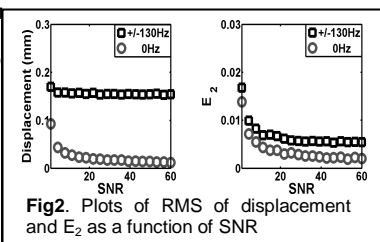


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**Introduction:** Accurate assessment of cardiac function plays an important role in the management of heart disease. Quantitative assessment of regional cardiac function may additionally improve the accuracy of detecting subtle wall motion abnormalities due to heart disease. While recently developed fast cine displacement-encoded with stimulated echoes (DENSE) MRI is a promising modality for the quantification of regional myocardial function [1], it has not been validated for clinical applications. Major limitations with in vitro validation studies in MRI include the difficulty in constructing an MR-compatible phantom that deforms like a left ventricle (LV) and has relaxation times comparable to those of the LV, and the availability of an accurate MR-compatible reference method. To circumvent such limitations, a numerical phantom was generated to model clinically relevant deformation of the heart. Therefore, the purpose of this simulation study was to validate the relative accuracy of fast cine DENSE MRI against the theoretical reference.

**Fig. 1.** Schematic diagram of the simulation. Theoretical displacement (lower left) is inputted to deform the end-diastolic tagged image, which is then processed for echo-combination DENSE reconstruction. Noise and  $B_0$  variation were incorporated as shown.  $U$ : displacement;  $\Delta F$ : off-resonant frequency.



characterize their relative contribution to displacement and strain. Specifically, in a stationary model (i.e. no motion), white Gaussian noise was included to simulate typical signal-to-noise ratio (SNR) values (e.g., 40 – 11) expected over multiple cardiac phases at 3T [1], and 130 Hz peak-to-peak  $B_0$  variation was incorporated to account for typical  $B_0$  variation within the heart at 3T [4]. In the second experiment, 20 additional cardiac frames were generated for each short-axis plane by deforming the end-diastolic image with user defined displacement fields, which were empirically derived to mimic typical LV deformation in control subjects over one cardiac cycle [5]. For apical and basal planes of the LV, the model was bulk rotated counter-clock wise and clock wise about its centroid with variable degrees on a frame-by-frame basis, respectively [6, 7]. Gaussian noise and systematic noise were incorporated as described above. For image reconstruction, the k-space was divided at frequency-encoding  $k_x = 0$ , and the echo-combination phase reconstruction was performed as previously described [1]. The theoretical and DENSE displacement maps were processed to calculate the second principal strain ( $E_2$ ), which is similar to circumferential shortening strain. The  $E_2$  maps in three short-axis planes were subdivided into 16 standardized segments [8]. For each segment, the mean  $E_2$  was calculated, and the mean  $E_2$  values were pooled for linear correlation and Bland-Altman analyses.

**Results:** Figure 2 shows plots of root-means-square (RMS) of displacement and  $E_2$  as a function of SNR. For displacement, the random error (i.e.  $\Delta F = 0\text{Hz}$ ) was inversely proportional to SNR, and the systematic error caused by  $\Delta F = 130\text{Hz}$  was approximately constant for  $\text{SNR} > 5$  and dominant over the random error. For  $E_2$ , the random noise error was inversely proportional to SNR, and the systematic error caused by  $\Delta F = 130\text{Hz}$  produced a bias. Note that the RMS of  $E_2$  was less than 0.01 for  $\text{SNR} > 5$ , and this corresponds to 5% error for typical end-systolic  $E_2$  of -0.2. In figure 3, the theoretical displacement maps (input) and the resulting tagged images (output) are shown at end systole. The apical and basal planes include counter-clock rotation of  $7^\circ$  and clock wise rotation of  $5^\circ$ , respectively. Figure 4 shows the corresponding  $E_2$  maps for both the theoretical reference (directly calculated from the inputted theoretical displacement) and DENSE reconstruction (calculated from the outputted tagged images with noise and  $B_0$  variation). For pooled data of 336 points, there was a strong correlation of  $E_2$  values between fast cine DENSE and the theoretical reference (slope = 1.02, intercept = 0.01, and  $R^2 = 0.99$ ). According to the Bland-Altman analysis, the corresponding  $E_2$  values were in good agreement (mean difference = 0.005; 95% limits of agreement were -0.007 and 0.017).

**Discussion:** This simulation study showed that  $E_2$  values produced by cine DENSE was linearly correlated and in good agreement with those produced by the theoretical reference. The computer simulation did not include complicated geometry such as wall thinning that may occur in myocardial infarction, and it did not include asymmetric deformation with respect to the centroid. More complex simulation may be necessary to model such conditions. The corresponding in vivo validation study is reported in [9]. We conclude that cine DENSE MRI is a validated method for clinical applications.

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**Fig. 3.** (Left) Theoretical displacement was used to generate the corresponding deformed (right) tagged image. H: horizontal; V: vertical.

**Fig. 4.** Corresponding  $E_2$  maps: (left) reference and (right) DENSE

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