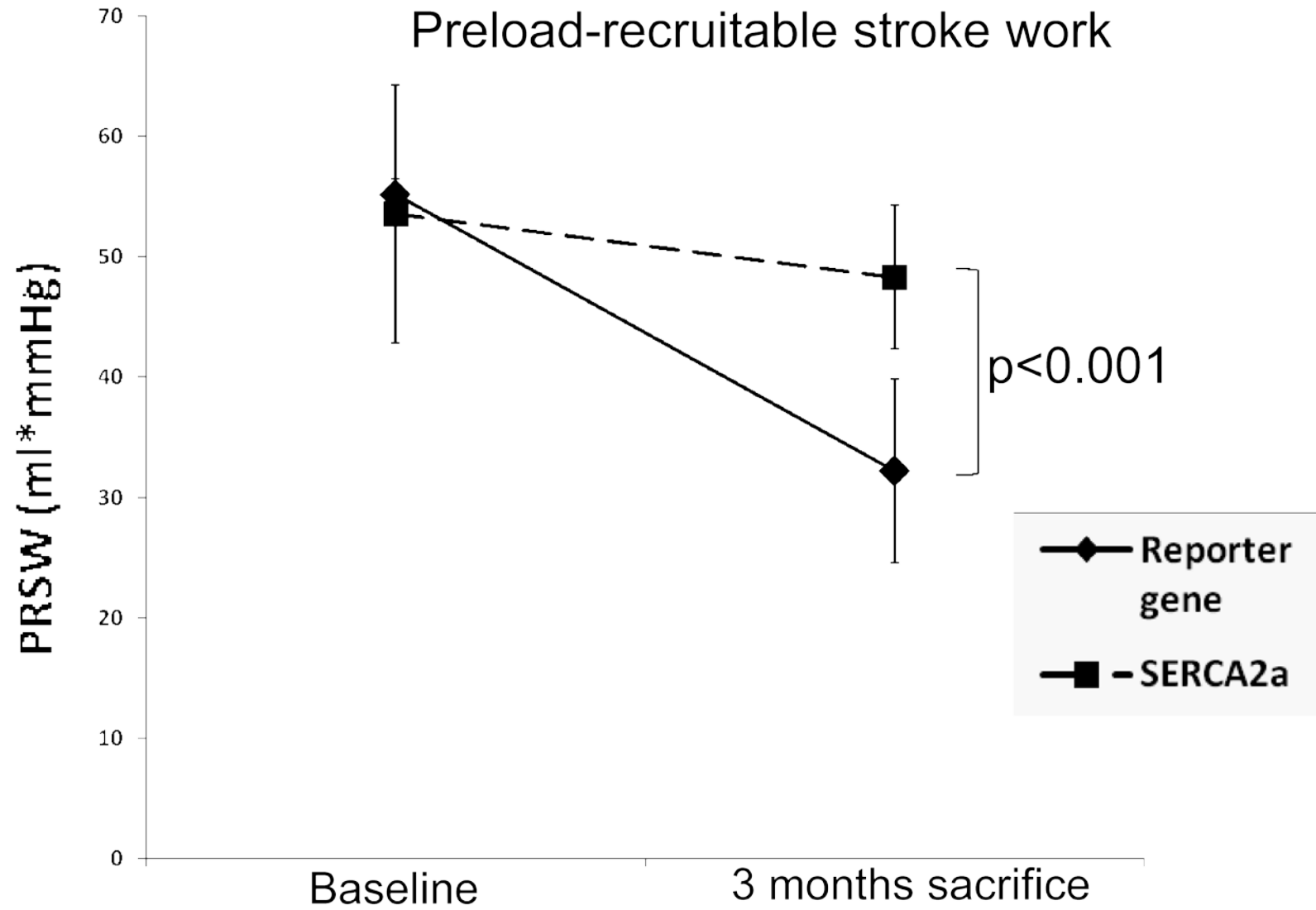
**LV remodeling can be
reversed if ischemic MR is
repaired early**

CAN THIS REMODELING BE RESCUED BY MOLECULAR REPAIR?

RONEN BEERI, ROGER HAJJAR



Preload-recruitable stroke work



INTERRUPTING THE VICIOUS CYCLE

LV remodeling can be reversed if ischemic MR is repaired early, and may be limited by molecular therapy that can be given intraop

Ischemic Mitral Regurgitation

Definition and mechanism

Good news about prognosis

**Good news and a challenge for
repair**

Case 2: Why does this 75 year-old woman have persistent heart failure and AF after CABG with annuloplasty?

PHILIPS

ET 4638069

12/30/2009

10:56:16

TISO.9

JPEG CR 19:1
MI 1.3

4638069

S5-1/MGH

FR 80Hz
16cm

M3

2D

63%
C 50
P Low
HGen



JPEG

100 bpm

PHILIPS ET 4638069
4638069

12/30/2009 10:56:53
S5-1/MGH

TIS2.6 JPEG CR 18:1
MI 1.1

FR 19Hz
17cm

2D
61%
C 50
P Low
HGen

CF
70%
2.5MHz
WF High
Med

M3 M4

+67.5

67.5
cm/s



JPEG

89 bpm

PHILIPS

ET 4638069

12/30/2009

10:56:16

TISO.9

JPEG CR 19:1
MI 1.3

4638069

S5-1/MGH

FR 80Hz
16cm

M3

2D

63%
C 50
P Low
HGen



JPEG

100 bpm

ANNULAR REDUCTION

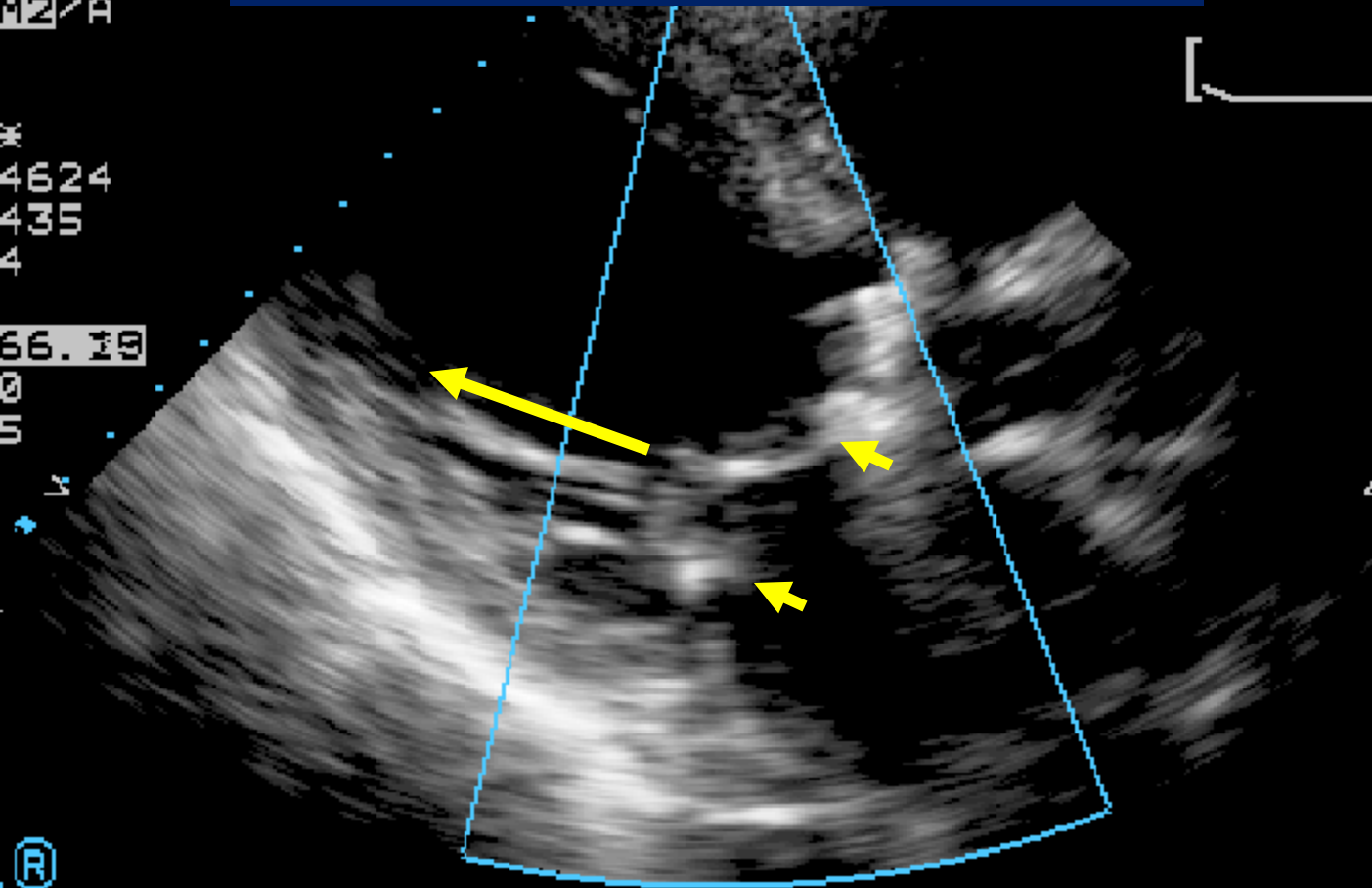
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22 DEC 04
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2/0/C/M2/A
MGH #8

MGH
WG 0494624
DENIM 435
0494624
01065
01166.19
GAIN 50
COMP 65
59BPM
16CM
17HZ

P T R
1.6 3.2

2.5MHZ
65

65



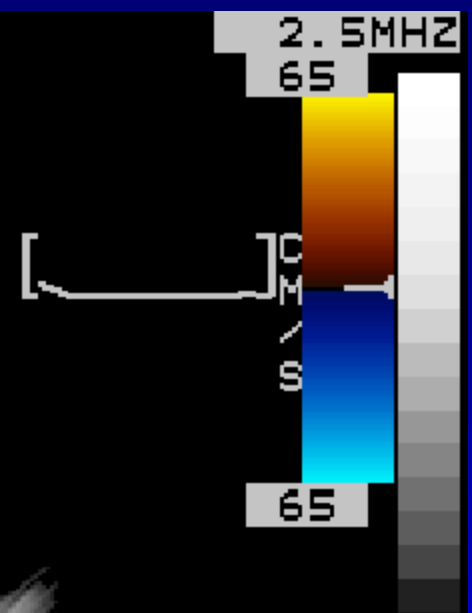
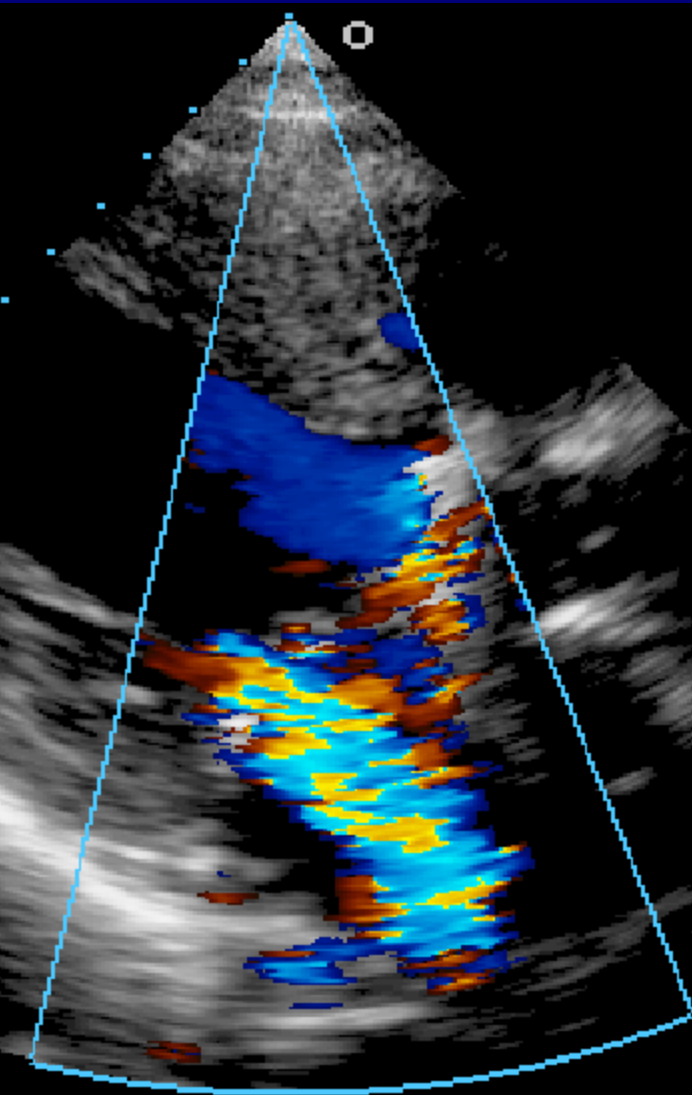
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S3
22 DEC 04
11:05:34
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MGH #8

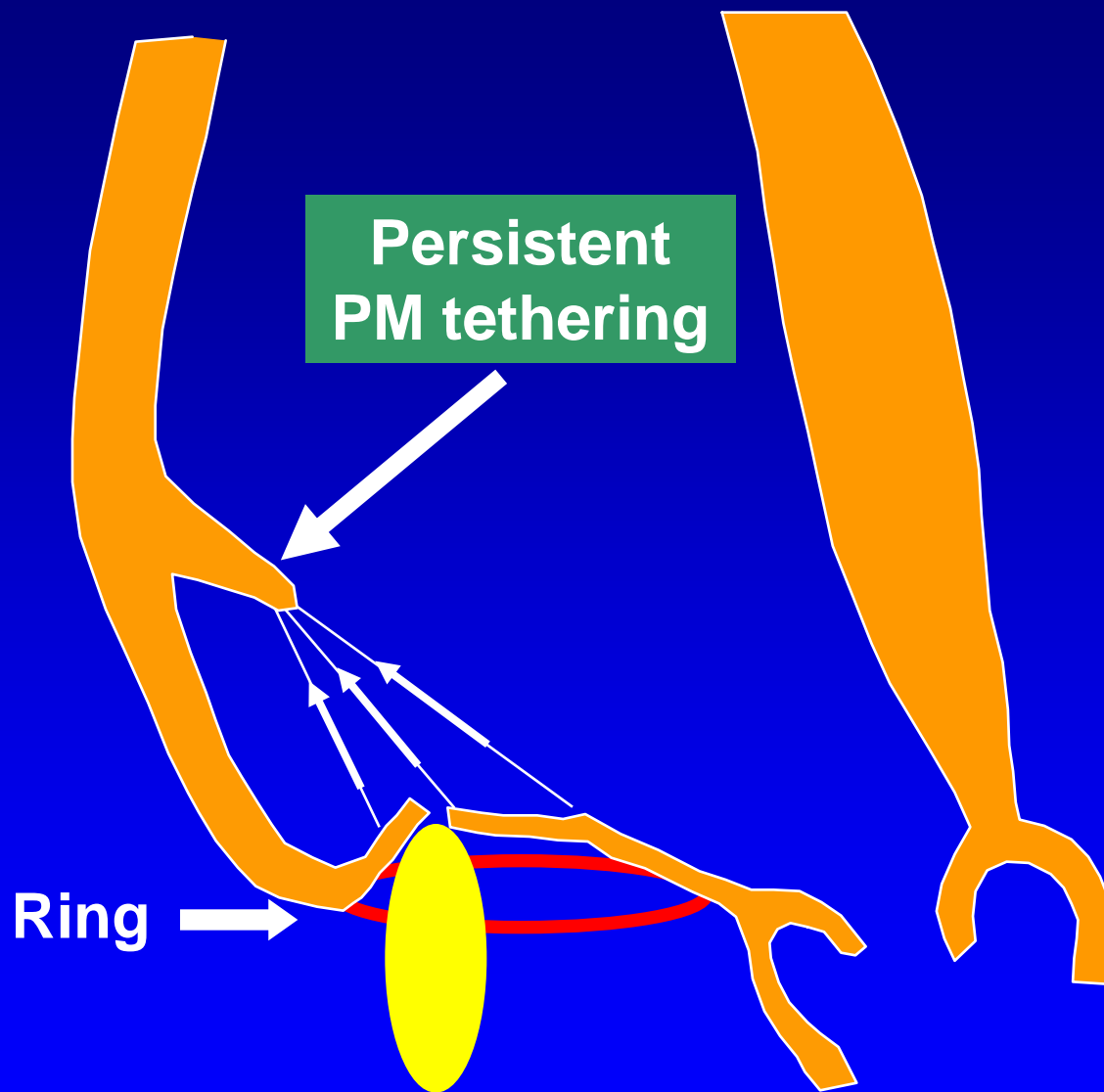
MGH
WG 0494624
DENIM 435
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01065
01166.25

GAIN 50
COMP 65
59BPM

16CM
17HZ



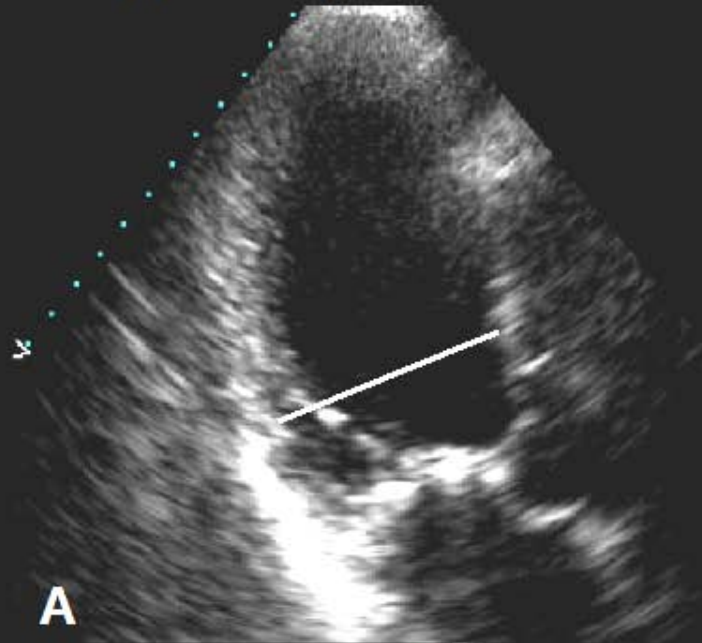
Limitations of ring annuloplasty



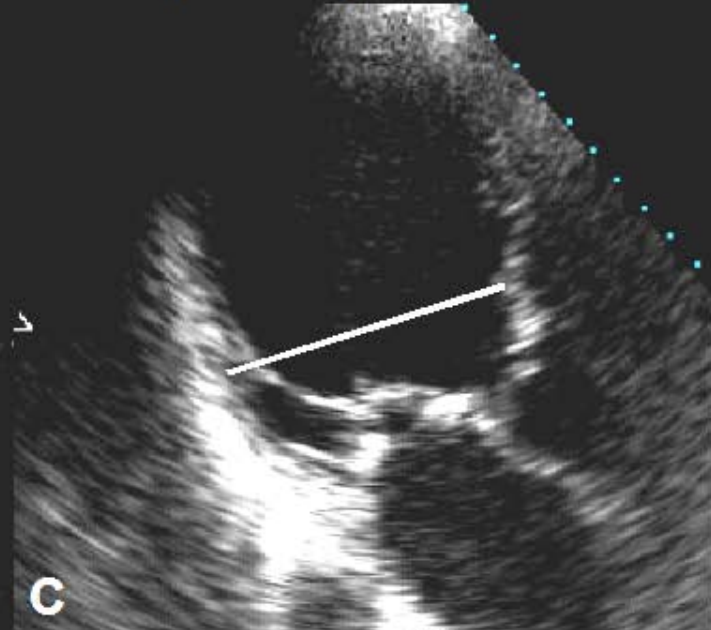
25-50% or more (MGH, Cleveland Clinic, Carlos Duran)

Early post-op: LVID=58mm

Late post-op: LVID=73mm

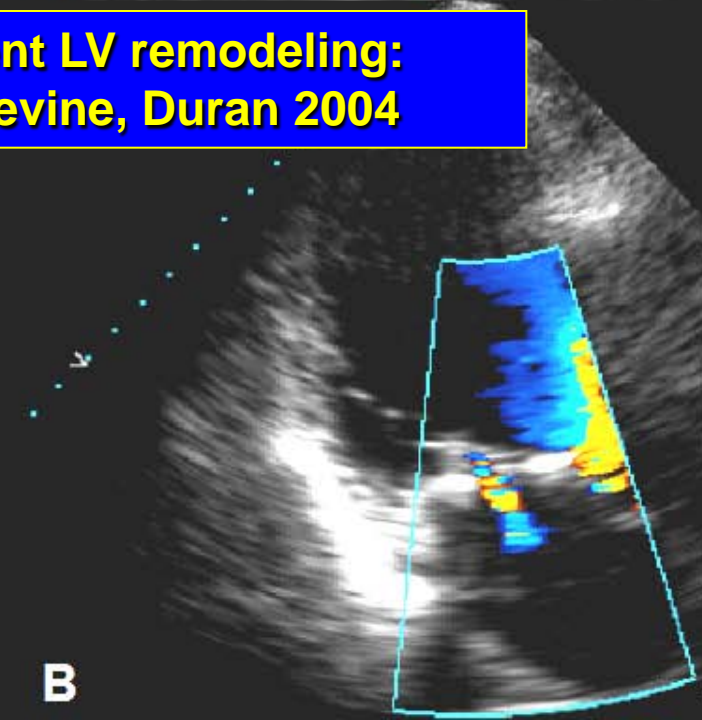


A

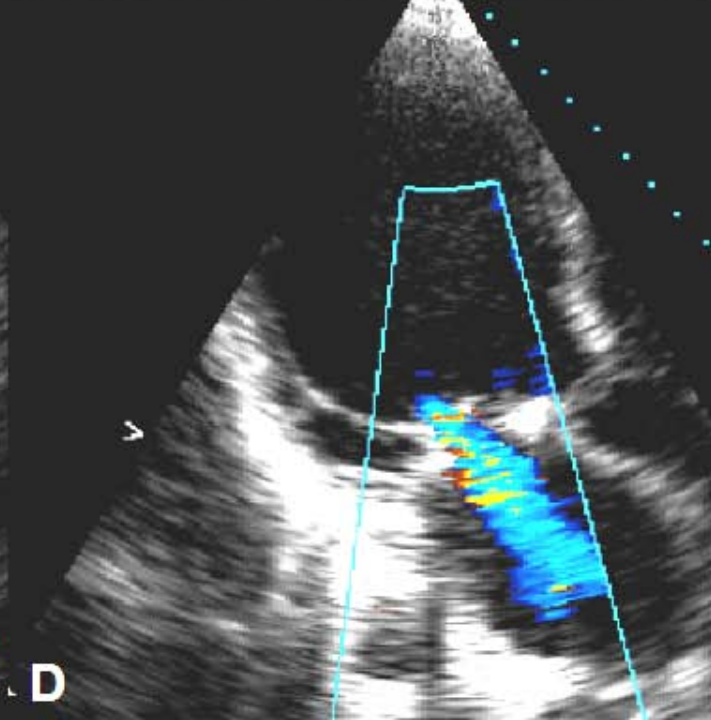


C

Persistent LV remodeling:
Hung, Levine, Duran 2004



B



D

ECHOCARDIOGRAPHY

ADVANCED IMAGING

+

MECHANISMS



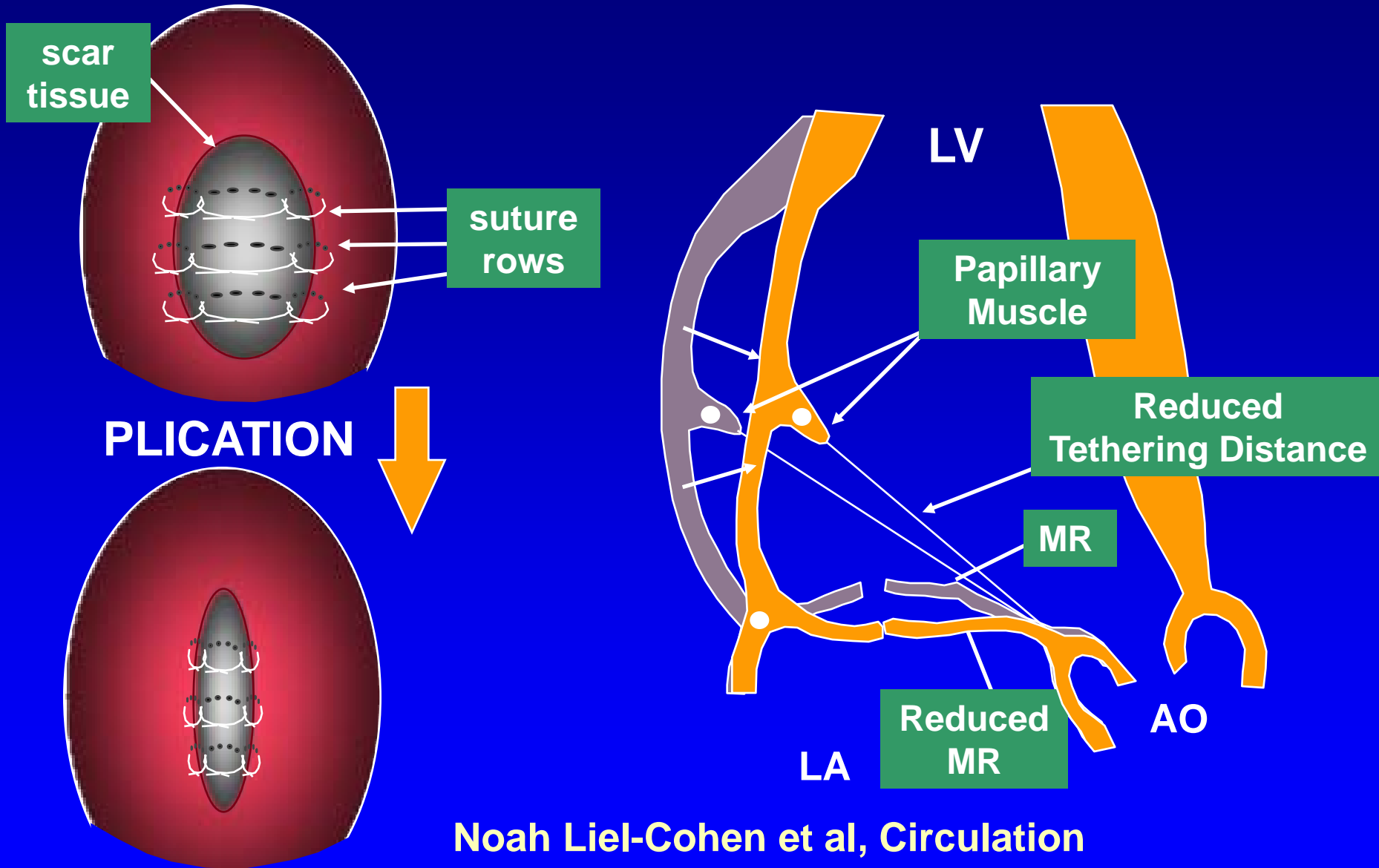
INNOVATIVE SOLUTIONS

NOAH LIEL-COHEN

**Soroka Medical Center,
Ben-Gurion University,
Beer Sheva, Israel**

Circulation 2000

Reverse Remodeling Procedure



Noah Liel-Cohen et al, Circulation
Procedure developed with J. Luis Guerrero

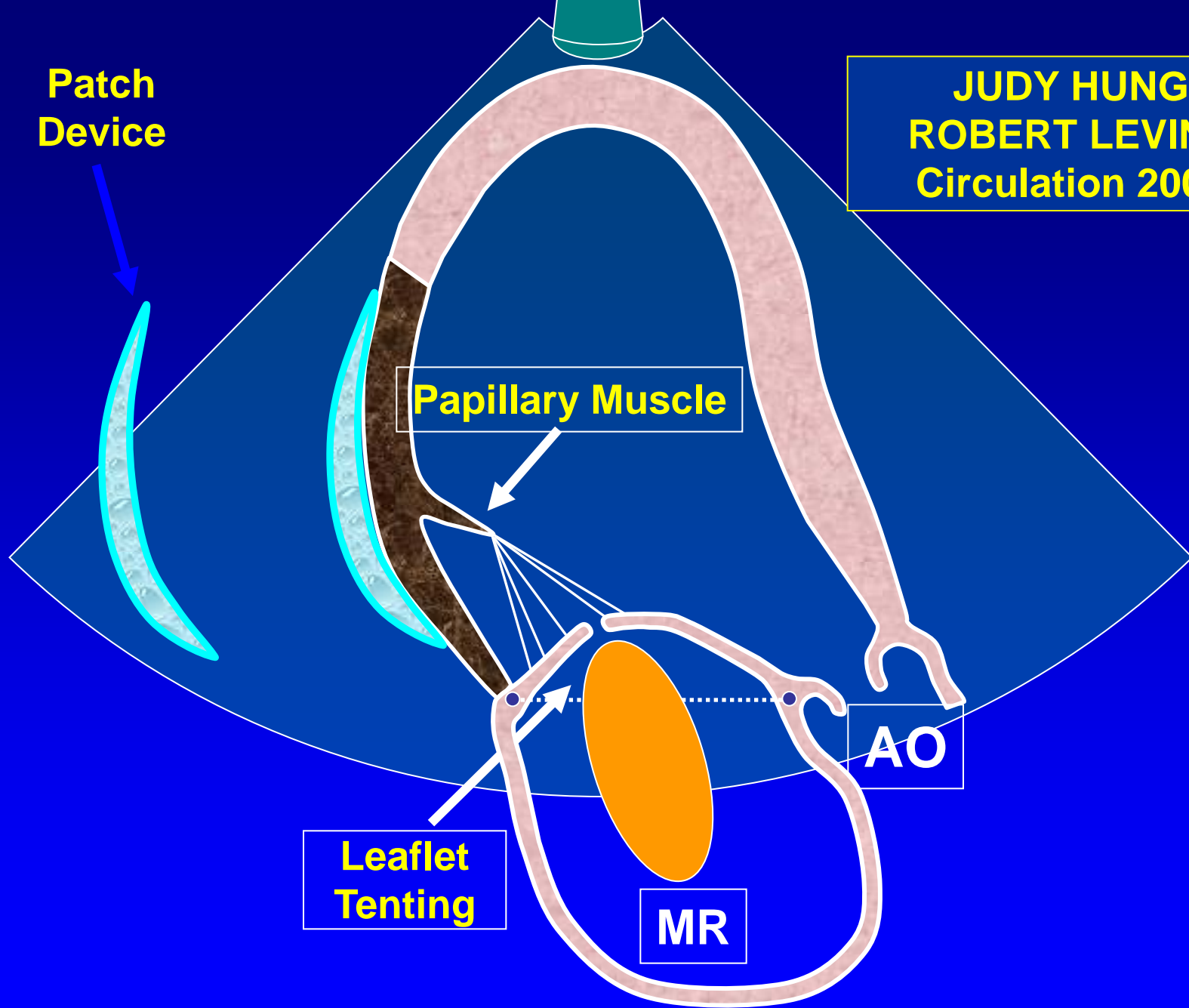
**PAPILLARY MUSCLE
REPOSITION BY LV WALL
RESHAPING**

**JUDY HUNG
ROBERT LEVINE
JORGE SOLIS**



Patch Device

JUDY HUNG
ROBERT LEVINE
Circulation 2002

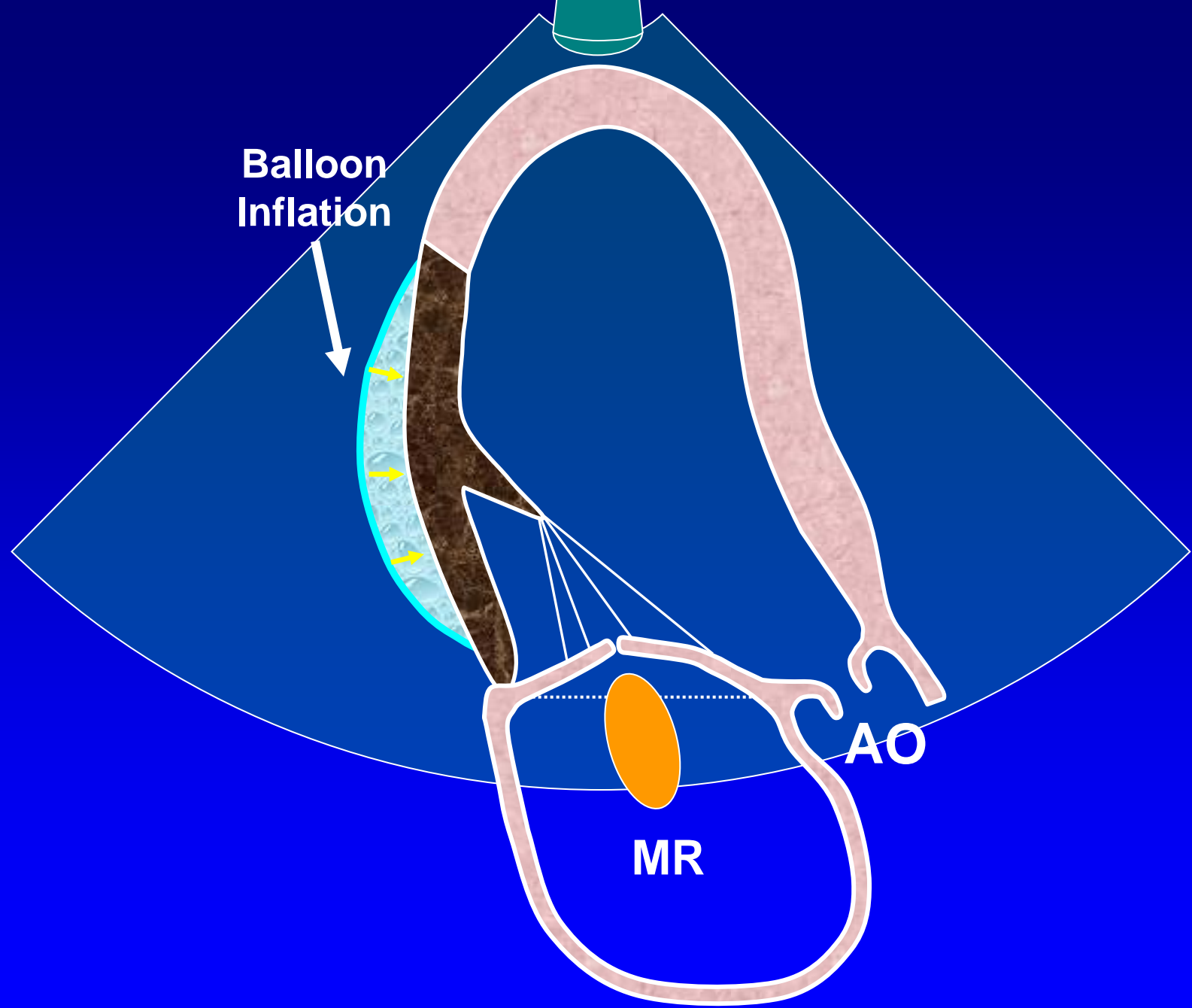


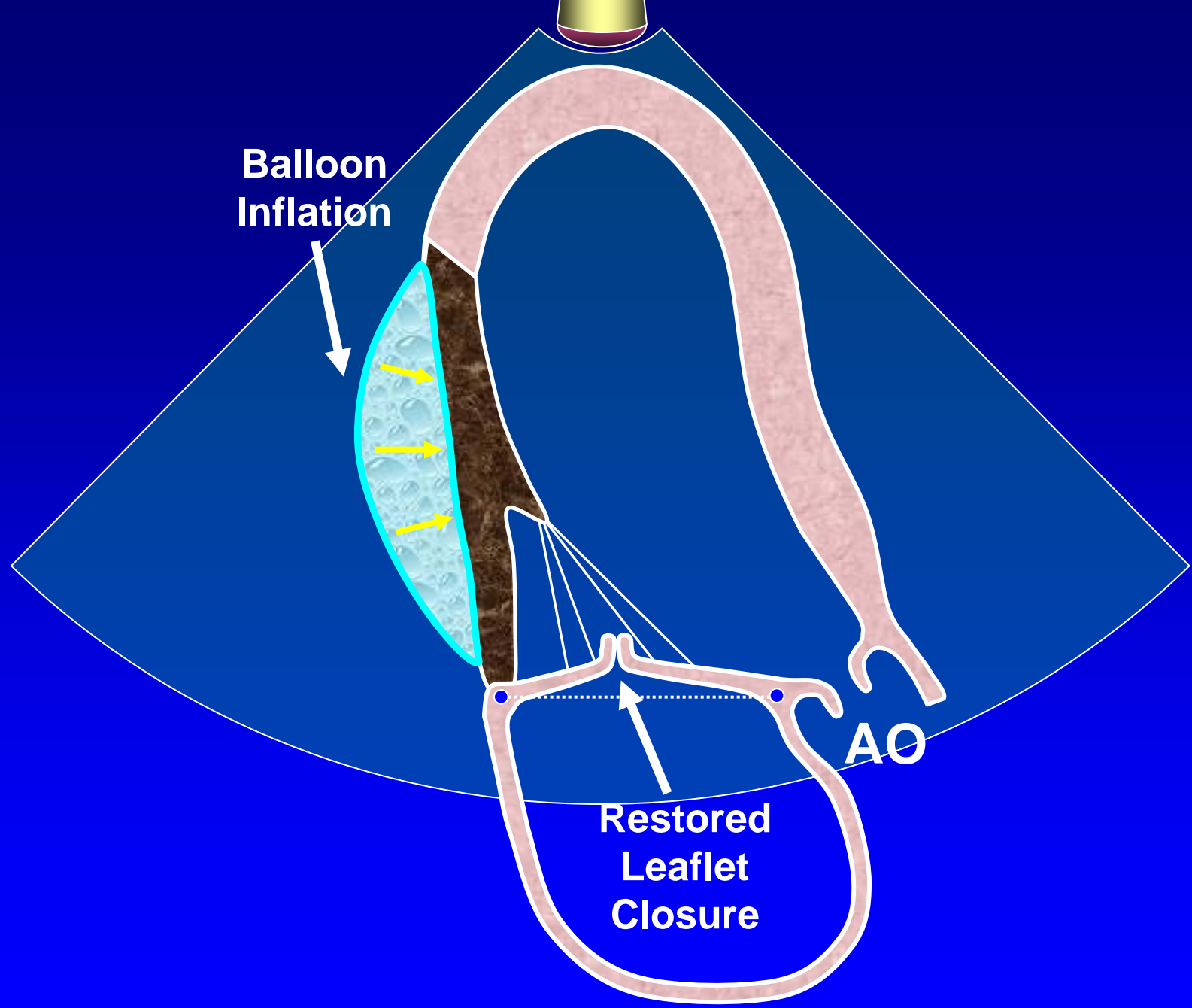
Papillary Muscle

AO

Leaflet
Tenting

MR



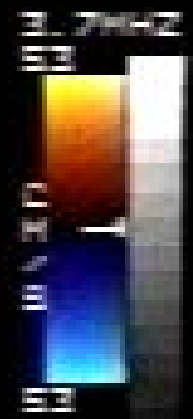


T19: 2.8 PAT T: 37.2C
T5812 TEE T: 37.2C
21 JUNE 21
18:14:46
PRIC 2/2/2/2/2
MCH 3-2

MCH TEE PATCH
01794 INF
62181
1842

21683.21
GAIN 100
COMP 0.8
1280PH

12CM
18HZ



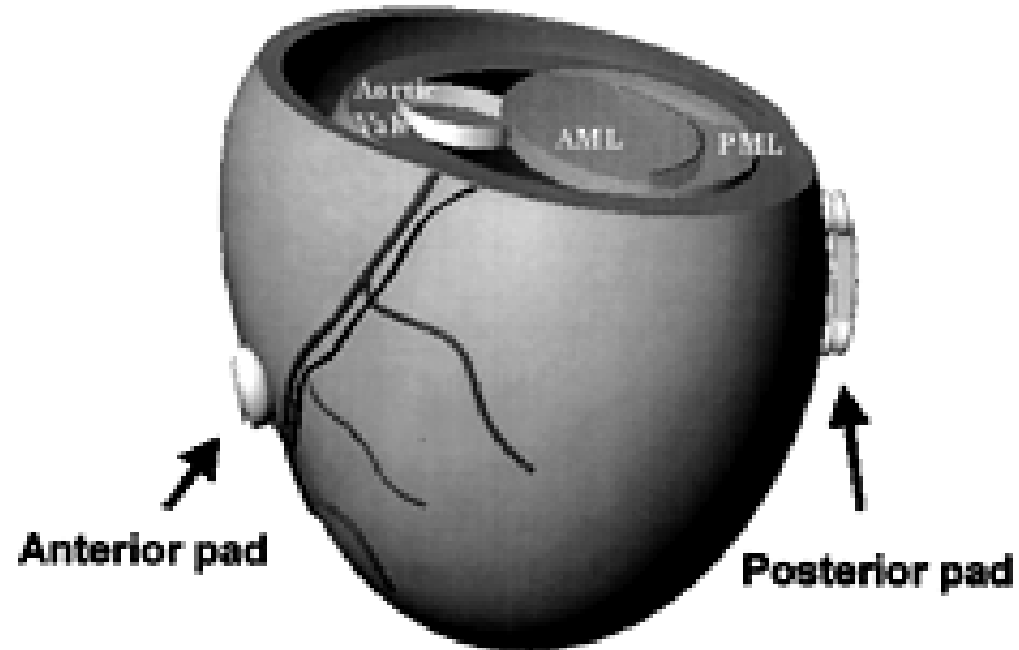
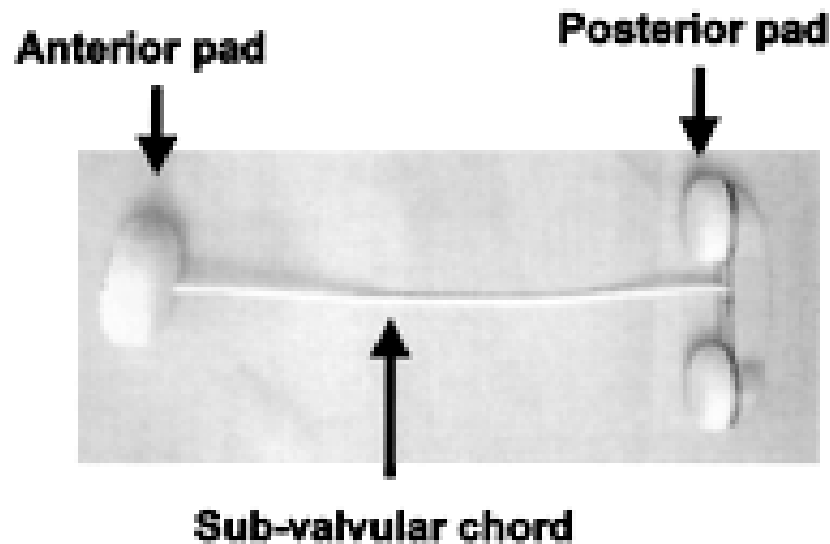


ADVANTAGES

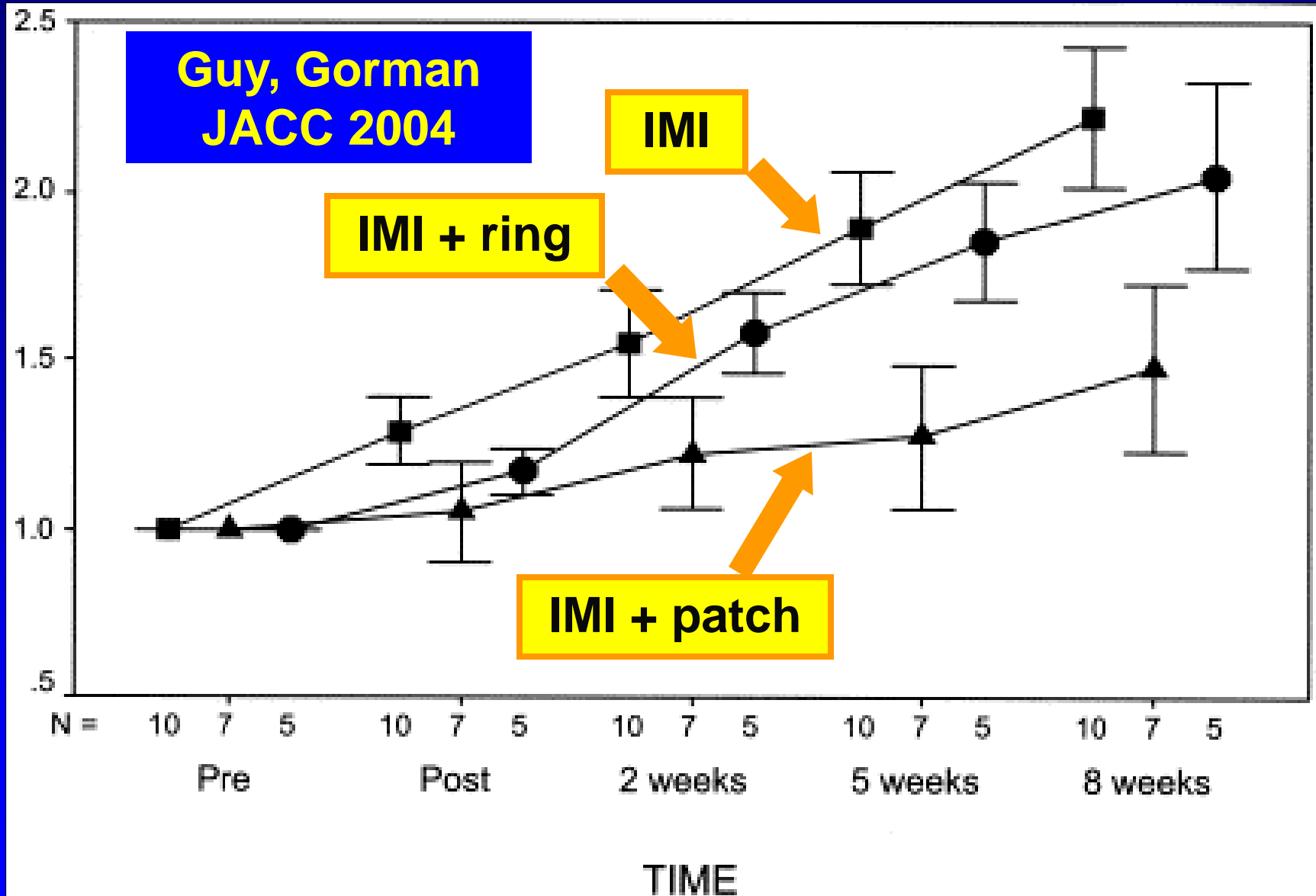
- Specifically allows targeted, individualized therapy, **adjustable** by echo guidance
- Can be applied in the beating heart because of echo monitoring

ALTERNATIVES

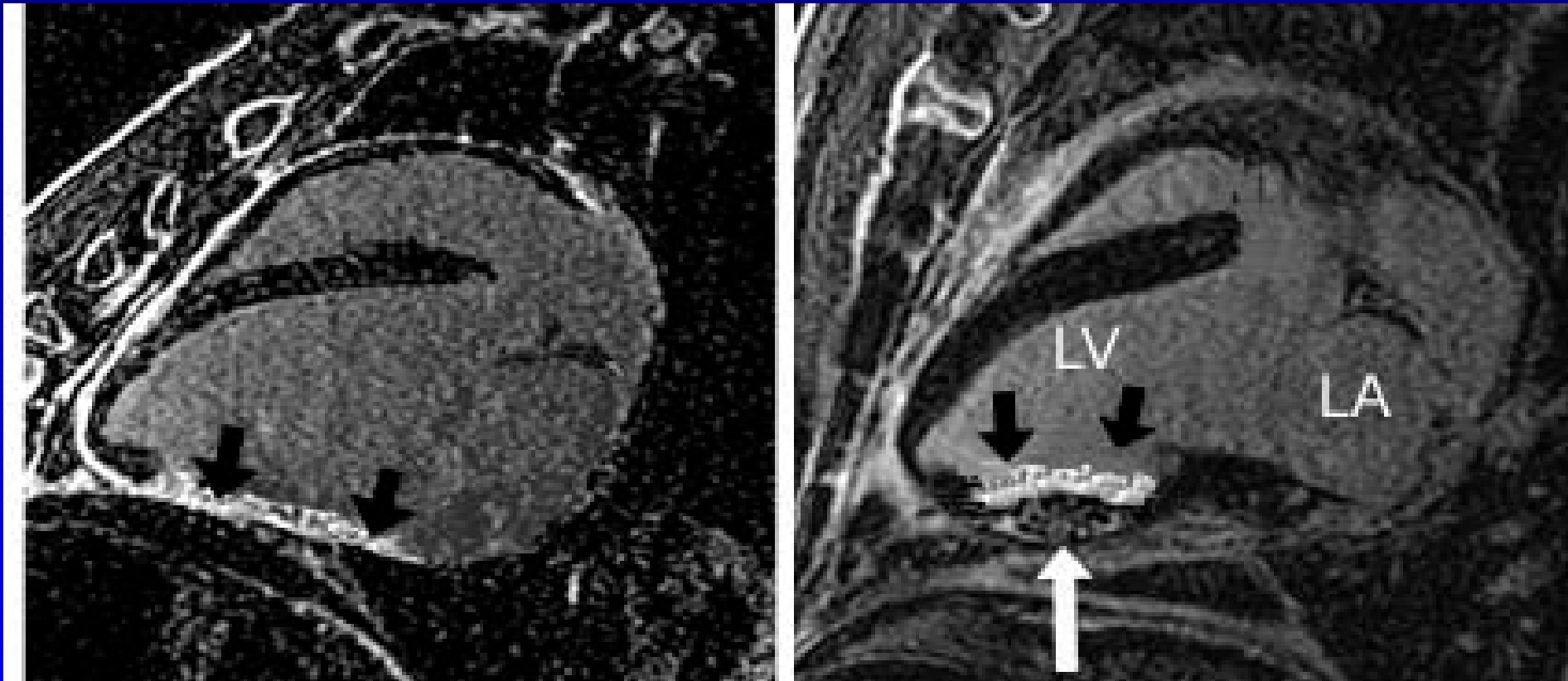
Coapsys aims to reduce tethering:



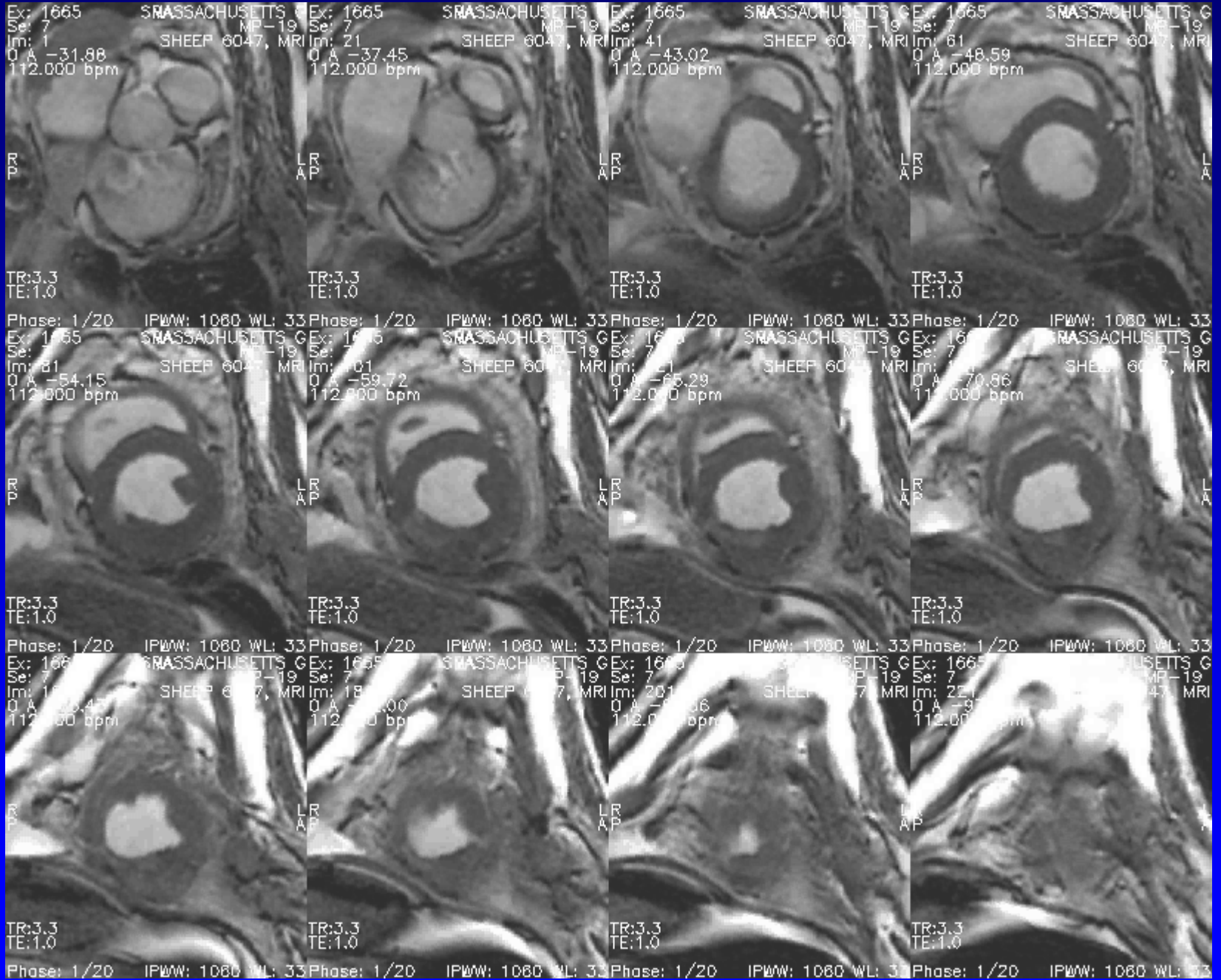
Local patching reduces global remodeling



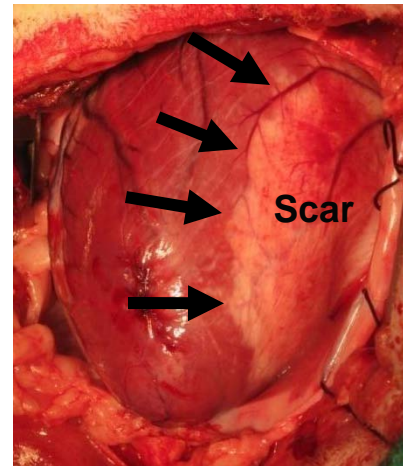
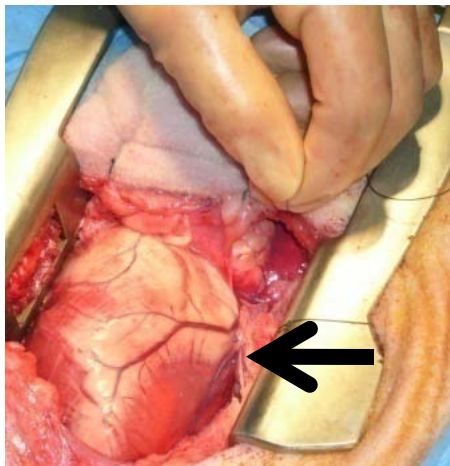
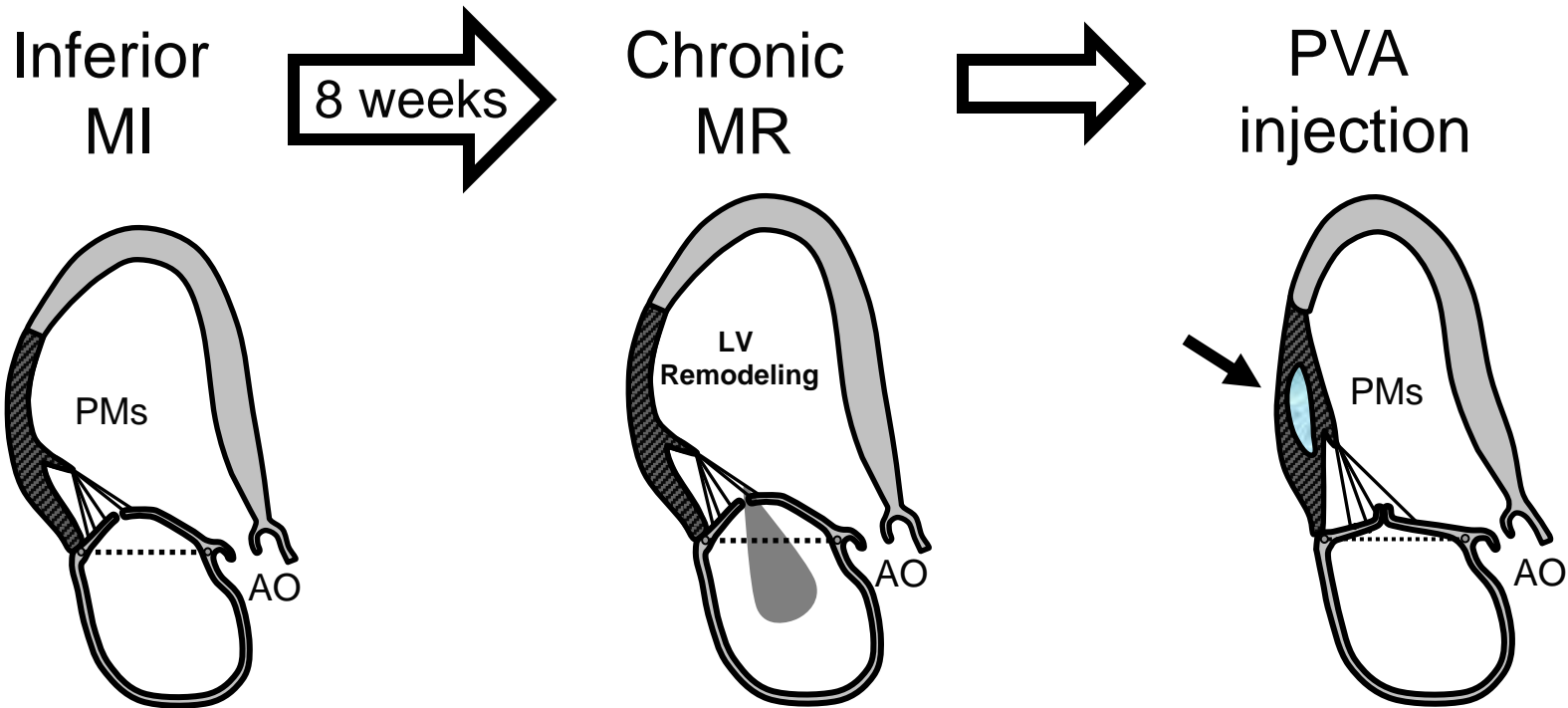
Local patch reduces MI expansion and global LV remodeling

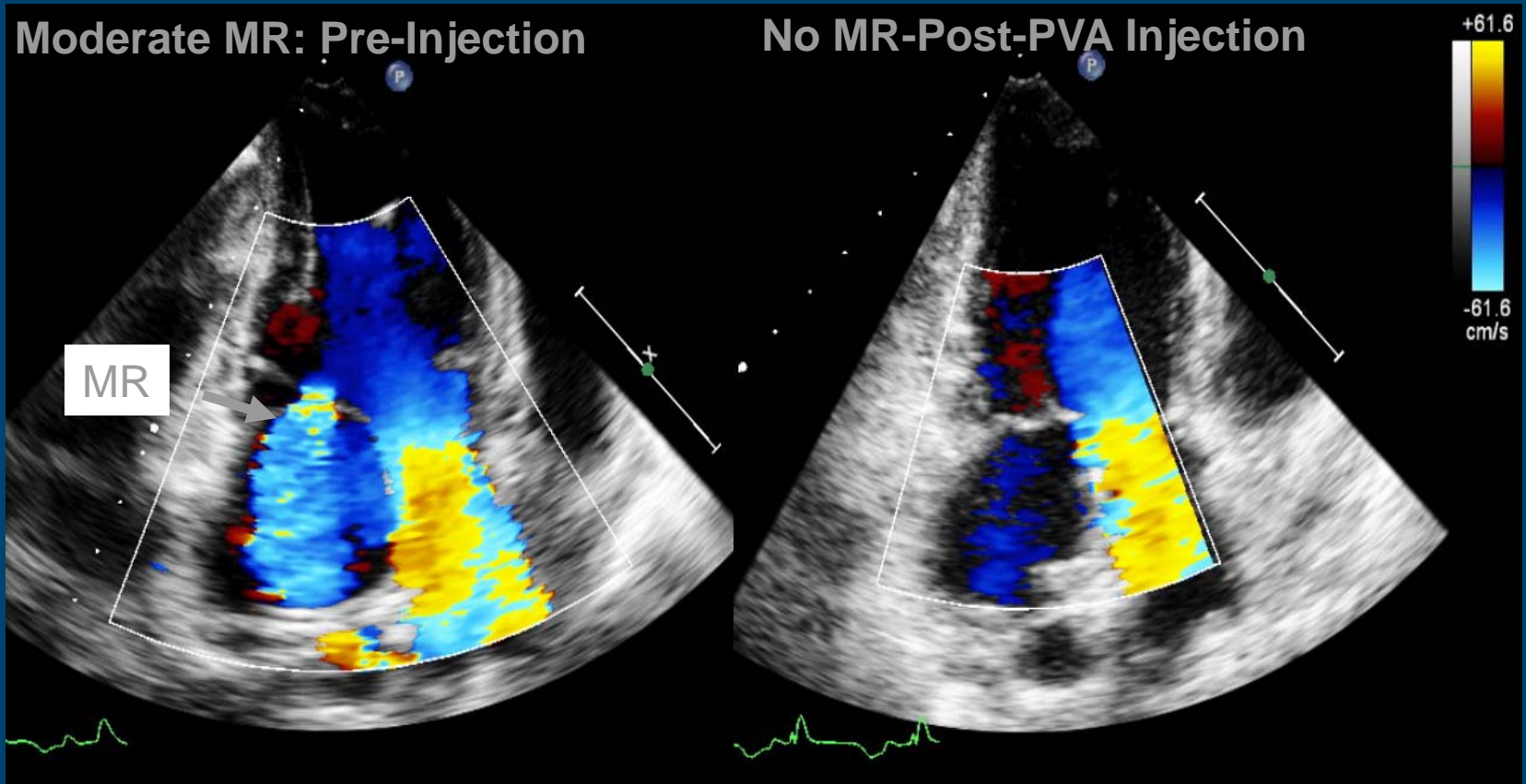


MIGUEL CHAPUT



Chronic Ischemic MR Model





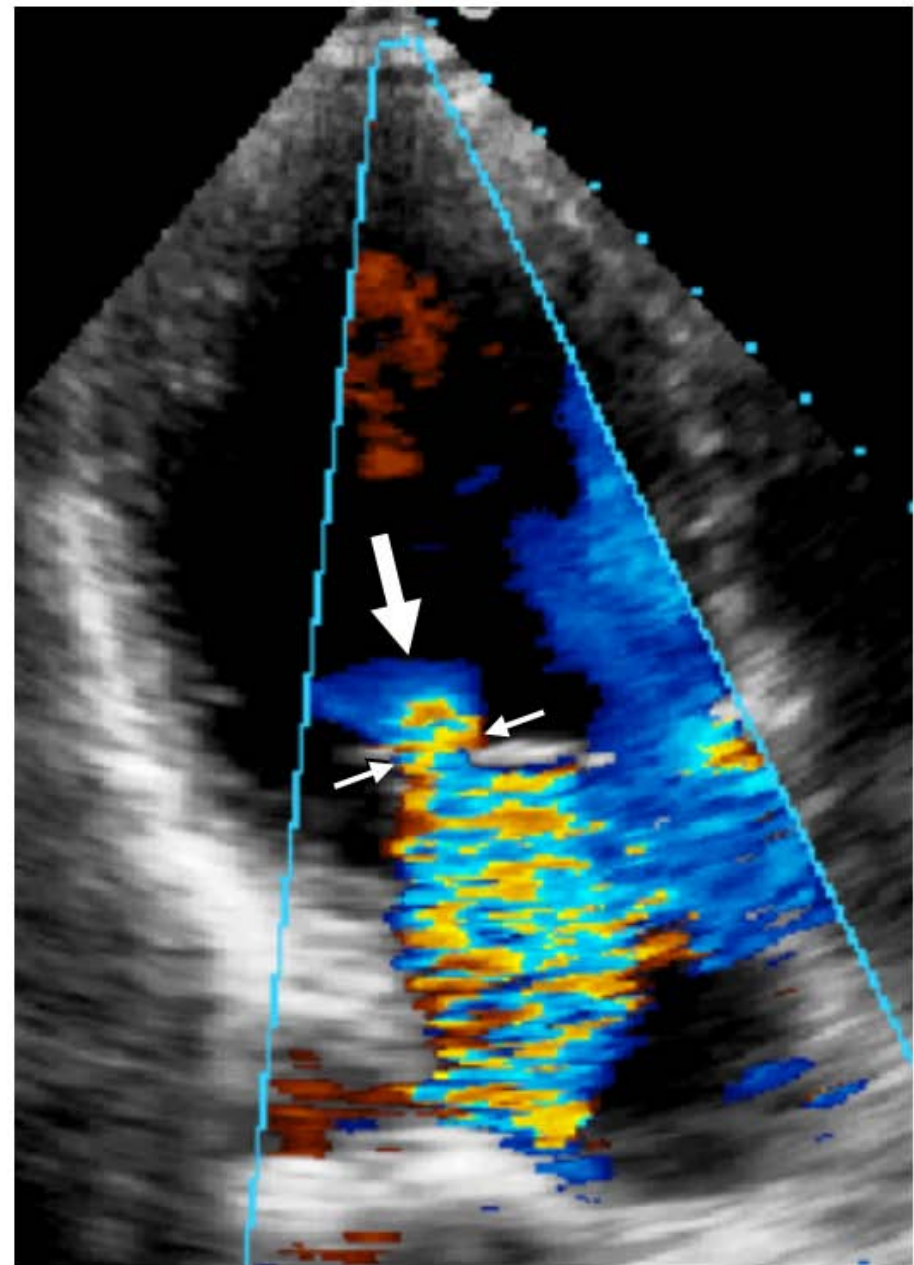
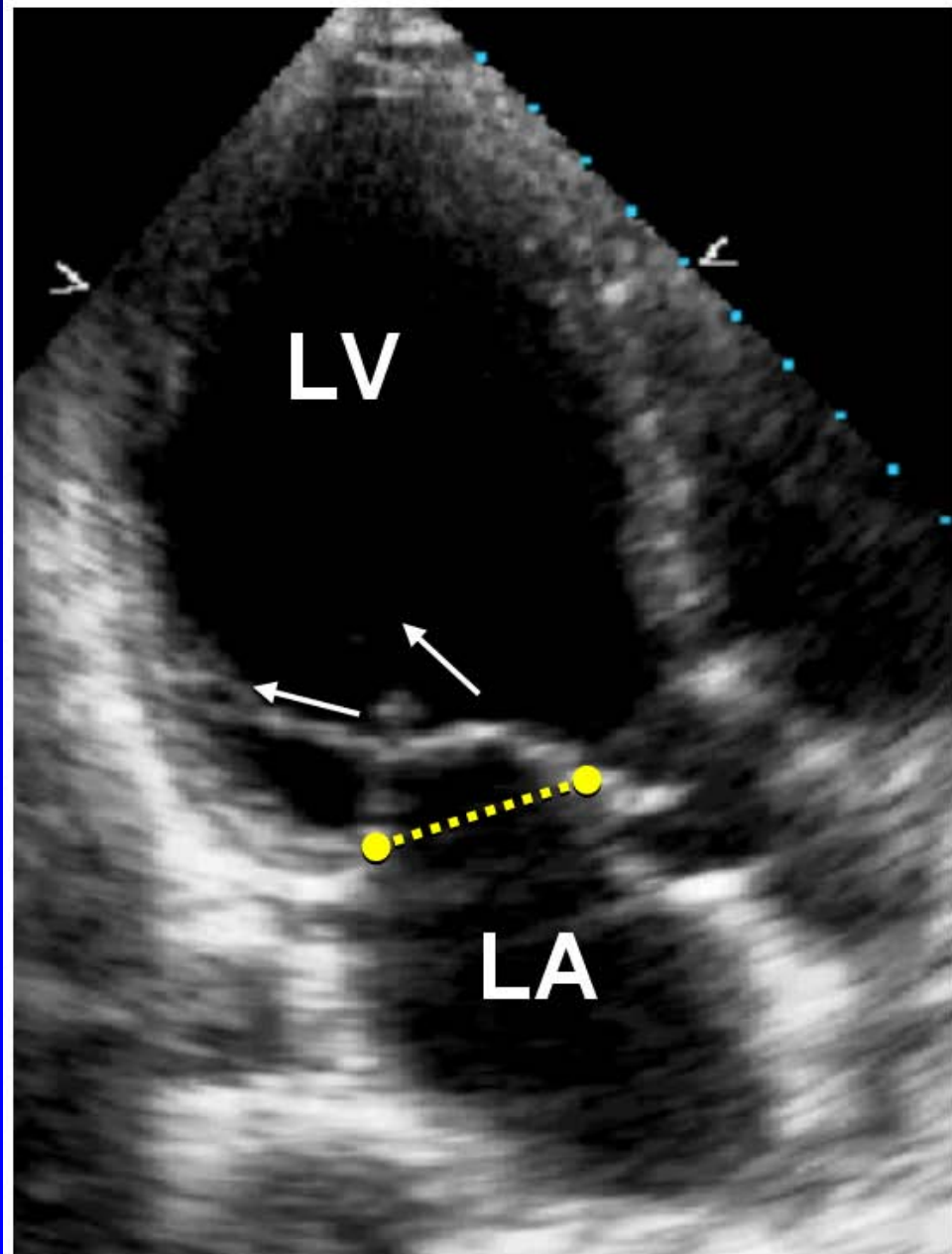
Ischemic Mitral Regurgitation

Definition and mechanism

Good news about prognosis

**Good news and a challenge for
repair**

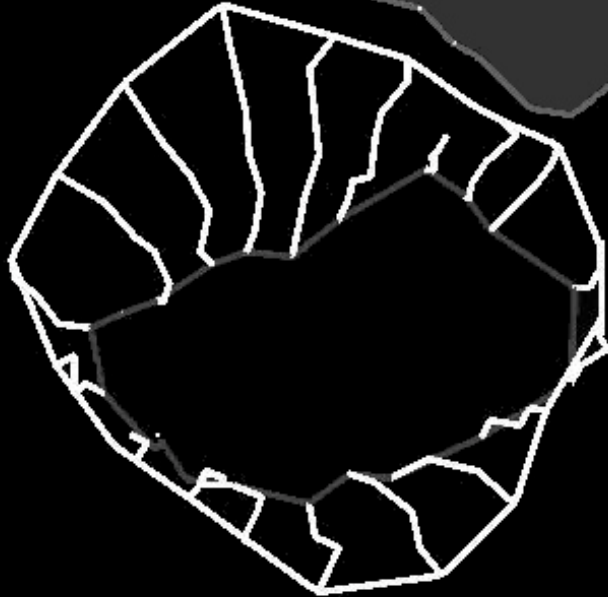
A mismatch between ventricular and valvular size



**Current thinking about therapy
assumes the size of the native
valve is fixed**

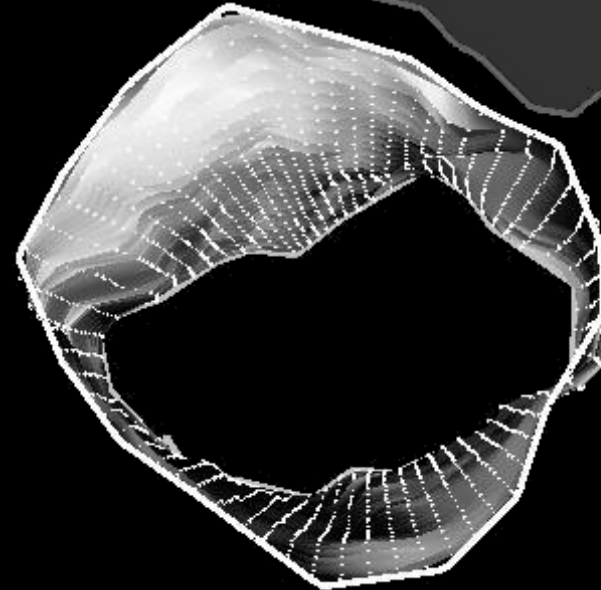
Traces

Ao



Surface

Ao

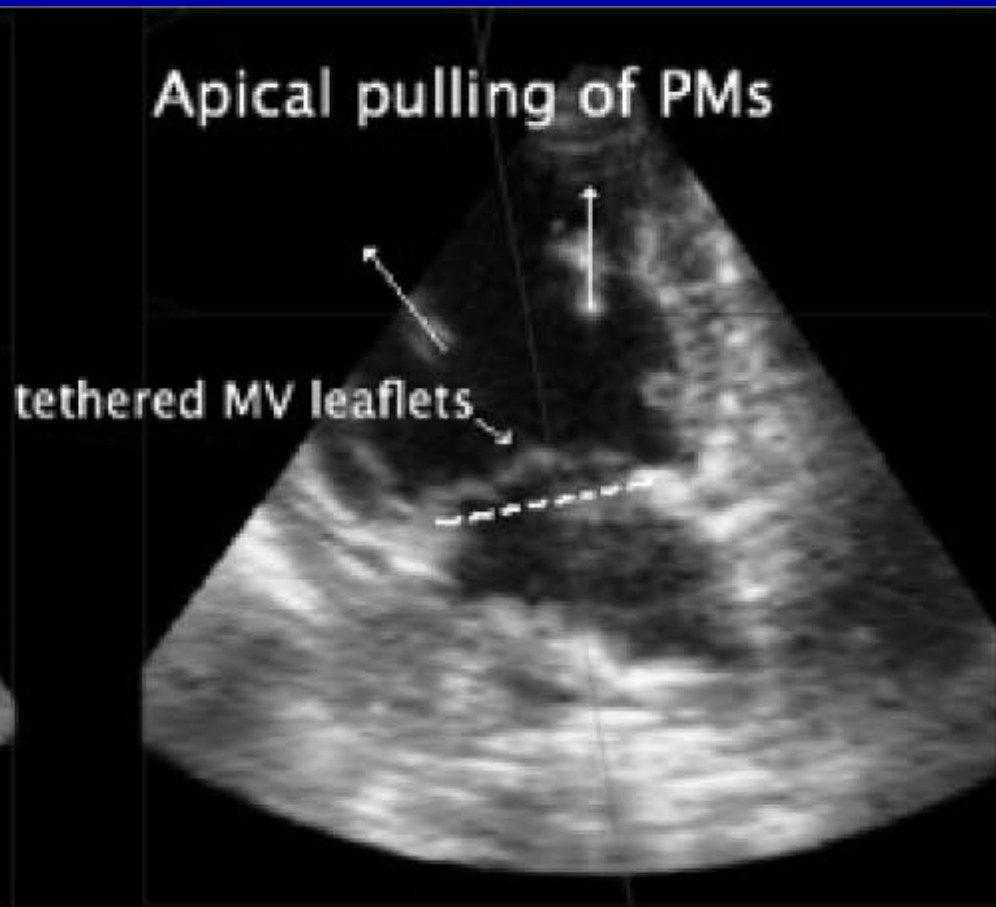
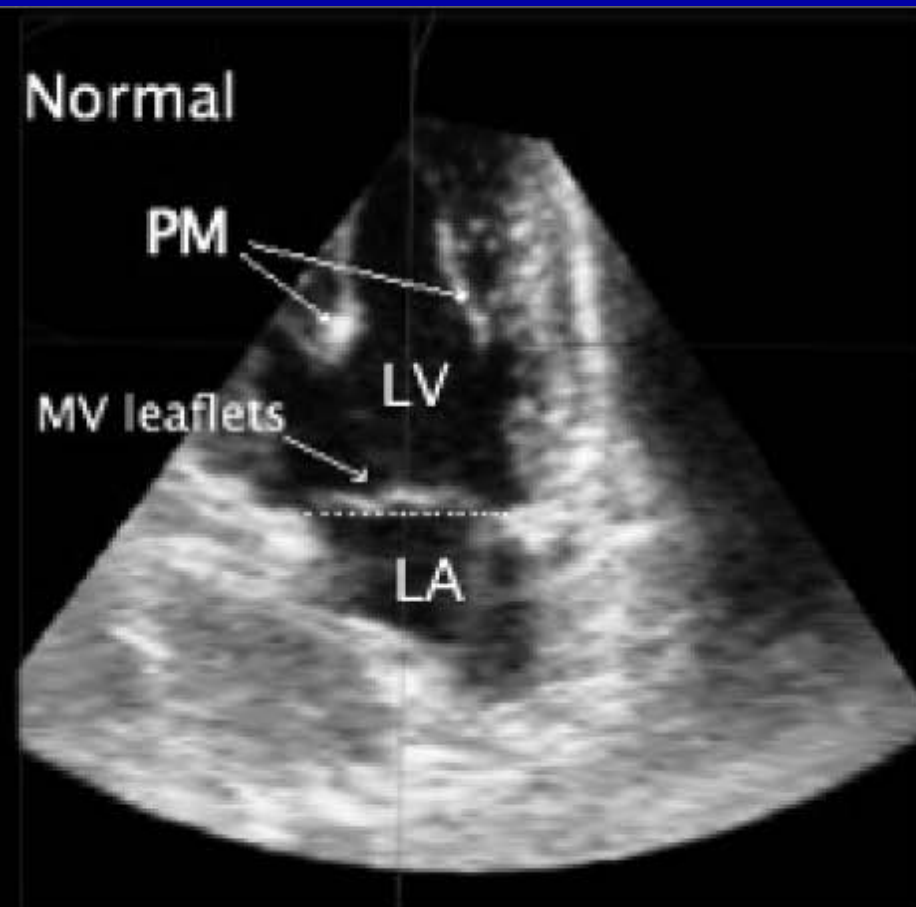


MIGUEL CHAPUT
MARK HANDSCHUMACHER
CIRCULATION 2008

To isolate the effect of tethering, we applied mechanical stretch to sheep MVs *in situ* over two months

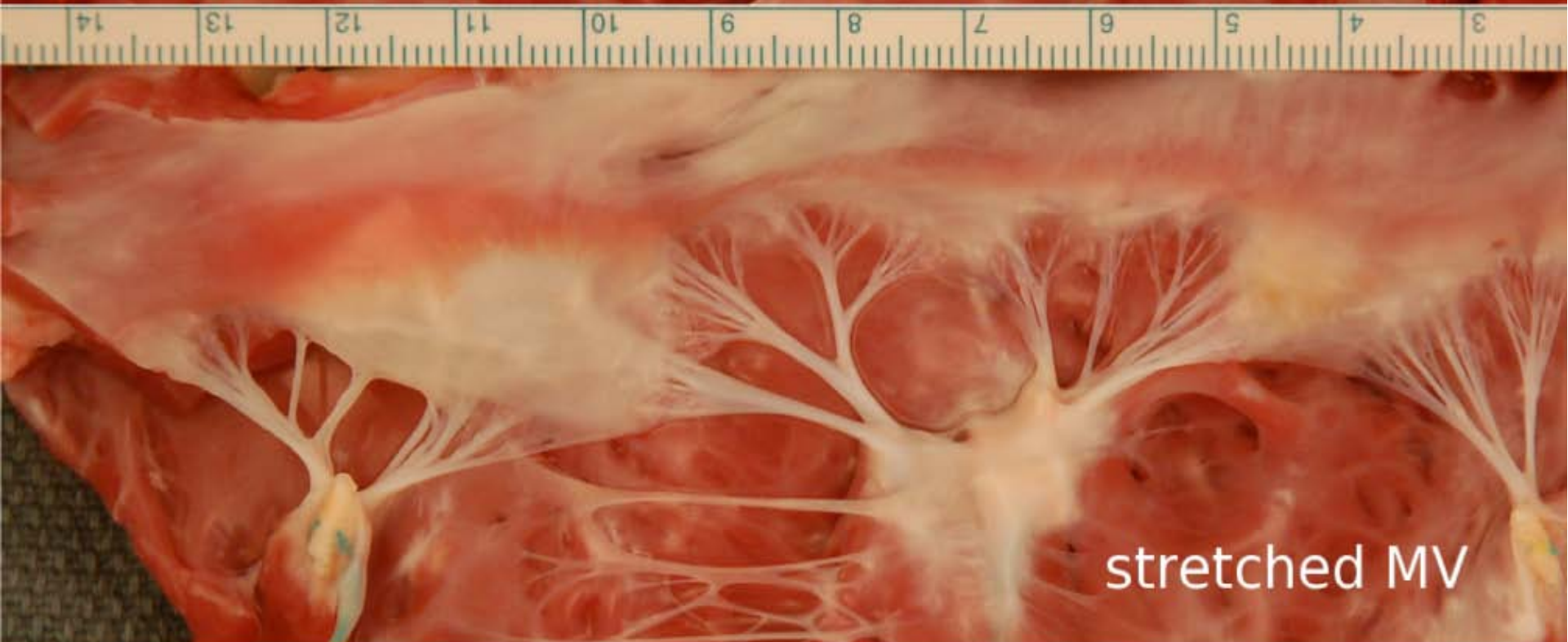
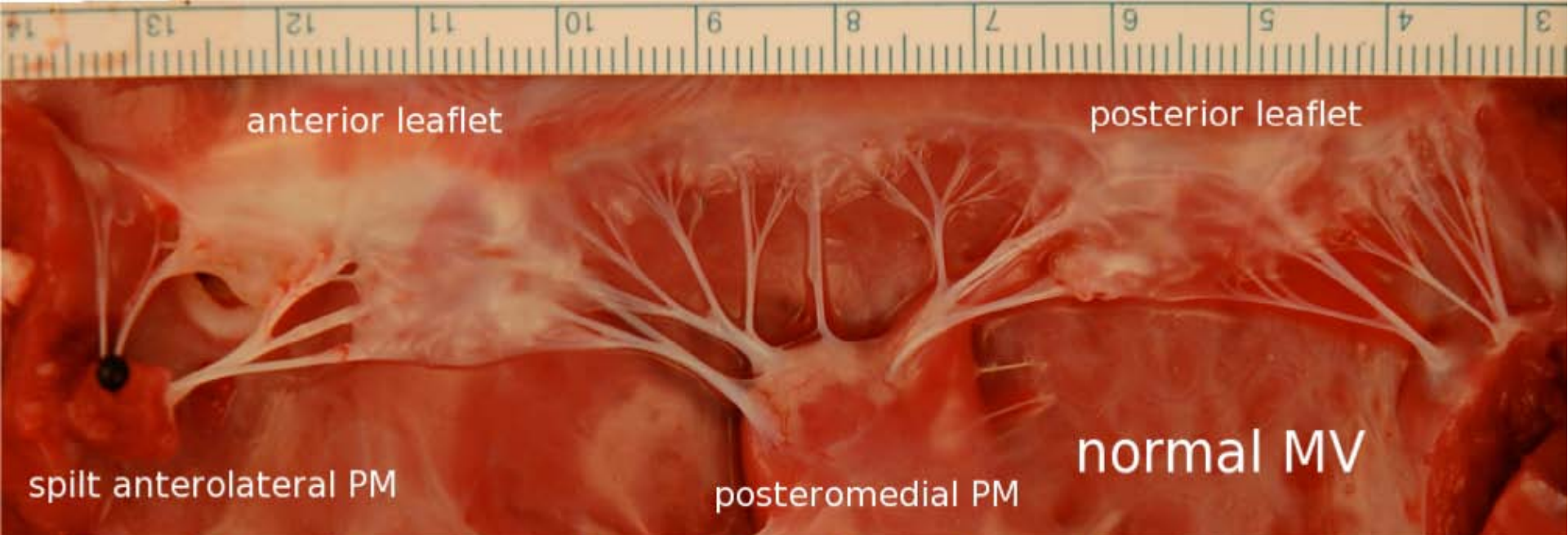
UNTETHERED MV

TETHERED MV



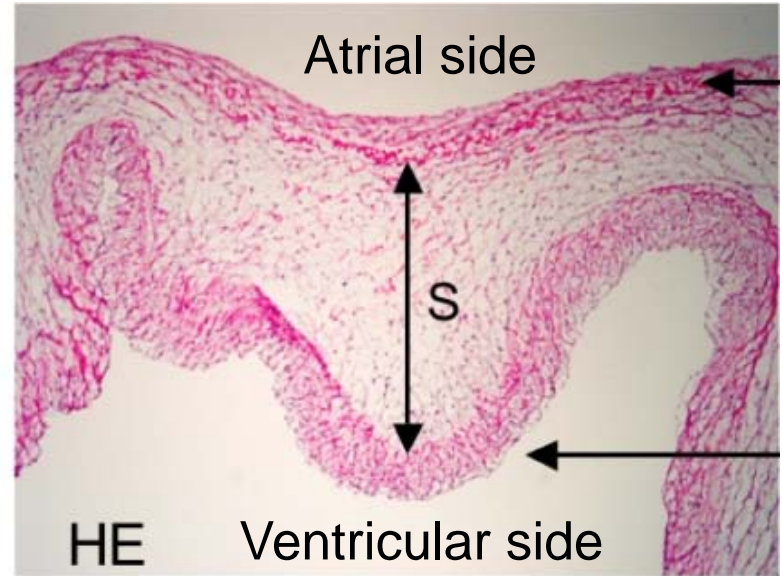
STRETCHED MITRAL VALVES (Dal-Bianco Circulation 2009):

**Active valve growth: Increased
area and thickness over two
months**



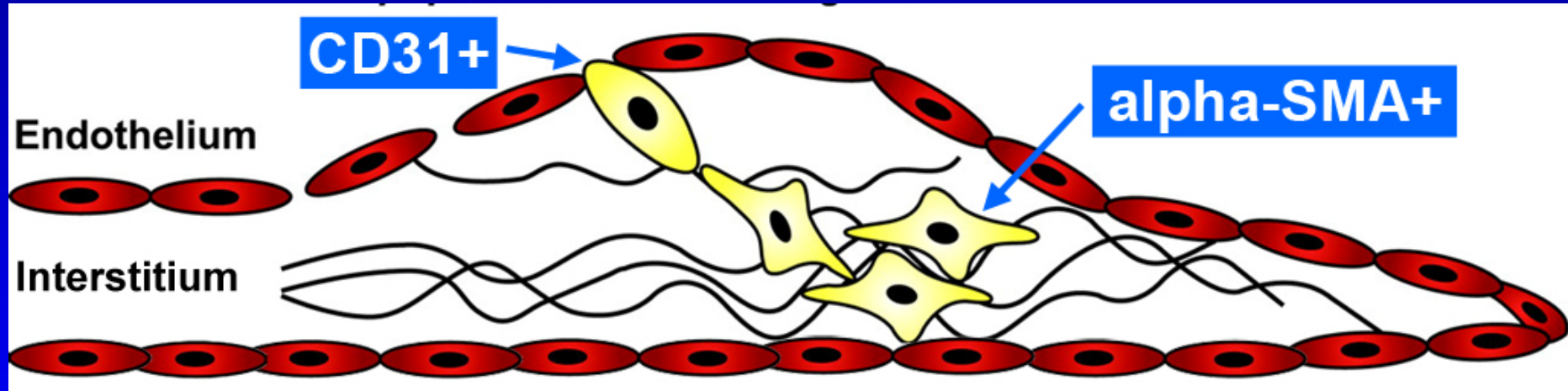
Unstretched MV

Tethered MV



How do valves grow?

Endothelial-mesenchymal transformation (EMT)

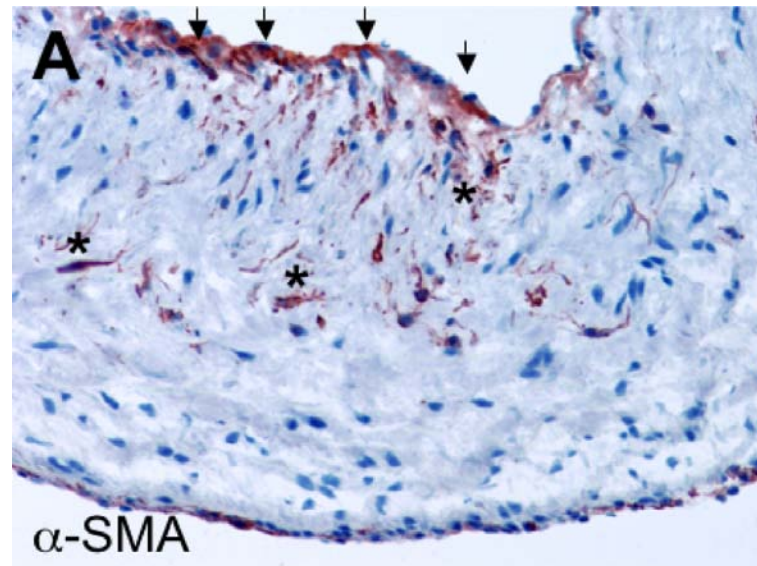
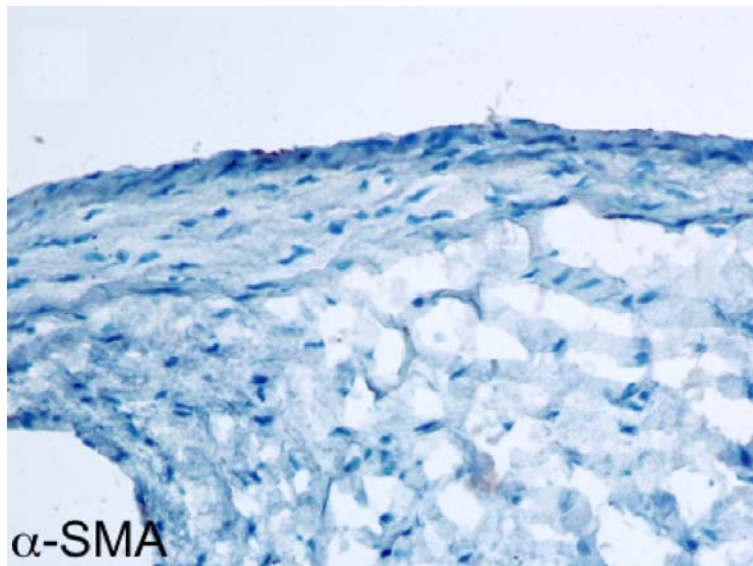
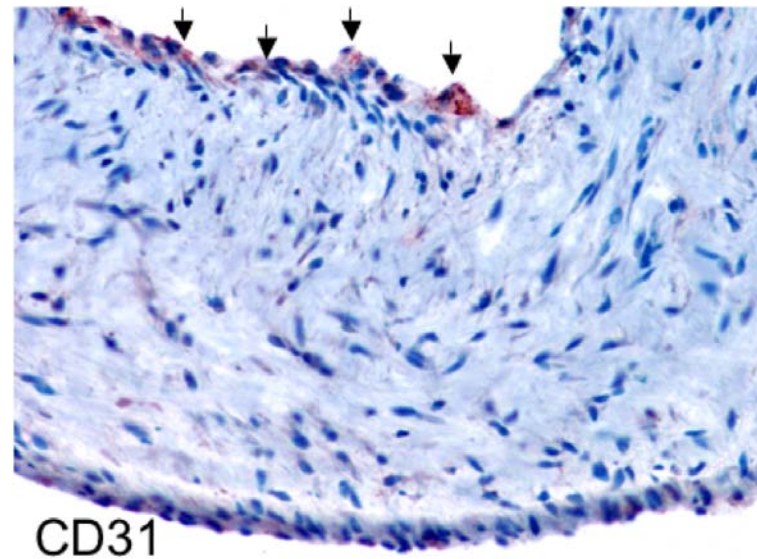
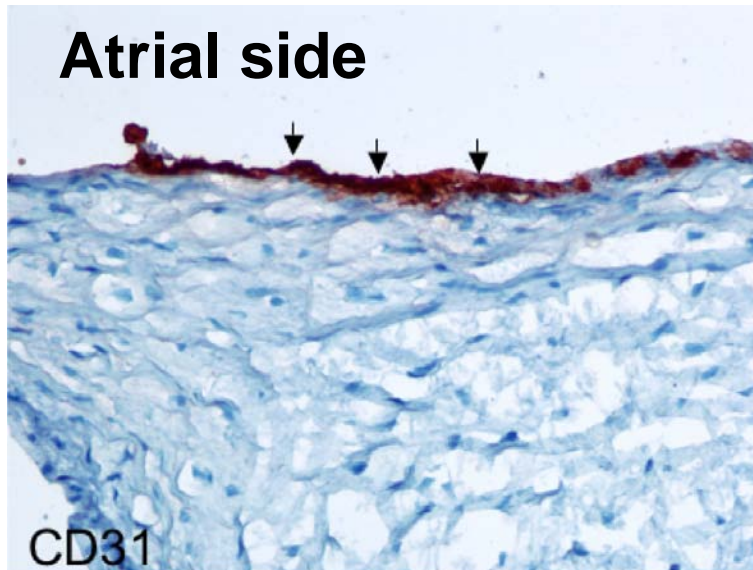


Armstrong EJ, Bischoff J, Circulation Research, 2004

Unstretched MV

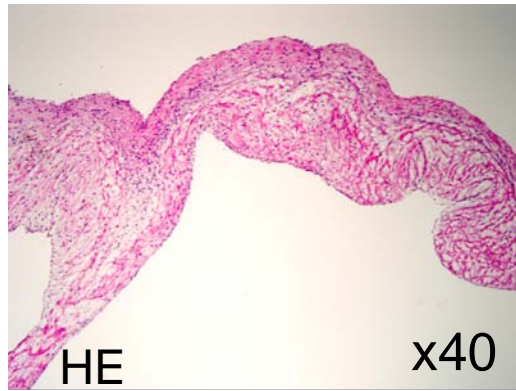
Tethered MV

Atrial side

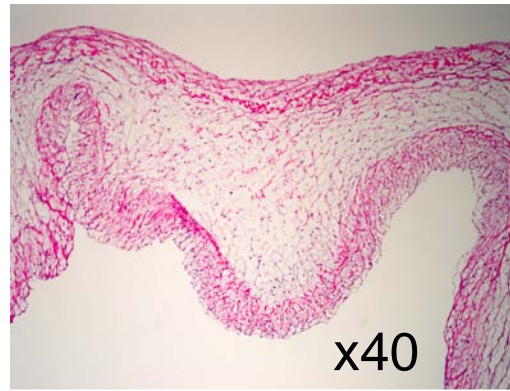


Tethering + MI produces markedly increases thickness

Normal MV



Tethered MV

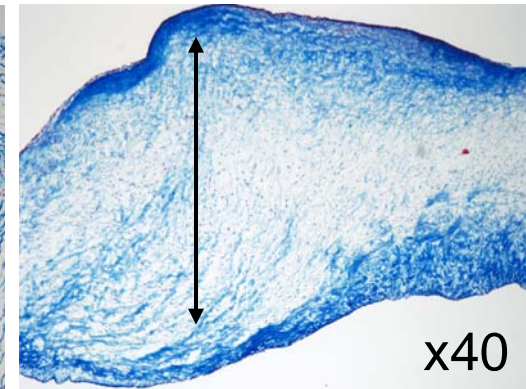
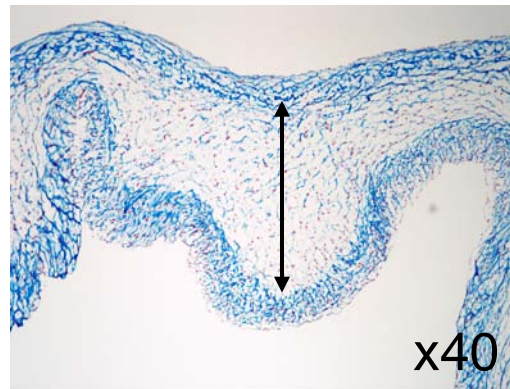
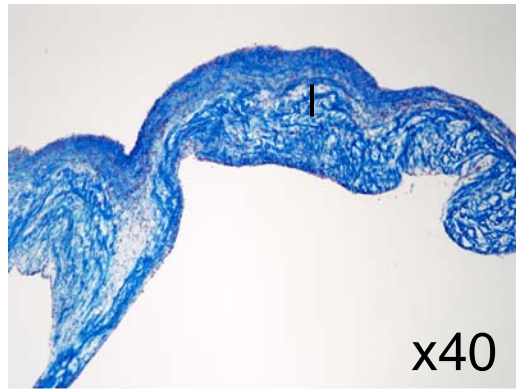


Tethered + MI MV



Atrial side

Ventricular side



« The living valve »

The mitral valve is dynamic, with the capacity to reactivate early growth processes in the adult valve

Ischemic Mitral Regurgitation

Definition and mechanism

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**Good news and a challenge for
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CLINICAL STUDIES OF OUTCOME FOLLOWING RING

**We can't tell whether MV
repair improves outcome if
the MV isn't repaired!**

Ischemic Mitral Regurgitation

Definition and mechanism

Good news about prognosis

Good news and a challenge: *Is it time to revive plication?*

Thank You !