MRI to assess arrhythmic risk post-MI

Jeffrey Goldberger, MD
Director, Cardiac Electrophysiology Research
Professor of Medicine

Disclosures

- **Research/Lectures - Boston Scientific, Medtronic. St. Jude**

SCD Epidemiology

- Sources of information
- Range 184,000 – 462,000
- Etiologies of SCD
  - Ventricular tachyarrhythmias – VT/VF
  - Bradyarrhythmias
  - Nonarrhythmic causes – aneurysm, PE, myocardial rupture

Variables Associated with Increased Risk for SCD

- Low EF
- VEA
- HRV, BRS, HR, HRR, HRT
- Repolarization abnormalities - QT interval, QT dispersion, T wave alternans
- Depolarization abnormalities - SAECG, QRS duration
- Functional class

AHA/ACC/HRS Scientific Statement

American Heart Association/American College of Cardiology/Heart Rhythm Society Scientific Statement on Noninvasive Risk Stratification Techniques for Identifying Patients at Risk for Sudden Cardiac Death

A Scientific Statement From the American Heart Association Clinical Cardiology Council Committee on Electrocardiography and Arrhythmias and the Epidemiology and Prevention Council

Jeffrey J. Goldberger, MD, FAHA, FACC, FHRS; Michael E. Cain, MD, FAHA, FACC, FHRS; Stefan H. Hohnloser, MD, FACC; Alan H. Kadish, MD, FAHA, FACC; Bradley P. Knight, MD, FACC; Michael S. Lauer, MD, FAHA, FACC; Barry J. Maron, MD, FACC; Richard L. Page, MD, FAHA, FACC, FHRS; Rod Passman, MD, MSCE, FACC; David Siscovick, MD, MPH, FAHA; William G. Stevenson, MD, FAHA, FACC, FHRS; Douglas P. Zipes, MD, FAHA, MACC, FHRS

Table. Summary of Noninvasive Risk-Stratification Techniques for Identifying Patients With Coronary Artery Disease Who Are at Risk for Sudden Cardiac Death (SCD)

Technique	Conclusion
1. **LVEF**	Although low LVEF has been effectively used to select high-risk patients for application of therapy to prevent sudden arrhythmic death, LVEF has limited sensitivity: the majority of SCDs occur in patients with more preserved LVEF.
2. ECG and Holter •Ectopy and **NSVT** •Signal averaged ECG •QRS duration •Heart rate variability •QT dynamics	In some populations, the presence of NSVT has been effectively used to select high-risk patients for application of therapy to prevent sudden arrhythmic death. This may also have limited sensitivity.
3. Exercise test/functional status •NYHA class •Heart rate recovery •T-wave alternans	

Circulation. 2008;118:1497-1518.

Table. Summary of Noninvasive Risk-Stratification Techniques for Identifying Patients With Coronary Artery Disease Who Are at Risk for Sudden Cardiac Death (SCD)

Technique	Conclusion
1. LVEF 2. ECG and Holter •**Ectopy** and NSVT •Signal averaged ECG •**QRS duration** •Heart rate variability •**QT dynamics** 3. Exercise test/functional status •**NYHA class** •**Heart rate recovery** •T-wave alternans	Clinical utility to guide selection of therapy has not yet been tested.

Circulation. 2008;118:1497-1518.

Table. Summary of Noninvasive Risk-Stratification Techniques for Identifying Patients With Coronary Artery Disease Who Are at Risk for Sudden Cardiac Death (SCD)

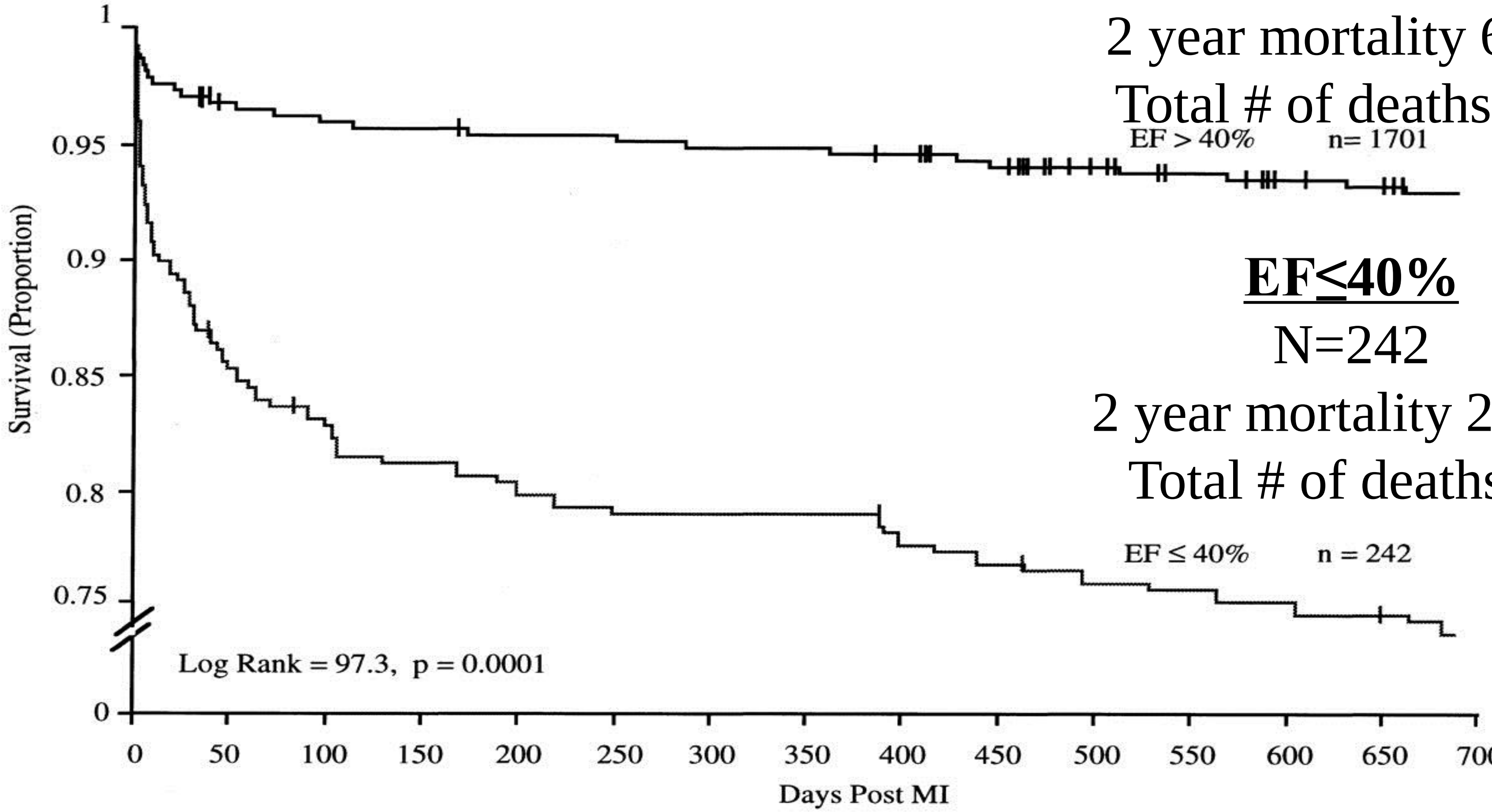
Technique	Conclusion
1. LVEF 2. ECG and Holter •Ectopy and NSVT **•Signal averaged ECG** •QRS duration **•Heart rate variability** •QT dynamics 3. Exercise test/functional status •NYHA class •Heart rate recovery **•T-wave alternans**	Clinical utility to guide selection of therapy has been tested, but not yet demonstrated.

Circulation. 2008;118:1497-1518.

GUSTO 2-YEAR SURVIVAL

EF>40%
N=1701
2 year mortality 6.8%
Total # of deaths 116

EF≤40%
N=242
2 year mortality 25.2%
Total # of deaths 61



EF > 40%	60	11	6	4	2	6	0	6	7	4	2	5	3
EF ≤ 40%	36	5	4	3	2	1	0	2	2	2	2	1	1

Cumulative Deaths per interval

Ross AM Circulation 1998; 97: 1549-1556

Oregon Sudden Unexpected Death Study

- **Multnomah County - 660,486; 2002-4**
- **714 SCD - 54/100,000**
- **Pre-SCD EF in 121 (17%)**

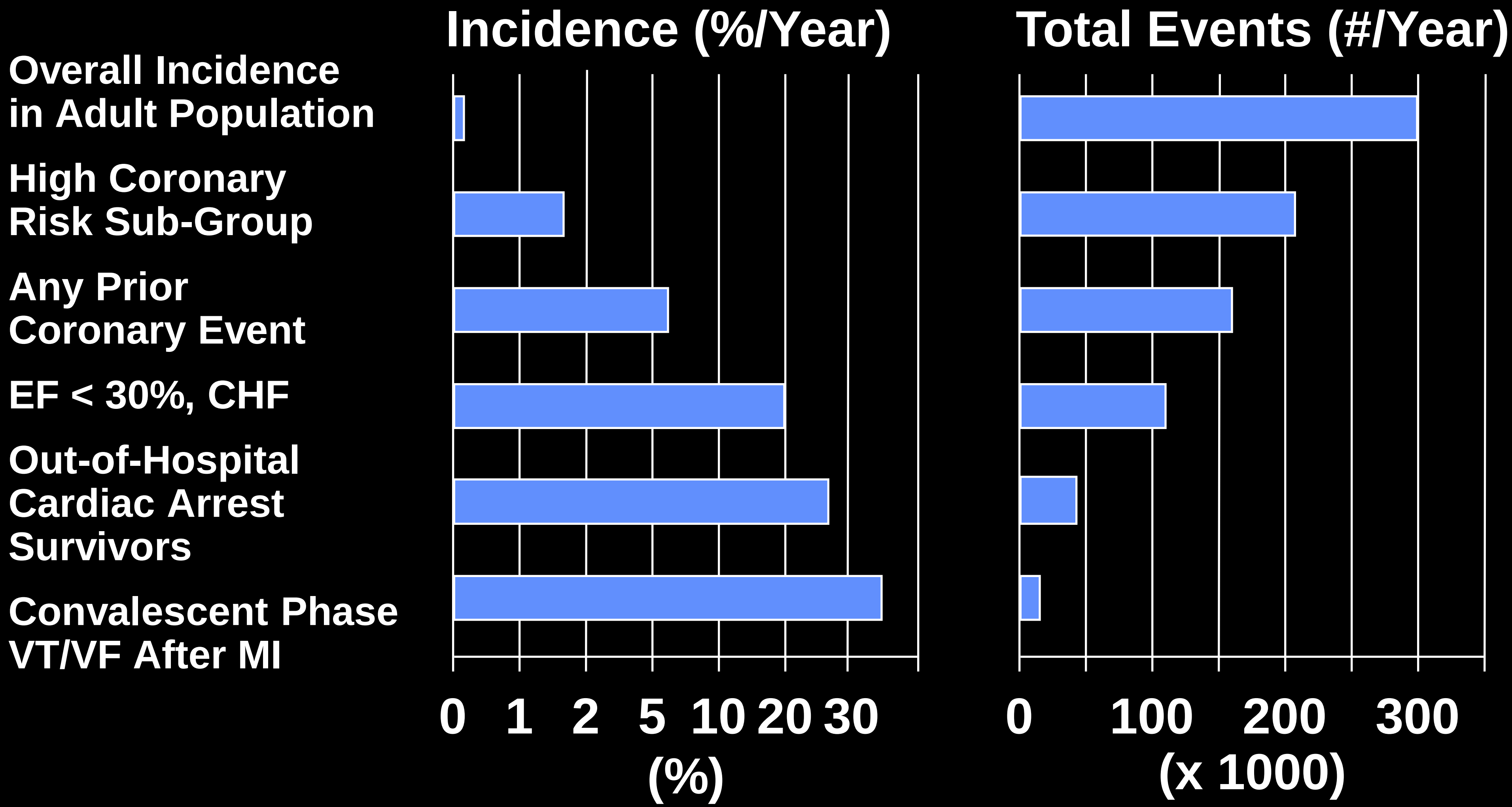
  Normal - 48%

  36-54% - 22%

  ≤35% - 30%

Stecker et al JACC 2006

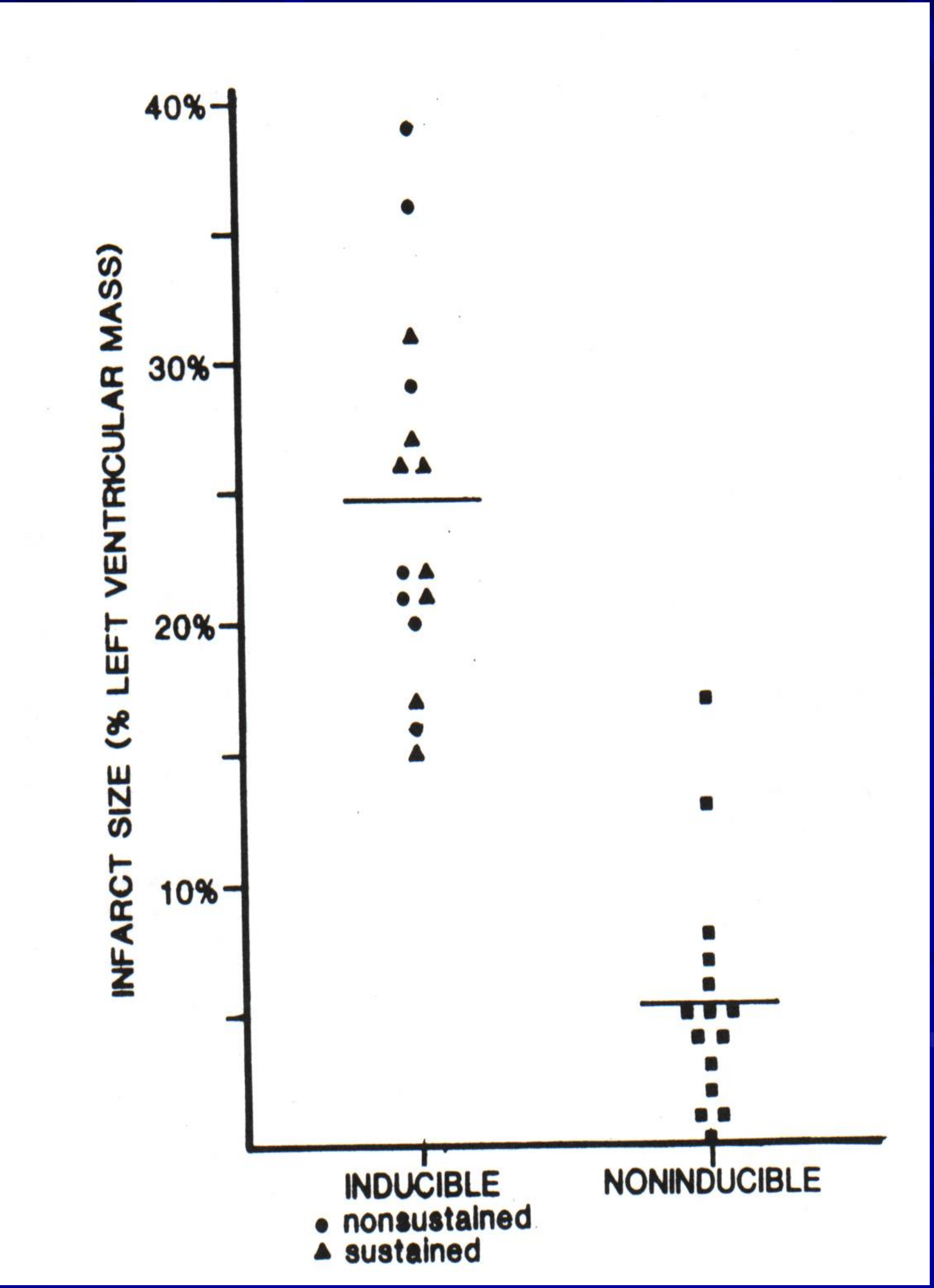
Sudden Cardiac Deaths – Incidence and Total Events



Myerburg RJ Circulation 1992;85(suppl I):I-2 – I-10.

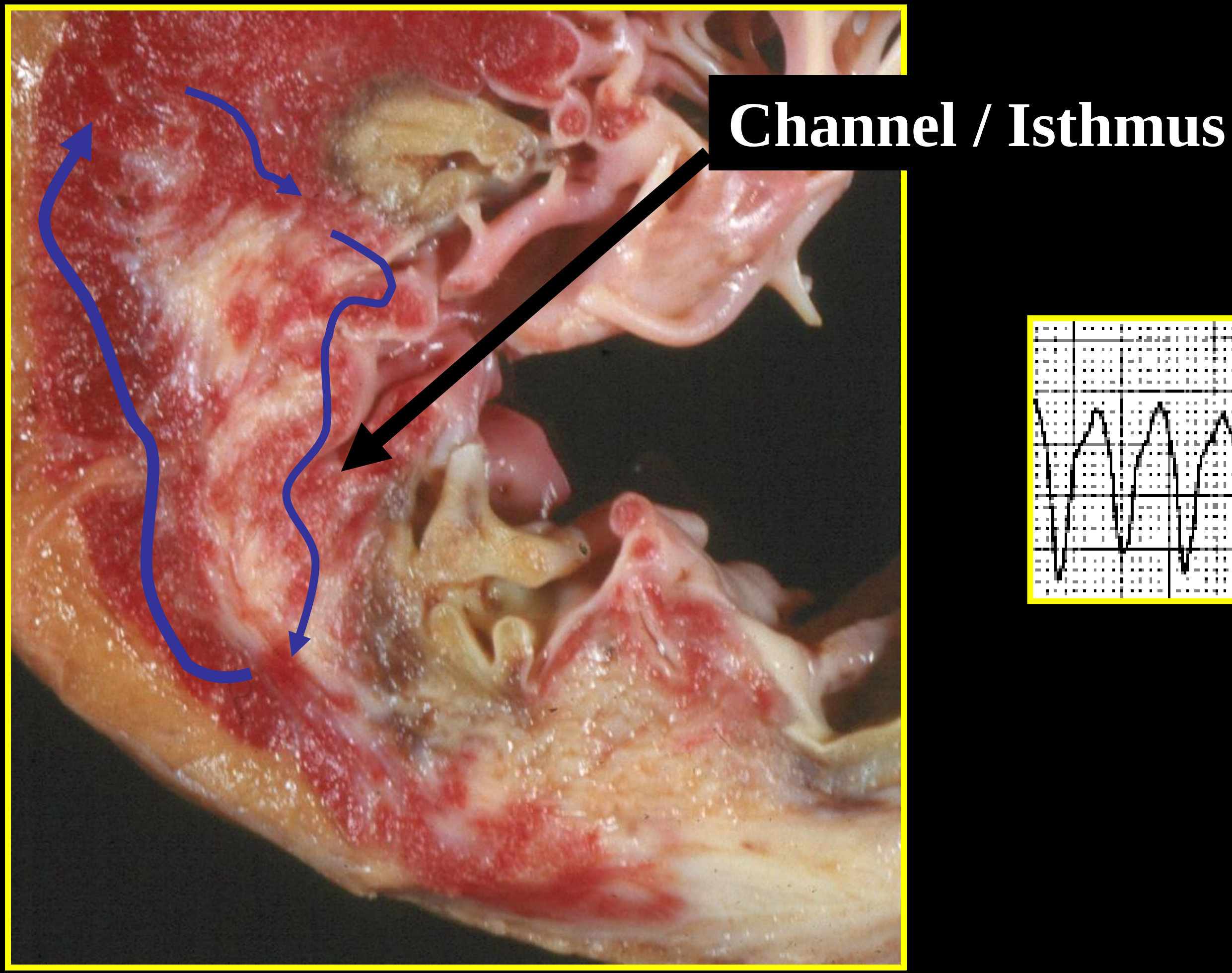
Canine Model

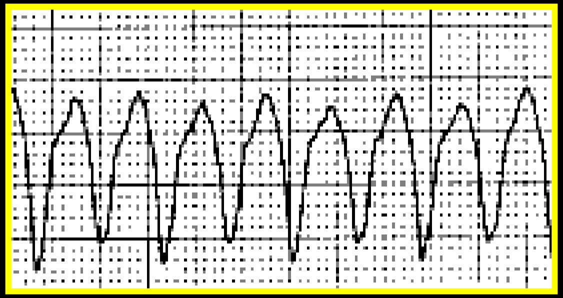
Extent of myocardial scar is related to inducibility of VT



Wilber et al *Am Heart J* 1985

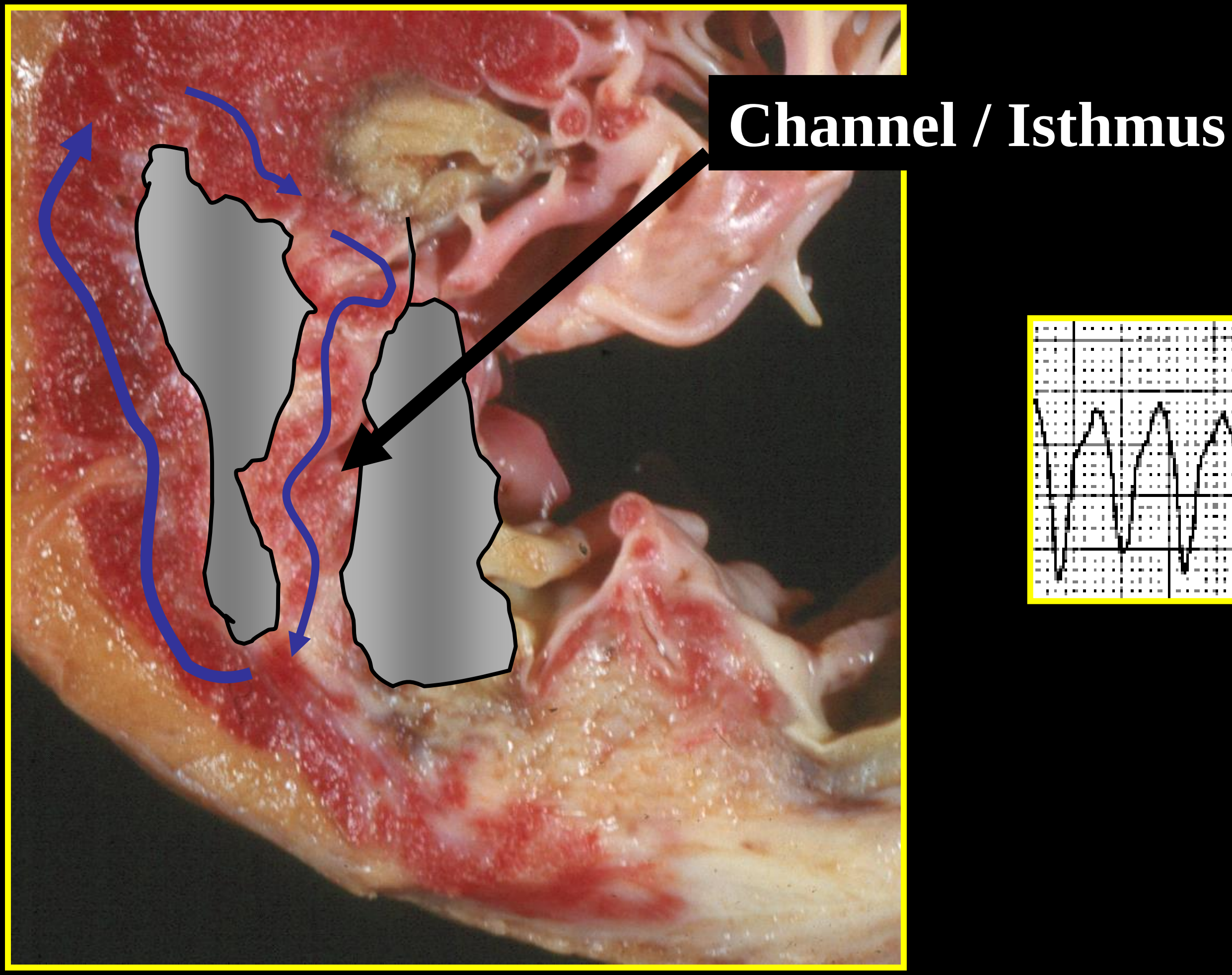
Sustained Monomorphic VT: Reentry in an infarct scar

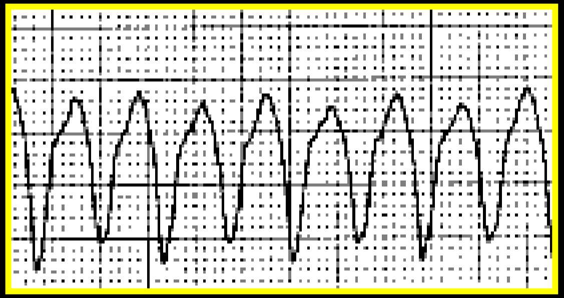




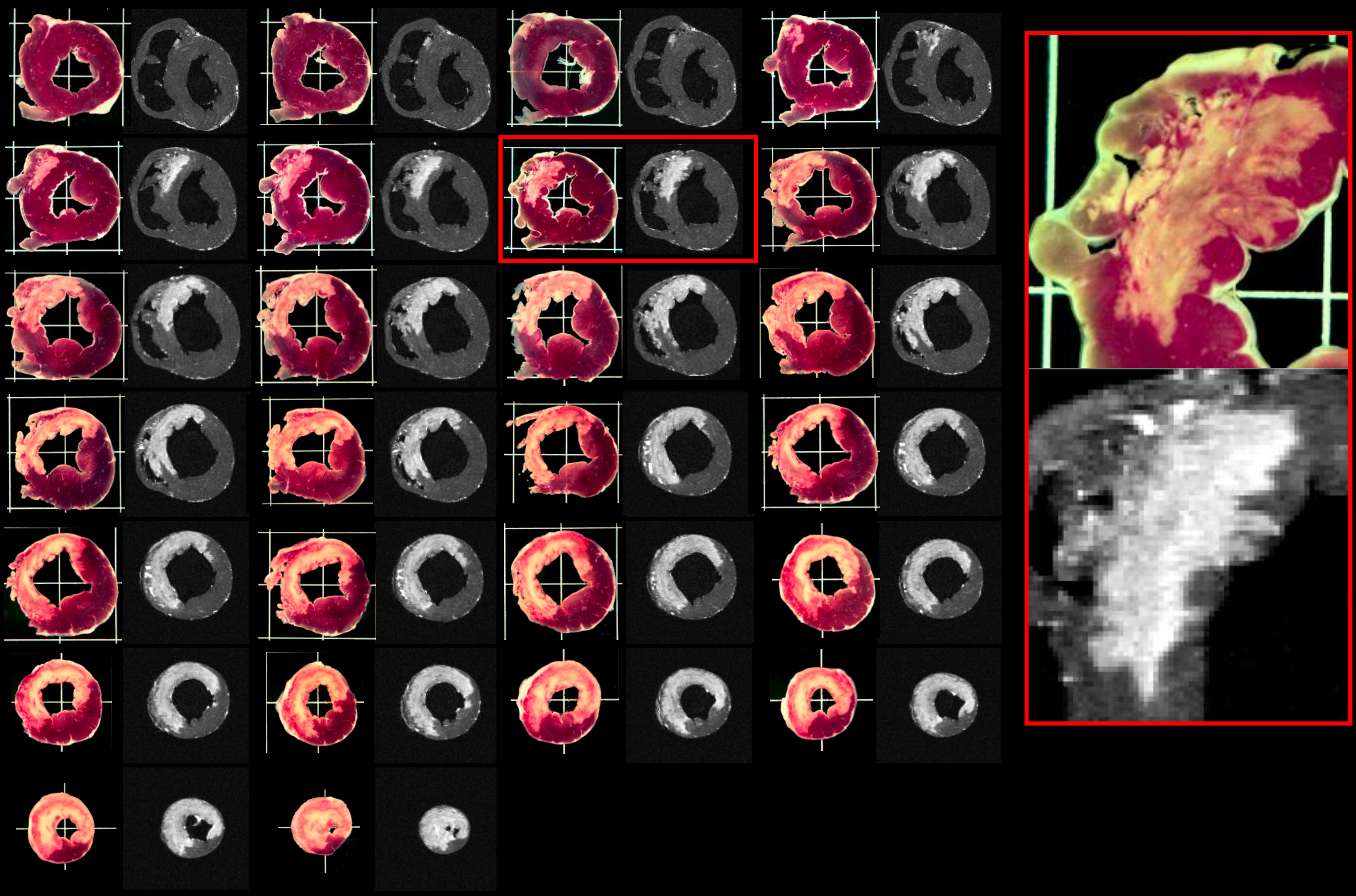
Courtesy of Bill Stevenson

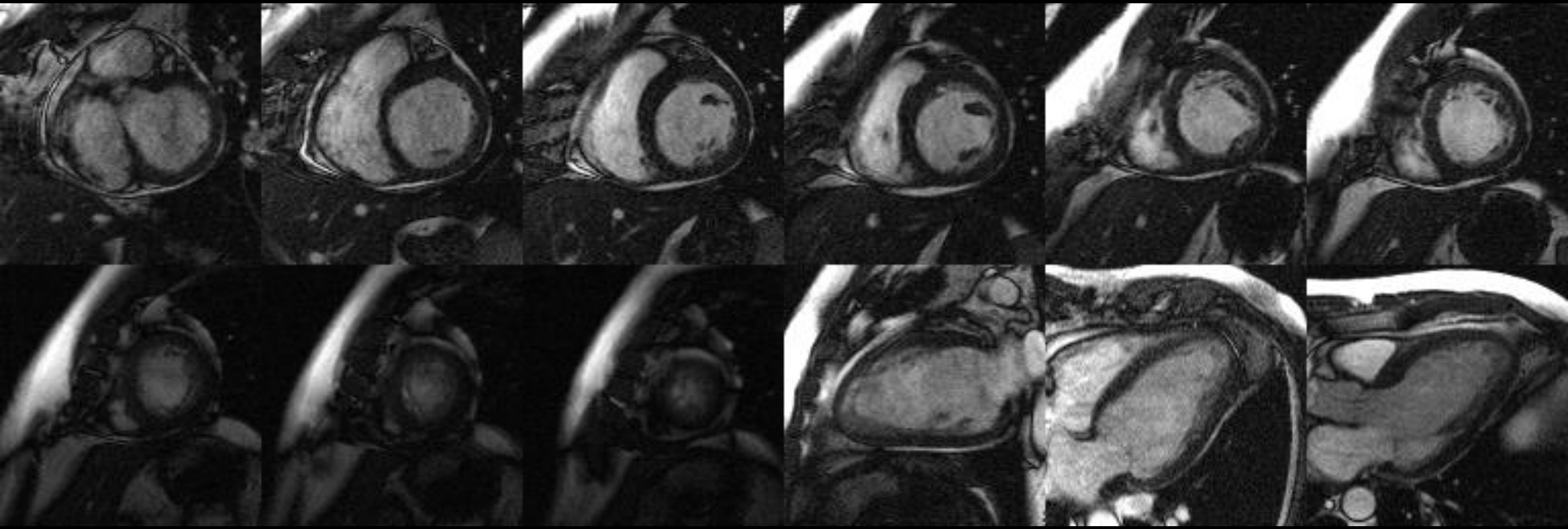
Sustained Monomorphic VT: Reentry in an infarct scar

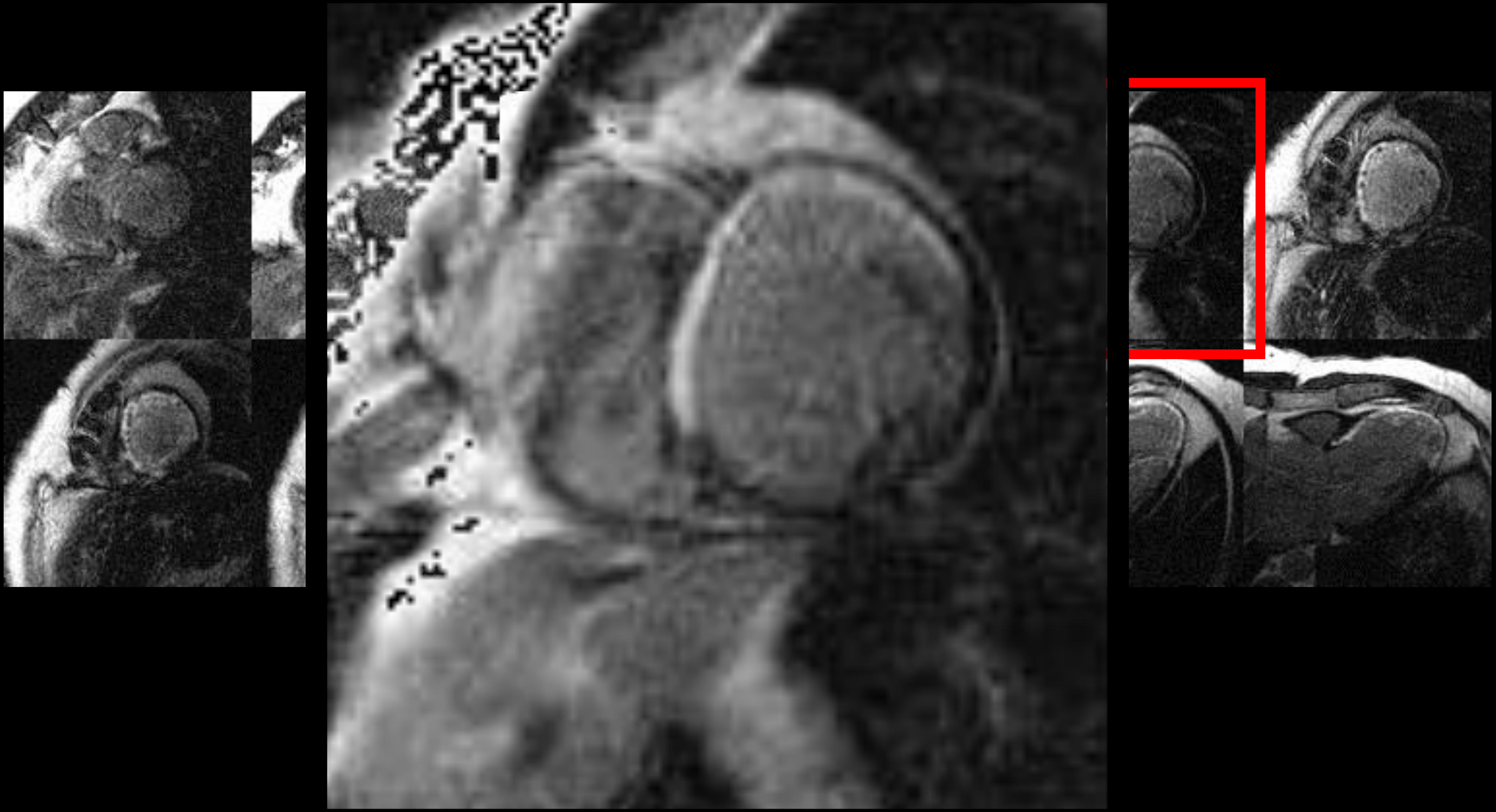


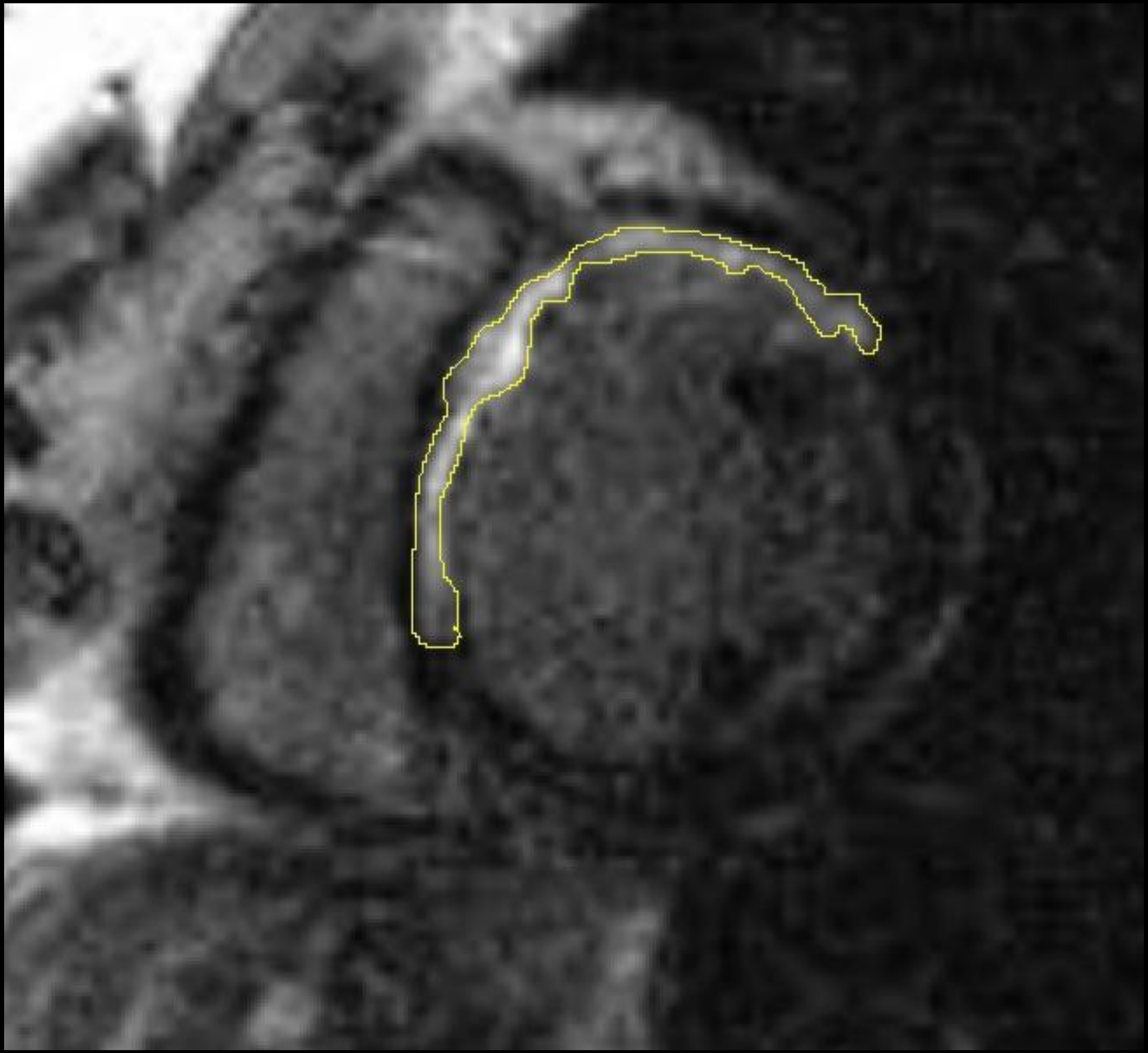


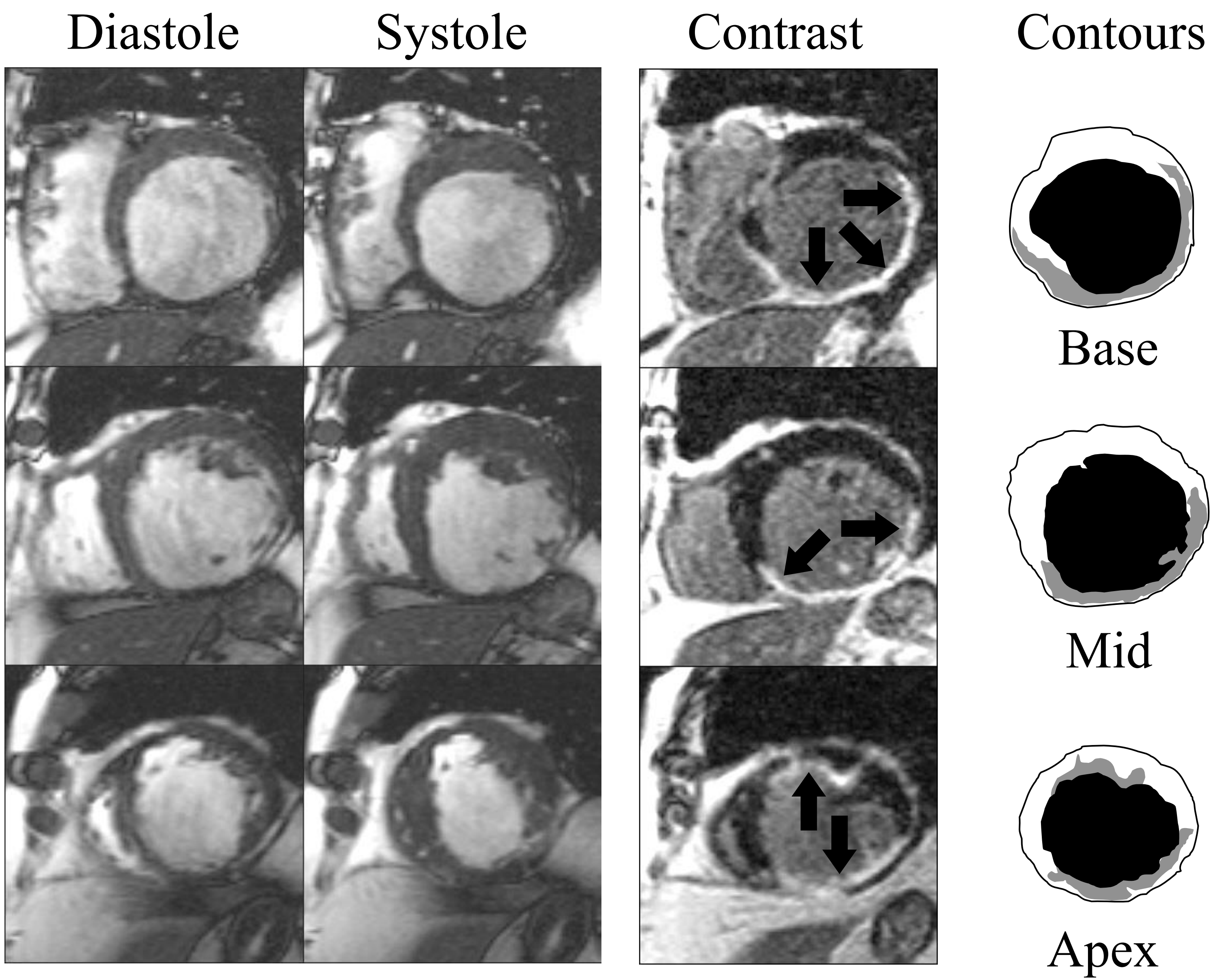
Courtesy of Bill Stevenson









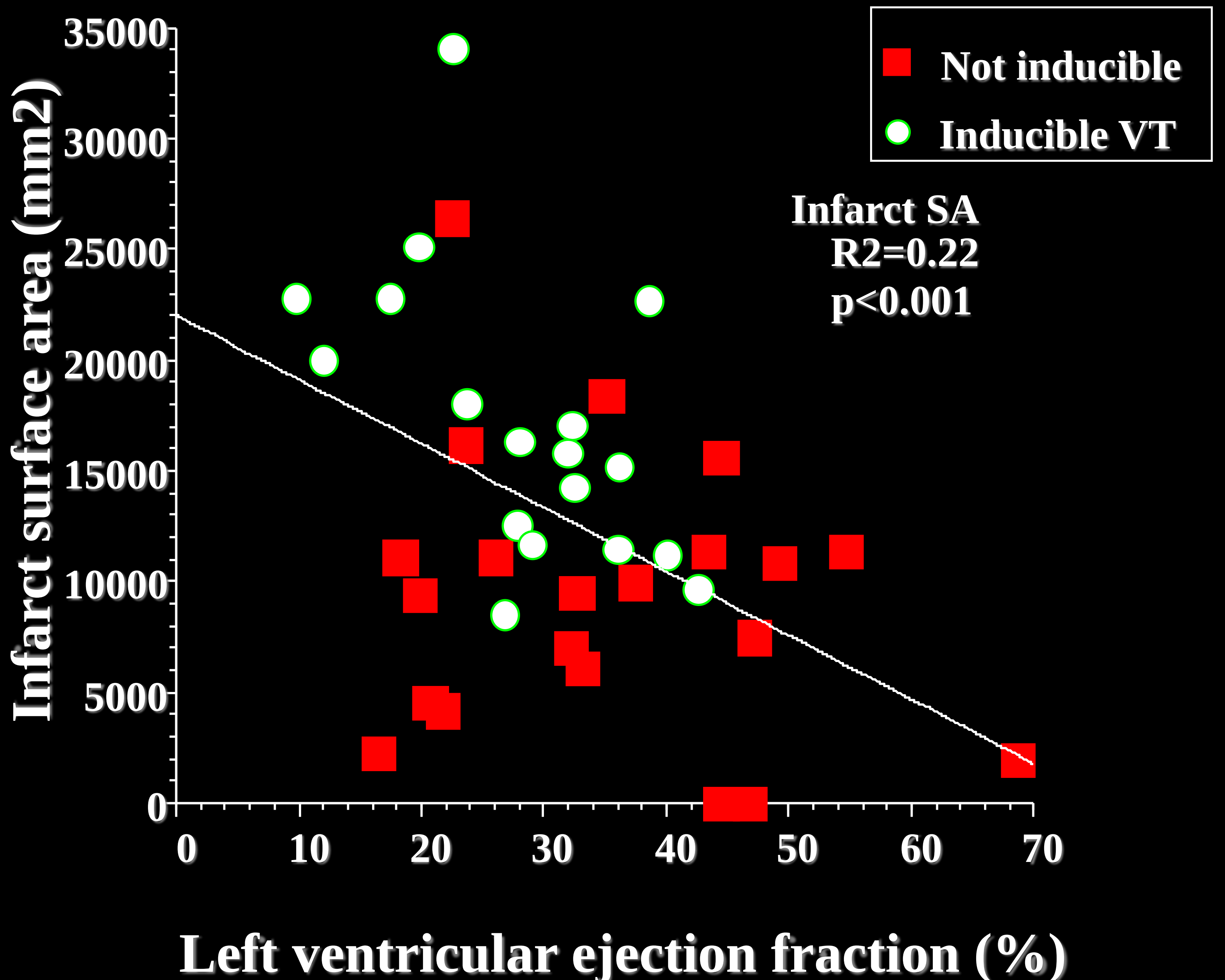

Diastole
Systole
Contrast
Contours
Base
Mid
Apex

Infarct Morphology Identifies Patients With Substrate for Sustained VT

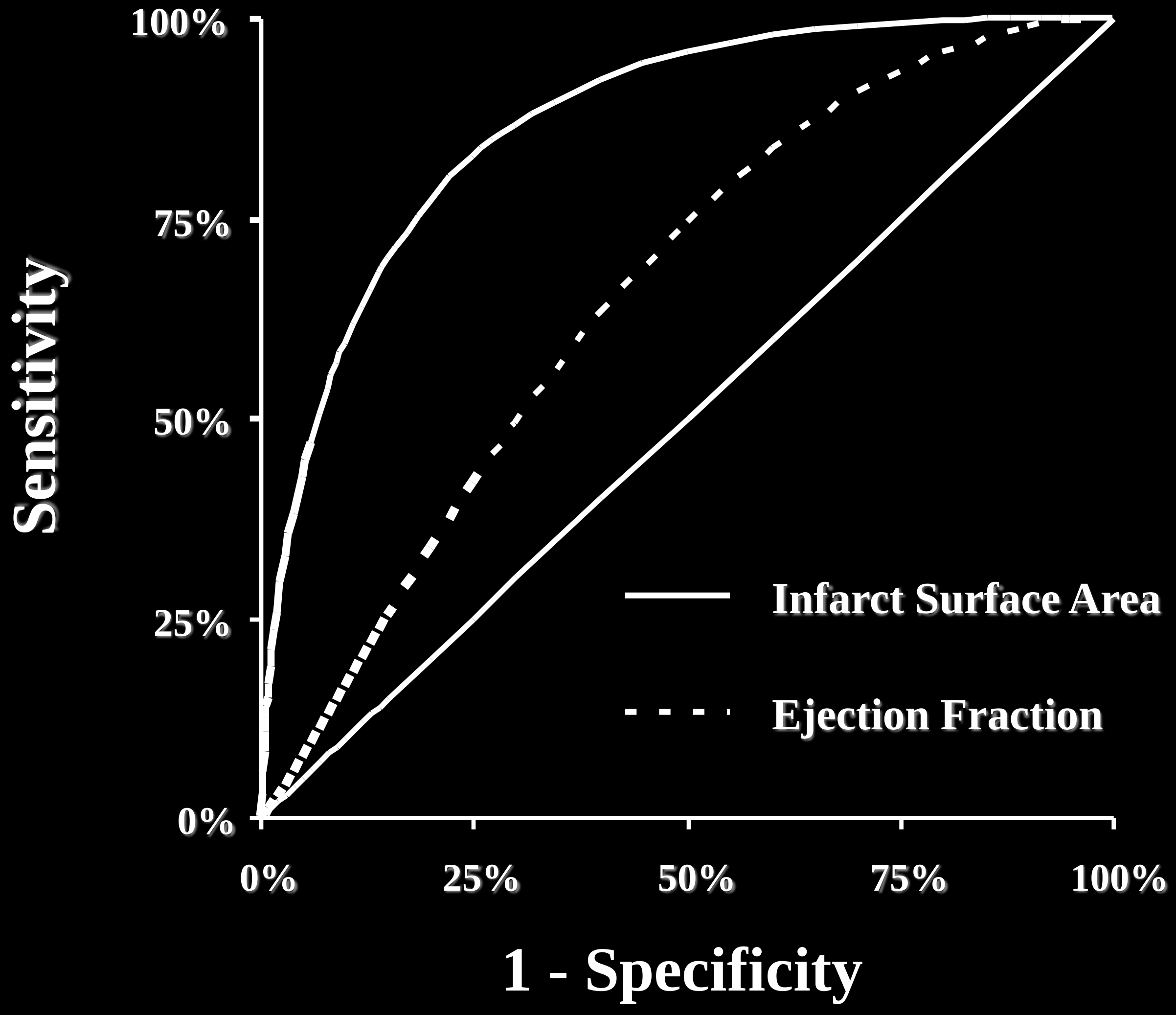
- 48 pts with CAD undergoing EPS
  - 21 not inducible EF 35 ± 3 %
  - 18 MVT EF 28 ± 2 %
  - 9 PVT/VF EF 34 ± 6 %
- MRI results

21 NI:	Inf mass 14 ± 3%	SA 93 ± 14 cm^2
18 MVT:	Inf mass 26 ± 3%	SA 172 ± 15 cm^2
	<0.009	<0.002

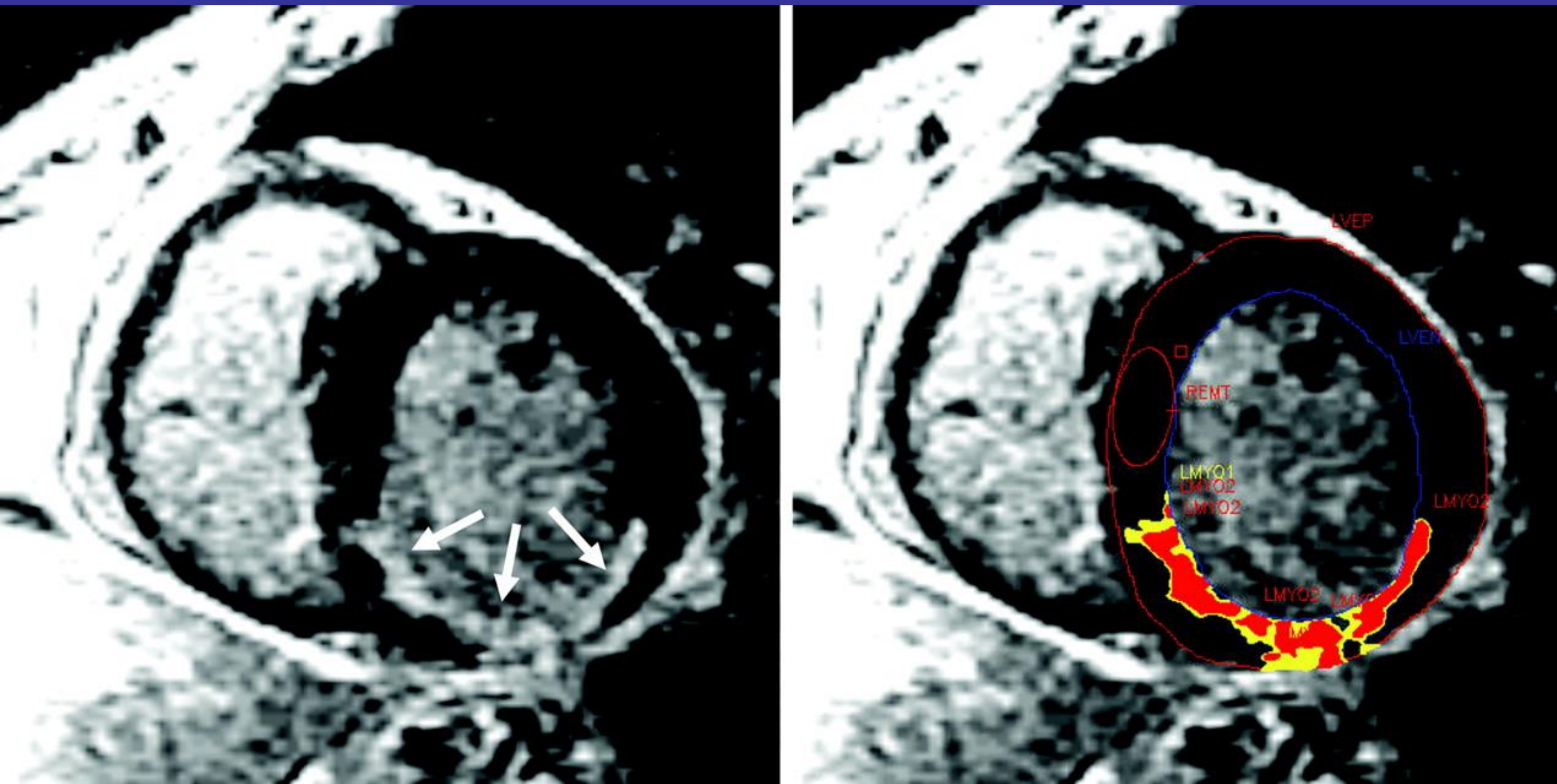
Bello, Goldberger JACC 2005


Not inducible
Inducible VT
Infarct SA
R2=0.22
p<0.001
Infarct surface area (mm2)
35000
30000
25000
20000
15000
10000
5000
0
0
10
20
30
40
50
60
70
Left ventricular ejection fraction (%)

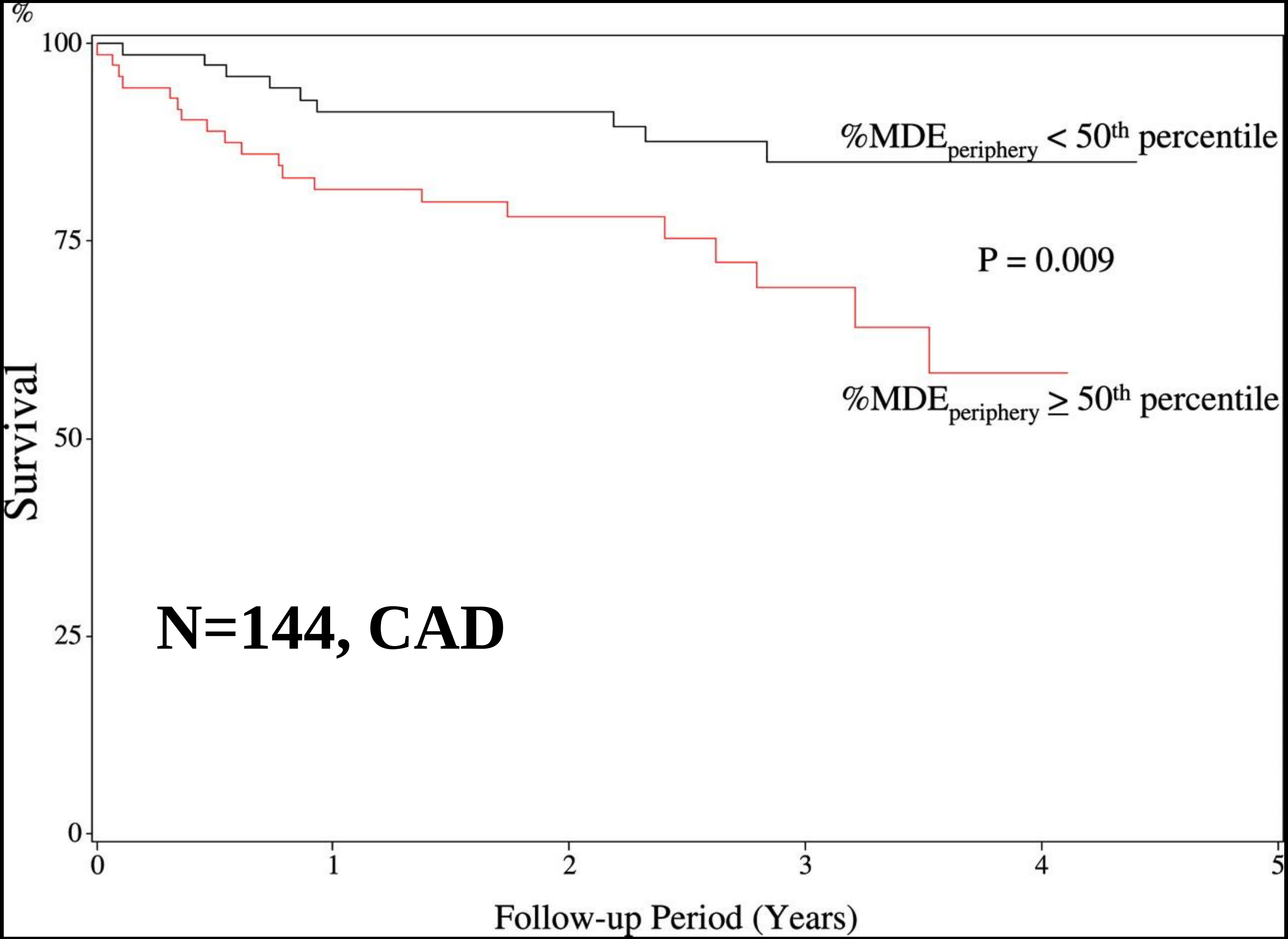
ROC Curves


100%
75%
50%
25%
0%
Sensitivity
0%
25%
50%
75%
100%
1 - Specificity
Infarct Surface Area
Ejection Fraction

64 y.o. male with IMI, LVEF 61%, 27% MDE $_{periph}$, died 11 mos post-MI

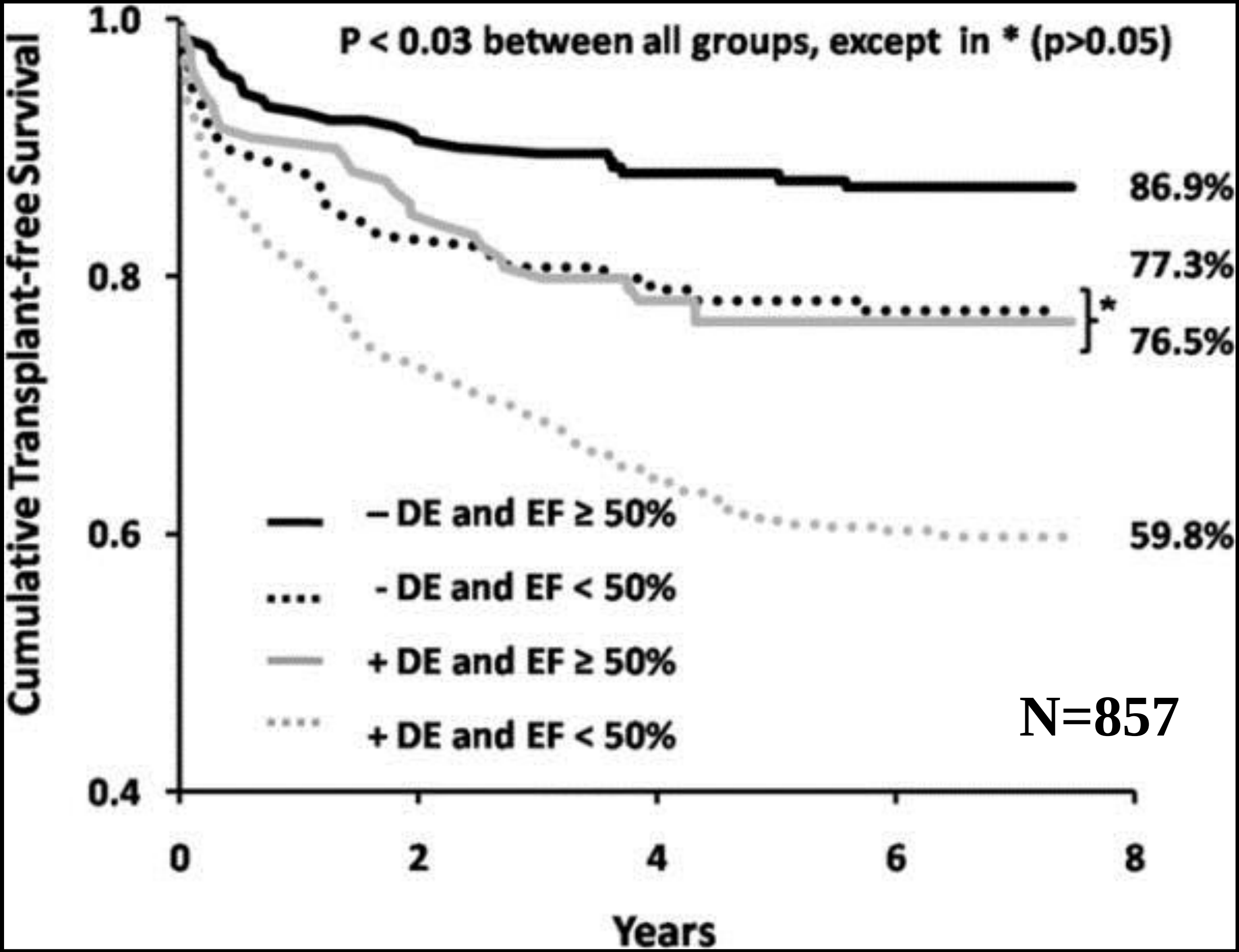


Yan et al   Circulation 2006



Yan et al   Circulation 2006

Prognostic Significance of DE MRI



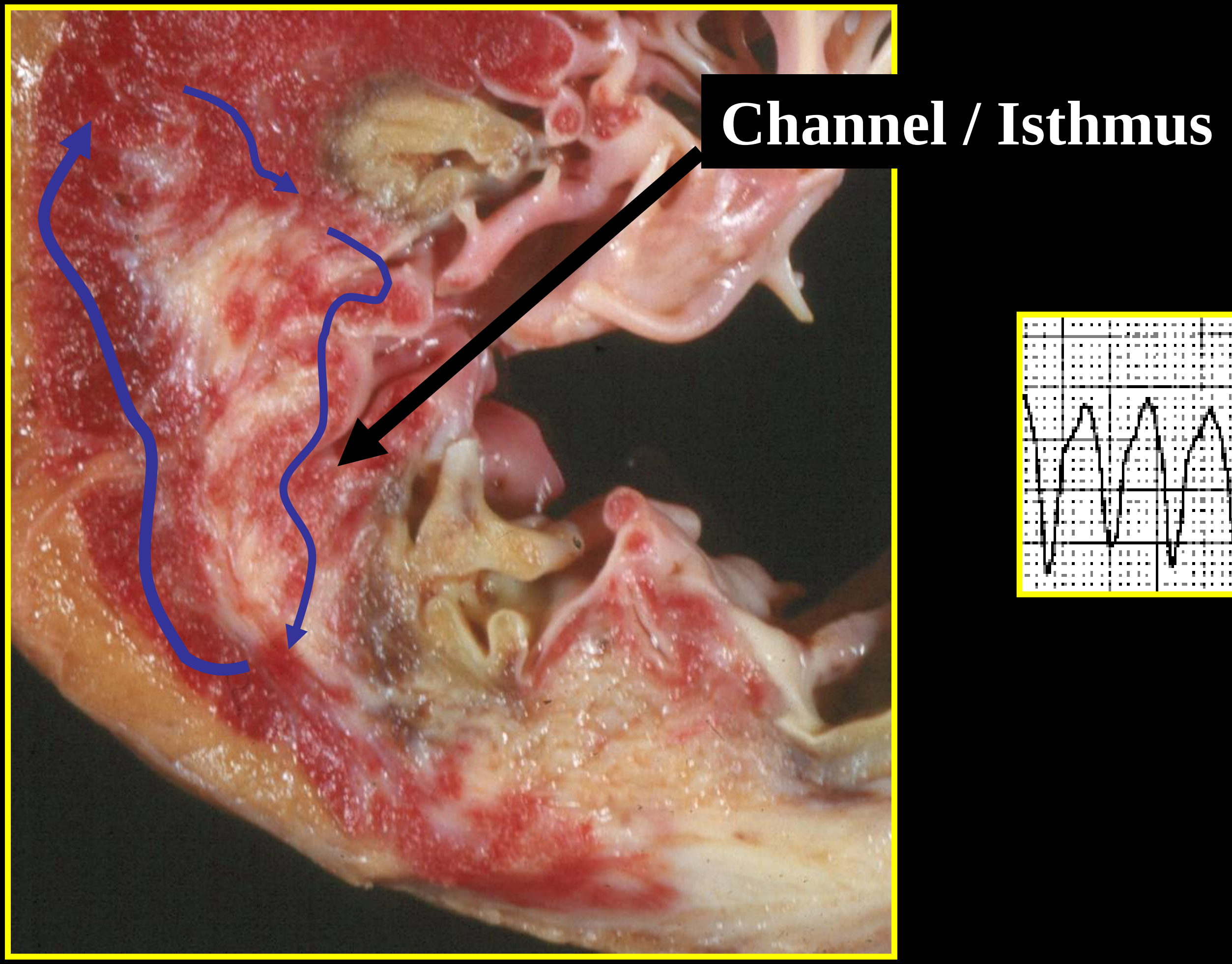
Cheong et al Circulation 2009

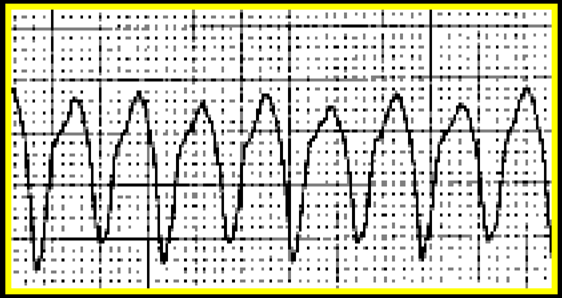
STUDY	Population	N	LVEF	Outcome	Finding
Bello 2005(13)	CAD referred for EPS	48	32%	Inducible VT	Infarct size better predictor than LVEF
Kwong 2006(4)	No known prior MI	195	54%	Death, MI, CV hosp, ICD rx	LGE strongest predictor of CV events
Yan 2006(9)	CAD with +LGE on CMR	144	44%	Mortality	Border zone independent predictor of mortality
Assomull 2006(14)	DCM	101	31%	Mortality + CV hosp	LGE only independent predictor
Schmidt 2007(7)	CAD, LVEF ≤ 35%, referred for ICD	47	27%	Inducible VT	Gray zone only predictive variable
Wu 2008(15)	CAD s/p STEMI	128	41%	Death, MI, CV hosp	Acute infarct size better predictor than LVEF
Yokata 2008(16)	CAD, EF≤50%, revasc ± ICD	86	26%	Death, CV hosp, revasc, VA	Infarct size was a predictor, not LVEF
Wu 2008(17)	DCM, LVEF≤35%	65	22%	Death, ICD rx, CV hosp	LGE only independent predictor
Cheong 2009(18)	Any pt w/ CMR, no infiltrative dz	857	39%	Transplant-free survival	Scar index and LVEF are independent predictors
Kelle 2009(19)	CAD	177	45%	Mortality + nonfatal MI	Spatial scar extent better predictor than LVEF
Roes 2009(8)	ICM, getting ICD	91	28%	Appropriate ICD rx	Gray zone only predictive variable
Kwon 2009(20)	CAD, LVEF < 45%	349	24%	Transplant-free survival	Infarct size was a predictor, not LVEF
Heidary 2010(21)	CAD, EF≤50%, revasc ± ICD	70	25%	Death, CV hosp, revasc, VA	Border zone and total scar are predictive, not LVEF
Bello 2011(22)	CAD	100	34%	Mortality	Infarct size and LVEF are independent predictors
Perez-David 2011(10)	CAD, ablation of monomorphic VT	36	32%	VT	More heterogeneous tissue channels in VT
Scott 2011(23)	CAD, getting ICD	64	30%	Appropriate ICD rx	Number of transmural segments most predictive
Iles 2011(24)	ICM and DCM getting ICD	103	26%	ICD rx	LGE predictive of ICD rx
Catalano 2012(25)	CAD	376	51%	Mortality+new onset HF	Infarct size and LVEF are independent predictors
Klem 2012(3)	ICM and DCM getting EPS±ICD	73	30%	SCD or ICD discharge	Infarct size is an independent predictor
Gao 2012(26)	ICM and DCM getting ICD	59	26%	SCD or ICD discharge	Infarct size is an independent predictor
Wu 2012(27)	+CAD(53%) and CAD, for EPS±ICD	137	26%	ICD rx/cardiac death	Gray zone predictive
Dawson(2)	Sustained or Nonsustained VT	373	60%	SCD, VT/VF, ICD rx	LGE only independent predictor

DETERMINE

- **CAD**
- **No current indication for ICD**
- **Infarct size > 10%**
- **Randomization to Optimal medical therapy or OMT + ICD**

Sustained Monomorphic VT: Reentry in an infarct scar





Courtesy of Bill Stevenson

Noninvasive Identification of Ventricular Tachycardia-Related Conducting Channels Using Contrast-Enhanced Magnetic Resonance Imaging in Patients With Chronic Myocardial Infarction

Comparison of Signal Intensity Scar Mapping and Endocardial Voltage Mapping

Esther Perez-David, MD,* Ángel Arenal, MD,* José L. Rubio-Guivernau, PHD,†
Roberto del Castillo, MD,* Leonardo Atea, MD,* Elena Arbelo, MD, PHD,‡
Eduardo Caballero, MD, PHD,‡ Verónica Celorrio, MD,* Tomas Datino, MD, PHD,*
Esteban Gonzalez-Torrecilla, MD, PHD,* Felipe Atienza, MD,* Maria J. Ledesma-Carbayo, PHD,†
Javier Bermejo, MD,* Alfonso Medina, MD, PHD,‡ Francisco Fernández-Avilés, MD, PHD*

Madrid and Las Palmas de Gran Canaria, Spain

JACC 2011

MR Signal Intensity Map

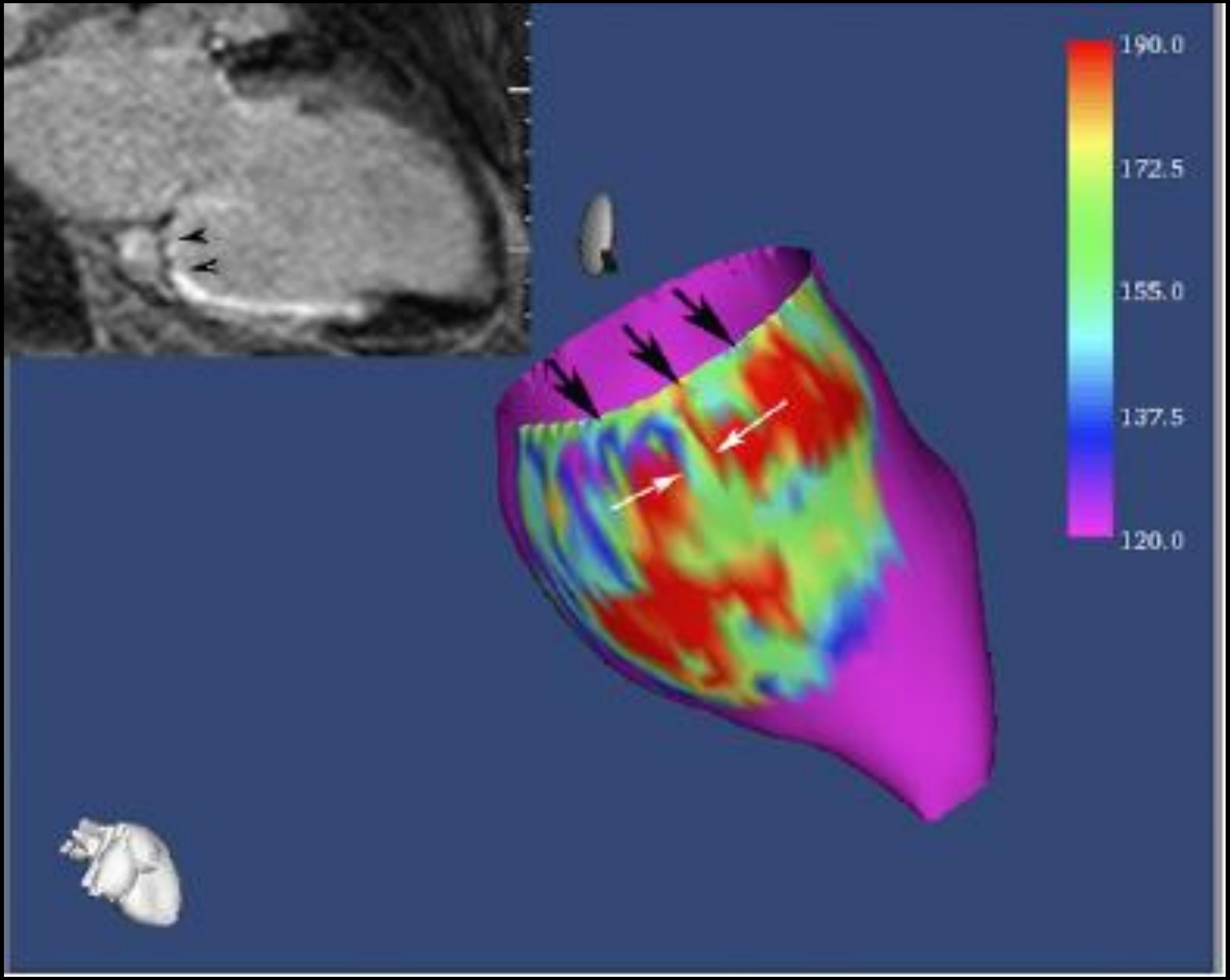


Table 3	Segment Location and Orientation of CC and SI Channels					
		Endocardial Voltage Mapping			Endocardial SI Mapping	
Patient #	Infarct Location	Channel n° and Segment Location	Orientation	VT-Related	Channel n° and Segment Location	Orientation
1	Ant	1: 3, 2, 1	Per		1: 3, 2, 1	Per
2	Inf	1: 6, 8	Para	+	1: 6, 8	Para
		2: 3, 5, 7	Para		2: 3, 5, 7	Para
3	Inf	1: 5, 6	Per	+	1: 5, 6	Per
4	Inf	1: 4, 6, 8	Para	+	1: 4, 6, 8	Para
5	Inf-Lat	1: 6, 8	Para		1: 6, 8	Para
		2: 6, 8, 5, 7	Per	+	2: 6, 8, 5, 7	Per
6	Ant					
7	Inf	1: 6	Para		1: 6	Para
		2: 6, 5	Para	+	2: 6, 5	Para
		3: 4, 6	Per		3: 4, 6	Per
8	Inf	1: 4, 6	Per		1: 4, 6	Per
9	Inf	1: 6, 8	Para	+	1: 6, 8	Para
10	Inf	1: 5, 6	Para	+	1: 5, 6	Para
11	Inf	1: 6	Para	+	1: 6	Para
12	Inf-Lat	1: 6	1: Para	+	1: 6	1: Para
		2: 5, 7, 6, 8	2: Per		2: 5, 7, 6, 8	2: Per
13	Inf	1: 6	Para	+	1: 6	Para
14	Ant	1–2	Para	+	1–2	Para
15	Inf	1: 6, 8	Para	+	1: 6, 8	Para
		2: 5, 6	Para		2: 5, 6	Para
		3: 4, 6	Per		3: 4, 6	Per
16	Ant	1: 2, 3	Para	+	1: 2, 3	Para
		2: 2, 3, 4	Per		2: 2, 3, 4	Per
17	Inf-Lat	1: 6, 8	Para	+	1: 6, 8	Para
		2: 4, 6	Per		2: 4, 6	Per
18	Inf	1: 6	Para	+	1: 6	Para

Journal of the American College of Cardiology

Published by Elsevier Inc.

Vol. 60, No. 5, 2012
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.03.029

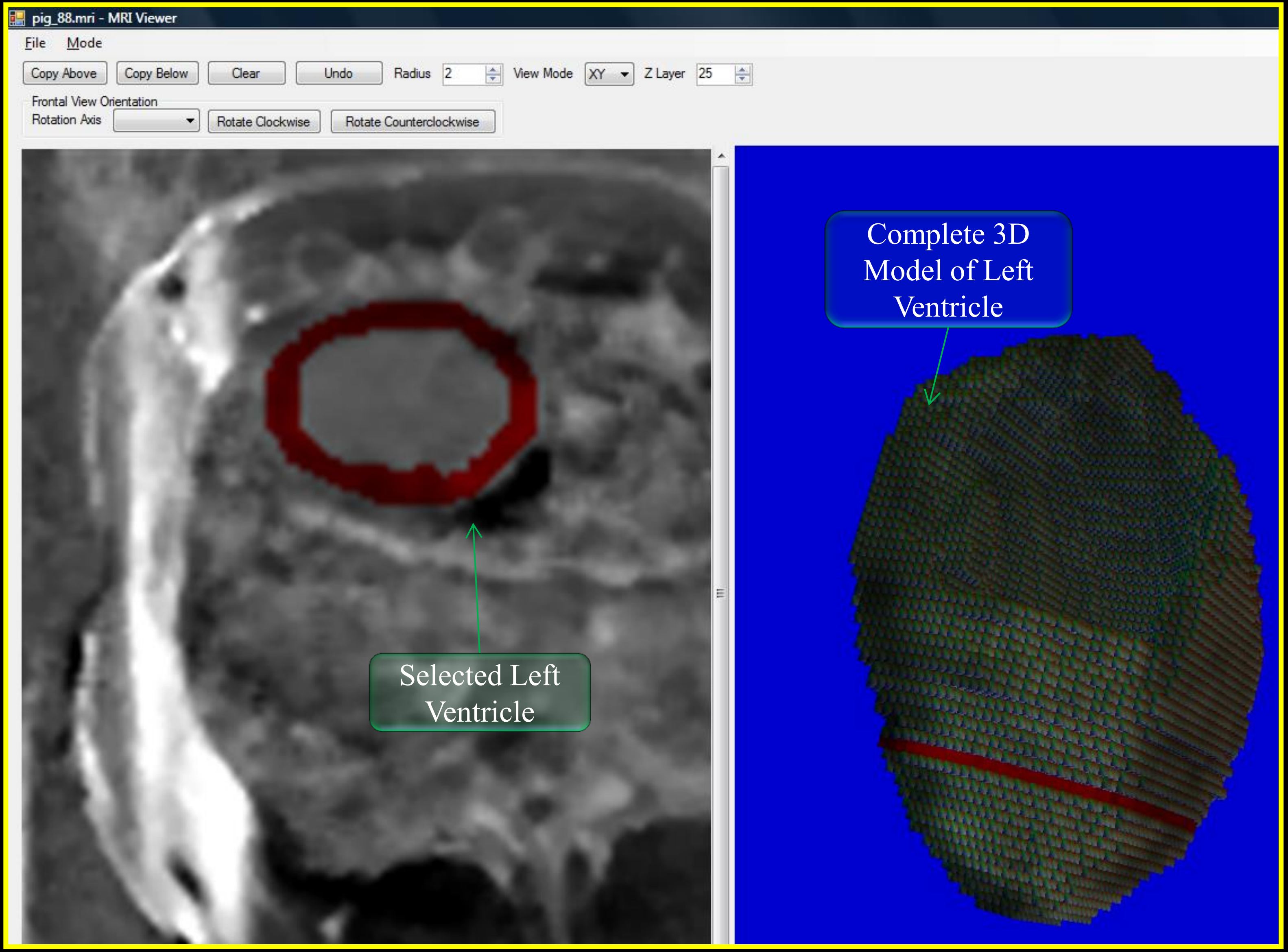
Virtual Electrophysiological Study in a 3-Dimensional Cardiac Magnetic Resonance Imaging Model of Porcine Myocardial Infarction

Jason Ng, PhD,* Jason T. Jacobson, MD,* Justin K. Ng, MS,* David Gordon, MD, PhD,*
Daniel C. Lee, MD,* James C. Carr, MD,† Jeffrey J. Goldberger, MD*

Chicago, Illinois

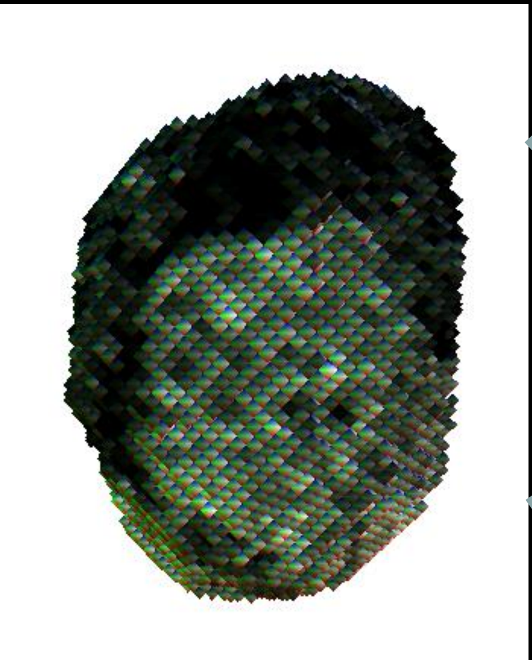
Virtual Electrophysiologic Testing Using Cardiac MRI

- 3D ceMRI to reconstruct LV and define scar
- At sites of normal LV - normal conduction
- At sites of scar - no conduction
- At border zone - slowed conduction
- Model propagation



pig_88.mri - MRI Viewer
File
Mode
Copy Above
Copy Below
Clear
Undo
Radius
2
View Mode
XY
Z Layer
25
Frontal View Orientation
Rotation Axis
Rotate Clockwise
Rotate Counterclockwise
Complete 3D Model of Left Ventricle
Selected Left Ventricle

Building the 3D Computer Model



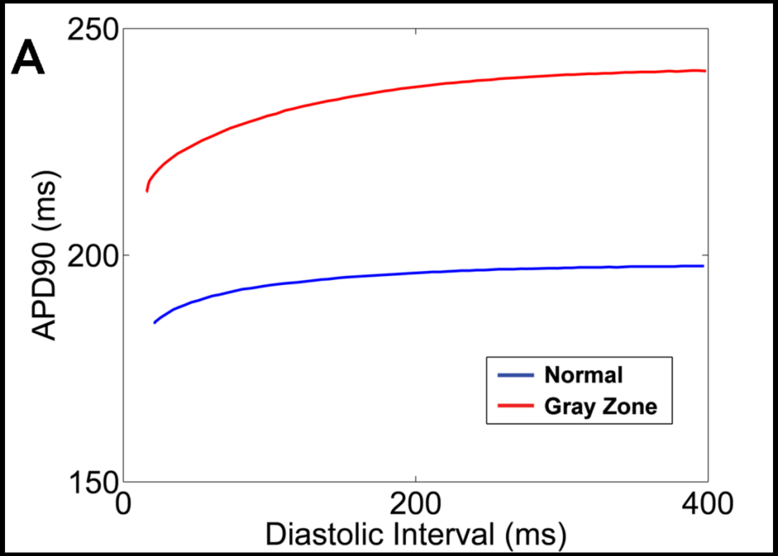
Normal → **Normal APD**
Normal conduction

Gray-zone → **Prolonged APD**
Slowed conduction

Hyper-enhanced → **No activation**
No conduction

Mathematical Model of the Action Potential

- Fenton-Karma 3 Variable Model
- Approximates Na^+, K^+, and Ca^{2+} dynamics
- Fast computation
- Restitution properties easily adjusted



Propagation equation

$$\frac{\partial V}{\partial t} = \frac{-(I_{ion} + I_{stim})}{C_m} + D\left(\frac{\partial^2 V}{\partial x^2} + \frac{\partial^2 V}{\partial y^2} + \frac{\partial^2 V}{\partial z^2}\right)$$

V = transmembrane potential

I_{ion} = Net ion current

I_{stim} = Stimulus current

C_m = Membrane capacitance

D = diffusion constant

Fenton-Karma 3-variable action potential model

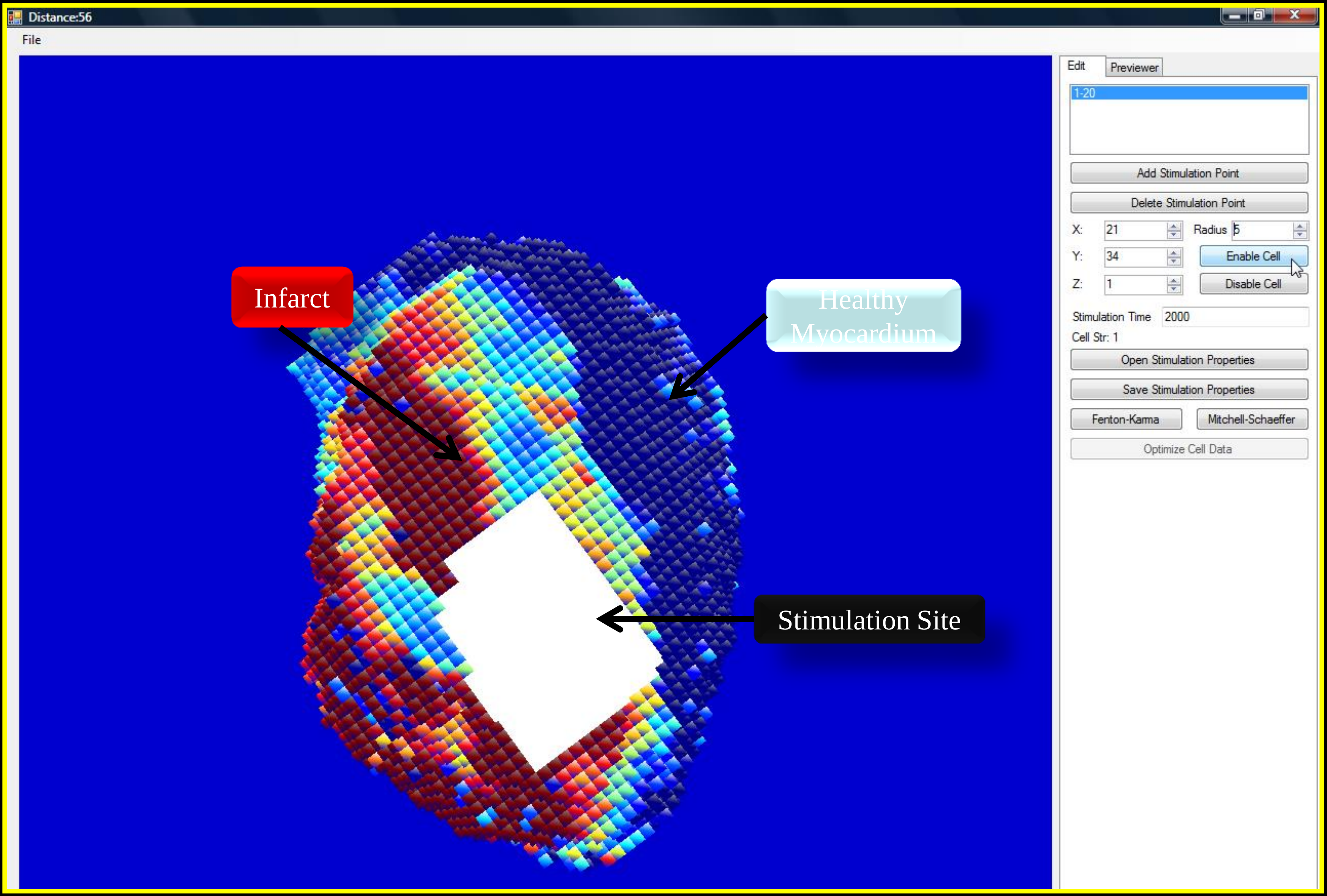
$$I_{ion} = J_{fi} + J_{so} + J_{si}$$

$$J_{\mathrm{fi}}(u;v) = -\frac{v}{\tau_d}\,\Theta(u-u_c)(1-u)(u-u_c),$$ (Fast inward current)

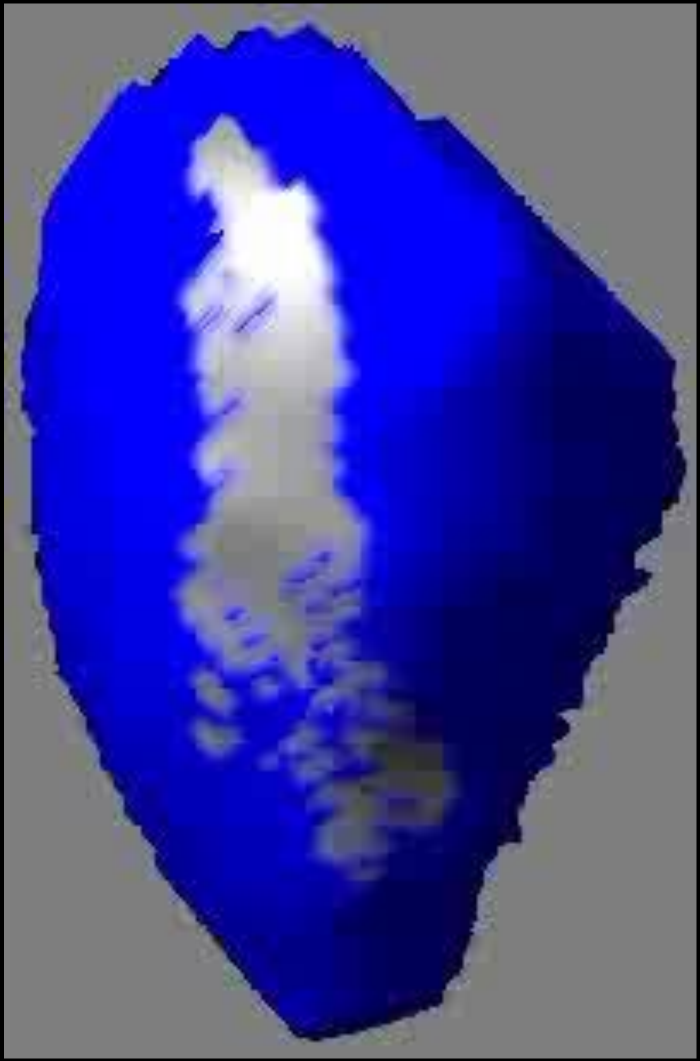
$$J_{\mathrm{so}}(u) = \frac{u}{\tau_o}\,\Theta(u_c-u) + \frac{1}{\tau_r}\,\Theta(u-u_c),$$ (Slow outward current)

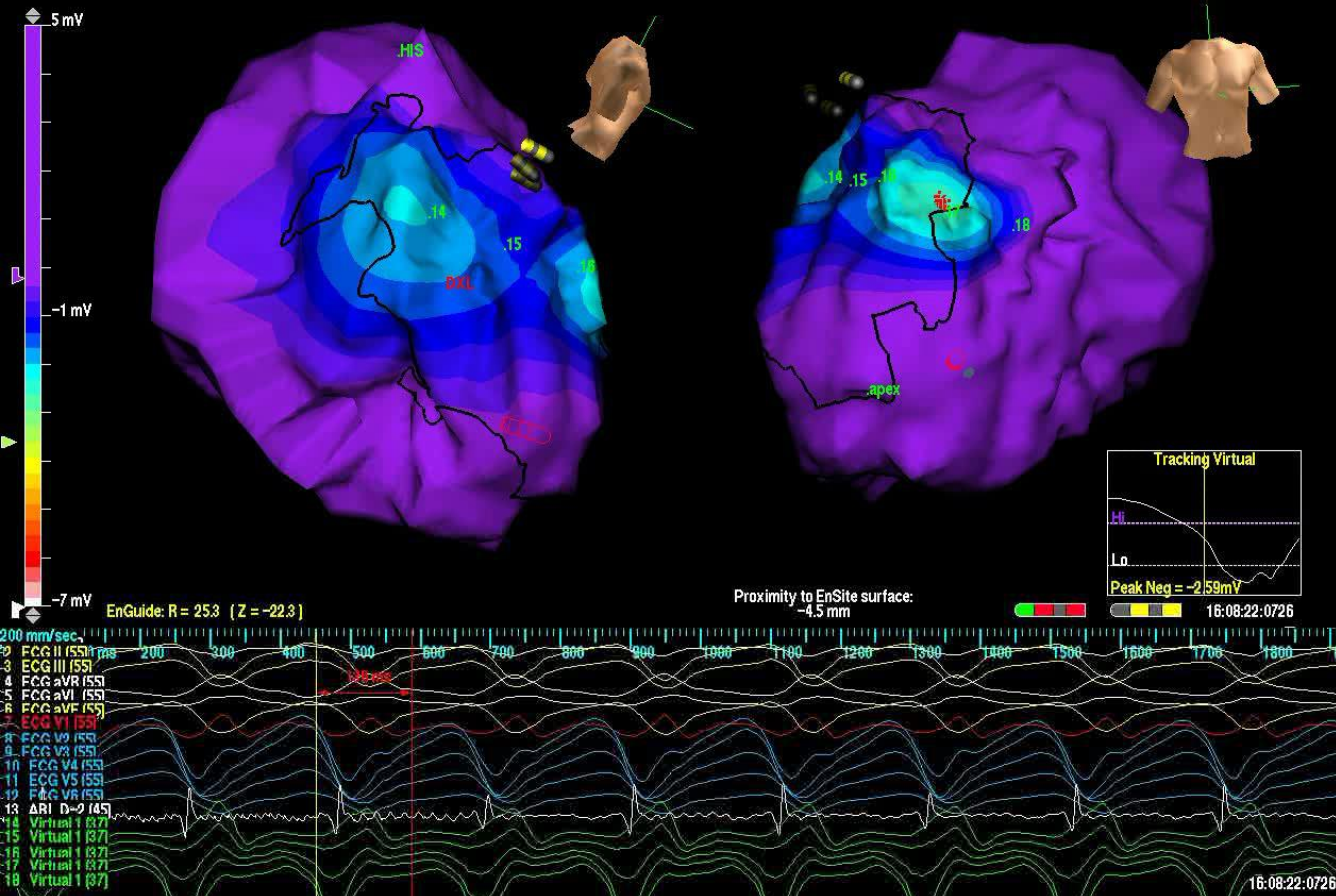
$$J_{\mathrm{si}}(u;w) = -\frac{w}{2\tau_{\mathrm{si}}}\,(1+\tanh[k(u-u_c^{\mathrm{si}})]).$$ (Slow inward current)

Partial differential equations solved by Euler forward method

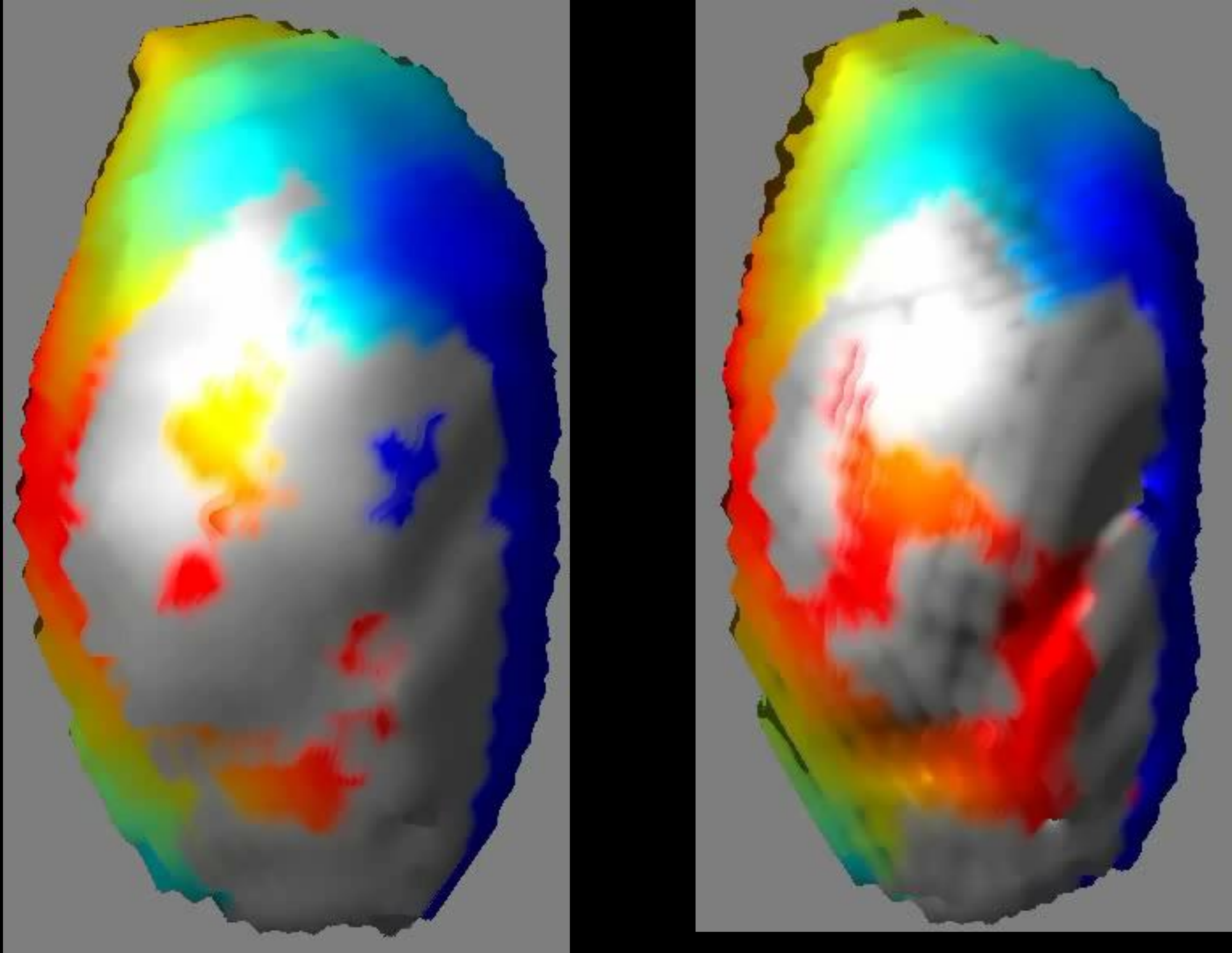

Distance:56
File
Edit
Previewer
1-20
Add Stimulation Point
Delete Stimulation Point
X: 21
Radius 5
Y: 34
Enable Cell
Z: 1
Disable Cell
Stimulation Time 2000
Cell Str: 1
Open Stimulation Properties
Save Stimulation Properties
Fenton-Karma
Mitchell-Schaeffer
Optimize Cell Data
Infarct
Healthy Myocardium
Stimulation Site

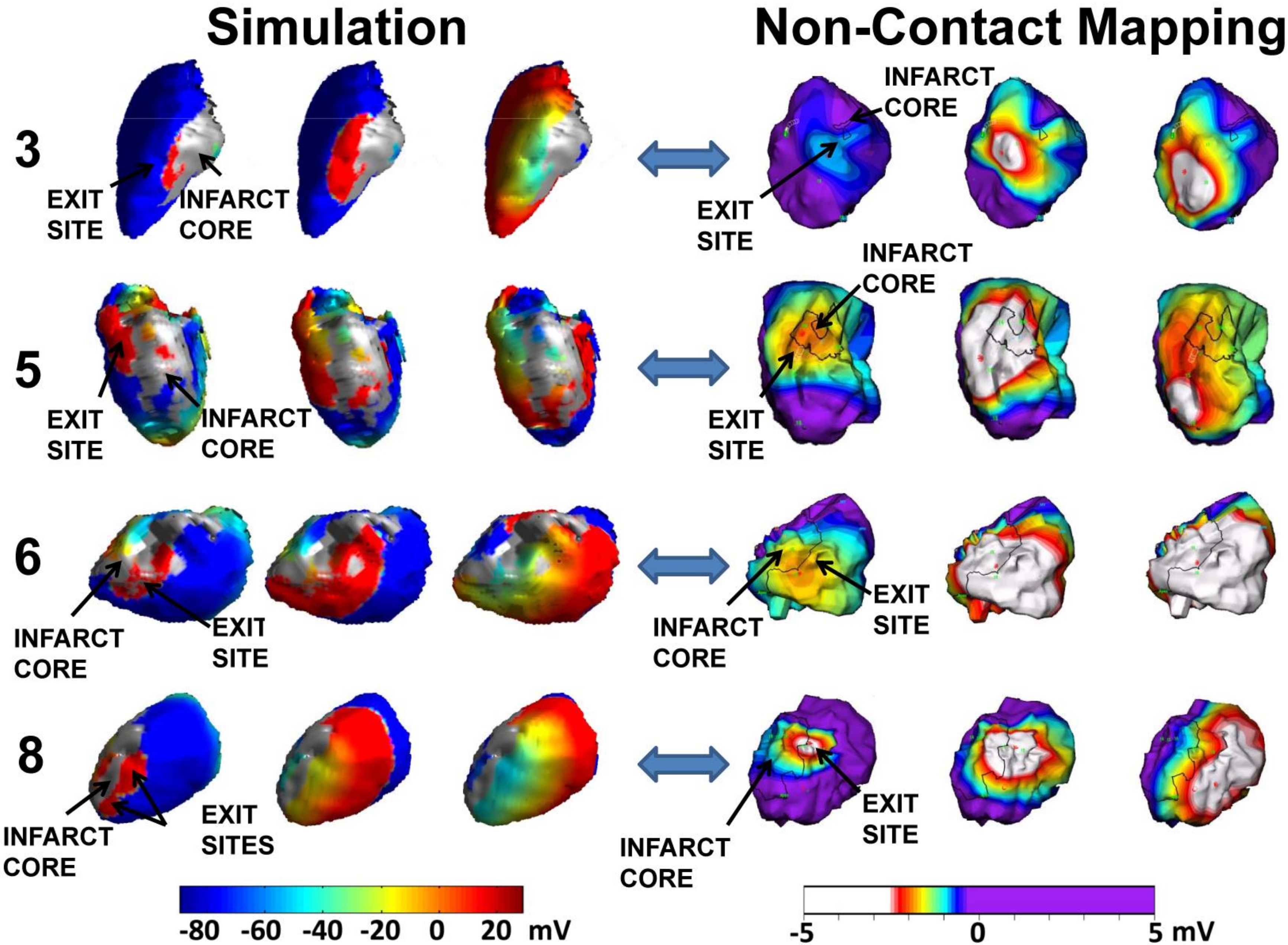
VT Induction Example



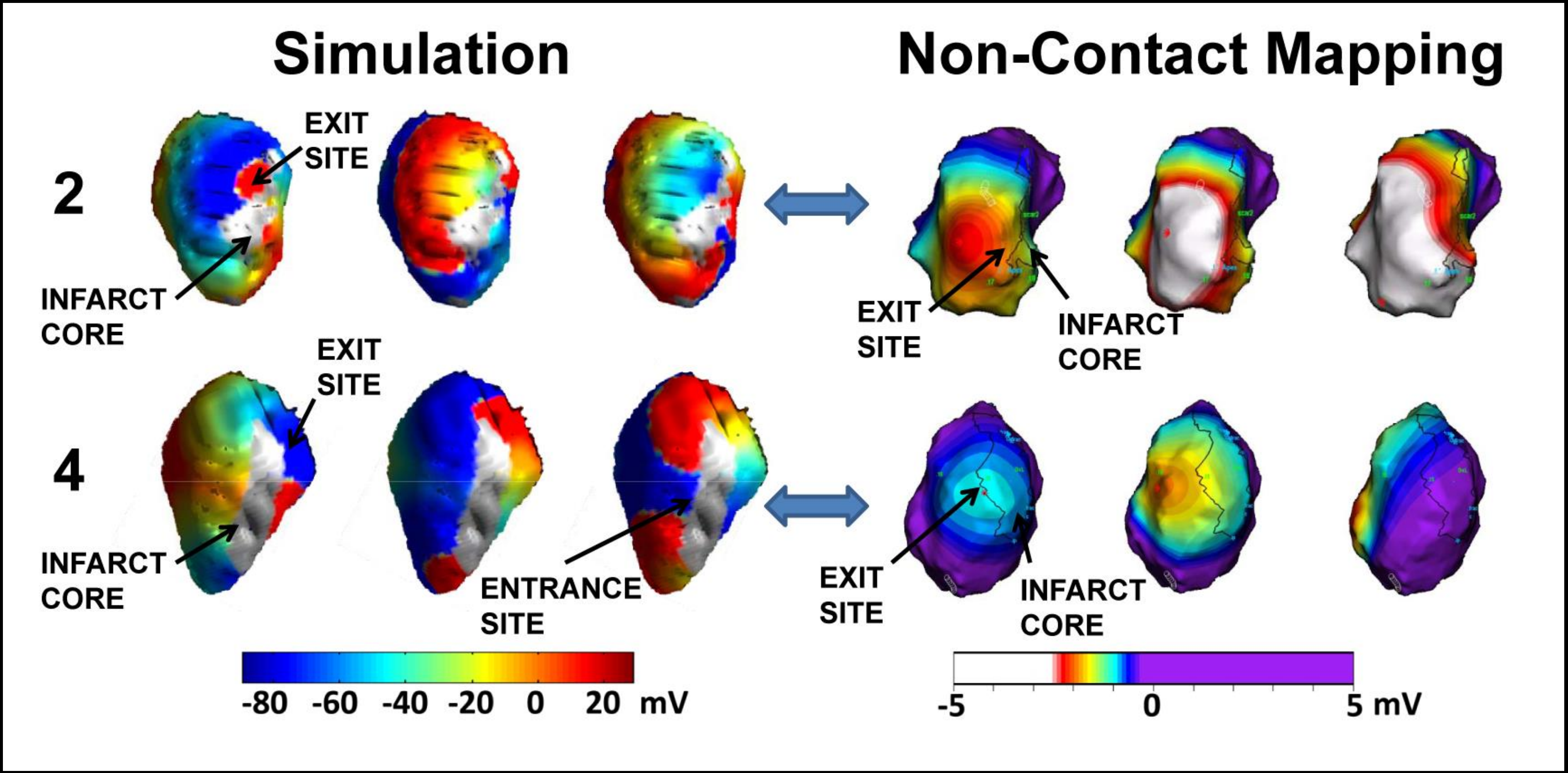


5 mV
-1 mV
-7 mV
.HIS
.14
.15
.18
DXL
.apex
Tracking Virtual
Hi
Lo
Peak Neg = -2.59mV
EnGuide: R = 25.3 (Z = -22.3)
Proximity to EnSite surface:
-4.5 mm
16:08:22:0726
200 mm/sec
2 ECG II (55)
3 ECG III (55)
4 ECG aVR (55)
5 ECG aVL (55)
6 ECG aVF (55)
7 ECG V1 (55)
8 ECG V2 (55)
9 ECG V3 (55)
10 ECG V4 (55)
11 ECG V5 (55)
12 ECG V6 (55)
13 ABL D-2 (45)
14 Virtual 1 (37)
15 Virtual 1 (37)
16 Virtual 1 (37)
17 Virtual 1 (37)
18 Virtual 1 (37)
16:08:22:0726





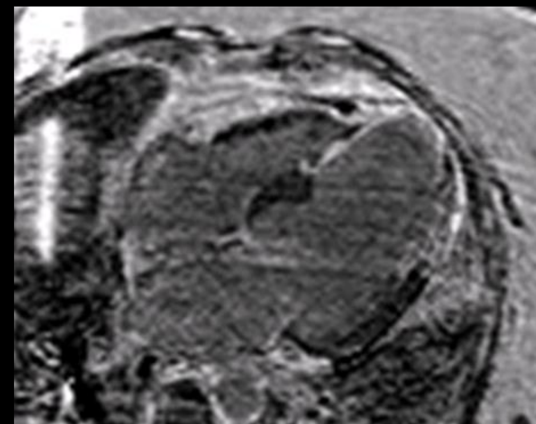
Simulation
Non-Contact Mapping
3
EXIT SITE
INFARCT CORE
INFARCT CORE
EXIT SITE
5
EXIT SITE
INFARCT CORE
INFARCT CORE
EXIT SITE
6
INFARCT CORE
EXIT SITE
INFARCT CORE
EXIT SITE
8
INFARCT CORE
EXIT SITES
INFARCT CORE
EXIT SITE
-80 -60 -40 -20 0 20 mV
-5 0 5 mV


Simulation
Non-Contact Mapping
2
4
EXIT SITE
INFARCT CORE
ENTRANCE SITE
-80 -60 -40 -20 0 20 mV
-5 0 5 mV

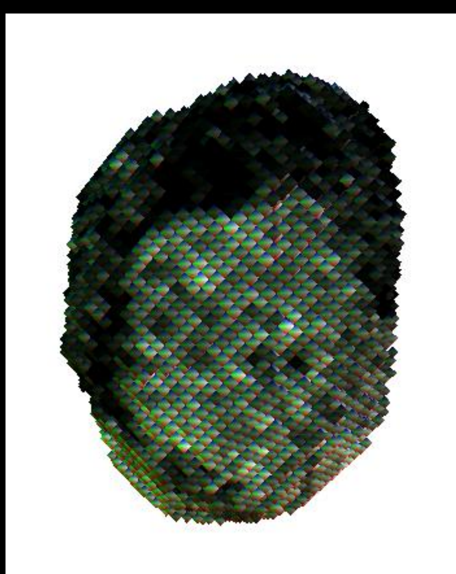
New Paradigm - Virtual Electrophysiologic Study (VEPS)

SCAN

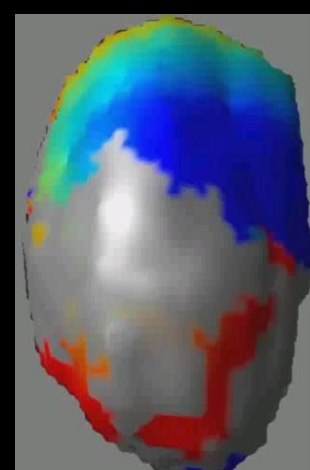
DE-MRI IMAGES



3D LV MODEL



VT INDUCTION SIMULATION



CLINICAL DECISION MAKING?

VEPS in Human MRIs

- 3D MRIs were collected from 16 patients with prior MI and 16 controls with no MI

	MI Patients (n=16)	**Controls (n=16)**	**P value**
Age (years)	64±10	55±10	***0.03***
Male	12 (75%)	10 (62.5%)	0.7
LVEF (%)	41.6±11.6	62.6±8.0	**<0.0001**
LV mass (g)	149.3±40.0	103.0±32.1	**0.0005**
LV Infarct %	13.2±8.8	N/A	

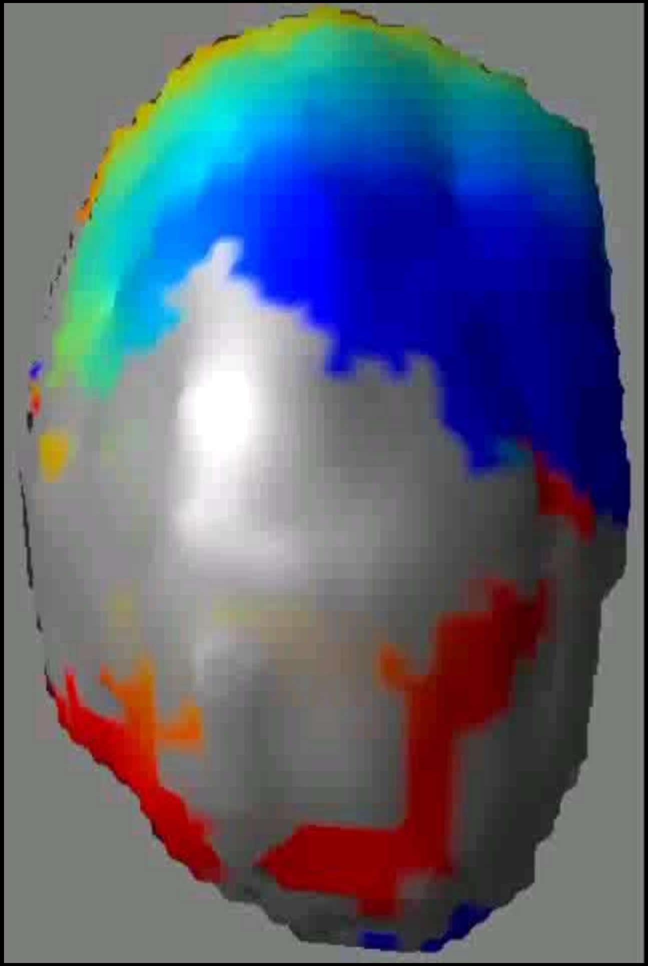
VEPS in Human MRIs

Results

- Six of 16 MI patients were inducible with VEPS
- None of the controls were inducible

	MI VEPS+ (n=6)	MI VEPS- (n=10)	P value
Age (years)	68±9	60±9	0.47
Male	4 (66%)	8 (80%)	0.6
LVEF (%)	34±9	46±11	***0.011***
LV mass (g)	149.8±39.6	149.0±34.5	0.45
LV Infarct %	20.0±8.9%	9.1±6.0%	***0.046***

Patient 1



MRI to assess arrhythmic risk post-MI

- MRI provides the best clinical method available to define infarct characterstics - ? substrate for VT
- Promising tool to improve upon LVEF as risk marker for arrhythmic SCD
- Enhanced imaging and data processing will make this more realistic