Deep-learning-based groupwise registration for motion correction of cardiac T_1 mapping

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Abstract. Quantitative T_1 mapping by MRI is an increasingly important tool for clinical assessment of cardiovascular diseases. The cardiac T_1 map is derived by fitting a known signal model to a series of baseline images, while the quality of this map can be deteriorated by involuntary respiratory and cardiac motion. To correct motion, a template image is often needed to register all baseline images, but the choice of template is nontrivial, leading to inconsistent performance sensitive to image contrast. In this work, we propose a novel deep-learning-based groupwise registration framework, which omits the need for a template, and registers all baseline images simultaneously. We design two groupwise losses for this registration framework: the first is a linear principal component analysis (PCA) loss that enforces alignment of baseline images irrespective of the intensity variation, and the second is an auxiliary relaxometry loss that enforces adherence of intensity profile to the signal model. We extensively evaluated our method, termed "PCA-Relax", and other baseline methods on an in-house cardiac MRI dataset including both pre- and post-contrast T_1 sequences. All methods were evaluated under three distinct training-and-evaluation strategies, namely, standard, one-shot, and test-time-adaptation. The proposed PCA-Relax showed further improved performance of registration and mapping over well-established baselines. The proposed groupwise framework is generic and can be adapted to applications involving multiple images.

Keywords: Quantitative Cardiac MRI · Groupwise Registration · Principal Component Analysis · Relaxometry.

1 Introduction

Quantitative MRI (qMRI) of the heart, such as T_1 and T_2 mapping [17,19], has become an increasingly important imaging modality for non-invasive examination of heart diseases [6]. In principle, the quantitative values of T_1 or T_2 relaxometry are inferred by fitting a known parametric model to a series of baseline images with different intensities and contrasts, assuming anatomical alignment. In practice, however, the alignment assumption is often violated by the involuntary respiratory and cardiac motion of patients [26], resulting in deteriorated

accuracy and precision of the quantitative mapping [9,10]. This makes motion correction an essential post-processing step for qMRI [15,23].

Conventionally, qMRI motion correction is performed in a pairwise fashion, by first selecting a single image or an average image as the *template*, and then registering the rest of the series to this template [3]. The choice of template, however, is nontrivial [12,20]. Some baseline images of qMRI can have extremely poor contrast depending on the acquisition setting and can fail catastrophically in pairwise registration. Such failure can severely undermine the final mapping quality. In contrast, groupwise registration, which registers all baseline images simultaneously, is a promising alternative. The groupwise paradigm avoids explicit selection of a template, and utilizes the shared information among all baseline images. The design of groupwise similarity, however, is not as straightforward as pairwise similarity. Aggregation of pairwise metrics was proposed to describe the groupwise alignment, including accumulated pairwise estimates [25] and the sum of variances [18]. Notably, Huizinga *et al.* [8] proposed a principle component analysis (PCA)-based metric that characterizes groupwise alignment without aggregating pairwise metric computation, in the Elastix framework [11].

The role of image registration in medical image analysis is well-established, with traditional optimization-based methods that optimize the deformation fields per dataset [3,8,11,15], and recent deep-learning-based methods that predict the deformation fields through a parameterized network[1,2,4,7,12,13,14,16,27]. Compared with iterative optimization-based methods, deep-learning-based methods promises much faster inference with competitive performances [2,4]. Interestingly, deep-learning-based methods can also be interpreted as amortized optimization on the training dataset, generalizable to in-domain data [2]. For qMRI, most deep-learning-based methods follow the pairwise paradigm, relying on the selection of a template [1,14]. A groupwise deep learning framework for qMRI was proposed recently, [13,28], but it still relies on the selection of a template and aggregates pairwise metrics as the groupwise loss.

With the MRI signal model known, physics-informed qMRI registration has been explored [24,5,26]. The methods are mostly optimization-based, which is typically slow, and the additional mapping loop further adds to the long computation. A recent work, PCMC-T1 [7], predicts motion-corrected baseline series by minimizing qMRI fitting error. However, the registration solely relied on the T_1 fitting error, which can be sensitive to the initial motion [23], while susceptible to shape collapse (*i.e.*, overfitting the signal model) [13].

In this work, to realize fast, template-free, physics-informed motion correction of T_1 mapping, we propose a novel groupwise registration framework. The groupwise registration makes use of PCA with a robust yet straightforward premise: the intensity profiles of all pixels should adhere to a low-rank model. This *implicitly* regulates anatomical alignment across baseline images. Furthermore, we design an auxiliary relaxometry loss, which *explicitly* incorporates the MR relaxometry into the registration, also in a groupwise manner. The second loss serves to refine the registration after PCA, given that it can be sensitive to motion and prone to overfit. We show that the proposed method, termed "PCA-Relax", sig-

nificantly outperformed established medical image registration baselines in our extensive experiments with different training-and-evaluation settings.

2 Method

2.1 Groupwise Image Registration

In quantitative MRI, a series of N baseline images are acquired for mapping, denoted by $I^N = \{I_i | i = 1, 2, \ldots, N\}$, where $I_i \in \mathbb{R}^{H \times W}$ is an image of size $H \times W$. The objective of groupwise registration is to align these images into a common coordinate system through parameterized 2D deformation fields $\phi^N = \{\phi_i | i = 1, 2, \ldots, N\}$, ensuring that all $I^N \circ \phi^N = \{I_i \circ \phi_i | i = 1, 2, \ldots, N\}$ align. The proposed deep-learning groupwise image registration framework is built upon the well-established VoxelMorph backbone [2]. As shown in Fig. 1, the parameterized network $\mathcal{R}_{\theta_1}$ takes I^N stacked along the channel dimension as input, and passes them through a U-Net architecture [21] to predict ϕ^N.

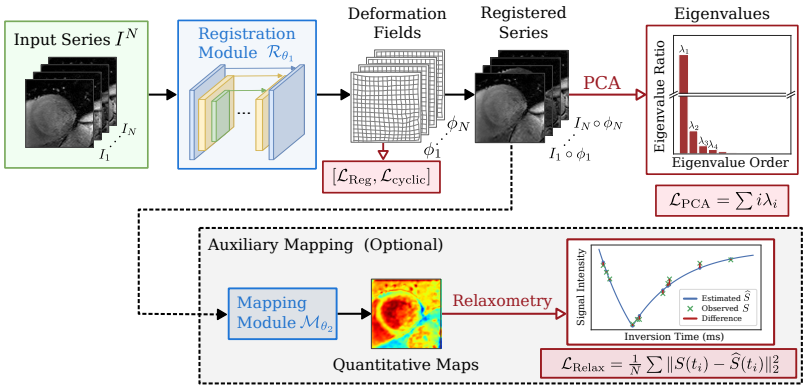

Fig. 1. An overview of the proposed template-free groupwise registration framework. It takes the baseline image series I^N through the registration module to predict ϕ^N. The warped series $I^N \circ \phi^N$ undergoes PCA decomposition to calculate the groupwise PCA loss without a template. If the auxiliary mapping module is enabled, the relaxometry loss is also activated to refine the registration module.

2.2 PCA-based Template-free Similarity Metric

In qMRI, the signal intensity $S_{(x,y)}$ at image coordinate (x, y), follows a parametric signal model. For T_1 mapping, with the widely adopted Modified Look-Locker inversion recovery (MOLLI) [17] sequence, the signal model is defined as follows:

$$S_{(x,y)}(t_i) = \left| C_{(x,y)} \left(1 - k_{(x,y)} \exp\left(-\frac{t_i}{T^*_{1\,(x,y)}} \right) \right) \right|, \tag{1}$$

where t_i is the inversion time of I_i. The parameters $C_{(x,y)}$, $k_{(x,y)}$ and $T^*_{1\,(x,y)}$ are the underlying tissue parameters at coordinates (x, y) to derive $T_{1\,(x,y)} = (k_{(x,y)} - 1)T^*_{1\,(x,y)}$. For a well-aligned MOLLI image series, the group of signal profiles has a low rank. This can be visually appreciated, as shown in Fig. 2 (d).

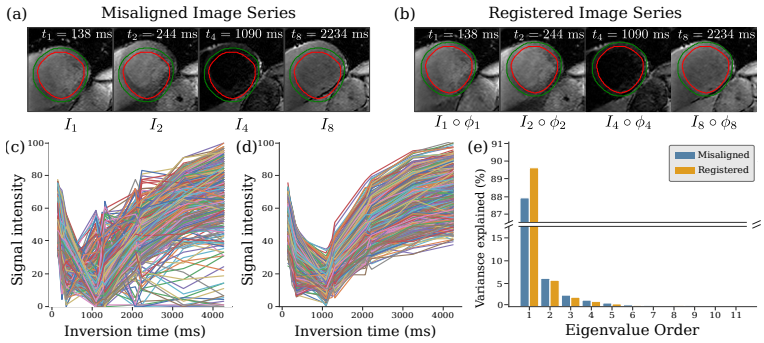

Fig. 2. Illustration of cardiac motion correction in qMRI. Sampled (a) misaligned and (b) registered series. Voxel-wise intensity curve for (c) misaligned and (d) registered series. And (e) the comparison of eigenvalues of the correlation matrix.

PCA provides an intuitive way to evaluate the groupwise alignment across all baseline images. By first rearranging the registered series $I^N \circ \phi^N$ into a data matrix $M \in \mathbb{R}^{HW \times N}$ such that each row represents a signal profile of length N, the alignment of all baseline images can be characterized by performing PCA decomposition on the normalized correlation matrix K:

$$K = \frac{1}{HW-1} \Sigma^{-1} (M - \overline{M})^\top (M - \overline{M}) \Sigma^{-1}, \tag{2}$$

$$K = U \Lambda U^\top, \quad \Lambda = \mathrm{diag}(\lambda_1, \lambda_2, \ldots, \lambda_N), \tag{3}$$

where $\Sigma = \mathrm{diag}(\sigma_1, \sigma_2, \ldots, \sigma_N)$ with σ_i being the standard deviation of each column, $\overline{M}$ is the column-wise mean matrix, U is the orthogonal matrix of eigenvectors, and $\lambda_1, \lambda_2, \ldots, \lambda_N$ are the eigenvalues of K in descending order. Ideally, the variance of K should be explained by the first few eigenvalues if all baseline images are aligned. However, motion can induce noisy or shifted row entries in M, resulting in a more scattered distribution of eigenvalues of K (Fig. 2 e). Therefore, we define the PCA loss as follows [8]:

$$\mathcal{L}_{\mathrm{PCA}} = \sum_{i=1}^{N} i\lambda_i. \tag{4}$$

Since $\sum_{i=1}^{N} \lambda_i$ equals to N given the normalized correlation matrix K, a smaller $\mathcal{L}_{\mathrm{PCA}}$ indicates a sharper energy concentration at the first few eigenvalues.

2.3 Auxiliary Relaxometry Loss

In principle, the aligned series should follow the MR signal model at each voxel, *e.g.*, as in Eq. 1. However, quantitative parameters (C, k, T_1^*) are normally estimated by least-square methods or grid search [5,24], lacking practical differentiability. This makes it difficult to integrate the physics prior into the deep learning registration framework. To incorporate the physics prior of relaxometry, we propose a *differentiable* qMRI mapping module and use it to further refine the PCA-based registration. We design an end-to-end U-Net [21] architecture to construct this module $\mathcal{M}_{\theta_2}$, parameterized by θ_2 [29]. The module takes stacked registered images $I^N \circ \phi^N$ and inversion times $t^N = \left\{t_i \in \mathbb{R}^{H\times W} | i = 1, 2, \ldots, N\right\}$ as input, and output parameter maps $[C, k, T_1^*] \in \mathbb{R}^{3\times H\times W}$. The mapping module is pre-trained, independently of the registration module, in a fully self-supervised fashion. The relaxometry loss is defined as the normalized fitting error:

$$\mathcal{L}_{\text{Relax}} = \frac{1}{NHW} \sum_{(x,y)\in\Omega} \sum_{i=1}^{N} \left\| S_{(x,y)}(t_i) - \widehat{S}_{(x,y)}(t_i) \right\|_2^2, \tag{5}$$

where Ω denotes the spatial domain of an image $I \in \mathbb{R}^{H\times W}$, $S_{(x,y)}(t_i)$ is the signal intensity of $I_i \circ \phi_i$ at (x, y), and $\widehat{S}_{(x,y)}(t_i)$ is the estimated intensity by evaluating Eq. 1 at (x, y). The differentiability of $\mathcal{L}_{\text{Relax}}$ is established through its sequential composition of $I^N \circ \phi^N$, $\mathcal{M}_{\theta_2}$, and signal model. We note that in our work, $\mathcal{L}_{\text{Relax}}$ is *optional* as shown in Fig. 1, and can be omitted if the registration problem is model-agnostic.

2.4 Regularization on Groupwise Deformation

In addition to the two template-free groupwise losses $\mathcal{L}_{\text{PCA}}$ and $\mathcal{L}_{\text{Relax}}$, we further regularize the deformation fields as regularly done. The first is the regularization loss $\mathcal{L}_{\text{reg}}$ [2] on deformation fields to ensure the spatial smoothness of ϕ^N:

$$\mathcal{L}_{\text{reg}} = \frac{1}{NHW} \sum_{(x,y)\in\Omega} \sum_{i=1}^{N} \|\nabla\phi_i(x, y)\|_2^2, \tag{6}$$

where ∇ denotes the spatial gradient operator.

Specific to groupwise registration is the cyclic consistency loss $\mathcal{L}_{\text{cyclic}}$ to prevent collapsing [8,12,28]:

$$\mathcal{L}_{\text{cyclic}} = \sqrt{\frac{1}{NHW} \sum_{(x,y)\in\Omega} \left(\sum_{i=1}^{N} \phi_i(x, y) \right)^2}, \tag{7}$$

which enforces the deformation fields to warp the baseline images to a "mean shape" of the group [8,20]. Therefore, the total loss is:

$$\mathcal{L}_{\text{total}} = \lambda_{\text{PCA}}\mathcal{L}_{\text{PCA}} + \lambda_{\text{reg}}\mathcal{L}_{\text{reg}} + \lambda_{\text{cyclic}}\mathcal{L}_{\text{cyclic}} + \lambda_{\text{Relax}}\mathcal{L}_{\text{Relax}}. \tag{8}$$

3 Experiments and Results

Data: We used an in-house cardiac MRI dataset including 50 subjects. Each subject has both pre-contrast and post-contrast MOLLI sequences (Philips 3.0T) with a fixed length $N = 11$. All images were resampled to a 1 mm resolution and center-cropped to a size of 128×128. The dataset was randomly split subject-wise to prevent data leakage: $(36, 4, 10)$ subjects were used for training, validation, and testing. To evaluate out-of-domain generalization, training involved only pre-contrast sequences, whereas validation and testing included both pre-contrast and post-contrast sequences.
Training-and-evaluation: We employed three train-and-evaluation settings to assess the registration performance. **Standard**: the model was trained on the training dataset and unchanged at inference time. **One-shot**: the model was randomly initialized and trained on the input T_1 mapping sequence. **Test-time Adaptation (TTA)**: the model was pre-trained on the training dataset and finetuned on the input image as in [2].
Comparison Study: The following scenarios were compared:

1. Raw: Original series without any registration.
2. VM-P: A pairwise registration baseline with the VoxelMorph backbone, which registered all baseline images to $I_{\text{template}} = I_1$, with normalized mutual information (NMI) loss.
3. VM-G: A template-based groupwise registration baseline with the VoxelMorph backbone, using $I_{\text{template}} = \frac{1}{N}\sum_{i=1}^{N} I_i \circ \phi_i$ as the template, and aggregated pairwise NMI loss.
4. PCA: Our template-free groupwise framework with $\mathcal{L}_{\text{PCA}}$.
5. PCA-Relax: Our template-free groupwise framework with $\mathcal{L}_{\text{PCA}}$ and $\mathcal{L}_{\text{Relax}}$.

Evaluation Metrics: We evaluated our proposed method in terms of T_1 mapping quality, as indicated by the fitting SD values [9]. Instead of evaluating tissue heterogeneity, the fitting SD measures the quality of curve fitting of the signal model at each voxel. The SD map is a clinically accepted metric to evaluate the quality of T_1 mapping [6,10,22,24], as it is difficult to compare contours or landmarks across the cardiac qMRI baselines given the varying contrast. We estimated the fitting SD following [9] and calculated the SD values in the myocardium region for each series, manually annotated by experienced radiologists.
Implementation Details: Our models were developed in PyTorch, with thorough hyper-parameter tuning on the validation split. The hyperparameters for PCA-Relax were set to $\lambda_{\text{PCA}} = 1, \lambda_{\text{reg}} = 10, \lambda_{\text{cyclic}} = 0.1, \lambda_{\text{Relax}} = 10$. For PCA, we set $\lambda_{\text{Relax}} = 0$. The models VM-P and VM-G utilized the NMI loss with $\lambda_{\text{NMI}} = 10$. For mapping module $\mathcal{M}_{\theta_2}$, the encoder features 5 convolutional layers with channel counts $[32, 32, 32, 64, 64]$; the decoder mirrors the encoder. We pretrained $\mathcal{M}_{\theta_2}$ for 100 epochs on the training split. The architecture of $\mathcal{R}_{\theta_1}$ is the same as $\mathcal{M}_{\theta_2}$. We used the ADAM optimizer, with learning rates of 5×10^{-4} for Standard, and 1×10^{-3} for One-shot, and TTA with early stopping after 500 iterations. Parametric fitting was performed using the Nelder-Mead algorithm

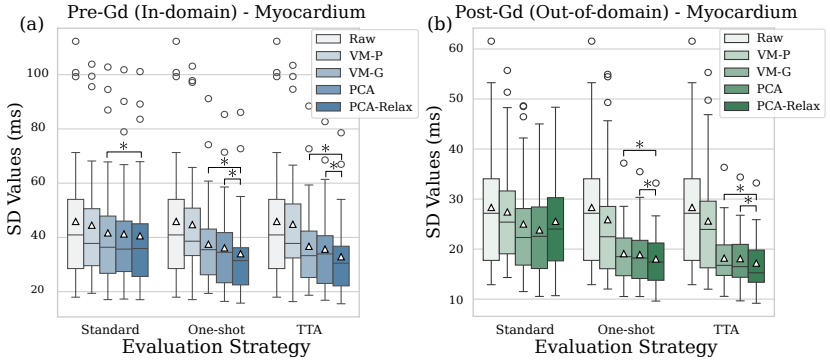

Fig. 3. Boxplots of T_1 SD values in the myocardium, with lower values indicating better motion correction: (a) Pre-Gd (in-domain) and (b) Post-Gd (out-of-domain). All five scenarios were evaluated in three training-and-evaluation settings. One-sided Wilcoxon signed-rank tests were conducted to compare the performance of PCA-Relax against that of PCA and VM-G. Statistically significance ($p < 0.05$) is labeled with *.

after registration. All experiments were conducted on an NVIDIA RTX 4090 GPU. Our code will be released on GitHub.

Results: We evaluated all four motion correction methods, as well as the raw data, on three training-and-evaluation settings. The box plots are shown in Fig. 3, with detailed statistics reported in Table 1. Our template-free registration baseline (PCA) outperforms the competitive VoxelMorph baselines (VM-P, VM-G) in all scenarios. Furthermore, for all-but-one settings, the SD maps are improved with the mapping module activated (PCA-Relax). However, the post-Gd results in the standard setting suggest that the mapping module may overfit when a domain shift exists. (Note that the training only included the pre-contrast T_1 mapping data.) One-shot optimization and TTA per sequence take only ≈ 20 secs with the groupwise framework, making TTA a valuable trade-off for refined registration for each new input sequence, with little extra time. Qualitative improvements in cardiac T_1 mapping are illustrated in Fig. 4.

4 Conclusion

In this work, we proposed a novel template-free, deep-learning-based, groupwise registration framework, to tackle the motion correction problem for cardiac T_1 mapping. Two groupwise losses were proposed and validated: a sequence-agnostic PCA loss and a sequence-specific relaxometry loss. We extensively evaluated the proposed method, PCA-Relax, with diverse training-and-evaluation strategies on an in-house cardiac T_1 mapping dataset. The proposed method demonstrated improved performance of registration and mapping over well-established baselines. The generic formulation of our groupwise framework allows easy extension to applications that involve multiple image registration.

Table 1. Mean and standard deviation of the T_1 SD values in the myocardium, with three training-and-evaluation strategies. **Bold** denotes the best results within the specific training-and-evaluation strategy and underline denotes the overall best results.

Method	Modality	SD Values (ms) ↓		
		Standard	One-shot	Fine-tuning
Raw	Pre-Gd	45.89 (±23.33)		
VM-P	Pre-Gd	44.50 (±21.56)	44.71 (±20.90)	44.84 (±21.33)
VM-G	Pre-Gd	41.67 (±21.24)	37.50 (±16.22)	36.72 (±15.73)
PCA	Pre-Gd	41.25 (±20.35)	36.15 (±15.44)	35.66 (±15.04)
PCA-Relax	Pre-Gd	**40.58** (±20.95)	**34.00** (±15.89)	**32.88** (±14.41)
Raw	Post-Gd	28.32 (±12.15)		
VM-P	Post-Gd	27.42 (±10.79)	25.86 (±12.10)	25.60 (±11.31)
VM-G	Post-Gd	25.00 (±10.28)	19.09 (±5.75)	18.19 (±5.46)
PCA	Post-Gd	**23.82** (±**9.44**)	18.89 (±5.85)	18.08 (±5.28)
PCA-Relax	Post-Gd	25.55 (±10.04)	**18.02** (±5.43)	**17.19** (±5.28)

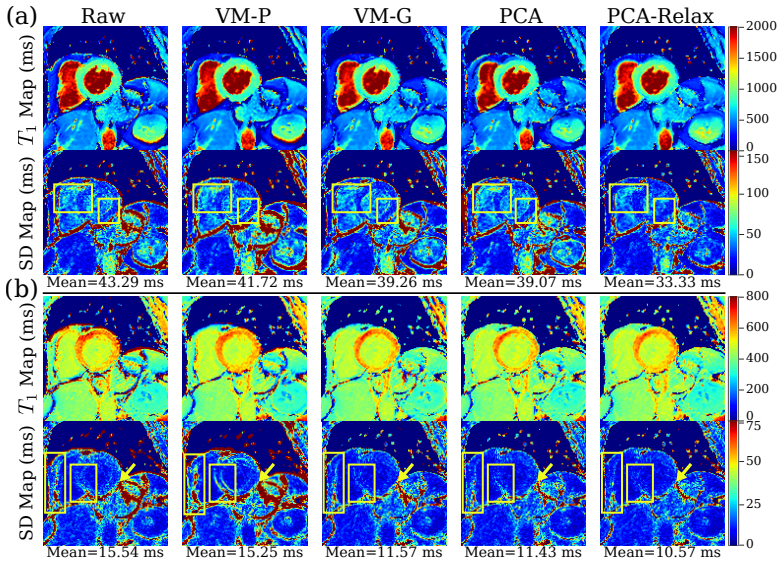

Fig. 4. Estimated T_1 and SD maps of a (a) pre-contrast and (b) post-contrast sequence with the TTA strategy. The mean values of the SD maps in the myocardium are reported. We highlight the difference in the SD maps with the yellow boxes and arrows.

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