Non-invasive evaluation of Myocardial Viability Using Magnetic Resonance Imaging

Raja Muthupillai, PhD, DABR, DABMP

Baylor St. Luke's Medical Center
CHI St. Luke's Health
Houston, TX 77030

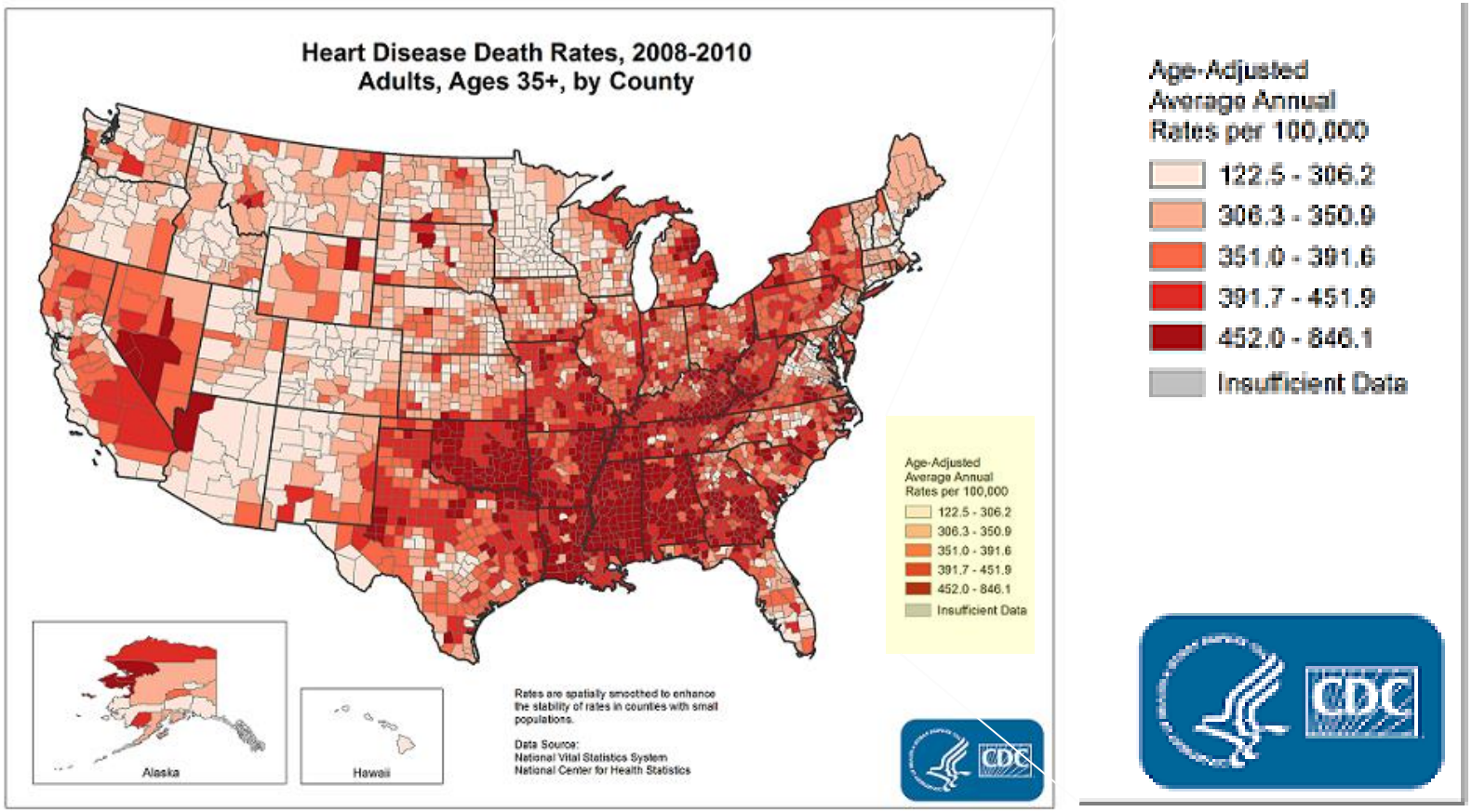
CHI St. Luke's Health

Texas Heart® Institute
at St. Luke's Episcopal Hospital

Disclosures

- Non-FDA approved use of Gadolinium-chelates for CMR applications

Cost of Heart Disease : Lives



610,000 deaths per year;1 in 4 deaths; ~50% due to CAD ; 109 Billion USD

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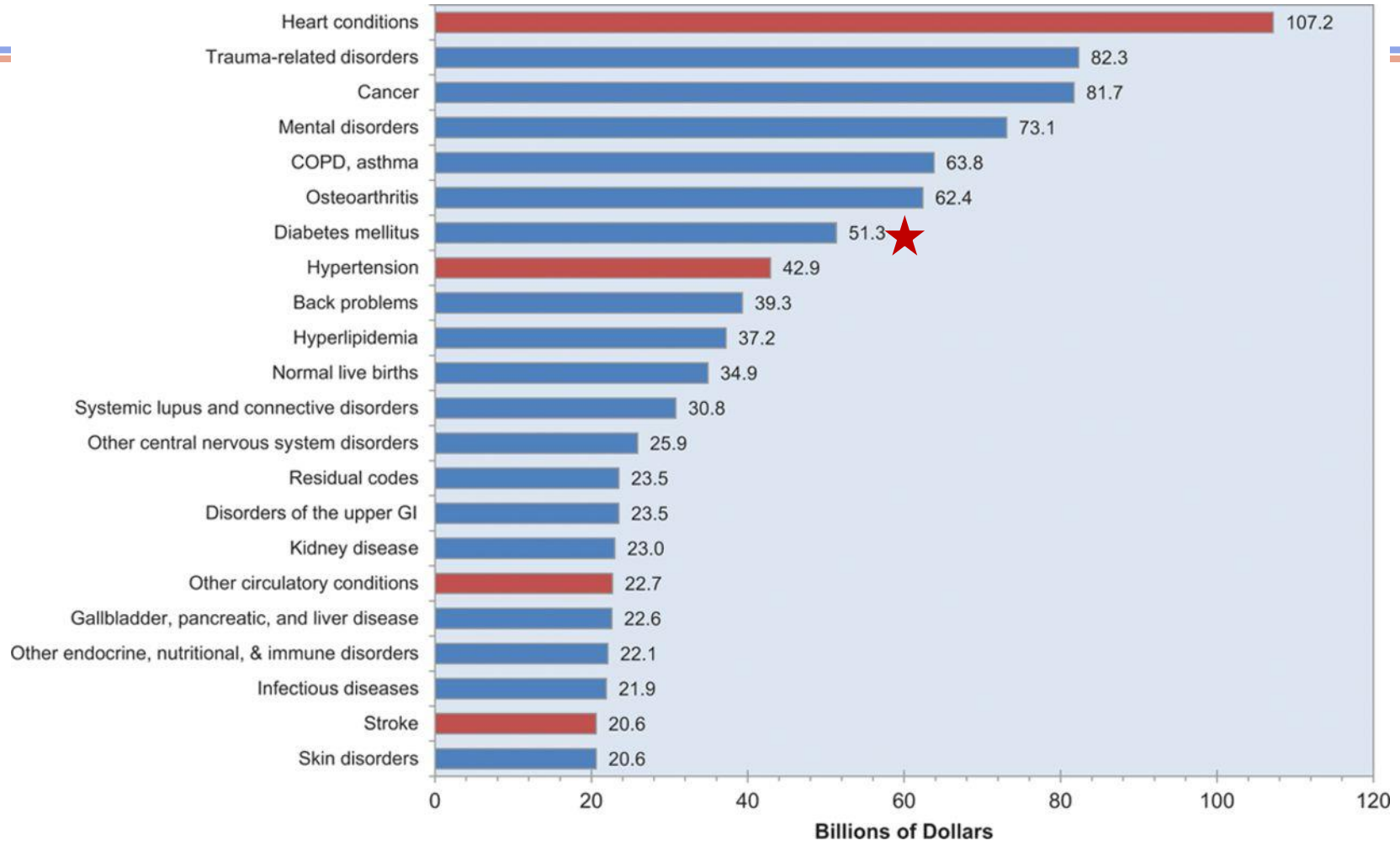
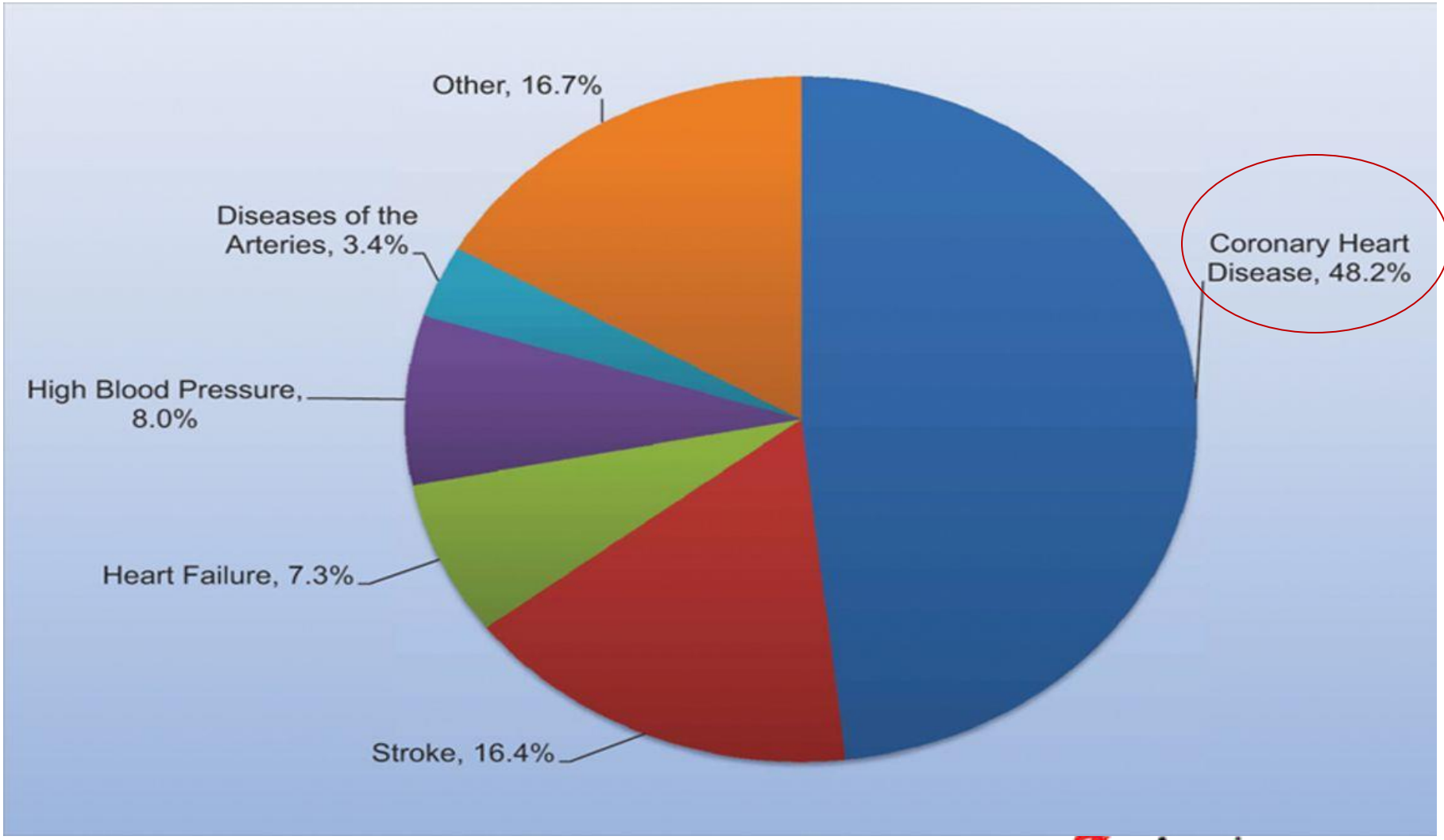
The 22 leading diagnoses for direct health expenditures, United States, 2010 (in billions of dollars).



Alan S. Go et al. Circulation. 2014;129:e28-e292

American Heart Association.

Deaths attributed to Heart Disease (%) (United States: 2010).



Alan S. Go et al. Circulation. 2014;129:e28-e292Heart Disease and Stroke Statistics—2014 Update

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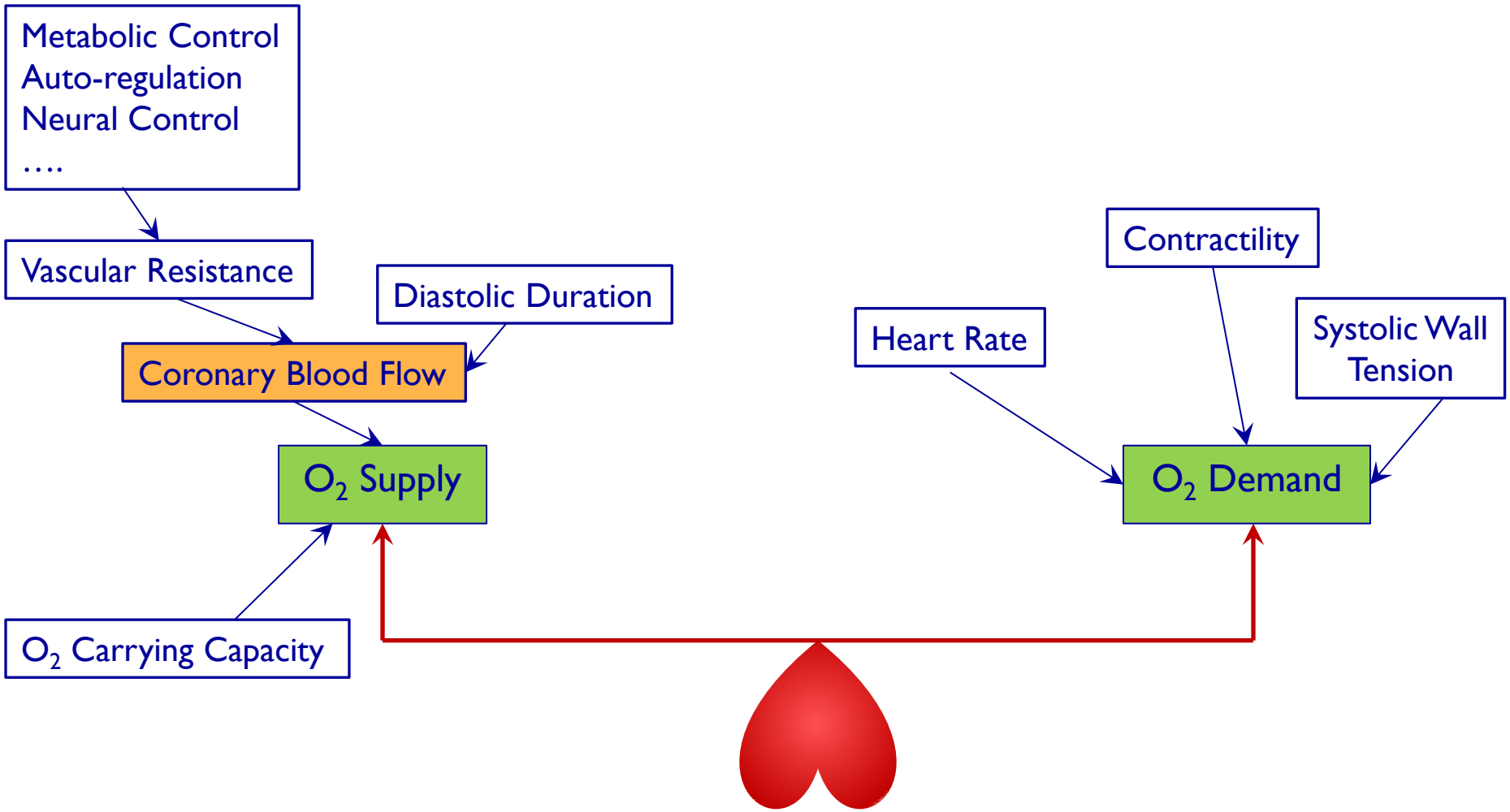
American Heart Association.

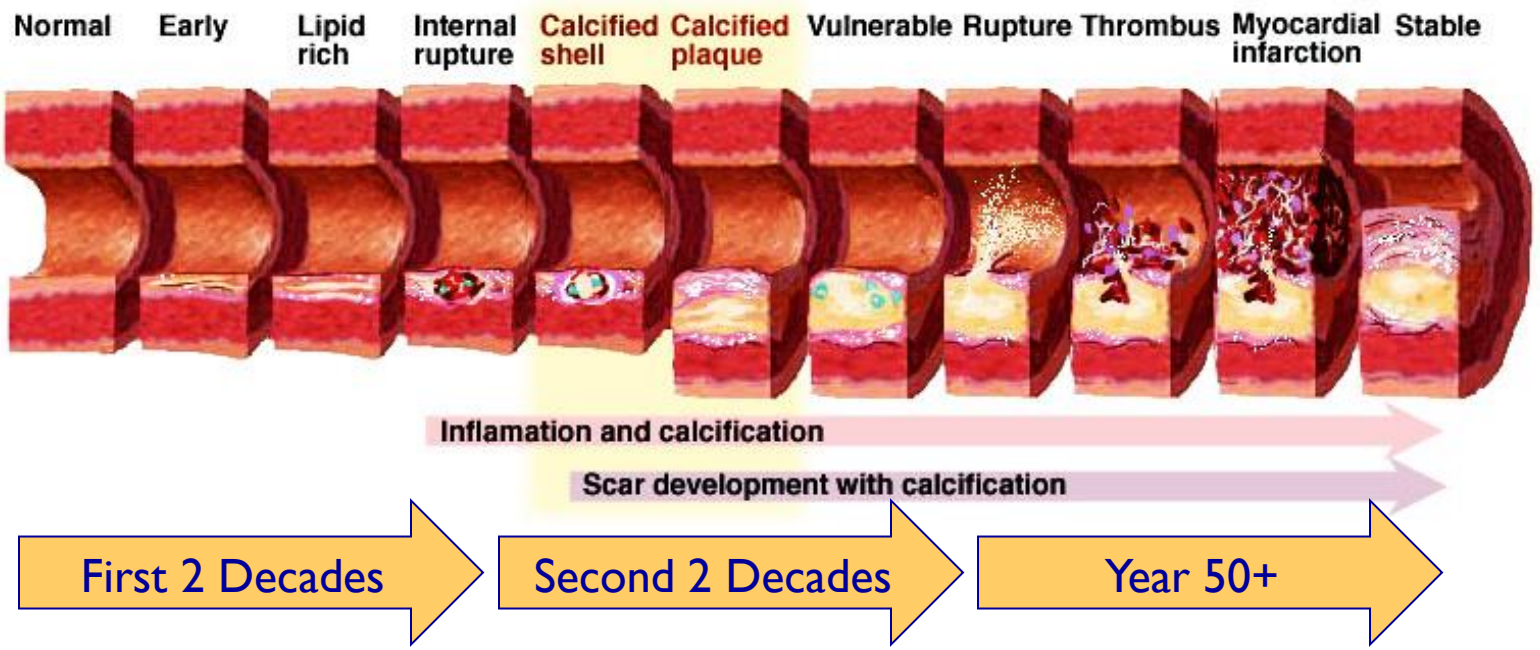
Heart Disease

- Ischemic Heart Disease
  - Inability to supply blood to meet demand
- Non-Ischemic Heart Disease
  - Hypertrophic Cardiomyopathy
  - Fatty/Fibrous Infiltration, e.g., Amyloidosis
  - Arrythmogenic RV Dysplasia
- Valvular problems
  - Valvular Incompetence
  - Valvular Stenosis
- Vascular problems
  - Dissections, Aneurysms
- Congenital Heart Disease

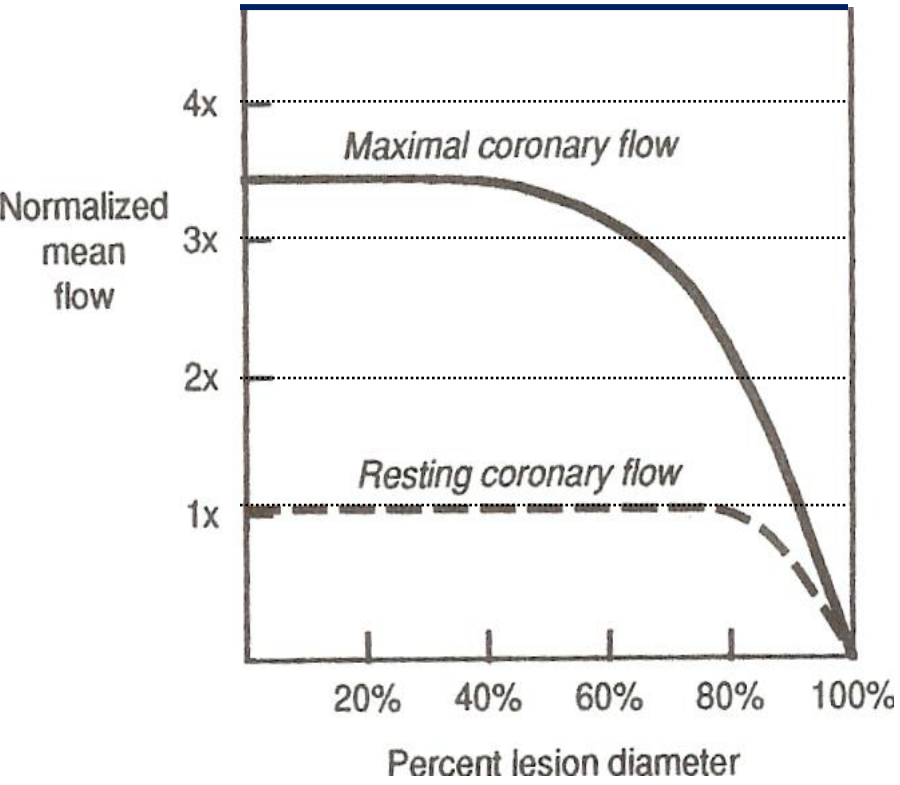
Myocardial Ischemia - I



Ischemic Heart Disease : Progressive

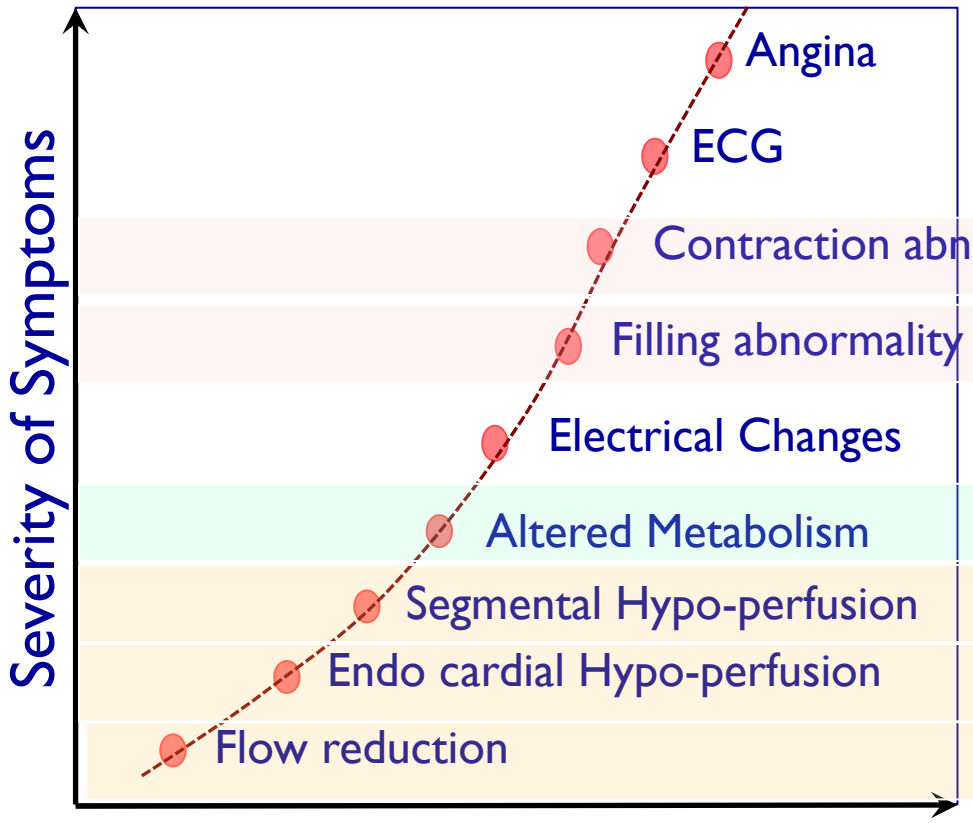


Perfusion Reserve : Adaptation



Adapated from: Gould KL, et al. AJC 1974

Ischemic Cascade and Imaging Windows



Echo, CMR

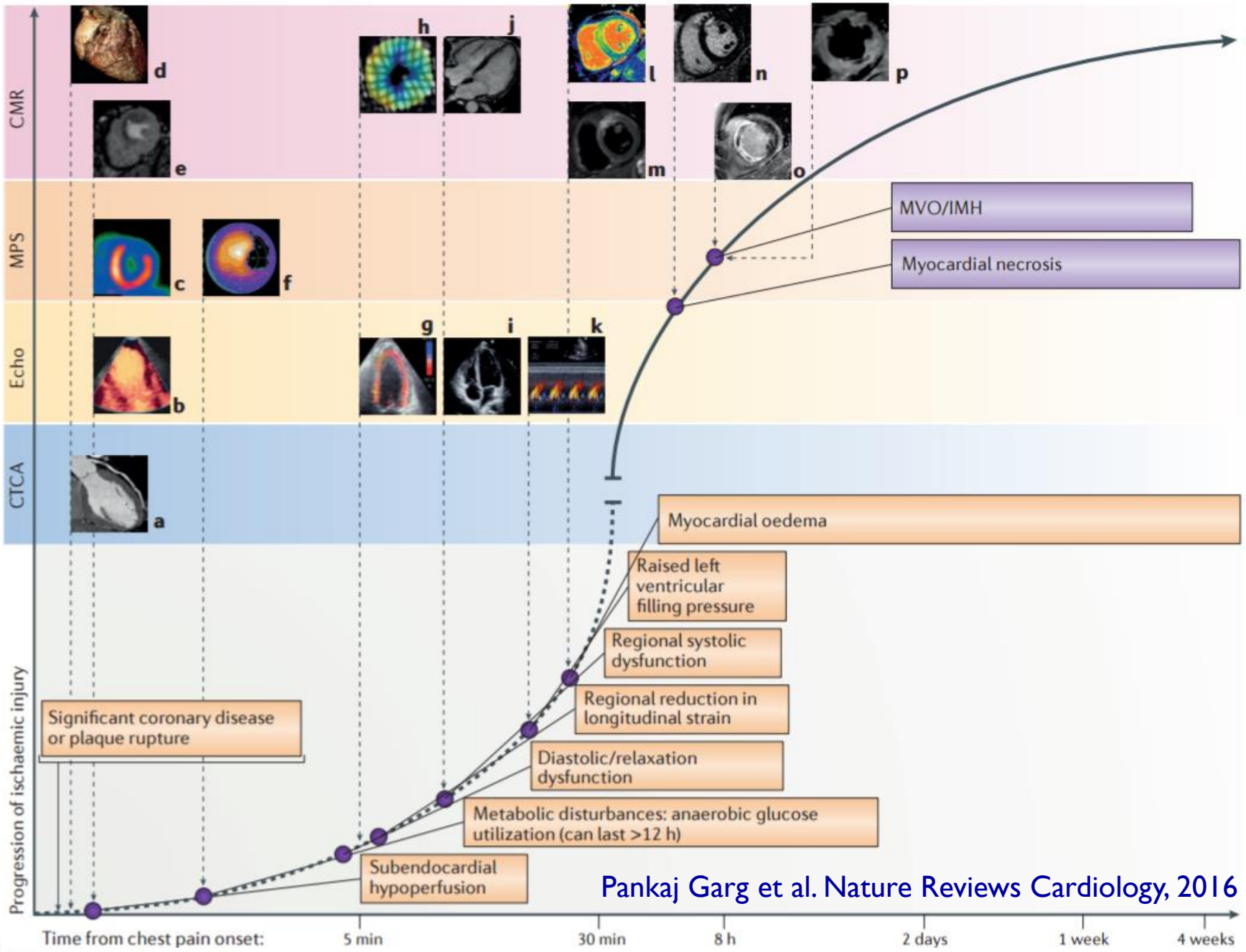
Echo, CMR

PET, CMR

PET/SPECT, CMR MPI

PET?, CMR MPI

PET/SPECT, CMR MPI



Pankaj Garg et al. Nature Reviews Cardiology, 2016

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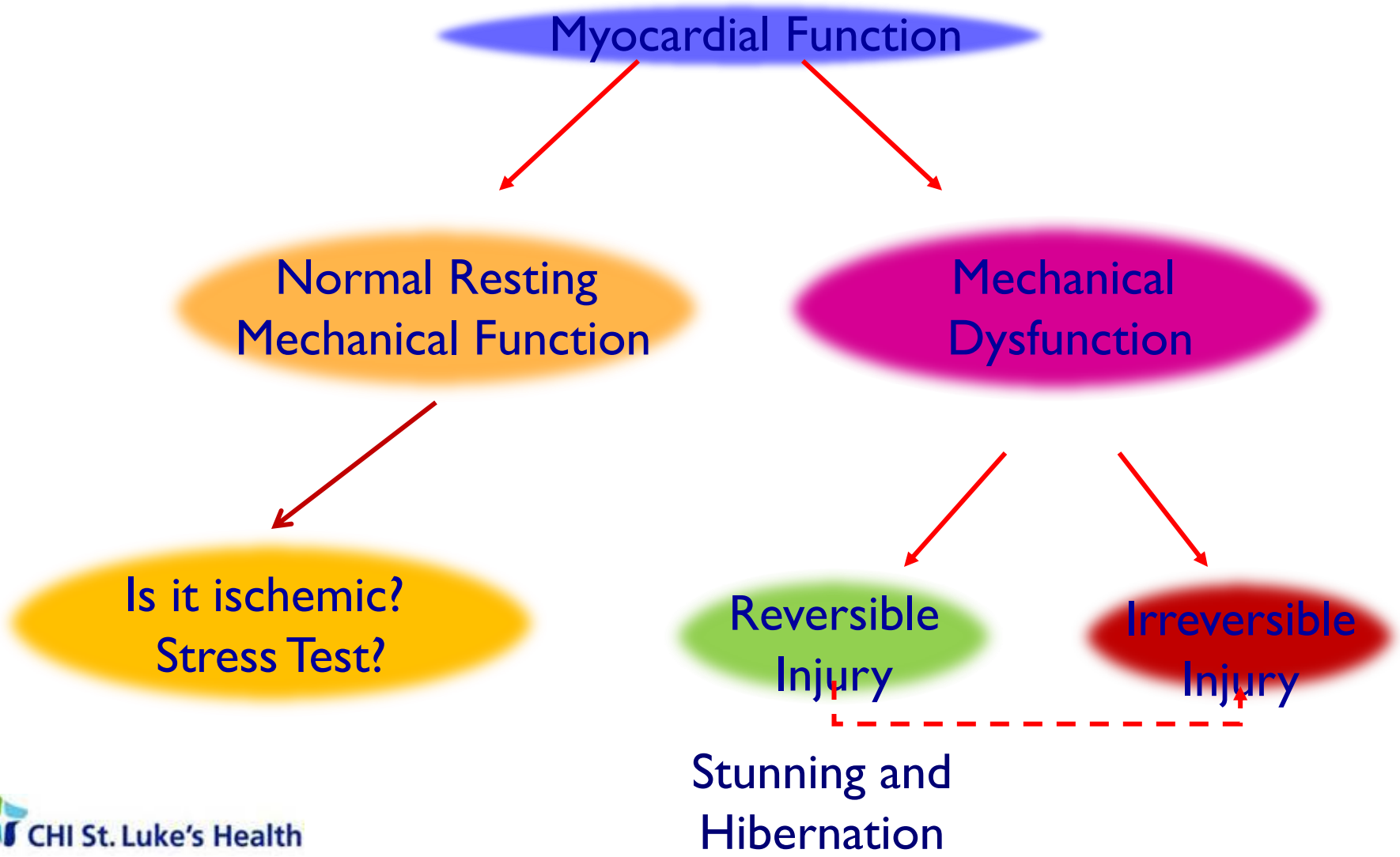
Myocardial Ischemia – Overview



Some Definitions

Ischemia: Impaired blood supply; inducible defect with stress

Stunning: Transient mechanical Dysfunction due to acute ischemic insult

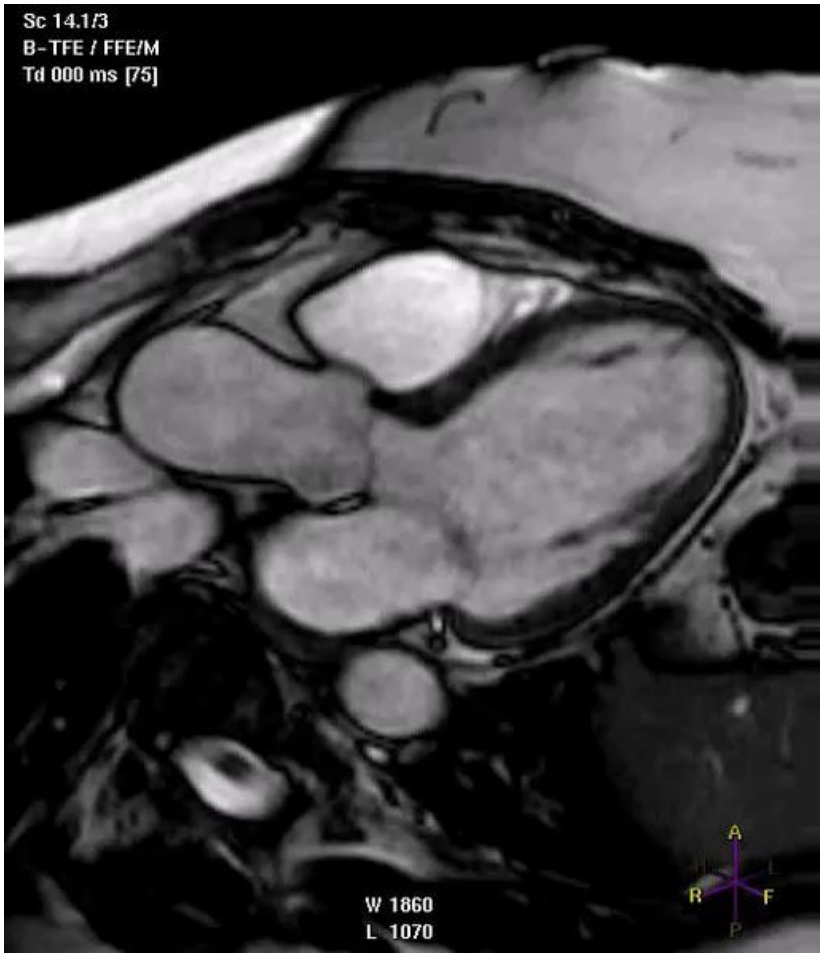
Hibernation: Adaptation to chronic ischemia via down-regulation.

Cell death: Loss of cell membrane integrity – irreversible injury either via apoptosis or necrosis.

Outline

- What is the clinical question regarding "viable" myocardium?
- Role of non-invasive imaging in evaluating myocardial viability
- MRI assessment of myocardial viability: Delayed Enhancement
- Technical Issues and Trouble shooting
- Conclusions

Clinical Problem : Wall motion



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Entirely normal?

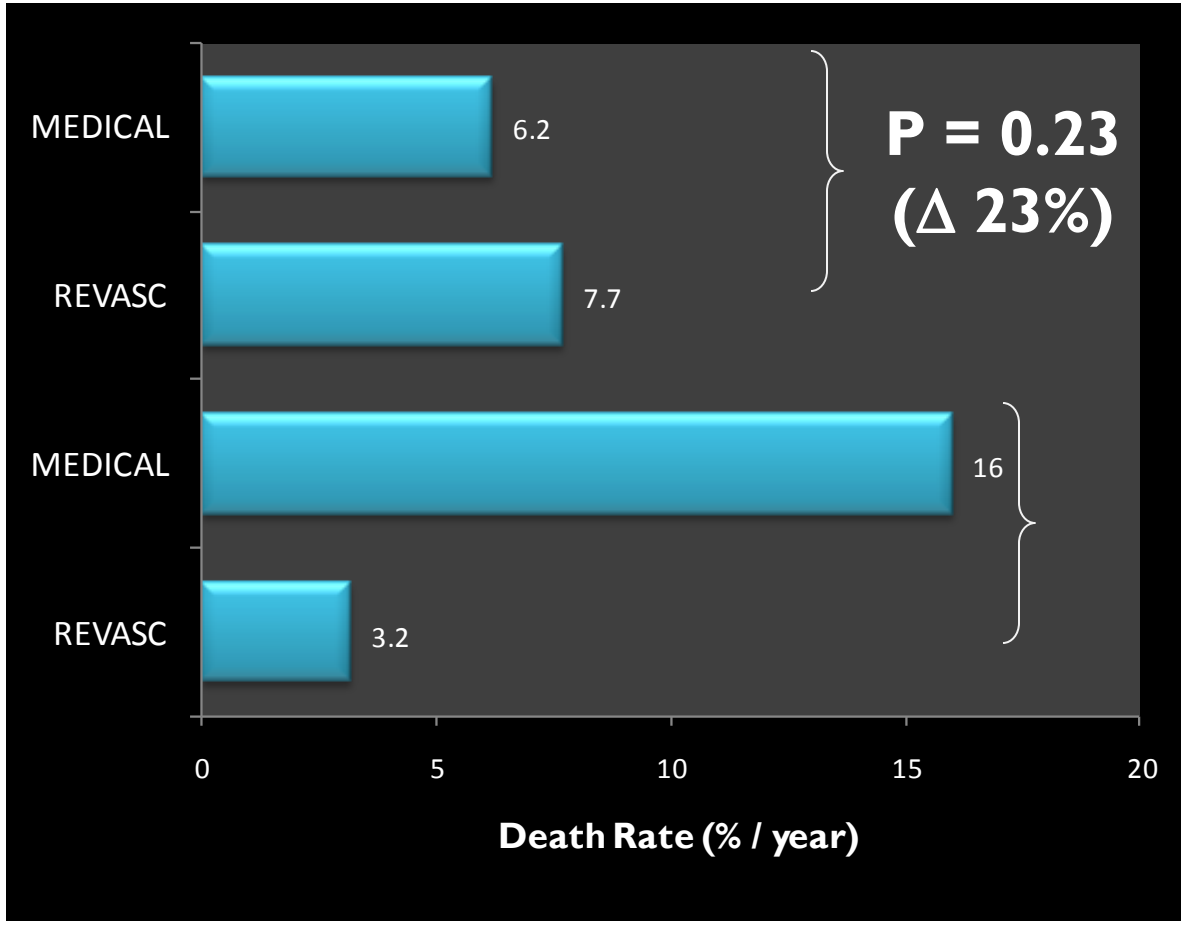
Dysfunction Treatable?

Dead meat or red meat?

- Ischemic myocardium will recover function after revascularization
- Dead or non-viable myocardium will NOT recover function
- Revascularization has non-negligible risk
- Revascularization of non-viable myocardium is associated with increased risk compared to mecical therapy

Why assess myocardial viability?

Death Rates in Patients +/- Revascularisation



P < 0.0001

(Δ 80%)

Meta-analysis > 3000 pts

PET, TI SPECT, ECHO

KC Allman at al. JACC 2002;39:1151-1158.

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Courtesy: Dr. Cheong, MD, BSLMC

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Imaging and myocardial viability

- Nuclear Scintigraphy
  - SPECT
  - PET
- Magnetic Resonance Imaging
  - Delayed Enhancement MRI
- Echocardiography
- Computed Tomography (Contrast Enhanced)

Myocardial dysfunction and Imaging

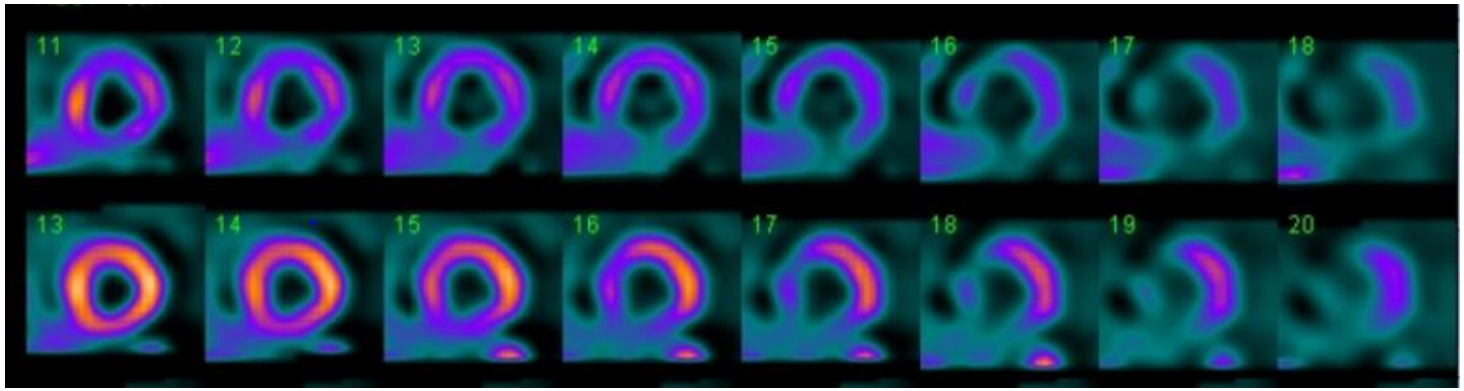
- Myocytes with cell membrane integrity
  - Radionuclide tracer uptake : PET/SPECT
  - "Fixed" Perfusion Defect Vs Inducible hypo perfusion

- Myocardium with preserved capacity to contract
  - Ability to recover function with low dose dobutamine
    - Low-dose dobutamine echocardiography
    - Low-dose dobutamine cardiac MR function

Nuclear Scintigraphy: Approach

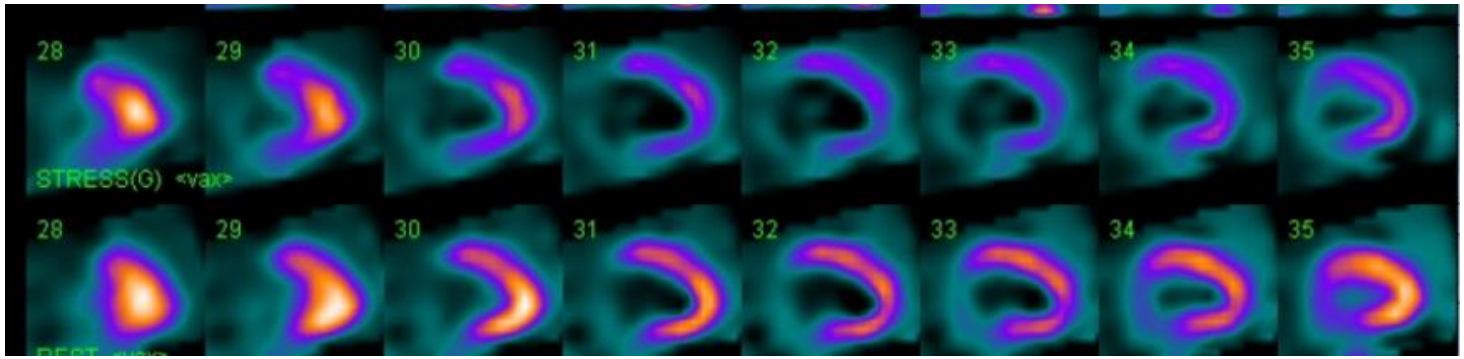
- Acquire Images during stress and rest
- A defect that is persistent during stress and rest is considered a “fixed” defect indicative of irreversible injury or non-viable myocardium
- A defect that is present only during stress is indicative of inducible ischemia or a reversible defect.

Myocardial Viability: Nuclear Scintigraphy



Stress

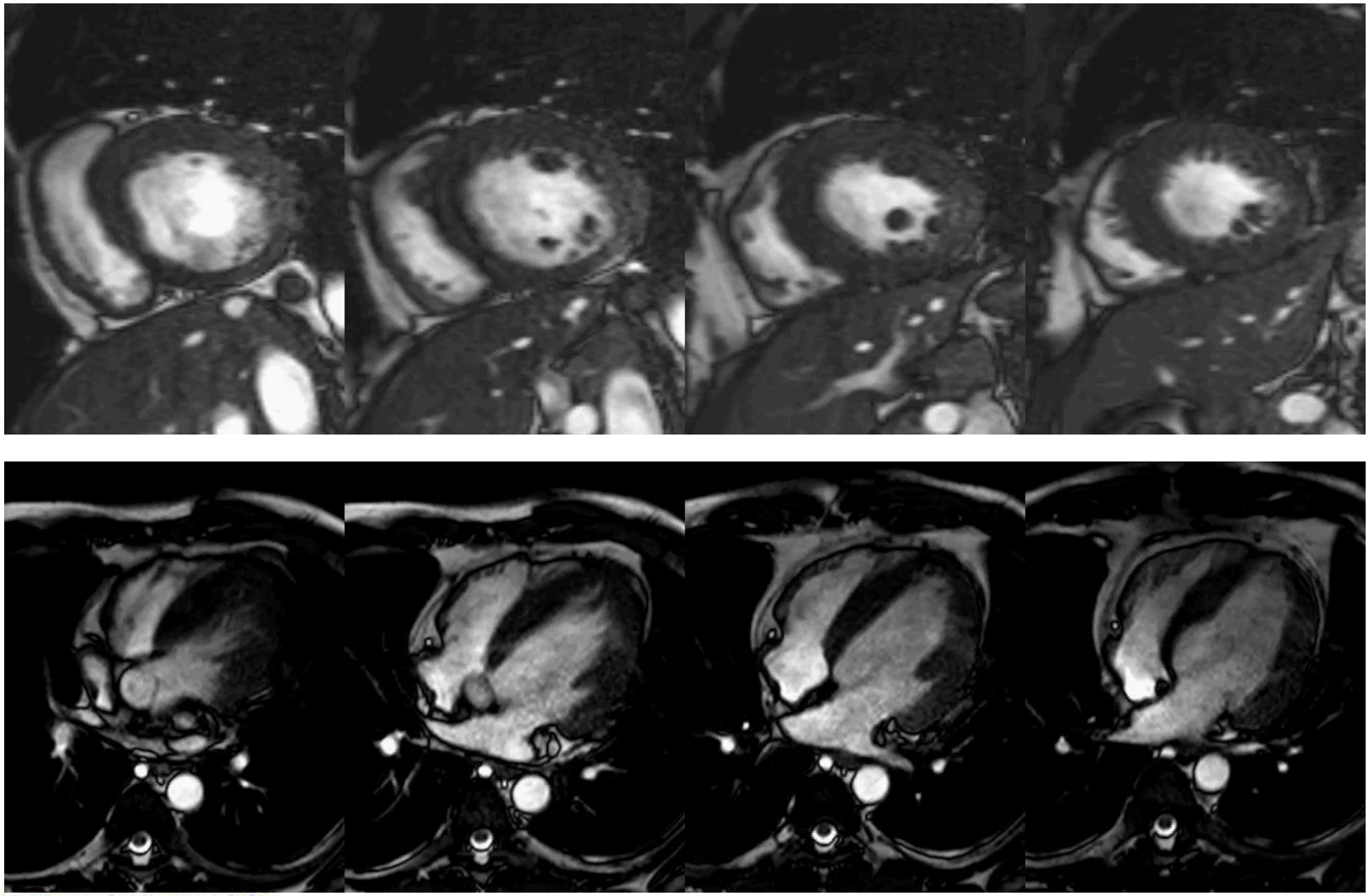
Rest



Stress

Rest

Regional WM Abnormality - MRI



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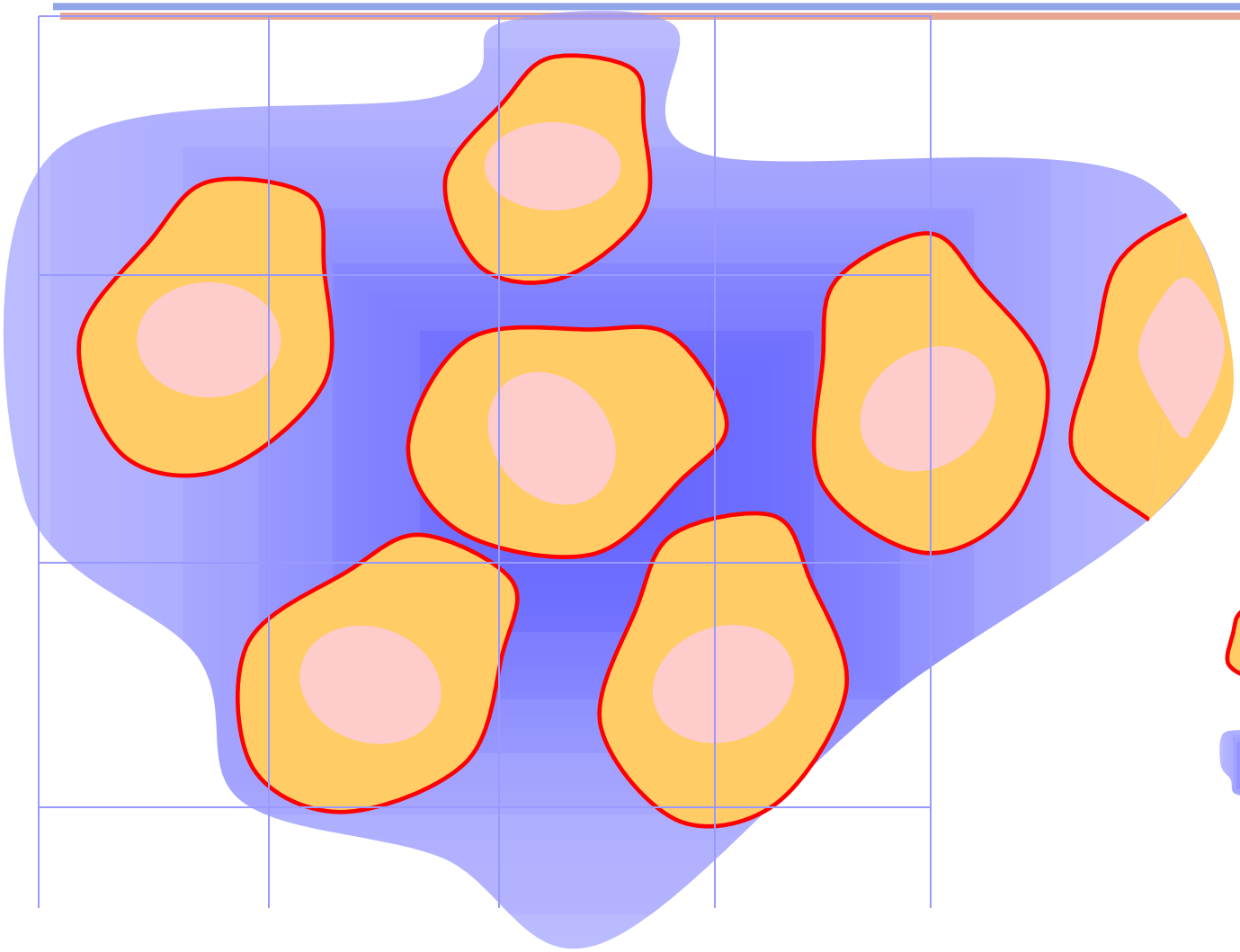
Myocellular matrix: Before Injury



Intact Myocytes

Distribution volume For Extracellular agent (0.3)

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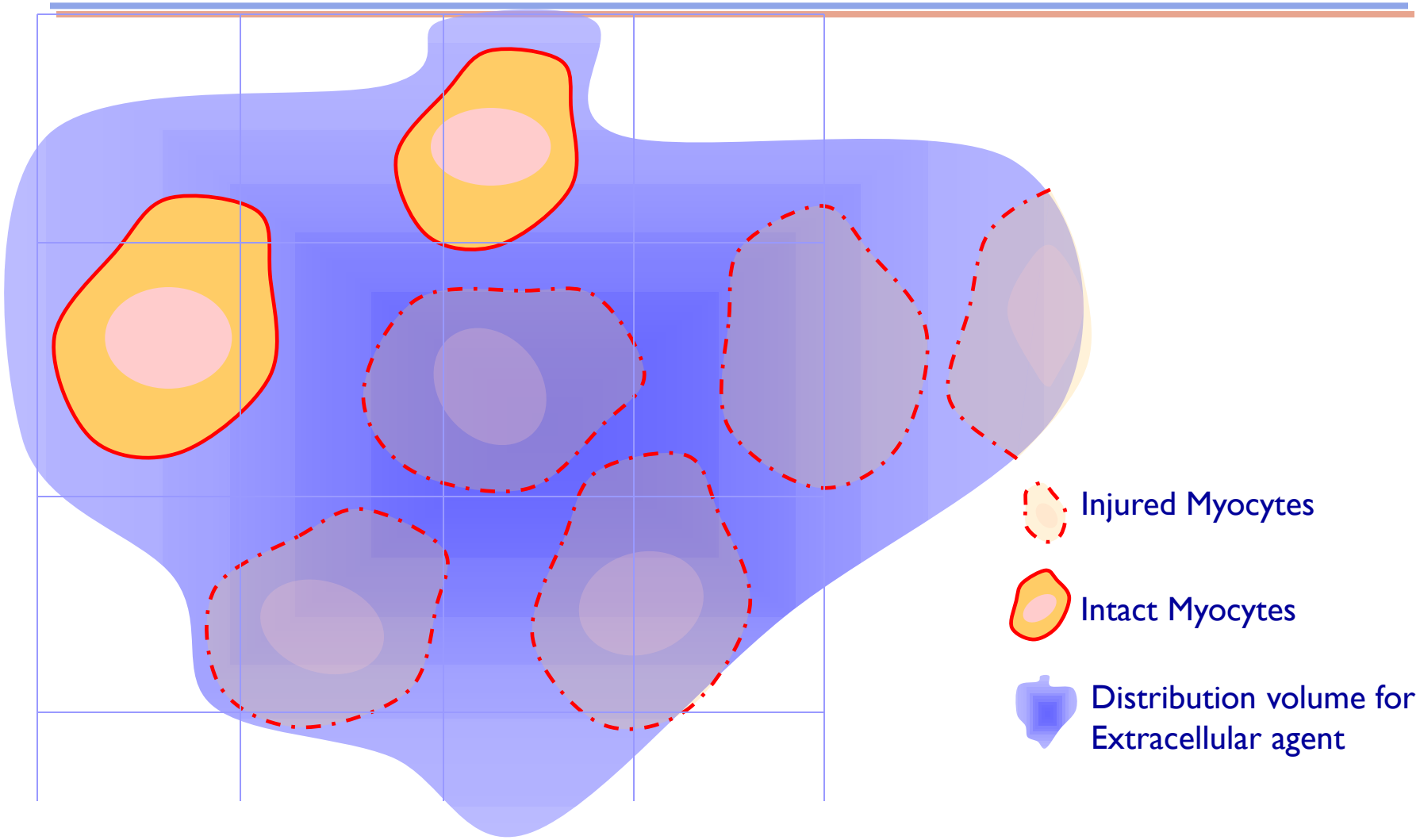
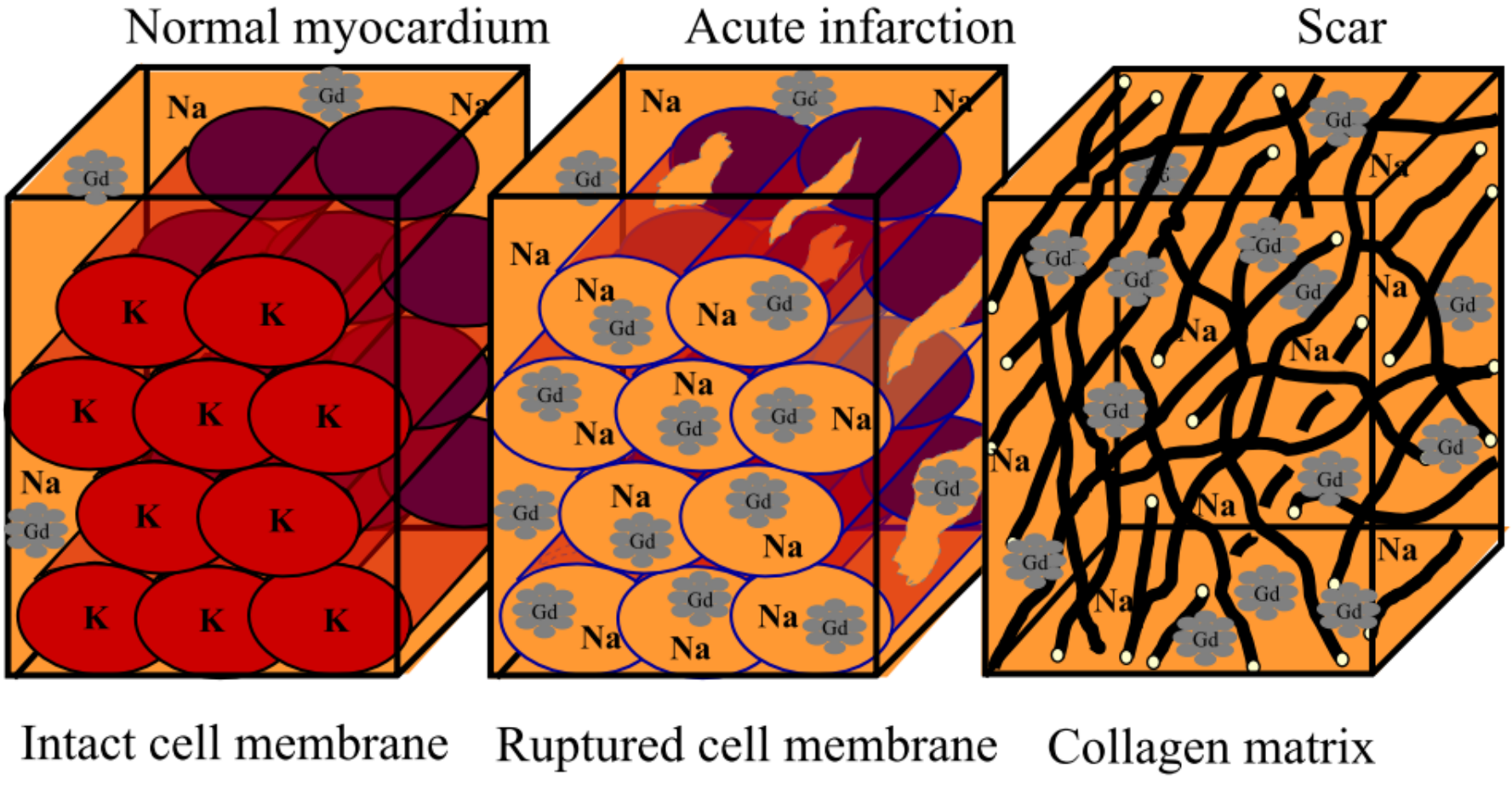
Irreversible Injury : Distribution volume (V_d) for Gd goes up



Mechanism of Delayed-Enhancement



H Mahrholdt et al. EHJ 2005;26:1461–1474

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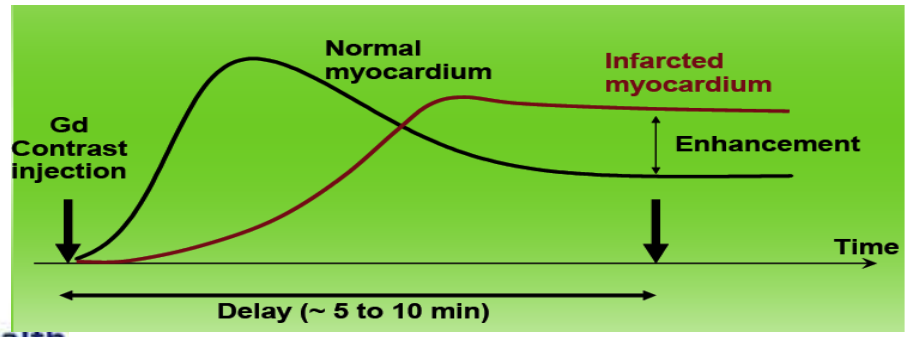
Courtesy: Dr. Benjamin Cheong, MD

Myocellular Injury and V_d

- Loss of cell membrane integrity
  - Increased Distribution volume for Gadolinium
- Chronic Case
  - Increased deposition of fibrous tissue – Collagen matrix
  - Increased distribution volume for an extracellular contrast medium
- **Differential Accumulation of Extravascular agent**



Delayed Enhancement Imaging : Overview

- Extra-cellular Contrast Administration to
  - Exploits the V_d difference between 'dead' Vs 'good'
- 10-15 minutes after Contrast Administration
  - Exploits the contrast agent kinetic differences
- Heavily T_1 weighted Sequence
  - Inversion Recovery Preparation

Pulse Sequence

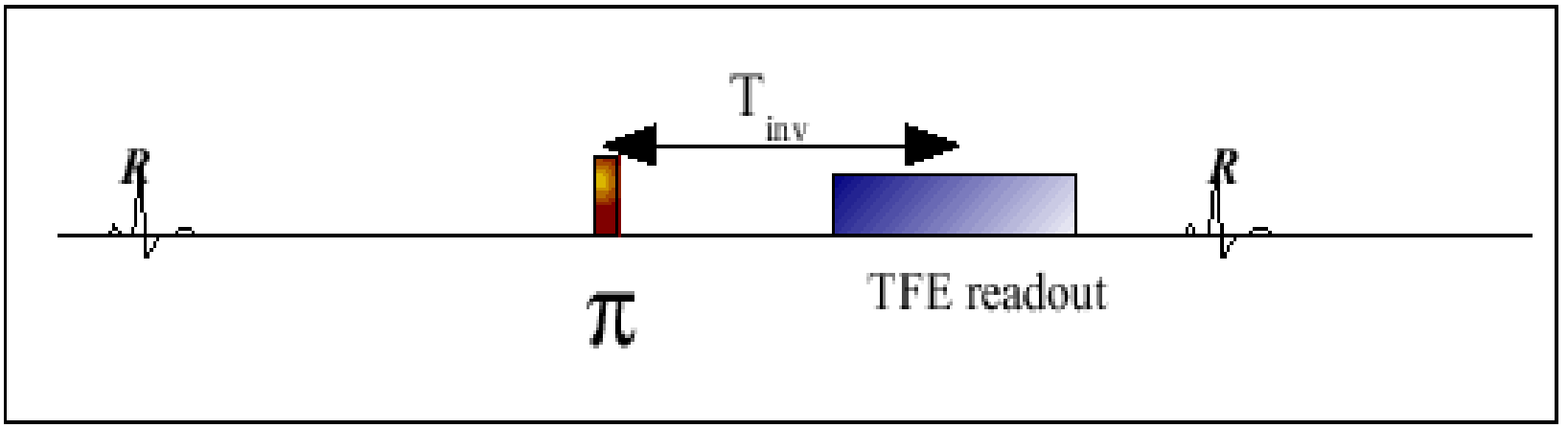
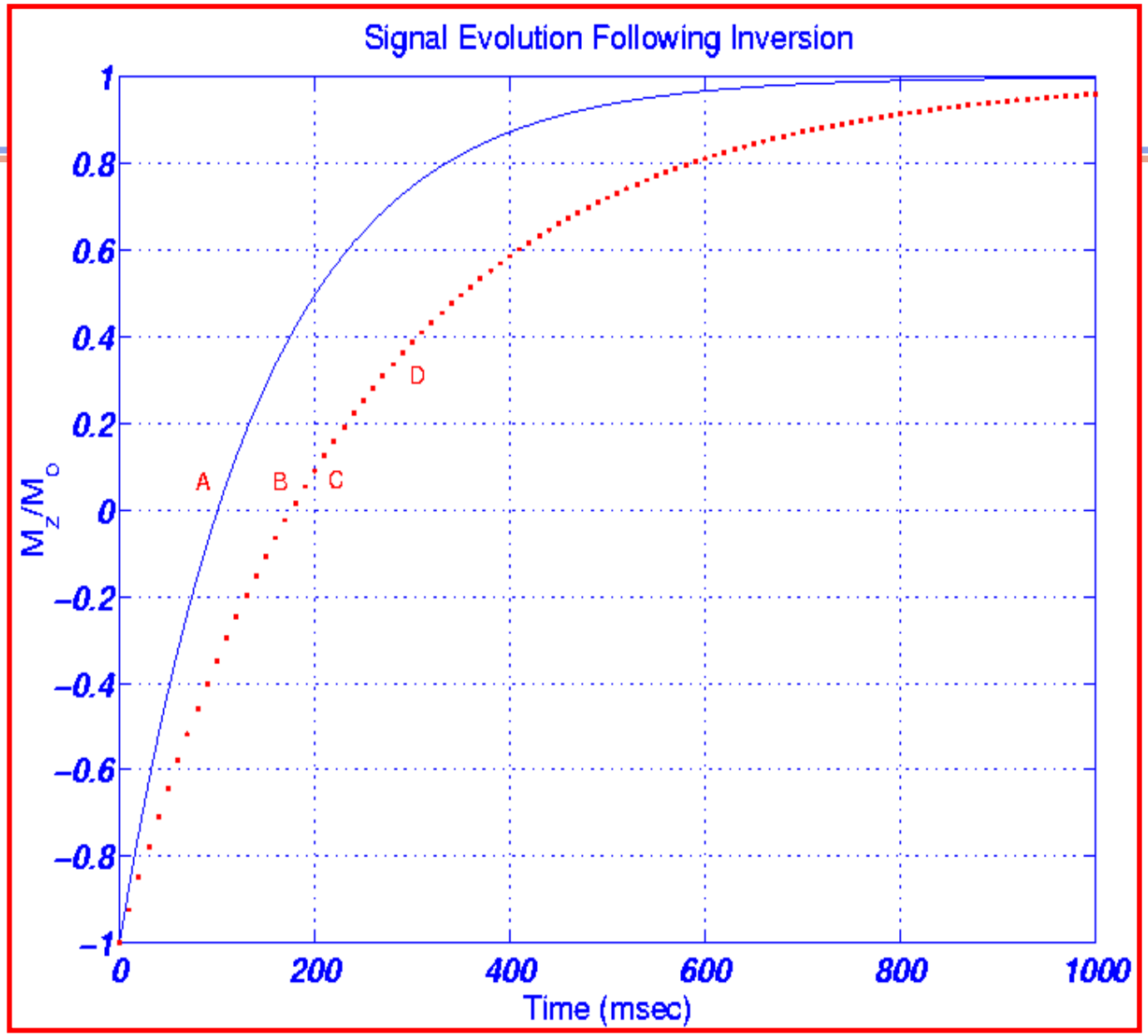
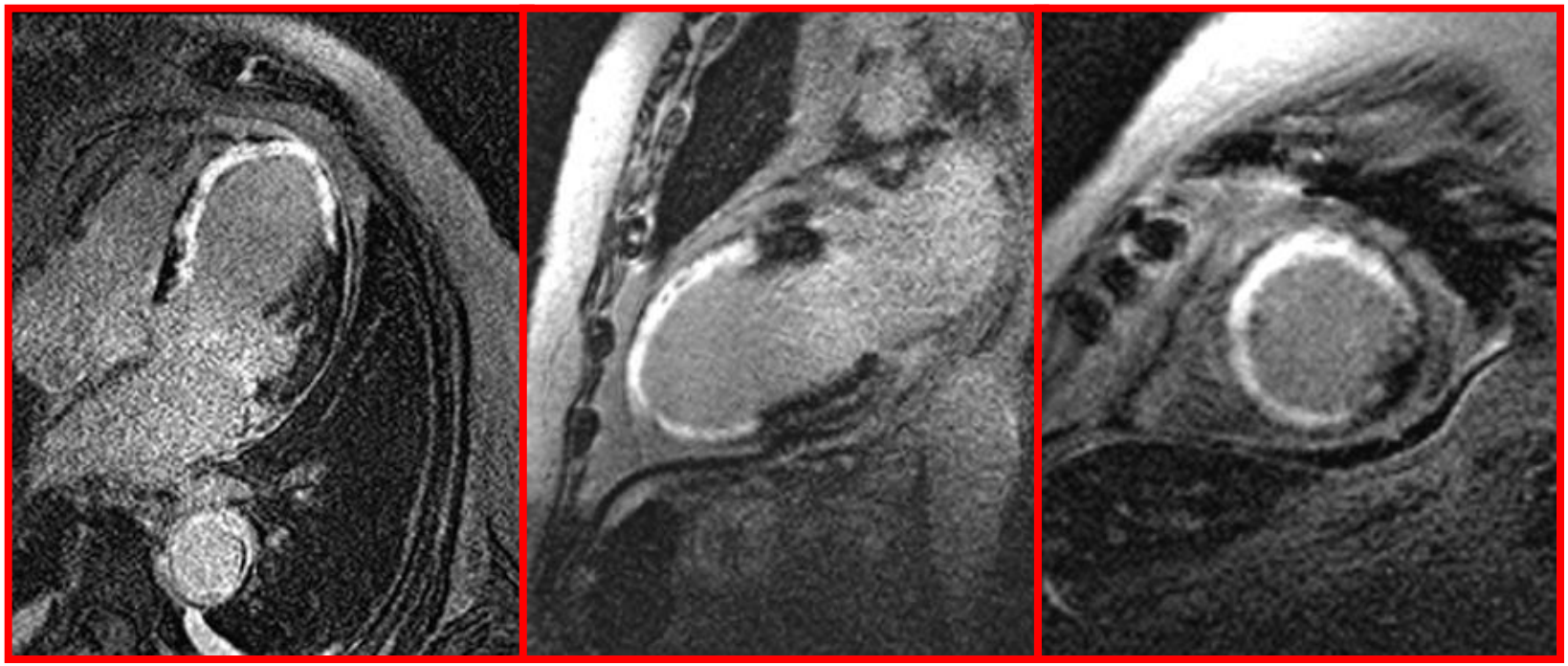


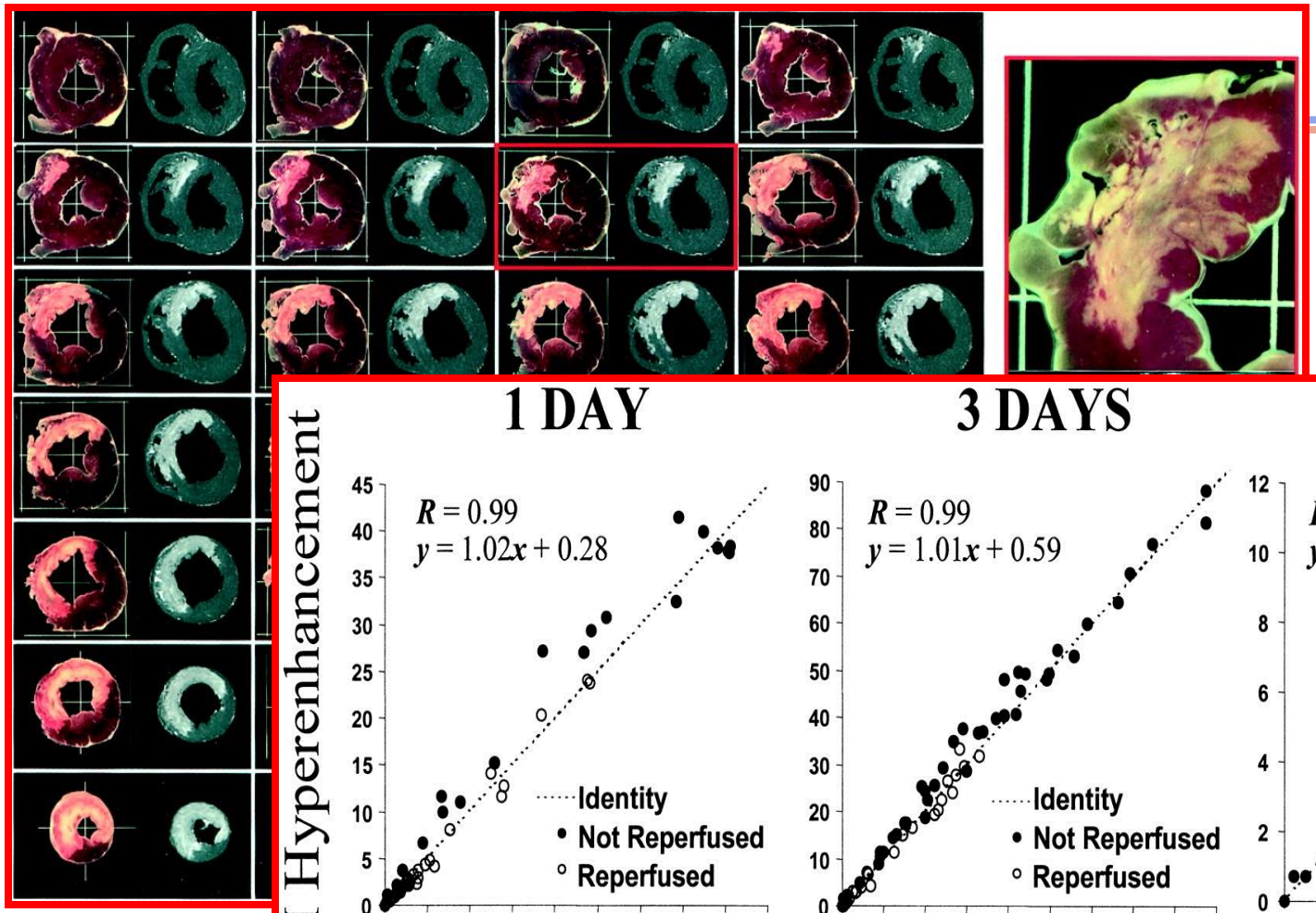
Figure 01: Pulse−sequence Schematic


Signal Evolution Following Inversion
1
0.8
0.6
0.4
0.2
0
−0.2
−0.4
−0.6
−0.8
−1
M_z/M_o
A
B
C
D
0
200
400
600
800
1000
Time (msec)

Delayed-Enhancement MRI



Delayed Enhancement in Acute MI



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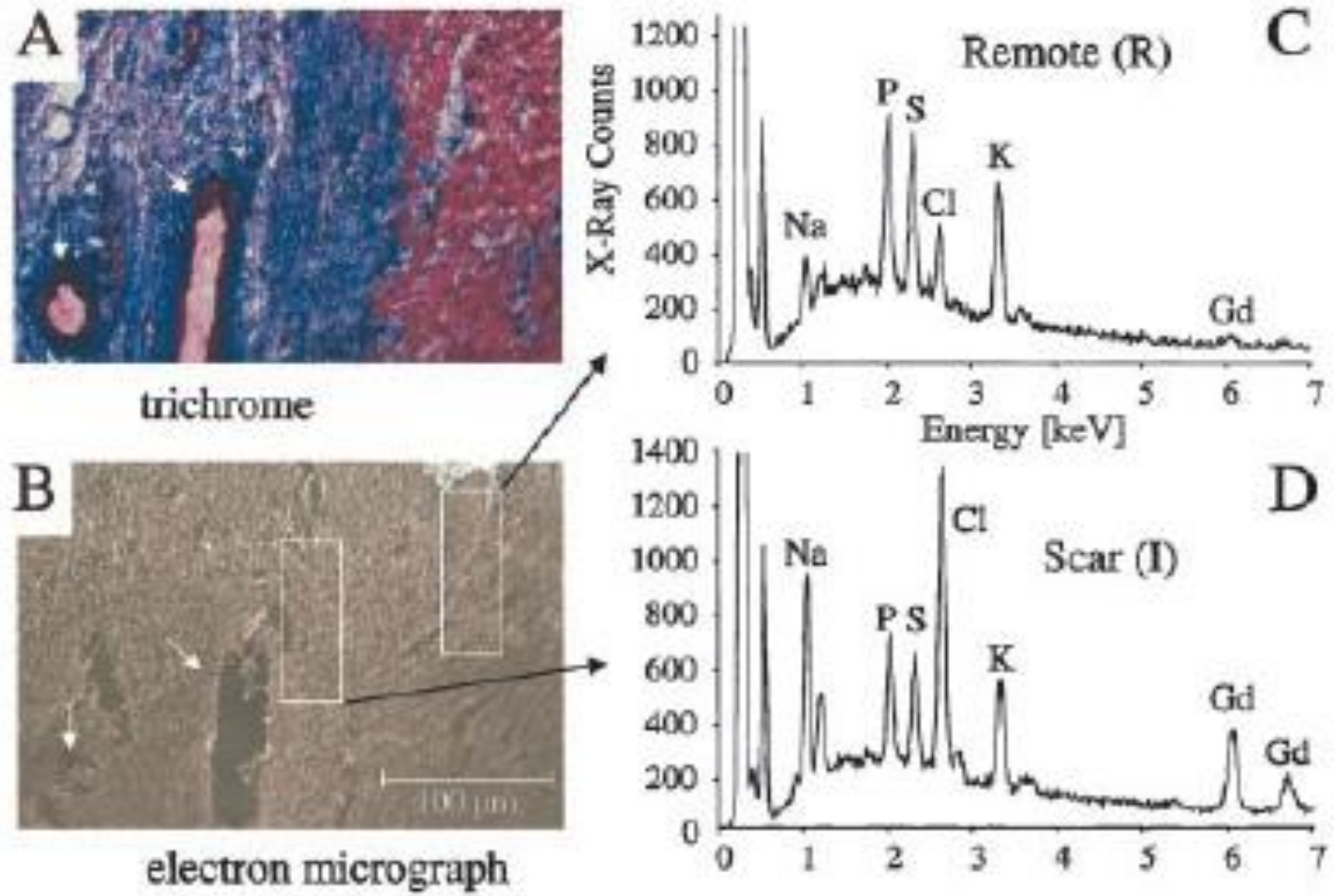
RJ Kim. Circulation 1999;100:1992-2002

Is Gadolinium really there?



Acute Gadolinium Deposition Skin Injury

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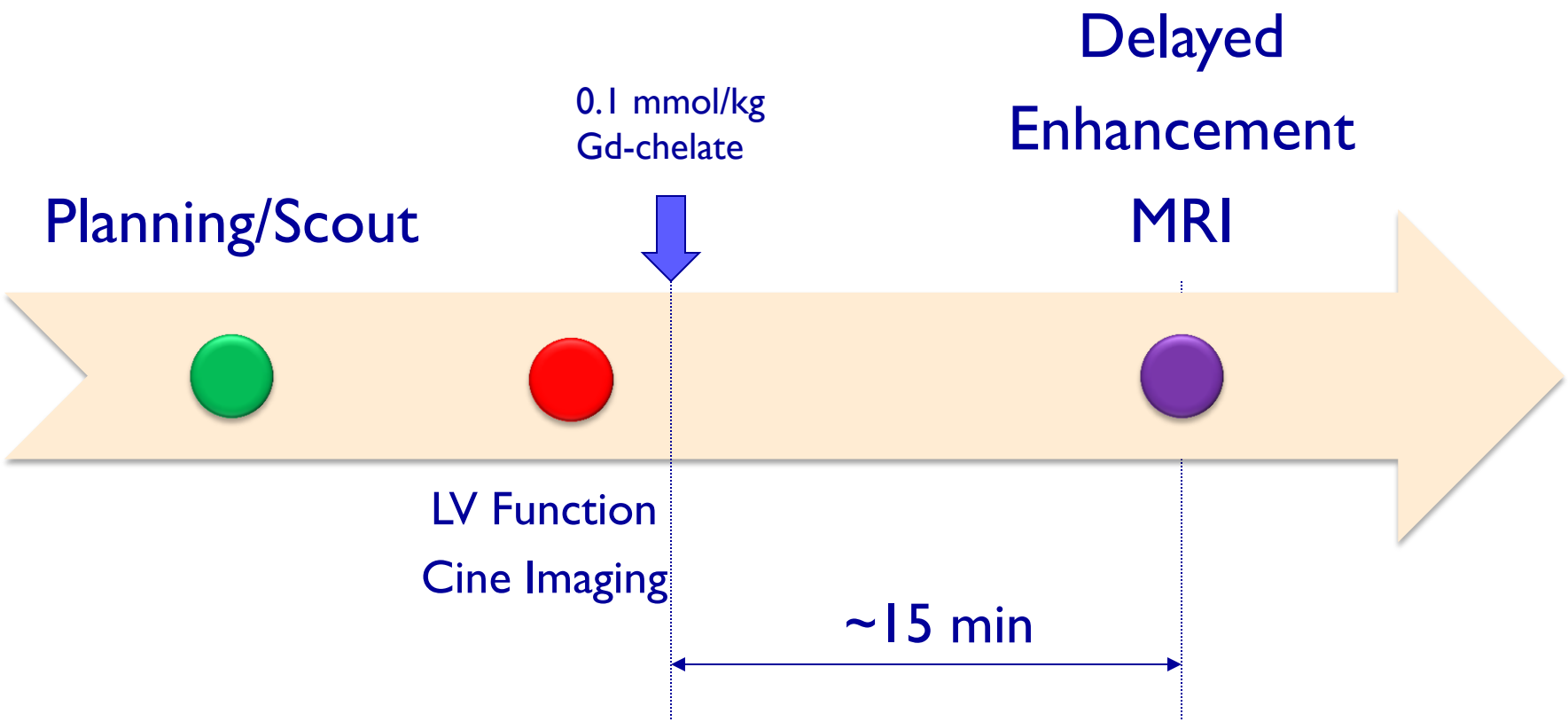
Delayed Enhancement MRI Protocol



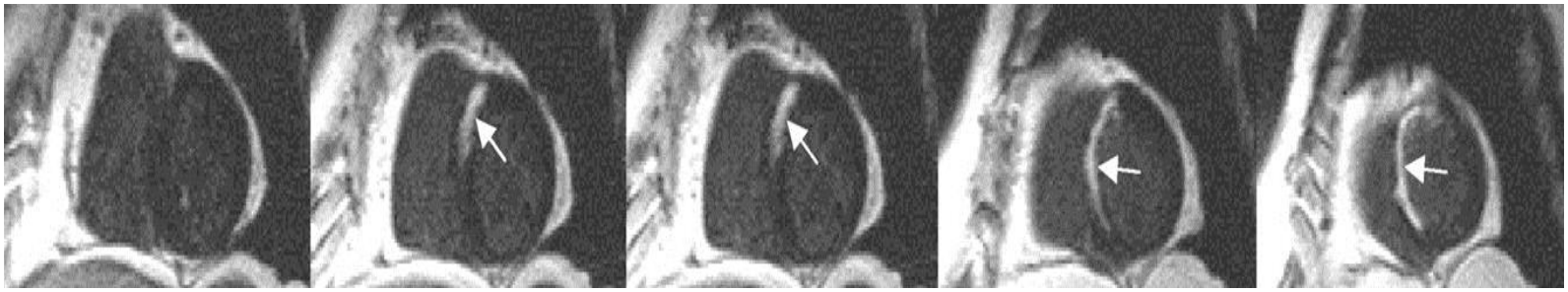
Clinical Decision making : DE-MRI

	Wall Motion Abnormality Absent	Wall Motion Abnormality Present
Delayed Enhancement Absent	Normal	Reversible Injury (Viable Myocardium)
Delayed Enhancement Present	Small Irreversible Injury?	Irreversible Injury

DE-MRI is highly reproducible

(in experienced hands)

OP 1
9th min
TI=300ms



OP 2
32rd min
TI=380ms

N= 20 patients (Chronic MI)
2 operators
Time between 2 scans ~ 20 to 25 mins
No extra gadolinium given

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H Madrholdt. Circ 2002;106:2322-2327.

DE-MRI Versus Other Modalities

	SPECT	PET	Stress Echo	DE-MRI
Spatial Resolution	10x10x10 mm^3	6x6x10 mm^3	NA	1.5 x1.5x 8 mm^3
Radiation Burden	Yes	Yes	No	No
Stress Required?	Yes	Yes	Yes	No

Imaging of myocardial viability

SPECT/PET	• Partial Volume Erros (Spatial Resolution) • Attenuation and Scatter artifacts • Estimate Function?
Stress Echo	• Functional information • Combined ability to evaluate valvular and LV function • Mis-registration between stress and rest views • Limitation of acoustic windows
MRI	• Ability to measure function, and viability in a single setting (and tissue characterization/perfusion) • Not suitable for claustrophobic patients or contraindicated for MR or MR contrast agent • Not suitable in patients with severe arrhythmias

CMR *vs* SPECT

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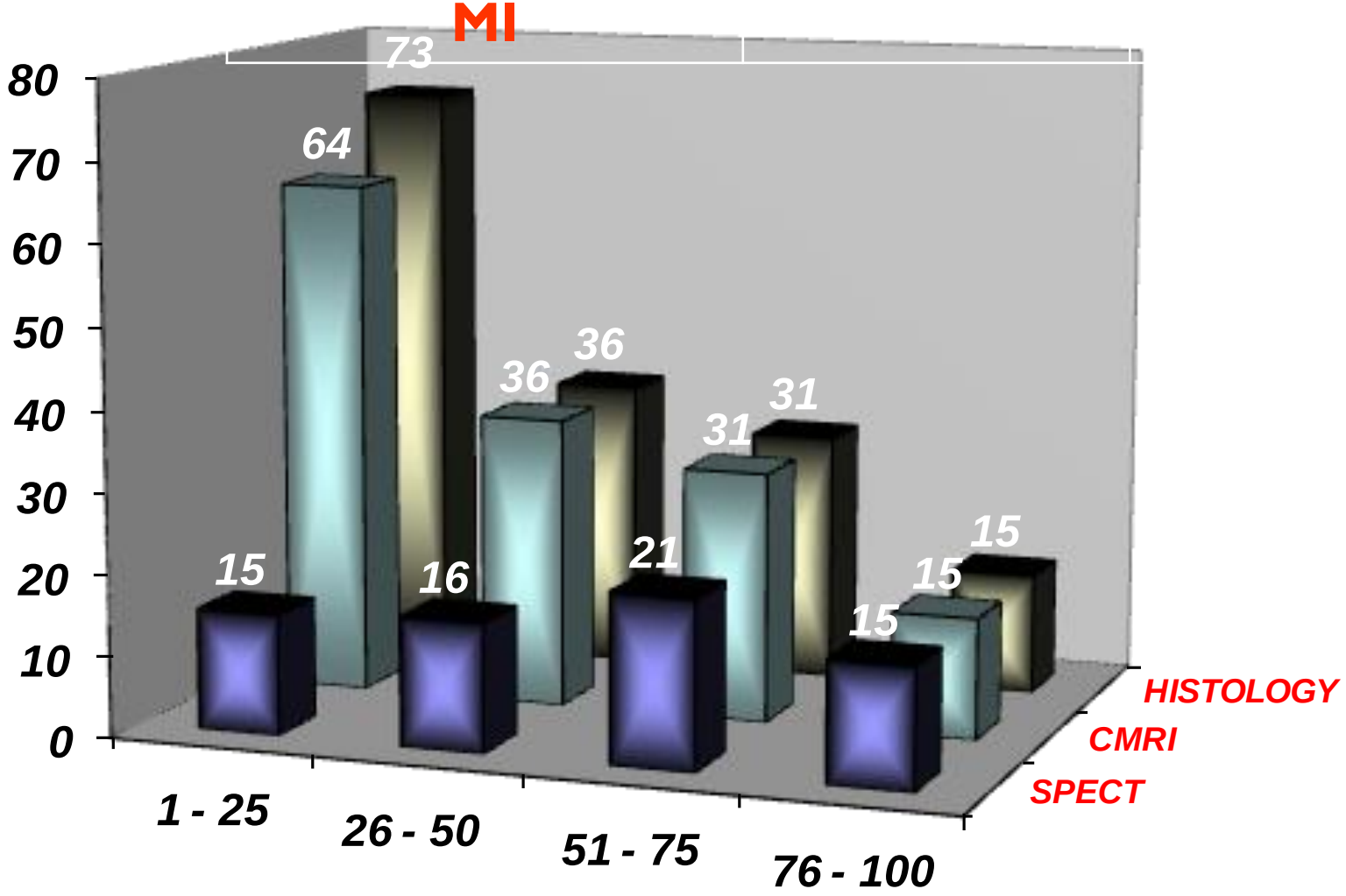
A Wagner. Lancet 2003;361:374-379

CMR *vs* SPECT

Number of Segments	*Segments* (n=109)	CMRI (%)	SPECT (%)
	Subendocardial	*100 (92%)*	*31 (28%)*



% Infarct per Segment by Histology

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A Wagner. Lancet 2003;361:374-379

CMR *vs* PET

Assessment of Myocardial Viability With Contrast-Enhanced Magnetic Resonance Imaging

Comparison With Positron Emission Tomography

Christoph Klein, MD; Stephan G. Nekolla, PhD; Frank M. Bengel, MD; Mitsuru Momose, MD; Andrea Sammer, MD; Felix Haas, MD; Bernhard Schnackenburg, PhD; Wolfram Delius, MD; Harald Mudra, MD; Dieter Wolfram, MD; Markus Schwaiger, MD

Background—Recent studies indicate that MRI, after administration of gadolinium-diethylenetriamine pentaacetic acid, can identify nonviable areas in dysfunctional myocardium. We compared MRI hyperenhancement with PET as a gold standard for detection and quantification of myocardial scar tissue.

Methods and Results—Thirty-one patients with ischemic heart failure (ejection fraction, 28±9%) were imaged with PET and MRI. Scar was defined as regionally increased MRI signal intensity 20 minutes after injection of 0.2 mmol/kg gadolinium-diethylenetriamine pentaacetic acid and as concordantly reduced perfusion and glucose metabolism as defined by PET. Sensitivity and specificity of MRI in identifying patients and segments (n=1023) with matched flow/metabolism defects was 0.96 of 1.0 and 0.86 of 0.94, respectively. Eleven percent of segments defined as viable by PET showed some degree of MRI hyperenhancement. Defect severity score based on visual analysis was 44.3±9.1 for PET and 47.6±11.1 for MRI (r=0.91, P<0.0001). Quantitatively assessed relative MRI infarct mass correlated well with PET infarct size (r=0.81, P<0.0001). Furthermore, MRI hyperenhancement was a better predictor of scar tissue than end-diastolic and end-systolic wall thickness or thickening.

Conclusions—In severe ischemic heart failure, MRI hyperenhancement as a marker of myocardial scar closely agrees with PET data. Although hyperenhancement correlated with areas of decreased flow and metabolism, it seems to identify scar tissue more frequently than PET, reflecting the higher spatial resolution. Additional functional studies after revascularization are required to define the significance of small islands of scar detected by MRI. **(*Circulation*. 2002; 105:162-167.)**

CMR *vs* PET

MRI vs PET	SENSITIVITY	SPECIFICITY
Transmural	*0.86*	*0.94*
Subendocardial / Transmural Scar	*0.83*	*0.88*

- 11% of segments identified by PET that are viable has subendocardial / transmural scar by MR (89/784)
- 55% of segments with subendocardial scar by MR were classified as normal by PET (51/93)

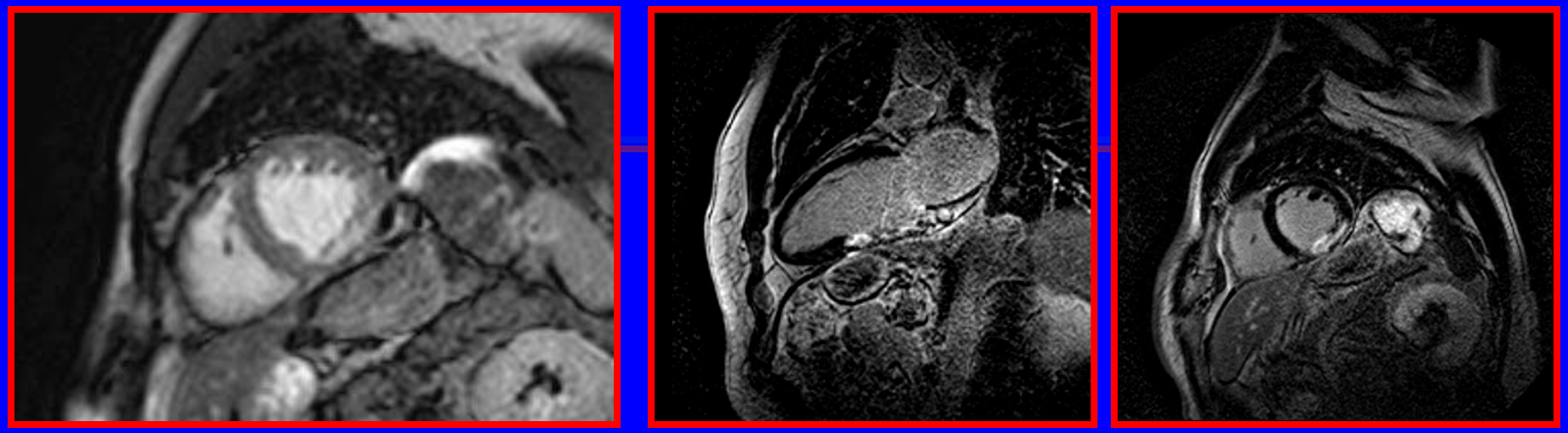
C Klein et al. Circ 2002;105:162-167

THI / SLEH Multicenter Viability Trial

Courtesy of Veronica Lenge, M.D.

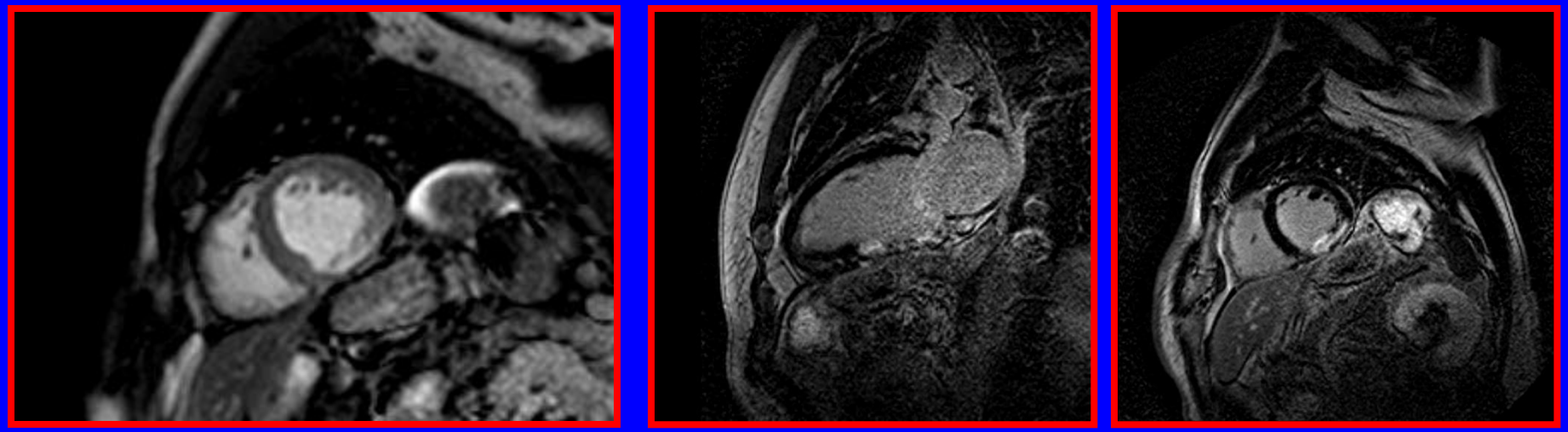
BASELINE

LVEDD: 221 cc, LVESV: 117 cc, EF: 47%



FOLLOW-UP

LVEDD: 228 cc, LVESV: 119 cc, EF: 48%



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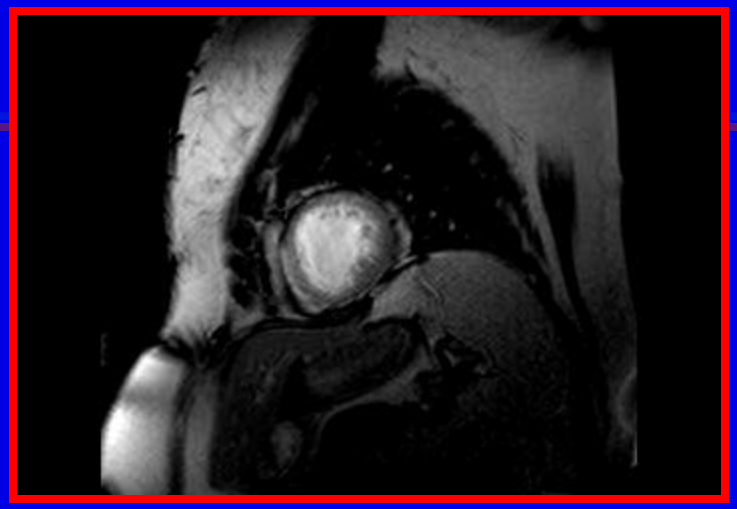
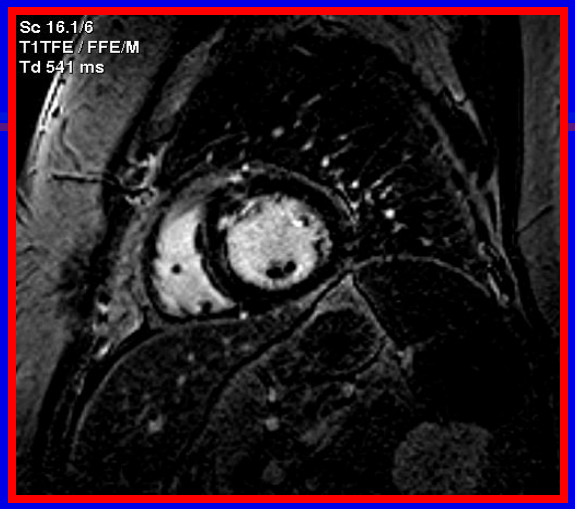
Courtesy of Veronica Lenge, M.D.

BASELINE

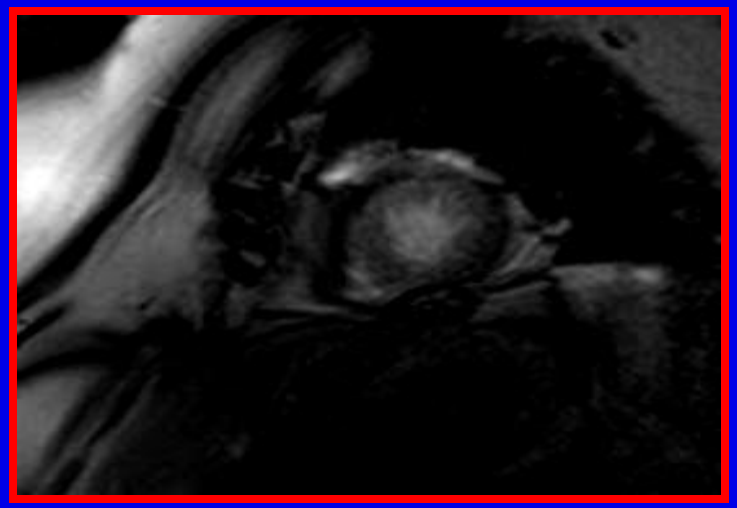
LVEDD: 203 cc, LVESV: 129 cc, EF: 37%

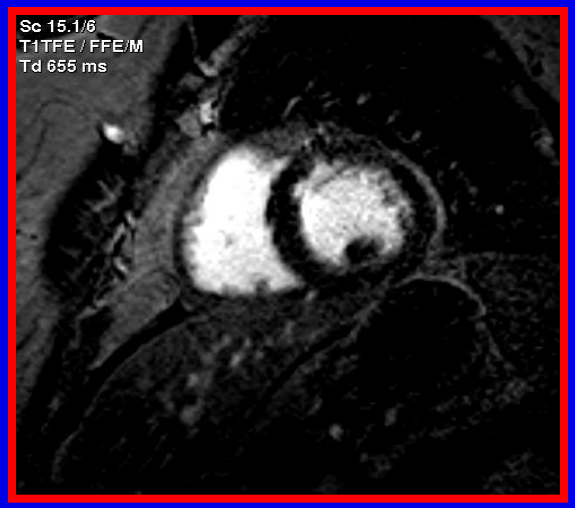




FOLLOW-UP

LVEDD: 166 cc, LVESV: 80 cc, EF: 52%





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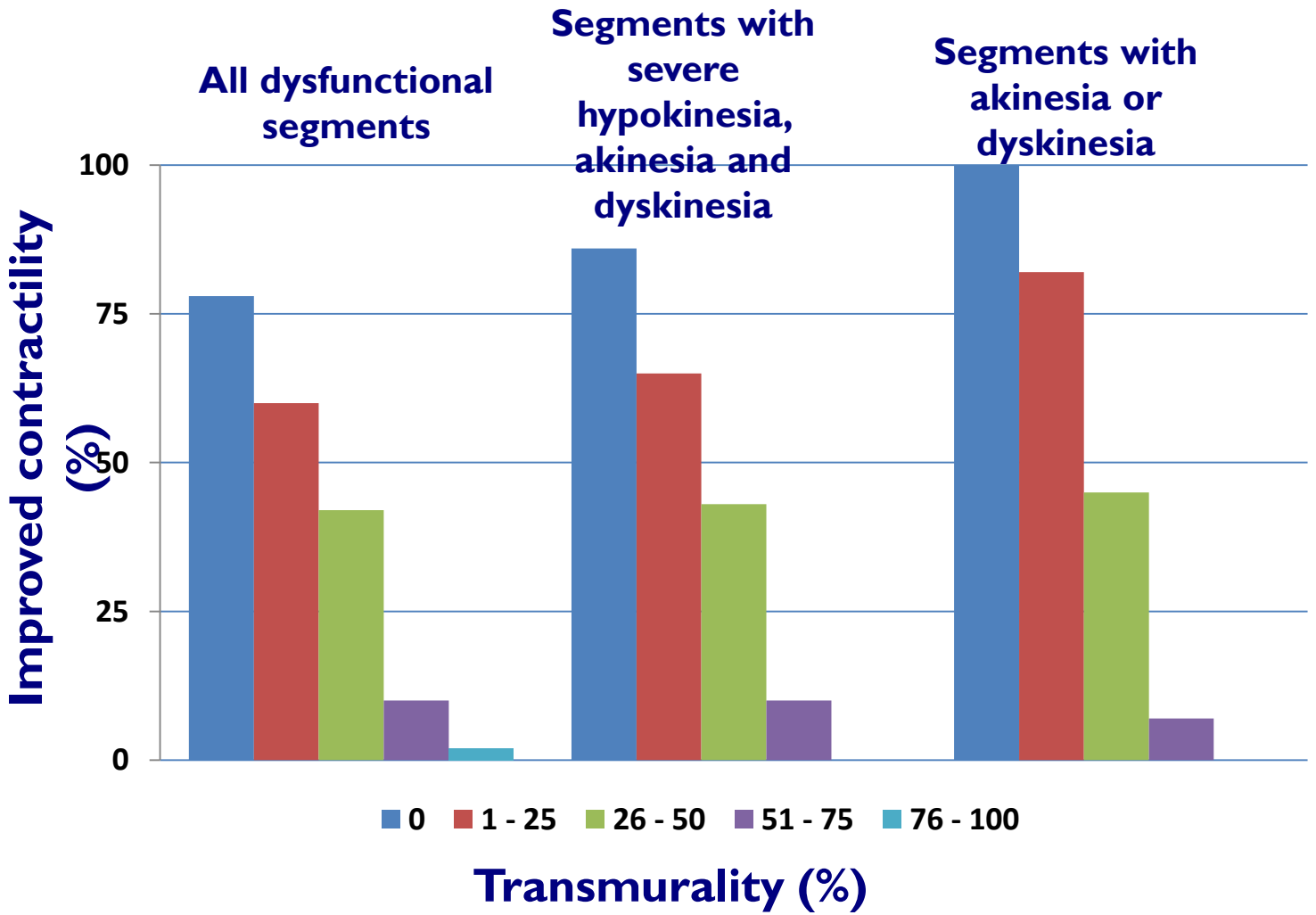
Courtesy of Veronica Lenge, M.D.

Extent of Scar and Functional Recovery



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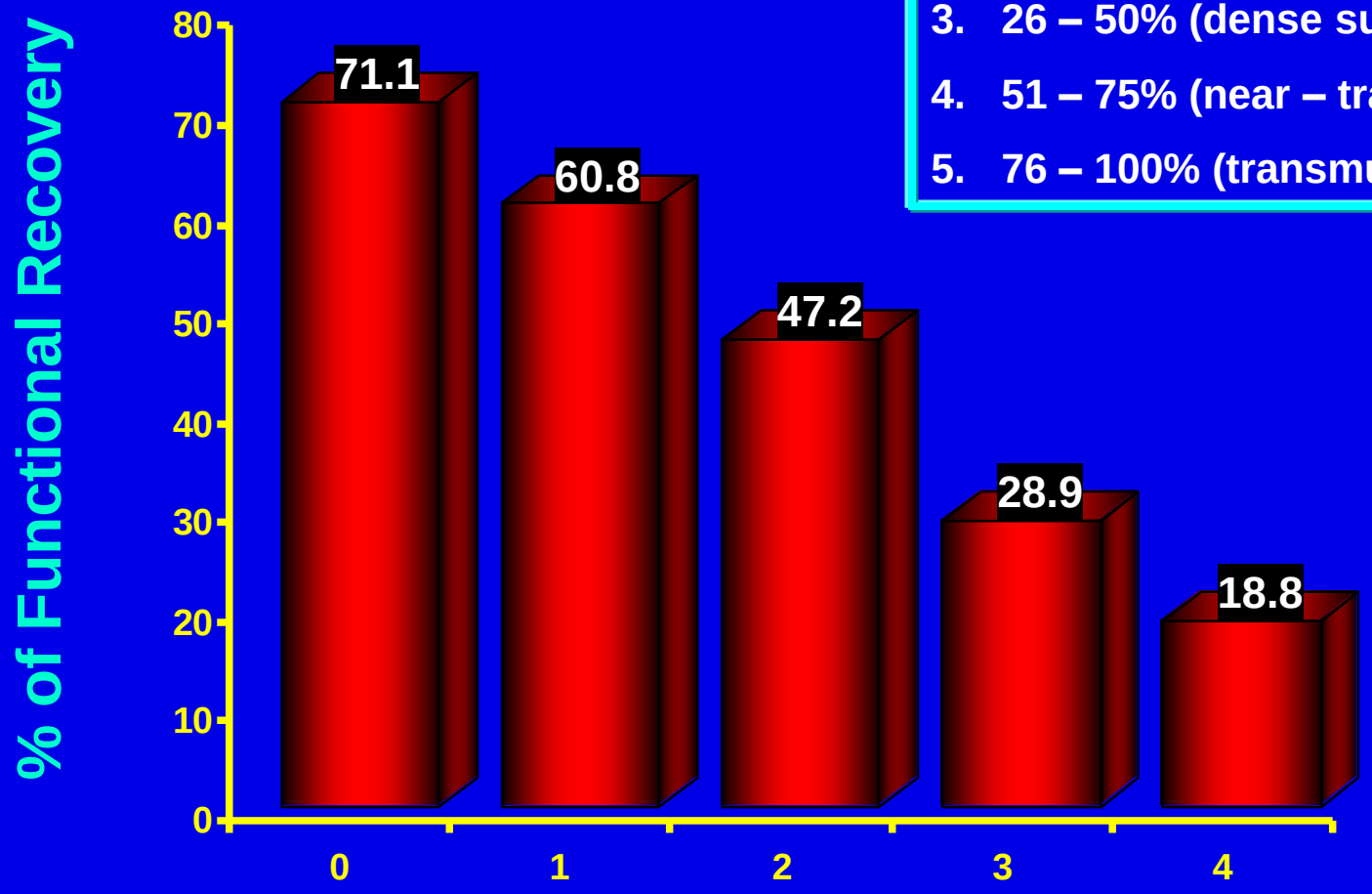
RJ Kim. NEJM 2000;343: 1445-1453

Results

SCAR SCORE

1. 0% (normal)
2. 1 – 25% (thin subendocardial)
3. 26 – 50% (dense subendocardial)
4. 51 – 75% (near – transmural)
5. 76 – 100% (transmural)



Courtesy of V. Lenge, M.D.

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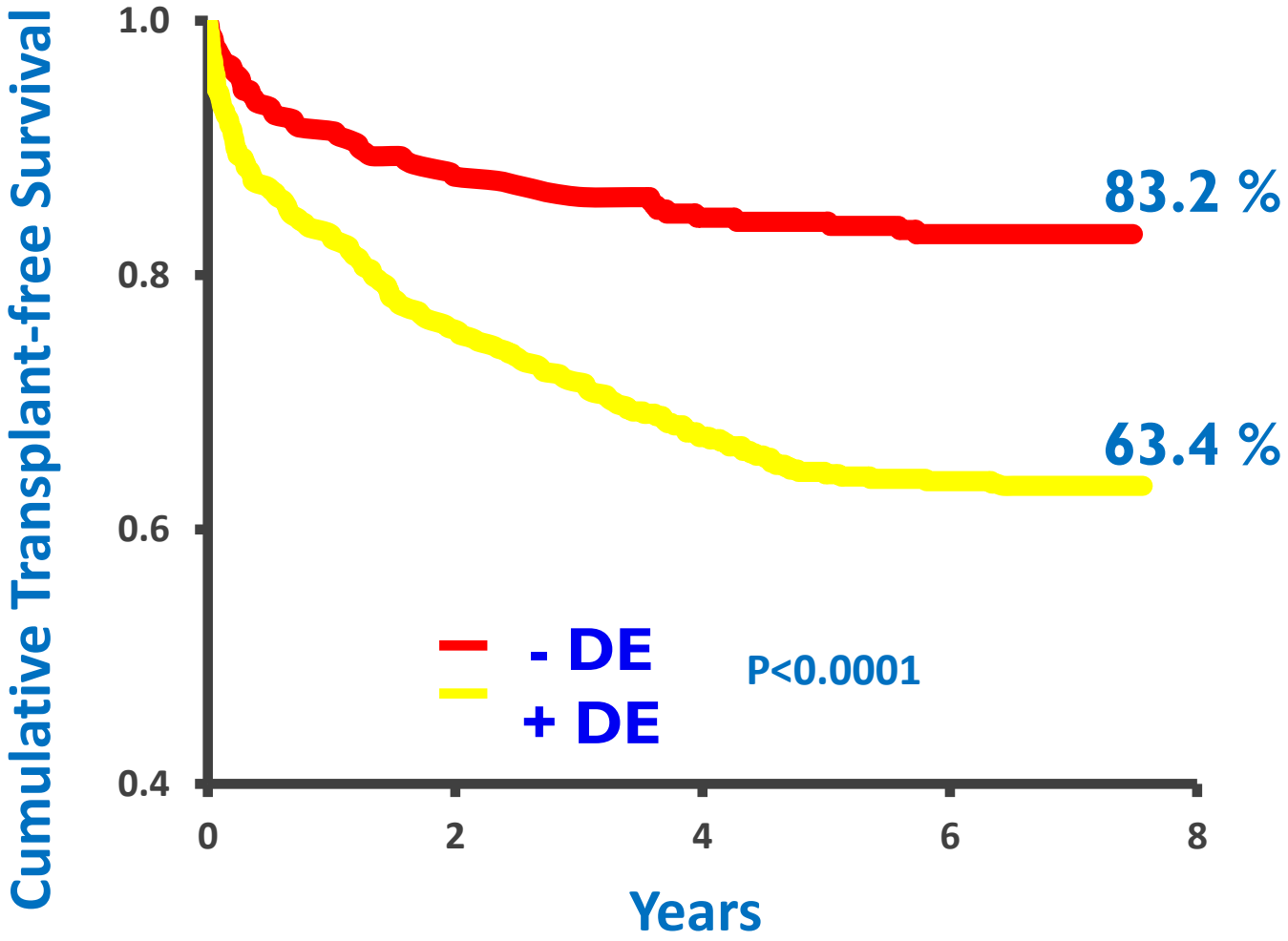
DE – MRI and Survival (n=842)



BYC Cheong et al. *Circ* 2009;120:2069–76.

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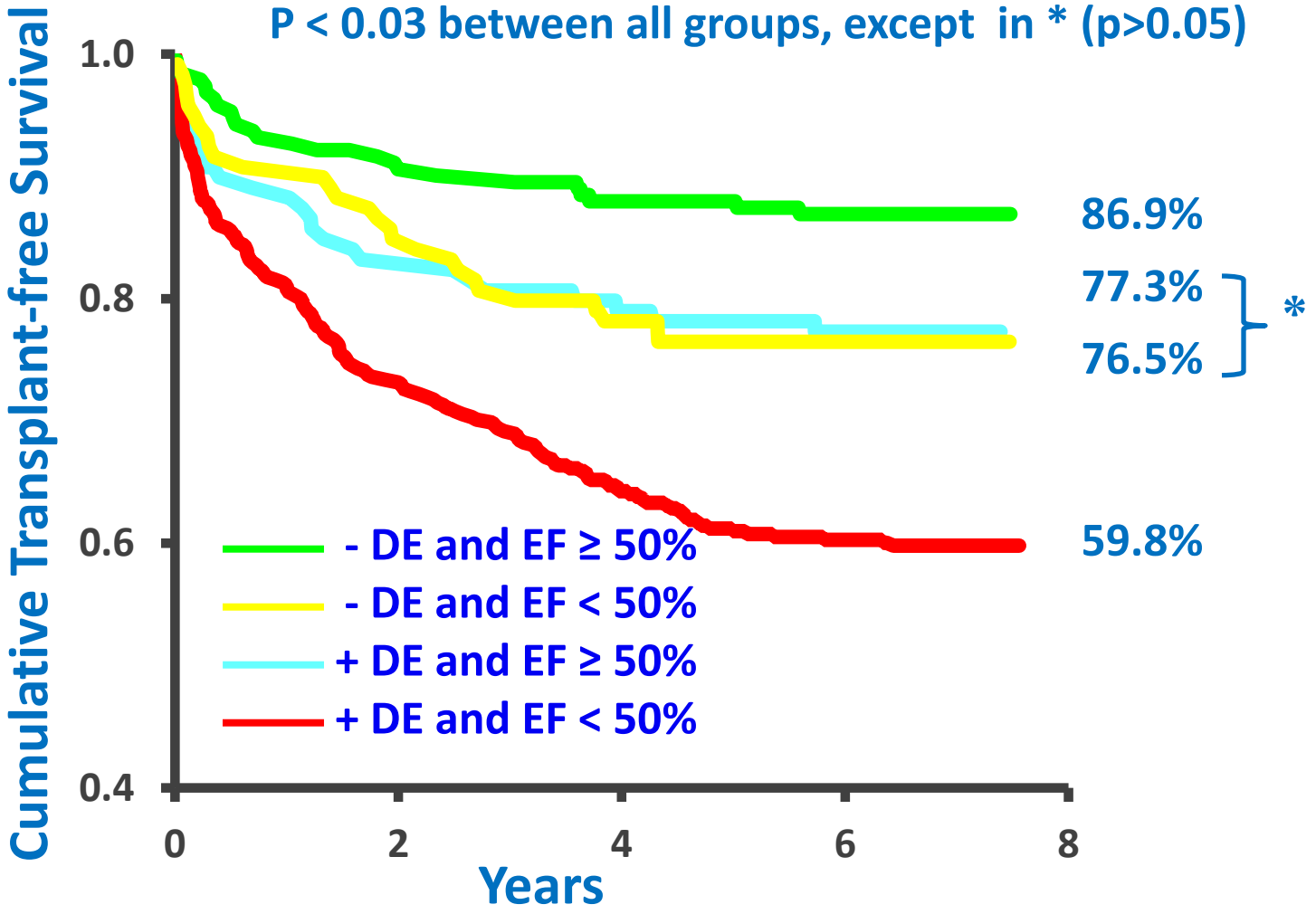
DE – MRI and Survival



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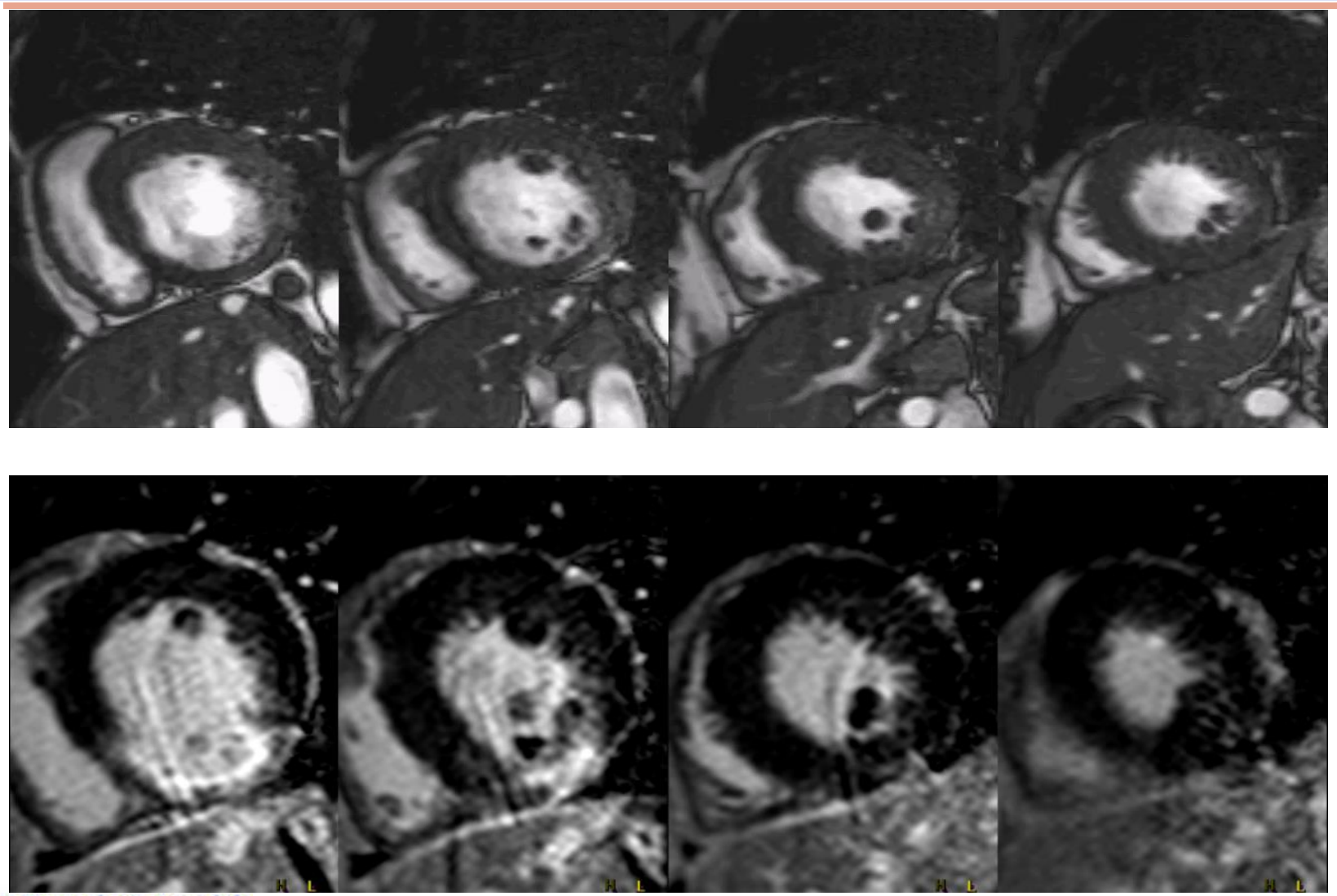
BYC Cheong et al. *Circ* 2009;120:2069–76.

Regional WM Abnormality - MRI



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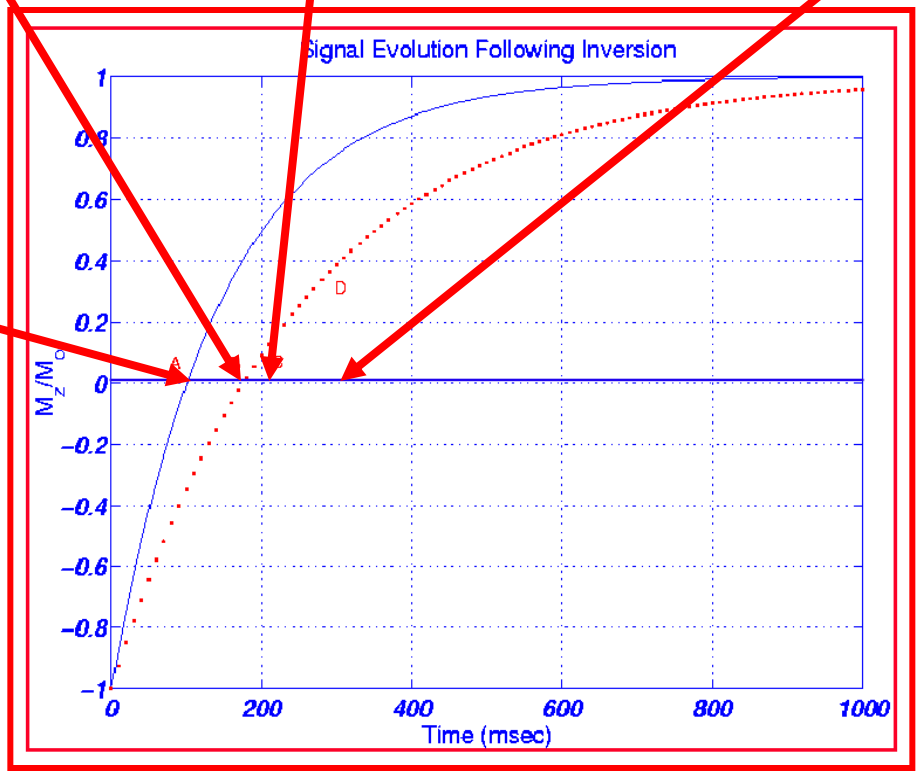
Issues: Determination of Inversion Delay in DE-MRI

- Continuous Washout of Gadolinium chelate
  - Dose and Type of Gadolinium-Chelate Injected (**0.2 mmol/kg**)
  - Time from Injection
- Protocol related parameters
  - Heart Rate variation results in different amounts of Mz
  - Profile order and type of readout



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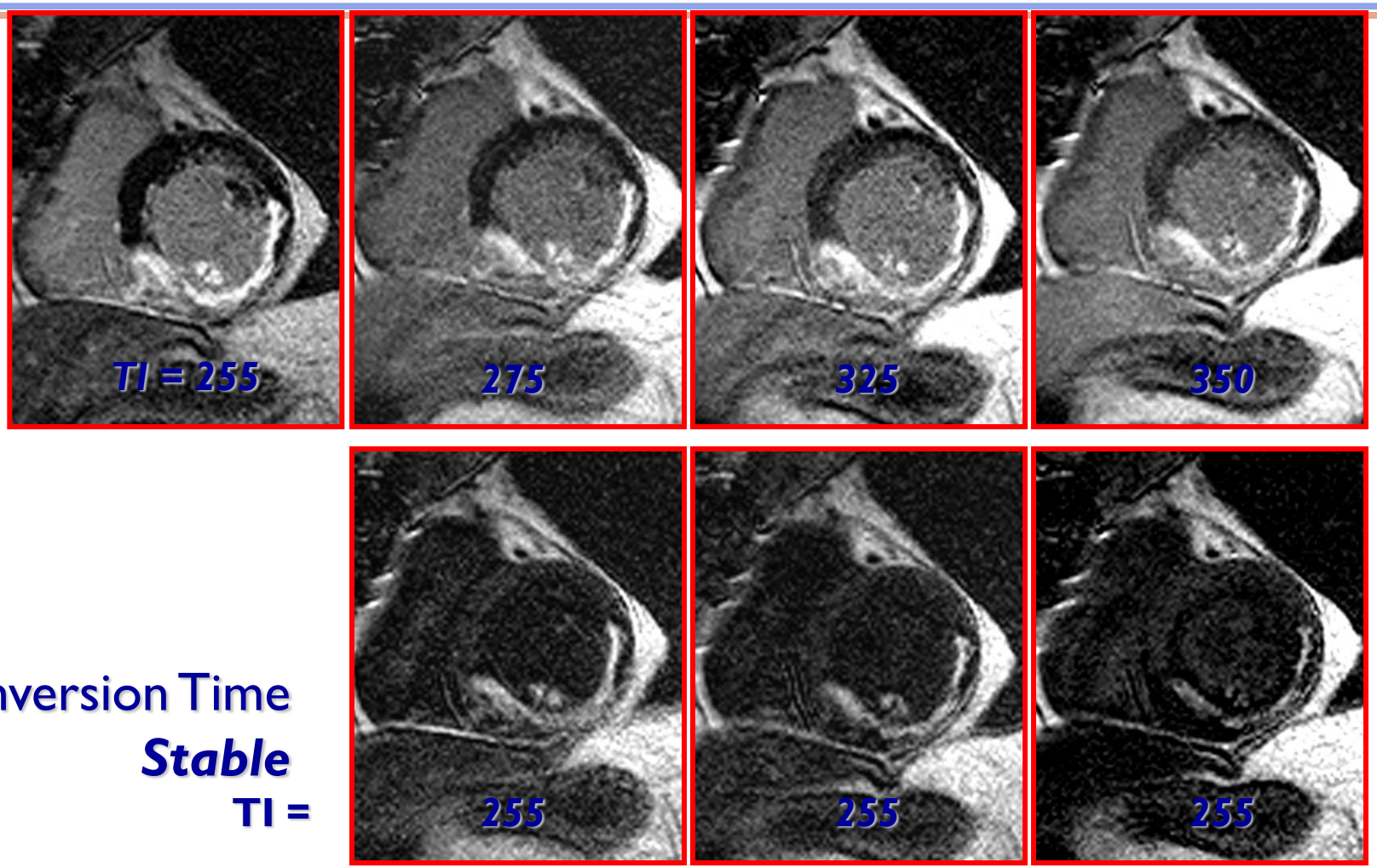
(1) Continued Washout of Gd-DTPA from myocardium

T = 10 min. *20 min.* *30 min.* *35 min.*

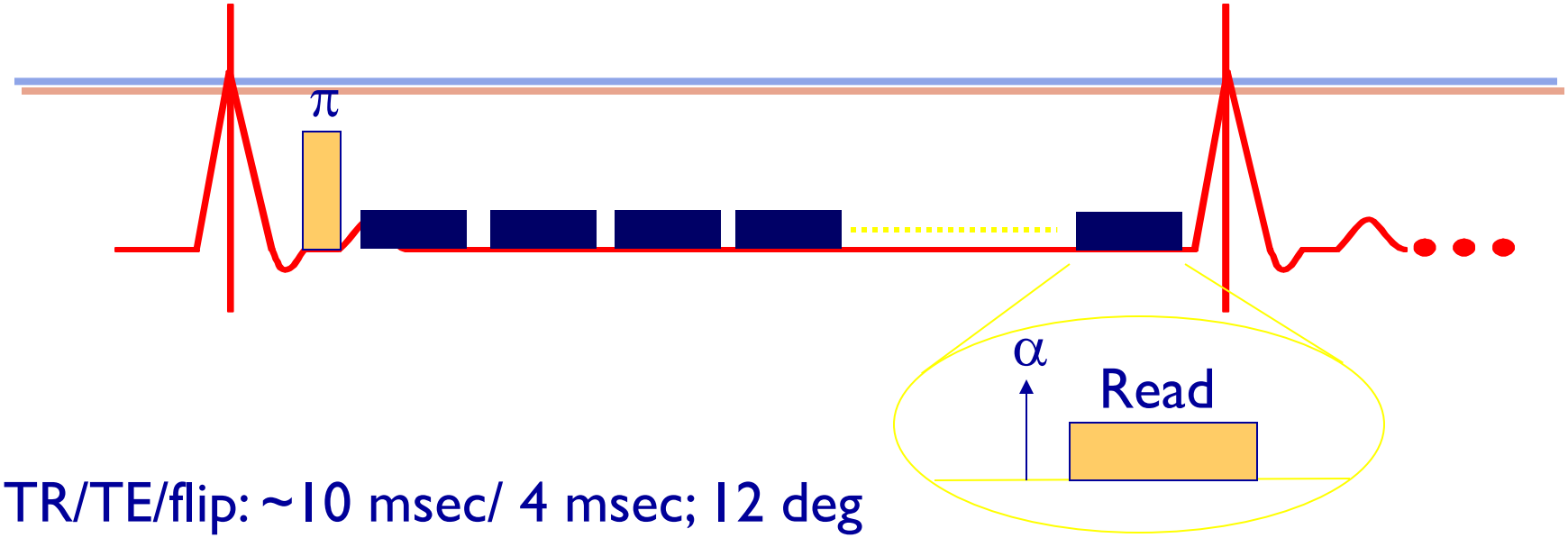


Inversion Time

Stable

TI =

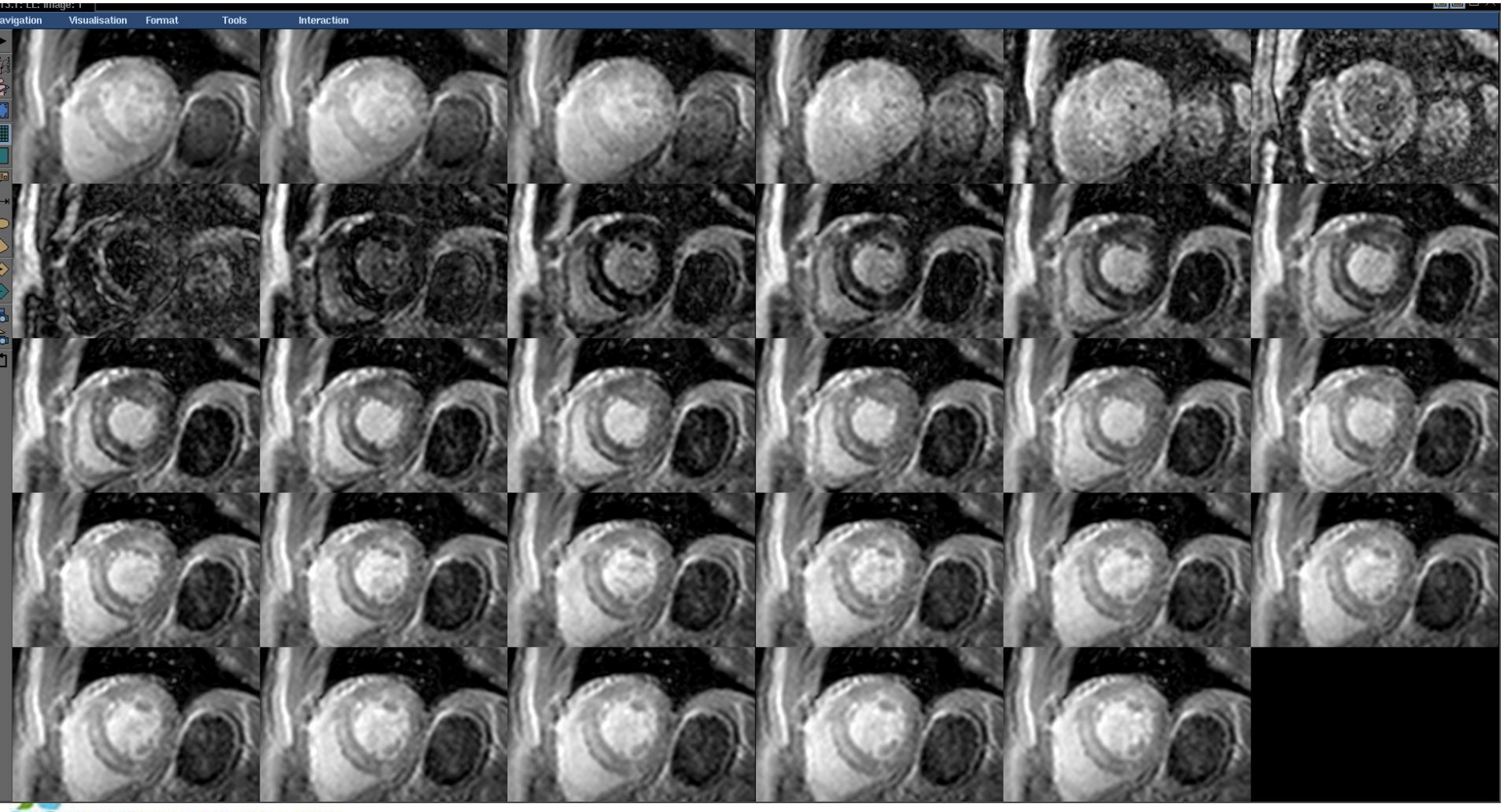
TI determination: Look-Locker method



- TR/TE/flip: ~10 msec/ 4 msec; 12 deg
- EPI readout; 5 lines/TR; VCG triggered
- FOV: 256 x 256 mm; matrix: 96 x 96 mm
- Acquired Voxel Size: 2.6 x 2.6 x 8 mm
- Temporal Resolution ~ 10 msec;
- Scan time: 17 heart beats

•DC Look, DR Locker, Phys. Rev. Lett. 20, 987, 1968

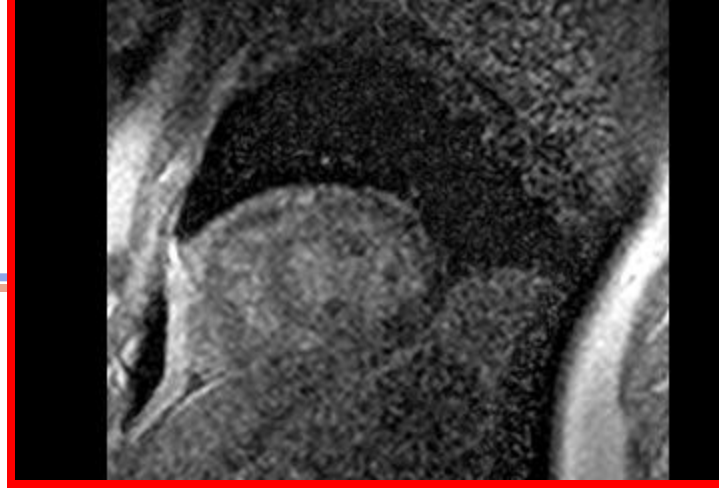
Look-Locker Approach

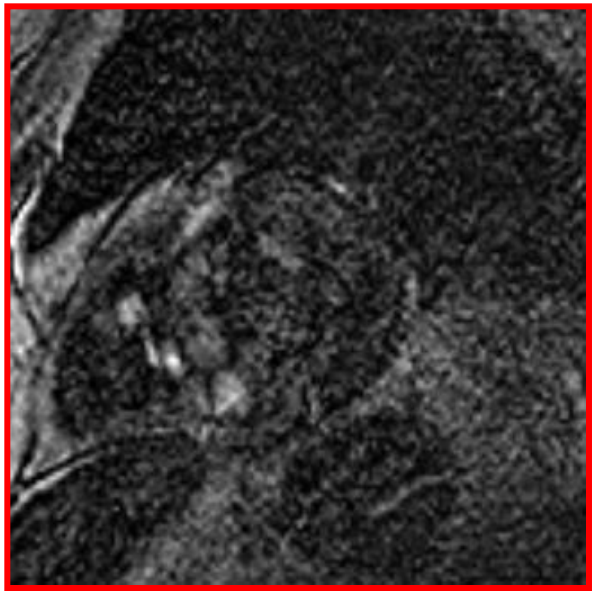


‘Look-Locker’ method for TI determination

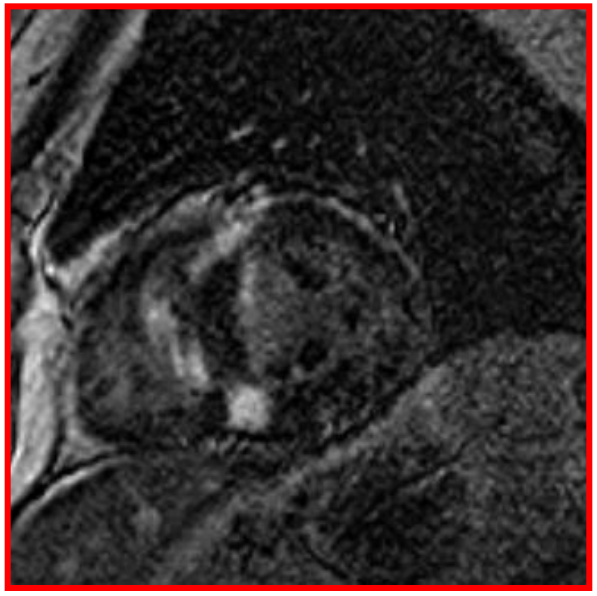
- Time between IR pulses should be the same for LL sequence and the DE-MRI sequence
- Look Locker gets you close to the TI for nulling; Choose a slightly longer TI (~15-20 ms) than determined by LL
- As contrast agent washes out, rerun LL sequence to get appropriate TI

Non-Ischemic CM

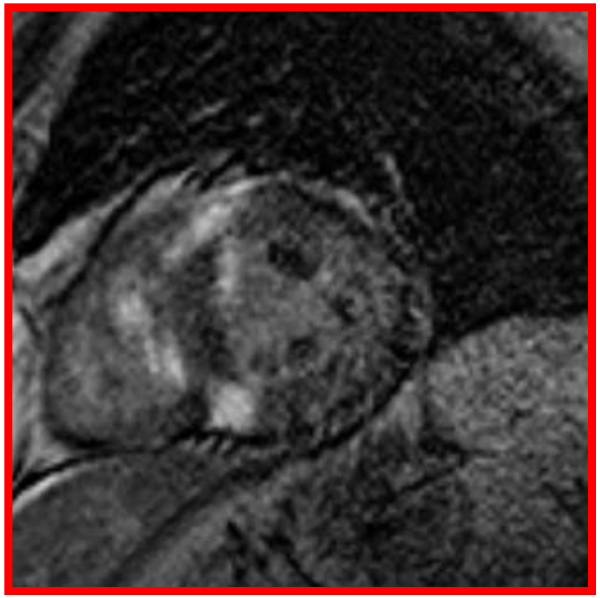




TI: 200



TI: 250



TI: 300

MRI Methods to evaluate ischemia

Normal

(< 50% Stenosis)

Quantitative?

Ischemia w/o Resting Mech Abn.

Perfusion Qualitative Anal.

Stunning/ Hibernation

DE+Resting Cine;

DE+Low Dose Dobutamine;

Dead Muscle

Delayed Enhancement; Resting Perfusion

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Summary

- What is the clinical question regarding "viable" myocardium?
  - Wall motion abnormality → Is it reversible?
- Role of non-invasive imaging in evaluating myocardial viability
  - Nuclear Scintigraphy, Stress Echo, MR
- MRI assessment of myocardial viability: Delayed Enhancement
  - Easy to use; Fx/Viability; Accurate and Reproducible
- Technical Issues and Trouble shooting
  - Choice of inversion delay time
- Conclusions

Thank you!