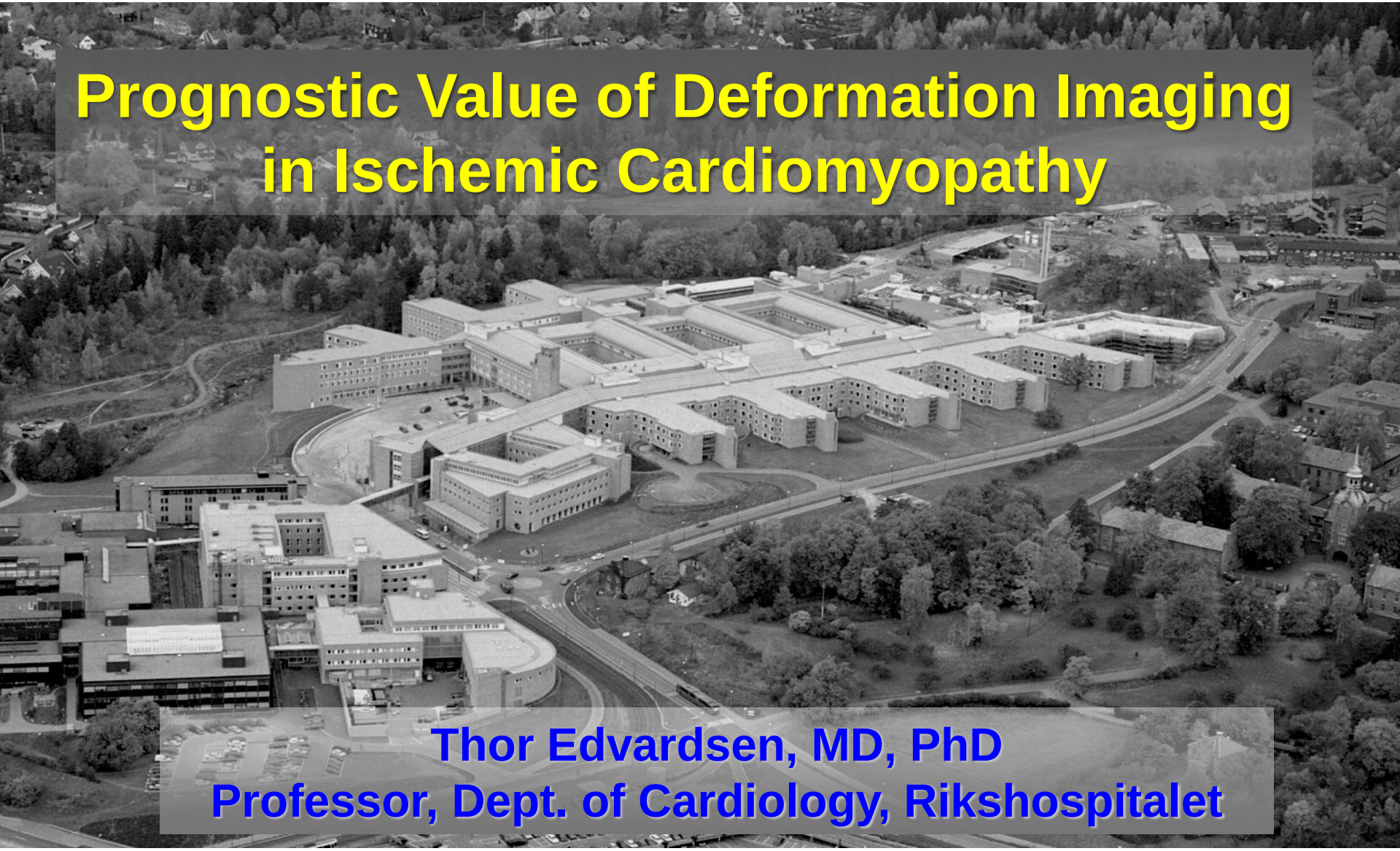
Prognostic Value of Deformation Imaging in Ischemic Cardiomyopathy

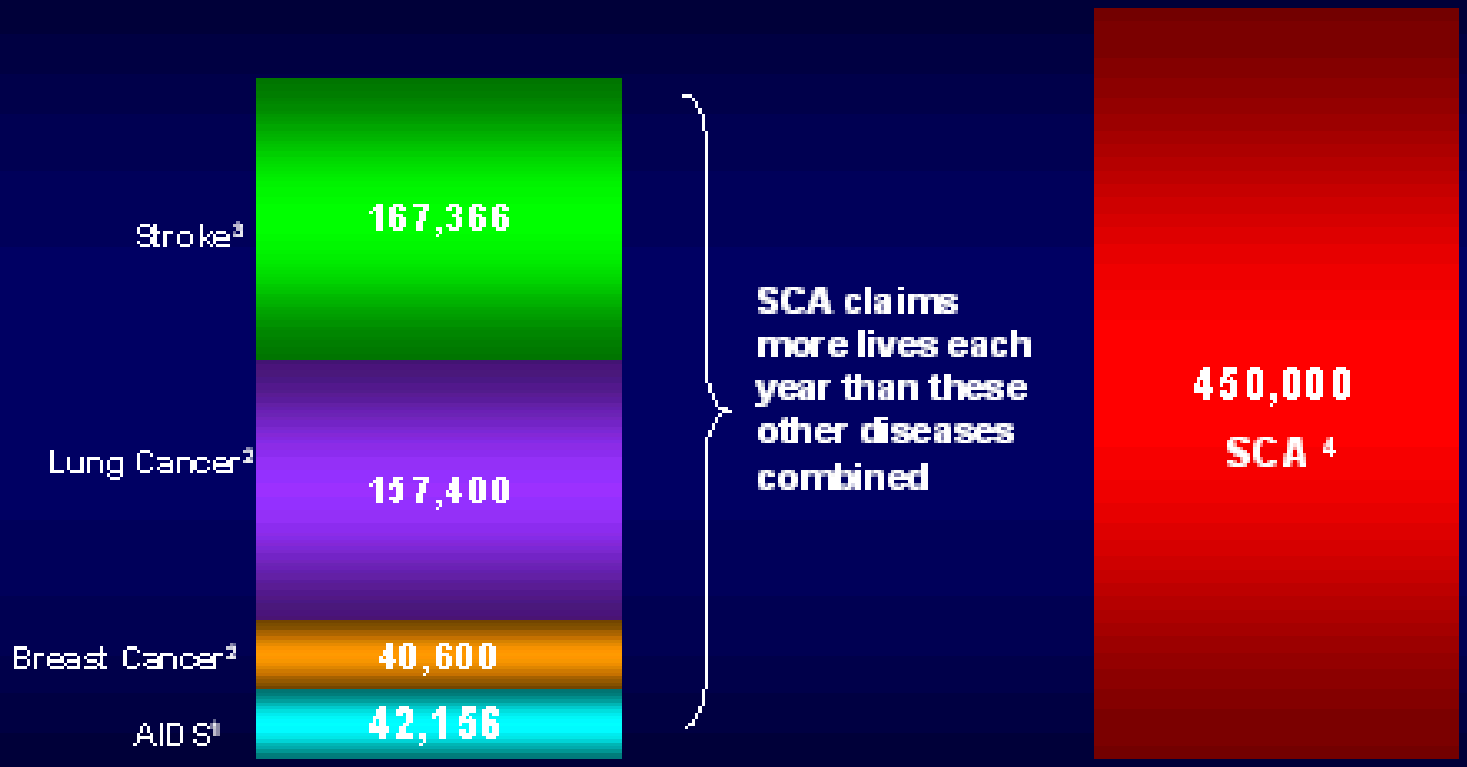


Thor Edvardsen, MD, PhD
Professor, Dept. of Cardiology, Rikshospitalet

Oslo University Hospital

Sudden cardiac arrest (SCA)

Magnitude of SCA in the US

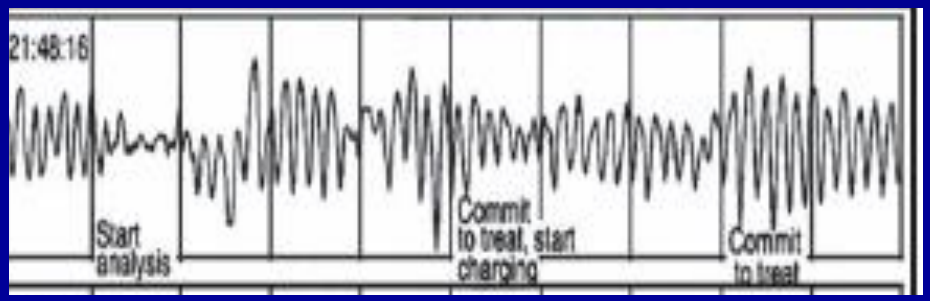


Norway:

1/1000 inhabitants/year - 5500/year

Questions

- Greatest challenge in cardiology?
- How to predict sudden cardiac death?



- < 40 years : 60-70% genetic cardiac diseases
- > 40 years: Coronary artery disease

Patients after mycoardial infarction

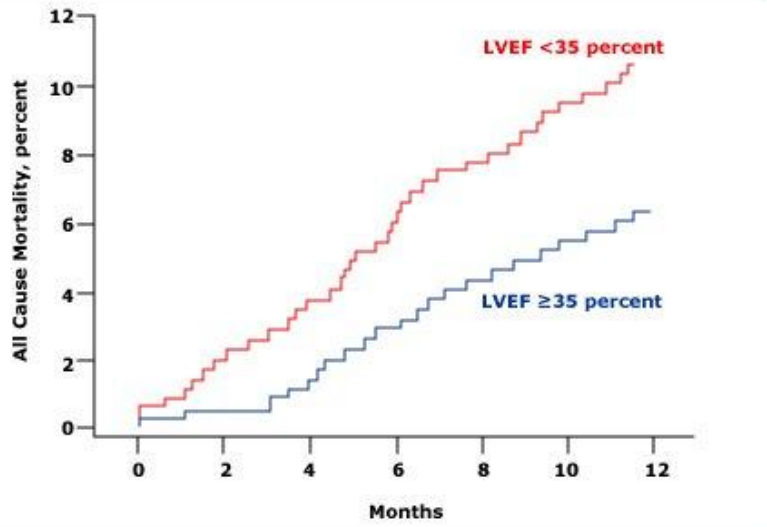
Acute MI

Scar development

Prognosis and EF

- Heart failure

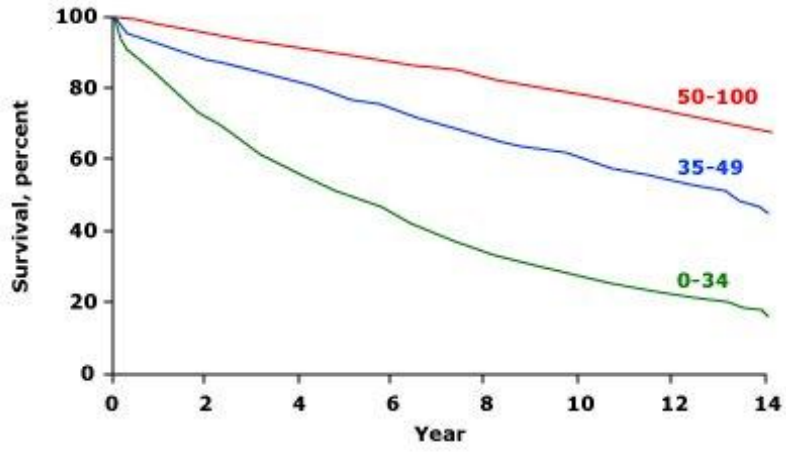
Mortality in heart failure is related to left ventricular function



Kaplan-Meier survival curves of 1172 patients in the SOLVD trials and registry show that a left ventricular ejection fraction (LVEF) <35 percent is associated with an increased all-cause mortality (risk ratio 1.8 compared to a LVEF ≥35 percent, p = 0.012). *Data from Quinones, MA, Greenberg, BH, Kopelen, HA, et al, for the SOLVD Investigators. J Am Coll Cardiol 2000; 35:1237.*

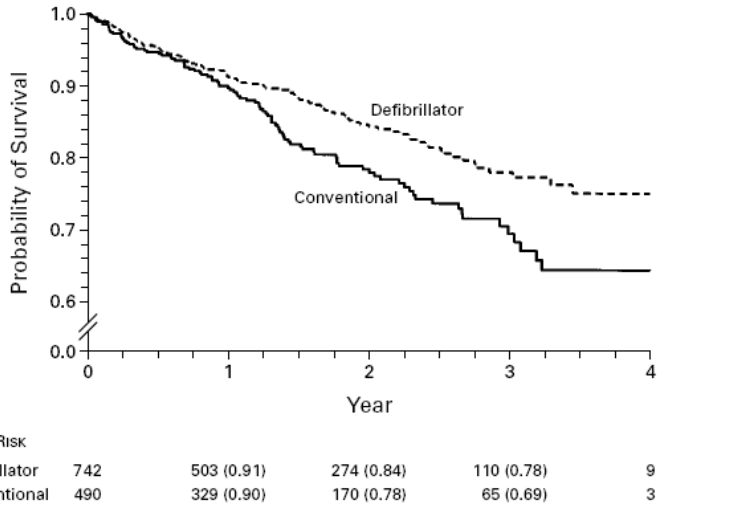
- CAD

Survival in coronary heart disease is related to left ventricular ejection fraction



Survival analysis during medical therapy of 23,467 patients enrolled in the CASS trial who had one, two, or three vessel disease shows that the overall 12 year survival is related to the left ventricular ejection fraction. *Data from Emond, M, Mock, MB, Davis, KB, et al, Circulation 1994; 90:2645.*

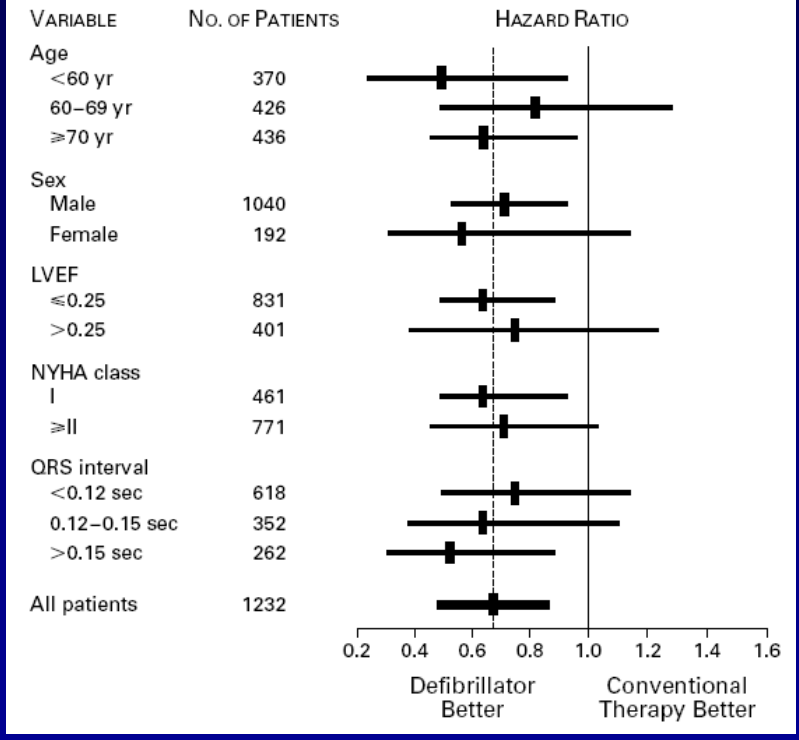
ICD and EF



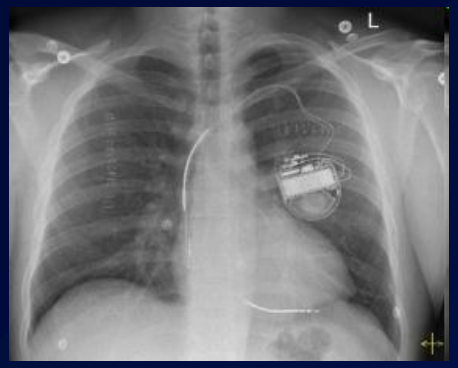
No. at Risk

Defibrillator	742	503 (0.91)	274 (0.84)	110 (0.78)	9
Conventional	490	329 (0.90)	170 (0.78)	65 (0.69)	3

Figure 2. Kaplan–Meier Estimates of the Probability of Survival in the Group Assigned to Receive an Implantable Defibrillator and the Group Assigned to Receive Conventional Medical Therapy.
The difference in survival between the two groups was significant (nominal P= 0.007, by the log-rank test).



Moss et al MADIT II
N Engl J Med. 2002



Post MI
Who needs ICD?

- Secondary prevention:
  - Survived heart arrest
  - VT with hemodynamic consequences

(AVID, CIDS, CASH)

- Primary prevention:
  - EF < 35%
  - EF < 40% and
    - Non sustained VT (Holter)
    - VT during an EP test

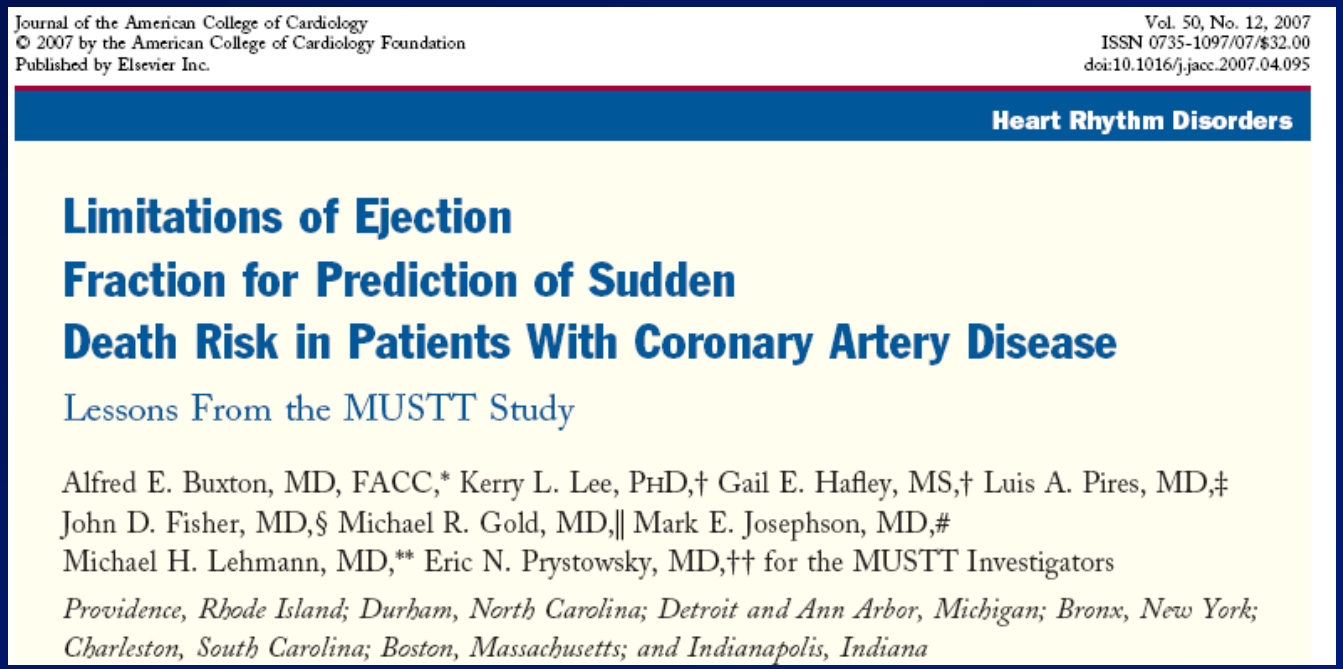
(MADIT2, SCDHeFT)

  - > 40 days after myocardial infarct

ACC/AHA/ESC 2006 Guidelines

Selection of post-MI patients for ICD

1. Many patients who not fulfill ICD indications experience arrhythmia
2. ICD never in use (1/15)



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Heart Rhythm Disorders

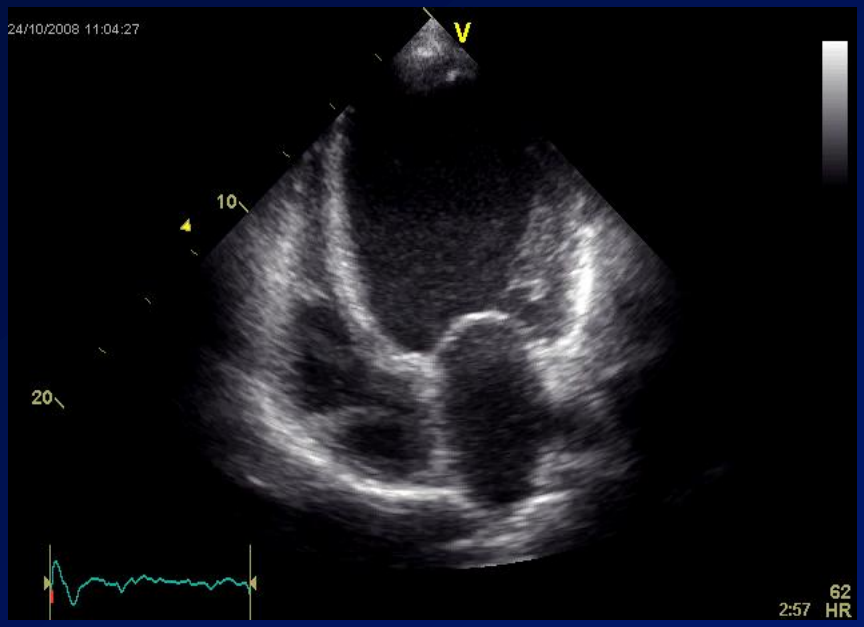
Limitations of Ejection Fraction for Prediction of Sudden Death Risk in Patients With Coronary Artery Disease

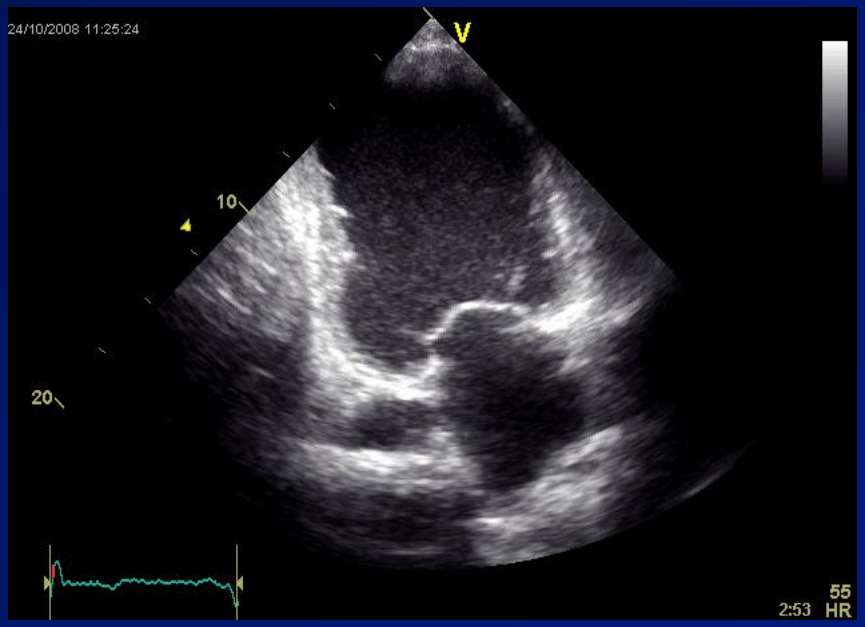
Lessons From the MUSTT Study

Alfred E. Buxton, MD, FACC,* Kerry L. Lee, PHD,† Gail E. Hafley, MS,† Luis A. Pires, MD,‡
John D. Fisher, MD,§ Michael R. Gold, MD,‖ Mark E. Josephson, MD,#
Michael H. Lehmann, MD,** Eric N. Prystowsky, MD,†† for the MUSTT Investigators

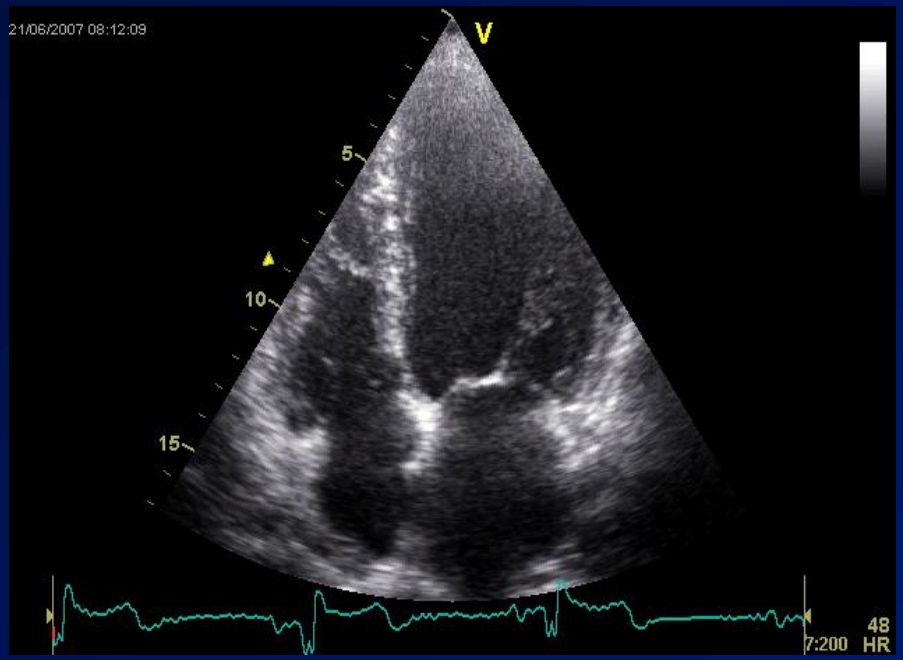
Providence, Rhode Island; Durham, North Carolina; Detroit and Ann Arbor, Michigan; Bronx, New York; Charleston, South Carolina; Boston, Massachusetts; and Indianapolis, Indiana

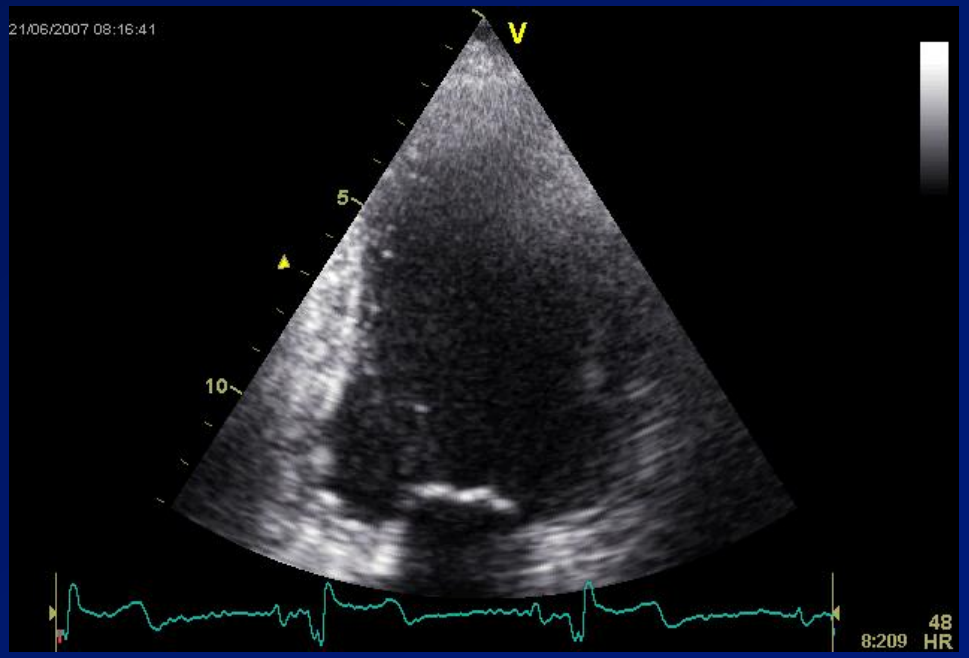
EF 20%, no arrhythmia



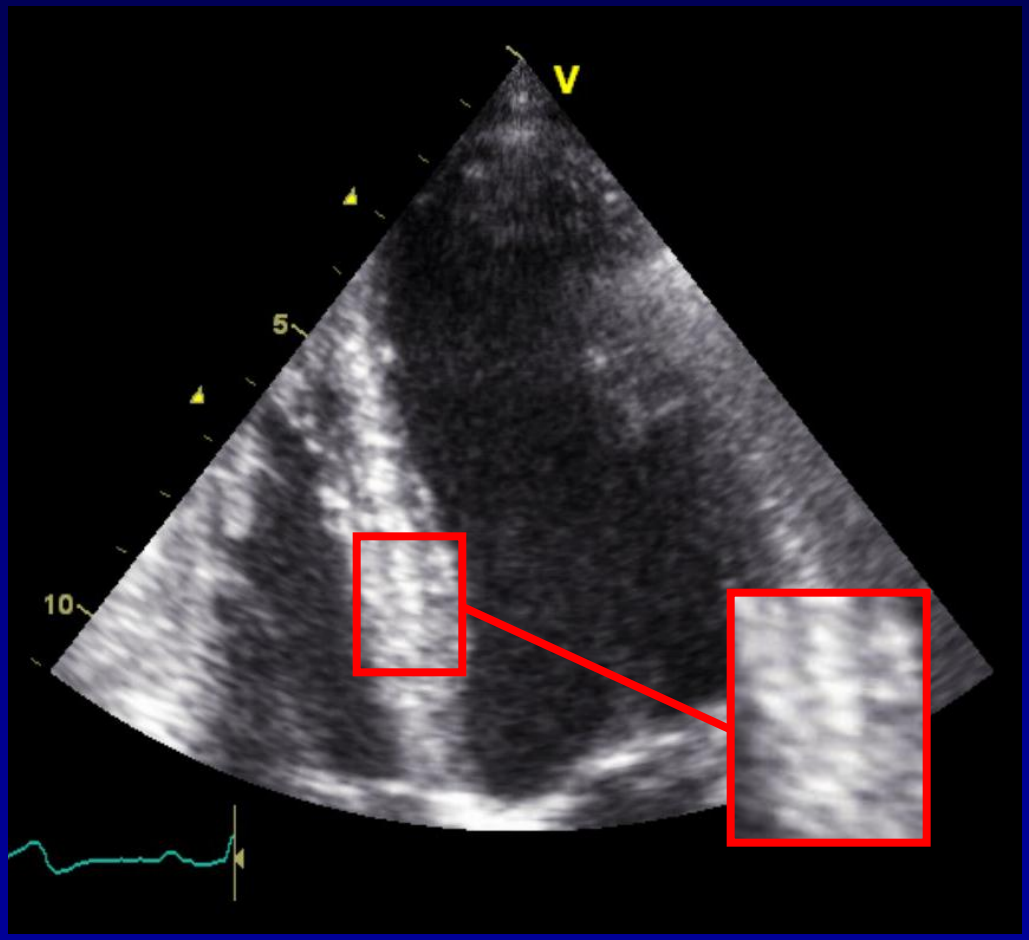


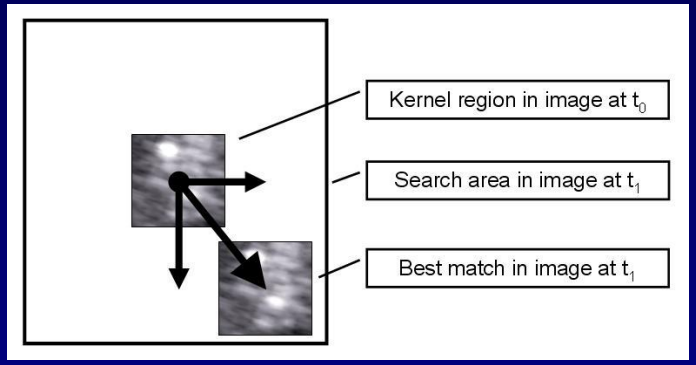
EF 50%, arrhythmia ICD





Speckle tracking





Noninvasive Myocardial Strain Measurement by Speckle Tracking Echocardiography

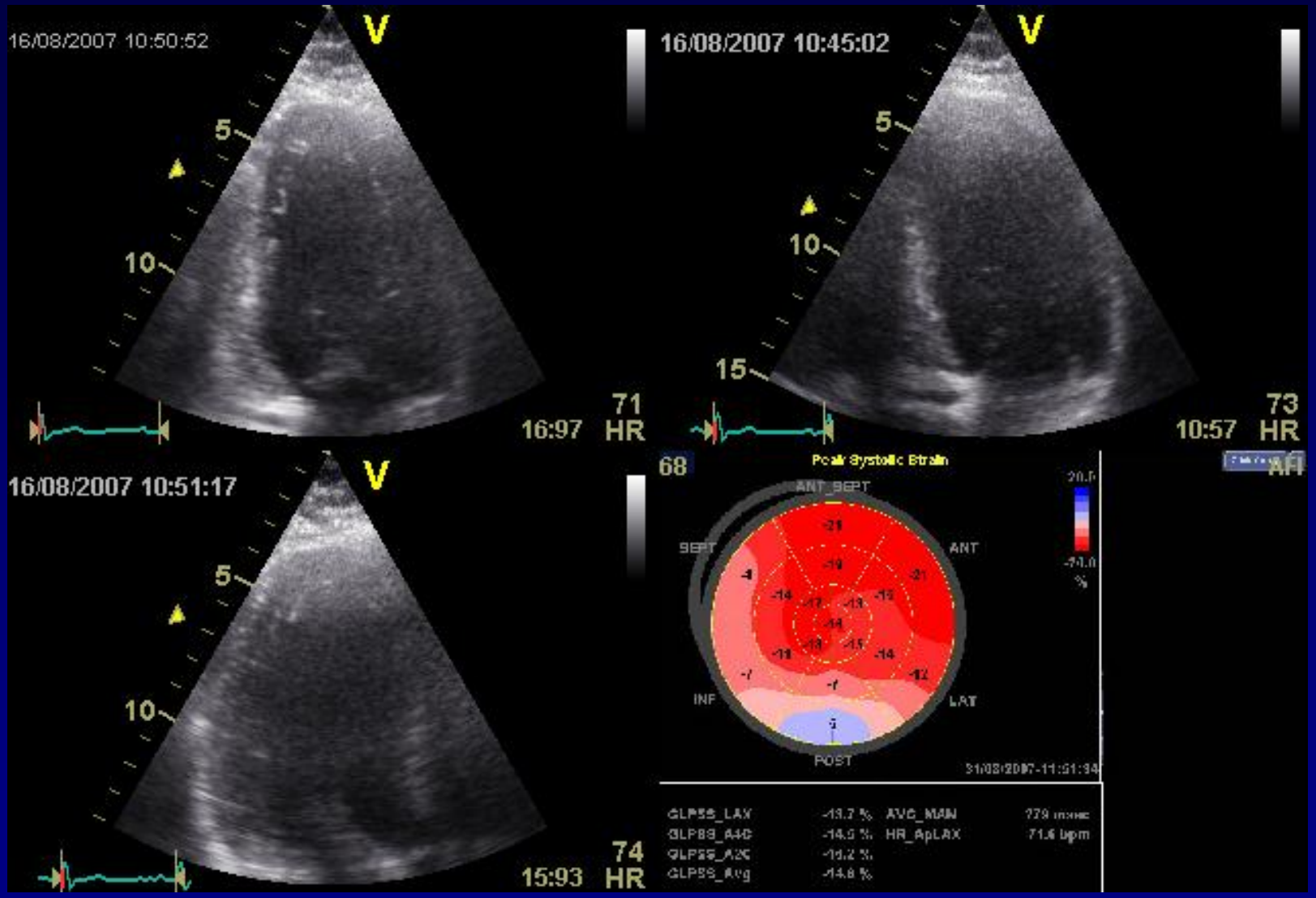
Validation Against Sonomicrometry and Tagged Magnetic Resonance Imaging

Brage H. Amundsen, MD,* Thomas Helle-Valle, MD,† Thor Edvardsen, PHD, MD,† Hans Torp, DRTECHN,* Jonas Crosby, MSC,* Erik Lyseggen, MD,† Asbjørn Støylen, MD, PHD,*‡ Halfdan Ihlen, MD, PHD,† João A. C. Lima, MD, FACC,§ Otto A. Smiseth, MD, PHD, FACC,† Stig A. Slørdahl, MD, PHD*‡

Trondheim and Oslo, Norway; and Baltimore, Maryland

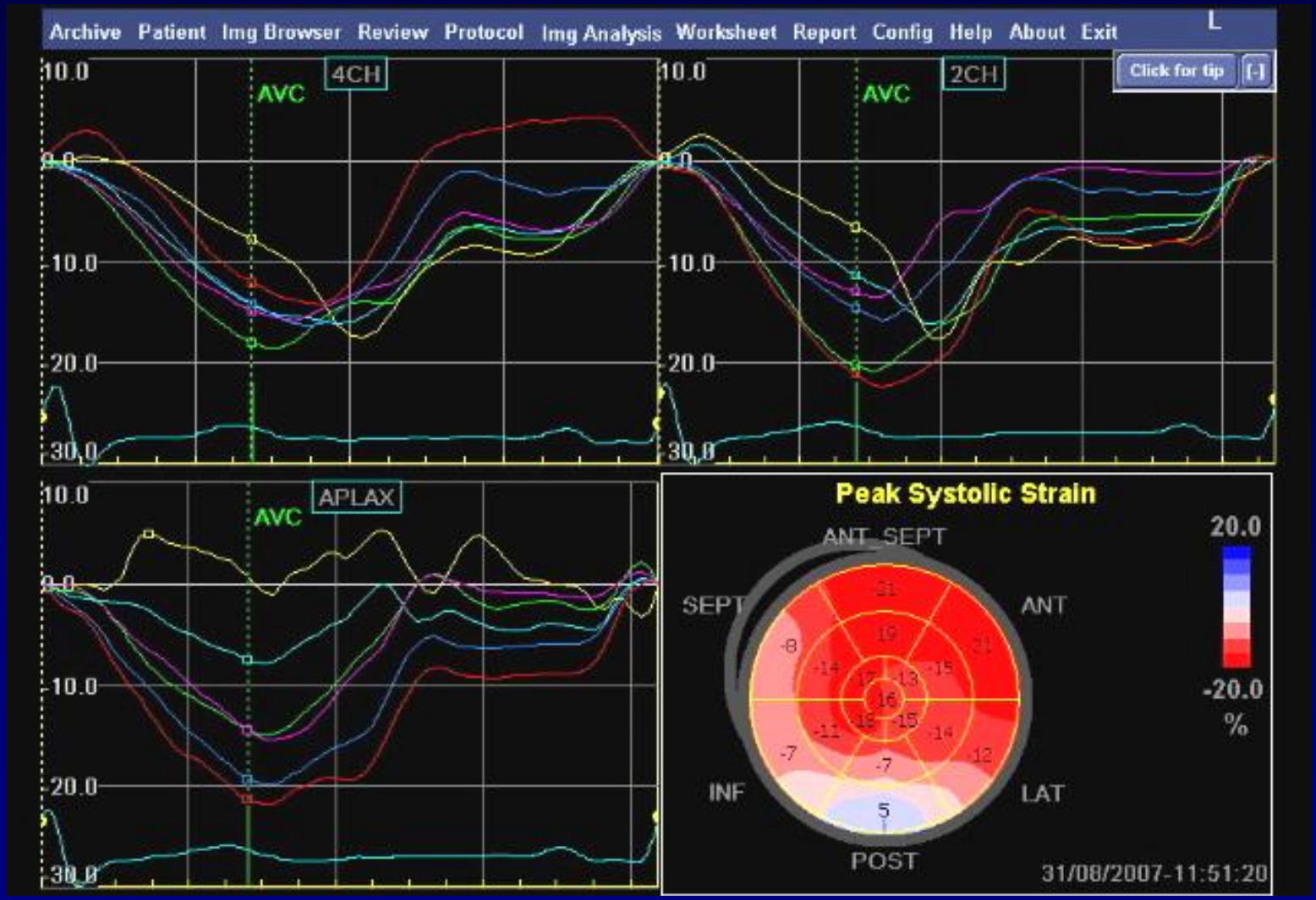
CONCLUSIONS Speckle tracking echocardiography provides accurate and angle-independent measurements of LV dimensions and strains and has potential to become a clinical bedside tool for quantifying myocardial strain. (J Am Coll Cardiol 2006;47:789–93)

Non ST elevation MI



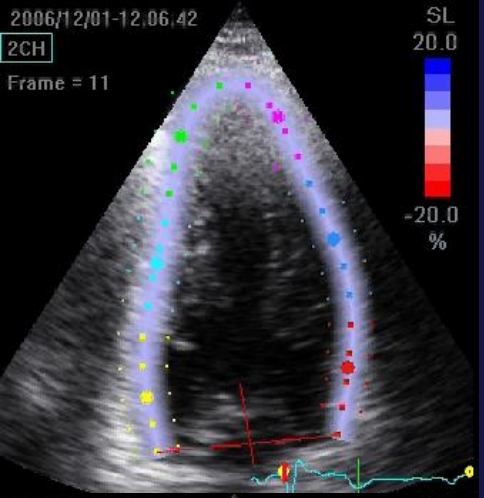
Courtesy of C Eek, MD

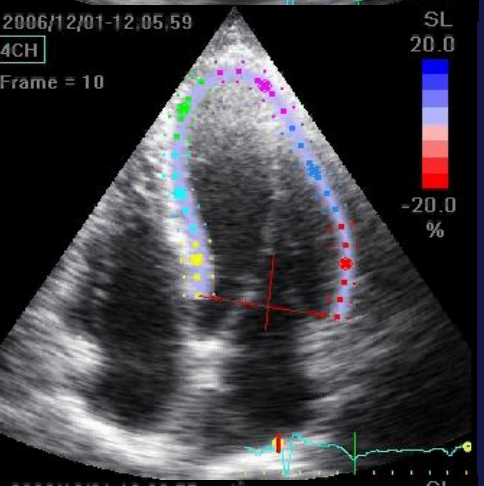
Non ST elevation MI

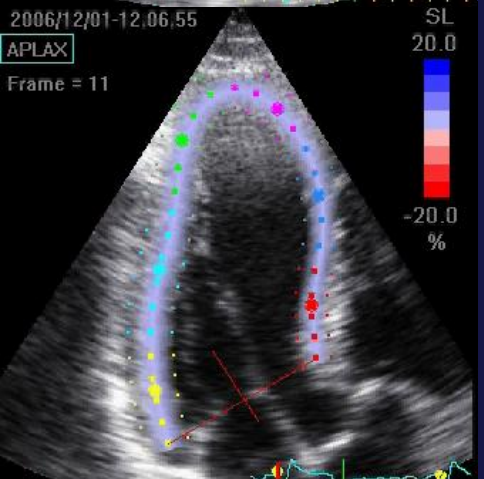


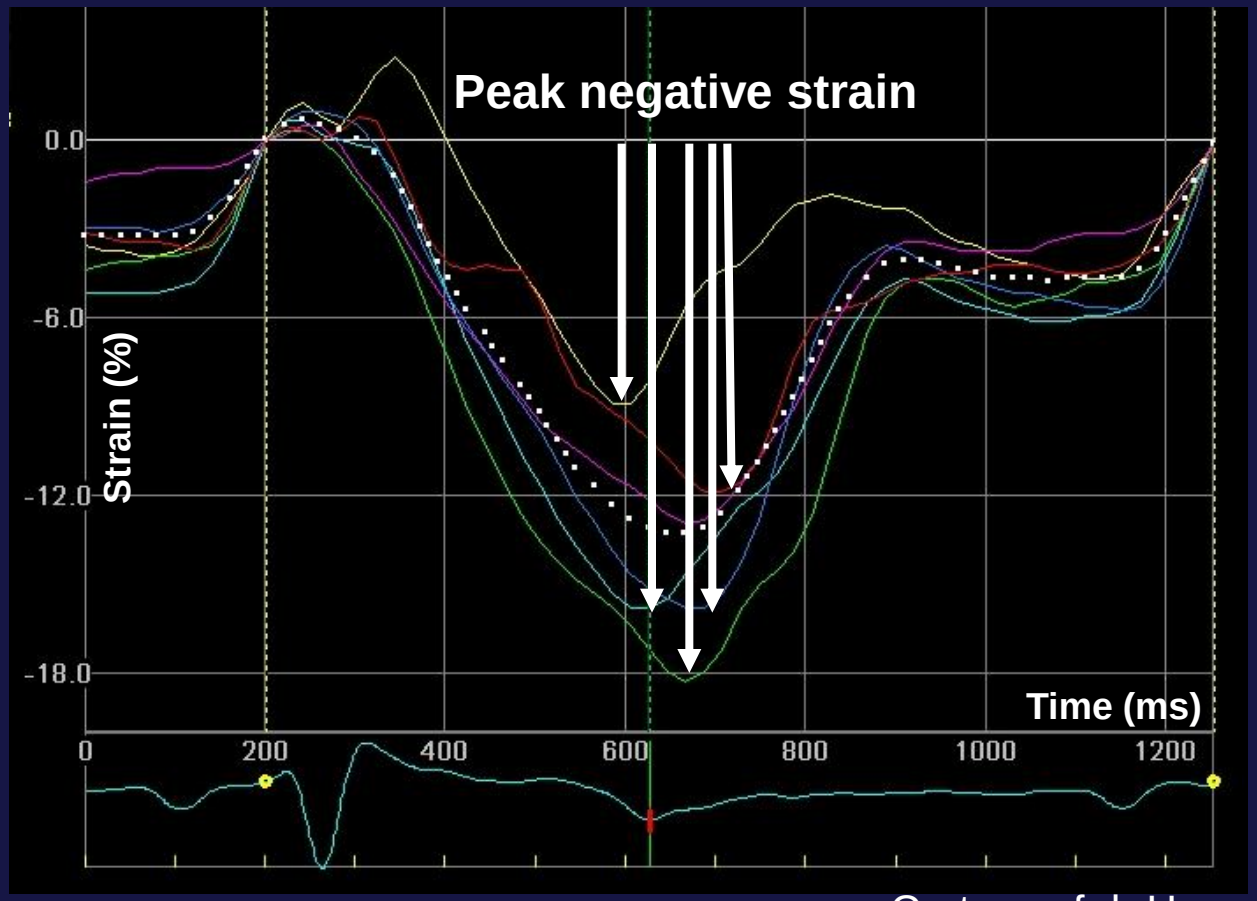
Methods

Global strain









Cortesy of dr Haugaa

Average of peak negative strain from 16 LV segments

Prediction of All-Cause Mortality From Global Longitudinal Speckle Strain

Comparison With Ejection Fraction and Wall Motion Scoring

Tony Stanton, MBChB, PhD; Rodel Leano, BS; Thomas H. Marwick, MBBS, PhD

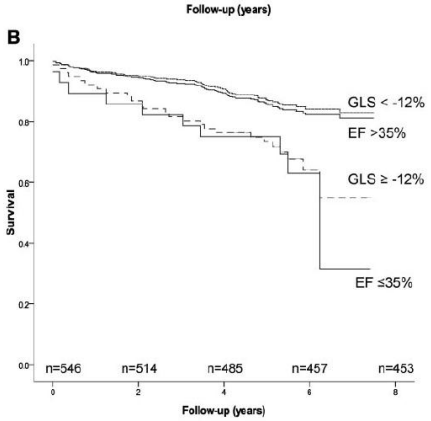


Figure 4. Kaplan-Meier curve depicting event-free survival for individuals using EF (A) with and without wall motion abnormalities (B) using EF and GLS cutoffs.

GLS = global longitudinal strain, EF = ejection fraction, WMSI = wall motion score index

- 546 unselected patients, known or suspected LV impairment
- 5.2±1.5 years
- 91 deaths

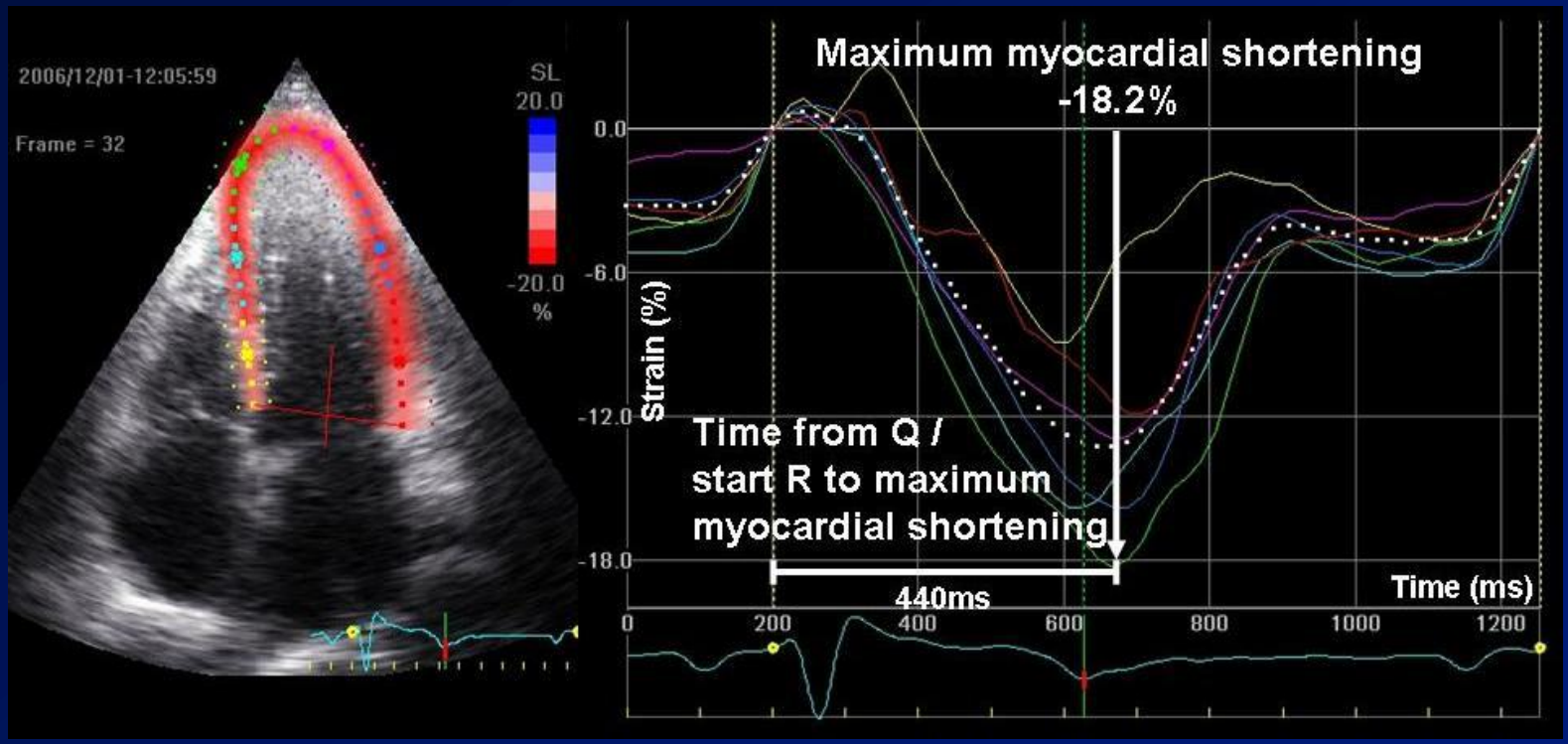
Table 4. Predictors of All-Cause Mortality and Overall Model χ^2 After Addition of Information Obtained From Imaging

Baseline+EF				Baseline+WMSI				Baseline+GLS			
	P	HR	95% CI		*P*	HR	95% CI		*P*	HR	95% CI
Age	<0.01	1.44	1.15–1.82	Age	<0.01	1.41	1.12–1.79	Age	<0.01	1.4	1.11–1.76
Diabetes	0.03	1.68	1.06–2.66	Diabetes	0.03	1.68	1.06–2.66	Diabetes	0.03	1.64	1.04–2.61
Hypertension	0.14	1.38	0.9–2.11	Hypertension	0.16	1.36	0.89–2.09	Hypertension	0.22	1.31	0.85–2.01
EF	0.03	1.23	1.02–1.5	WMS	<0.01	1.28	1.08–1.53	GLS	<0.001	1.45	1.19–1.77
Significance from baseline			Model χ^2	Significance from baseline			Model χ^2	Significance from baseline			Model χ^2
P=0.04			25.3	*P*<0.01			28.6	*P*<0.001			34.9

Model χ^2 from baseline=20.2.

Conclusions—GLS is a superior predictor of outcome to either EF or WMSI and may become the optimal method for assessment of global left ventricular systolic function. (*Circ Cardiovasc Imaging*. 2009;2:356-364.)

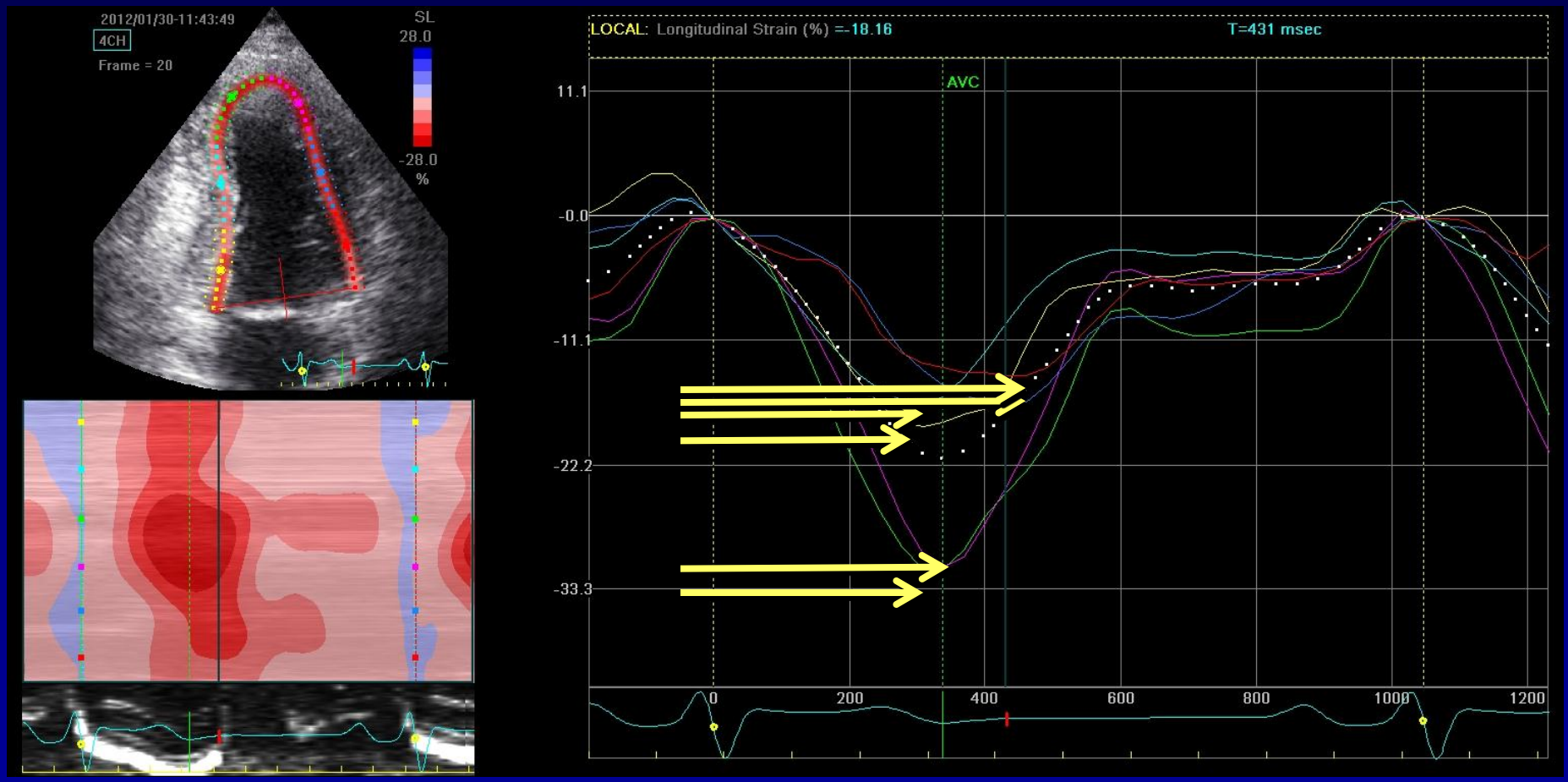
Amplitudes or durations?



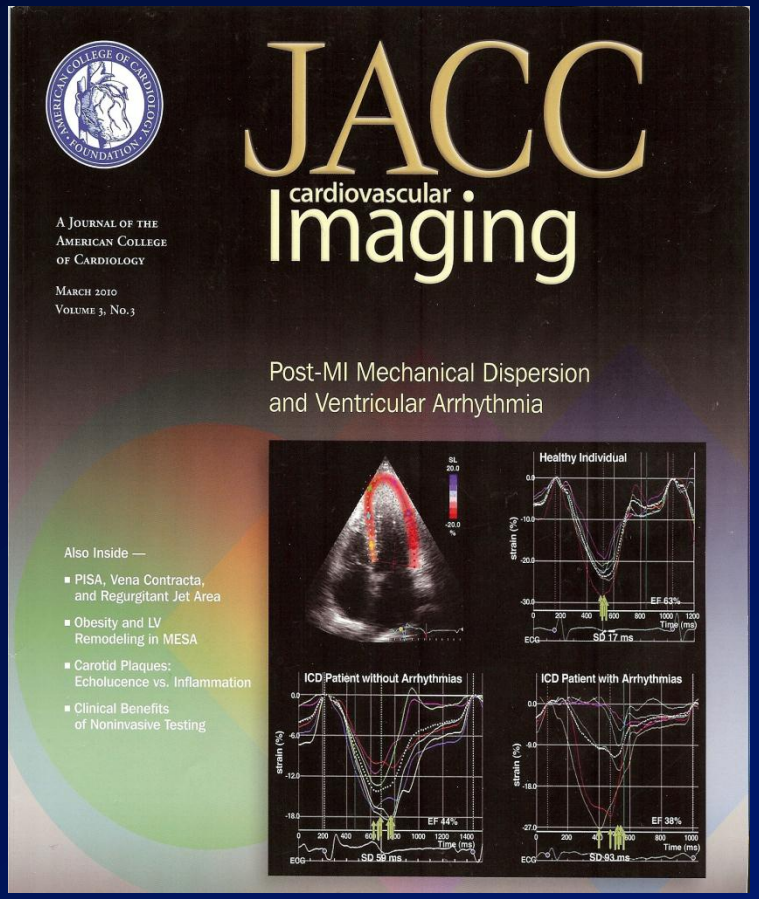
Global strain – average strain from 16 LV segments
Mechanical dispersion – SD of duration of systole in 16 LV segments

Mechanical dispersion

=SD of TIME to max shortening in 16 LV segments



Myocardial mechanical dispersion
85 patients after mycoardial infarction with ICD



Mechanical Dispersion Assessed by Myocardial Strain in Patients After Myocardial Infarction for Risk Prediction of Ventricular Arrhythmia

Kristina H. Haugaa, MD,*† Marit Kristine Smedsrud, MD,*† Torkel Steen, MD, PhD,‡ Erik Kongsgaard, MD, PhD,* Jan Pål Loennechen, MD, PhD,§‖ Terje Skjaerpe, MD, PhD,‖ Jens-Uwe Voigt, MD, PhD,¶ Rik Willems, MD, PhD,¶ Gunnar Smith, MD,‡ Otto A. Smiseth, MD, PhD,* Jan P. Amlie, MD, PhD,* Thor Edvardsen, MD, PhD*

Oslo and Trondheim, Norway; and Leuven, Belgium 2010

EDITOR'S PAGE

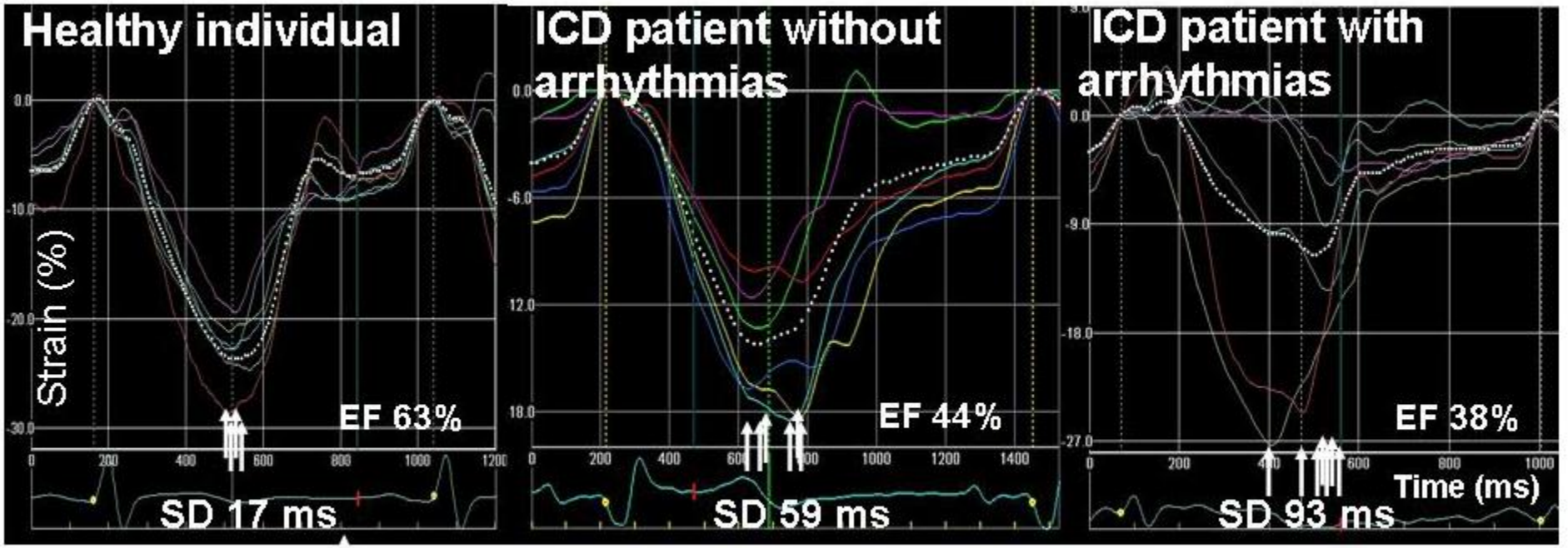
Is Mechanical Dispersion a Raven of Ventricular Arrhythmias?

William A. Zoghbi, MD,* Jagat Narula, MD, PhD†

2.3 (0.6-5.5) years follow up

Myocardial mechanical dispersion
85 patients after mycoardial infarction with ICD

N=23 **N=47** **N=38**



2.3 (0.6-5.5) years follow up

K Haugaa et al, JACC CV Imag 2010

Table 2. Echocardiographic Findings in 85 Patients With an ICD, 20 Control Patients With a Previous MI, and 23 Healthy Individuals

	Healthy Individuals (n = 23)	Control Patients With Previous MI (n = 20)	ICD Patients Without Arrhythmic Events During Follow-Up (n = 47)	ICD Patients With Arrhythmic Events During Follow-Up (n = 38)	p Value*
EF (%)	62 ± 7	55 ± 9	34 ± 11†	35 ± 9†	<0.001
EF >35%, no. (%)	23 (100)	20 (100)	21 (45)†	22 (58)†	<0.001
LVEDV (ml)	107 ± 28	110 ± 26	188 ± 68†	202 ± 86†	<0.001
LVESV (ml)	42 ± 13	51 ± 19	126 ± 59†	132 ± 66†	<0.001
Global strain (%)	−21.6 ± 2.8	−15.9 ± 2.5‡	−11.2 ± 4.0†	−10.0 ± 3.7†	<0.001
Mechanical dispersion (ms)	22 ± 10	45 ± 15§	56 ± 13§	85 ± 29‡	<0.001
Delta contraction duration (ms)	70 ± 33	145 ± 55§	195 ± 65§	335 ± 115‡	<0.001

Values are mean ± SD unless otherwise indicated. Multiple comparisons are obtained with the Bonferroni post hoc test. *p Values for analysis of variance, *F* test, and chi-square test, †$p < 0.05$ compared with healthy individuals and control patients with previous MI, ‡$p < 0.001$ compared with all other groups, §$p < 0.001$ compared with healthy individuals. Global strain: average value of the maximum myocardial shortening in 16 left ventricular (LV) segments; mechanical dispersion: SD of time interval from electrocardiogram (ECG) onset Q/onset R-wave to maximum myocardial shortening in 16 LV segments; delta contraction duration: difference between longest and shortest duration of time from ECG onset Q/onset R-wave to maximum myocardial shortening in a 16-segment model.

EF = ejection fraction; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; other abbreviations as in Table 1.

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Table 3. Predictors of Arrhythmias During Follow-Up That Require Appropriate ICD Therapy in a Total of 85 Post–MI Patients With an ICD by Cox Regression Analysis

	Variable			
	Primary Prevention Criteria Patients (n = 44), HR (95% CI)	p Value	Secondary Prevention Criteria Patients (n = 41), HR (95% CI)	p Value
Univariate analyses				
Age (per 5-yr increase)	1.12 (0.90–1.40)	0.30	1.14 (0.88–1.48)	0.33
Sex (male vs. female)	1.04 (0.23–4.56)	0.95	5.42 (0.72–40.8)	0.10
Heart rate (per 5-beats/min increase)	0.96 (0.77–1.19)	0.69	0.90 (0.74–1.08)	0.25
QRS (per 10-ms increase)	0.76 (0.50–1.15)	0.20	0.97 (0.76–1.24)	0.78
QTc (per 10-ms increase)	1.02 (0.94–1.10)	0.71	0.95 (0.79–1.14)	0.56
Amiodarone therapy (yes vs. no)	1.54 (0.35–6.86)	0.57	1.06 (0.40–2.86)	0.91
Revascularization therapy (yes vs. no)	1.01 (0.39–2.62)	0.97	0.97 (0.36–2.59)	0.95
nsVT/inducible VT (yes vs. no)	2.62 (0.59–11.56)	0.21		
EF (per 5% increase)	0.80 (0.59–1.08)	0.15	1.13 (0.90–1.42)	0.30
Global strain (per 1% increase)	0.84 (0.71–0.99)	0.03	1.00 (0.89–1.12)	0.98
Mechanical dispersion (per 10-ms increase)	1.25 (1.10–1.43)	<0.01	1.30 (1.09–1.55)	<0.01
Delta contraction duration (per 10-ms increase)	1.05 (1.01–1.08)	<0.01	1.06 (1.02–1.10)	<0.01
Multivariate analyses				
Age (per 5-yr increase)	1.20 (0.93–1.55)	0.15	1.23 (0.94–1.59)	0.14
Sex (male vs. female)	0.92 (0.18–4.78)	0.92	3.80 (0.50–29.44)	0.20
EF (per 5% increase)	0.90 (0.56–1.45)	0.68	1.10 (0.83–1.46)	0.51
Global strain (per 1% increase)	0.92 (0.76–1.11)	0.37		
Mechanical dispersion (per 10-ms increase)	1.24 (1.07–1.43)	<0.01	1.31 (1.08–1.58)	<0.01

CI = confidence interval; EF = ejection fraction; HR = hazard ratio; nsVT = nonsustained ventricular tachycardia; inducible VT = inducible ventricular tachycardia in electrophysiology study; other abbreviations as in Table 1.

Do they work when EF > 35%?

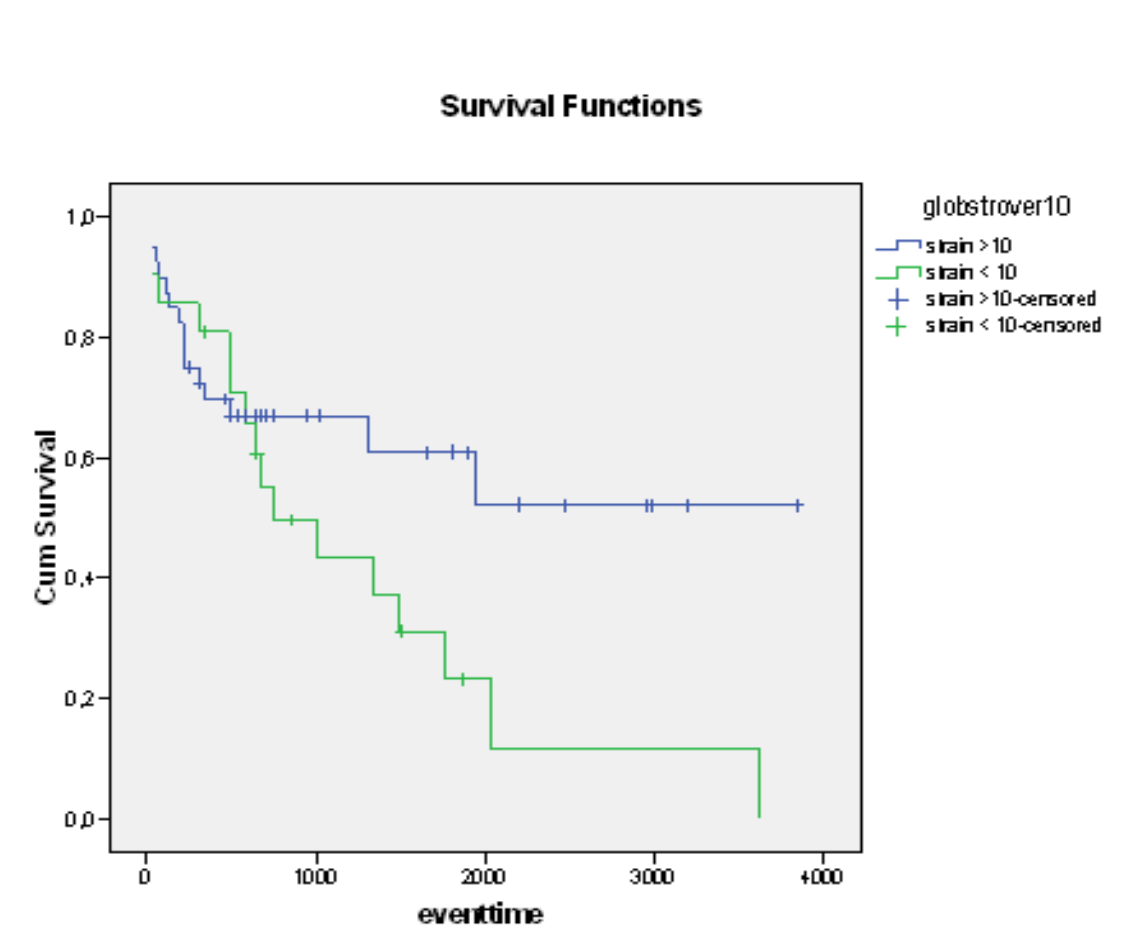
Table 4. Separate Results From 42 ICD Patients With an EF <35% and 43 ICD Patients With an EF >35%

	EF <35%			EF >35%		
	Without Arrhythmic Events During Follow-Up (n = 26)	With Arrhythmic Events During Follow-Up (n = 16)	p Value*	Without Arrhythmic Events During Follow-Up (n = 21)	With Arrhythmic Events During Follow-Up (n = 22)	p Value*
Age (yrs)	60 ± 9	64 ± 8	0.52	64 ± 10	67 ± 11	0.32
EF (%)	27 ± 5	27 ± 5	0.99	44 ± 8	41 ± 5	0.23
Global strain (%)	−8.9 ± 2.2	−7.2 ± 3.0	0.04	−14.0 ± 4.0	−12.0 ± 3.0	0.05
Mechanical dispersion (ms)	52 ± 13	93 ± 31	<0.001	61 ± 12	80 ± 27	0.01
Delta contraction duration (ms)	170 ± 40	340 ± 120	<0.001	225 ± 80	280 ± 110	0.06
QRS duration (ms)	104 ± 14	107 ± 26	0.88	95 ± 13	101 ± 28	0.49
ICD secondary prevention, no. (%)	12 (46)	3 (19)	0.07	11 (52)	15 (68)	0.29
ICD primary prevention, no. (%)	14 (54)	13 (81)	0.07	10 (48)	7 (32)	0.29

Values shown are mean ± SD unless otherwise indicated. *p Values for analysis of variance *F* test. Mechanical dispersion = standard deviation of time interval from onset Q/onset R wave to maximum myocardial shortening in 16 LV segments; Delta contraction duration = difference between longest and shortest duration of time from ECG onset Q/onset R to maximum myocardial shortening in a 16 segment model.

Abbreviations as in Tables 1 and 2.

Prediction of arrhythmia Global strain -10%



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Mechanical dispersion

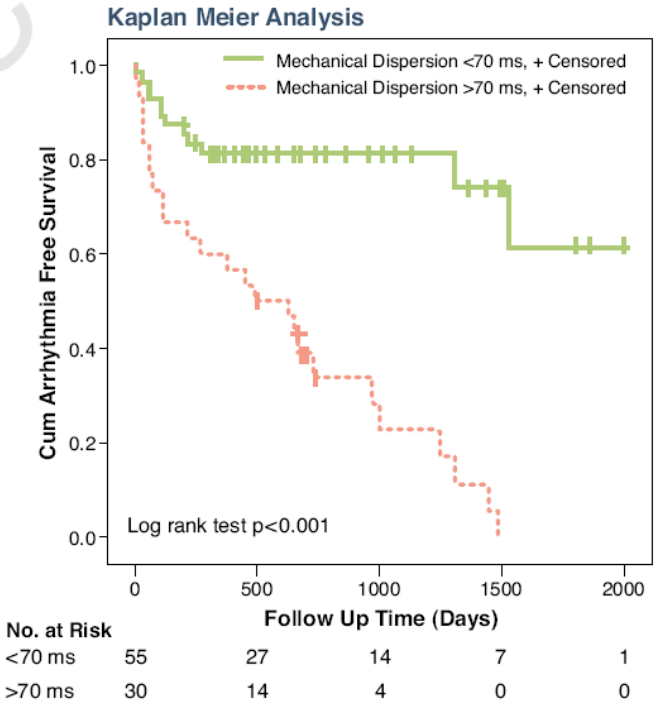


Figure 3. Kaplan-Meier Arrhythmia-Free Survival in 85 Post-MI Patients With an ICD

Kaplan-Meier plot demonstrates arrhythmic–event free survival in 85 post–myocardial infarction (MI) implantable cardioverter-defibrillator (ICD) patients. Mechanical dispersion is defined as the SD of the time to maximum myocardial shortening in a 16-segment left ventricular model and reflects the heterogeneity of myocardial contraction throughout the ventricle. Patients with mechanical dispersion >70 ms show a higher arrhythmic event rate.

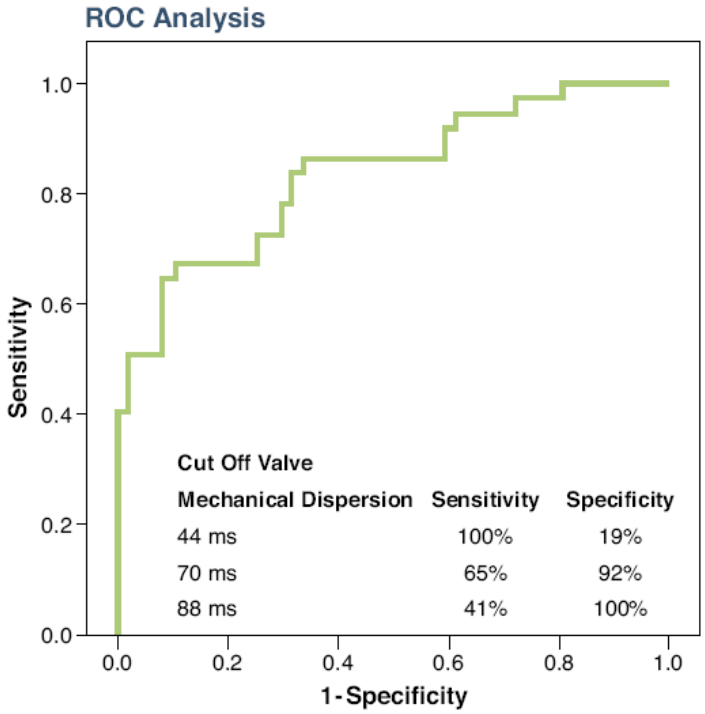


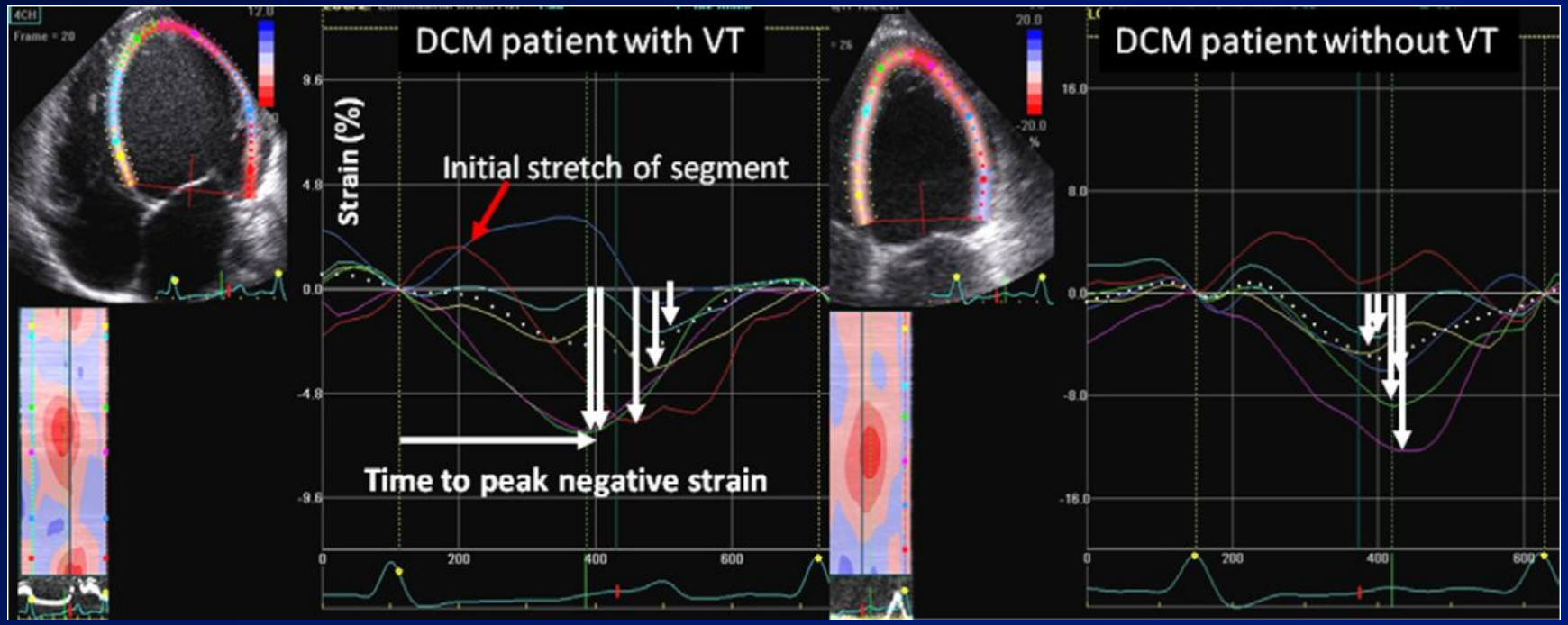
Figure 4. ROC Curve for the Ability of Mechanical Dispersion to Identify Arrhythmic Events During Follow-Up in 85 Post-MI ICD Patients

The cutoff value for mechanical dispersion of 41 ms provided 100% sensitivity and a value of 88 ms provided 100% specificity in predicting arrhythmic events. The optimal cutoff value was 70 ms for a sensitivity of 65% and a specificity of 92% in predicting arrhythmic events. Area under the curve: 0.84 (95% confidence interval: 0.75 to 0.92). ROC = receiver operator characteristic.

Risk Assessment of Ventricular Arrhythmias in Patients with Nonischemic Dilated Cardiomyopathy by Strain Echocardiography

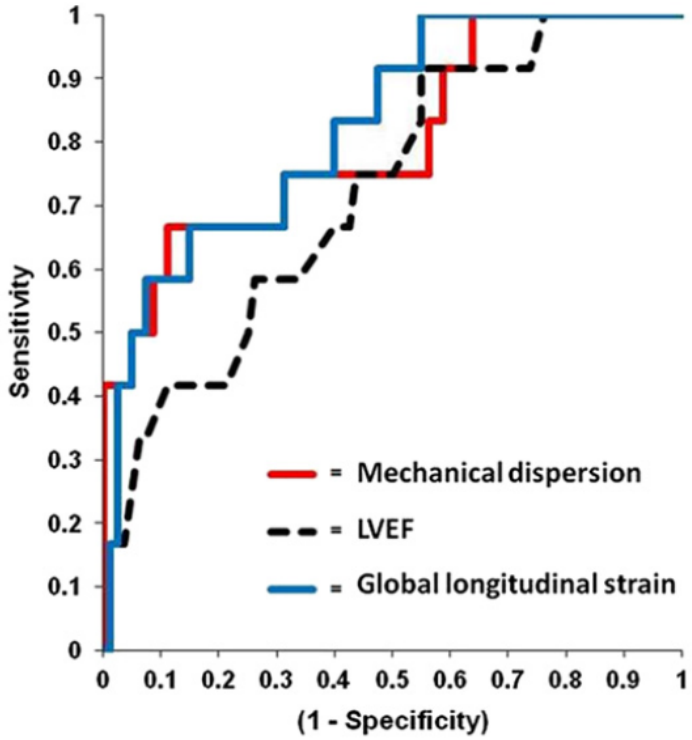
Kristina H. Haugaa, MD, PhD, Björn Goebel, MD, Thomas Dahlslett, MD, Kathleen Meyer, MD, Christian Jung, MD, Alexander Lauten, MD, Hans R. Figulla, MD, PhD, Tudor C. Poerner, MD, PhD, and Thor Edvardsen, MD, PhD, *Oslo, Norway; Jena, Germany*

JASE 2012



EF and prognosis

- Risk prediction of ventricular arrhythmias in patients with non ischemic dilated cardiomyopathy (DCM) is challenging
- Guidelines for ICD and CRT-D indications are based on LV ejection fraction (EF)
- EF is insufficient as an arrhythmic risk predictor
- Myocardial strain by echocardiography can accurately quantify ventricular function and has been proven to be more accurate than EF

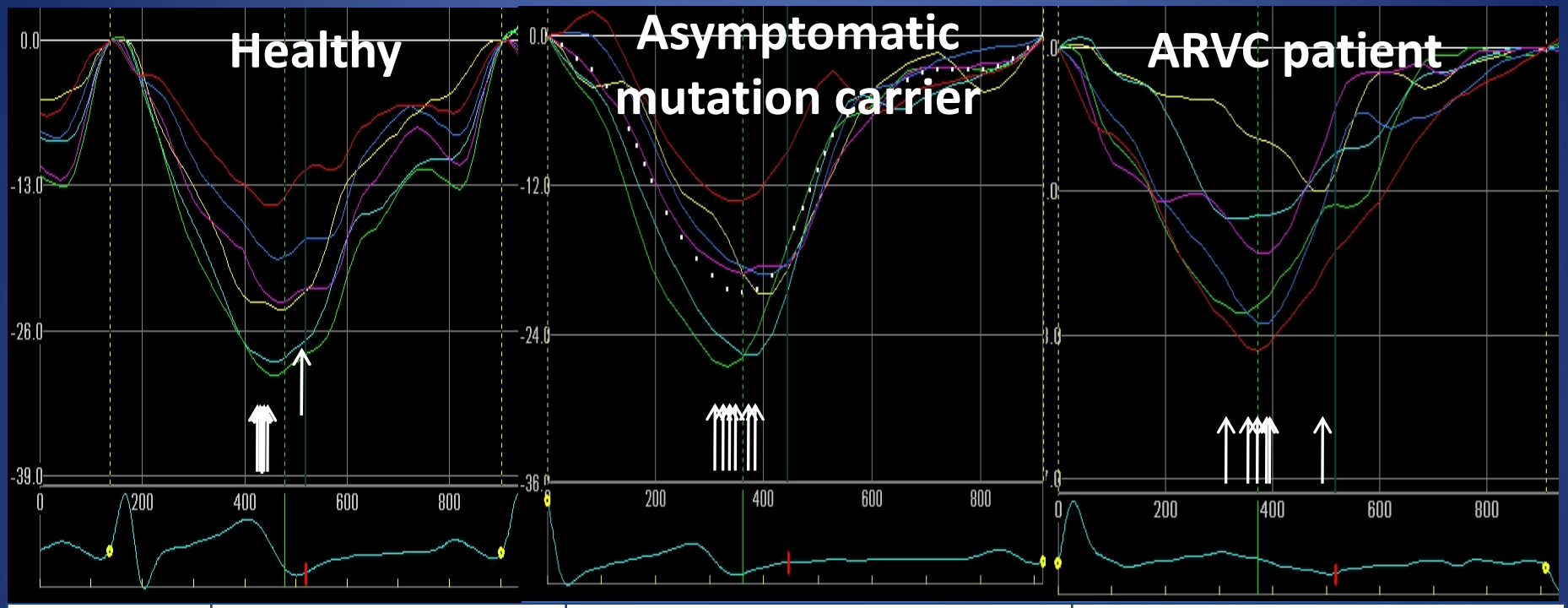


Parameter	Area under curve (95% CI)	Optimal cut off	Sensitivity (%) (95%CI)	Specificity (%) (95%CI)
Mechanical dispersion	0.80(0.65-0.95)	72 ms	67(35-90)	89(80-95)
Global strain	0.82(0.70-0.95)	-7.1 %	67(35-90)	85(75-92)
LVEF	0.72(0.57-0.87)	40 %	92(61-100)	45(34-56)

K Haugaa et al, JASE 2012

Arrhythmogenic Right Ventricular Cardiomyopathy

ARVC - Mechanical dispersion



LV Dispersion	22 ± 8ms	42 ± 13ms*	64 ± 25ms†
RV Dispersion	15 ± 8ms	33 ± 20ms*	53 ± 25ms†

Mean±SD, Bonferroni Post hoc correction

*P<0.01 compared to healthy controls

† P<0.01 compared to healthy controls and asymptomatic mutation carriers

Sarvari et al , EHJ 2011

Infarct Tissue Heterogeneity by Magnetic Resonance Imaging Identifies Enhanced Cardiac Arrhythmia Susceptibility in Patients With Left Ventricular Dysfunction

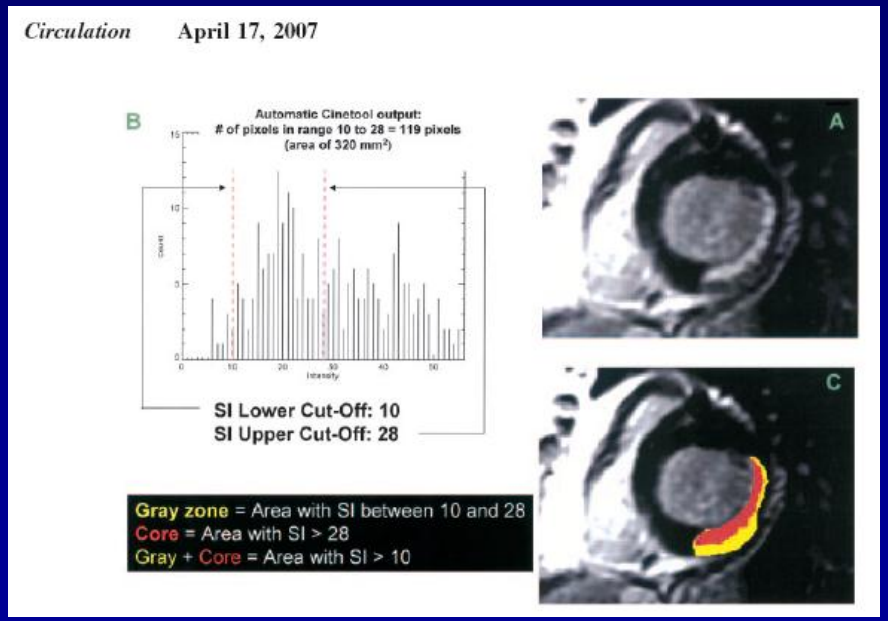
André Schmidt, MD*; Clerio F. Azevedo, MD*; Alan Cheng, MD; Sandeep N. Gupta, PhD; David A. Bluemke, MD, PhD; Thomas K. Foo, PhD; Gary Gerstenblith, MD; Robert G. Weiss, MD; Eduardo Marbán, MD, PhD; Gordon F. Tomaselli, MD; João A.C. Lima, MD; Katherine C. Wu, MD

Circ 2007

TABLE 2. MRI Indices According to Inducibility Status at Electrophysiology Study

Variable	Noninducible for MVT (n=27)	Inducible for MVT (n=20)	*P*
MRI LVEF	0.30±0.10	0.29±0.07	0.79
LV end-diastolic volume, mL	220±70	228±57	0.68
LV end-systolic volume, mL	156±61	162±44	0.71
LV end-diastolic mass, g	146±46	132±30	0.23
Infarct location, n (%)			0.23
Anterior±other territory	15 (56)	15 (75)	
Inferior and/or lateral only	12 (44)	5 (25)	
No. of coronary territories with hyperenhancement (%)			0.1*
Single vessel	21 (78)	19 (95)	
Two vessel	6 (22)	1 (5)	
Transmural infarct extent: % of sectors grouped by quartiles of transmurality			
No infarct	51±15	45±9	0.11
1% to 25% infarct transmurality	8±4	7±2	0.61
26% to 50% infarct transmurality	8±3	8±5	0.88
51% to 75% infarct transmurality	11±5	12±5	0.39
76% to 100% infarct transmurality	23±14	28±11	0.17
Extent of hyperenhancement, g			
Total (core+gray)	34±17	40±11	0.17
Infarct core	21±10	21±5	0.95
Gray zone	13±9	19±8	0.015

*With a logistic regression model in which gray zone extent and number of coronary territories with hyperenhancement were included, only gray zone extent was statistically significant in predicting inducibility (P=0.03).



Summary

- **Global strain:**
  - an excellent parameter for quantification of myocardial function
  - it will replace the current method for assessment of LV function
  - can predict prognosis
  - an excellent tool to predict sudden cardiac death

Heterogeneity of cardiac contraction seems to be a marker of increased arrhythmogenecity

Mechanical dispersion:

- a promising parameter for predicting malignant arrhythmias
- time consuming
- more studies should be done