Myocardial Fibrosis

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JOHNS HOPKINS
MEDICINE

MESA

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Introduction

- Myocardial fibrosis is a well-known marker of heart disease

- Related to:
  - lower ventricular systolic function
  - adverse ventricular remodeling
  - adverse cardiac outcomes

Iles *et al*. JACC 2008
Flett *et al*. Circ Imaging, 2010

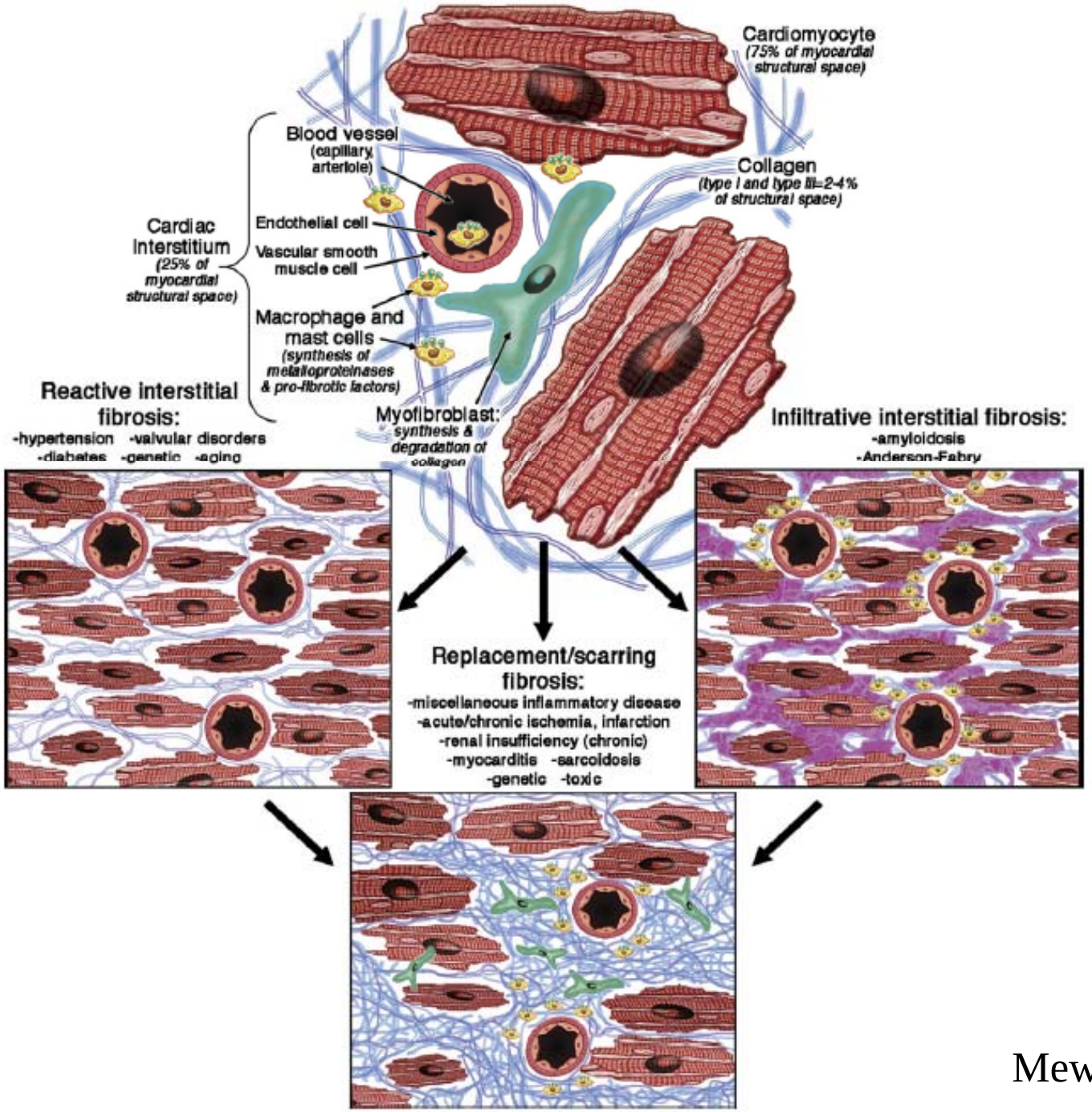
Mewton N *et al*. JACC 2011
Sibley *et al*. Radiology, 2012

Myocardial fibrosis

In cardiomyopathies of various etiologies, myocardial fibrosis is associated with:

- increased ventricular wall stress and stiffness
- cardiac mechanical dysfunction
- symptomatic heart failure

Mewton N et al. *Journal of the American College of Cardiology.* Feb 22 2011;57(8):891-903.



Replacement

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LGE

Interstitial

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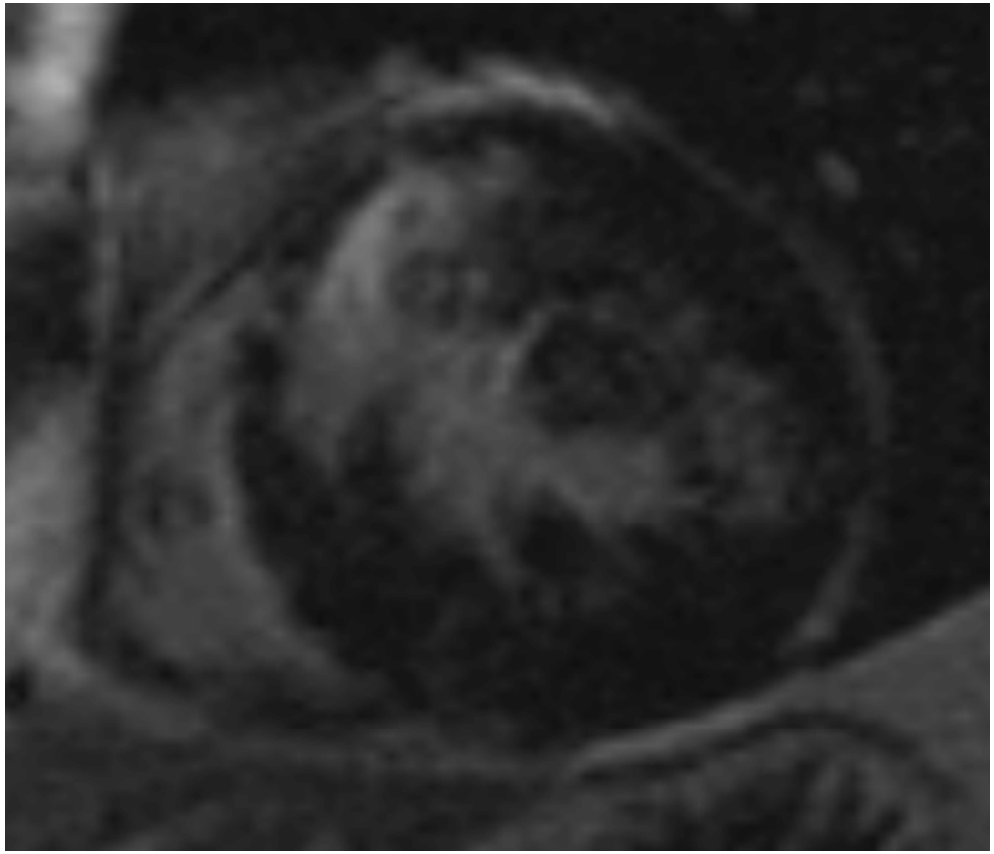
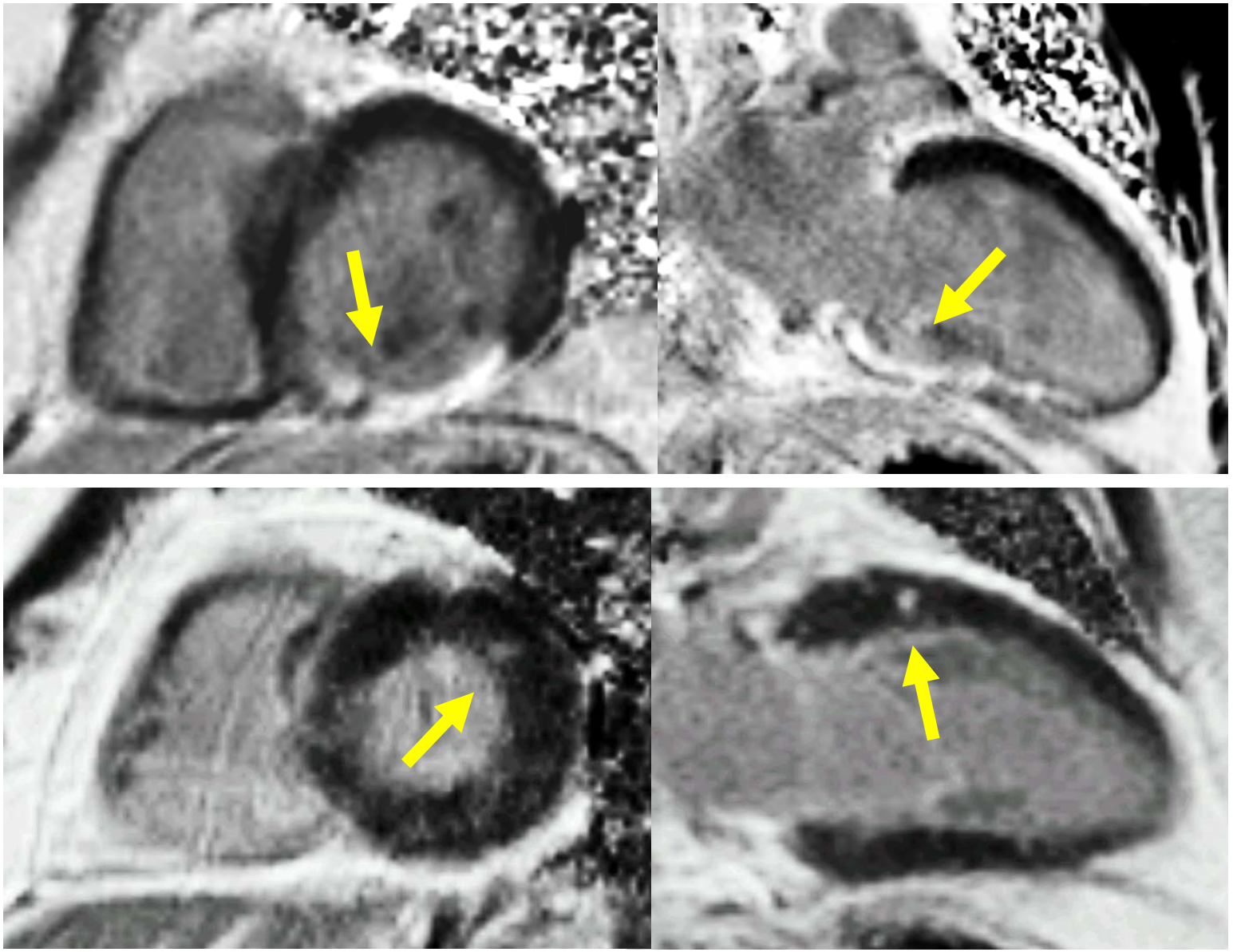
T1 Mapping

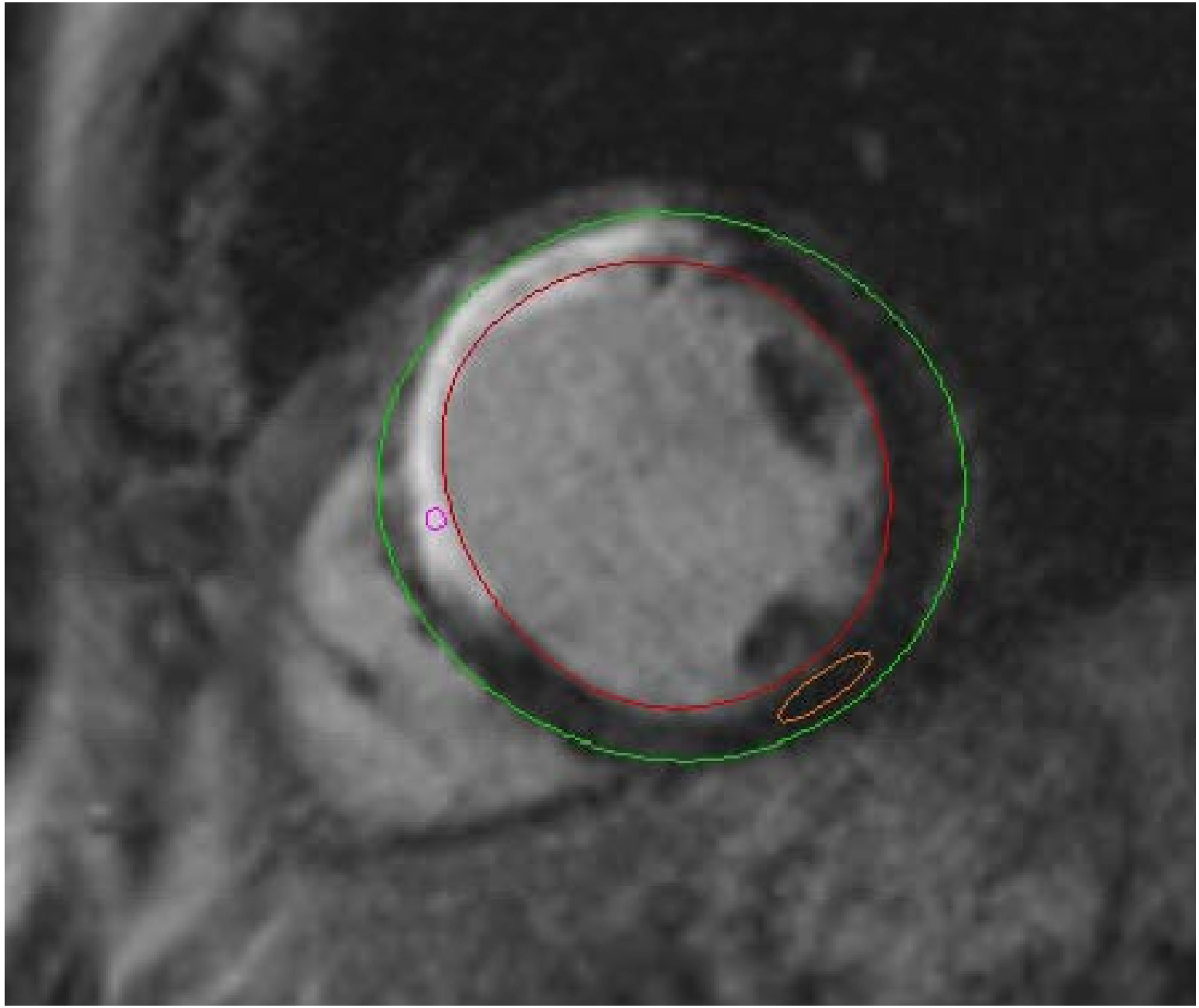
Mewton N *et al*. JACC 2011



LATE GADOLINIUM ENHANCEMENT (LGE)

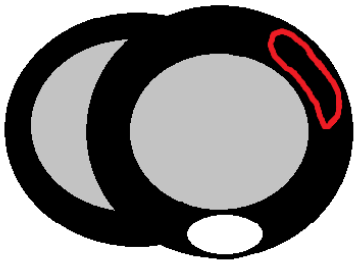
Late Gadolinium Enhancement CMR

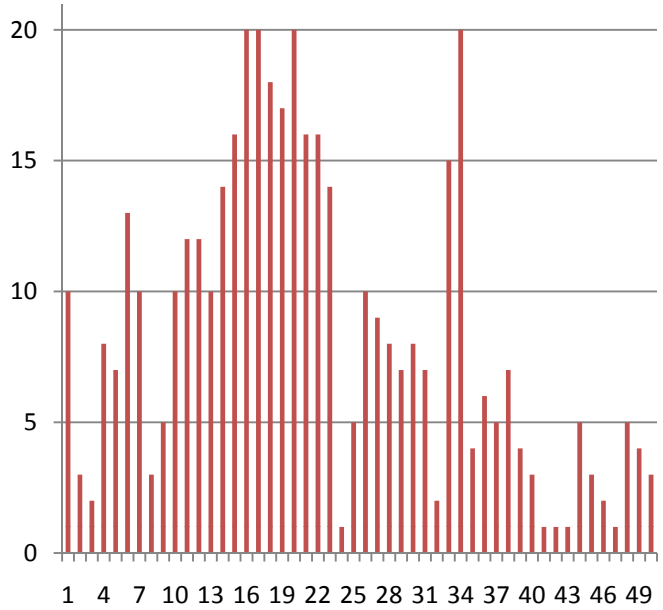




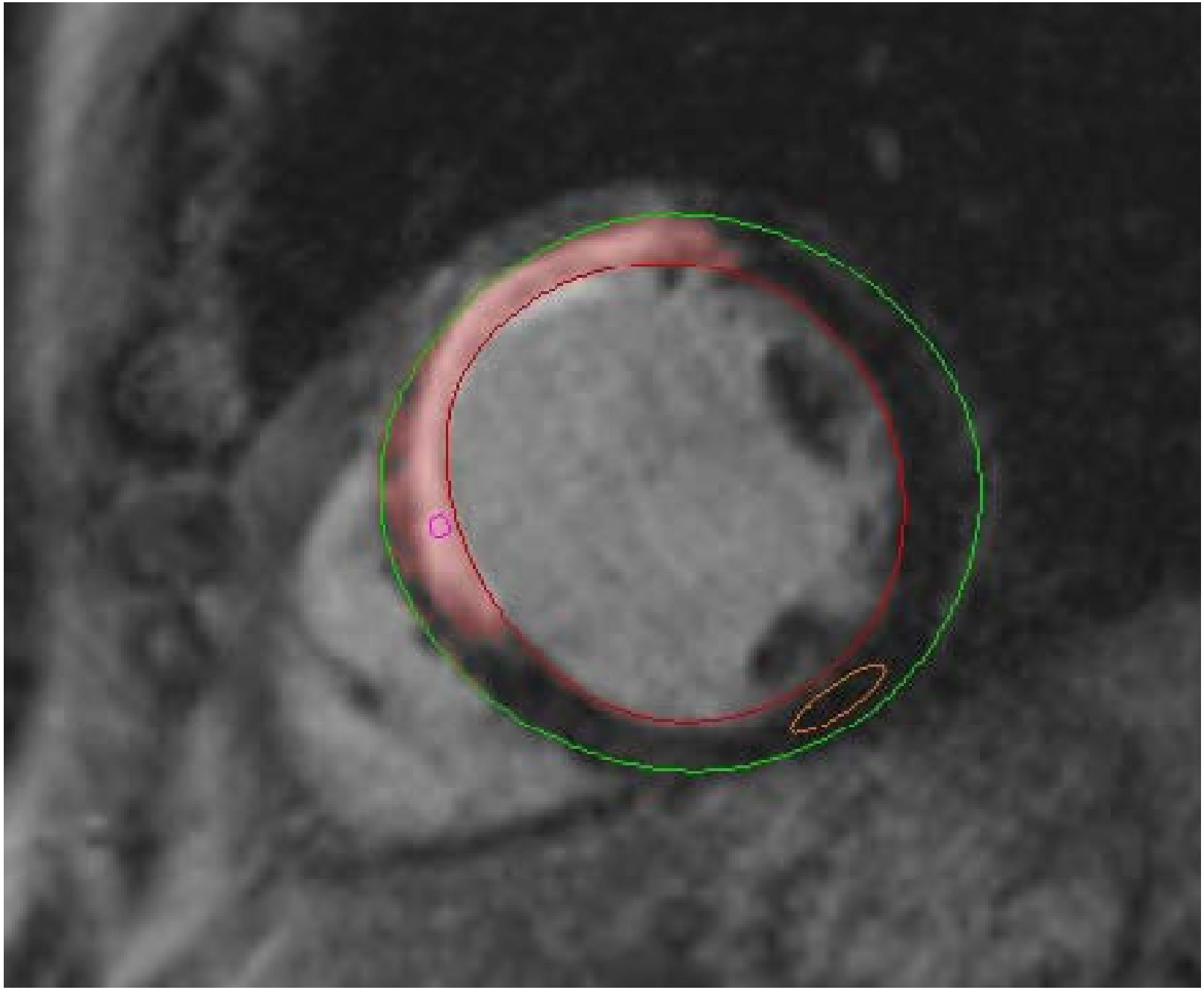
n-SD + Mean

Remote myocardial mean plus n-SD

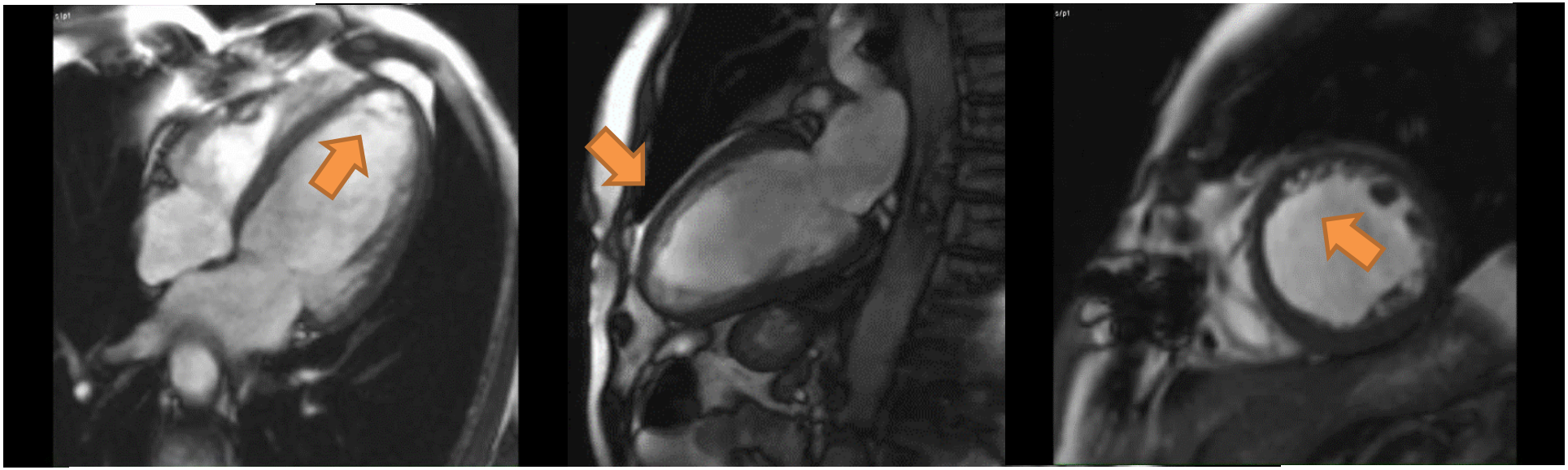




1. Visual assessment of LGE sequences;
2. Conventional planimetry at the short axis view (endo and epicardial borders) in the positive cases;
3. In a positive slice, a ROI is placed in the hyper-enhanced area and in the normal myocardium (remote area);
4. Intensity threshold calculation by the software and semi-automated quantification (with visual correction for artifacts and partial volume effect)



No-Gad Studies with scar?



Participant ineligible for gadolinium study (GFR = 35.2 mL/min/1.73 m^2)

Cath post MI from 08/26/2004 with lesion ≥ 75% in LAD, RCA and LCx

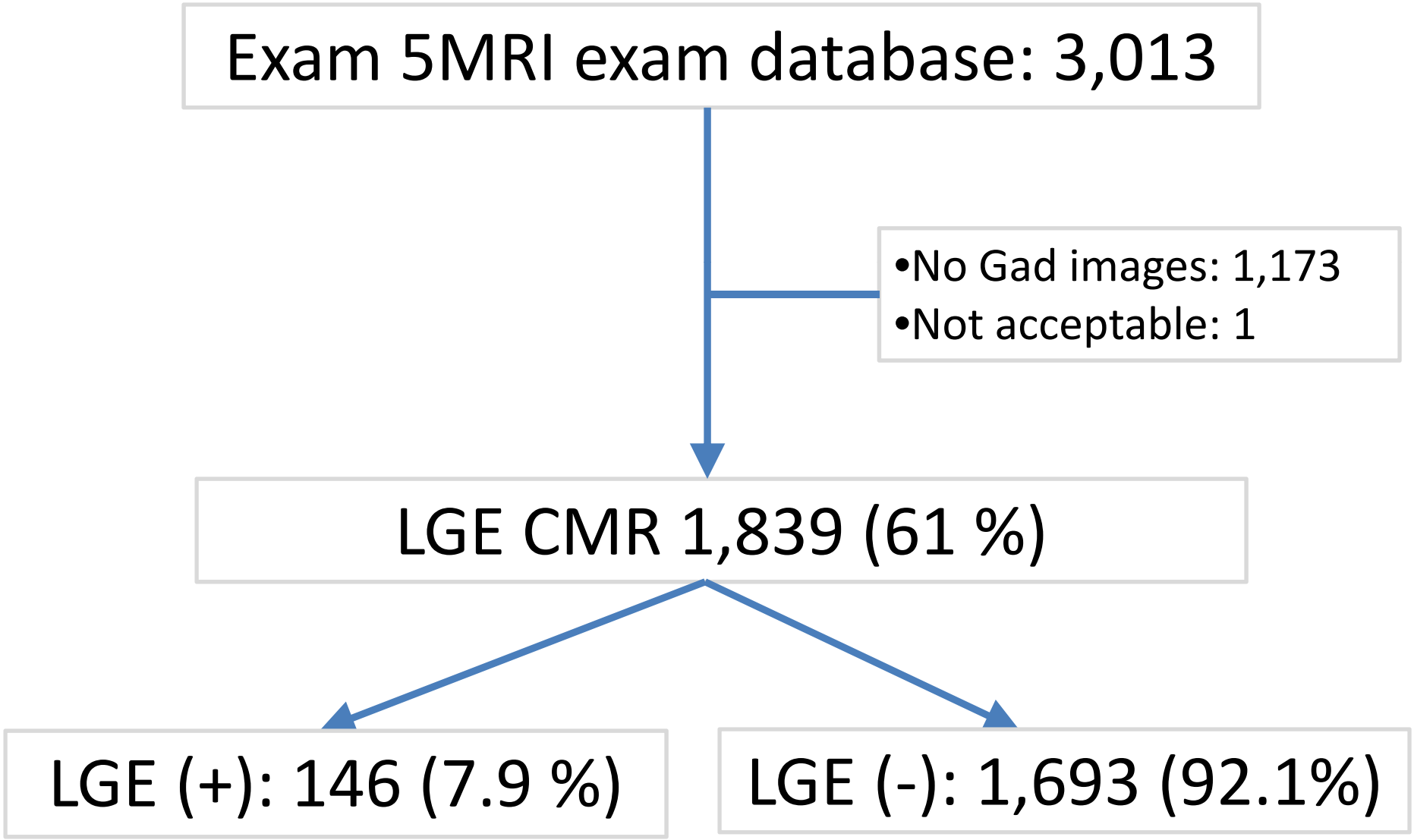
Objective

- We sought to describe determinants of myocardial scar in the Multi-Ethnic Study of Atherosclerosis (MESA)

Late Gadolinium Enhancement CMR

- LGE CMR is used to identify myocardial scar (dense myocardial fibrosis) due to ischemic and non-ischemic heart diseases
- Phase sensitive inversion recovery segmented gradient recalled echo sequence
- 15 minutes after intravenous administration of 0.15 mmol/kg gadolinium based contrast agent

CMR in MESA

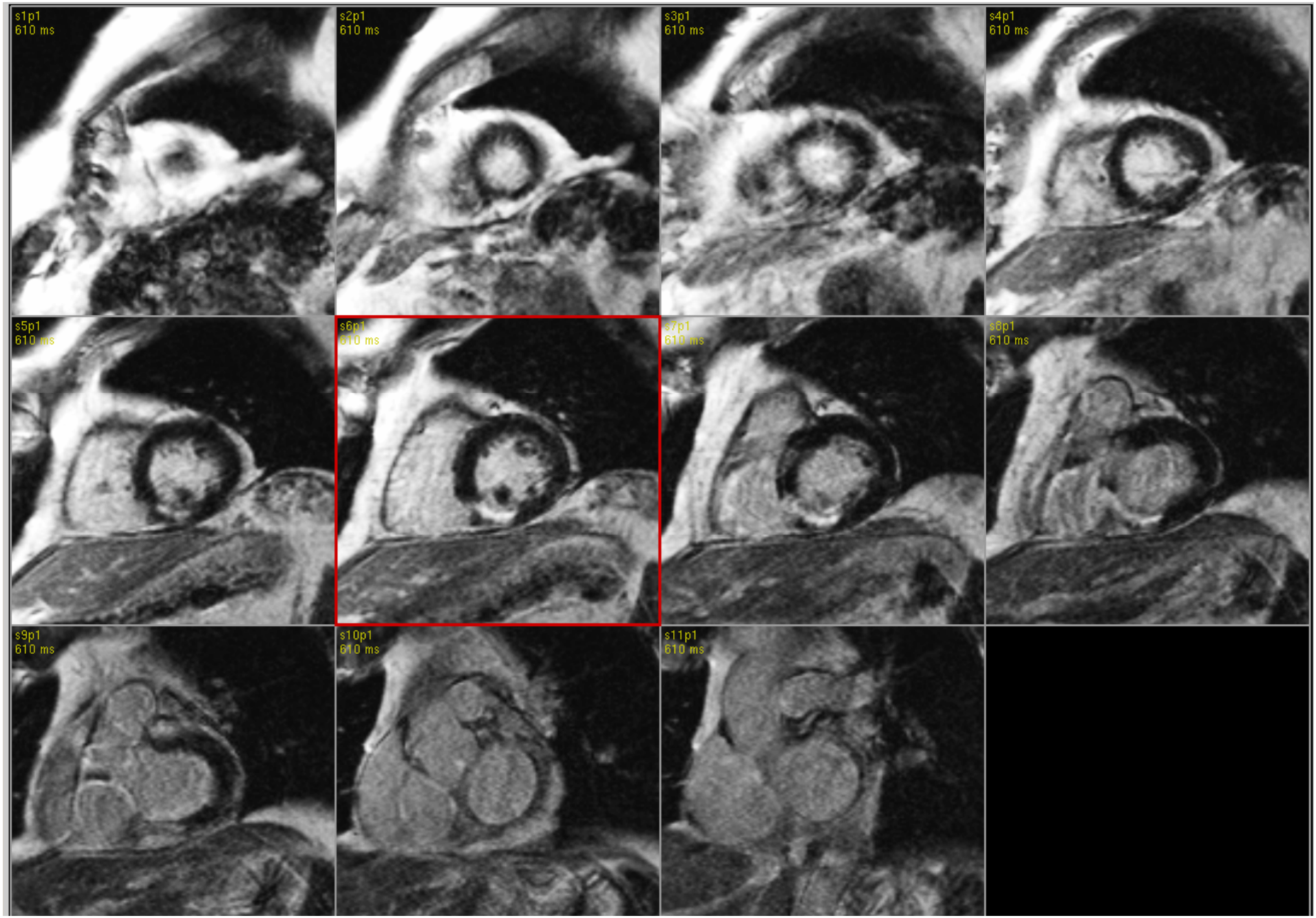

Exam 5MRI exam database: 3,013
•No Gad images: 1,173
•Not acceptable: 1
LGE CMR 1,839 (61 %)
LGE (+): 146 (7.9 %)
LGE (-): 1,693 (92.1%)

Methods

- 1,839 subjects underwent LGE-CMR as part of a 10-year follow up exam (2010-2012)
- The associations of risk factors and imaging measures with myocardial scar were assessed with logistic regression models

Methods

- Model 1 was adjusted for age, gender, race/ethnicity, blood pressure, hypertension medication, smoking status, diabetes, renal function and lipids
- Model 2 included model 1 + imaging phenotype:
  - LV mass/volume ratio + calcium score + carotid IMT + aortic diameter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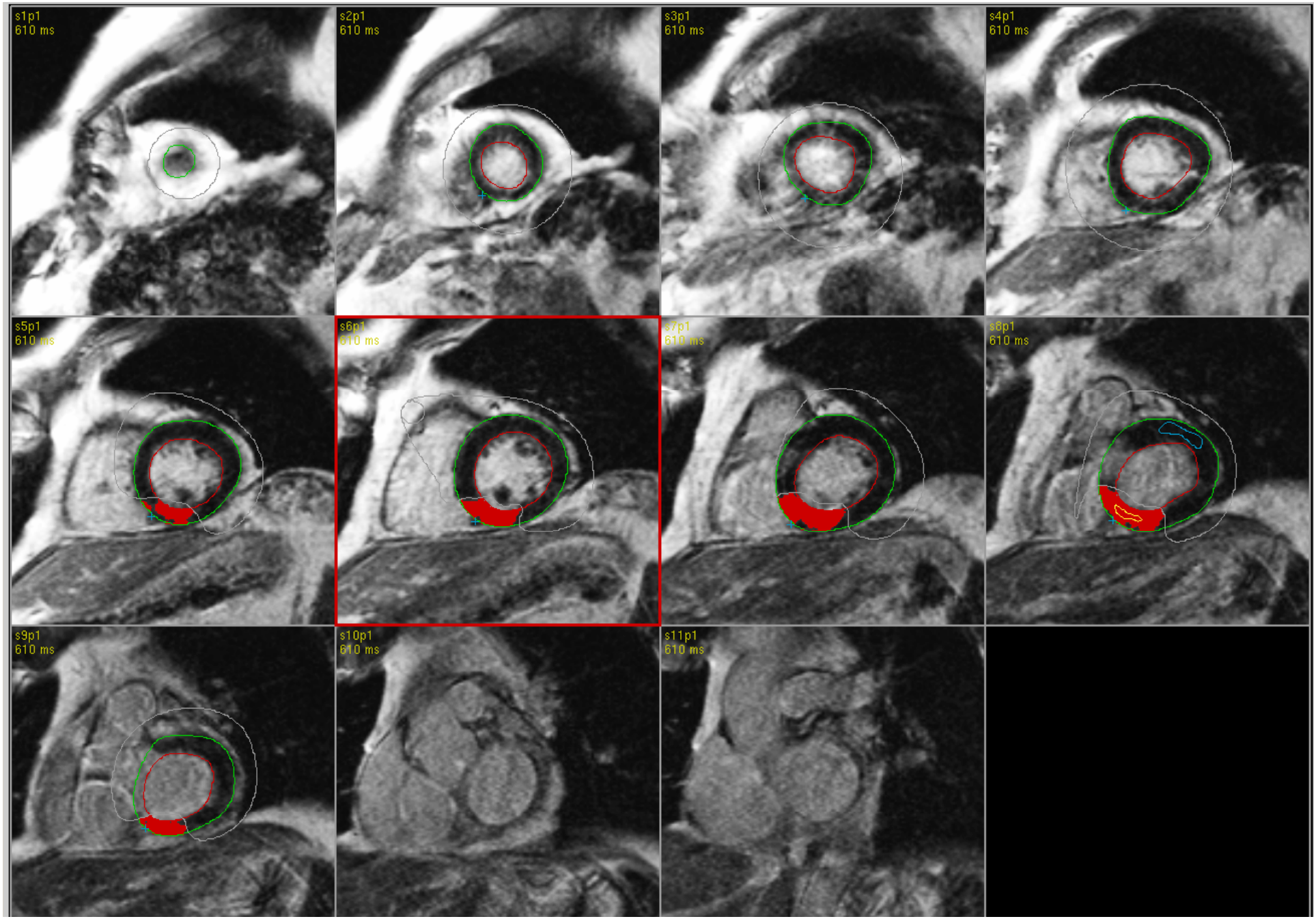
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VILLRIM, EXAM5-ECG2 ID:8017948 08-JUN-2011 11:40:21 MESA-DUPE ROUTINE RETRIEVAL

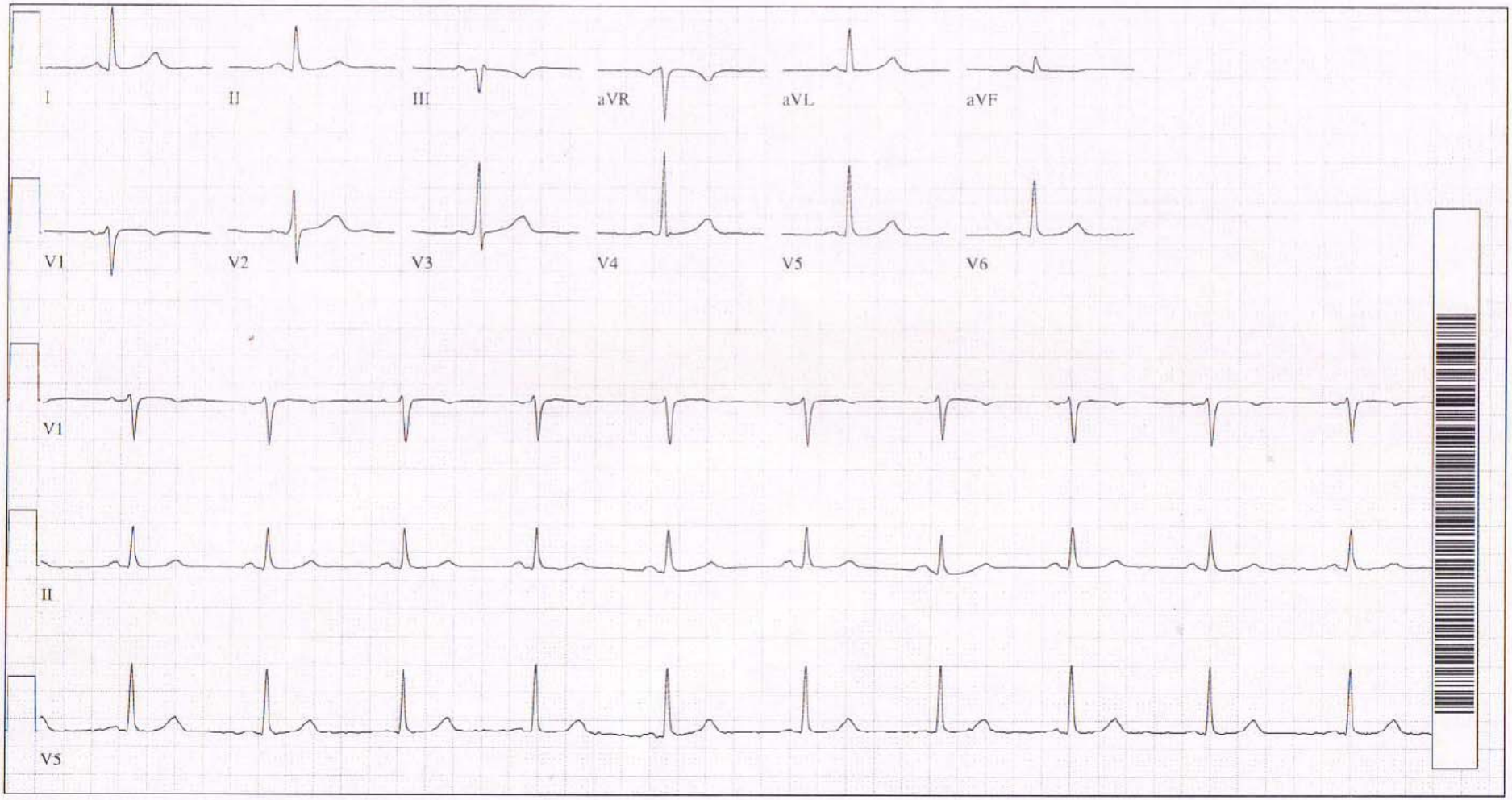
17-JUN-1950 (60 yr)		Vent. rate	62	BPM	Normal sinus rhythm
Male	Hispanic	PR interval	130	ms	Normal ECG
79in	286lb	QRS duration	96	ms	
Room:		QT/QTc	446/452	ms	
Loc:1000		P-R-T axes	49 11	-4	

Technician:MICHELLE CHAN
Test ind:

Med:

Referred by: MESA 2 UCLA 80 Confirmed By: Charles Campbell

Normal sinus rhythm
Normal ECG



25mm/s 10mm/mV 40Hz 7.1.1 12SL 21 CID: 80

SID: 8017948 EID:1 EDT: 09:14 10-JUN-2011 ORDER:

Results

- The prevalence of myocardial scar was 7.9% (146/1,839) by LGE-CMR
- Chinese/Hispanic ethnicities were less likely to have myocardial scar compared to Caucasians

Table - Myocardial Scar by LGE CMR

	Baseline (N=1,839)	**LGE + at 10-year follow-up Model 1** OR [95%CI], p value
Demographics		
Age (years)	62 ± 10	**1.05 [1.03-1.08], <0.001**
Male (%)	48	**6.34 [3.7-10.7], <0.001**
Clinical and Laboratory		
Systolic Blood Pressure (mmHg)	122 ± 33	**1.01 [1.0-1.02], 0.01**
Total Cholesterol (mg/dl)	194 ± 35	1.00 [0.99-1.10], 0.24
HDL (mg/dl)	50 ± 14	0.99 [0.97-1.10], 0.49
Lipid lowering medication (%)	17	0.97 [0.60-1.50], 0.91
Current smoker (%)	12.5	**1.95 [1.17-3.24], 0.01**
Diabetes (%)	22	1.5 [0.81-2.58], 0.205
eGFR (mL/min/1.73 m^2)	81 ± 14	1.0 [0.99-1.01], 0.516

Table - Myocardial Scar by LGE CMR

	Baseline (N=1,839)	**LGE + 10-year follow-up Model 2** OR [95%CI], p value
Demographics		
Age (years)	62 ± 10	1.02 [0.99-1.05], 0.11
Male (%)	48	**4.6 [2.46-8.67], <0.001**
Clinical and Laboratory		
Systolic Blood Pressure (mmHg)	122 ± 33	1.1 [0.99-1.02], 0.19
Total Cholesterol (mg/dl)	194 ± 35	1.0 [0.99-1.10], 0.32
HDL (mg/dl)	50 ± 14	1.0 [0.98-1.02], 0.56
Lipid lowering medication (%)	17	0.83 [0.48-1.4], 0.53
Current smoker (%)	49	1.76 [0.97-3.21], 0.06
Diabetes (%)	22	1.68 [0.86-3.25], 0.12
eGFR (mL/min/1.73 m^2)	81 ± 14	1.0 [0.99-1.02], 0.47

Table - Myocardial Scar by LGE CMR

	Baseline (N=1839)	LGE + at 10 years follow-up **Model 2** OR [95%CI], p value
Intimal-medial thickness (US)		
Max. common carotid (mm)	0.82±0.16	2.81 [0.77-10.20], 0.12
Calcium score by CT		
Log (agatston score+1)	1.6±2.2	**1.2 [1.08-1.31], <0.001**
Cardiac MRI		
Mass/ Volume Ratio (g/ml)	1.14±0.2	0.34 [0.1-1.4], 0.137
Asc. Aortic diameter (mm)	31±4	1.03 [0.96-1.08], 0.47

CMR defined myocardial scar

- EDIC, Turkbey et al: Circulation 2011; 18:124
  - Type 1 diabetes, 741 patients
  - Age (pts with scar): **52±6 years**
  - Prevalence of scar: 4.3%
- Kwong et al: Circulation 2008; 118:1011
  - Symptomatic Type 2 diabetes, 107 patients
  - Age (scar present): **63 ±13 yrs**
  - Prevalence of scar: 28%
- SMART study Heart 2009; 95:728
  - 480 Patients with arterial disease or vascular risk factors
  - Age: whole sample **53±12 yrs**
  - Prevalence of scar: 9.4%

CMR defined myocardial scar (continued)

- Barbier et al. (*JACC* 2006; 48:765)
  - Age: **70 year olds in Upsalla, Sweden, 248 subjects**
  - Prevalence of scar: 29%

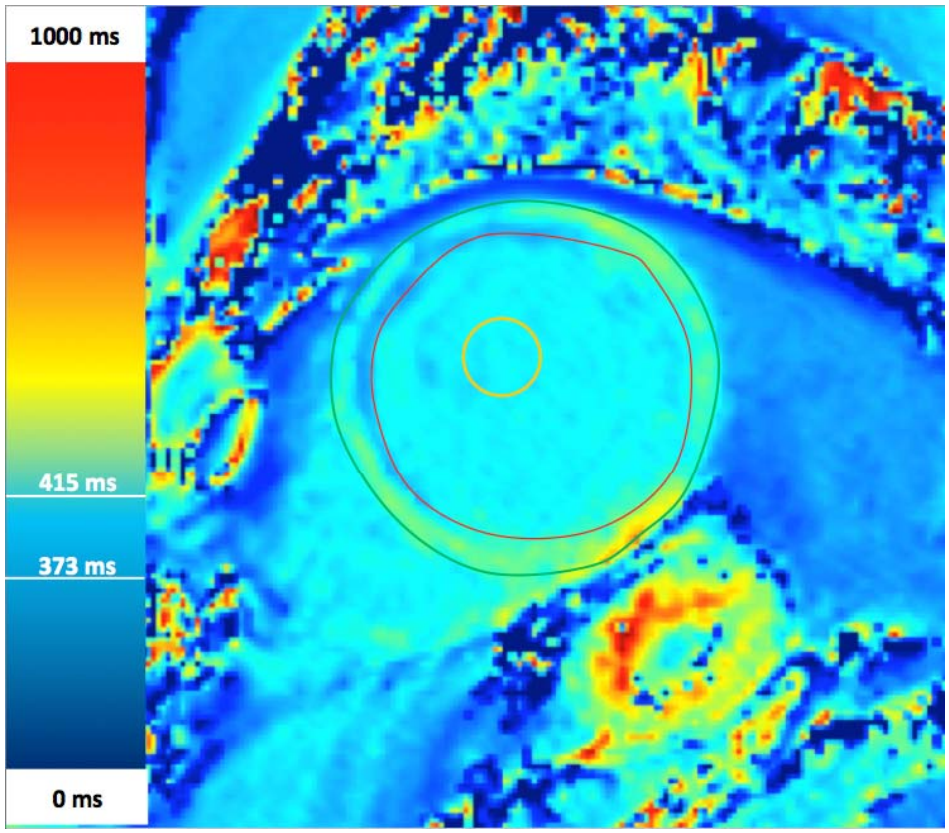
No GFR Criteria

- Schelbert et al. (*JAMA* 2012; 308)
  - **76 yrs in Iceland,** 936 subjects
  - Prevalence of scar: 27%

No GFR Criteria

Summary

- In a large multi-center cohort, the prevalence of myocardial scar was 7.9% (mean age, 72), substantially lower than in Iceland (29%) and Sweden (27%)
- In the multivariable model, age, male gender, systolic blood pressure, and current smoking status were associated with myocardial scar ($p<0.001$)
- From the imaging variables, only CAC was significantly associated with the presence of myocardial scar

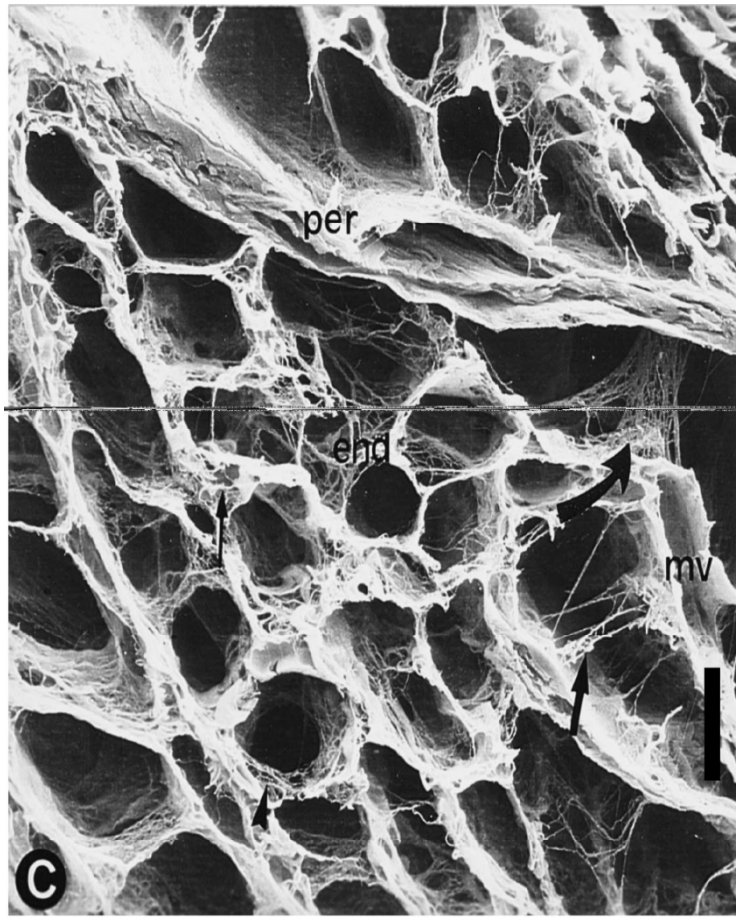


T1 MAPPING

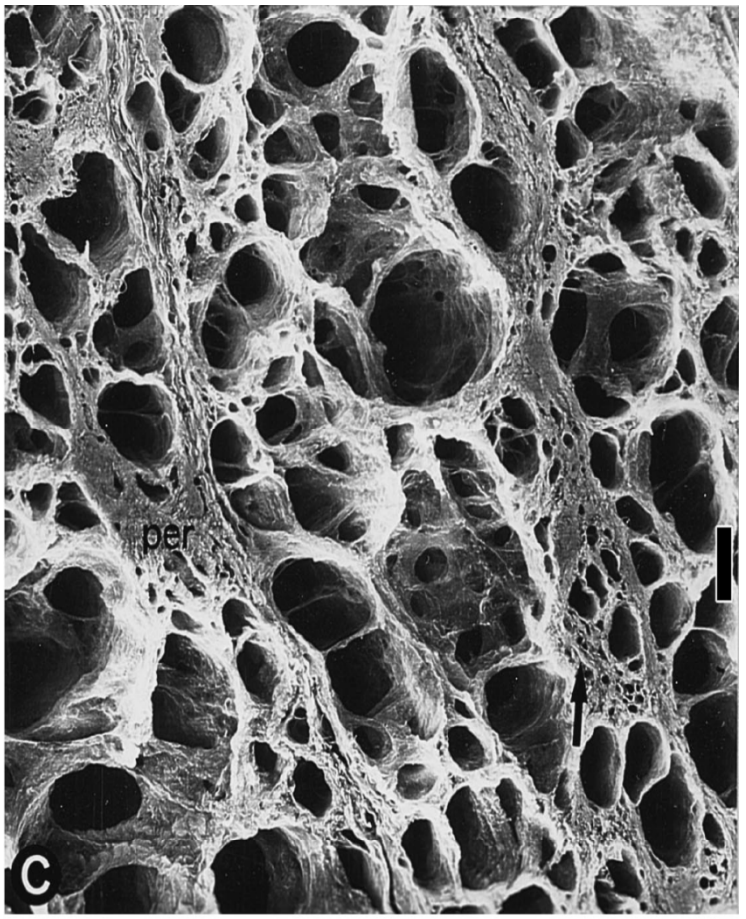
Pathologic fibrosis and connective tissue matrix in left ventricular hypertrophy due to chronic arterial hypertension in humans

Marcos A. Rossi

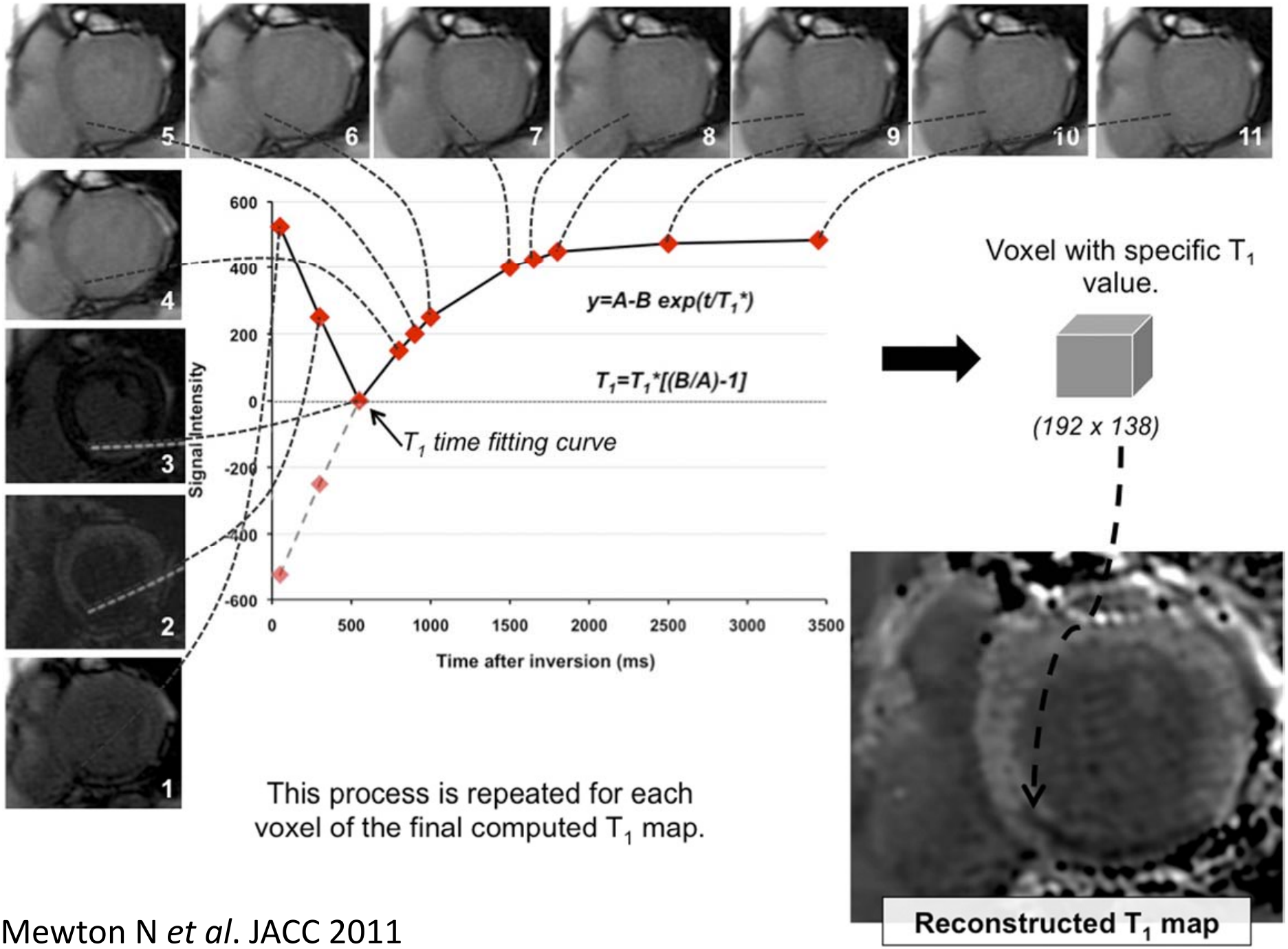
Normal



Hypertrophied

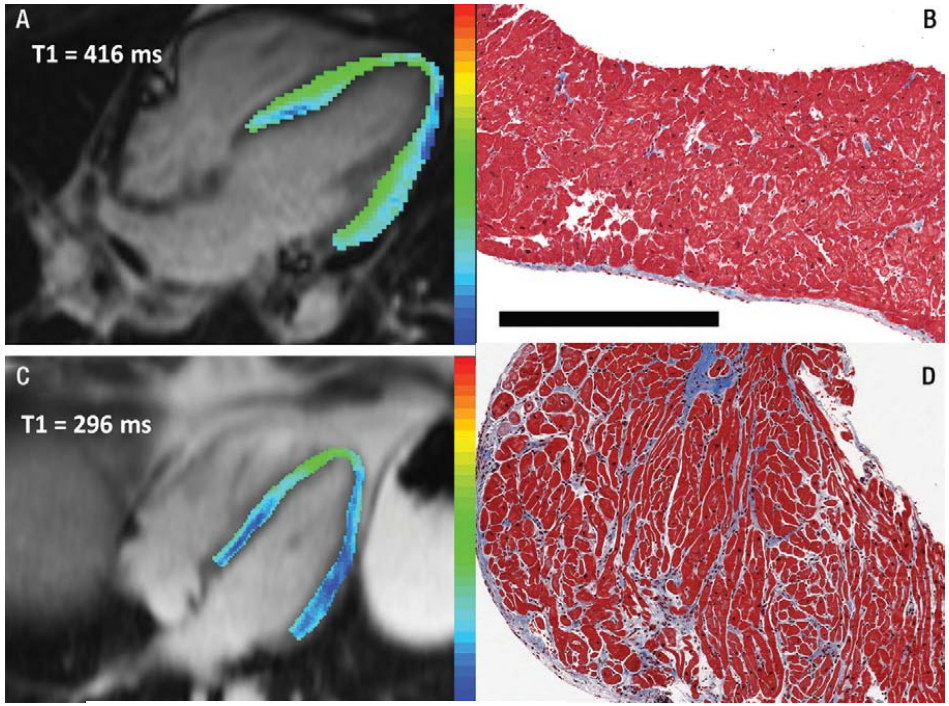


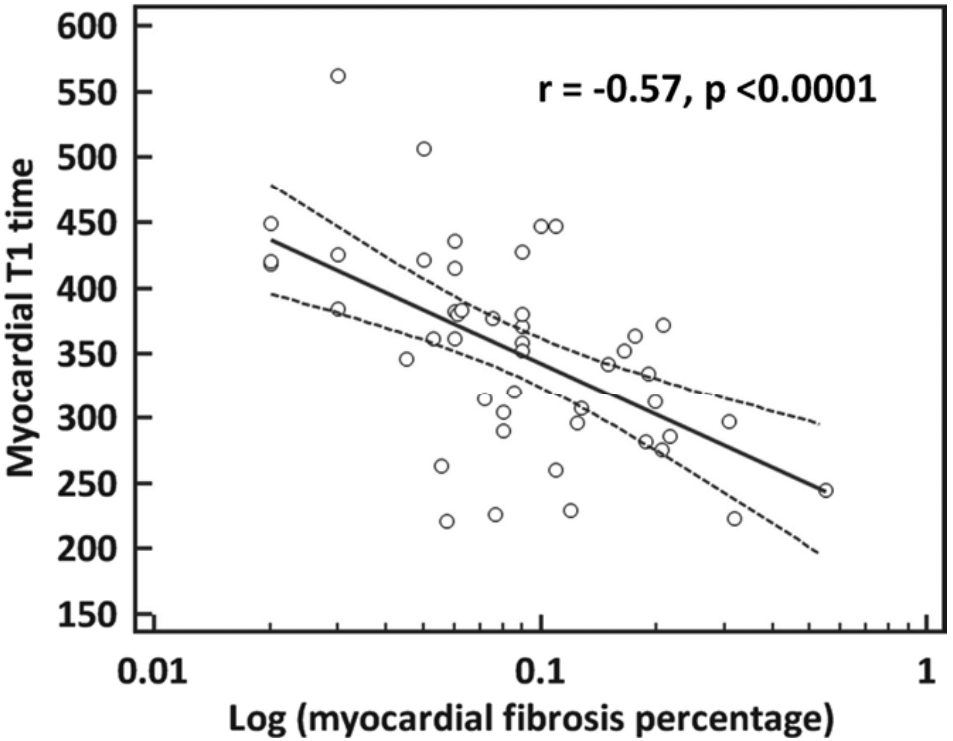
Rossi, MA. J Hypertens 1998

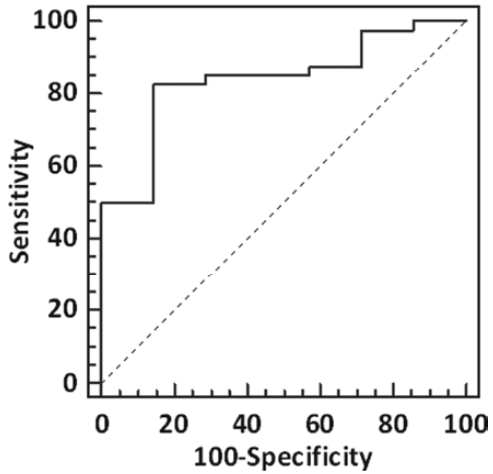


Mewton N *et al*. JACC 2011

T1 Mapping in Cardiomyopathy at Cardiac MR: Comparison with Endomyocardial Biopsy[1]







For histologic fibrosis greater than 5% of myocardial volume.
AUC = 0.84
(95% CI: 0.70, 0.93;
P < 0.0001)

Sibley, CT. *Radiology* 2012

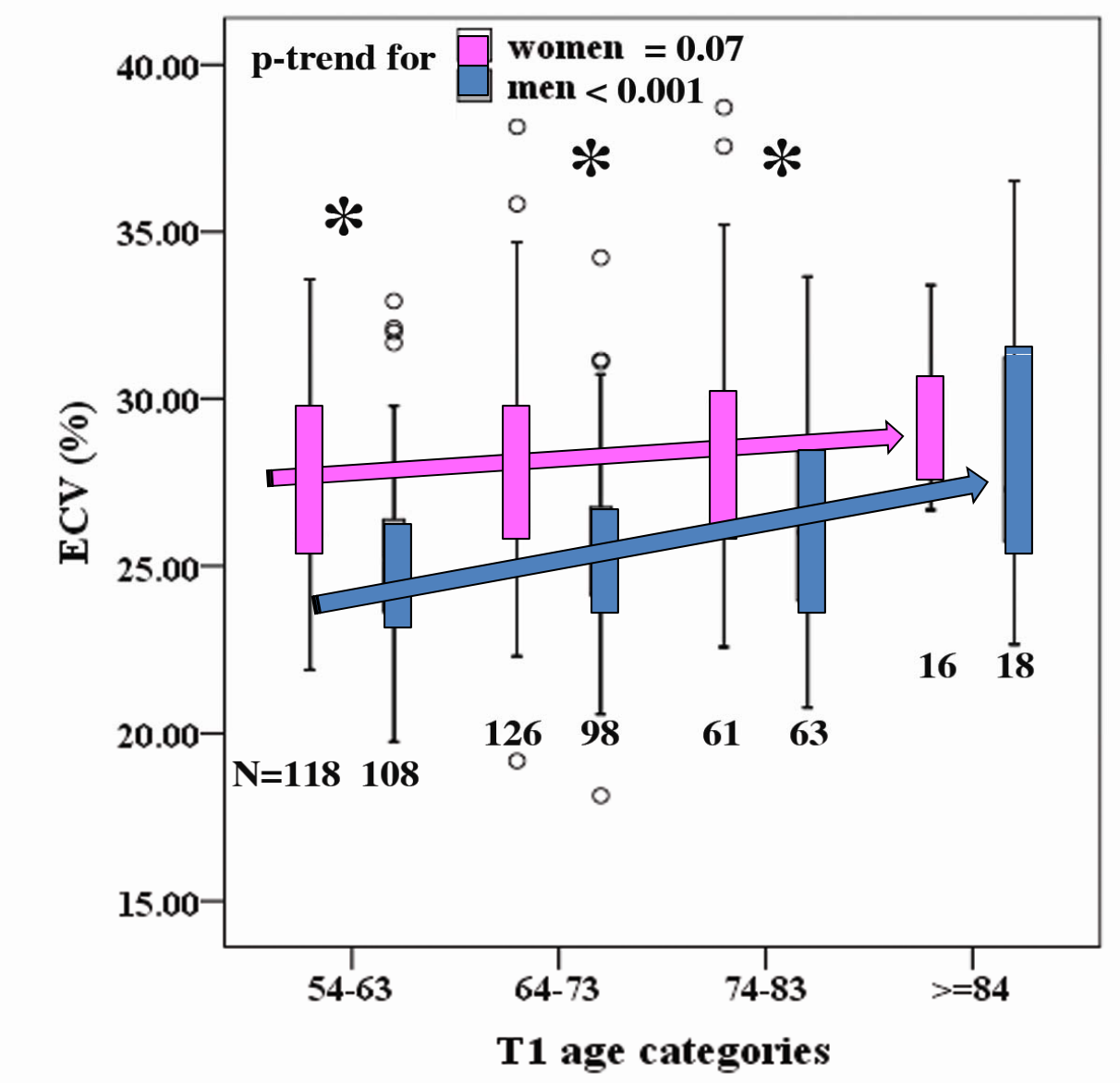
DETERMINANTS OF INTERSTITIAL FIBROSIS EVALUATED BY MR T1 MAPPING: MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS (MESA)

This analysis was presented at the 2012 AHA scientific sessions by Chia-Ying Liu, PhD

Methods

- **Model 1:** Age, gender, Race/ethnicity, smoking status, hypertension medication, total cholesterol, lipid lowering medication, diabetes, obesity (BMI ≥ 30 kg/m^2)
- **Model 2:** Model 1 + LV mass/volume ratio + calcium score + carotid IMT + aortic diameter.

ECV in age quartiles without any adjustments (Liu et al. JACC 2013)



Scar variables from MESA 5 data

- In the Exam 5 dataset currently:
  - Scar of any size (yes/no)
- Variables to be merged into Exam 5 data in early 2014
  - Percent scar
  - Clinically significant (> 5%) (yes/no)
  - Transmural (yes/no)
  - Ischemic (yes/no)
  - Location – (apex, base, mid)

Thank you