

Research Article

## Assessment of The Regional and Global Myocardial Function by Myocardial Mri Tagging

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### Abstract

**Background:** Strain was so sensitive even for subclinical disorders with segmental analysis of wall motion and matching size of infarction in correlation with reduced strain percentage values according to the degree of involvement of each patient. On other side, strain is not specified only for ischemic heart disease but also implicated by no ischemic condition. CMR is the best modality for imaging LV systolic function and myocardial mass. **Methods:** A total of 20 patients with history of previous ischemic heart disease referred for cardiac magnetic resonance imaging because of suspected progression of coronary artery disease will be included in the study. Most patients who need mild sedation may be given 2-10 mg of diazepam by mouth. Since accurate peak detecting in the ECG is critically important for good-quality scans, several systems have been designed to provide superior detection. **Results:** P value for all examined segments which was significant measuring  $<0.001$  in this study (P value  $<0.05$  was considered significant) which confirm high sensitivity of strain in relation to CMR enhancement. **Conclusion:** myocardial tagging promises to continue to enhance our understanding of the mechanical complexities underlying the function of the normal and pathological heart.

**Keywords:** MRI, MRI tagging, Ventricular function, Regional wall motion and Strain analysis.

### Introduction

Cardiovascular disease is the leading cause of death in the United States. Each year, over 1.0 million U.S. residents have myocardial infarctions, roughly one-third of whom die<sup>(1)</sup>. Although there has been a dramatic reduction in the death rate due to cardiovascular disease over the past 40 years, it still accounts for 22% of all deaths. The socioeconomic importance of heart disease provides important motivation for development of new radiological tools for noninvasive imaging of the coronary arteries diseases and cardiac diseases in general<sup>(1)</sup>. While invasive imaging techniques, especially selective conventional coronary angiography, will remain essential for planning and guiding catheter-based and surgical treatment of significantly stenotic coronary lesions, the comprehensive and serial assessment of asymptomatic or minimally symptomatic stages of coronary artery disease (CAD) for preventive purposes will eventually need to rely on noninvasive imaging techniques<sup>(1)</sup>. Cardiovascular

imaging with tomographic modalities, including computed tomography (CT) and magnetic resonance imaging has great potential for providing valuable information<sup>(2)</sup>. The invention of magnetic resonance (MR) imaging in 1972 is associated with leaps and bounds, which is attributable to rapid technologic advances in several areas, including magnet technology, gradient coil design, radiofrequency (RF) technology, and computer engineering<sup>(3)</sup>. In conjunction with the fast technologic development, there has been phenomenal growth in the number of MR applications including the structural information as well as functional information of various kinds; such as blood flow, cardiac function, biochemical processes, tumor kinetics, and blood oxygen levels<sup>(3)</sup>. The importance for rapid data acquisition to minimize motion-induced artifacts and to maximize cardiac coverage during the myocardial passage of the contrast agent is a big hinder for firstpass perfusion MR imaging. Spatial undersampling methods, such as sensitivity

encoding (SENSE), can provide some of the necessary data acquisition speed but are associated with an SNR defaults<sup>(1)</sup>. Myocardial tagging is an MR imaging method that uses a sequence of RF pulses to presaturate thin planes of myocardium prior to imaging. In our study we will try to assess the myocardial tagging as a method of choice in the determinants of the regional and global myocardial function based on tracking of the myocardial wall motion aiming to achieve increased spatial and temporal resolutions while decreasing the imaging time.

### **Magnetic resonance anatomy of the heart**

For imaging of the heart with cardiovascular MR it is necessary to understand imaging planes in relation to both the axes of the body and the axes of the heart. This allows accurate description of cardiovascular anatomy and reliable standardization between the various cardiovascular imaging modalities. The transverse or axial plane is beneficial for morphology and the relationships of the four cardiac chambers and the pericardium. The connection between the ventricles and the great vessels can be analyzed by the sagittal images, while frontal or coronal images are most useful for investigation of the left ventricular outflow tract (LVOT), the left atrium, and the pulmonary veins<sup>(2)</sup>. The global positioning of the heart in the thorax depends on the optimal planes, which is more vertical in young individuals and more diaphragmatic in elderly persons. Whoever these images are sufficient for assessment of the overall morphology of the heart, quantitative measurements of wall thickness and cavity dimensions as well as functional data cannot be obtained accurately, since the planes are not perpendicular to the wall or the cavity, with the consequence that partial volume effects and obliqueness can introduce a large overestimation of the true dimensions<sup>(3)</sup>. A transverse or axial scout view at the level of the left ventricle (LV) is acquired initially to obtain the correct inclinations for imaging in the cardiac axes<sup>(4)</sup>. A new plane is used on this image running through the apex of the LV and the middle of the left atrioventricular (AV), mitral, valve. This yields the vertical long-axis (VLA) plane. A plane chosen on this image to transect the LV apex and the middle of the mitral ring yields the horizontal long-axis (HLA) plane. The short-axis (SA) plane can now be done perpendicular

to both the VLA and HLA. From a SA plane at the level of the mitral valves, the four-chamber view can be acquired (4Ch)<sup>(5)</sup>. The plane for the 4Ch view passes from the most superior mitral valve, "anterolateral" papillary muscle to the inferior angle of the right ventricle (RV) anteriorly, usually through the mid-point of the interventricular septum. A true-SA plane can now be done off the 4Ch view perpendicular to the interventricular septum. The anterior and inferior walls of the left ventricle are not exactly parallel, and no single plane is absolutely perpendicular to both walls, so the inclination of the short axis slices is not always simple. A compromise can be made, by using a short-axis plane oriented parallel to the mitral valve ring. Furthermore, when a SA stack is being prescribed for ventricular volume calculations, the imaging plane is often best positioned parallel to the AV valves, between the anterior and posterior AV grooves<sup>(6)</sup>.

### **Techniques for Myocardial Tissue Tagging**

The regional myocardial function can be quantified by insertion of invasive surgical implantation of physical markers within the myocardium itself and then tracking their motion using external imaging.

However, this method is impractical for clinical application<sup>(7)</sup>. The myocardial tissue tagging is introduced as a magnetic resonance based noninvasive imaging method for tracking myocardial motion<sup>(8)</sup>. Noninvasive markers, known as tags, are created within the tissue by locally induced perturbations of the magnetization with selective radiofrequency saturation of multiple, thin tag planes in a plane perpendicular to the imaging plane prior to image acquisition. These perturbations then produce regions of reduced signal intensity that appear as dark lines in the acquired images<sup>(9)</sup>. The spatial modulation of magnetization (SPAMM) is developed upon this technique to allow the application of tags in two orthogonal directions that, combined, form a grid of sharp intrinsic tissue markers<sup>(10)</sup>. Tags are typically created upon detection of the QRS complex of the electrocardiogram (ECG). The resulting tags then follow myocardial motion during the cardiac cycle, thus reflecting the underlying myocardial deformation. However, fading of the tag lines close to end-diastole, as a result of T1 tissue relaxation, has limited its application to

the systolic part of the cardiac cycle. Although spoiled gradient echo imaging is the commonly used sequence for tag generation at the widely available 1.5T magnets, recent studies<sup>(14)</sup> have proposed implementing steady state free precession (SSFP) to achieve better contrast and longer tag persistence. The tag lines can be applied in the short or long axis cardiac planes to facilitate three dimensional (3D) strain analysis<sup>(15)</sup>. Motion quantification techniques are divided into: a) Differential optical flow-based methods that track motion by assessment of the temporal and spatial changes of image intensity. b) Tag segmentation methods based on tracking of tag lines as in Find tags<sup>(16)</sup> and SPAMMVU<sup>(17)</sup> analysis. c) Phase-based analysis methods which are the bases for Harmonic phase (HARP) analysis<sup>(18)</sup>.

#### Measurement of Deformation:

The myofiber arrangement within the left ventricle changes gradually from a right-handed helix in the subendocardium to a left-handed helix in the subepicardium, passing by a circumferential arrangement in the mid wall. So; complex patterns of deformation and changes in shape are produced upon muscle contraction or relaxation. Tagging analysis allows quantification of these multiplanar regional deformations and, in turn, offers a dynamic multidimensional measure of myocardial function<sup>(19)</sup>.

**Strain:** Each element of strain is a measurement of the fractional or the percent change of length in a specific direction where  $L_0$  is the original

fiber length before tag deformation and  $L$  is the current length<sup>(19)</sup>.  $Strain = \frac{L - L_0}{L_0}$

In 3D space, myocardial strain can be represented by two different coordinate systems:

1) The radial-fiber-cross fiber coordinate system, which is based on the fiber direction within the myocardial tissue and thus, requires a precise knowledge of fiber orientation angles<sup>(20)</sup>.

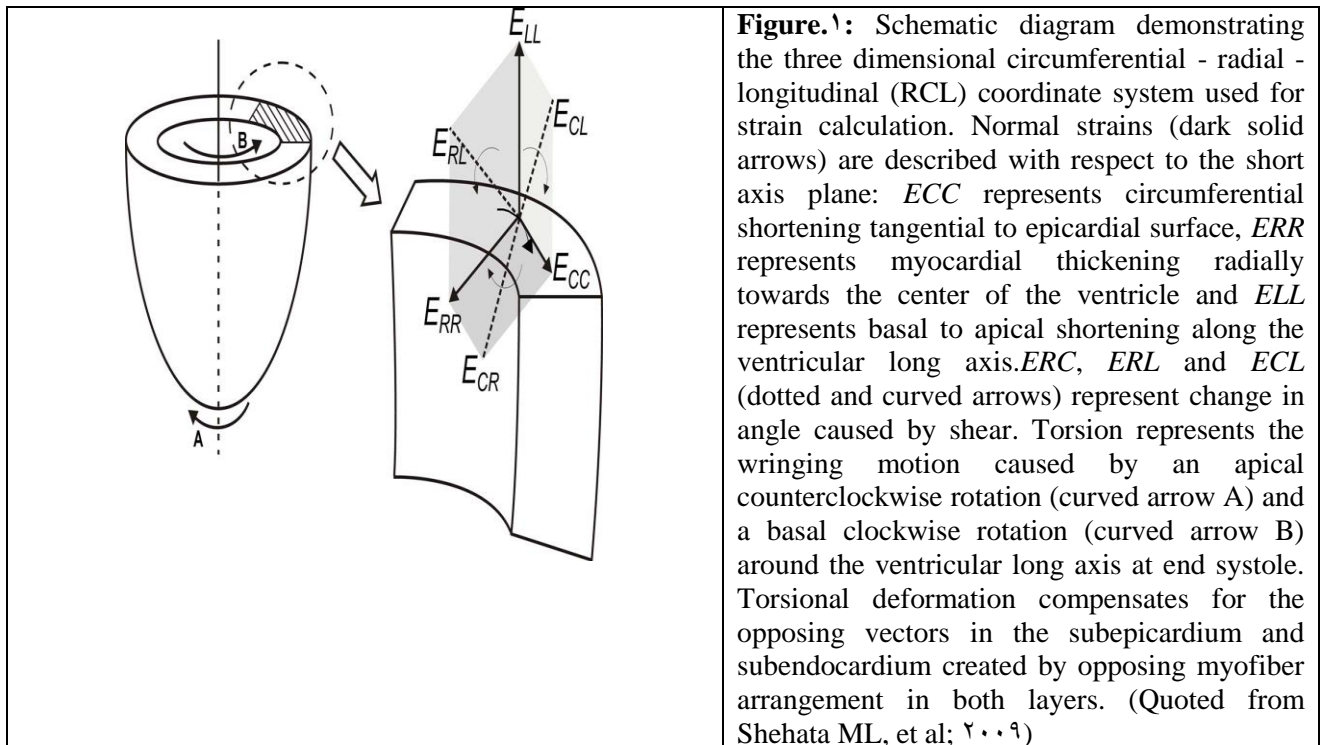
2) The radial-circumferential-longitudinal (RCL) coordinate system.

- Circumferential strain (ECC) describes the circumferential shortening in the short axis plane in a direction tangential to the epicardial surface.

- Radial strain (ERR) describes myocardial thickening in a radial direction towards the center of the ventricle.

- Longitudinal strain (ELL) represents the apical shortening along the ventricular long axis. The RCL coordinate system is based on the cardiac geometry<sup>(21)</sup>.

In the RCL coordinate system, ECC, ERR, and ELL represent the normal strain elements of myocardial deformation in 3D space, whereas ERC, ERL, and ECL represent strain changes that occur in a plane between two of these three initially orthogonal normal directions known as shear strains<sup>(22)</sup>. The later component, ECL, represents the shear in the circumferential - longitudinal plane and is usually referred to as torsion (Fig. 1.1).



**Strain Rate**<sup>(13)</sup> (SR) represents the time derivative of strain values or strain changes per unit time. Strain rate is calculated by taking the change in strain (S) between two time frames and dividing this by the time (t) difference between these two frames:

$$SR_{12} = \frac{st_2 - st_1}{t_2 - t_1}$$

LV diastolic function using strain rate analysis revealed significant reduction of regional diastolic strain rate, reflecting regional diastolic dysfunction, among individuals with asymptomatic LV hypertrophy compared to healthy controls<sup>(14)</sup>. The study revealed that early diastolic strain rate could be assessed in 80% (692/872) of all segmental analyses. The atrial-induced strain rate could be assessed in 32% (277/872) of all segmental analyses.

### Subjects and Methods

A total of 20 patients with history of previous ischemic heart disease referred for cardiac magnetic resonance imaging because of suspected progression of coronary artery disease will be included in the study. Exclusion criteria: Implanted pacemakers & defibrillators, automatic implanted cardiac defibrillator, aneurysm surgical clips and carotid artery vascular clamp. CMR is a long examination (20 to 60 minutes) that requires patient cooperation. Claustrophobia, which occurs in a small percentage of cases, can lead to the cancellation

of the study. Patients should be informed that they will have to remain motionless during the exam and that the system generates some loud noise. The patient should avoid excessive swallowing, and respiration should be as regular as possible, avoiding large diaphragm movements. Most patients who need mild sedation may be given 2-10 mg of diazepam by mouth. Since accurate peak detecting in the ECG is critically important for good-quality scans, several systems have been designed to provide superior detection. These systems use the spatial information in a vector cardiogram (VCG) to improve R-wave detection in the MRI environment. Similar to cardiac triggering, acquisitions can be triggered by the respiratory cycle. By use of a respiratory belt, excitation and signal readout is guided to the period of end-expiration. In cardiac MRI, this technique presumes that cardiac and respiratory gating are combined. All patients had undergone the MRI study. MR imaging were performed at the University Hospital Ain Shams in a 1.5-T scanner (Philips Medical Systems, Achieva).

Prior to imaging, an intravenous line were be introduced into the same arm (right or left) to allow for injection of Gd-DTPA (0.1 mmol/kg). The patients were placed supine and a cardiac coil positioned over the heart and four MR-compatible electrocardiographic electrodes will be applied for cardiac gating of the images. Many troubleshooting was occurring during the patient's examination including: Poor lead contact, unchecked electrode connections, respiratory motion non coordination, posterior lead placement, Switch leads and arrhythmias.

### Statistical analysis

Using SPSS program version 13, the following tests were done: Mean standard deviation, standard deviation, T test of independent samples and  $\chi^2$  = Pearson chi square test.

### Results

A total of 80 patients with history of previous ischemic heart disease referred for cardiac magnetic resonance imaging unit because of suspected progression of coronary artery disease will be included in the study. The patients were referred to the MRI unit at Ain Shams University Hospital from December 2011 to September 2012. This study was divided into five groups according to presence or absence of infarction, wall motion abnormalities and presence or absence of infarction. **Group one** with history of IHD, showed no wall motion abnormalities and no infarction corresponding to negative strain results. This group identified the capability of strain to be good precursor of subclinical disorders which may be of equivocal clinical diagnosis, yet the test is not established in the routine work. **Second group** showed wall motion abnormalities in patient presented with

IHD, no infarction were detected at post Gadolinium study. This group showed reduced overall systolic function with no definite element of fibrosis. However, strain results were positive confirming how strain is sensitive even in absence of infarction, but it is not specific for IHD. Strain may give positive results in other disorders as non IHD, cardiomyopathy. So, it may be of little value if the no definite element of precursors of infarction. **Third group** showed IHD patients with wall motion abnormalities and subendocardial infarction as well as positive strain results. This group shows sensitivity of strain with more characterization according to the involved vessel and related supplied segment of the myocardium. This more appreciated in cases which showed areas of microvascular obstruction which shows positive up slope of the strain curve instead of normal down slope (figure. 2). **Fourth group** showed IHD patients with wall motion abnormalities and subendocardial and transmural infarction as well as positive strain results. This group showed similar results to the previous one, in addition to more effect of combined infarction upon the strain percent values corresponding to the size of infarction. **Fifth group** showed IHD patients with wall motion abnormalities and transmural infarction as well as positive strain results. The transmural infarction may have a major effect upon the strain curves matching with size and affected area of transmural infarction. Table (1) shows P value for all examined segments which was significant measuring  $<0.001$  in this study (P value  $<0.05$  was considered significant) which confirm high sensitivity of strain in relation to CMR enhancement.

Table 1: Agreement between strain with CMR for significance.

		CMR				Test of sig.
		-ve		+ve		
		No	%	No	%	
Ant basal	-ve	24	73.2	2	17.7	FE p = 0.073
	+ve	14	37.8	10	82.3	
Ant mid	-ve	18	64.3	0	0.0	FE p = 0.001*
	+ve	10	35.7	22	100.0	
Ant apical	-ve	18	64.3	2	8.3	FE p = 0.000*
	+ve	10	35.7	22	91.7	
Ant-lat basal	-ve	22	71.1	0	0.0	FE p = 0.008*
	+ve	14	38.9	14	100.0	
Ant-lat mid	-ve	16	57.1	4	18.2	FE p = 0.099
	+ve	12	42.9	18	81.8	
Ant-lat apical	-ve	16	71.0	0	0.0	FE p = 0.002*
	+ve	10	38.0	24	100.0	
Inf-lat basal	-ve	20	72.0	0	0.0	FE p = 0.003*
	+ve	12	37.0	18	100.0	
Inf-lat mid	-ve	16	77.7	2	7.7	FE p = 0.004*
	+ve	8	33.3	24	92.3	
Inf-lat apical	-ve	16	77.7	0	0.0	FE p < 0.001*
	+ve	8	33.3	26	100.0	
Inferior basal	-ve	18	70.0	2	10.0	FE p = 0.018*
	+ve	12	40.0	18	90.0	
Inferior mid	-ve	14	73.7	2	7.1	FE p = 0.007*
	+ve	8	36.3	26	92.9	
Inferior apical	-ve	16	77.7	0	0.0	FE p < 0.001*
	+ve	8	33.3	26	100.0	
Ant-sept basal	-ve	20	72.0	0	0.0	FE p = 0.003*
	+ve	12	37.0	18	100.0	
Ant-sept mid	-ve	16	77.7	0	0.0	FE p < 0.001*
	+ve	8	33.3	26	100.0	
Ant-sept apical	-ve	14	73.7	0	0.0	FE p = 0.001*
	+ve	8	36.3	28	100.0	
Inf-sept basal	-ve	18	70.0	2	10.0	FE p = 0.018*
	+ve	12	40.0	18	90.0	
Inf-sept mid	-ve	16	71.0	2	8.3	FE p = 0.011*
	+ve	10	38.0	22	91.7	
Inf-sept apical	-ve	4	18.2	0	0.0	FE p = 1.000
	+ve	18	81.8	28	100.0	
Over all	-ve	302	70.9	18	4.0	$\chi^2$ p < 0.001*
	+ve	194	39.1	386	96.0	

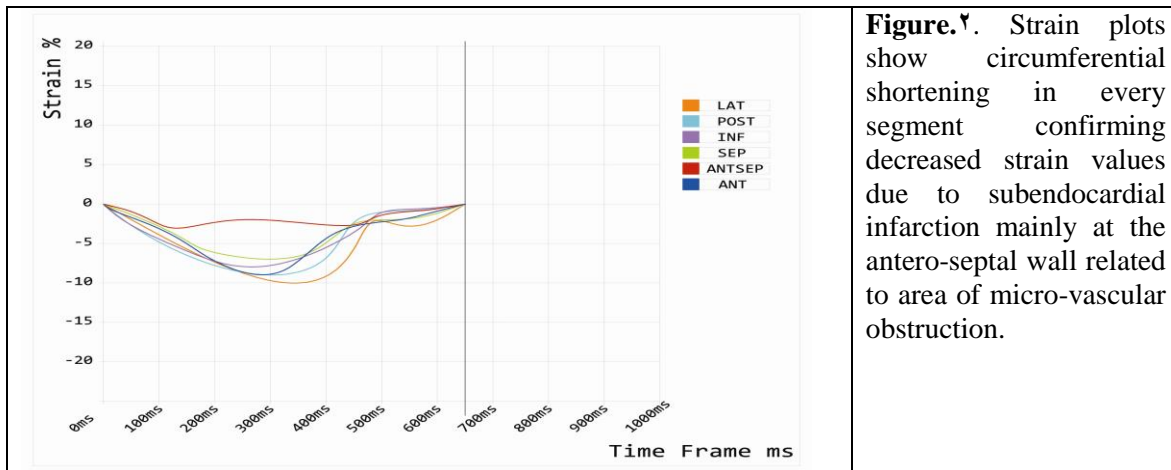
P: p value for comparing between the two studied group,

FE: Fisher Exact test,

$\chi^2$ : Chi square test

\*: Statistically significant at  $p \leq 0.05$





**Figure.2.** Strain plots show circumferential shortening in every segment confirming decreased strain values due to subendocardial infarction mainly at the antero-septal wall related to area of micro-vascular obstruction.

### Discussion

The importance of quantifying strain for detecting wall motion abnormalities in MI was recently demonstrated by Gotte et al.<sup>(14)</sup> Specifically, strain analysis (both radial and circumferential strains) of tagged images was directly compared with wall thickening in 13 normal subjects and 13 patients with a first anterior MI. Imaging was performed 3 to 4 months after MI and included short-axis cine CMR of the entire left ventricle and myocardial tagging in basal, mid-ventricular, and apical short-axis slices. Whereas both wall thickening and strain were significantly reduced in patients compared with normal subjects, only strain analysis of tagged images detected a significant difference in function when infarct-related segments were compared with remote segments within the patient group. For detecting infarct related segments, as defined by ECG and angiography, the sensitivity and specificity of wall thickening were 79% and 92%, respectively, whereas the sensitivity and specificity of strain were 92% and 99%, respectively.

The correlation with EF was also higher for both radial and circumferential strain than for wall thickening. These results suggest the potential importance of wall strain imaging more broadly, as well as the importance of accurate, reliable, and easy-to-use methods for strain imaging. In this study we used mid-wall LV circumferential strain (ECC) as a best parameter for assessment of the regional function which is matched with Shehatta et al., 2009<sup>(15)</sup> confirming that mid wall LV circumferential strain (ECC) is the most frequently computed parameter for quantifying regional

function. This particular strain measure is favored, in part, due to myocardial geometry contributing an abundance of tagging data around the mid wall myocardial circumference compared to along the width of radial wall thickness which is matched with Moore et al., 2000.<sup>(16)</sup>

Kuijjer et al.<sup>(17)</sup> showed that ECC data less sensitive to noise and more suitable for assessing the transmural strain gradient. In the normal heart, circumferential strain increases gradually from the base towards the apex. With respect to transverse regions, the greatest shortening is consistently observed in the anterior and lateral myocardial segments with the least deformation seen in the inferior wall. Additionally, ECC is seen to increase from epicardium towards endocardium, which is also confirmed in our study. Fonseca et al., 2003<sup>(18)</sup> and Oxenham et al., 2003<sup>(19)</sup> observed that aging was associated with little change in peak circumferential shortening when referring to expected normal patterns of regional myocardial deformation in correlation with aging effects. Relatively prolonged time to peak shortening in older compared to younger subjects was noted as well as aging related diastolic dysfunction was evident in the form of reduced peak rate of relaxation of ECC, which was confirmed in our study.

Due to the strong association between regional myocardial dysfunction and markers of prevalent coronary disease, multiple studies have used tagging to further explore its relation with myocardial ischemia. Rosen et al.<sup>(20)</sup> examined the relationship between regional coronary

perfusion reserve and regional myo-cardial function in a subset of 45 symptom-free MESA participants who underwent adenosine stress CMR perfusion scans. In this study, reduced coronary perfusion reserve was associated with reduced regional systolic function, which was evident in this study. Moreover, infarcted myocardium in the setting of microvascular obstruction demonstrated reduced regional systolic circumferential shortening in relation to the extent of obstruction which was evident in four cases in this study matching also with Gerber et al., 2008<sup>(70)</sup>. On other hand patients with minimal element of ischemia who proved by CMR to be free of infarction showed negative strain analysis results.

Another intermediate group which was free of infarction but had wall motion abnormalities and reduced overall systolic function; this group shows positive strain analysis. This is can be explained by fact that strain is sensitive but not specific for IHD. This condition was matched with Jeung et al.<sup>(71)</sup> told that strain is generally impaired in ischemic heart disease and cardiomyopathy, but the most diagnostically significant finding is the early identification of contractile dysfunction on the basis of longitudinal and circumferential strain reduction in patients with apparently preserved systolic function. Thus, strain impairment appears to be a sensitive and promising marker of subclinical disease, with the potential for improving patient management, this was evident in this study represented by higher sensitivity and lower specificity for tagging method. Myocardial tagging can assess the contractile reserve for ischemic patient in addition to accessibility for investigators to elucidate the mechanisms related to post-infarct ventricular remodeling. In particular, myocardial tagging is able to define changes in regional function involving the infarcted myocardium versus areas remote from the infarcted myocardium. Kramer et al.<sup>(72)</sup> found reduced circumferential segmental shortening in adjacent compared to remote myocardium, reflecting the probable effect of increased wall stress on LV remodeling which was evident in our study.

A comparative study between low-dose dobutamine stress echocardiography and MR tissue tagging (infusion of 0 and 10 -g/kg/min dobutamine) was performed by Kramer et al.,

2002<sup>(73)</sup>. The investigators showed that both techniques are sensitive and accurate for the prediction of functional improvement after reperfused myocardial infarction. The sensitivity and specificity of dobutamine MR tissue tagging were 82% and 79%, respectively, with an overall accuracy of 76%. The introduced results here shows little difference to our results where sensitivity and specificity were 90 % and 71%, respectively with the same overall accuracy of 76%. Gotte et al.<sup>(74)</sup> made a direct comparison between strain and wall thickening analysis, strain analysis was found to be superior in discriminating infarct from remote myocardium. In this study, the perfusion territory of the culprit vessel was considered the infarct region. For detecting dysfunctional myocardium, wall thickening analysis had a sensitivity of 79% and a specificity of 92%, whereas strain analysis showed a sensitivity of 92% and a specificity of 99%. The global ejection fraction correlated better with averaged myocardial strain than with wall thickening. In this study strain expresses the local myocardial deformation and was prone to important physiologic heterogeneities. Normal peak systolic strain is in the range of -10% to -20% for the circumferential components (fiber shortening) which was in agreement with Jeung et al., . We also agree with Jeung et al., 2012<sup>(71)</sup> that simple visual analysis of tag deformation is possible and provides an immediate impression of the regional abnormal contraction pattern with greater discrimination capabilities than are available with basic cine views. However, the post-processing procedures open the door to much more interesting quantitative analysis. This analysis may be performed on the reconstructed image itself using optical flow or some other tracking algorithm; however, this approach is quite cumbersome compared with the more convenient automatic (operator-independent) harmonic phase analysis method described by Osman et al.<sup>(75)</sup>

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