OVERVIEW

- *Strain and Strain Rate – Definitions*
- *Why it is important?*
- *Clinical Applications in the CCF Echo Lab*
- *Future Perspectives*

Cleveland Clinic

OVERVIEW

- *Strain and Strain Rate – Definitions*
- *Why it is important?*
- *Clinical Applications in the CCF Echo Lab*
- *Future Perspectives*

Cleveland Clinic

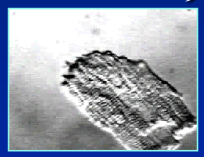
Myocardial Strain: What is It?

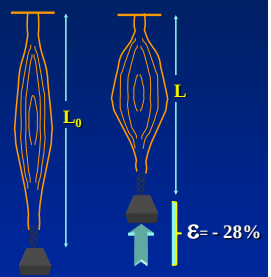
- ***Strain** is defined as the **deformation** of an object, normalized to its original shape.*
- ***Strain Rate (SR)** should be understood as the rate of myocardial **deformation** over a period of time.*
- $Strain\ Rate\ (SR) = \frac{Strain}{time}$

Cleveland Clinic

Strain Calculation

- $Strain\ (\varepsilon) = \frac{L - L_0}{L_0}$
- $Strain\ (\varepsilon) = \frac{7 - 9}{9}$





Mirsky and Parmley. Circ Res, 1973

Cleveland Clinic

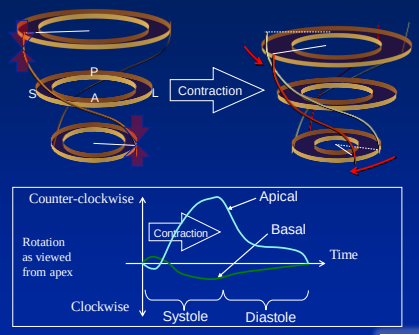
Strain or deformation

- *Units → Dimensionless*
- *Lengthening → Positive value*
- *Shortening → Negative value*

Cleveland Clinic

Cleveland Clinic

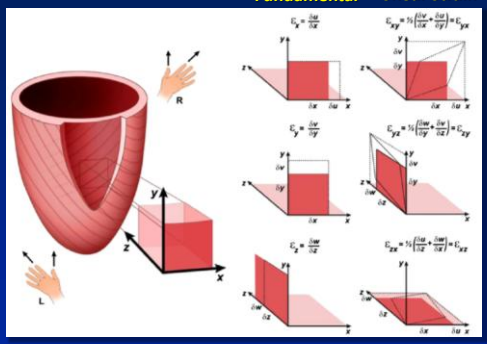
Strain and Torsion



Notomi et al. Circulation 2005; 111: 1141-7

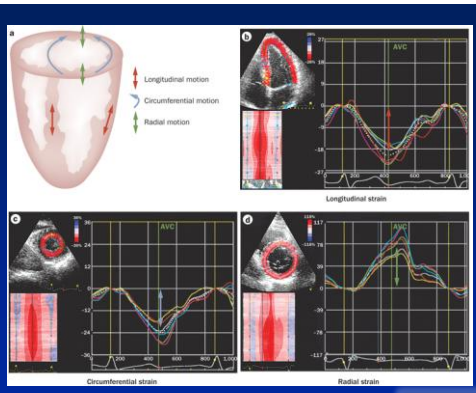
Cleveland Clinic

Fundamental Shear Strain



Geyer H et al. JASE 2010;23:351-69

Cleveland Clinic



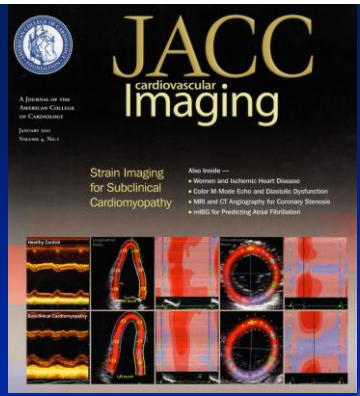
Ozkan A, Marwick TH. Nat Rev Cardiol. 2011;8(9):494-501

Cleveland Clinic

OVERVIEW

- *Strain and Strain Rate – Definitions*
- *Why it is important?*
- *Clinical Applications in the CCF Echo Lab*
- *Future Perspectives*

Cleveland Clinic



Cleveland Clinic

Strain in Myocardial Disease

- *Importance of Longitudinal Strain*
  - Longitudinal fibers are predominant in the subendocardial region
  - Most vulnerable component of LV mechanics and therefore most sensitive to the early presence of myocardial disease.

Table 1 Classification of cardiac mechanics in heart failure

Functional impairment	Longitudinal mechanics	Circumferential mechanics	Radial mechanics	Torsional mechanics	Global EF	Diastolic filling pressures	Clinical syndrome
Predominant subendocardial dysfunction	Marked impairment	Preserved	Preserved/minimal impairment	Preserved	Preserved/minimal impairment	Elevated	Diastolic HF/HFNEF
Predominant subepicardial dysfunction	Preserved/minimal impairment	Marked impairment	Minimal impairment	Marked impairment	Preserved/minimal impairment	Elevated	Diastolic HF/HFNEF
Transmural dysfunction	Marked impairment	Marked impairment	Marked impairment	Marked impairment	Marked impairment	Elevated	Systolic HF

EF, Ejection fraction; HF, heart failure; HFNEF, heart failure and normal ejection fraction.

Geyer H et al. JASE 2010;23:351-69

Cleveland Clinic

BRIEF REPORT

Myocardial Strain Measurement With 2-Dimensional Speckle-Tracking Echocardiography

Definition of Normal Range

Thomas H. Marwick, MD,* Rodel L. Leano, BS,* Joseph Brown, BS,* Jing-Ping Sun, MD,† Rainer Hoffmann, MD,‡ Peter Lysyansky, PhD,§ Michael Becker MD,‡ James D. Thomas, MD†

Brisbane, Australia; Cleveland, Ohio; Aachen, Germany; and Haifa, Israel

The interpretation of wall motion is an important component of echocardiography but remains a source of variation between observers. It has been believed that automated quantification of left ventricular (LV) systolic function by measurement of LV systolic strain from speckle-tracking echocardiography might be helpful. This multicenter study of nearly 250 volunteers without evidence of cardiovascular disease showed an average LV peak systolic strain of −18.6 ± 0.1%. Although strain was influenced by weight, blood pressure, and heart rate, these features accounted for only 16% of variance. However, there was significant segmental variation of regional strain to necessitate the use of site-specific normal ranges. (J Am Coll Cardiol Img 2009;2:80–4) © 2009 by the American College of Cardiology Foundation

JACC Cardiovascular Imaging

Cleveland Clinic

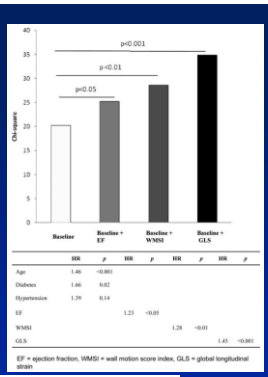
Table 1. Left Ventricular 2-Dimensional Longitudinal Strain and SRs in Subjects at Different Sites

Parameter	Peak Systolic Strain (%)	Peak Systolic SR (1/s)	Early Diastolic (E) SR (1/s)	Late Diastolic (A) SR (1/s)
Mean ± SEM	−18.6 ± 0.1	−1.10 ± 0.01	1.55 ± 0.01	1.02 ± 0.01
Lower 95% limit	−18.5	−1.09	1.54	1.01
Upper 95% limit	−18.7	−1.11	1.56	1.03

Selected for tracking quality (TQ) <3.
SR = strain rate.

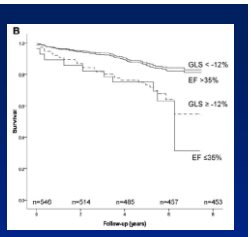
JACC Cardiovascular Imaging

Cleveland Clinic



	HR	p	HR	p	HR	p	HR	p
Age	1.46	<0.001						
Diabetes	1.66	0.02						
Hypertension	1.39	0.14						
EF			1.23	<0.05				
WMSI					1.28	<0.01		
GLS							1.45	<0.001

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



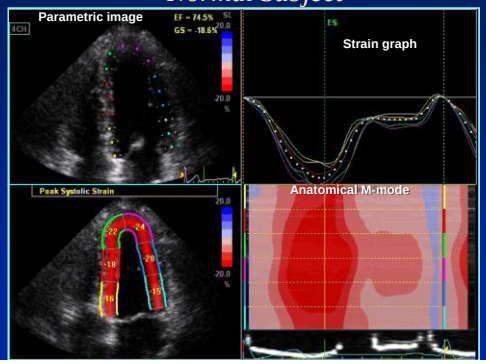
Staton et al. Circ CV Imaging 2009;2:356-64

Circulation Cardiovascular Imaging

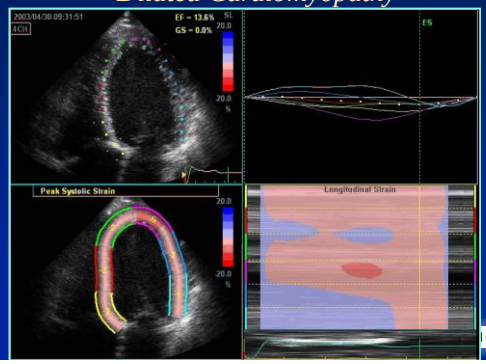
American Heart Association Learn and Live

Cleveland Clinic

Longitudinal Strain
Normal Subject



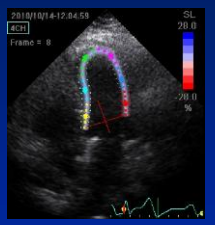
Longitudinal Strain
Dilated Cardiomyopathy



Clinic

Caveats of Speckle-Tracking derived Strain

- *Highly dependent on image quality and acquisition. (ie: reverberation, attenuation artifacts, etc)*
- *Excessive or limited region-of-interest width (don't include the pericardium!).*
- *Technical proficiency for image acquisition and measurements.*
- *Cannot do it in the presence of IV myocardial contrast for LVO.*



Cleveland Clinic

OVERVIEW

- *Strain and Strain Rate – Definitions*
- *Why it is important?*
- *Clinical Applications in the CCF Echo Lab*
- *Future Perspectives*

Cleveland Clinic

Early detection of cardiotoxicity from chemotherapy

Cleveland Clinic

Chemotherapy Associated with LV Dysfunction

Chemotx Agent	Incidence	Frequency of use
Antracyclines (Doxorubicin)	3-26%	+++
Cyclophosphamide	7-28%	+++
Trastuzumab (Herceptin)	2-28%	++

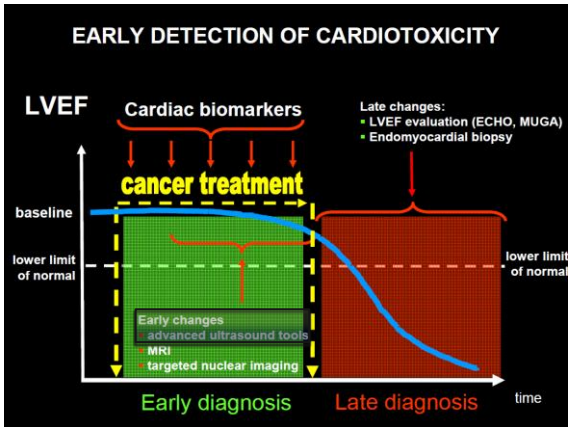
Yeh ET, Bickford CL. JACC 2009;53:2231–47.

Cleveland Clinic

What's the classic and current defition of chometherapy related cardiotoxicity?

- *Symptomatic reduction >5% to an EF<55%*
- *Asymptomatic reduction >10% to an EF <55%*

Cleveland Clinic



Use of myocardial deformation imaging to detect preclinical myocardial dysfunction before conventional measures in patients undergoing breast cancer treatment with trastuzumab

James L. Hare, MBBS,[a] Joseph K. Brown, BSc,[a] Rodel Leano, BSc,[a] Carly Jenkins, MSc,[a] Natasha Woodward, MBBS,[b] and Thomas H. Marwick, MBBS, PhD[a] *Brisbane, Australia*

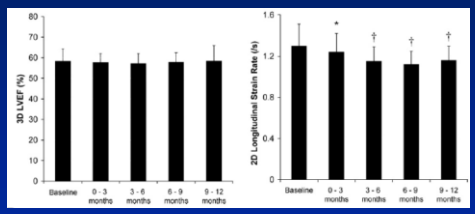
Background Trastuzumab prolongs survival in patients with human epidermal growth factor receptor type 2–positive breast cancer. Sequential left ventricular (LV) ejection fraction (EF) assessment has been mandated to detect myocardial dysfunction because of the risk of heart failure with this treatment. Myocardial deformation imaging is a sensitive means of detecting LV dysfunction, but this technique has not been evaluated in patients treated with trastuzumab. The aim of this study was to investigate whether changes in tissue deformation, assessed by myocardial strain and strain rate (SR), are able to identify LV dysfunction earlier than conventional echocardiographic measures in patients treated with trastuzumab.

Methods Sequential echocardiograms (n = 152) were performed in 35 female patients (51 ± 8 years) undergoing trastuzumab therapy for human epidermal growth factor receptor type 2–positive breast cancer. Left ventricular EF was measured by 2- and 3-dimensional (2D and 3D) echocardiography, and myocardial deformation was assessed using tissue Doppler imaging and 2D-based (speckle-tracking) strain and SR. Change over time was compared every 3 months between baseline and 12 months.

Conclusions Myocardial deformation identifies preclinical myocardial dysfunction earlier than conventional measures in women undergoing treatment with trastuzumab for breast cancer. (Am Heart J 2009;158:294-301.)

Cleveland Clinic

3D LVEF vs. Longitudinal Strain Rate



Hare JL et al. Am Heart J. 2009;158(2):294-301

Cleveland Clinic

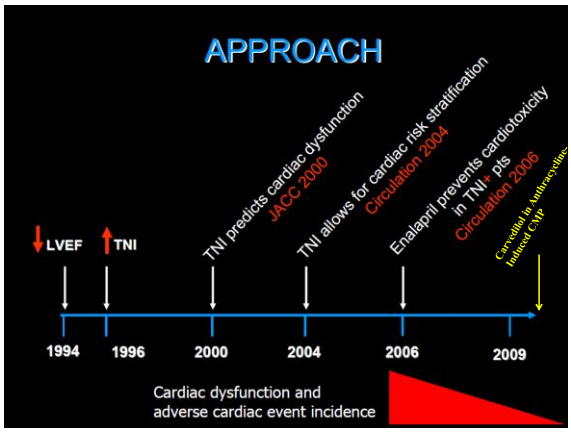
Early Detection and Prediction of Cardiotoxicity in Chemotherapy-Treated Patients

Heloisa Sawaya, MD, PhD[a], Igal A. Sebag, MD[a], Juan Carlos Plana, MD[c], James L. Januzzi, MD[a], Bonnie Ky, MD[e], Victor Cohen, MD[e], Sucheta Gosavi, MD[a], Joseph R. Carver, MD[e], Susan E. Wiegers, MD[e], Randolph P. Martin, MD[b], Michael H. Picard, MD[a], Robert E. Gerszten, MD[a], Elkan F. Halpern, PhD[c], Jonathan Passeri, MD[a], Irene Kuter, MD[b], and Marielle Scherrer-Crosbie, MD, PhD[a,b]

***Objectives:** To evaluate if more sensitive echocardiographic measurements and biomarkers could predict later cardiac dysfunction in chemo-treated patients.*

	Sensitivity	Specificity	PPV	NPV
10% decrease longitudinal strain	7/9 (78%)	27/34 (79%)	7/14 (50%)	27/29 (93%)
Increased cTnI at 3 months	6/9 (67%)	28/34 (82%)	6/12 (50%)	28/31 (90%)
10% decrease Long strain and increased cTnI at 3 months	5/9 (55%)	33/34 (97%)	5/6 (83%)	33/37 (89%)
10% decrease Long strain or increased cTnI at 3 months	8/9 (89%)	22/34 (65%)	8/20 (40%)	22/23 (97%)

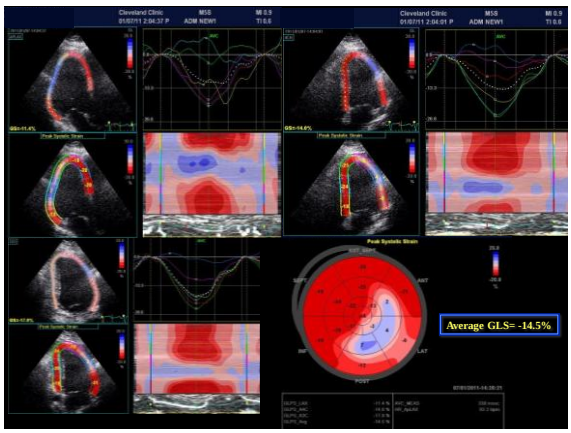
Am J Cardiology 2011;107(9):1375-80

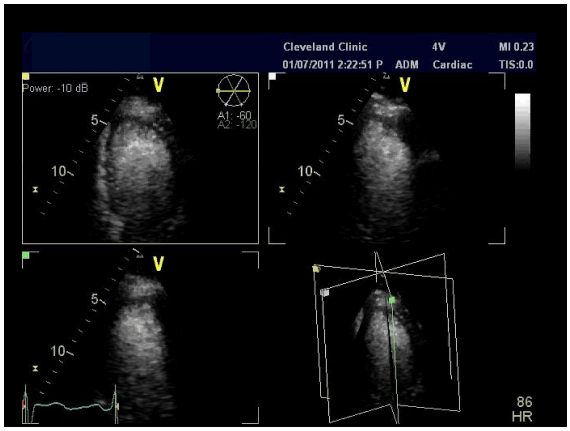


Clinical Example

- *52yo female with history of breast CA ($T_{1c}N_1M_0$) dx in 07/2000.*
  - **S/p Modified radical mastectomy w/ adjuvant Chemotx**
  - **Adriamycin/Doxorubicin (12yrs prior) + XRT**
- *Recurrence 8 yrs after w/ mets*
  - **Herceptin 2yrs + XRT**
- *Mild exertional dyspnea (walking up 5 flights of steps). No PND/orthopnea.*
- *Longstanding edema, due to varicose veins.*
- *No angina.*
- *Hypotensive symptoms with Anti-HTN Rx in past.*

Cleveland Clinic

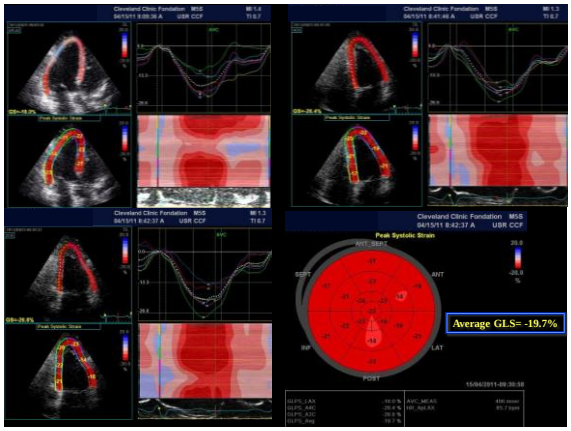


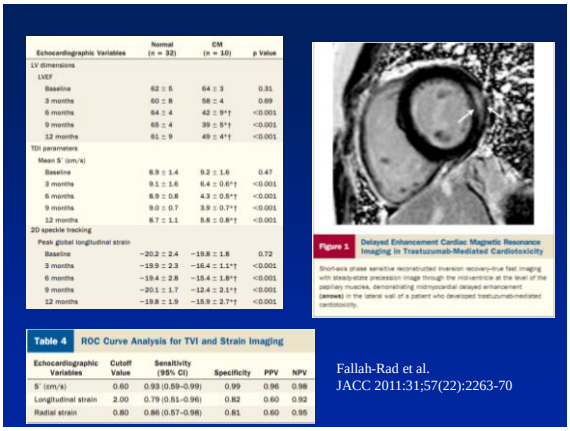


Clinical Example

- Patient was started on Ramipril 2.5 mg in AM and 5 mg PM
- Bisoprolol 2.5 mg/day was added 2 weeks after and titrated up to 5 mg/day over 1 month.
- Tolerated well, except for mild cough.
- Follow-up Echo in 1 and 3 months

Cleveland Clinic





Echocardiographic Variables	Normal (n = 32)	CM (n = 10)	p Value
LV dimensions			
LVEF			
Baseline	62 ± 5	64 ± 3	0.31
3 months	60 ± 8	58 ± 4	0.69
6 months	64 ± 4	42 ± 9*†	<0.001
9 months	65 ± 4	39 ± 5*†	<0.001
12 months	61 ± 9	49 ± 4*†	<0.001
TDI parameters			
Mean S′ (cm/s)			
Baseline	8.9 ± 1.4	9.2 ± 1.6	0.47
3 months	9.1 ± 1.6	6.4 ± 0.6*†	<0.001
6 months	8.9 ± 0.8	4.3 ± 0.5*†	<0.001
9 months	9.0 ± 0.7	3.9 ± 0.7*†	<0.001
12 months	8.7 ± 1.1	5.8 ± 0.8*†	<0.001
2D speckle tracking			
Peak global longitudinal strain			
Baseline	−20.2 ± 2.4	−19.8 ± 1.8	0.72
3 months	−19.9 ± 2.3	−16.4 ± 1.1*†	<0.001
6 months	−19.4 ± 2.8	−15.4 ± 1.8*†	<0.001
9 months	−20.1 ± 1.7	−12.4 ± 2.1*†	<0.001
12 months	−19.8 ± 1.9	−15.9 ± 2.7*†	<0.001

Figure 1 Delayed Enhancement Cardiac Magnetic Resonance Imaging in Trastuzumab-Mediated Cardiotoxicity

Short-axis phase sensitive reconstructed inversion recovery–true fast imaging with steady-state precession image through the mid-ventricle at the level of the papillary muscles, demonstrating midmyocardial delayed enhancement (arrows) in the lateral wall of a patient who developed trastuzumab-mediated cardiotoxicity.

Table 4 ROC Curve Analysis for TVI and Strain Imaging

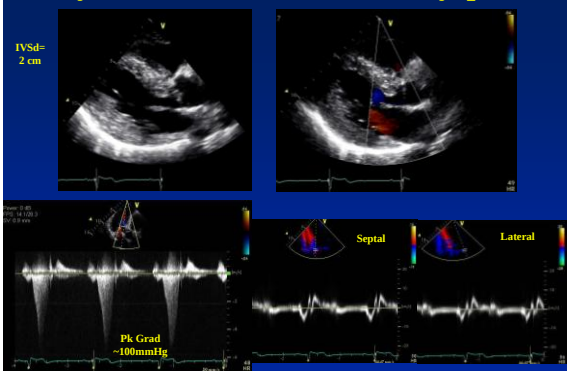
Echocardiographic Variables	Cutoff Value	Sensitivity (95% CI)	Specificity	PPV	NPV
S′ (cm/s)	0.60	0.93 (0.59–0.99)	0.99	0.96	0.98
Longitudinal strain	2.00	0.79 (0.51–0.96)	0.82	0.60	0.92
Radial strain	0.80	0.86 (0.57–0.98)	0.81	0.60	0.95

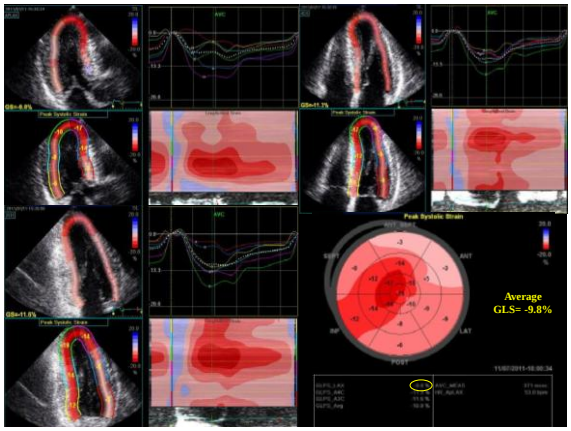
Fallah-Rad et al.
JACC 2011:31;57(22):2263-70

Strain in HCM

Cleveland Clinic

45 yo female with exertional dyspnea





Correlation of regional function and myocardial fibrosis in HCM

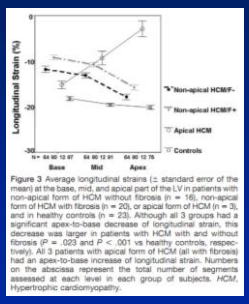


Figure 3 Average longitudinal strains (± standard error of the mean) at the base, mid, and apical part of the LV in patients with non-apical form of HCM without fibrosis (n = 16), non-apical form of HCM with fibrosis (n = 20), or apical form of HCM (n = 3), and in healthy controls (n = 23). Although all 3 groups had a significant apex-to-base decrease of longitudinal strain, this decrease was larger in patients with HCM with and without fibrosis ($P = .023$ and $P < .001$ vs healthy controls, respectively). All 3 patients with apical form of HCM (all with fibrosis) had an apex-to-base increase of longitudinal strain. Numbers on the abscissa represent the total number of segments assessed at each level in each group of subjects. *HCM*, Hypertrophic cardiomyopathy.

- N=72 (39 w/ HCM and 23 controls)
- Mean end-systolic Long strain correlated well with total myocardial fibrosis (r=0.46, p=0.003)
- Longitudinal, circumferential, and radial strains are decreased in patients with HCM even in the absence of fibrosis.
- Myocardial fibrosis is associated with depressed longitudinal strain in patients with HCM.

Popovic Z et al. JASE 2008;21:1299-1305

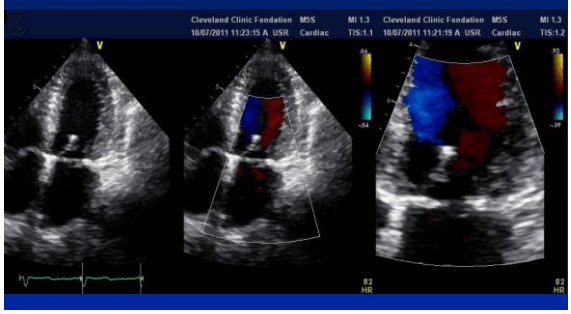
Cleveland Clinic

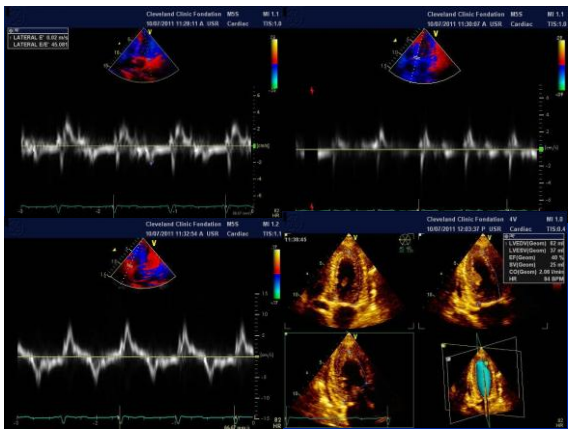
Other Clinical Applications of Strain

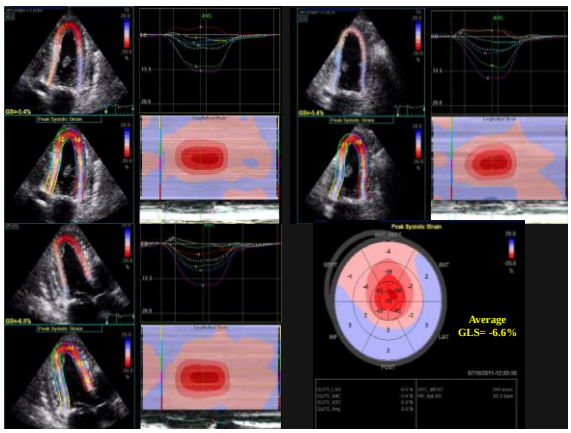
- *Correlation of regional function and myocardial fibrosis in cardiomyopathies. (ie: amyloid, DCM, etc)*
- *Pericardial Diseases*
- *Regional and Global Function of other cardiac chambers (ie: LA, RV).*
- *Could it be measured with/post contrast?*

Cleveland Clinic

67 yo female with adv COPD, s/p robotic MV repair (5 mos prior) with progressive HF symptoms







FINAL DIAGNOSIS

A. Skin, left lower abdomen, punch biopsy
- No evidence of amyloidosis identified (see comment).

COMMENT
Sections demonstrate relatively normal benign fibroadipose tissue. A Congo red stain is negat
also reviewed this

808/kmr 10/17/2011

FINAL DIAGNOSIS

BONE MARROW CORE BIOPSY, CLOT SECTION, TOUCH IMPRINT, ASPIRATE & PERIPHERAL BLOOD SMEAR (A-C):
- PLASMA CELL NEOPLASM.
- PRIMARY AMYLOIDOSIS.
- NORMOCELLULAR MARROW (APPROXIMATELY 40%) WITH TRILINEAGE HEMATOPOIESIS AND INCREASED PLASMA CELLS, APPROXIMATELY 20% OF CELLULARITY WITH KAPPA LIGHT CHAIN RESTRICTION BY IMMUNOSTAINS.
- DECREASED IRON STORES.
- SEE COMMENT.

Comment: The patient has a history of congestive heart failure and monoclonal protein with IgA kappa light restriction. The current bone marrow is normocellular for age and shows trilineage hematopoiesis. CD138 positive plasma cells showing kappa light chain restriction are increased, which may represent approximately 20% of the total cellularity. Congo red stain is positive for amyloid deposit. Overall, morphologic and immunohistochemical findings are consistent with plasma cell neoplasm and primary amyloidosis. Correlation with clinical and cytogenetic findings is suggested.

CBC (10-19-2011): WBC 21.0; Hgb 9.1; MCV 80.9; RDW 18.7; Plts 182
Differential (%): Segs 84; Lymphs 4; Monos 12; Eos 0. 6 nRBCs per 100 WBCs

Cleveland Clinic

Differentiation of Hypertrophic Cardiomyopathy and Cardiac Amyloidosis from Other Causes of Ventricular Wall Thickening by Two-Dimensional Strain Imaging Echocardiography

Jing Ping Sun, MD[a,*], William J. Stewart, MD[b], Xing Sheng Yang, MD, PhD[a], Robert O. Donnell, MD[a], Angel R. Leon, MD[a], Joel M. Felner, MD[a], James D. Thomas, MD[b], and John D. Merlino, MD[a]

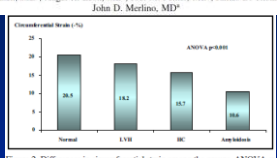
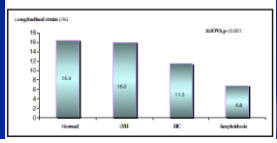
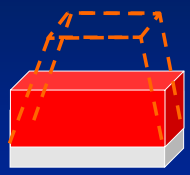


Figure 2. Differences in circumferential strain among the groups. ANOVA = analysis of variance; LVH = LV hypertrophy.



Cleveland Clinic

Constrictive Pericarditis



Muscle

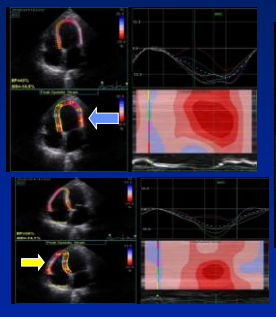
Pericardium

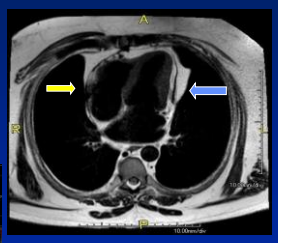
Constricted pericardial shell tethers the myocardium

Cleveland Clinic

Regional LV and RV Free Wall Longitudinal Strain by Speckle Tracking is Reduced in Patients with Constrictive Pericarditis: An MRI Correlation Study

Arun Dahiya, Zoran B Popovic, M Chadi Alraies, João L. Cavalcante, L. Leonardo Rodriguez, Scott Flamm, Allan L. Klein

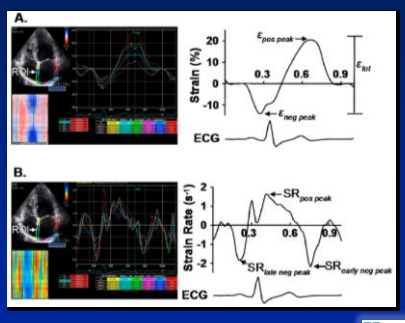




J Am Coll Cardiol. 2011;57(17):E339

Cleveland Clinic

Understanding LA function (contractile, conductive and reservoir)

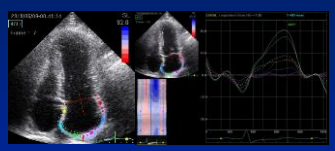


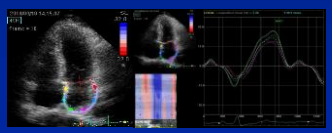
Saraiva R et al. JASE 2010;23:172-80

Cleveland Clinic

Functional Recovery of the Left Atrium after Pericardiectomy Demonstrated by Speckle Tracking Imaging

Hirohiko Motoki, MD, PhD, Andrew C. Y. To, MBChB, Roberto M Saraiva, MD, PhD, Arun Dahiya, MD, Mazen Hanna, MD, Chadi Alraies, MD, Juan Carlos Plana, MD, Thomas H. Marwick, MD, PhD, Allan L. Klein, MD.

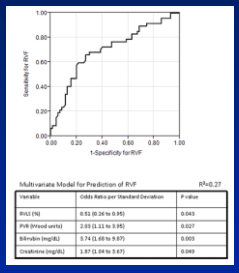




JASE 2011

Cleveland Clinic

Can RVLS predict RV failure post LVAD implantation?



Multivariate Model for Prediction of RVF R^2=0.27

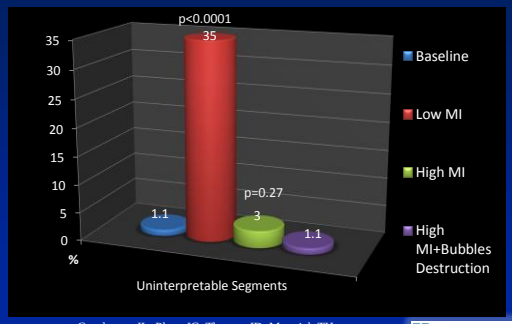
Variable	Odds Ratio per Standard Deviation	P value
RVLS (%)	0.51 (0.26 to 0.95)	0.043
PVR (Wood units)	2.03 (1.11 to 3.95)	0.027
Bilirubin (mg/dL)	3.74 (1.68 to 9.67)	0.003
Creatinine (mg/dL)	1.87 (1.04 to 3.67)	0.049

- N=117 patients undergoing LVAD implant.
- RV failure defined as need for RVAD or use of inotropic > 14 days.
- VVI measure RVLS on pre-procedural echocardiograms.
- 40% pts had RV failure.
- Cutoff value of -9.6% predicted RV failure w/ specificity of 76% and sensitivity of 68% with ROC=0.70.
- RVLS was independent predictor of RV failure.

Grant AD, Starling RC, Smedira NG, Marwick TH.
Circulation 2011;124:A11333

Cleveland Clinic

Feasibility of STLS assessment in the presence of LV contrast

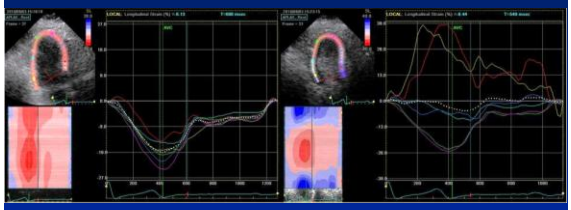


Cavalcante JL, Plana JC, Thomas JD, Marwick TH
Circulation 2011;124:A17415

Cleveland Clinic

Just an example…

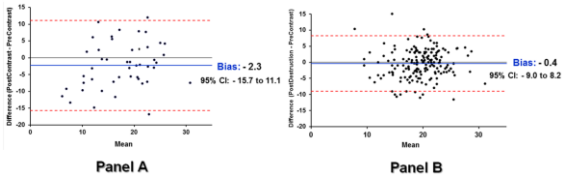
PRE-CONTRAST **POST-CONTRAST with LOW MI**



Cavalcante JL, Plana JC, Thomas JD, Marwick TH
Circulation 2011;124:A17415

Cleveland Clinic

Bland–Altman Plot Analysis of STLS measurements



Panel A Panel B

Cavalcante JL, Plana JC, Thomas JD, Marwick TH
Circulation 2011;124:A17415

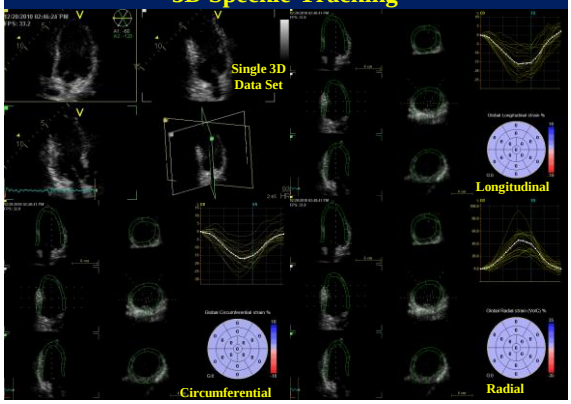
Cleveland Clinic

OVERVIEW

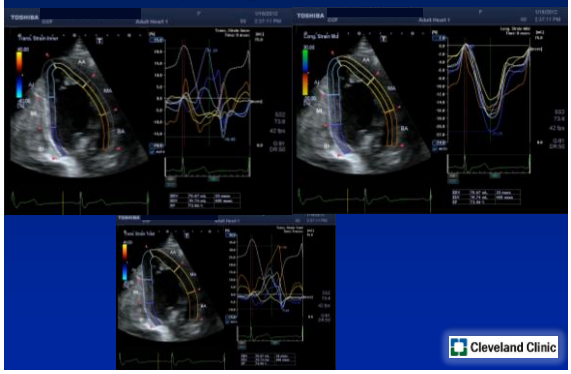
- *Strain and Strain Rate – Definitions*
- *Why it is important?*
- *Clinical Applications in the CCF Echo Lab*
- *Future Perspectives*

Cleveland Clinic

3D Speckle-Tracking



Layer Specific Strain



Cleveland Clinic

Strain and Strain Rate

- Free from Translation and Tethering
- Highly dependent on image quality
- Robust and sensitive marker of functional changes of subclinical disease.
- It can quantify global and regional myocardial function, adding incremental value to standard measurements.

Cleveland Clinic

Strain and Strain Rate – What's Ahead?

- Multicenter trials are needed to further confirm and establish the incremental value of this method.
- Standardization of the measurements across vendors and different platforms.
- Significance of these measurements needs to be considered in the context of

early detection of subclinical abnormality → early intervention

Cleveland Clinic

Thanks!!