Robust motion correction for myocardial T1 and extracellular volume mapping by principle component analysis-based groupwise image registration

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Robust Motion Correction for Myocardial T_1 and Extracellular Volume Mapping by Principle Component Analysis-Based Groupwise Image Registration

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Background: Myocardial tissue characterization by MR T_1 and extracellular volume (ECV) mapping has demonstrated clinical value. The modified Look–Locker inversion recovery (MOLLI) sequence is a standard mapping technique, but its quality can be negatively affected by motion.
Purpose: To develop a robust motion correction method for T_1 and ECV mapping.
Study Type: Retrospective analysis of clinical data.
Population: Fifty patients who were referred to cardiac MR exam for T_1 mapping.
Field Strength/Sequence: 3.0T cardiac MRI with precontrast and postcontrast MOLLI acquisition of the left ventricle (LV).
Assessment: A groupwise registration method based on principle component analysis (PCA) was developed to register all MOLLI frames simultaneously. The resulting T_1 and ECV maps were compared to those from the original and motion-corrected MOLLI with pairwise registration, in terms of standard deviation (SD) error.
Statistical Test: Paired variables were compared using the Wilcoxon signed-rank test.
Results: The groupwise registration method demonstrated improved registration performance compared to pairwise registration, with the T_1 SD error reduced from 31 $\pm$ 20 msec to 26 $\pm$ 15 msec ($P < 0.05$), and ECV SD error reduced from 4.1 $\pm$ 3.6% to 2.8 $\pm$ 2.0% ($P < 0.05$). In LV segmental analysis, the performance was particularly improved in lateral segments, which are most affected by motion. The running time of groupwise registration was significantly shorter than that of the pairwise registration, 17.5 $\pm$ 3.0 seconds compared to 43.5 $\pm$ 2.2 seconds ($P < 0.05$).
Data Conclusion: We developed an automatic, robust motion correction method for myocardial T_1 and ECV mapping based on a new groupwise registration scheme. The method led to lower mapping error compared to the conventional pairwise registration method in reduced execution time.
Level of Evidence: 3
Technical Efficacy: Stage 1

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Myocardial T_1 mapping is a useful quantitative tool for objective characterization of myocardial tissue in both ischemic and nonischemic cardiomyopathies.[1,2] With native (precontrast) and postcontrast T_1 mapping, the extracellular volume (ECV) fraction of the myocardial tissue can be estimated. ECV mapping provides an objective way to assess tissue characteristics in absolute values, enabling comparison among studies using different T_1 mapping techniques.[3–5] In addition, it has the potential to identify diffuse tissue fibrosis, which cannot reliably be assessed from late gadolinium enhanced (LGE) MRI.[6] Clinical studies have demonstrated the prognostic and diagnostic significance of ECV and T_1 measurements in various patient cohorts.[7,8]

In clinical practice, the modified Look–Locker inversion recovery (MOLLI) sequence is an established technique

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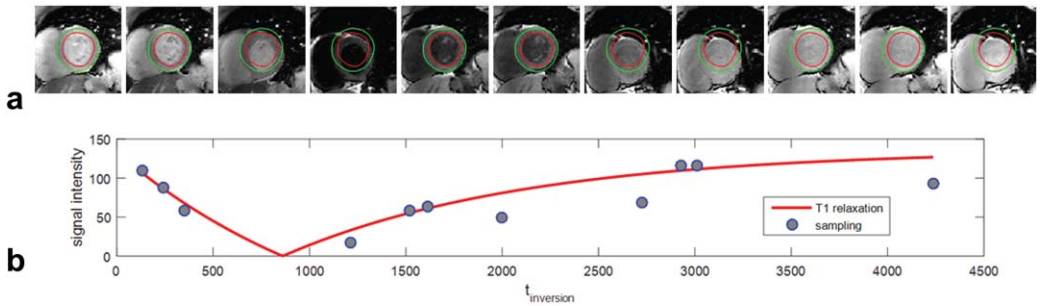

FIGURE 1: a: The MOLLI sequence from a patient who could not perform proper breath-hold. The myocardial borders were annotated on the first frame and copied to the other frames as reference. b: The sampled relaxation (blue dots) deviates from the intrinsic T_1 relaxation (red curve).

for T_1 mapping: within a single breath-hold, it acquires data across 11 heart beats at the end-diastole phase during which the heart is the most stable.[9] By breath-hold and ECG-gating, the MOLLI sequence minimizes the motion involved in T_1 mapping. In recent years, more techniques have been developed, including the shortened MOLLI (ShMOLLI),[10] saturation recovery single-shot acquisition (SASHA),[11] and saturation pulse prepared heart rate independent inversion recovery (SAPPHIRE).[12] Although all sequences use a single breath-hold and ECG-gating to suppress motion artifacts, in subgroups of patients the inability to hold breath can still negatively affect the quality of T_1 mapping. As an example, Fig. 1 shows the MOLLI frames and T_1 sampling from a subject who could not properly perform breath-hold, and the subsequent T_1 sampling that deviates from the intrinsic T_1 relaxation curve. Potentially, motion can alter not only the cardiac position but also the image intensity, both reducing the T_1 mapping quality. In recent years, free-breathing T_1 mapping methods have also been proposed that do not require a breath-hold[13,14]; however, the protocols take longer to acquire and are therefore still impractical for clinical practice.

The quality of ECV mapping is profoundly dependent on the quality of both precontrast and postcontrast T_1 maps. An issue that has seldom been addressed is the potential misalignment between precontrast and postcontrast MOLLI acquisition, which is another source of error for ECV mapping. The misalignment would cause additional error and further reduce the sensitivity and specificity of ECV maps in differentiating healthy from diseased tissue.

In practice, the misalignment within a MOLLI sequence, or between precontrast and postcontrast MOLLI sequences, can be corrected manually by visually aligning each frame to a reference frame, or automatically by registering each frame to a reference frame through image registration. In the literature, a synthetic motion correction method was proposed, which introduces synthesized T_1 images into registration, taking into consideration the specific T_1-relaxation pattern. All these methods are of pairwise by nature, ie, each registration involves only two frames out of the full set, lacking in regularization of the entire sequence. With real T_1 mapping data, it often occurs that particular frames are of very poor contrast, resulting in occasional registration failure that is difficult to predict or prevent.

The purpose of this work was to develop a postprocessing method that can robustly correct for the motion between slices in the MOLLI sequence, for both myocardial T_1 and ECV mapping.

Materials and Methods

Patients and MR Acquisition

Fifty patients (age 50 ± 17, 16 female) who were scheduled for a regular cardiovascular MR exam at Leiden University Medical Center were included in the study. The patients were referred for cardiac MR for cardiovascular investigation, including ischemic, nonischemic, and idiopathic cardiomyopathy. All acquisitions were performed on a 3.0T Ingenia MR-scanner (Philips Healthcare, Best, The Netherlands). The ECG-triggered breath-hold MOLLI sequence was acquired in three short-axis slices: apical, mid, and basal. Typical acquisition parameters were: repetition time (TR) 2.4 msec, echo time (TE) 1.1 msec, flip angle (FA) 20°, acquired resolution 1.7 × 2.1 × 10 mm, reconstructed resolution 1.25 × 1.25 × 10 mm^3, field of view (FOV) 300 × 300 mm, and reconstruction matrix 256 × 256. Both precontrast and postcontrast T_1 mapping was acquired using the same 3-3-5 scheme provided by the manufacturer. Postcontrast T_1 mapping was acquired 15–20 minutes after bolus injection of 0.15 mmol per kg body weight of gadolinium-based contrast material (Dotarem, Guerbet, France). For all patients, the hematocrit level was measured within 1 week before or after the MR acquisition. For each slice of the MOLLI sequence, the endocardial and epicardial contours of the left ventricle (LV) were manually drawn in the first frame by an experienced observer to define the region of myocardium.

The Dutch Central Committee on Human-related Research allows use of anonymous data without prior approval of an Institutional Review Board, provided that the data are acquired for regular patient care and that the data contain no identifiers that could be traced back to the individual patient. All data used for this study were acquired for clinical treatment, and were stripped of any identifying information.

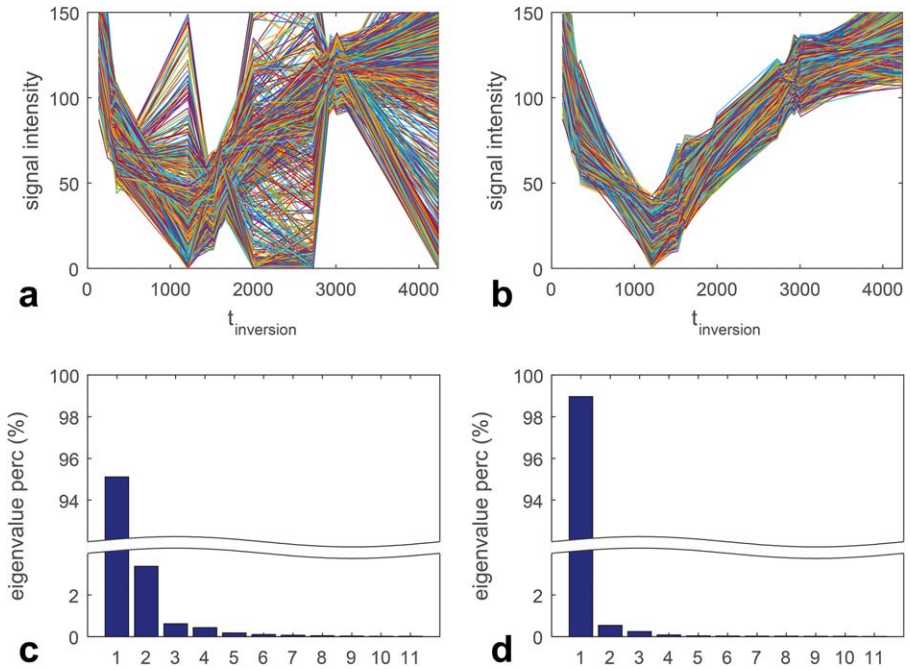

FIGURE 2: Illustration on alignment and eigenvalues. a: The group of T_1 relaxation curves per voxel from misaligned MOLLI frames (from the same example as in Fig. 1). b: The group of T_1 relaxation curves per voxel from motion-corrected MOLLI frames. c: The eigenvalue distribution (normalized to the total energy) of misaligned T_1 relaxation curves. d: The eigenvalue distribution of aligned T_1 relaxation curves.

Registration Algorithm

Compared to the pairwise registration approach that is conventionally used, we propose to use an advanced groupwise registration for motion correction in T_1 mapping,[13] which registers all frames in the MOLLI sequence simultaneously, instead of one by one. The registration is modeled by a set of transformation parameters μ. For each frame in the MOLLI sequence I_i, there is a transformation $T_i(x;\mu_i)$, $i = 1,2,\ldots N$, where x is the image coordinate and N is the number of frames. The registration is then formulated as an optimization problem to seek the optimal $\mu = (\mu_1,\mu_2,\ldots\mu_N)$, a vector containing all individual transformation parameters:

$$\hat{\mu} = \text{argmax}_{\mu} S(\mu) \tag{1}$$

where $S(\mu)$ is the similarity function that measures the similarity of all transformed images $I_i(T_i(x;\mu_i))$ with respect to each other, in a groupwise manner.

In this work, the similarity function covers all frames, based on principle component analysis (PCA), a mathematical method to capture the main modes of variation in data.[14] Given that the MOLLI frames follow the T_1 relaxation rule, the spectrum of eigenvalues from PCA, indicating the energy of variation in eigenmodes, is expected to sharply peak at the first few eigenvalues. When motion misaligns a frame, the T_1 relaxation pattern is disturbed at the voxel level, hence the mode is less strong and the spectrum of eigenvalues is expected to be less sharply peaked. An extreme case is that the eigenvalues would be nearly evenly distributed when complete misalignment removes any pattern at all. Figure 2 illustrates the phenomenon in motion-corrupted and motion-corrected T_1 relaxation curves. As such, a groupwise metric based on eigenvalues can be derived from PCA to measure the alignment of all frames altogether, as proposed previously[13,15]:

$$S(\mu) = \sum_{i=1}^{m} i\lambda_i(\mu) \tag{2}$$

in which λ_i is the i^{th} eigenvalue from PCA, weighted by i to balance the disparity of values. The first m eigenvalues were taken to estimate the similarity between all frames; in this study m is set to 3 given that the T_1 relaxation curve is parameterized by 3 variables.

To accommodate the small change of cardiac shape at end-diastole, possibly caused by variability among heart rates, we adopted a nonrigid uniform B-spline transformation for $T_i(x;\mu_i)$, with a coarse grid size identical to the diameter of the LV, estimated from the manual contour. An adaptive stochastic gradient descent optimization method was used, with a multiresolution strategy.[16]

The groupwise registration is scalable to the number of frames N. For motion correction of a precontrast or a postcontrast MOLLI sequence $N = 11$. For motion correction of precontrast and postcontrast MOLLI sequences together, all frames were pooled into the same registration in Eq. (1) and $N = 22$.

T_1 and ECV Mapping

T_1 mapping was performed by fitting the 3-parameter T_1 relaxation formula, using the Levenberg–Marquardt algorithm, on the registered frames:

$$f(TI) = A - B \cdot \exp\left(-\frac{TI}{T_1^*}\right) \tag{3}$$

in which $f(TI)$ is the longitudinal magnetization recovery curve, parameterized by A, B, and T_1^*. The T_1 values were derived from the three parameters as $T_1 = \left(\frac{B}{A} - 1\right) T_1^*$.

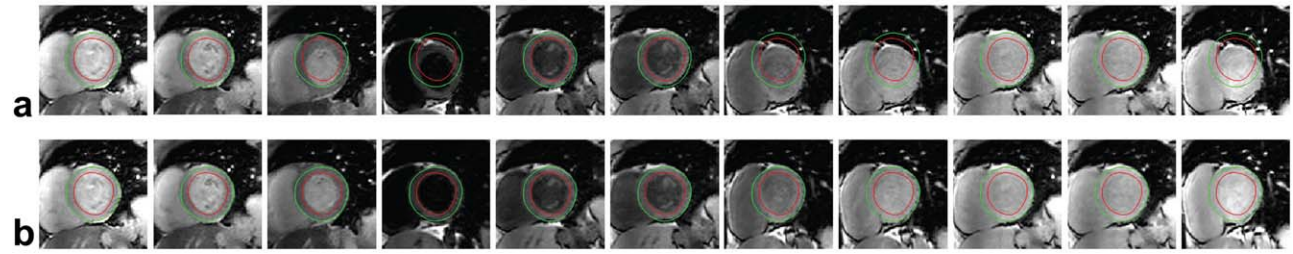

FIGURE 3: An example of motion correction by groupwise registration. a: the original uncorrected MOLLI. b: the motion-corrected MOLLI with groupwise registration. The location of the epicardial and endocardial contour is identical in all frames.

The ECV map was computed from the precontrast and postcontrast T_1 map using:

$$ECV = (1-h)\frac{\Delta R_{myo}}{\Delta R_{blood}} \quad (4)$$

where h is the hematocrit level, $R = 1/T_1$ is the relaxation rate, and Δ denotes the difference between precontrast and postcontrast relaxation rate. The blood relaxation rate R_{blood} was computed as the median value within the endocardial region (blood pool).

To evaluate the quality of T_1 and ECV mapping, we used the standard deviation (SD) map as proposed previously.[17] The SD map presents a quantitative pixelwise estimation of the mapping errors, applicable to both T_1 and ECV map. The SD map can be used as a confidence metric for the mapping quality.[17]

Validation

To evaluate the performance of motion correction by groupwise registration, we compared the mapping error of T_1 in the follow five scenarios:

1. ORG: the original uncorrected MOLLI;
2. PW: the motion-corrected MOLLI with pairwise registration;
3. SYN: the motion-corrected MOLLI with pairwise registration through synthetic image estimation, a state-of-art motion correction method[18];
4. GW: the motion-corrected MOLLI with the proposed groupwise registration, with precontrast and postcontrast MOLLI processed separately;
5. GW2: the motion-corrected MOLLI with the proposed groupwise registration, with precontrast and postcontrast MOLLI grouped together.

In scenario (2), the registration was pairwise, registering each frame to the first reference frame. In scenario (3), the registration was also pairwise, registering each frame to the synthetic frame with similar contrast.[18] For fair comparison, the spline grid parameter, optimization method, and number of iterations for optimization were all set to be the same in pairwise and groupwise registration. The only difference is the optimization metric used: for pairwise registration it is the pairwise mutual information, while for groupwise registration it is the presented groupwise PCA metric. In the first four scenarios, the precontrast and postcontrast T_1 map was registered by aligning the center of the manually annotated contours. We quantified the mapping error for T_1 and ECV mapping in the myocardial region of interest (ROI), as manually annotated.

Lateral segments of the LV are known to be more susceptible to motion artifacts than septal segments.[19,20] We evaluated segmental performance of the T_1 mapping, based on the American Heart Association (AHA) standard of 17 LV segments.[21] In our dataset, each patient has three short-axis slices, at apical, mid, and basal, covering segments from 1 to 16. We quantified two measures in the 16 segments: 1) the mean T_1 mapping error within each segment, and 2) the SD of ECV values within each segment. The second measure quantifies the variation of ECV map at segment level, which can be sensitive to misalignment.

Statistical Analysis

Continuous variables were expressed as mean ± SD. Paired variables were compared using the Wilcoxon signed-rank test, assuming no underlying distribution. $P < 0.05$ was considered significant. The Pearson's correlation coefficient was computed to evaluate the correlation between variables.

The registration algorithm was implemented using the Elastix toolbox,[22] and the other processing steps were developed in the MatLab environment (v. R2015b, MathWorks, Natick, MA).

Results

T_1 Values and T_1 Fitting Accuracy

The motion correction methods (1–4) were successfully applied to all 50 subjects. An example of motion correction is shown in Fig. 3, with the 11 MOLLI frames before and after motion correction by the proposed groupwise registration (scenario 1 vs. 4). The location of the epicardial and endocardial contours was identical in all frames to provide reference.

The resulting mean myocardial T_1 and ECV values within the myocardium ROI per subject after motion correction with the developed groupwise registration method (GW2) are shown in Fig. 4, plotted against the T_1 and ECV values from the original uncorrected MOLLI. The Pearson correlation coefficient was 0.96 for the precontrast T_1, 0.99 for the postcontrast T_1, 0.97 for the ECV values.

The four different motion-correction methods were applied to the precontrast and postcontrast MOLLI sequences in all subjects. The T_1 mapping error was computed in the ROI of myocardium. Figure 5 shows the mapping error of T_1 value (in msec) and ECV (in %) map of the error in the ROI for the five different scenarios.

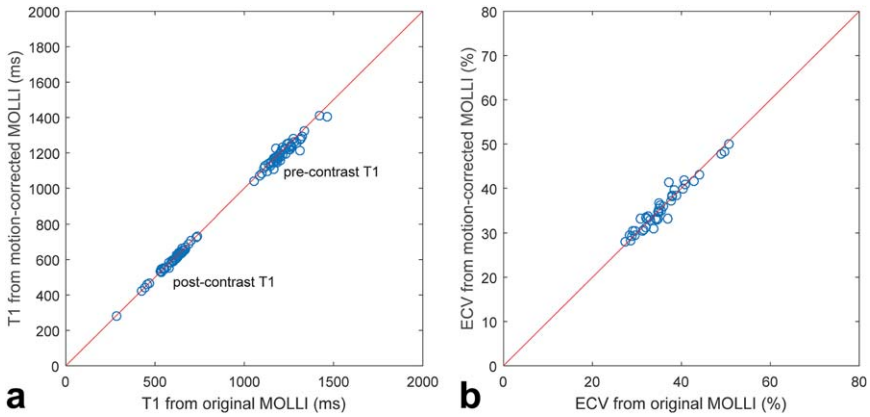

FIGURE 4: T_1 (a) and ECV (b) values from the original MOLLI and from the motion-corrected MOLLI by the groupwise registration methods.

The mean SD error of T_1 mapping in the ROI was 26 ± 15 msec for the groupwise registration (GW), significantly lower than that of the original (ORG) 30 ± 20 msec ($P < 0.05$) and pairwise registration (PW) 31 ± 20 msec ($P < 0.05$). It was not significantly different from pairwise registration with synthetic image (SYN) 26 ± 16 msec ($P = 0.4$), or groupwise registration with precontrast and postcontrast sequences (GW2) 26 ± 15 msec ($P = 0.7$).

The mean SD error of ECV mapping in the ROI was 3.3 ± 2.2% for the groupwise registration (GW), significantly lower than that of the original (ORG) 4.2 ± 2.9% ($P < 0.05$) and pairwise registration (PW) 4.1 ± 3.6% ($P < 0.05$). It was not significantly different from pairwise registration with synthetic image (SYN) 3.3 ± 2.1% ($P = 0.8$). However, it significantly outperformed by groupwise registration with precontrast and postcontrast sequences (GW2) 2.8 ± 2.0% ($P < 0.05$).

ECV Map

Two examples of ECV maps, from the original, pairwise, synthetic, and groupwise registration are shown in Fig. 6. The first example shows a subject with good breath-hold, and second example shows a subject with poor breath-hold. It can be observed from the figure that in the example of good breath-hold, all methods produced comparable results, while in the example of poor breath-hold, the groupwise registration led to reduced error and more uniform performance across the myocardium.

Evaluation in AHA Segments

We computed the T_1 and ECV mapping error per AHA segment (1 to 16) for all subjects in Figs. 7 and 8, respectively, from all different motion correction methods. It can be observed that the inferior and lateral segments[4–6,10–12] were associated with higher mapping error, compared to septal segments,[2,3,8,9,14] as suggested in the literature.[19,20] In Figs. 7f and 8f, it can be observed that the groupwise registration method performed better compared to the pairwise methods in correcting for the trend in segments.

Execution Performance

Executed on a 3.5 GHz Intel Xeon computer with 32 GB RAM, for each short-axis slice the running time of motion correction was 43.5 ± 2.2 seconds for pairwise registration, 56.2 ± 4.2 seconds for pairwise registration with synthetic image estimation, 17.5 ± 3.0 seconds for groupwise registration with 11 frames, and 26.2 ± 4.9 for groupwise

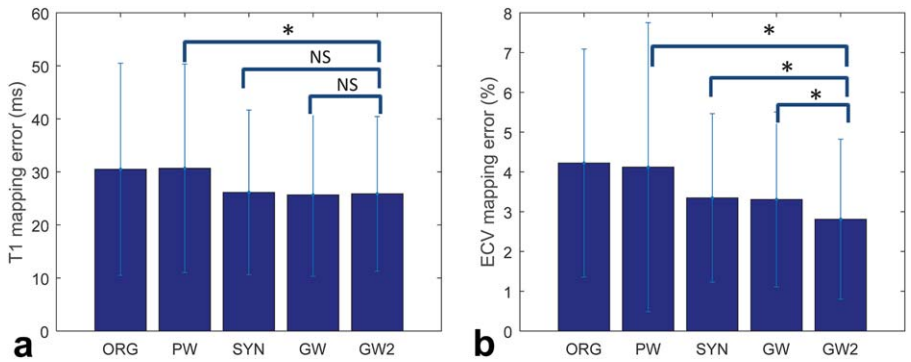

FIGURE 5: The mean (a) and STD (b) of T_1 mapping error of the original and four different motion-corrected MOLLI sequences. "ORG" denotes the original uncorrected sequence, "PW" denotes pairwise motion correction, "SYN" denotes pairwise motion correction with synthetic image, "GW" denotes groupwise motion correction of precontrast and postcontrast MOLLI separately, "GW2" denotes groupwise motion correction of precontrast and postcontrast MOLLI together.

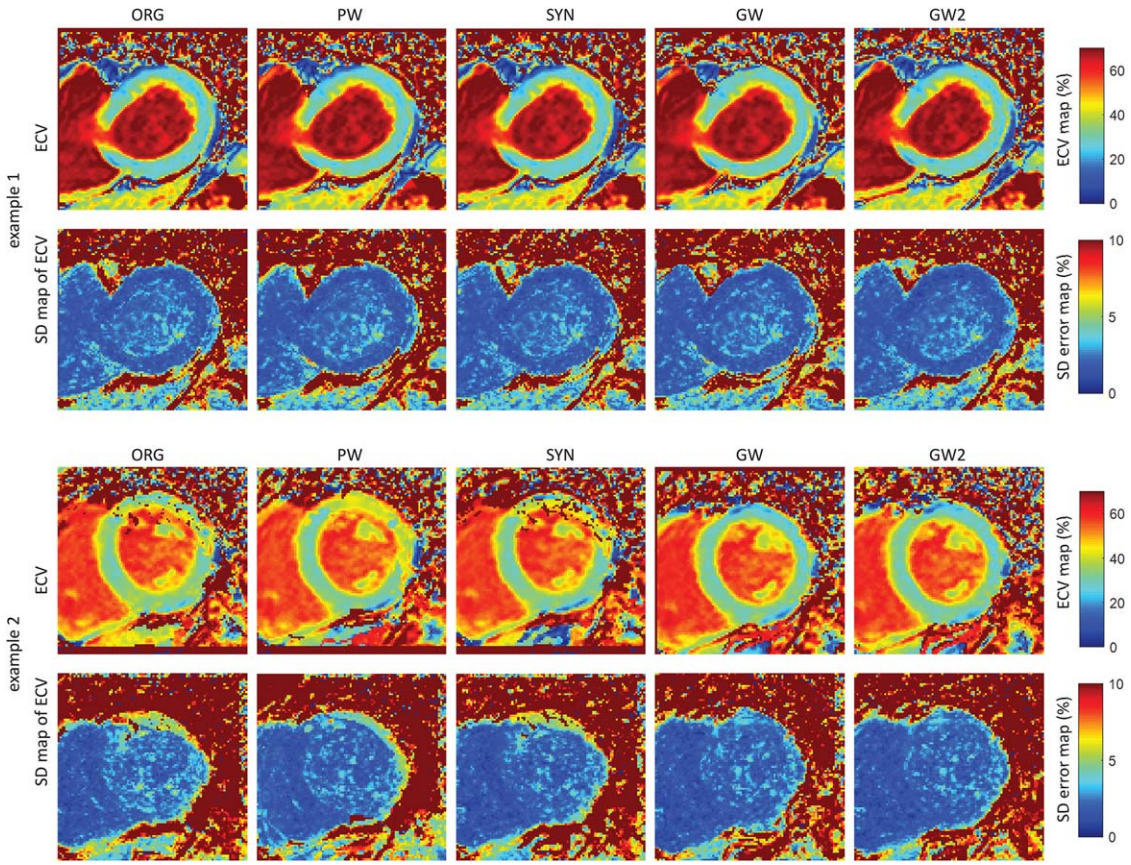

FIGURE 6: Two examples of the resulting ECV map and its corresponding SD error map from different motion correction methods. In each example, the upper row is the ECV map and the lower row is the error map. From left to right: "ORG" denotes the original sequence, "PW" denotes pairwise motion correction, "SYN" denotes pairwise motion correction with synthetic image, "GW" denotes groupwise motion correction of precontrast and postcontrast MOLLI separately, "GW2" denotes groupwise motion correction of precontrast and postcontrast MOLLI together. Example 1 is a case with little motion, in which all methods had comparable results, while in Example 2 the groupwise methods led to lower SD error, in particular in the anterior wall.

registration with 22 frames. The two groupwise registration methods were significantly faster compared to the two pairwise methods ($P < 0.05$). However, we note that the speed of groupwise registration can also be largely improved with parallelization, taking advantage of multiple cores by running the image registration for multiple slices in parallel. The groupwise registration method with two acquisitions is significantly slower than the groupwise registration method with one acquisition, because the computational cost increases nonlinearly with the number of frames.

Discussion

In this study we presented a robust motion-correction method to simultaneously align all frames from the MOLLI sequences. The method demonstrated improved performance compared to the conventional pairwise method, in terms of T_1 mapping error and SD of ECV map.

Quantification of ECV has shown promise to identify myocardial tissue characteristics in an objective and reproducible manner.[3] However, the range of ECV values can overlap between patient groups and healthy controls,[5] limiting its sensitivity and specificity in clinical application. As such, the significant reduction of SD error in ECV mapping by our method is of high clinical interest.

In practice, registration between precontrast and postcontrast T_1 maps has rarely been addressed, mostly done by rigidly aligning manual contours, while in reality the misalignment can be large and nonrigid, given the considerable time interval between precontrast and postcontrast acquisition. In this work we were able to address motion correction using a unified groupwise registration strategy by pooling both precontrast and postcontrast sequences in one registration process. As demonstrated by the results, the GW2 method that aligned all 22 frames in two MOLLI sequences produced the best ECV mapping performance. The method is not only accurate but also objective, as it does not necessitate the manual drawing of precontrast and postcontrast contours.

A disadvantage of the conventional pairwise registration is that the registration of each frame is independently performed while not globally regulated. In a MOLLI sequence, there are often one or two frames with extremely poor contrast, close to the signal nulling point of inversion recovery. It is difficult to correctly register such frames to a

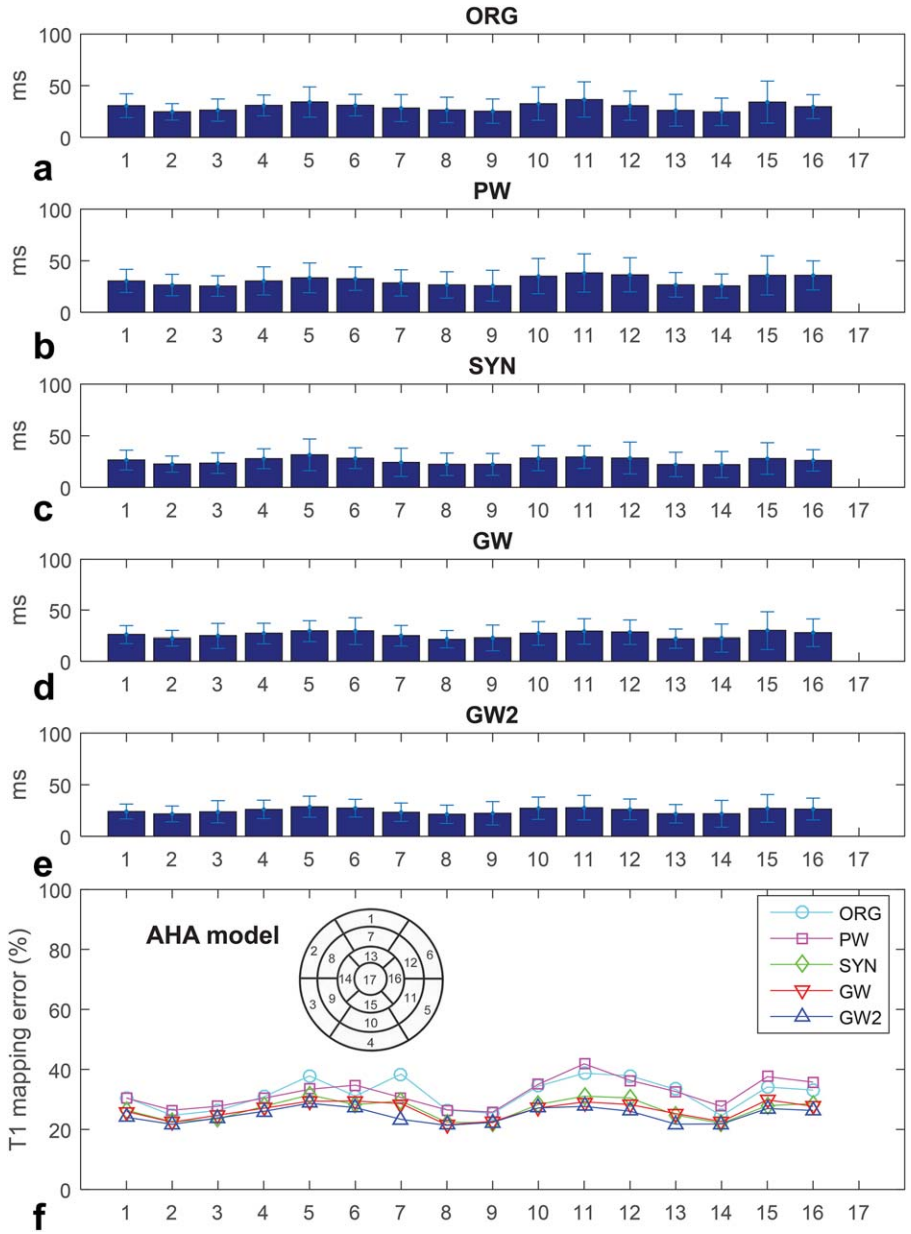

FIGURE 7: The mean T_1 mapping error per AHA segment. Subfigures a–e show different scenarios: (a) original sequence, (b) pairwise motion correction, (c) motion correction with synthetic image, (d) groupwise motion correction of precontrast and postcontrast MOLLI separately, and (e) groupwise motion correction of precontrast and postcontrast MOLLI together. Subfigure (f) compares the mean mapping error of all methods in one view. The two groupwise methods ("GW" and "GW2") resulted in lower T_1 mapping error compared to the rest, especially in the lateral segments.[4–6,10–12]

reference frame, since there is not sufficient information. In a worst case, if the reference frame has poor contrast, the registration of the whole sequence would have poor performance. Although the state-of-art registration techniques work well in most frames with reasonable contrast, the one or two failing frames can still significantly deteriorate the quality of T_1 mapping. Although the state-of-art registration techniques work well in most frames with reasonable contrast, the one or two failing frames can still significantly deteriorate the quality of T_1 mapping. The motion-correction method using synthetic image estimation addresses the problem by creating synthetic frames with similar image contrast for more robust registration performance. In this work, the method demonstrated significantly improved performance compared to the original pairwise registration. However, the method remains essentially pairwise. Furthermore, the synthetic image can become unreliable if the initial misalignment is large. In contrast, the proposed groupwise registration method tackles the problem by searching for a global optimum, taking into account all frames simultaneously by maximizing the pattern across all frames.

In this work we also investigated the segmental performance of T_1 and ECV mapping with the standardized AHA heart model. It has been known that lateral segments are

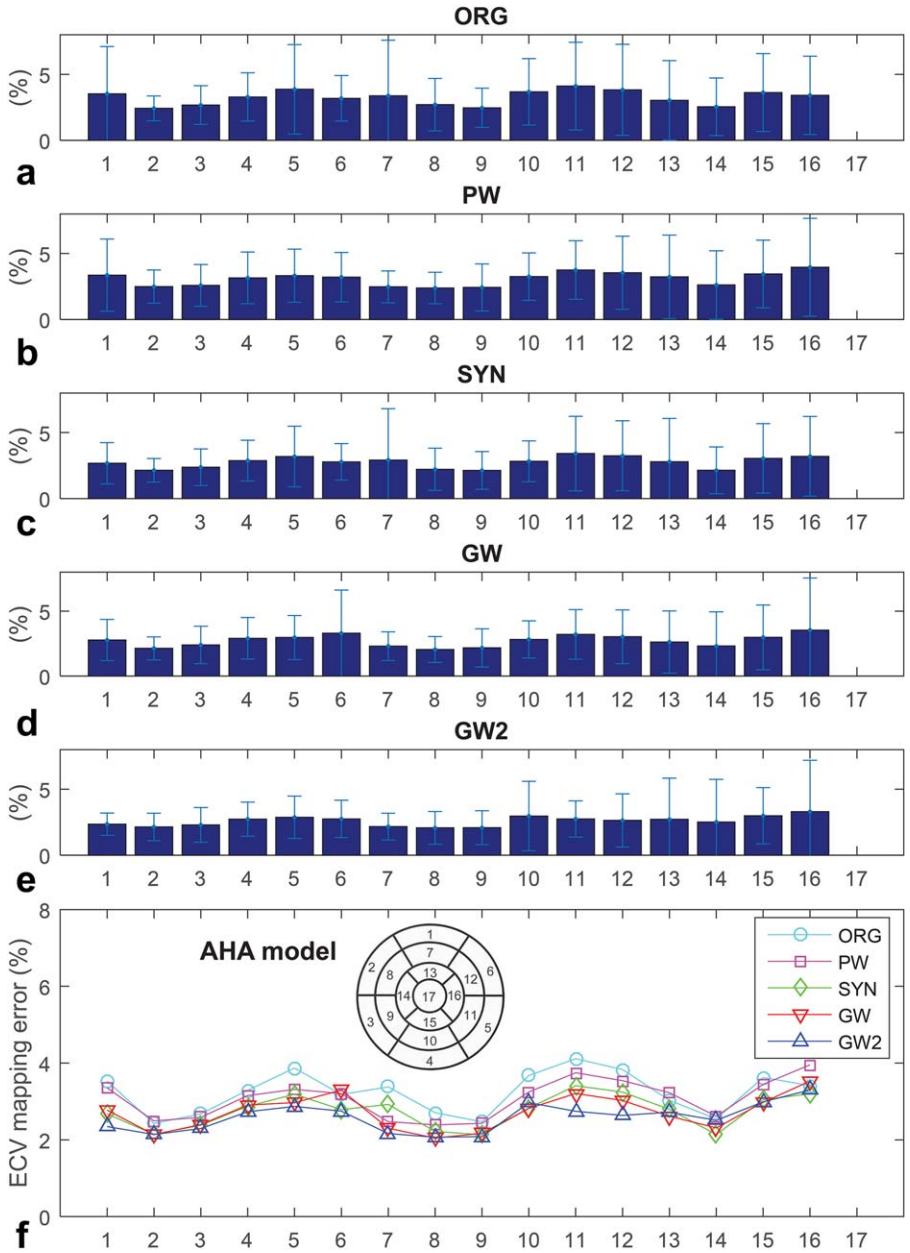

FIGURE 8: The mean ECV mapping error per AHA segment. Subfigures a–e show different scenarios: (a) original sequence, (b) pairwise motion correction, (c) motion correction with synthetic image, (d) groupwise motion correction of precontrast and postcontrast MOLLI separately, and (e) groupwise motion correction of precontrast and postcontrast MOLLI together. Subfigure (f) compares the mean mapping error of all methods in one view. The two groupwise methods ("GW" and "GW2") resulted in lower T_1 mapping error compared to the rest, especially in the lateral segments.[4–6,10–12]

more susceptible to motion artifact than septal segments, and our results show that the groupwise registration method acts to correct for the disparities between septal and lateral segments, reducing the trend caused by motion.

The proposed groupwise registration strategy is shown to be efficient in computation. By performing one comprehensive registration step instead of $N-1$ registration steps, it significantly reduces the computational effort of repetitively deriving the gradient of cost function for each registration.

The presented groupwise registration method for MOLLI can be generic in the sense that it can also apply to other T_1 sequences such as ShMOLLI, SASHA, or SAPPHIRE and potentially also to other quantitative sequences such as T_2* mapping. The registration is scalable to N, and the PCA criteria do not assume any particular form of dynamic change, while robust to varying image contrast.

A limitation of the study is that a real reference standard, such as histology or a moving T_1 phantom, is lacking and we could only compare the performance to the standard MOLLI itself. In the meantime, we are aware of fact that our method only acts as a postprocessing method, and cannot address the accuracy issue related to MR pulse

sequences.[6] Nevertheless, the proposed method can still improve the T_1 mapping precision by better alignment prior to fitting, in particular in cases of poor breath-hold.

Most subjects in our study could hold their breath reasonably well. Ideally, it would be desirable to also include patients with systematically degraded breath-hold to better demonstrate the benefit of our motion correction method. The proposed method is expected to work directly for such data with larger motion, but further study is warranted

In conclusion, we developed an automatic, robust motion correction method for myocardial T_1 and ECV mapping based on groupwise registration of the MOLLI frames. Our results show that the method led to lower errors in T_1 and ECV estimation, both overall and in segments, compared to conventional pairwise registration, in reduced execution time.

Acknowledgments

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