

## **A New Speckle Tracking Algorithm can Accurately Analyze Left Ventricular Wall Motion - a Multicenter Study by the Israeli Echocardiography Research Group**

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**Introduction:** Left ventricular wall (WM) motion assessment is crucial in echocardiogram interpretation, but despite technology improvements no automatic tool yet replaced visual reading. We hypothesized that 2D strain, a new speckle-tracking technique, can assess WM automatically with high concordance to visual assessment.

**Methods:** Echocardiograms (3 apical views, 18 segments) of 105 patients (ten duplicated), (28 healthy, 62 AMI, 15 dilated cardiomyopathy) were blindly read by 10 readers. Segments were scored: normal-dyskinetic (1-4). Segmental “gold-standard” for visual scoring (VSS) was computed using majority score assigned to each segment. 2DS was applied and segmental peak systolic strain (PSS) determined [Vivid 7, AFI(GE)]. PSS scores were divided: <-14% normal, -14 to -11% hypokinetic, - 11 to 2% akinetic, >2% dyskinetic.

**Results:** 1890 segments were analyzed, 66% categorized by VSS as normal and 30% as abnormal (13.5% hypokinetic, 12.1% akinetic and 1.7% dyskinetic), (4% unscorable). The sensitivity and specificity of PSS vs. VSS for identifying normal vs. abnormal segments was 88% and 85%. 85% of normal and 88% of akinetic segments were correctly identified by PSS. Kappa values for VSS inter and intra observer variability (4 categories): 0.50 and 0.57. When dichotomized into normal (score 1) and abnormal (2-4), inter and intra observer variabilities were 0.65 and 0.71. For PSS, Kappa values for inter and intra observer variability were 0.71 and 0.77, and when dichotomized, 0.79 and 0.83.

**Conclusions:** Automated PSS can accurately distinguish normally and abnormally contracting segments with good agreement to visual assessment by experienced echocardiographers, thus may assist WM analysis performed by less experienced readers.

## **Reduction in Mitral Regurgitation in Patients Undergoing Cardiac Resynchronization Treatment: Assessment of Predictors by Two Dimensional Radial Strain Echocardiography**

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**Background.** Cardiac resynchronization treatment (CRT) is associated with reduction in mitral regurgitation (MR), however few studies have defined specific predictors of acute MR reduction. We hypothesized that left ventricular (LV) mechanical dyssynchrony in mid-LV segments corresponding to papillary muscles insertion sites can predict early MR reduction post CRT, due to improved synchrony in papillary muscle contraction. We utilized the novel approach of 2-D radial strain (2-DRS) to evaluate our hypothesis.

**Methods.** We evaluated 32 pts undergoing CRT (mean age 64±17 years, 54% male) with MR grade ≥3 determined by MR jet area/left atrial area ratio (JA/LAA) (grade 1, MRJA/LAA <20% to grade 4, MRJA/LAA >40%). Radial mechanical activation sequence maps were constructed using 2-DRS from mid-LV circumferential sites. Responders were defined as patients with post-CRT (1.9±1.0 months) reduction in MR to MRJA/LAA < 25%.

**Results.** The percent reduction in LV end-systolic volume was significantly higher in responders (p=0.03), as was improvement in LVEF (p=0.007). Post CRT, 67% of responders had mild or no MR and 33% had mild to moderate MR, while 70% of non-responders had grade 3 or 4 MR (p=0.0001). Significant delay of time-to-peak 2-DRS in the mid posterior and inferior segments prior to CRT was found in responders compared with non-responders (580±58 vs. 486±94, p=0.002 and 596±79 vs. 478±127 ms, p=0.005, respectively). Responders also had higher peak positive systolic 2-DRS in the posterior and inferior segments compared to non-responders (22±13 vs. 12±7%, p=0.01 and 17±9 vs. 9±7%, p=0.02, respectively). Logistic regression analysis showed that the difference in pre-CRT infero-anterior time-to-peak radial strain of >110 ms and MRJA/LAA <40% as well as 2-DRS >18% in the posterior wall were significant predictors of post-CRT improvement in MR.

**Conclusion.** 2-D radial strain can quantify LV dyssynchrony and predict post-CRT improvement in MR. Presence of a significant time-to-peak delay on 2-DRS between inferior and anterior LV segments, preserved strain of posterior wall and MRJA/LAA <40% were found to be associated with significant MR reduction in patients post CRT.

## Is Left Ventricular Diastolic Dysfunction Associated with Elevated Pulmonary Artery Pressure in Patients with Preserved Left Ventricular Ejection Fraction?

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**Background and Objectives:** The role of isolated left ventricular (LV) diastolic dysfunction (DDFx) as a cause of pulmonary hypertension is unclear. The objectives of our study were: 1) to determine the distribution of pulmonary artery systolic pressure (PAP) in patients with advanced LV DDFx and preserved LV ejection fraction (LVEF); 2) to examine whether the severity of LV DDFx is related to PAP.

**Methods:** The computerized database of the echocardiography laboratory at our institution was used to identify consecutive patients with preserved LVEF ( $\geq 50\%$ ), advanced LV DDFx (pseudonormal or restrictive LV filling patterns), and no significant left-sided valve disease, in whom PAP was estimated. Advanced LV DDFx was defined as mitral inflow E/A ratio  $\geq 1.0$  and echocardiographic evidence of elevated LV filling pressures (at least one of the following: pulmonary venous systolic/diastolic flow ratio [PV S/D]  $< 1$ , mitral inflow E/mitral annular e' ratio  $\geq 15$  [septal aspect of annulus], or E/e' ratio  $\geq 10$  [lateral annulus]).

**Results:** During the study period (44 months) – 407 patients fulfilled the inclusion criteria (age:  $70 \pm 10$  yrs; 43% male). PAP was  $< 35$  mmHg in 57 (14%) patients, 35-49 mmHg in 201 (49%) patients, 50-69 mmHg in 133 (33%) patients, and  $\geq 70$  mmHg in 16 (4%) patients. The PAP in patients with variable degrees of LV diastolic filling abnormalities is presented in the Table.

Diastolic parameters	Terciles of Diastolic Parameters			P for trend
	I	II	III	
Mitral inflow E/A ratio				
Tertiles (ranges)	$< 1.4$	1.4-1.7	$> 1.7$	
PAP	$43 \pm 11$	$46 \pm 11$	$48 \pm 13$	$< 0.0001$
E wave deceleration time (DT)				
Tertiles (ranges)	$< 170$	170-200	$> 200$	
PAP	$50 \pm 14$	$46 \pm 11$	$43 \pm 9$	$< 0.0001$
PV S/D ratio				
Tertiles (ranges)	$< 0.6$	0.6-0.8	$> 0.8$	
PAP	$51 \pm 14$	$46 \pm 13$	$44 \pm 10$	$< 0.0001$
Left atrial (LA) diameter				
Tertiles (ranges)	$< 4.3$	4.3-4.7	$> 4.7$	
PAP	$42 \pm 11$	$45 \pm 11$	$48 \pm 14$	0.01

Greater abnormalities of LV filling (increasing values of E/A ratio and LA diameter and decreasing values of DT and PV S/D ratio) were associated with higher PAP. Female gender was associated with higher PAP ( $P=0.002$ ) and there was an interaction between gender, the severity of DDFx, and its association with PAP. For example - PAP in the 3rd tertile of E/A ratio was higher in women ( $50 \pm 13$  mmHg) than in men ( $45 \pm 13$  mmHg).

**Conclusions:** PAP is significantly elevated in a large proportion of patients with advanced LV DDFx and preserved LVEF. More severe abnormalities of LV filling (reflecting more severe LV DDFx) are associated with higher PAP, suggesting a cause-and-effect relationship. Gender appears to modify this relationship, suggesting that women are more prone to developing pulmonary hypertension under these circumstances.

## Differential Effects of Afterload on Left Ventricular Long-Axis and Short-Axis Function: Insights from a Clinical Model of Patients with Aortic Valve Stenosis Undergoing Aortic Valve Replacement

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**Background and Objective:** The differential effects of left ventricular (LV) afterload on longitudinal versus circumferential ventricular mechanics is largely unknown. The objective of our study was to examine the changes in LV deformation early after aortic valve replacement (AVR) in patients with aortic valve stenosis (AS), using 2-D myocardial strain imaging.

**Methods:** Paired echocardiographic studies before and early [7±3 days] after AVR, were analyzed in 29 patients (age: 72±9 yrs, 45% men) with severe AS. All patients had normal LV ejection fraction (LVEF) and no segmental wall motion abnormalities. Long-axis (longitudinal) myocardial function was assessed from 3 apical views (average of 18 segments from 4-chamber, 2-chamber, and long-axis views). Short-axis (circumferential) function was assessed from mid-LV and apical short-axis views (separate averages of 6 segments in each view). Myocardial deformation (strain), strain rate (SR), and LV twist (counterclockwise systolic rotation of apex relative to mid-LV) were measured using the 2-D Velocity Vector Imaging software (VVI, Siemens, Mountainview, CA).

**Results:** AVR resulted in a significant drop in transaortic pressure gradients (peak and mean gradients dropped from 93±13 to 35±1 and from 55±12 to 18±6 mmHg, respectively, p<0.001 for both), whereas LV size and LVEF did not change early post-AVR. The changes in myocardial longitudinal and circumferential function are listed in the Table.

	Pre-AVR	Post-AVR	p
Peak systolic strain (%)			
Longitudinal	-12.1±2.9	-15.3±3.4	<0.001
Circumferential			
Mid-LV	-27.6±6.2	-24.1±3.9	<0.001
Apex	-31.3±8.4	-31.6±6.3	NS
Early diastolic SR (%/sec)			
Longitudinal	0.49±0.16	0.65±0.22	<0.001
Circumferential			
Mid-LV	1.31±0.58	1.06±0.27	<0.001
Apex	1.44±0.54	1.53±0.46	NS
LV twist (°)	3.1±2.6	5.3±2.7	<0.001

Following AVR: 1) longitudinal systolic strain increased, whereas mid-LV circumferential strain decreased; 2) longitudinal early diastolic SR increased, whereas mid-LV circumferential strain decreased; 3) LV twist increased.

**Conclusions:** In this clinical model of significant afterload reduction (patients with severe AS undergoing AVR), afterload reduction resulted in differential effects on LV long-axis versus short-axis function (systolic and diastolic) without a change in overall LV performance (LVEF). These findings provide new insights into the mechanical adaptation of the LV to chronic afterload elevation and its response to acute unloading.

## **Strain Imaging Improves the Accuracy of Dipyridamole Stress Echocardiography in Detecting Coronary Artery Disease**

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Stress echocardiography is a cost-effective tool for noninvasive diagnosis of coronary artery disease. Several physical and pharmacological stresses have been used in combination with echocardiographic imaging including exercise, dobutamine and dipyridamole. The use of dipyridamole stress echocardiography (DE) for the diagnosis of mild to moderate coronary artery disease is controversial since dipyridamole stress is believed to mainly produce flow heterogeneity rather than ischemia. Myocardial strain imaging provides quantitative segmental analysis of myocardial function. It has been shown recently that segmental analysis of systolic strain rate has prognostic information that is independent and incremental to standard wall motion score index in dobutamine echocardiography. We sought to determine whether segmental quantification of DE using strain imaging improves the accuracy of standard DE in detecting coronary artery disease as defined by stress perfusion scintigraphy. We performed DE and Th-201 gated SPECT simultaneously in 73 patients with suspected or known coronary artery disease. DE images were analyzed using customized software to measure peak systolic longitudinal strain. Fifty-one patients had abnormal perfusion by SPECT. Standard DE revealed wall motion abnormalities in 24 patients while 57 patients had abnormal longitudinal systolic strain. The overall concordance between SPECT and wall motion assessment was 57% ( $k=0.30$ ). The concordance between SPECT and DE using strain imaging was 80% ( $k=0.52$ ). Analysis of agreement between SPECT and DE using strain imaging by coronary territory ( $n=218$ ) revealed concordance of 82% at the LAD territory, 84% at the RCA territory and 68% at the circumflex territory. We conclude that myocardial strain imaging improves the accuracy of standard DE in detecting coronary artery disease. DE with strain imaging allows routine use of vasodilators in stress echocardiography.

## **Ultrasound Echocardiographic Assessment of Transmural Inhomogeneity of the Left Ventricular Contraction during the Heart Cycle**

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**Objectives:** The normal adult left ventricle (LV) is characterized by regional nonuniformity. A spiral structure of the fibers around the LV generates rotation of the LV during contraction and relaxation. The inhomogeneity of the human heart was investigated better with magnetic resonance tagging. We evaluated rotation and circumferential strain over the LV in normal subjects using novel echocardiography based signal processing method.

**Methods:** Circumferential strain and the myocardial rotation were calculated at 3 levels (apical, papillary muscle and mitral valve) from short-axis ultrasound echo cines in 11 normal subjects, utilizing speckle tracking imaging (UFI, GE Healthcare Inc., and Technion, Israel) and a novel signal processing method. This new method enabled high temporal and spatial resolution measurements of the myocardial velocities, so that the circumferential strain and the myocardial rotation were evaluated during a full heart cycle for 3 myocardial layers.

**Results:** A significant transmural difference was found in the myocardial rotation and circumferential strain. The rotation is larger in the endocardium and decreases towards the epicardium, while the apex and base rotate in counter directions (apex level: endocardium  $7.7\pm 3.4$  [deg], midwall  $5.0\pm 2.3$  [deg], epicardium  $3.6\pm 2.0$  [deg], Papillary muscle level: endocardium  $1.4\pm 2.4$  [deg], midwall  $1.8\pm 2.1$  [deg], epicardium  $2.3\pm 1.3$  [deg], mitral valve level: endocardium  $-4.4\pm 2.0$  [deg], midwall  $-1.9\pm 2.4$  [deg], epicardium  $-0.5\pm 2.1$  [deg]). Similarly, the circumferential strain is larger at the endocardium than at the epicardium. Furthermore, the circumferential strain is larger at the apex level than at the base level.

**Conclusion:** Transmural inhomogeneities of the left ventricular rotation and of the circumferential strain can be evaluated by echocardiography based method, and may serve as a simple, affordable and commonly available diagnostic modality.

## Successful Restoration of Function of Frozen/Thawed Isolated Rat Hearts

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**Introduction** Long-term organ preservation for transplantation may allow optimal donor-recipient matching with potential reduction in the incidence and severity of rejection. Complete cessation of metabolism may be obtained by freezing. Previous attempts to freeze intact mammalian hearts were limited to  $-3.6^{\circ}\text{C}$ , restricting tissue ice content to 34%. We hypothesized that our freezing method will allow recovery of function of the intact rat heart after freezing to  $-8^{\circ}\text{C}$ , a temperature at which most of the tissue water is frozen. **Methods** Isolated rat hearts were attached to a Langendorff apparatus. After normothermic perfusion, cold cardioplegia was induced followed by perfusion with a cryoprotecting agent. Hearts were then frozen to  $-8^{\circ}\text{C}$ ; thawed, and reperfused for 1hr. Recovery was tested by means of haemodynamic parameters, ATP and phosphocreatine content and electron microscopy scanning. **Results** All frozen/thawed hearts regained normal electric activity. At  $-8^{\circ}\text{C}$ , ice content was over 64%. The hearts maintained over 80% viability although energy stores, as represented by ATP and phosphocreatine were depleted compared to the control hearts. Integrity of muscle fibers and intracellular organelles after thawing and reperfusion, as demonstrated by electron microscopy, was maintained. **Conclusion** We demonstrate for the first time, the feasibility of functional recovery following freezing and thawing of the isolated rat heart while maintaining structural integrity and viability.

## **Repair of Ischemic Mitral Regurgitation: Comparison Between Flexible and Rigid Annuloplasty Rings**

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**Introduction:** The surgical treatment of ischemic mitral valve regurgitation (IMR) usually involves implantation of an annuloplasty ring. We compared results of mitral valve repair using a flexible or a rigid annuloplasty ring in patients with IMR undergoing coronary artery bypass grafting (CABG) and mitral valve repair.

**Methods:** One hundred and seventy patients underwent CABG with mitral valve annuloplasty. A flexible ring was implanted in 118 and a rigid ring in 52. Age and clinical profile, degree of left ventricular dysfunction and degree of MR (mean 3.2) were similar between both groups.

**Results:** Operative mortality was 9% in each group. Late follow-up (58+30 months for flexible and 14+7 months for rigid groups) was available in 88%. For the flexible and rigid ring group respectively: mean NYHA class was 1.9 and 1.6, with 33% and 14% in NYHA class III-IV (p=0.03). There was no difference in LV function or dimensions. Mean MR grade was 1.3 and 0.7 respectively for flexible and rigid ring groups (p=0.006). At late follow-up, 29 patients (34%) in the flexible group had residual MR of moderate degree or greater compared with 6 (15%) in the rigid group (p=0.03). TI gradient was 39 and 34 mmHg (p=ns), however the degree of reduction was greater in the rigid group (p<0.001). Late mortality was observed in 33 patients, all in the flexible group.

**Conclusions:** Clinical and hemodynamic results are better with rigid mitral annuloplasty rings compared to flexible rings. This may be due to ring design which dictates not only the annular diameter, but also annular configuration. Longer follow-up is needed to determine differences in survival.

## **Multiple Arterial Revascularization Using the Tangential K-Graft Technique**

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**BACKGROUND:** Complete arterial revascularization of the left ventricle with two conduits can be achieved even in triple vessel disease, using a T-configuration. However, kinks, tension and technical errors in constructing this end-to-side anastomosis can jeopardize the entire revascularization. Hypoperfusion and ignored diagonal branches are also troublesome. The tangential K-graft composite technique attempts to resolve these issues. We present our new surgical technique - Tangential (K-graft) and its intermediate clinical and physiological outcome.

**METHODS:** From July 2002 to September 2007, 194 consecutive patients underwent multiple arterial grafting using the Tangential K-graft technique. One end of the free graft is anastomosed end-to-side, the other sequential side-to-side anastomoses are constructed parallel to the coronary artery, and the other end of the free arterial conduit is anastomosed end-to-side to a diagonal or intermediate branch. After the left internal thoracic artery (LITA) is attached to the left anterior descending artery (LAD), a wide-open side-to-side free right ITA or radial artery (RA) to LITA anastomosis - resembling the letter "K" - is constructed.

**RESULTS:** Mean age was 66 (range 31 to 81). 74 patients (38%) were older than 70, 70 patients (36%) suffered from diabetes mellitus. 17 (8.8%) cases were emergent. Left ventricle ejection fraction (EF) ranged from 18% to 72% (mean  $52 \pm 13\%$ ). The number of distal anastomoses of the left ventricle per patient was averaged 3.9(mean). In 167patients (86 %) both IMA's and in 27 patients (17%) any IMA and RA were used. 15 patients (7.7%) were undergoing first-time reoperation. Eighteen patients (8.7%) were operated on by off-pump coronary arteries bypass (OPCAB) technique. Cross-clamp was  $79 \pm 13$  minutes, and bypass time was  $98 \pm 16$  minutes. Operative mortality was 1.55% (n=3). There was 1.55% (n=3) perioperative myocardial infarction, and one patient (0.79%) sustained permanent stroke. Deep sternal wound infection occurred in 4 patients (2 %) and six (3%) had superficial wound infections. During the follow-up in 27 arbitrary patients studied early postoperatively no of them had recurrent angina or intervention. Newly released 64-slice multidetector CT scanner verified patency in all 27 patients.

**CONCLUSIONS:** The K-grafting technique was found to be safe, and has the potential of increasing the ease and versatility with which the surgeon can perform total grafting to the left system using only two arterial conduits.

## Neontal Brain Protection Using Innominate Artery Cannulation for Continuous Brain Perfusion in Complex Aortic Arch Repairs

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**Introduction:** Traditionally, deep hypothermic circulatory arrest has been used when complex neonatal arch surgery was performed. Recently, the use of antegrade cerebral perfusion (ACP) has been advocated as means of brain protection. Two basic techniques have been used; either suturing a gortex shunt to the innominate artery, or direct cannulation of the ascending aorta with sliding of the cannula to the innominate artery when ACP is performed. Both techniques require additional surgical maneuvers to complete. For the last year we have been using direct innominate artery cannulation when ACP is performed.

**Materials and Methods:** During 2007, 6 neonates [Norwood (3), IAA VSD (2), severe coarctation (1)], and 1 child [intracardiac Willms tumor] underwent complex arch surgery using innominate artery cannulation and ACP. Median age was 1 week (range- 1week-3.5yrs), median weight was 3 kg (range 2.4-12kg). Innominate artery cannulation was accomplished using 8 french modified cannula inserted 3 mm into the innominate artery and directed into the ascending aorta enabling 200cc/kg flow. CPB times: mean 176±66 min, median 221 and ranges were 104-268 minutes. ACP times: mean 49±27 minutes, median 40 minutes, range 26-84 minutes.

**Results:** All patients survived the operation without neurologic damage, there were no clinical seizures. Innominate artery cannulation accommodated appropriate flows and de-cannulation was performed without complications.

**Conclusion:** Innominate artery cannulation and ACP is a safe and effective technique for brain protection in neonates and infants undergoing complex arch surgery.