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*World J Cardiol* 2017 April 26; 9(4): 296-395



### MINIREVIEWS

- 296 Pacemaker recycling: A notion whose time has come  
*Runge MW, Baman TS, Davis S, Weatherwax K, Goldman E, Eagle KA, Crawford TC*
- 304 Coronary artery disease detection - limitations of stress testing in left ventricular dysfunction  
*Bomb R, Kumar S, Chockalingam A*
- 312 Feature tracking cardiac magnetic resonance imaging: A review of a novel non-invasive cardiac imaging technique  
*Rahman ZU, Sethi P, Murtaza G, Virk HUH, Rai A, Mahmood M, Schoondyke J, Albalbissi K*

### ORIGINAL ARTICLE

#### Basic Study

- 320 Dissection of Z-disc myopalladin gene network involved in the development of restrictive cardiomyopathy using system genetics approach  
*Gu Q, Mendsaikhan U, Khuchua Z, Jones BC, Lu L, Towbin JA, Xu B, Purevjav E*

#### Retrospective Cohort Study

- 332 Blood conservation pediatric cardiac surgery in all ages and complexity levels  
*Karimi M, Sullivan JM, Linthicum C, Mathew A*
- 339 Bilateral vs unilateral internal mammary revascularization in patients with left ventricular dysfunction  
*Popovic B, Maureira P, Juilliere Y, Danchin N, Voilliot D, Vanhuyse F, Villemot JP*

#### Retrospective Study

- 347 QT prolongation is associated with increased mortality in end stage liver disease  
*Kim SM, George B, Alcivar-Franco D, Campbell CL, Charnigo R, Delisle B, Hundley J, Darrat Y, Morales G, Elayi SC, Bailey AL*
- 355 Determinants of percutaneous coronary intervention success in repeat chronic total occlusion procedures following an initial failed attempt  
*Cuevas C, Ryan N, Quirós A, Del Angel JG, Gonzalo N, Salinas P, Jiménez-Quevedo P, Nombela-Franco L, Nuñez-Gil I, Fernandez-Ortiz A, Macaya C, Escaned J*

#### Observational Study

- 363 Speckle tracking echocardiography to assess regional ventricular function in patients with apical hypertrophic cardiomyopathy  
*Saccheri MC, Cianciulli TF, Morita LA, Méndez RJ, Beck MA, Guerra JE, Cozzarin A, Puente LJ, Balletti LR, Lax JA*

- 371 Inter-ethnic marriages and severity of coronary artery disease: A multicenter study of Arabian Gulf States  
*Daoulah A, Al-kaabi S, Lotfi A, Al-Murayeh M, Nasser SA, Ahmed W, Al-Otaibi SN, Alama MN, Elkhateeb OE, Plotkin AJ, Malak MM, Alshali K, Hamzi M, Al Khunein S, Abufayyah M, Alsheikh-Ali AA*

**META-ANALYSIS**

- 378 Contrast use in relation to the arterial access site for percutaneous coronary intervention: A comprehensive meta-analysis of randomized trials  
*Shah R, Mattox A, Khan MR, Berzingi C, Rashid A*

**CASE REPORT**

- 384 Three-dimensional optical coherence tomography reconstruction of bifurcation stenting using the Szabo anchor-wire technique  
*Yu K, Hundal H, Zynda T, Seto A*
- 391 Conservative management of aortic root rupture complicated with cardiac tamponade following transcatheter aortic valve implantation  
*Vannini L, Andrea R, Sabaté M*

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## Feature tracking cardiac magnetic resonance imaging: A review of a novel non-invasive cardiac imaging technique

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### Abstract

Cardiovascular disease is a leading cause of morbidity and mortality globally. Early diagnostic markers are gaining popularity for better patient care disease outcomes. There is an increasing interest in noninvasive cardiac imaging biomarkers to diagnose subclinical cardiac disease. Feature tracking cardiac magnetic resonance imaging is a novel post-processing technique that is increasingly being employed to assess global and regional myocardial function. This technique has numerous applications in structural and functional diagnostics. It has been validated in multiple studies, although there is still a long way to go for it to become routine standard of care.

**Key words:** Feature tracking cardiac magnetic resonance imaging; Feature tracking; Myocardial tagging

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**Core tip:** Feature tracking cardiac magnetic resonance imaging (FT-CMR) is novel non-invasive imaging technique that is being used commonly in assessment of different cardiac disorders. FT-CMR utilizes standard steady-state free precession sequences and is simpler, more practical and easily available. It has been validated in multiple studies. The objective of our literature review is to look at the current literature regarding validation, normal and abnormal values, advantages and limitations of FT-CMR in

research and clinical trials.

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## INTRODUCTION

Cardiovascular diseases constitute a major global public health burden. It accounts for about one third (30.9%) of patient mortality worldwide<sup>[1]</sup>. Due to increasing economic burden and shrinking resources, there is a major shift in strategy towards prevention and early detection of cardiac disease worldwide.

Among non-invasive diagnostic techniques, cardiac magnetic resonance imaging (MRI) is a gold standard. Strain imaging on cardiac magnetic resonance imaging (CMR) through myocardial tagging was in vogue since the ground-breaking work of Zerhouni in 1988. Since then many imaging sequences have been designed to measure the global and regional function of myocardium. However, most of these sequences are fraught with fading of tag lines in diastole, long the breath-hold time which are cumbersome in acutely ill and advanced cardiac failure and those with coexistent pulmonary diseases.

Strain imaging using Echocardiographic measurements obtained using tissue Doppler is limited by noise interference and angle dependency. While speckle tracking has largely overcome these issues, it is often limited by image quality CMR with feature tracking is a novel technique which uses myocardial deformation for global and segmental functional analysis. Feature tracking uses different myocardial strain patterns including longitudinal, radial and circumferential strain measurements for global and segmental functional assessment<sup>[2]</sup>. Strain on feature tracking is not dependent on loading conditions, unlike ejection fraction, and it is actually a ratio of initial and final myocardial lengths during different portions of myocardial cycle. Strain is equal to  $L - L_0/L_0$ , where L is final length and  $L_0$  is initial length.

Strain is a measure of myocardial deformation, longitudinal strain is measured in long axis while circumferential and radial strains are measured in short-axis. As cardiac magnetic resonance feature tracking (CMR-FT) is less time consuming due to no prolonged post processing times involved, it may have a better future value in quick assessment of myocardial mechanics<sup>[2]</sup>. It has been well studied in last few years and it has shown to play a great role in the diagnosis of multiple cardiac conditions as detailed below. The purpose of our literature review was to assess its integration in routine clinical care for the assessment of myocardial function to avoid unnecessary invasive diagnostic, e.g., intravascular ultrasound and cardiac catheterization.

## VALIDATION OF CMR AS NOVEL IMAGING MODALITY

Feature-tracking (FT) is a novel technology which is used to calculate strain for the assessment of cardiovascular disease, is not a validated technique at the moment, against a standard myocardial tagging analysis for any strain parameter. It needs to be validated before incorporating it into routine clinical practice. We will compare CMR-FT with other diagnostic modalities such as echocardiogram to assess its equivalence vs superiority or inferiority. Echocardiographic measurements obtained using tissue Doppler imaging are limited by noise interference and angle dependency. While speckle tracking has largely overcome these issues, it is often limited by image quality. In order to label it as standard of care, we also need to look for inter study, inter and intra observer reproducibility of CMR feature tracking (Table 1).

Taylor *et al*<sup>[3]</sup> studied 20 healthy volunteers and measured myocardial strain using FT. They found FT highly reproducible within operators and needed a short analysis time of  $3 \pm 1$  min.

Augustine *et al*<sup>[4]</sup> used feature tracking in 145 healthy individuals to measure different myocardial deformation parameters including radial, circumferential and longitudinal strain, and segmental levels based on age and gender and recorded the normal values. They found these values to be similar when compared to prior studies based on age and gender. They also used myocardial tagging in 20 of these subjects to measure these same values and compared them with those obtained by feature tracking. Feature tracking measurements of circumferential but not longitudinal or radially directed global strain showed reasonable agreement with myocardial tagging and acceptable inter-observer reproducibility. Similarly, Schuster *et al*<sup>[2]</sup> studied feature tracking measurements in 20 healthy subjects with 2 sets of measurements, one at baseline and other after 4 wk. They found that FT-CMR had reasonable intra observer reproducibility in different groups of individuals. It was most reproducible for left ventricular circumferential strain measurements while it was least reproducible for right ventricular longitudinal strain.

Use of Feature tracking was not only studied in primary cardiovascular disease patients but was also used to study left ventricular radial and circumferential strain to assess anthracycline induced cardiotoxicity. Both circumferential and radial strain detected subclinical cardiac dysfunction in this cohort. Feature tracking was compared with harmonic phase imaging analysis (HAARP). Circumferential strain was found to be a robust and reproducible index in this study while radial strain did not show much promise<sup>[5]</sup>.

To assess the reproducibility of myocardial strain, FT was compared with tagging in a small patient cohort of left bundle branch block (LBBB) and hypertensive cardiomyopathy. It concluded that peak circumferential strain and time to peak circumferential strain are not good

Table 1 Validation studies at glance

Ref.	Technique compared	Cardiac disease	Population studied (n)	Results of validation
Taylor <i>et al</i> <sup>[10]</sup>	-	Healthy individuals	55	FT is highly reproducible within operators, requiring a short analysis time
Augustine <i>et al</i> <sup>[4]</sup>	Myocardial tagging	Healthy individuals	145	FT measurements of circumferential strain showed reasonable agreement with myocardial tagging
Schuster <i>et al</i> <sup>[2]</sup>	-	Healthy individuals	20	FT showing reasonable intra-observer reproducibility in different groups of individuals
Lu <i>et al</i> <sup>[5]</sup>	HAARP	Anthracycline induced cardiomyopathy	26	Circumferential strain was found to be a robust and reproducible index of myocardial deformation
Hor <i>et al</i> <sup>[7]</sup>	HAARP	Duchenne muscular dystrophy	233	Good correlation between CMR-FT and HAARP for the mean circumferential strain values
Morton <i>et al</i> <sup>[8]</sup>	-	Healthy individuals	16	FT had good inter-study reproducibility for global strain analysis
Kempny <i>et al</i> <sup>[9]</sup>	STE and simple EBD	ToF	25	Feature tracking showed better inter observer reproducibility for circumferential or radial left ventricular and longitudinal right ventricular global strain when compared to STE
Padiyath <i>et al</i> <sup>[10]</sup>	2D echocardiography	20 patients with ToF and 20 healthy controls	40	Reasonable agreement between FT and 2D echo in measurement of global circumferential strain and global longitudinal strain for the left ventricle
Harrild <i>et al</i> <sup>[12]</sup>	Myocardial tagging	HCM	24	Closer agreement between 2 modalities in measuring time to peak strain
Orwat <i>et al</i> <sup>[13]</sup>	Trans-thoracic echocardiogram with speckle tracking	HCM	40	Trans-thoracic echocardiogram with speckle tracking. They found decent agreement between left ventricular longitudinal strain measurements between the 2 modalities while the agreement for circumferential strain not encouraging

HCM: Hypertrophic cardiomyopathy; EBD: Endocardial border delineation; STE: Speckle tracking echocardiography; ToF: Teratology of Fallot; HAARP: Harmonic phase imaging analysis; CMR-FT: Cardiac magnetic resonance feature tracking; FT: Feature tracking; 2D: 2-Dimensional.

indices in this patient population. Although it was well designed study, but due to small sample size ( $n = 20$ ) it would be far from conclusive<sup>[6]</sup>.

Another well designed study on large cohort ( $n = 233$ ) Duchene Muscular Dystrophy (DMD) patients stratified into various groups based on EF and late gadolinium enhancement (LGE) after age and gender matching. There was a good correlation between CMR-FT and HAARP for the mean circumferential strain values ( $-13.3\% \pm 3.8\%$  for CMR-FT vs  $13.6\% \pm 3.4\%$  for HAARP) with an  $r = 0.899$ <sup>[7]</sup>.

Morton *et al*<sup>[8]</sup> imaged 16 healthy individuals with CMR feature tracking 3 times in a single day and different time points to look for inter-study reproducibility. They concluded that CMR-FT had good inter-study reproducibility for global strain analysis while it was poor for segmental strain. Though, they did not find any diurnal variation in strain measurements<sup>[8]</sup>.

Kempny *et al*<sup>[9]</sup> used feature tracking for biventricular myocardial function assessment in 28 patients of repaired Teratology of Fallot (ToF) and healthy 25 controls and compared it with speckle tracking echocardiography (STE) and simple endocardial border delineation (EBD). They found close agreement between right and left ventricular global strain. Inter observer agreement for features tracking and STE was moderate for longitudinal left ventricular global strain while feature tracking showed better inter observer reproducibility for circumferential or radial left ventricular and longitudinal right ventricular global strain when compared to STE. Feature tracking

showed poor reproducibility for regional strain. The relative systolic length change of endocardial border as measured by EBD was similar to feature tracking global strain<sup>[9]</sup>. Similarly studying similar population and comparing this novel technique with 2D echocardiography, Padiyath *et al*<sup>[10]</sup> studied myocardial mechanics in 20 patients with Teratology of Fallot and 20 healthy controls using 2D STE echocardiography and FT-CMR. They found reasonable agreement between the 2 modalities in measurement of global circumferential strain and global longitudinal strain for the left ventricle ( $9.5\%$  and  $16.4\%$  inter modality variability, respectively) while right ventricular global longitudinal strain had an inter modality variability of  $25.7\%$ . Also, the global radial strain measurements had high inter modality and inter observer variability<sup>[10]</sup>. When compared with 2D echocardiography for right ventricular strain assessment, CMR-FT showed reasonable agreement with 2D echo in these assessments<sup>[11]</sup>.

In hypertrophic cardiomyopathy (HCM) patients, feature tracking was compared with myocardial tagging in 13 normal subjects and 11 patients of HCM patients, showing closer agreement between 2 modalities in measuring time to peak strain while agreement was more modest in measuring magnitude of the peak strain<sup>[12]</sup>. Orwat *et al*<sup>[13]</sup> studied feature tracking myocardial measurements in 20 healthy volunteers (10 male, mean age  $24 \pm 3$  years) and 20 patients with HCM (12 male, mean age  $47 \pm 19$  years) and compared them with trans-thoracic echocardiogram with speckle tracking. They found decent agreement between left ventricular longitudinal

strain measurements between the 2 modalities while the agreement for circumferential strain and strain rate was not encouraging. There was high reproducibility for left ventricular peak global strain measurements as compared to strain rate<sup>[13]</sup>.

Validity of FT-CMR was also studied in patients with recent or past myocardial infarction patients. Gao *et al*<sup>[14]</sup> examined 3 healthy controls and 41 patients with either recent or past MI to assess left ventricular strain and compared with DENSE [displacement encoding with stimulated echoes in cardiac functional magnetic resonance imaging (MRI)]. He found good agreement in peak circumferential and peak radial strain values in patient population although peak radial strain measurements in healthy patients was overestimated in healthy controls when using cine CMR as compared to DENSE<sup>[14]</sup>. Also in aortic stenosis patients ( $n = 30$ ), a reasonable agreement was found in deformation measurements as measured from myocardial strain using FT as compared to tagging technique<sup>[15]</sup>. In another study, Schneeweis *et al*<sup>[16]</sup> measured circumferential strain by using speckle tracking echocardiography (STE), FT and myocardial tagging and compared these three modalities. They found that FT and Tagging had moderate agreement in global circumferential strain analysis while agreement was poor for segmental analysis. No agreement was found between CMR (FT and MT) based global and segmental circumferential strain measurements and ST based values<sup>[16]</sup>.

Anwar *et al*<sup>[17]</sup> studied 15 single ventricle Fontan ("Fontan" is a procedure done in pediatric patients who have 1 functional ventricle when born) patients with FT and compared it with tagging. They found moderate agreement between these 2 modalities in the assessment of circumferential strain<sup>[17]</sup>.

## REFERENCE VALUES OF FT-CMR FOR NORMAL AND DISEASED PATIENTS

Feature tracking imaging could reliably be used to assess myocardial function in patients with early dysfunction. Multiple parameter datasets are available for radial systolic strain values, circumferential strain values, circumferential strain, longitudinal endocardial systolic strain, longitudinal strain and segmental reproducibility for systolic strain measurements<sup>[18]</sup>. Similarly, Taylor *et al*<sup>[19]</sup> studied the values for feature tracking in a cohort of 108 cardiomyopathy patients and 55 normal healthy controls. Healthy controls ( $n = 55$ , age:  $42.9 \pm 13$  years, LVEF:  $70\% \pm 5\%$ , QRS:  $88 \pm 9$  ms) and patients with cardiomyopathy ( $n = 108$ , age:  $64.7 \pm 12$  years, LVEF:  $29\% \pm 6\%$ , QRS:  $147 \pm 29$  ms) underwent FT-CMR for the assessment of the circumferential uniformity ratio estimate (CURE) and radial uniformity estimate ratio (RURE) based on myocardial strain (both CURE and RURE: 0 to 1; 1 = perfect synchrony). CURE ( $0.79 \pm 0.14$  vs  $0.97 \pm 0.02$ ) and RURE ( $0.71 \pm 0.14$  vs  $0.91 \pm 0.04$ ) were lower in patients with cardiomyopathy than in healthy controls (both  $P < 0.0001$ ). CURE [area under the receiver-operator

characteristic curve (AUC): 0.96], RURE (AUC: 0.96) and an average of these [CURE: RURE atrioventricular groove (AVG), AUC: 0.98]. They concluded that measures like CURE and RURE provide absolute differentiation between patients with cardiomyopathy and normal healthy controls with a sensitivity of 90%, specificity of 98% at a cut-off of 0.89<sup>[19]</sup>. Buss *et al*<sup>[20]</sup> and Shang *et al*<sup>[21]</sup> measured reference values in 110 healthy adult patients and 115 healthy pediatric patients. Their work was based on the fact that some observational studies of left ventricular function in adults suggest that global longitudinal strain correlate with EF, and is superior to EF as a predictor of outcome. Also, Kadiyala *et al*<sup>[22]</sup> measured values of myocardial strain in 60 normal subjects and tabulated them for reference.

### Features tracking algorithm

Proto-type software is TomTec (Diogenes Medical, Germany). Different algorithms are available for strain measurement. Elnakib *et al*<sup>[23]</sup> suggested the algorithm shown in Table 2.

### Clinical applications of feature tracking

Assessment of left ventricular function is a key application of CMR. Feature tracking imaging is a fast and rapid method that provides an objective and reliable measurement of left ventricular function. CMR-FT is a novel promising technique to diagnose structural and functional heart disease. It provides a rapid a method to diagnose these conditions without long and watchful waiting processing times<sup>[3]</sup>. In 1 study<sup>[7]</sup>, analysis of a complete data set using Feature Tracking was quicker than by tagging ( $8.8 \pm 4.7$  min vs  $15.4 \pm 4.9$  min,  $P < 0.05$ ). It does not require any extra imaging sequences and can be applied to any imaging sequence.

**Structural heart disease:** In single ventricular patients, feature tracking could help to identify ventricular dysfunction based on specific type of defect present. Moore *et al*<sup>[24]</sup> collected the data from 25 control subjects and 30 patients with single ventricle (right or left) and used feature tracking for mechanical dyssynchrony and strain analysis in these patients. They concluded that analysis of circumferential strain is abnormal in single ventricle patients despite normal ejection fraction<sup>[24]</sup>. In patients after repair of coarctation of aorta, FT can detect early systolic dysfunction. Kutty *et al*<sup>[25]</sup> used FT to identify abnormal strain patterns as indication of early systolic dysfunction despite normal ejection fraction in 81 patients 10-13 years after repair for coarctation of aorta. It was noted that global longitudinal strain measurements were worse in the presence of left ventricular hypertrophy<sup>[25]</sup>. FT was found to be better, fast and reliable method in quantification of wall mechanics and strain after 10 healthy subjects were examined with CMR-FT to for quantitative wall motion assessment during intermediate dose dobutamine stress CMR<sup>[26]</sup>. In addition to diagnosing early cardiac dysfunction in structural heart disease patients, FT allows quantitative elaboration of myocardial tissue and blood flow<sup>[27]</sup>. Fifteen patients with

**Table 2** Feature tracking algorithm

Algorithm	Strain estimation algorithm
Step 1	Wall borders segmentation Segment the LV wall from cine CMR
Step 2	For each image, find the centerline of the LV wall as follows Start with the inner border of the LV wall Solve the Laplace equation between the inner and outer wall borders to find the corresponding outer points to the defined inner points in step 2(a) Pick the points located equidistant from the corresponding point-pairs Form the centerline ( <i>i.e.</i> , mid-wall border) using a closed spline fit for the selected points
Step 3	Tracking For each two successive images, solve the Laplace equation between their respective inner borders, mid-walls, and outer borders Track the co-allocated points at the inner, mid-wall, and outer edges of the first image frame (defined in step 2) throughout the cardiac cycle
Step 4	Strain estimation Estimate the circumferential strains by tracking the change in distance between tracked points on the same border ( <i>i.e.</i> , inner, mid-wall, and outer borders) Estimate the radial strains by tracking the change in distance between radially oriented tracked points

CMR: Cardiac magnetic resonance imaging; LV: Left ventricle.

ischemic cardiomyopathy were enrolled in 1 study for viability assessment *via* feature tracking measurements. FT imaging was done both at rest and during low-dose dobutamine stress. Feature tracking was found to be a reliable method for quantitative assessment of myocardial viability in patients with ischemic cardiomyopathy<sup>[28]</sup>. Feature tracking was also useful in identifying higher indexes of left ventricular dyssynchrony which were associated with ventricular tachycardia and death in patients with repaired tetralogy of Fallot<sup>[29]</sup>. This technique was also used to study the impact of transcatheter pulmonary valve placement on biventricular strain and synchrony in patients with right ventricular outflow tract conduit dysfunction which showed improved right and left ventricular global strain and left ventricular synchrony, showing the value of feature tracking in this patient population<sup>[30]</sup>. Role of feature tracking in the diagnosis of muscular dystrophy associated cardiomyopathy has been evaluated in some studies. Rosales *et al.*<sup>[31]</sup> found the role of FT in diagnosis of Limb Girdle Dystrophy associated cardiac dysfunction including cardiomyopathy with systolic dysfunction, myocardial fibrosis and diastolic dysfunction.

**Ischemic cardiomyopathy:** Usefulness of FT is not only limited to structural heart diseases, it has been studied extensively in patients with ischemic cardiomyopathy secondary to coronary artery disease. In a study by Buss *et al.*<sup>[32]</sup>, FT was used in 74 patients with first STEMI 2-4 d after reperfusion. Circumferential strain analysis provided an objective method in the assessment of infarct size<sup>[32]</sup>. They found similar utility of FTI in another study of 54 patients with first time STEMI<sup>[33]</sup>.

**Non-ischemic cardiomyopathies:** FT doesn't limit its usefulness in ischemic and structural heart disease patients, non-ischemic cardiomyopathies can also be managed early in the course if FT is used. Breuninger *et al.*<sup>[34]</sup> used FT to assess myocardial strain in 88 patients with

dilated cardiomyopathy and 30 healthy controls and found it to be reliable in analyzing global myocardial function. Steinmetz *et al.*<sup>[35]</sup> studied 26 patients with uncorrected Ebstein's anomaly and 10 healthy controls with FT to measure right and left ventricular deformation and dyssynchrony which showed RV intraventricular dyssynchrony and reduced RV global strain in patients with Ebstein's Anomaly as compared to healthy controls. Buss *et al.*<sup>[33]</sup> studied 210 patients with dilated cardiomyopathy with FT and noted that LV longitudinal strain assessment *via* FT was an independent predictor of patient survival and thus a helpful diagnostic tool for risk stratification in this patient population beyond clinical parameter and standard CMR<sup>[32]</sup>. Similarly, in hypertrophic cardiomyopathy (HCM) patients, Smith *et al.*<sup>[36]</sup> used FT to follow 30 HCM pediatric patients (14.1 ± 3.2 years) and the relationship of LGE (present in 17 of those patients) to adverse clinical outcome (defined as cardiac death non sustained Ventricular tachycardia, ventricular fibrillation and appropriate AICD discharge) over a period of 26.9 mo. They found LGE presence in these pediatric patients comparable to adult population in terms of decreased myocardial strain and adverse clinical outcome<sup>[36]</sup>. Thavendiranathan *et al.*<sup>[37]</sup> studied 30 patients with myocarditis and takotsubo cardiomyopathy with CMR and feature tracking and they found it a rapid and reliable method to diagnose myocardial injury in these conditions<sup>[37]</sup>. Petryka *et al.*<sup>[38]</sup> used FT in 137 children with known or suspected HCM, DCM or LV non compaction to measure strain and its prognostic significance. Circumferential Strain measurements in these patients were thought to be valuable in predicting adverse outcome.

**Advanced heart failure:** Cardiac resynchronization therapy (CRT) provides both morbidity and mortality benefit in advanced heart failure patients. Measurement of left ventricular mechanical dyssynchrony in these patients might provide prognostic information along with QRS duration. Onitsha *et al.*<sup>[39]</sup> studied 72 patients

to assess left ventricular dyssynchrony using CMR-FT and speckle tracking echocardiography with promising results concluding FT as a reasonable technique for patients with more marked dyssynchrony.

**Cardio-oncology:** Use of feature tracking for the diagnosis of chemotherapy-induced cardiomyopathy has been established in multiple studies<sup>[5,40]</sup>. In another study, Kowallick *et al.*<sup>[41]</sup> used this technique to measure left atrial mechanics in 10 healthy controls, 10 patients with HCM and 10 patients with heart failure with preserved LVEF (HFpEF). They concluded that FT reliably differentiated between healthy controls and patients with impaired left ventricular relaxation based on LA longitudinal strain and strain rate measurements<sup>[41]</sup>.

**Other diseases:** A small study identified the role of feature tracking in diagnosing myocardial abnormalities in patients with Churg-Strauss syndrome and Wegener's Granulomatosis and in clinical remission with normal EKG and transthoracic echocardiogram<sup>[30]</sup>. Feature tracking could also be useful in the diagnostic workup of left ventricular hypertrophy and the detection of early cardiac involvement in Anderson Fabry's disease which is an X-linked lipid storage disorder (characterized by multi organ involvement and premature death due to cardiac failure, renal failure, stroke and arrhythmias), with potential for therapy monitoring<sup>[42]</sup>. Strain measurements using feature tracking should play a major role in instituting early therapy for cardiomyopathy in patients with Duchenne Muscular Dystrophy associated cardiomyopathy and other similar cardiomyopathies where abnormal strain patterns precede the systolic dysfunction<sup>[43,44]</sup>. These measurements could also be helpful in following paroxysmal atrial fibrillation patients after ablation therapy to look for the presence and reversibility of cardiac dysfunction<sup>[29]</sup>. Bratis *et al.*<sup>[45]</sup> found FT to be helpful in differentiating between normal controls and Kawasaki Disease patients in a study of 29 KD convalescent patients and 10 healthy controls.

## FUTURE DIRECTION

Despite recent surge in the number of studies looking at this diagnostic modality, we still need large randomized trials. More studies are needed to assess the role of feature tracking in the assessment of right ventricular/right and left atrial dysfunction<sup>[11]</sup>. Further refinements are needed to overcome poor reproducibility in left ventricular segmental strain measurements and right ventricular strain measurements<sup>[27]</sup>.

## CONCLUSION

CMR-FT is a new and potentially useful noninvasive technique for measuring myocardial strain from routine cine CMR images using feature-tracking algorithms that were initially designed for echocardiographic strain analysis. FT-CMR tracks tissue voxel motion using standard steady-state

free precession sequences and is simpler, more practical and easily available and less time consuming than other CMR-based strain techniques for global and segmental myocardial function analysis. It needs to be further studied and validated for routine use in current clinical practice.

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