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Temporal 3D Lagrangian strain from 2D slice-followed cine DENSE MRI

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Summary

A quantitative analysis of myocardial mechanics is fundamental to the understanding of cardiac function, diagnosis of heart disease and assessment of therapeutic intervention. In clinical practice, most cardiac imaging analyses are performed in 2D due to the limited scan time available. However, the obtained information from a 2D measurement is limited. This paper presents a method to obtain temporal evolutions of transmural 3D Lagrangian strains from two intersecting 2D planes of slice-followed cine displacement encoding with stimulated echoes (DENSE) data using a bilinear-cubic polynomial element to resolve strain from the displaced myocardial positions. The method was validated against an analytical standard and has been applied to *in vivo* data acquired on a 3 T magnetic resonance system from a healthy volunteer to quantify systolic strains at the anterior-basal region of left ventricular myocardium. The method demonstrates accurate results when validated in the analytical model, and the *in vivo* results agree within experimental accuracy with values reported in the literature. Even with a short scan time, this method provides the full 3D Lagrangian strain tensor from two 2D DENSE measurements.

Keywords: myocardium; kinematics; magnetic resonance; transmural, deformation

Introduction

A quantitative analysis of myocardial mechanics is fundamental to the understanding of cardiac function, diagnosis of heart disease and assessment of therapeutic intervention.

Myocardial strain has been analyzed extensively with surgically implanted markers and beads (Carlhall, *et al.* 2008; Cheng, *et al.* 2005; Costa, *et al.* 1999; Waldman, *et al.* 1988). This data has the advantage of true material tracking of myocardial points during temporal analysis, in the sense that the beads are fixed into the myocardium and thus physically move with the myocardium. Noninvasive imaging techniques such as magnetic resonance imaging (MRI), computer tomography (CT) and tissue Doppler are used extensively for research purposes and as clinical tools for visualization and analysis of heart motion. Among these modalities, MRI-based techniques are often used to measure myocardial motion and deformation. A number of MRI techniques have been developed to quantify myocardial motion, including myocardial tagging (Axel & Dougherty 1989; Zerhouni, *et al.* 1988), phase contrast velocity encoding (Pelc, *et al.* 1991) and displacement encoding with stimulated echoes (DENSE) (Aletras, *et al.* 1999).

In clinical practice, most cardiac imaging analyses are performed in 2D due to the limited scan time available. However, the obtained information from a 2D measurement is limited as in-plane displacements maximally accomplish the 2D strain tensor. Although measured in a 2D plane, 3D displacements can be obtained with slice-followed DENSE MRI. In a recent paper, Spottiswoode *et al.* (Spottiswoode, *et al.* 2008) described how the two in-plane strain components of the 3D Lagrangian

strain tensor can be obtained from a single 2D acquisition of slice-followed DENSE MRI. In a sequel paper, Hess et al. (Hess, *et al.* 2009) quantified the entire 3D strain tensor from 2D DENSE in-plane displacement measurements in two adjacent slices in conjunction with a single SENC through-plane strain measure, utilizing constant-strain assumptions within 4-voxel tetrahedral volumes to resolve strain. Although thorough, this method requires three separate measurements of myocardial displacements to obtain the 3D strain tensor. This approach also assumes strain to be homogeneous within each finite tetrahedral volume and determines the average strain in this region.

The method presented in this paper combines the benefits from 2D and 3D measurements. Even with a short scan time, this method provides the full 3D Lagrangian strain tensor from two 2D DENSE measurements. Temporal evolutions of transmural 3D Lagrangian strains from two intersecting 2D planes of slice-followed cine DENSE data are obtained using a bilinear-cubic polynomial element to resolve strain from the displaced myocardial positions. The method is validated against an analytical standard in both an ideal situation and with noise added to the analytical model. To illustrate the method, 3D strains during systole are presented at an anterior-basal region of the left ventricular (LV) myocardium, resulting from data acquired at the intersection of a long axis sagittal plane with a short axis basal plane.

Methods

Imaging protocol

Time resolved myocardial displacement data from a healthy volunteer were acquired by a 3 T MR scanner (Philips Achieva, Philips Medical Systems, Best, The Netherlands) using an in-house implemented ECG triggered cine DENSE sequence with k -space segmented EPI readout. The initial reference position was encoded at end diastole (ED), defined by the ECG R-wave peak. Displacement was measured in a basal short axis and a long axis sagittal (approximately orthogonal to a four chamber view). These views were measured using slice-following to enable true myocardial tracking in three dimensions (Fischer, *et al.* 1994). Data were acquired during multiple end expiratory breath holds. The undesirable signal component arising from the T_1 relaxation was suppressed by complementary encoding with RF phase cycling (Fischer, *et al.* 1993); which also increases signal-to-noise ratio (SNR) by averaging. Further suppression of the T_1 relaxation signal component was achieved with a regional k -space filter. The following imaging parameters were used during data acquisition; repetition/echo time (TR/TE) 8.4/3.9 ms, 10 degree flip angle, k -space segmentation factor 3, EPI factor 7, SENSE factor 2, temporal resolution 40 ms, FOV 350x350 mm, slice thickness 8 mm, acquisition matrix size 128x120, reconstructed pixel size 1.46x1.46 mm, displacement encoding strength 0.35 cycles/pixel. In order to reduce influence of off-resonance fat signal, the fat shift direction was chosen to displace most of the fat surrounding the heart away from the myocardium.

The measurements were approved by the local ethical review board and informed consent was obtained from the healthy volunteer. The epicardial and endocardial

contours were manually delineated based on image intensity in the magnitude images for all cardiac phases.

Phase unwrapping

In DENSE the phase of the MRI signal is proportional to the myocardial displacement. The phase acquired with MRI is however arithmetic modulo 2π , which can be represented by wrapping the phase into the interval $-\pi$ to π . This property results in spatial phase discontinuities as the phase wraps, which need to be unwrapped in order to obtain the correct displacement. Using the segmentation to outline the myocardium, the MRI phase was unwrapped (Moon-Ho Song, *et al.* 1995) using a multigrid solver to the Poisson equations (Farneback, *et al.* 2007).

Region selection

The intersection line of the two planes was used to define a region of the LV myocardium for subsequent transmural and temporal analysis of Lagrangian strain. By combining displacement data from both 2D planes near the intersection, 3D Lagrangian strains could be computed within this region. Figure 1 shows, in magnitude images, the intersection of the two planes. In both planes myocardial elements were selected within a region along the intersection line, within 1.8 mm from the intersection, in the reference configuration. These material points were used in the subsequent strain analysis.

The two planes were mapped by rigid body translation and rotation to account for tracking variability between the two separate scans, caused by differences in breathhold position and slice orientation. At each time frame, the long axis plane was translated to assure that the centroid of the selected myocardial points in the long axis plane coincided with the centroid of the selected myocardial points in the short axis

plane. The long axis plane was then rotated to assure alignment of the intersection line at each time frame. This mapping assured that the intersection of the two planes coincided over the complete cardiac cycle.

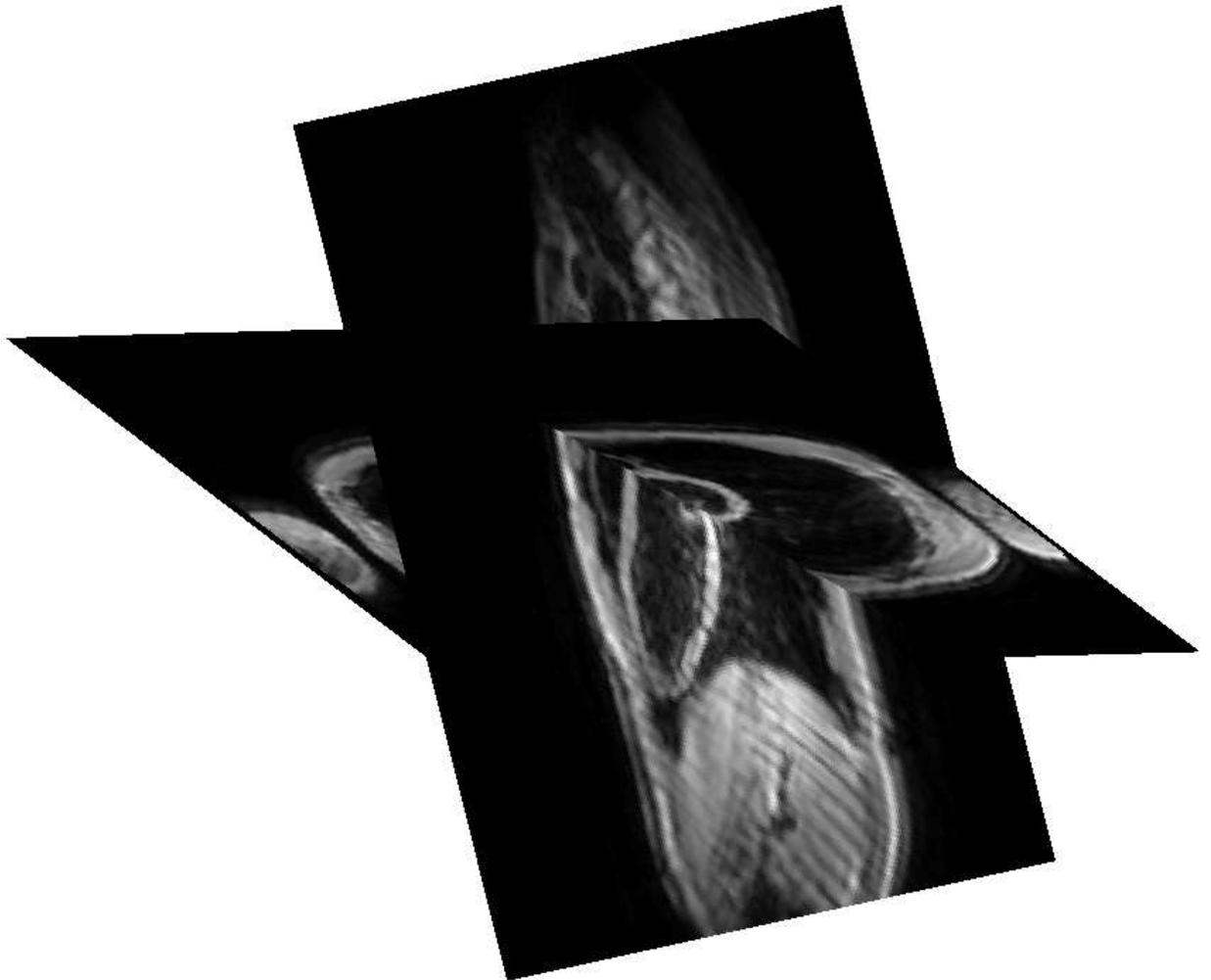


Figure 1: Intersection of 2D planes. The long axis sagittal plane intersecting the short axis basal plane shown in magnitude images. Myocardial elements are selected in both planes within a region along the intersection line in the reference configuration.

A local Cartesian cardiac coordinate system was defined at the intersection region, with axes along the radial (X_R), circumferential (X_C) and longitudinal (X_L) directions of the LV. The radial axis was defined as the intersection vector of the two planes, the circumferential axis as orthogonal to X_R in the short axis plane, and the longitudinal

axis as normal to the short axis image plane. The long axis plane was at an angle β from the short axis plane. The cardiac axes are illustrated in Figure 2.

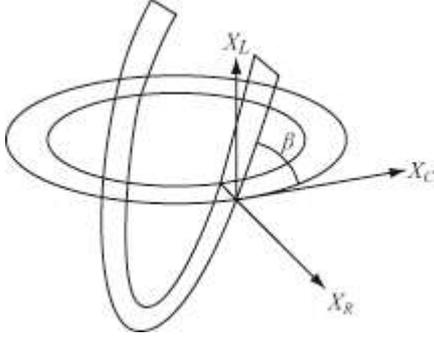


Figure 2: Cardiac coordinate system. The short axis plane is spanned by the radial (X_R) and circumferential (X_C) axes, with the longitudinal axis (X_L) defined as normal to the plane. The angle between the two planes is β .

Slice-followed DENSE acquires displacements at any time t_n relative to a reference configuration of the myocardium, at the spatial coordinates $\mathbf{s}=(s_x, s_y, s_z)$. The (s_x, s_y) coordinate relate to the encoded 2D plane while the s_z -values are given by the displacements in the through-plane direction. The spatial coordinates $\mathbf{S}=(S_x, S_y, S_z)$ of the myocardium in the reference configuration at time T_0 were derived by adding the inverse displacements to the spatial coordinates at the current configuration; $\mathbf{S}(t_1) = \mathbf{s} + \mathbf{f}^{-1}(\mathbf{s}, t_1)$, illustrated in Figure 3. The material coordinates of myocardial points at the region of interest were identified in the reference configuration, $\mathbf{X}(\mathbf{S})$, and tracked for each temporal frame to obtain the Lagrangian displacements of the cine DENSE data.

Resolving 3D Lagrangian strain

Myocardial strain was computed from the acquired data using a polynomial least squares fitting method for strain estimation (Kindberg, *et al.* 2007). The mapping from reference to deformed configuration was modeled by a polynomial function of the coordinate of the material point in the reference configuration. This polynomial position field gives an estimate $\hat{\mathbf{x}}$ of the measured coordinate \mathbf{x} and can be of

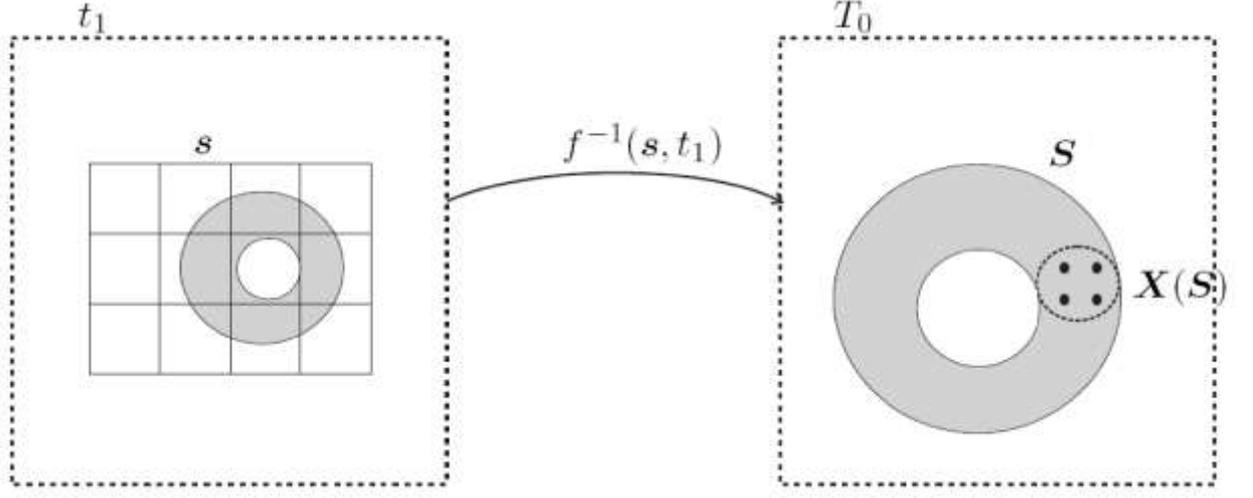


Figure 3: Current and reference configurations. The myocardial coordinates in the reference configuration \mathbf{S} are acquired by adding the inverse displacements f^{-1} to myocardial coordinates at the current configuration \mathbf{s} . $\mathbf{X}(\mathbf{S})$ are the material coordinates of myocardial points at the region of interest

different order in the different reference coordinate directions depending on the number of material points along each dimension. For the data in this study, a bilinear-cubic polynomial, linear in X_C and X_L and cubic in X_R , was fitted to the myocardial positions in each time frame. For the material point with position vector (X_R, X_C, X_L) in the reference configuration, the polynomial

$$\hat{x}_i = (a_{1i} X_R^3 + a_{2i} X_R^2 + a_{3i} X_R + a_{4i}) (a_{5i} X_C + a_{6i}) (a_{7i} X_L + a_{8i})$$

$$= [X_R^3 X_C X_L, \dots, 1] \cdot \begin{bmatrix} c_{1i} \\ \vdots \\ c_{16i} \end{bmatrix} \quad (1)$$

was a bilinear-cubic estimate of the coordinate x_i in the current configuration where a_{ki} and c_{li} are sets of constants and $i=R,C,L$. The constants c_{li} were determined at each time frame by minimizing the squared difference between the measured and the estimated coordinates of the myocardial material points. Strain was quantified by differentiation, and the Lagrangian strain tensor was given by

$$E_{IJ} = \frac{1}{2} \left(\frac{\partial \hat{x}_i}{\partial X_I} \frac{\partial \hat{x}_i}{\partial X_J} - \delta_{IJ} \right) \quad (2)$$

where each of the indices I, J and i refer to the set of R, C, L directions, δ_{IJ} is the Kronecker delta and summation over i is implied.

Validation

A previously presented analytical model (Kindberg, Karlsson, Ingels & Criscione 2007; McCulloch & Omens 1991) was used to evaluate the strain computation. Briefly, the model is a thick-walled cylinder that deforms to resemble the LV during systole. The cylinder was adapted to experimental data with inner radius $R_i = 21.0$ mm and outer radius $R_o = 29.6$ mm at the reference configuration, and inner radius $r_i = 16.8$ mm at the deformed configuration. Material points were sampled at six transmural positions through the cylinder wall within a short axis plane and a long axis plane, respectively, within 1.8 mm from the intersection of the two planes. Strains were computed within the region of intersection using the method described above, and were compared with the analytical strains (\tilde{E}_{IJ} , where each of the indices I and J refer to the set of R, C, L directions).

Noise sensitivity of the strain quantification was analyzed by adding noise to the analytical model. The noise had normalized distributions, with mean value of zero and standard deviation 0.25 mm in the in-plane directions and 0.70 mm in the through-plane direction, for each slice respectively.

Results

Analytical validation

The absolute errors of the estimated strains, $\varepsilon_{IJ} = \left| \tilde{E}_{IJ} - E_{IJ} \right|$, integrated through the wall of the cylinder, were for the ideal situation $\varepsilon_{RR} = 3.7 \cdot 10^{-3}$ for the radial strain, $\varepsilon_{CC} = 9.6 \cdot 10^{-4}$, $\varepsilon_{LL} = 4.5 \cdot 10^{-5}$, $\varepsilon_{CR} = 2.0 \cdot 10^{-4}$, $\varepsilon_{LR} = 1.5 \cdot 10^{-4}$ and $\varepsilon_{CL} = 1.9 \cdot 10^{-4}$, with mean value $8.8 \cdot 10^{-4}$. The mean absolute error of the estimated strains for the case with noise was 0.06 (range 0.04 to 0.07)

In vivo strains

In the *in vivo* data set, an anterior-basal region of the LV myocardium was defined at the intersection of the two planes. The angle between the two planes was $\beta = 96^\circ$. The reference frame was at ED for all frames. The systolic temporal analysis started at 100 ms after ED (referred to as near-ED below). The anterior-posterior distance through the LV was computed to illustrate the changes in LV volume (LVV) (Ingels, *et al.* 1975). Minimum LVV occurred approximately at 380 ms after ED, which was regarded as ES in the subsequent analysis. The number of material points across the wall within the selected region increased during systole due to systolic wall thickening. The total number of material points within the region of interest was 34 at near-ED and 44 at ES, approximately distributed along five transmural columns. Strains are displayed at three transmural depths; subendocardium, midwall and subepicardium, defined as 25%, 50% and 75% of wall thickness.

The temporal evolutions of all six strain components from near-ED to ES at the anterior-basal LV region are shown in Figure 4 and the end-systolic strains are

tabulated in Table 1. During the interval, midwall E_{RR} increased from zero to 0.52, midwall E_{CC} decreased from zero to -0.21 and midwall E_{LL} decreased to -0.14.

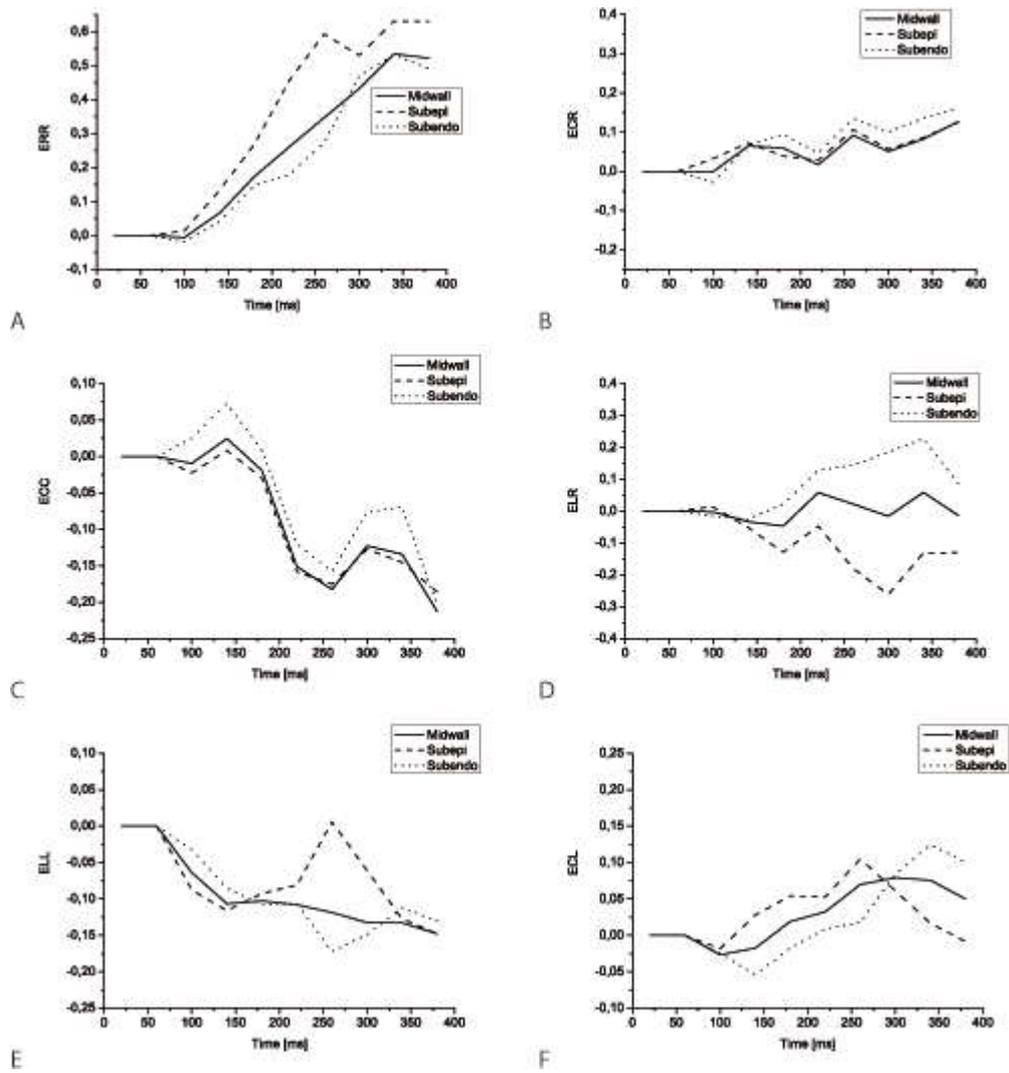


Figure 4: Myocardial systolic strains. Temporal evolutions from near-ED to ES of all six 3D strain components at three transmural levels at the anterior basal region. A) E_{RR} , B) E_{CR} , C) E_{CC} , D) E_{LR} , E) E_{LL} , F) E_{CL} .

Discussion

Spottiswoode et al. (Spottiswoode, Zhong, Lorenz, Mayosi, Meintjes & Epstein 2008) have shown that displacements acquired by slice-followed DENSE MRI in one image plane allows for the calculation of the in-plane 3D normal strains and shear. In order to obtain the entire strain tensor, 3D displacements from more than one plane are needed. In a recent paper, Hess et al. (Hess, Zhong, Spottiswoode, Epstein & Meintjes 2009) suggest two parallel planes of 2D cine DENSE combined with one SENC acquisition to formulate the 3D strain from constant-strain tetrahedra within a region of 16 mm thickness. Although elegant and straight forward, this approach assumes strain to be homogeneous within each finite tetrahedral volume and determines the average strain in this region. The current paper suggests utilizing of a bilinear-cubic polynomial element to resolve strain at the intersection of two planes of slice-followed cine DENSE.

The method suggested herein was validated using an analytical model adapted to the *in vivo* data. Noise sensitivity was analyzed in the analytical model by adding noise to each coordinate direction in the deformed configuration and computing the absolute strain errors. The noise levels evaluated were chosen to be representative for the noise of the *in vivo* data in this study.

To illustrate the method, 3D strains during systole were presented at an anterior-basal region of the LV myocardium. The observed *in vivo* temporal evolutions of systolic strains agree to within experimental accuracy with the values previously reported at ES as $E_{RR} = 0.42 \pm 0.21$, $E_{CC} = -0.20 \pm 0.03$, $E_{LL} = -0.15 \pm 0.03$, $E_{RC} = E_{CR} = 0.05 \pm 0.06$, $E_{RL} = E_{LR} = -0.05 \pm 0.05$ and $E_{CL} = 0.01 \pm 0.04$ for the anterior basal midwall of healthy human volunteers from MR tagging (Moore, *et al.* 2000), and from cine DENSE and

SENC at the anterior equatorial midwall (Hess, Zhong, Spottiswoode, Epstein & Meintjes 2009) where $E_{RR} = 0.43 \pm 0.16$, $E_{CC} = -0.20 \pm 0.04$ and $E_{LL} = -0.09 \pm 0.03$ reported as principal strains along the radial and approximate circumferential and longitudinal directions, respectively. The relatively high spatial resolution of DENSE allows for analyses of transmural distributions of strain. There is, to our knowledge, no previous study of transmural distributions of systolic shear strains in the antero-basal wall of normal human hearts. Saber et al. reported longitudinal-radial shear strain from a 2D long-axis plane acquired in canine subjects using DENSE MRI (Saber & Wen 2004). Despite different species and different LV regions in the two studies, our transmural distribution of E_{LR} , with positive values at the subendocardium and negative at the subepicardium, agrees qualitatively with their end-systolic transmural distribution reported at the lateral wall.

The polynomial model was chosen aiming to resolve transmural strain based on sparse data, and the acquisition was designed to match this model. The lower polynomial order along the myocardial wall and the higher transmural polynomial order reflect the assumption that the fiber orientation is more or less constant at a certain transmural depth, within the region of interest, while at the same time allowing for transmural variation. With more densely sampled data, a finite element method might be a more suitable choice.

Segmentation of the myocardium was performed by manual contouring of the endocardial and epicardial borders in the magnitude images for all cardiac phases. This is a laborious process and the most time-consuming component of the analysis. Introduction of an automated segmentation technique might speed up this part of the analysis (Spottiswoode, *et al.* 2009).

The fat shift direction of the EPI readout was chosen to reduce any potential influence of the fat tissue surrounding the heart by selecting the fat shift direction that displaces a majority of the fat away from the myocardium. An alternative approach to reduce influence of off-resonance fat signal would be to use a water-selective 1-1 SPAMM preparation pulse.

The in-plane and through-plane point spread function of the acquisition differs as a trade-off between, on one hand, providing high spatial resolution transmurally while, on the other hand, providing sufficient signal-to-noise ratio in the MRI signal. This difference in point spread function has two main effects. Firstly, the voxel shape is anisotropic. Hence the displacement acquired reflects the motion in this anisotropic volume. Secondly, the accuracy of the in- and through-plane displacement differs. This difference is a consequence of the anisotropic voxel size and the choice to use the same displacement encoding strength in all direction in terms of cycles/pixel to produce the same signal drop due to deformation.

Considering natural variations between breath holds there will be a certain degree of misregistration of the two slices. This issue was addressed by guiding the volunteer during the acquisition (to reduce the misregistration itself) and by using rigid body translation and rotation compensation in the strain analysis. These two ways to reduce the influence of misalignments do mostly take into account that the position of the heart may differ between the two acquisitions.

The method has been demonstrated to quantify all six components of the 3D Lagrangian strain tensor along the transmural intersection of two slice-followed cine DENSE planes. The method demonstrated accurate results when validated in an analytical model, and was applied to *in vivo* data acquired on a 3 T MR system from a

healthy volunteer. The *in vivo* results agree within experimental accuracy with values reported in the literature.

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TABLES

Table 1: End systolic strains at the anterior basal region.

Component	Subendo	Midwall	Subepi
E_{RR}	0.49	0.52	0.63
E_{CC}	-0.20	-0.21	-0.19
E_{LL}	-0.13	-0.14	-0.15
E_{CR}	0.16	0.13	0.13
E_{LR}	0.09	-0.01	-0.13
E_{CL}	0.10	0.05	-0.01