Advances in Cardiovascular Imaging

Cardiovascular Magnetic Resonance Myocardial Feature Tracking
Concepts and Clinical Applications

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Abstract—Heart failure–induced cardiovascular morbidity and mortality constitute a major health problem worldwide and result from diverse pathogeneses, including coronary artery disease, nonischemic cardiomyopathies, and arrhythmias. Assessment of cardiovascular performance is important for early diagnosis and accurate management of patients at risk of heart failure. During the past decade, cardiovascular magnetic resonance myocardial feature tracking has emerged as a useful tool for the quantitative evaluation of cardiovascular function. The method allows quantification of biaxial and bi-ventricular mechanics from measures of deformation: strain, torsion, and dyssynchrony. The purpose of this article is to review the basic principles, clinical applications, accuracy, and reproducibility of cardiovascular magnetic resonance myocardial feature tracking, highlighting the prognostic implications. It will also provide an outlook on how this field might evolve in the future. (Circ Cardiovasc Imaging, 2016;9:e004077. DOI: 10.1161/CIRCIMAGING.115.004077.)

Key Words: cardiomyopathies ▫ coronary artery disease ▫ deformation imaging ▫ heart failure ▫ life expectancy ▫ magnetic resonance imaging ▫ strain

Advances in medical care and newer therapies for acquired and congenital heart disease (CHD) have substantially increased life expectancy. The field of cardiovascular imaging has evolved from obtaining qualitative diagnostic information toward more quantitative assessment methods. Recognizing the importance of measuring myocardial function in the management of heart disease, several indices including velocity of contractile shortening and end-systolic stiffness have been introduced.1 The lack of ideal indices of contractility led the cardiology community at large to choose ejection fraction (EF), which has remained the reference standard of ventricular function for decades, despite its inability to assess regional function.2 The superior index for the assessment of global and regional myocardial function is myocardial strain, a quantity of deformation that represents the percent change in dimension from a resting state to one achieved after application of a force or stress.3 Myocardial strain measurement was first achieved by using cardiovascular magnetic resonance (CMR) tagging methods in the late 1980s,4 allowing for the first time to directly visualize and quantify deformation without having to implant a physical marker.

Myocardial strain assessed by CMR tagging has been shown to be a more sensitive and earlier marker of contractile dysfunction than EF in multiple studies.5,6 Because of requiring prospective image acquisition using time consuming protocols, CMR tagging has not gained wide popularity in routine clinical practice.7 A simpler solution became available with the development of software analogous to speckle tracking echocardiography (STE) that tracks intramyocardial features detected between the epicardial and endocardial myocardial tissue boundaries.8 This newer technique—CMR feature tracking (CMR-FT)—tracks the actual borders and follows them over time; in contrast to STE, no intramyocardial features are tracked.9 FT has led to more automation of quantitative analysis with much less time consumption than tagged imaging methods.5

Software capable of accurately measuring global and regional myocardial deformation from steady state free precession CMR images holds great potential in the clinical and research settings. The ability to automatically track cardiac structures allows users to follow changes of dimensions as well as velocities, displacement, strain and strain rate (SR) to potentially differentiate normal from abnormal heart function. Therefore, it is not surprising, that FT has attracted much interest in the CMR community. The majority of CMR-FT studies
have used the Diogenes and Cardiac Performance Analysis-MR software provided by TomTec Imaging systems (TomTec, Unterschleissheim, Germany). Other vendors including Toshiba (Tokyo, Japan) and more recently Circle (Calgary, Canada) have released alternative FT software platforms. The purpose of this article is to summarize the basic principles, evolving clinical applications, accuracy and reproducibility data of CMR-FT. The article will also highlight the prognostic implications of this technique and provide future perspectives.

Technical Considerations: A Peek Inside the Black Box

All CMR-FT techniques and STE, as well as other cardiac motion analysis tools are based on optical flow technology. In principle, the features tracked by CMR-FT are anatomic elements that are different along the cavity–myocardial tissue boundary and are found by methods of maximum likelihood in 2 regions of interest between 2 frames. The CMR-FT software’s automatic border tracking algorithm is initiated after manually tracing either the endocardial or both the endocardial and the epicardial borders in the frame with the best separation of the cavity–myocardial tissue boundary, usually at end diastole (Figure 1). The border tracking proceeds by tracking each feature along the contour, based on a hierarchical algorithm and combining 1-dimensional (1D) tracking (guaranteeing high accuracy because of the spatial restriction, Figure 2), and 2D tracking (necessary to properly detect the spatially extended features in the 2D space, Figure 3). To precisely capture the geometric displacement of the border, the tracking must first be performed in the direction orthogonal to the border itself where the feature is more recognizable (cavity–myocardial tissue boundary). The software automatically tracks the features along this direction by performing transmural cuts passing through and orthogonal to the original manual tracing for all the points through time over the cardiac cycle. In this way, the evolution along a transmural cut can be represented for all instants at once in a 2D representation, where 1 axis is the distance along the line and the other axis is the time similar to the M-mode technique in echocardiography (Figure 2). The border tracking is then automatically performed along this space-time image.

To ensure high accuracy, the underlying hierarchical algorithm makes use of all available information, including tissue–cavity interface, CMR imaging specifics (temporal and spatial resolution, signal/noise ratio, and frame rate), periodicity and type of motion, and spatial coherence. This allows flexible adaptation of the tracking by increasing or reducing the size of the search window within which a given point is tracked between 2 frames (Figure 3). In theory, this is useful to compensate for additional motion (for example, mitral annular motion or high amounts of inward or outward through plane motion).

Recent work in a small number of healthy volunteers has demonstrated differences in strain measurements between 2 types of CMR-FT solutions. Prospective investigations in larger numbers of patients are needed for solutions from multiple vendors to be used interchangeably. Furthermore, precise assessment of regional myocardial function is valuable. Notably, all 2D techniques of deformation including CMR-FT, STE, and CMR tagging have lower reproducibility at the regional level. This is because of through plane motion effects, with tags, features, or speckles fading/leaving the imaging plane between end diastole and end systole. Newer 3D approaches of tagging and STE may rectify this problem but are also limited in terms of temporal and spatial resolution. Therefore, further studies and stronger evidence are needed to enable widespread clinical use.

Preclinical and Clinical Validation

CMR-FT was tested on simulation data from a series of artificial computer-generated loops that enabled testing of the image analysis procedure under simple and perfectly controlled conditions. The results of the simulation studies demonstrated that the errors in all cases were small for integral quantities (radius and strain) and slightly larger for differential quantities (velocities and SR) as a result of the latter being a derivative of the former. These studies demonstrated that the quality of the results had lower spatial resolution and that higher frame rates (above 25 Hz) were not beneficial if not accompanied by an increase in spatial resolution. In real-life CMR acquisitions, the process is more complex than just taking the spatial and temporal resolution into consideration. Image acceleration techniques (SENSE, GRAPPA, and k-t BLAST) increase frame rate, altering signal/noise ratio and thus may reduce tracking accuracy. Future studies assessing the impact of spatial and temporal resolution on the tracking accuracy of CMR-FT would be important to undertake.

CMR-FT assessment of global circumferential strain (GCS) was tested against the reference standard tagged imaging in Duchenne muscular dystrophy patients and
There have been numerous pediatric and adult validation studies that compared CMR-FT to tagging and STE in acquired and CHD, which will be summarized later in this article. The Table shows the average imaging resolution parameters for CMR-FT, CMR tagging, and STE. STE has superior spatial and temporal resolution, whereas the CMR techniques are often associated with inherently better image quality.

Quantitative Assessment of Cardiovascular Physiology

**Applications in Adults**

CMR-FT offers incremental clinical information in the adult population. The technique can be applied for the quantification of right and left ventricular (LV) systolic and diastolic function using strain and SR imaging as well as myocardial torsion and diastolic recoil quantification. The study of atrial physiology using strain and SR imaging has recently been explored. CMR-based deformation assessments of all cardiac chambers have become possible with FT, which could not reliably be achieved with myocardial tagging for the relatively thin-walled right ventricular (RV) and atrial myocardium.

**Ventricular Performance**

CMR-FT has been applied for ischemia and viability detection, cardiomyopathies, pulmonary hypertension, and quantification of dyssynchrony. Reference values for LV circumferential, radial and longitudinal strain have been published recently.

Assessment of ventricular deformation at rest and with inotropic stimulation using dobutamine has provided clinically relevant data in health and disease states. Schneeweis et al demonstrated the ability to use circumferential short-axis strain to identify inducible ischemia during intermediate and high-dose dobutamine stimulation. This is in line with previous evidence from myocardial tagging suggesting that quantification of wall motion with strain enhances diagnostic accuracy when compared with visual analysis for the detection of ischemia during high-dose dobutamine stress. Schneeweis et al have reproduced an important finding that quantitative impairments of myocardial strain defined by strain encoding imaging already occur at intermediate dobutamine levels. Because CMR-FT does not require the acquisition of extra sequences (when compared with strain encoding imaging) and the risk of adverse events when diagnosing coronary disease at intermediate dobutamine levels is low, there could be clinical benefit of using CMR-FT during ischemia testing. The role of strain imaging is well established in the assessment of myocardial hibernation by quantifying contractile reserve during low-dose dobutamine stress. The incremental diagnostic value of contractile reserve quantification has been demonstrated previously using 3D myocardial...
tagging techniques. There is evidence to suggest that similar information can be derived from CMR-FT strain parameters, with circumferential short-axis strain shown to accurately identify the presence of hibernation (contractile reserve) in patients with ischemic cardiomyopathy. However, a prognostic benefit of CMR-FT assessment in the setting of ischemic heart disease has not yet been demonstrated.

CMR-FT–derived myocardial strain assessment is useful for the classification of cardiomyopathies of nonischemic origin, including dilated cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy. In addition to ventricular strain, rotational mechanics and diastolic recoil can also be quantified using CMR-FT (Figure 4). LV rotational indices of twist and untwist rate have been used to differentiate cardiomyopathies and have revealed disease-specific patterns of rotation in hypertrophic cardiomyopathy and cardiac amyloidosis.

There is mounting evidence from tissue Doppler and STE that mechanical dyssynchrony is associated with adverse outcomes. Recently, the feasibility of CMR-FT for the assessment of dyssynchrony has been demonstrated. Taylor et al introduced a CMR-FT–based measure of dyssynchrony using the circumferential and radial uniformity ratio estimates that had initially been validated based on myocardial tissue tagging. Either circumferential or radial strains are being plotted against spatial locations using the 48 evenly spaced tracked points. In the presence of perfect synchrony, all points experience the same strain (synchronous contraction of all walls with an index of 1) at a given point in time, whereas in completely dysynchronous conditions opposing points will experience opposite strains (contraction of one wall and dilation of the opposing wall with an index of 0). Taylor et al demonstrated almost absolute discrimination between nonischemic cardiomyopathy and healthy volunteers using this methodology. It is important to note that dyssynchrony may not follow a perfectly synchronous pattern with alterations only between opposing locations but may involve more complex patterns that may not necessarily be detected using the circumferential and radial uniformity ratio estimates. Onishi et al used CMR-FT to calculate the differences in time points of the maximum peak radial strain and found reasonable agreements with STE using this approach. Whether or not the uniformity ratio estimates, the Onishi approach, or the more established classical systolic dyssynchrony index (based on the SD of the regional time to peak in volume or strain change) is most appropriate will need to be investigated in future studies.

**Atrial Physiology**

Beyond quantification of systolic and diastolic ventricular function, the applicability of CMR-FT has recently been extended to global longitudinal left atrial (LA) strain and SR analysis (Figure 4). This methodology permits derivation of quantitative strain and SR parameters for each of the 3 functional components of atrial physiology: (1) the reservoir phase is characterized by collection of pulmonary venous return during ventricular systole, and reservoir function is indicated by global peak longitudinal total strain ($\varepsilon_T$) and global peak-positive SR (SRs). (2) Conduit phase describes the passage of blood to the LV during early ventricular diastole. Global longitudinal passive strain ($\varepsilon_P$) and global peak early negative SR (SRe) are indices of LA conduit function. (3) Contractile booster pump function describes the intensity of atrial contraction leading to augmentation of ventricular filling during late ventricular diastole and can be quantified measuring global longitudinal active strain ($\varepsilon_A$) and global peak late-negative SR (SRa) during atrial contraction (Figure 4). Close correlation of impaired LA function and replacement and diffuse myocardial fibrosis as determined by late gadolinium enhancement and T1-mapping has been demonstrated. It is interesting to speculate whether increased LV stiffness is associated with diffuse myocardial fibrosis and the resulting impaired atrial performance could be a sensitive marker of early diastolic impairment. Our group has identified different patterns of LA impairment associated with different diseases. Patients with hypertrophic cardiomyopathy exhibit an increased contractile (booster pump) function, whereas patients with heart failure with preserved EF show impaired booster pump function compared with healthy controls. Both hypertrophic cardiomyopathy and heart failure with preserved EF patients show impaired LA reservoir and conduit function when compared with healthy controls. In theory, similar assessments of right atrial physiology can be derived from the 4-chamber view, which is however more susceptible to breathing motion with associated higher variability.

**Applications in CHD**

CMR-FT offers several advantages compared with echocardiography in the CHD population. Most of these patients, adults in particular have poor acoustic windows secondary to their body size and previous surgical procedures. The RV can be especially difficult to image reliably in patients with CHD because of its retrosternal location and dilatation. CMR does not have these limitations and generally provides good quality data sets suitable for CMR-FT analysis. Higher temporal resolution of 2D echocardiography is an advantage over CMR (Table); however, greater signal/noise ratio makes CMR-FT potentially superior to STE in image quality and border tracking. In our experience, CMR-FT–derived LV global longitudinal strain (GLS) has the best intermodality agreement among the indices measured, followed by GCS, whereas global radial strain (GRS) shows more degrees of divergence between CMR-FT and STE. Within CMR-FT, GCS reaches the highest reproducibility followed by GLS and GRS.
This pattern of reproducibility differs slightly from reports of interobserver agreement in the echocardiography literature where GLS shows slightly higher reproducibility than GCS. The precise reason for this difference is unknown at the present time. Among CHD, CMR-FT has been applied for the study of ventricular function in tetralogy of Fallot (TOF), coarctation of the aorta, and in forms of single ventricle (Figure 5). Harrild et al used CMR-FT to quantify indices of RV and LV strain and synchrony before and a median of 6 months after transcatheter pulmonary valve implantation in patients with dysfunctional right ventricular outflow tract conduits (18 patients with repaired TOF). Pulmonary valve implantation was associated with an improvement in LV longitudinal and circumferential strain and, in the cohort of patients with predominant pulmonic stenosis, an improvement in RV circumferential strain. The improvement in RV circumferential but not longitudinal strain may suggest regional differences of the impact of RV pressure load; infundibular function being more affected than free wall function. Among patients with primary pulmonary regurgitation, LV longitudinal synchrony improved, whereas electric measures of synchrony did not.

Another study in adult patients with TOF found close agreement between LV GLS and GCS derived by STE and FT and poor agreement for LV GRS. There was also a good agreement between the RV GLS measurements on FT and STE. The inter- and intraobserver agreements were comparable for LV GLS by CMR-FT and STE. For LV GCS and especially GRS, the agreements on FT were better compared with STE. In addition, interobserver agreement for RV GLS was superior for CMR-FT. Several FT-derived parameters of RV function were related to exercise capacity in TOF patients. The VE/Vco₂ slope correlated with RV circumferential strain and the peak power achieved on exercise correlated with RV longitudinal strain.

A study of 15 adult Fontan subjects imaged with both techniques made similar observations. The agreement between CMR and echocardiography was poor. Good or moderate interobserver variability was seen for FT (coefficients of variability 6.6% and 14.3% for circumferential and longitudinal strain), and FT indices correlated with age at Fontan completion, New York Heart Association class, and peak oxygen uptake on cardiopulmonary exercise testing. Using an earlier prototype of CMR-FT software, Truong et
observed differences in circumferential strain and apical rotation, as well as marked dyssynchrony in a heterogenous cohort of single ventricle hearts compared with controls. They attributed abnormal mechanics in single ventricles to abnormal cardiac looping.

Our group has investigated CMR-FT in patients with repaired coarctation of the aorta. In the population with coarctation of the aorta, LV GLS was significantly more reduced in the presence of LV hypertrophy (compared with normal LV mass), whereas GCS and GRS were similar. This finding suggests that deformation in the LV subendocardial longitudinal fibers may be more affected, relative to subepicardial and circumferential midwall fibers in this population. Similar alterations in LV GLS with preservation of radial and circumferential deformation have been described in systemic hypertension, indicating that an abnormal pattern of LV deformation results from afterload-induced myocardial hypertrophy.

Normal ranges for CMR-FT indices in the pediatric age group considering age, sex, and allometry have become recently available. More studies correlating CMR-FT indices with clinical outcomes are needed in pediatric and adult CHD imaging.

Prognostic Implications
The prognostic implications of STE-derived GLS are well established. Stanton et al have reported incremental prognostic value and superior mortality prediction with GLS compared with EF; and wall motion score index in 546 consecutive patients referred for echocardiography. Only recently, similar evidence became available from CMR-FT. Buss et al followed 210 patients with dilated cardiomyopathy who underwent conventional CMR with subsequent CMR-FT-derived assessment of radial, circumferential, and longitudinal strain measurements during a period of 5.3 years. They found significant associations of all strain parameters with mortality. However, GLS was found to be an independent and superior predictor of outcome when compared with radial and circumferential strain, N-terminal of the prohormone brain natriuretic peptide, EF, and scar burden as defined by late gadolinium enhancement mass.

The pathophysiological significance of GLS has been studied in the context of cardiac adaptation in adult life after preterm birth. This investigation consisted of 234 subjects aged between 20 and 39 years, of which 102 were born preterm and prospectively followed. All subjects underwent CMR including CMR-FT-based quantification of systolic (strain) and diastolic function (SR) as well as advanced assessment of cardiac anatomy using the cardiac atlas approach. A uniquely changed 3D cardiac anatomy was found in preterm born individuals with shorter and hypertrophied LV. Furthermore, these ventricles had decreased GLS as well as systolic and diastolic SR and twist mechanics. Whether the changes in GLS are associated with clinical outcomes in this group compared with patients with cardiomyopathy or simply consequent to the altered anatomy and shorter ventricular length is unknown. The circumferential strain and EF in preterm born adults was preserved, which may however suggest different pathophysiological mechanisms when compared
with patients with dilated cardiomyopathy. These differences should be explored in future longitudinal studies. Additional evidence comes from a retrospective case–control study of TOF. Moon et al. found that every measure of strain (RV and LV, longitudinal and circumferential) by CMR-FT was more impaired among patients who experienced death or ventricular tachycardia compared with an age-matched group who did not experience these outcomes. Impaired RV longitudinal strain was associated even more strongly with death and ventricular tachycardia than reduced LV strain. Associations of LV GLS, GCS, GRS, and RV GLS with death and nearly missed death were recently prospectively demonstrated in a large cohort of repaired TOF at a median follow-up of 7.4 years.56

There is also evidence from STE to suggest that quantitative measures of LA function carry prognostic information.57 From an inception cohort of the MESA study, it was shown that impairment of LA function precedes development of heart failure in the general population.11 Inoue et al. demonstrated the potential of CMR-FT–derived LA dynamics to improve risk stratification of cerebrovascular events in patients with atrial fibrillation. Because the assessment of CMR-FT–based atrial performance analysis has only recently been validated,22,43 widespread prognostic information is currently lacking and future studies are awaited. Notwithstanding these considerations, the data from our group demonstrate reasonable agreement between STE and CMR-FT–derived ventricular GLS. Interchangeability of GLS between modalities might be feasible, with consequent easy clinical applicability.44

Future Applications

There is evidence to suggest that FT techniques may also be applicable to imaging modalities other than echocardiography and CMR. Buss et al. have reported the feasibility of 2D FT using computed tomographic images and demonstrated a close agreement with STE. Tee et al. have demonstrated that such methods can discriminate normal from experimental cardiomyopathies in the porcine model. This methodology may well represent an alternative in the setting of limited ultrasound windows and in the presence of general contraindications to CMR.

Although 3D models for STE and MR tagging have been introduced, CMR-FT is limited to 2D acquisitions at the present time. Technical improvements including correction for through-plane motion and development of 3D CMR-FT have the potential for improving the accuracy and reproducibility of deformation measurements especially at the regional level. Preliminary data suggest that such improvements may be achievable using steady state free precession data based on modeling approaches.61 If those refinements can be achieved, cardiac deformation imaging using CMR-FT may well become fully established in routine clinical practice.

Conclusions

The current review provides an overview of the technical aspects, reproducibility, and clinical use of CMR-FT. CMR-FT has developed into a promising technique with diagnostic and prognostic implications. In particular, global LV circumferential short-axis as well as global LV and LA longitudinal long-axis strains demonstrate good reproducibility. Further technical refinements may allow robust assessments of regional myocardial mechanics. Continued technical development, clinical application, and future studies are needed to support our understanding of the relevance of this tool in heart failure pathophysiology, disease progression, and risk stratification.

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Disclosures

None.

References


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