# *Quantification of Left Atrial Deformation using Cardiovascular Magnetic Resonance Myocardial Feature Tracking*

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**Abstract:** Cardiovascular Magnetic Resonance myocardial feature tracking (CMR-FT) is a quantitative technique tracking tissue voxel motion on standard steady-state free precession (SSFP) cine images to assess myocardial deformation. The present work demonstrates the feasibility and reproducibility of CMR-FT for quantitative assessment of left atrial (LA) strain and strain rate (SR). Furthermore, the technique was applied to patients with hypertrophic cardiomyopathy (HCM) to address the determinants and the degree of LA dysfunction in the course of HCM.

**Zusammenfassung:** Das kardiovaskuläre Magnetresonanz Feature Tracking (CMR-FT) ist ein Verfahren, das durch ein Tracking der Herzwandbewegung eine Quantifizierung der myokardialen Deformation anhand von konventionellen cine steady-state free precession (SSFP) Aufnahmen erlaubt. Die vorliegende Arbeit zeigt, dass das CMR-FT eine Analyse des links atrialen (LA) strain und und strain rate (SR) erlaubt. Darüber hinaus wurde das Verfahren bzgl. der Reproduzierbarkeit validiert und bei Patienten mit Hypertropher Kardiomyopathie (HCM) angewendet, um das Ausmaß der LA Dysfunktion im Verlauf der Erkrankung zu charakterisieren.

## Motivation

The field of cardiovascular imaging has evolved from obtaining qualitative diagnostic information toward quantitative assessment methods. Recognizing the importance of measuring myocardial function in the management of heart disease, several indexes including left atrial (LA) functional parameters have been introduced (1).

Cardiovascular Magnetic Resonance myocardial feature tracking (CMR-FT) is a quantitative technique tracking tissue voxel motion on standard steady-state free precession (SSFP) cine images to assess myocardial deformation. The importance of LA deformation assessment is increasingly recognized in a variety of cardiovascular disease states, e.g. hypertrophic cardiomyopathy (HCM). LA deformation can be assessed with echocardiographic speckle tracking (STE). However atrial deformation quantification has never previously been demonstrated with CMR.

Accordingly, we sought to determine the feasibility and reproducibility of CMR-FT for quantitative LA strain and strain rate (SR) analysis. In a following step, the technique was applied to patients with HCM to address the determinants and the degree of LA dysfunction in the course of HCM.

## Material and Methods

In a first project, 10 healthy volunteers, 10 patients with HCM and 10 patients with heart failure and preserved ejection fraction (HFpEF) were studied at 1.5 Tesla to demonstrate the feasibility and the reproducibility of LA CMR-FT on an intra- and inter-observer level. LA longitudinal strain and SR parameters were derived from SSFP 4- and 2-chamber cine images using dedicated CMR-FT software (2D CPA MR, TomTec, Germany) (**Figure 1**).

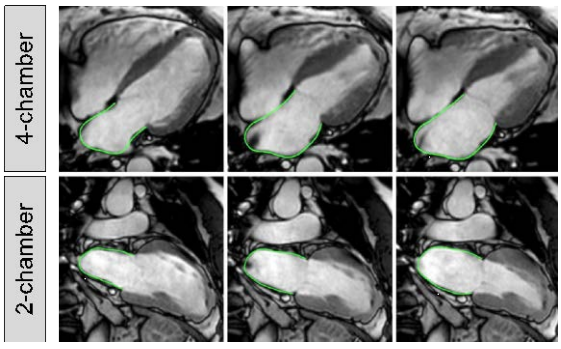


**Fig. 1**: **Left atrial CMR feature tracking.** Representative example of left atrial tracking in the 4-chamber and 2-chamber view in a patient with hypertrophic cardiomyopathy.

The technique permits derivation of quantitative strain and SR parameters for each

of the 3 functional components of LA physiology (**Figure 2**): 1.) the reservoir phase is characterized by collection of pulmonary venous return during ventricular systole and is indicated by global peak longitudinal total strain ($\varepsilon_s$) 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 ($\varepsilon_e$) and global peak early negative SR (SRe) are indexes 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 2**).

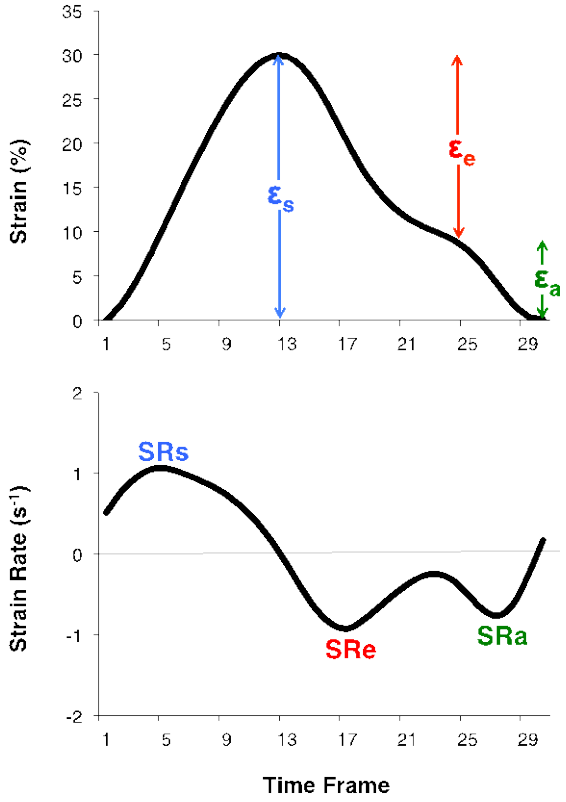


**Fig. 2**: **Left atrial strain and strain rate profiles.** Left atrial function comprises reservoir, conduit and contractile booster pump function. Total strain ($\varepsilon_s$) and peak positive strain rate (SRs) correspond to reservoir function. Passive strain ($\varepsilon_e$) and peak early negative strain rate (SRe) correspond to conduit function. Active strain ($\varepsilon_a$) and peak late negative strain rate (SRa) correspond to contractile booster pump function.

A second project addressed the reducibility on an inter-study level, which is particularly important to validate the applicability of this novel technique for CMR-based LA deformation analysis in studies with repeated measurements. 16 healthy volunteers underwent CMR imaging at 9:00 (Exam A), 9:30 (Exam B) and 14:00 (Exam C). LA strain and SR were quantified based on CMR-FT as described above. Exams A and B were compared to assess the inter-study reproducibility. Morning (fasting) and afternoon scans (non-fasting) were compared to address possible diurnal variation of LA function.

In a third project, CMR-FT was applied to 73 patients with HCM and 23 age-and gender-matched controls who underwent CMR imaging including left ventricular (LV) late gadolinium enhancement (LGE). The degree of HCM was evaluated according to the extent of LV fibrosis (Non-LGE; mild LGE≤10%; intermediate LGE 11-19%; severe LGE≥20%). LA reservoir, conduit and contractile functions were quantified by CMR-FT derived strain and SR using the above described methodology.

## Results

LA strain and SR parameters could be derived from SSFP images in all subjects in the first project. There was impaired LA reservoir function in HCM and HFpEF ($\varepsilon_s$ [%]: HCM 22.1±5.5, HFpEF 16.3±5.8, Controls 29.1±5.3, p<0.01) and impaired LA conduit function as compared to healthy controls ($\varepsilon_e$ [%]: HCM 10.4±3.9, HFpEF 11.9±4.0, Controls 21.3±5.1, p<0.001). LA booster pump function was increased in HCM while decreased in HFpEF ($\varepsilon_a$ [%]: HCM 11.7±4.0, HFpEF 4.5±2.9, Controls 7.8±2.5, p<0.01). Observer variability was excellent for all strain and SR parameters on an intra- and inter-observer level as determined (**Table 1**) (2).

**Table 1:** Intra-observer and inter-observer reproducibility for LA strain ($\varepsilon$) and strain rate (SR) parameters.

| | **Intra-observer** | **Inter-observer** |
|---|---|---|
| | **ICC (95%CI)** | **ICC(95%CI)** |
| **$\varepsilon_s$** | 0.98 (0.93-1.00) | 0.98 (0.92-1.00) |
| **$\varepsilon_e$** | 0.97 (0.90-0.99) | 0.96 (0.84-0.99) |
| **$\varepsilon_a$** | 0.99 (0.96-1.00) | 0.99 (0.98-1.00) |
| **SRs** | 0.97 (0.88-0.99) | 0.96 (0.82-0.99) |
| **SRe** | 0.97 (0.90-0.99) | 0.95 (0.78-0.99) |
| **SRa** | 0.99 (0.93-1.00) | 0.99 (0.96-1.00) |

ICC, intraclass correlation coefficient; $\varepsilon$, strain; SR, strain rate

The results of the second project showed good inter-study reproducibility for all LA strain and SR parameters. Inter-study reproducibility was

better for strain than for SR parameters. Reservoir function showed the best reproducibility (ICC 0.94-0.97, Coefficient of Variation [CoV] 4.5-8.2%), followed by conduit (ICC 0.78-0.97, CoV 8.2-18.5%) and booster pump function (ICC 0.71-0.95, CoV 18.3-22.7). LA dynamics were not measurably affected by diurnal variation between morning and afternoon scans (3).

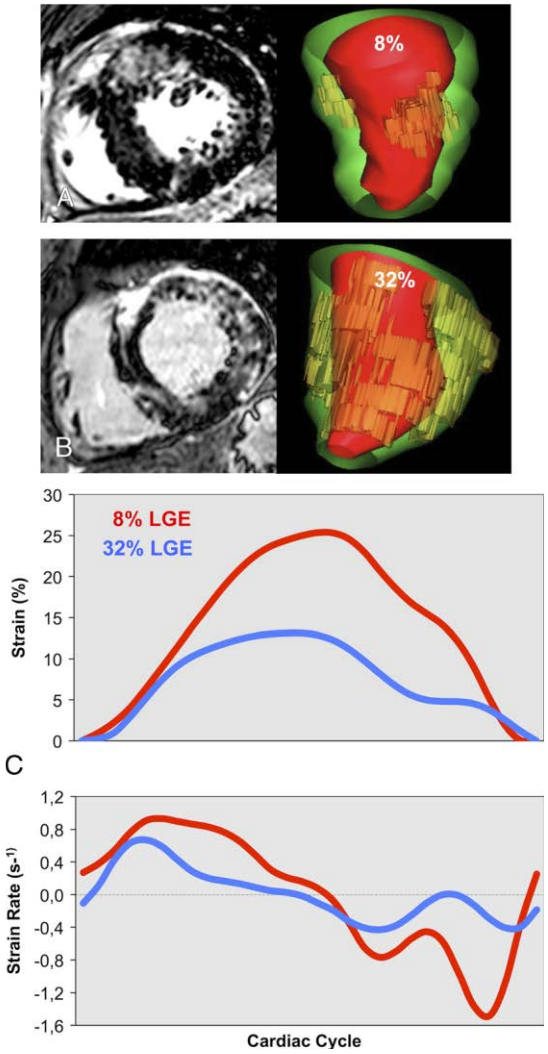


**Fig. 3**: **Comparison of LA deformation in a HCM patient with mild and a HCM patient with severe fibrosis.** HCM patient with mild (8%) LV LGE (**A**), HCM patient with extensive (32 %) LV LGE (**B**). Presented are basal short-axis scar images (**left**) and 3D LV scar models (**right**) which are generated after segmenting the whole short-axis scar stack (red: endocardium; green: epicardium; yellow: areas of LGE). Corresponding LA strain (**C**) and LA strain rate (**D**) profiles showing impaired LA dynamics in the patient with extensive LGE.

The results of the third project demonstrated that LA mechanics were associated with the extent of LV LGE (p=0.033 to p<0.001) in patients with HCM, but not with the LV mass extent or maximum wall thickness (p=0.108 to p=0.964) as derived from multivariable regression analyses. LA function decreased according to the increase in extent of LV fibrosis. Compared to age- and gender matched healthy controls, LA conduit function was impaired in HCM with no LGE already (LA emptying fraction [LAEF] Conduit: 32±7% vs. 26±14, p=0.037) (**Figure 3**). Conversely, LA contractile booster pump function was impaired in HCM with severe LGE only (LAEF Booster: 40±8% vs. 20±10%, p<0.001; for controls vs. LGE≥20%, respectively) (4).

## Discussion

CMR-FT can be used to calculate myocardial deformation indexes for the quantification of LA performance. The examined parameters have been validated with respect to reproducibility on an intra- and inter-observer as well as an inter-study level. Furthermore, LA deformation indexes have been initially applied to a clinical study with the aim to characterize LA abnormalities in patients with HCM.

LA deformation quantification comprises challenges that are not present when dealing with ventricular deformation imaging. These include the insertion of pulmonary veins and the presence of the LA appendage, the thin LA wall and the variable LA geometry. Notwithstanding these facts, the results of our research approach have shown good performance and reproducibility of CMR-FT derived LA deformation analysis. MR tagging representing the current reference standard for myocardial strain assessment has not proved useful for LA function analysis since the LA myocardium appears too thin to be adequately labeled by grid lines. The same applies to displacement encoding with stimulated echoes (DENSE), which has not been validated for LA strain and SR quantification so far. Thus, CMR-FT represents the only CMR based technique that allows for LA strain and SR imaging at the current time. CMR-FT benefits from high quality CMR images allowing robust contouring of the thin LA myocardium. Remarkably, CMR includes the acquisition of standardized and highly reproducible imaging planes. As a consequence, we were able to demonstrate good inter-study reproducibility of CMR-FT derived LA strain and SR, which is particularly important in longitudinal studies with repeated measurements.

Predominantly there is evidence from STE to suggest that quantitative measures of LA function carry prognostic information (1). Because the assessment of CMR-FT–based LA performance analysis has been validated only recently (2,3), widespread prognostic information is currently lacking and future studies are awaited. Specifically, LA

deformation indexes proved useful for disease staging and detection of early myocardial deterioration in HCM as demonstrated above. Consequently, the association of clinical outcome with LA mechanics will need to be addressed in future investigations.

## Conclusions

The present work demonstrates the feasibility of CMR-FT as a promising tool for the quantification of LA deformation. CMR-FT reliably distinguished LA function between healthy volunteers and patients with different origins of LV diastolic dysfunction. Reproducibility of LA deformation indexes was good on an intra- and inter-observer as well as an inter-study level. Finally, LA functional abnormalities as derived from CMR-FT demonstrated an association with LV hypertrophy and fibrosis in patients with HCM. Furthermore, these deformation indexes have proven useful for disease staging and early detection of cardiac deterioration in patients with HCM with superiority over conventional LV functional parameters. Further studies in larger cohorts should follow to establish the clinical utility and the prognostic implications of the investigated CMR-FT derived myocardial deformation indexes.

## References

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