Role of Feature Tracking Myocardial Strain Analysis with Cardiac Magnetic Resonance in Cases of Hypertrophic Cardiomyopathy

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Abstract

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Background: The feature tracking (CMR-FT) method of cardiovascular magnetic resonance (CMR) allows for the measurement of global strain impairment using routinely acquired cine CMR images. **Aim of the study:** to evaluate the role of Cardiac magnetic resonance feature tracking analysis in detection of myocardial deformation in cases of hypertrophic cardio myopathy. **Study subjects:** A total number of 60 cases were included in our study, 30 of them had hypertrophic cardiomyopathy as diagnosed by echocardiography while the other 30 were normal (control cases). All of them were enrolled for MRI examination of the heart from January 2020 to April 2021. Tracking myocardial strain analysis with cardiac magnetic resonance were assessed among all cases. **Results:** global strain analysis by feature tracking cardiac magnetic resonance (FT-CMR) showed good capability in assessment of myocardial scarring and contractility disorders in cases of hypertrophic cardiomyopathy and enables myocardial deformation analysis without lengthening the imaging protocol or the timing of the CMR examination. The results yielded high sensitivity and specifity in the longitudinal and circumferential directions. global longitudinal strain was the most sensitive and specific value that yielded excellent significant correlation with the myocardial scar burden while radial strain was the least sensitive tool of assessment and showed wide variability. **Conclusion**: Cardiovascular magnetic resonance feature tracking approaches have evolved as a useful tool for assessing cardiovascular function quantitatively using numerous parameters such as strain, strain rate, and torsion.

Introduction:

Analysis of cardiac magnetic resonance feature tracking is steadily establishing itself as a reliable approach for assessing cardiovascular function quantitatively by assessing cardiac fibre deformation directly. Strain parameters determined from feature-tracking can detect minimal cardiac abnormalities before they appear clinically, enabling for early identification of primitivecardiomyopathies, in patients with heart failure of diverse etiologies, diagnosis of cardiac involvement in systemic disorders, detection of drug-related cardiac toxicity, risk stratification, and monitoring of treatment effects are all of great importance.**(1)**

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CMR is the gold standard for assessing cardiac morphology and function without the limitations of anatomical plane restrictions. Cardiac magnetic resonance feature tracking (CMR-FT), which was introduced in 2009, allows for the assessment of cardiac deformation on routinely obtained b-SSFP cine images. CMR-FT is widely utilized in cardiovascular research and is becoming more common in clinical practice. It has been used to examine a wide range of cardiovascular disorders and provides for comprehensive and reliable assessments of heart function.(2).

In the Western world, cardiovascular disorders are the main cause of death and morbidity. Early detection of primitive myocardial illnesses, cardiac involvement in systemic diseases, drug-related cardiac toxicity, risk stratification and monitoring of treatment effects in patients with heart failure of various etiologies all require assessment of cardiac function. Ejection fraction determination using various imaging modalities is considered the gold standard for assessing heart function. However, cardiovascular magnetic resonance feature tracking techniques have evolved as a more accurate tool for measurement of cardiovascular function in recent years with several parameters including strain, strain-rate, torsion, and mechanical dispersion. By directly assessing cardiac fibre deformation, this imaging technique offers exact assessment of ventricular and atrial mechanics.(1).

Heart function analysis is critical for diagnosing, risk stratifying, and monitoring treatment response in a variety of cardiac diseases. Left ventricular ejection fraction (LVEF), which is defined as the ratio of systolic output to end diastolic volume and measured using a variety of techniques including ventricular angiography, 2D and 3D echocardiography, cardiac single proton emission tomography, computed tomography, and cardiac magnetic resonance imaging, has traditionally been the gold standard for evaluating cardiac function (CMR). LVEF is used to assess the risk of sudden cardiac death (SCD) in patients with ischemic and non-ischemic cardiomyopathies, with LVEF less than 35 percent indicating the need for a primary preventive implanted cardioverter defibrillator (ICD). LVEF measures are suggested for routine cardiomyopathy screening, early detection of cardiac involvement in systemic immune-mediated diseases, and cardiac toxicity in cancer patients. Over the last decade, new imaging modalities for evaluating global and regional myocardial mechanics, such as echo and CMR myocardial strain, have gradually emerged as superior tools for evaluating global and regional myocardial mechanics, highlighting the limitations of LVEF, particularly in evaluating regional myocardial function and detecting early stage insidious cardiac disorders. (1).

Aim of the study:

The aim of the current study was to to evaluate the role of Cardiac magnetic resonance feature tracking analysis in detection of myocardial deformation in cases of hypertrophic cardio myopathy.

Subjects and Methods:

A total number of 60 cases were included in our study, 30 of them had hypertrophic cardiomyopathy as diagnosed by echocardiography while the other 30 were normal (control cases). All of them were enrolled for MRI examination of the heart from January 2020 to April 2021.

Inclusion criteria:

- Patients diagnosed with hypertrophic cardiomyopathy by echocardiography.

Exclusion criteria:

- Patients with absolute or relative contraindications to magnetic resonance imaging e.g. cardiac pacemaker, intra-ocular metallic foreign body, claustrophobia, etc. ….
- Any clinical morbidity contra-indicating anesthesia induction during the examination in un-cooperative patients where sedation is a must.

METHODS

Patient preparation and Set up:
Prior to the test, no specific instructions are needed. Medications should not be stopped. A brief medical history was obtained first. The patients were next evaluated for MR imaging contraindications. All nylon or metal-containing underwear was removed. Static electricity may produce artefacts in the former, and picture deterioration in the latter.

Height, weight, heart rate, and rhythm were all measured prior to the test. Each patient's or relative's participation in the research was thoroughly described. To assess patients' capacity to hold their breath for a lengthy period of time in cooperative patients, they were asked to take a deep breath and then hold it without pushing (i.e., Valsalva maneuver).

Magnetic Resonance Imager:
Magnetic resonance imaging studies were performed using a Philips Achieva, (1.5 Tesla) & Siemens Aera, Germany (1.5 Tesla) by using a phased-array cardiac coil.

Patient position:
All of the patients were evaluated head first in the supine posture. To alleviate back strain and ensure the patient's comfort, the patient's knees and legs may be raised.

The patient wears headphone provided with the MRI equipment to minimize repeated gradient noise while also hearing the breath hold instructions.

ECG Lead positioning:
On the anterior chest wall, four ECG pads were placed: the first is 1 cm to the left of the xyphisternum, the second and third are aligned at 90° to each other, with the first electrode forming the right angle and the distance between the electrodes 15 cm. The fourth electrode is positioned underneath the first.

The ECG leads were attached. The green lead to the first pad, the red lead to the second pad, the white lead to the third pad, and the black lead to the fourth pad.

The QRS complex is then examined on the MRI monitor, and the lead sites are adjusted as needed. The MRI monitor also detects the patient's heart rate, which is used to calculate the cardiac frequency, which should be similar to the patient's heart rate.

The Coil:
The cardiac coil utilised was the SENSE (sensitivity encoding) (6 element phased-array coil, receive only). It is made composed of a stiff bottom section and a flexible top section. Two phased-array coil elements are found in the bottom portion, while four phased array coil elements are found in the top part.

The coil is placed on the patient's chest such that the top portion of the coil's midline is just below the sterno-clavicular notch and the lower part is underneath the patient. Four straps are used to securely secure it to the patient. The magnet's connection is inspected.

The Respiratory Sensor:

Under the coil, the respiratory sensor is positioned over the largest region of respiratory movement (abdomen or thorax). The sensor is secured with a strap. As the respiratory wave emerges on the monitor, the respiratory signal is examined and utilised to identify the patient's breathing rhythm and synchronise breath hold instructions with the patient's capabilities.

Sedation and anesthesia:

In patients younger than five years old and un-cooperative ones, we used either general anesthesia or chloral

Cardiac MR Examination:

Imaging protocol: The patients done a routine MR examination that included the following steps:

1. Scout images were yielded in orthogonal orientations for planning of the long-axis and short-axis views.

2. Functional cine images (essential to measure ventricular volumes and functions as well as serves as raw data for post-processing feature tracking myocardial strain analysis): In short axis view, two and four chamber views, electrocardiographic gated, steady state free precision (SSFP) sequences were used. The following settings were used to produce slices during repeated breath-holds 1 cm apart:

TR/TE: 4.4/2.5   FOV: 300
Phases: 25   NSA: 1
Matrix: 128x128   Band width: 125 kHz
Flip angle: 15°   Scan Time: 0.07-0.12 sec.
Slice thickness: 8mm   Slice number: 8-11

3. Standard delayed gadolinium enhancement imaging (mandatory to quantify scar burden):

Starting 10–15 minutes after intravenous injection of gadolinium chelate contrast material (0.1– 0.2 mmol/kg), performed after utilising look locker to identify the optimum period of delay by employing Segmental inversion recovery balanced turbo field echo (IR-b-TFE). The following settings were used to collect contrast-enhanced photos in the same orientation as the cine images (short axis plane) and at least one of the long axis planes:

TR/TE: 3.8/1.86   FOV: 300
TI: 260-350   NSA: 1
Matrix, 128x128   Bandwidth: 125 kHz
Flip angle: 15°   Scan Time: 9-15 sec.
Slice thickness: 8mm   Slice number: 8-11

Image analysis:

Images (DICOM) were transferred to a workstation equipped with a dedicated cardiac software package for further analysis:

Statistical analysis:

1) Assessment of the ventricular volumes and function:

With the use of commercially available software, global functional parameters were obtained from cine MRI. During systole and diastole, the endocardial boundaries of both ventricles were manually drawn using short axis pictures. Simpson's rule was used to determine the LV end-diastolic volume (EDV) and end-systolic volume (ESV).Subsequently, stroke volume (SV) and ejection fraction (EF) was calculated using EDV and ESV values.

The ventricular ejection fraction is classified into: **Normal**: 55-75%, **Border line**: 40-54% and **low**: <40%.

2) Assessment of associated myocardial scarring:-

It is a crucial factor in predicting prognosis in such cases. There are many causes and underlying etiological factors precipitating myocardial ischemia and scarring including increased myocardial mass and hence more demand of vascular supply in addition to muscular hypertrophy affecting the wall of the feeding coronary arteries inducing luminal attenuation, subsequent vascular compromise and ischemia.

3)Feature tracking myocardial strain analysis:

Circumferential, longitudinal and radial myocardial strain analysis of the different myocardial segments were derived from the routine short axis cine images by post processing with the aid of special dedicated commercially available software. It acts as a quantitative assessment of segmental myocardial contractility.

4)Assessment of associated congenital anomalies:

Through the detailed visual assessment of the cardiac anatomy in the different planes and different pulse sequences.

Results:

The study group included 60 patients (36 male and 24 female subjects) and the results were analyzed as follows:

I- Descriptive statistics

- tables 1, 2 , 3 illustrate the descriptive statistics across the cases and the normal control subjects including:

o Number of subjects.

o Minimum, maximum and mean values of the scar percentage and myocardial strain analysis in the three different directions (longitudinal, circumferential and radial).

o Standard deviation.

Tables 4 describes the relation between the global myocardial strain analysis in HCM cases versus normal control subjects which showed high significance (P-value less than 0.01) regarding the strain values in peak longitudinal and peak circumferential directions while being insignificant in the radial direction.

Correlation was analyzed across the HCM cases (30 cases included in our study) between the scar burden of the myocardium and the myocardial strain analysis in the three different directions using Pearson's correlation. It revealed significant correlation (p-value equals 0.01) between the global longitudinal peak strain analysis and total myocardial scar burden while being of less significance in the other two directions (0.216 and 0.307 in the circumferential and radial directions respectively) as detailed in the table 5.

The three scatter 1, 2, 3 plot curves illustrate the inverse relationship between the myocardial strain analysis in the three different directions and the myocardial scar burden i.e. as the scar burden increases the global strain values decrease, more apparent and significant in the longitudinal direction (putting in consideration that the different directions of the curves in both longitudinal and circumferential directions as compared with the radial one is due to the negative values normally given for the former two directions based on their orientation during myocardial deformation and contraction).

The ROC (receiver operating characteristic) curves 4 analyze and illustrate the sensitivity and specifity of the three directions of the myocardial strain analysis in terms of assessing the area under curve (AUC).It proved to be highly significant (sensitive and specific) along the longitudinal direction, significant in the circumferential strain while non- significant only in the radial direction

Table (1) illustrating the descriptive statistics across the cases.

	N	Minimum	Maximum	Mean	Std. Deviation
TOTAL SCAR	30	.6	27.0	9.853	7.2570
GLOBAL PEAK LONGITUDINAL STRAIN	30	-18.170695176470588	-3.917857529411760	-12.202660611764705	3.569526305728644
GLOBAL PEAK CIRCUMFERENTIAL STRAIN	30	-30.584957937500008	3.207524812500000	-19.083212447916672	5.568298374788155
GLOBAL PEAK RADIAL STRAIN	30	-2.881851411764710	70.201863058823530	42.289408609803920	15.076100084629338

Table (2) illustrating the descriptive statistics across the normal control subjects

	N	Minimum	Maximum	Mean	Std. Deviation
TOTAL SCAR	0				
GLOBAL PEAK LONGITUDINAL STRAIN	30	-24.196054117647060	-20.534828235294118	-22.499878857843140	.982393651714478
GLOBAL PEAK CIRCUMFERENTIAL STRAIN	30	-24.675300000000004	-19.833750000000000	-22.311361754166670	1.255772529516027
GLOBAL PEAK RADIAL STRAIN	30	40.827341176470600	48.339269411764710	44.284378019607840	2.300077121308407

Table (3) illustrating the descriptive statistics across the whole study population.

	N	Minimum	Maximum	Mean	Std. Deviation
GLOBAL PEAK LONGITUDINAL STRAIN	60	-24.196054117647060	-3.917857529411760	-17.351269734803918	5.804706446398666
GLOBAL PEAK CIRCUMFERENTIAL STRAIN	60	-30.584957937500008	3.207524812500000	-20.697287101041670	4.320268845235711
GLOBAL PEAK RADIAL STRAIN	60	-2.881851411764710	70.201863058823530	43.286893314705885	10.739199423683411

Table (4) illustrating the Hypothesis Test Summary

	Null Hypothesis	Test	Sig.^{a,b}	Decision
1	The distribution of GLOBAL PEAK LONGITUDINAL STRAIN is the same across categories of SUBJECTS.	Independent-Samples Mann-Whitney U Test	<.001	Reject the null hypothesis.
2	The distribution of GLOBAL PEAK CIRCUMFERENTIAL STRAIN is the same across categories of SUBJECTS.	Independent-Samples Mann-Whitney U Test	<.001	Reject the null hypothesis.
3	The distribution of GLOBAL PEAK RADIAL STRAIN is the same across categories of SUBJECTS.	Independent-Samples Mann-Whitney U Test	.478	Retain the null hypothesis.
a. The significance level is .050.				
b. Asymptotic significance is displayed.				

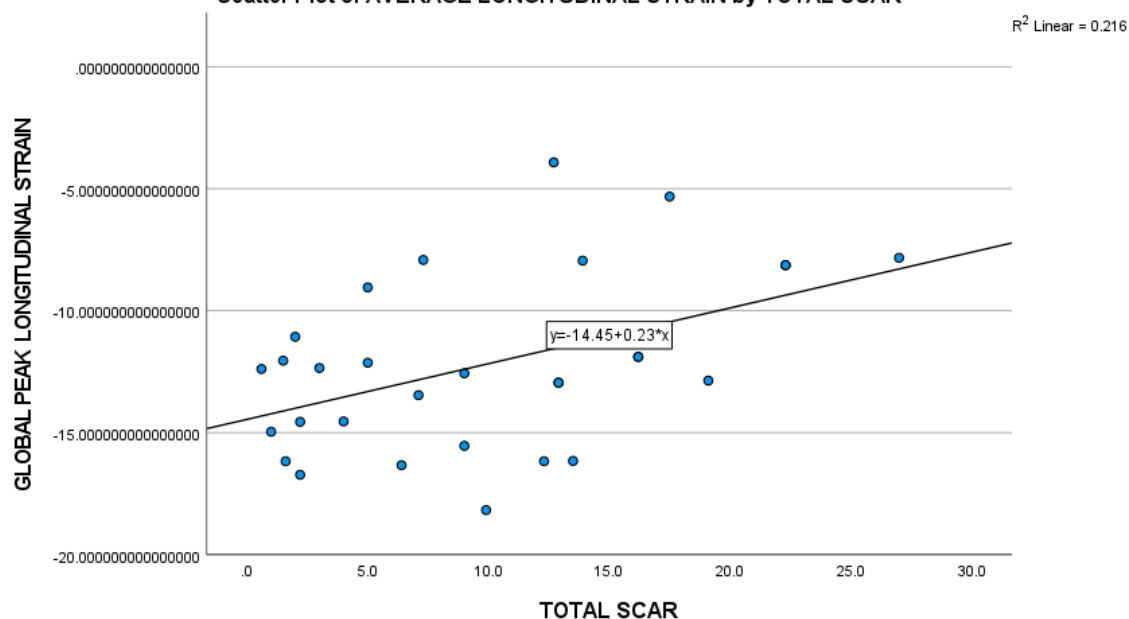**Table (5) Correlation was analyzed across the HCM cases**

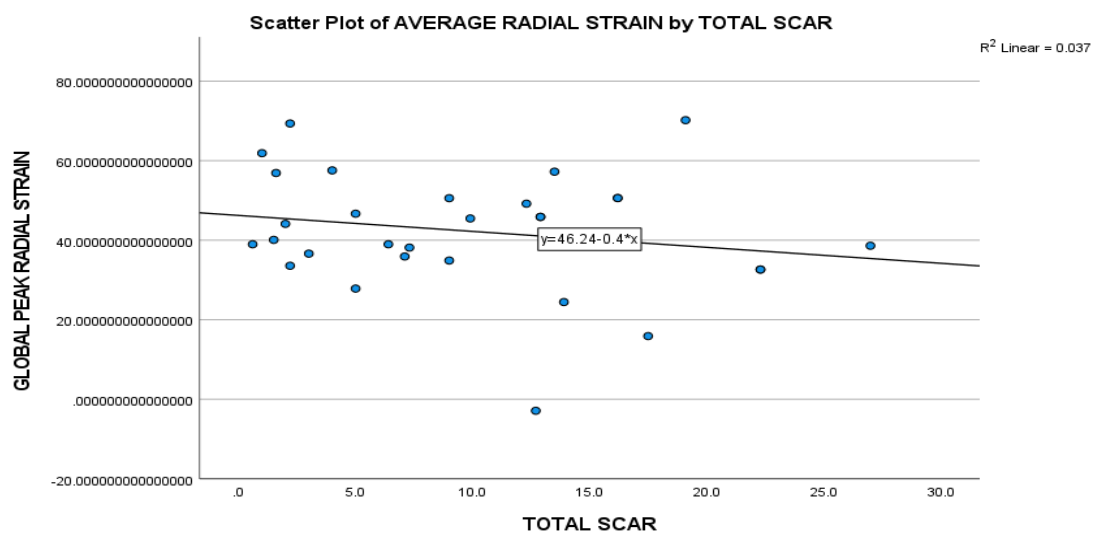|		TOTAL SCAR	GLOBAL PEAK LONGITUDINAL STRAIN	GLOBAL PEAK CIRCUMFERENTIAL STRAIN	GLOBAL PEAK RADIAL STRAIN
TOTAL SCAR	Pearson Correlation	1	.464**	.233	-.193
	Sig. (2-tailed)		.010	.216	.307
	N	30	30	30	30

**. Correlation is significant at the 0.01 level (2-tailed).

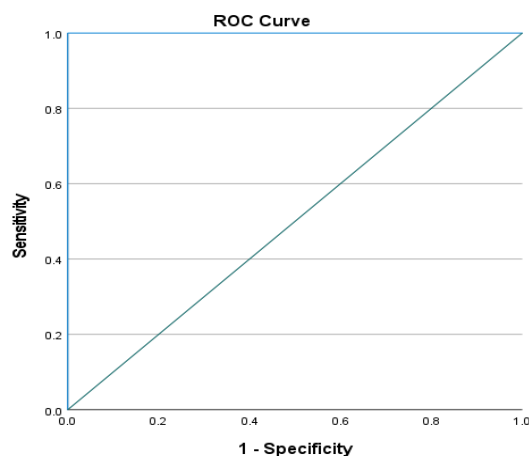

Scatter Plot of AVERAGE LONGITUDINAL STRAIN by TOTAL SCAR

Scatter Plot of AVERAGE CIRCUMFERENTIAL STRAIN by TOTAL SCAR

Scatter Plot of AVERAGE RADIAL STRAIN by TOTAL SCAR

R^2 Linear = 0.037

$y=46.24-0.4*x$
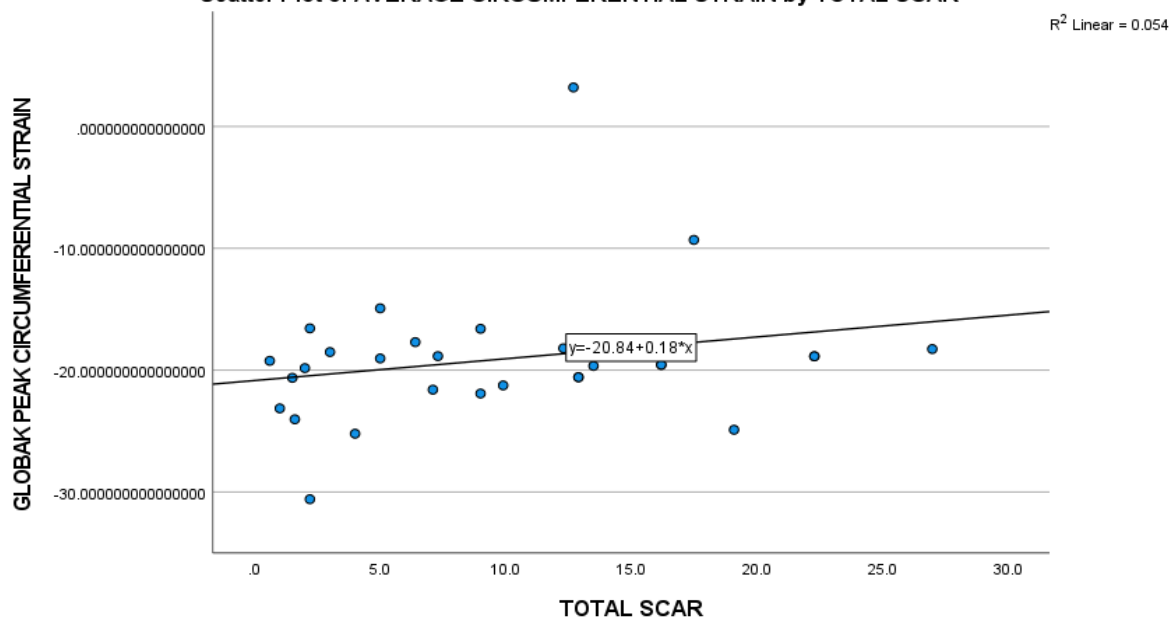
ROC Curve

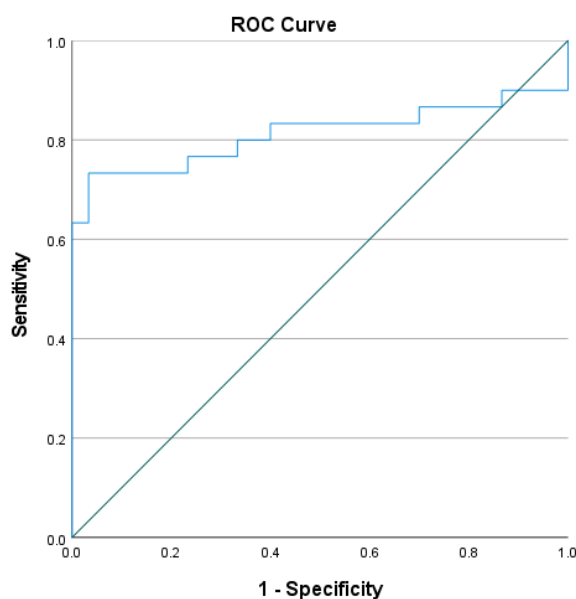## ROC curve of the longitudinal strain.

Area Under the Curve

Table (4):Test Result Variable(s):   GLOBAL PEAK LONGITUDINAL STRAIN

Area	Std. Error[s]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
1.000	.000	.000	1.000	1.000

a. Under the nonparametric assumption

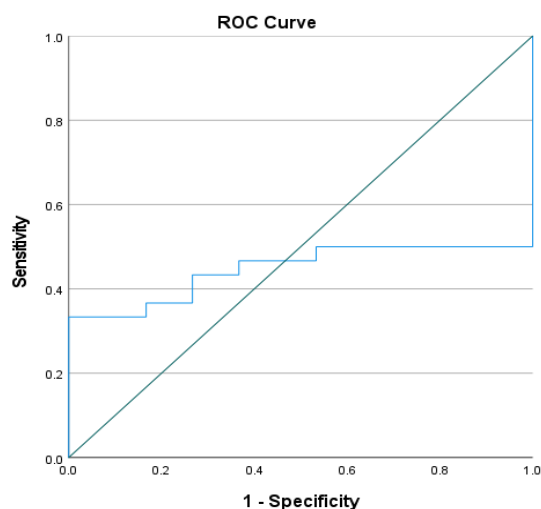ROC curve of the circumferential strain.

Area Under the Curve

Test Result Variable(s):   GLOBAL PEAK CIRCUMFERENTIAL STRAIN

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.812	.064	.000	.687	.937

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5
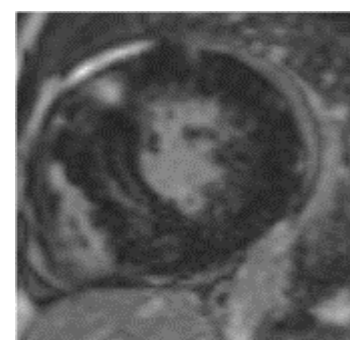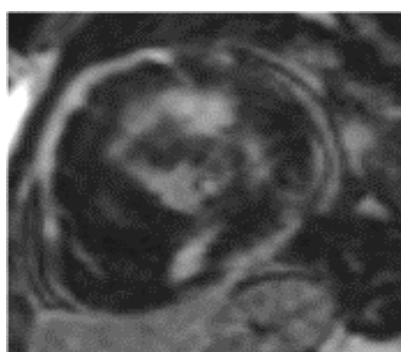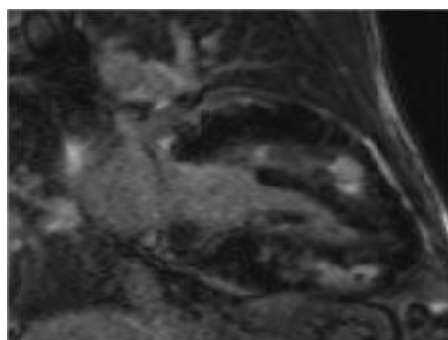

ROC curve of the radial strain.

Area Under the Curve

Test Result Variable(s): GLOBAL PEAK RADIAL STRAIN

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.447	.085	.478	.279	.614

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

a. LGE 2 chamber view. b. LGE short axis view at apical level. c. LGE short axis view at basal level.

Fig. 1 -LGE 2 chamber and short axis images at different myocardial levels showing patchy hyperenhancement keeping with scattered myocardial fibrosis
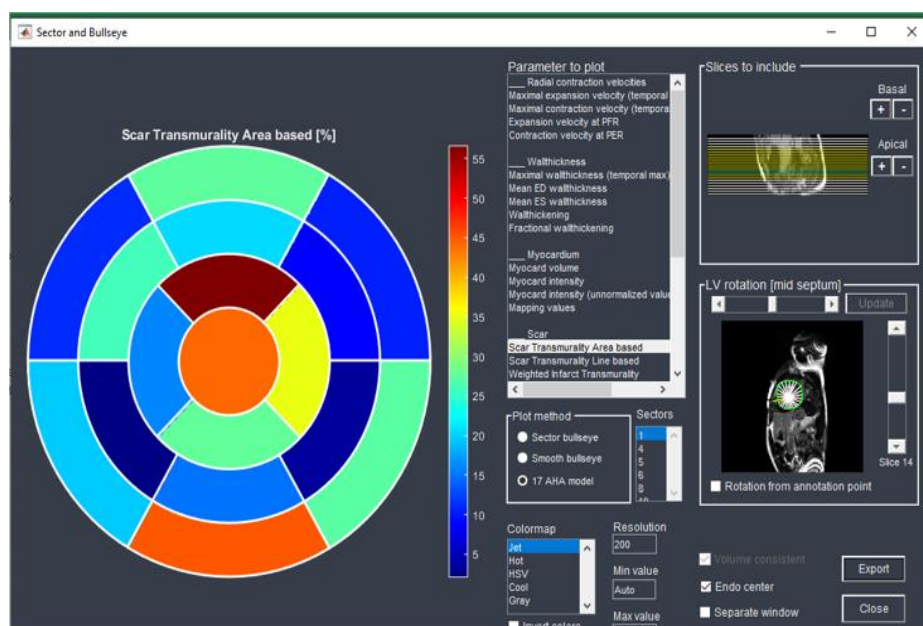

Fig 2. 69-17 segment model of the American heart association (AHA) bull's eye representation shows the distribution of scar in the different myocardial segment of the left ventricle
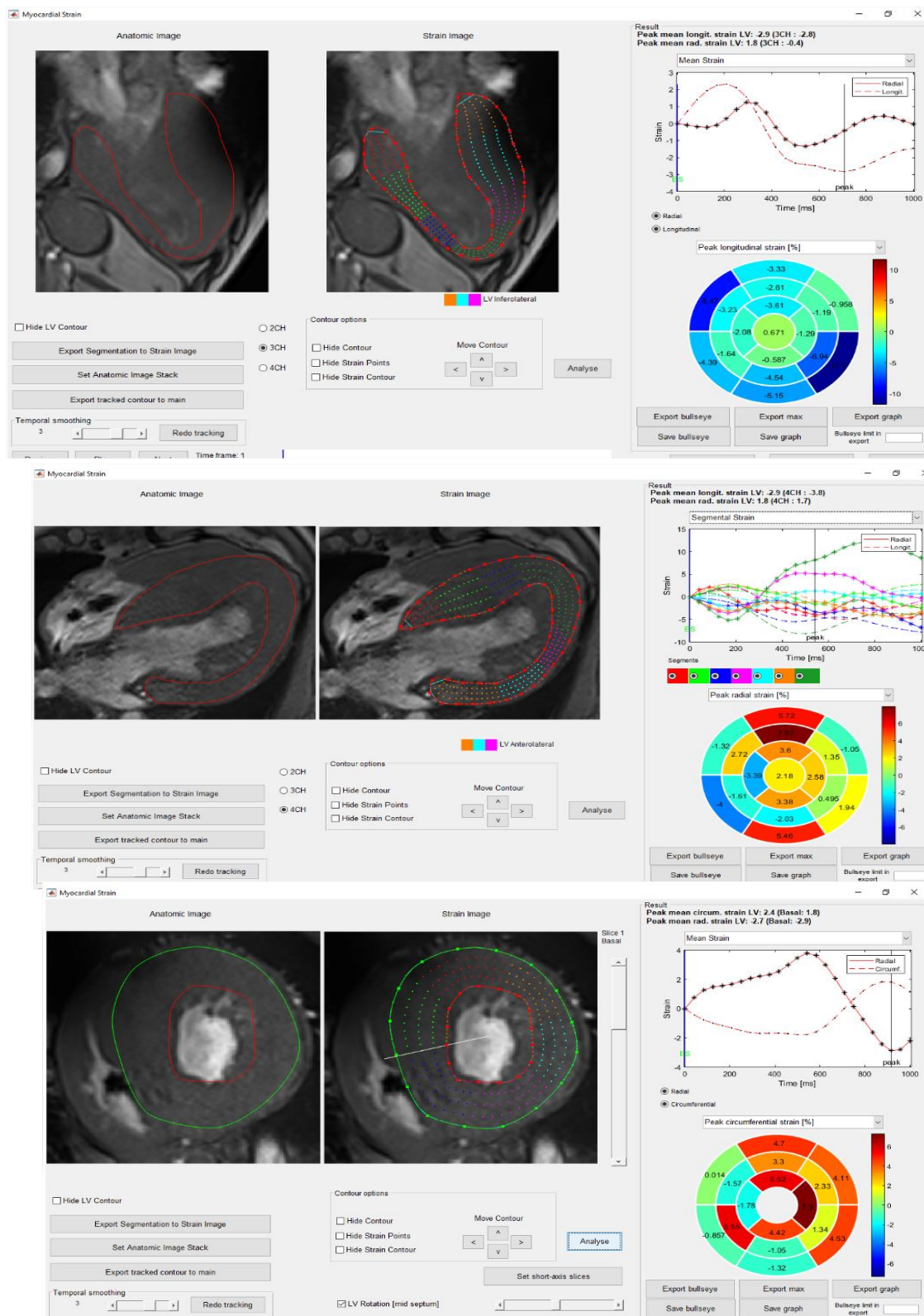
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Fig.3-Illustrative feature tracking images in longitudinal, radial and circumferential directions showing variable degree of impaired strain analysis in the different myocardial segments with overall results being significant after analysis in comparison with the scar burden, especially in the longitudinal direction

Case study: 28 years old male patient diagnosed as hypertrophic cardiomyopathy by echocardiography presented with recurrent cardiac arrest and ventricular arrhythmia, **CMR Findings:** Concentric LV hypertrophy, On late gadolinium hyper-enhancement images: Multiple scattered patches of enhancement are noted.

Discussion

Hypertrophic cardiomyopathy is a primary cardiac illness defined by increased ventricular wall thickness, myocyte enlargement and enhanced myocardial fibrosis that is unrelated to any underlying condition. The clinical signs of HCM vary greatly amongst people, with symptoms ranging from mild exertional difficulty in breathing to heart failure. Many patients' clinical courses are punctuated by arrhythmias, both atrial and ventricular, thromboembolic events, and sudden cardiac death, all of which enhance morbidity and mortality from HCM.(3)

During cardiac contraction, vectors in the radial, circumferential, and longitudinal directions may be used to describe myocardial deformation. Positive strain values are recorded in the radial direction owing to thickening in the radial direction during ventricular contraction, while negative strain values are found in the circumferential and longitudinal directions during systole.(4)

Following the various directions in which the myocardium deforms may be used to determine longitudinal, circumferential, and radial strain. The longitudinal shortening from the base to the apex is measured by longitudinal strain, which is a negative metric. Radial strain is the radially directed myocardial deformation towards the LV cavity's centre, which represents LV thickening and thinning motion throughout the cardiac cycle; positive values indicate thickening and thinning motion. Circumferential strain is the shortening of LV myocardial fibres around the circular perimeter as viewed from a short-axis perspective, and it is denoted by a negative sign.(5)

Due to the decreased contractility of myofibroblasts, which take lace instead of the myocytes following an infarct, scar tissue causes locally altered strain behaviour of the myocardium.

Due to the lower ability of contraction of myofibroblasts, which replace myocytes following an infarction, scar tissue causes locally altered strain behaviour of the myocardium.

In the last two decades, various techniques for assessing global and local myocardial deformation, such as myocardial tagging tissue displacement encoding with stimulated echoes and strain encoded imaging, have evolved. (4)

All of these approaches, with myocardial tagging as the gold standard for assessing myocardial strain, have one thing in common: sequences must be obtained in addition to an already lengthy clinical protocol. Using routinely obtained steady-state free precession (SSFP) cine sequences as input, myocardial feature tracking (FT) was introduced for myocardial strain assessment. Myocardial boundaries can be recognised and movement of myocardial segments tracked during the cardiac cycle using optical flow methods or non-rigid image registration and segmentation algorithms.(4)

This study examined global and segmental myocardial deformation indices using feature tracking cardiac magnetic resonance (FT-CMR) in patients with hypertrophic cardiomyopathy suffering from variable degrees of myocardial affection in terms of contractility disorders and scarring. The feasibility of using strain analysis by CMR for quantitative detection of regional and global myocardial motion abnormalities, contractility disorders and scarring.

According to our results, global strain analysis by feature tracking cardiac magnetic resonance (FT-CMR) showed good capability in assessment of myocardial scarring and contractility disorders in cases of hypertrophic cardiomyopathy and enables myocardial deformation analysis without lengthening the imaging protocol or the timing of the CMR examination. The results yielded high sensitivity and specifity in the

longitudinal and circumferential directions (as illustrated in the previous chapter throughout the ROC curves). Furthermore, it showed significant correlation (yielding a P value of 0.01) between global strain analysis in the longitudinal vector direction and the scar burden.

In our study global strain analysis proved to be of better reproducibility unlike the segmental one which agreed with the study done by **(6)**.

Cavus et al., (7) CMR at 1.5 T was used to study 144 HCM patients and 16 healthy controls. Using widely accessible software, analyses were conducted on regular steady-state free precession cine (SSFP) CMR data. Global left ventricular (LV) strain was assessed as longitudinal (LV_{LAX}-GLS), circumferential (LV_{LAX}-GCS) and radial strain (LV_{LAX}-GRS) on long-axis (LAX) and as LV_{SAX}-GCS and LV_{SAX}-GRS on short-axis (SAX). **(4)** has studied 46 patients known CAD (diagnosis of CAD since > 7 month), ischemic scars (> 4 months old) and 24 healthy controls. Both studies found significantly decreased global strain values in cases as compared to healthy controls which agrees with our study results.

In our study, global longitudinal strain was the most sensitive and specific value that yielded excellent significant correlation with the myocardial scar burden while radial strain was the least sensitive tool of assessment and showed wide variability. These results agree with those yielded from the study done by

Faragli et al., (7) which included animal models in the study.

Furthermore, the study done by **spath et al., (9)** on cases of aortic stenosis yielded that GLS correlates with established markers of myocardial fibrosis.

Conclusion

Feature tracking cardiac magnetic resonance has good capability in assessment of myocardial scarring and contractility disorders in cases of hypertrophic cardiomyopathy and enables quantitative analysis of myocardial deformation without lengthening the imaging protocol or the CMR examination The GLS was the most sensitive, specific and significant correlator with myocardial scar burden which agrees with previous studies as being an important indicator of myocardial disorder.

Limitations

There are study limitations that must be acknowledged, some of which is that it is a relatively new technique with still deficient similar studies to be compared with, also the unequal gender distribution with more males included in the study.

In addition, more studies with larger number of patients may be needed for confirmation of our results.

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