

Learning-based motion artifact removal networks for quantitative R_2^* mapping

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Purpose: To introduce two novel learning-based motion artifact removal networks (LEARN) for the estimation of quantitative motion- and B_0 -inhomogeneity-corrected R_2^* maps from motion-corrupted multi-Gradient-Recalled Echo (mGRE) MRI data.

Methods: We *train* two convolutional neural networks (CNNs) to correct motion artifacts for high-quality estimation of quantitative B_0 -inhomogeneity-corrected R_2^* maps from mGRE sequences. The first CNN, LEARN-IMG, performs motion correction on complex mGRE images, to enable the subsequent computation of high-quality motion-free quantitative R_2^* (and any other mGRE-enabled) maps using the standard voxel-wise analysis or machine learning-based analysis. The second CNN, LEARN-BIO, is trained to directly generate motion- and B_0 -inhomogeneity-corrected quantitative R_2^* maps from motion-corrupted magnitude-only mGRE images by taking advantage of the biophysical model describing the mGRE signal decay.

Results: We show that both CNNs trained on synthetic MR images are capable of suppressing motion artifacts while preserving details in the predicted quantitative R_2^* maps. Significant reduction of motion artifacts on experimental in vivo motion-corrupted data has also been achieved by using our trained models.

Conclusion: Both LEARN-IMG and LEARN-BIO can enable the computation of high-quality motion- and B_0 -inhomogeneity-corrected R_2^* maps. LEARN-IMG performs motion correction on mGRE images and relies on the subsequent analysis for the estimation of R_2^* maps, while LEARN-BIO directly performs motion- and B_0 -inhomogeneity-corrected R_2^* estimation. Both LEARN-IMG and LEARN-BIO jointly process all the available gradient echoes, which enables them to exploit spatial patterns available in the data. The high computational speed of LEARN-BIO is an advantage that can lead to a broader clinical application.

KEYWORDS

convolutional neural networks, deep learning, gradient recalled echo, motion correction, MRI, R_2^* mapping, self-supervised deep learning

1 | INTRODUCTION

Multi-Gradient-Recalled-Echo (mGRE) sequences accompanied by correction of magnetic field inhomogeneity artifacts^{1,2} are used in different MRI applications to produce quantitative maps related to biological tissue microstructure in health and disease (e.g., References 2-9). However, involuntary physical motion and subtle anatomical fluctuations during the mGRE signal acquisition can lead to undesirable artifacts during the estimation of these quantitative maps. It is therefore important to develop methods that reduce the sensitivity of the estimated quantitative maps to the motion artifacts in the MR images.

A number of methods have been developed over the years for the prevention, mitigation, or correction of motion artifacts in MR images.¹⁰⁻²² Deep learning (DL) methods have also been recently introduced for motion-correction in MRI due to their speed and quality of reconstruction.²³⁻²⁸ Despite the recent activity, DL is yet to be investigated in the context of quantitative B_0 -inhomogeneity-corrected estimation of R_2^* maps from mGRE signals. One of the key challenges in this context is the sensitivity of the quantitative maps to the motion artifacts.²⁹

In this paper, we propose two convolutional neural networks (CNNs) for recovering high-quality quantitative R_2^* maps from the motion-corrupted mGRE images. Both of our methods, referred to LEARN-IMG and LEARN-BIO, are trained on motion-free mGRE images and their simulated motion-corrupted counterparts. LEARN-IMG follows the traditional supervised training strategy in order to correct the motion on the complex mGRE images. The high-quality motion-free and B_0 -inhomogeneity-corrected R_2^* maps can be subsequently computed by applying the standard nonlinear least squares (NLS) analysis that also accounts for the effect of background B_0 field gradients (herein we use Voxel Spread Function [VSF] approach¹) on the motion-corrected output images. On the other hand, LEARN-BIO is trained to directly map the magnitude-only motion-corrupted mGRE images to motion-free and B_0 -inhomogeneity-corrected R_2^* maps. The key feature of LEARN-BIO is that it is fully self-supervised, in the sense that it does not need ground-truth quantitative R_2^* maps for training. Instead, it is trained using only the mGRE images and the biophysical model connecting the mGRE signal with biological tissue microstructure that includes contribution of magnetic field inhomogeneities to the mGRE signal decay (described in terms of a factor $F(t)$ ¹), and our knowledge of the analytical biophysical model connecting the mGRE signal with biological tissue microstructure. LEARN-BIO is related to our recent method RoAR³⁰ that trains CNNs to learn a mapping from Gaussian noise

corrupted mGRE images to noise-free R_2^* maps. However, unlike LEARN-BIO, RoAR does not account for motion during training, which is the focus of the current work.

Both of our approaches, LEARN-IMG and LEARN-BIO, are trained on pairs of motion-corrupted and motion-free MR images without requiring the ground truth quantitative R_2^* maps, which might be challenging to obtain in some settings. The advantage of LEARN-IMG is that its training is decoupled from the quantitative mapping procedure, which means that the training does not need any prior knowledge of the biophysical model or pre-estimation of the $F(t)$ functions. Instead, LEARN-IMG is used to produce motion-artifact-free mGRE images. Consequently, it has the flexibility to enable the successive estimation not just R_2^* but also various mGRE-based quantitative maps (e.g., $R2t^*$,^{3,4} cellular density⁶). The key advantage of LEARN-BIO is that by using $F(t)$ during training, it learns to compensate for macroscopic magnetic field inhomogeneities to produce motion-artifact-free and B_0 -inhomogeneity-corrected R_2^* maps. As a result, the trained LEARN-BIO can be directly applied to the motion-corrupted mGRE images without precomputing $F(t)$ or using any additional fitting methods, resulting in a much faster computation of the quantitative maps.

We train both of our CNN models on synthetic motion-corrupted data generated using our motion simulation pipeline. We show that both approaches are capable of removing motion artifacts on synthetic as well as experimental datasets and produce high-quality in vivo quantitative maps. Quantitative and qualitative evaluations are conducted to demonstrate the robustness and effectiveness of the proposed methods.

2 | METHODS

2.1 | The mGRE sequences and biophysical model

In the R_2^* approximation, the mGRE signal from a single voxel can be expressed as:³¹

$$S(t) = S_0 \cdot \exp(-R_2^* \cdot t - i\omega t) \cdot F(t), \quad (1)$$

where t denotes the gradient echo time, $S_0 = S(0)$ is the signal intensity at $t = 0$, and ω is a local frequency of the MRI signal. The complex valued function $F(t)$ in Equation (1) describes the effect of intra- and intervoxel macroscopic magnetic field inhomogeneities on the mGRE signal. The failure to account for such inhomogeneities is known to bias and corrupt the recovered R_2^* maps. In this paper we use the VSF approach¹ for calculating $F(t)$. In the VSF approach,¹ effects of macroscopic magnetic field

inhomogeneities (background gradients) on formation of mGRE signal are evaluated from the same complex mGRE dataset that is used for calculating tissue-specific parameters of a biophysical model. They are accounted for by including in the biophysical model the term $F(t)$ that is calculated for each imaging voxel based on the values of mGRE signal phase and amplitude in this and surrounding voxels. The latter is important due to amplified signal leakage effects from the neighboring voxels (Fourier leakage) in the presence of magnetic field inhomogeneities.³² In a standard approach, the R_2^* maps, ω maps, and S_0 are jointly estimated from three-dimensional (3D) mGRE signals acquired at different echo times t by fitting Equation (1) with precalculated $F(t)$ on a voxel-by-voxel basis to experimental data by applying the NLLS analysis. However, mGRE images are often affected by motion artifacts resulting from subject movement during MRI scan. In this paper we propose two learning-based approaches that can compute motion- and B_0 -inhomogeneity-corrected R_2^* maps from motion-corrupted mGRE data.

2.2 | Motion artifacts simulation procedure

Here we present our motion generation pipeline where various levels of motion artifacts can be introduced into motion-free MR images through manipulation of k-space data, which allows us to obtain pairs of motion-free and motion-corrupted images for training our CNNs. Specifically, denote the spatial motion-free mGRE images of N echo times (e.g., $N = 10$ in our data) at slice index ℓ as

$$\mathbf{s}_\ell = (\mathbf{s}_\ell^1, \dots, \mathbf{s}_\ell^N), \quad (2)$$

where each component $\mathbf{s}_\ell^n \in \mathbb{C}^{y \times z}$ in $\mathbf{s}_\ell$ denotes a two-dimensional (2D) complex image extracted from 3D MR volume at slice ℓ for one of the echo times. Let $\mathbf{u}_\ell \in \mathbb{C}^{k_y \times k_z \times N}$ denote the k-space maps of $\mathbf{s}_\ell$ such that

$$\mathbf{u}_\ell = \mathbf{F}\mathbf{s}_\ell \quad \text{and} \quad \mathbf{s}_\ell = \mathbf{F}^{-1}\mathbf{u}_\ell, \quad (3)$$

where $\mathbf{F}$ and $\mathbf{F}^{-1}$ represent the Fourier and inverse Fourier transforms. We model the motion artifacts in the MR images as the consequences of a series of physical motions, such as shifts or rotations, that result in perturbations of blocks of k-space lines during corresponding motions. We therefore replace certain k-space lines of the motion-free MR images with those of their motion-corrupted versions to synthesize motion artifacts. Specifically, in our data, for each point in k_z , we collect $N = 10$ echoes of k-space data along the k_y direction in $\mathbf{u}_\ell$. Considering the fact that k-space scanning in the frequency-encoding direction (k_y)

is much faster than the physical movement, we assume that all 10-echo lines along k_y suffer from the same motion effects (it takes about 50 ms to get 10 gradient echoes in our approach—see Dataset section). We illustrate this motion generation method in a 2D slice-based manner which can be easily extended to 3D mGRE data by including the slice dimension. In particular, we represent the motion artifacts within a scan of slice ℓ as

$$\mathbf{T} = (\mathbf{T}_1, \dots, \mathbf{T}_J), \quad (4)$$

where $\mathbf{T}_j$ denotes the j th motion movement during the k-space data collection of $\mathbf{s}_\ell$ and J is the total number of motions. Let the binary map $\mathbf{M}_j$ indicate the frequencies that are miscollected during the j th motion (with 1 in those k-space locations and 0 otherwise), simulating the time and duration of each sudden motion. Then, the final k-space maps after J motions can be computed as

$$\tilde{\mathbf{u}}_\ell[J] = \left(\mathbf{I} - \sum_{j=1}^J \mathbf{M}_j \right) \odot \mathbf{u}_\ell + \sum_{j=1}^J \mathbf{M}_j \odot \mathbf{F}\mathbf{T}_j(\mathbf{s}_\ell), \quad (5)$$

where $\mathbf{I}$ denotes a binary map with all ones and $\odot$ denotes the element-wise multiplication of two maps. As a result, our synthetic motion-corrupted images with J motions can be computed as

$$\tilde{\mathbf{s}}_\ell[J] = \mathbf{F}^{-1}(\tilde{\mathbf{u}}_\ell[J]). \quad (6)$$

By changing the total number of motions J in addition to the location and duration of each physical motion indicated by $\mathbf{M}_j$, one can control the type and level of motion artifacts introduced to the motion-free images, and thus synthesize a variety of realistic motion-corrupted images. Notably, motion artifact generation can be conducted sequentially as the relationship between motion-corrupted images $\tilde{\mathbf{s}}_\ell[j-1]$ with the first $j-1$ motions and $\tilde{\mathbf{s}}_\ell[j]$ with the first j motions in $\mathbf{T}$ is

$$\tilde{\mathbf{s}}_\ell[j] = \mathbf{F}^{-1}((\mathbf{I} - \mathbf{M}_j) \odot \mathbf{F}(\tilde{\mathbf{s}}_\ell[j-1]) + \mathbf{M}_j \odot \mathbf{F}\mathbf{T}_j(\mathbf{s}_\ell)). \quad (7)$$

This k-space lines-replacement-based motion artifacts generation pipeline is used to simulate the motion-corrupted data for training our CNNs. Specifically, we focus on the artifacts introduced by in-plane translational and 3D rotational movements where the subject is assumed to lie still during the examination with several swift translations or rotations of the head occurring during the process. It is important to note that although the effect of global motion on the acquired k-space data is well established where translational motion induces a linear phase shift and rotational motion causes the same degree of rotation in the k-space data, our pipeline is actually more flexible as we can allow the k-space manipulation for

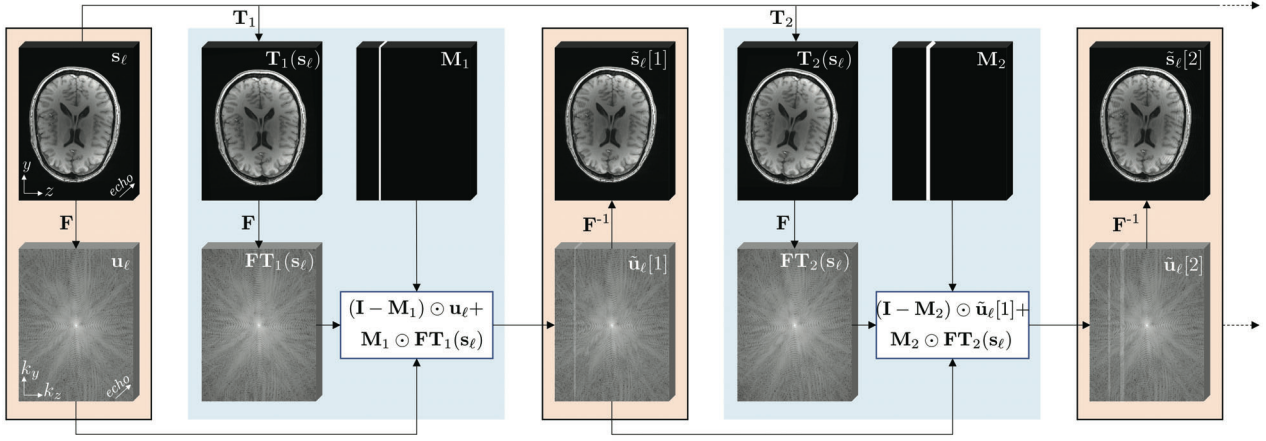


FIGURE 1 Illustration of the motion corruption simulation pipeline for given example images $\mathbf{s}_\ell$. We assume all N echoes at the given slice ℓ are corrupted by the same motion artifacts. $\mathbf{T}_1$ models the first shift and rotation when certain k-space lines at $\mathbf{u}_\ell$, indicated by $\mathbf{M}_1$, are replaced by the k-space lines of the moved object, generating the first N echoes of motion-corrupted images $\tilde{\mathbf{s}}_\ell[1]$. Similarly, the second motion represented by $\mathbf{T}_2$ and $\mathbf{M}_2$ further corrupts $\tilde{\mathbf{s}}_\ell[1]$ by generating images $\tilde{\mathbf{s}}_\ell[2]$ with stronger artifacts. The process can be repeated a desired number of times

more motion types (i.e., deformation and scaling) of different organs and we are not restricted to global motions. Figure 1 illustrates an example where the motion artifacts are due to two consecutive rigid motions.

2.2.1 | Method 1: LEARN-IMG

As defined in Equation (2), given the motion-free complex spatial mGRE images of N echo times at slice ℓ as $\mathbf{s}_\ell$, we represent the corresponding absolute value of $\mathbf{S}_0$ and true $\mathbf{R}_2^*$ maps as

$$\mathbf{p}_\ell = (\mathbf{S}_0, \mathbf{R}_2^*). \quad (8)$$

Let $\{\text{Re}(\hat{\mathbf{s}}_\ell), \text{Im}(\hat{\mathbf{s}}_\ell)\} = \mathcal{I}_\theta(\{\text{Re}(\tilde{\mathbf{s}}_\ell), \text{Im}(\tilde{\mathbf{s}}_\ell)\})$ denote our neural network LEARN-IMG that computes an estimate $\hat{\mathbf{s}}_\ell$ of the unknown motion-free $\mathbf{s}_\ell$ given the motion-corrupted mGRE signal $\tilde{\mathbf{s}}_\ell$. The operators $\text{Re}(\cdot)$ and $\text{Im}(\cdot)$ denote the real and imaginary parts of a complex number, and vector θ denotes the trainable set of weights in the CNN. The 3D convolutional structure of LEARN-IMG allows it to take both the complex statistical relationships between pixels and the echo times into account, and therefore enhances the motion correction performance and robustness of the model. As illustrated in Figure 2A, the training of our network is carried out by minimizing the empirical loss over a training set consisting of L slices $\{(\tilde{\mathbf{s}}_\ell, \mathbf{s}_\ell)\}_{\ell=1, \dots, L}$, as follows

$$\min_{\theta} \sum_{\ell=1}^L \mathcal{L}(\mathcal{I}_\theta(\{\text{Re}(\tilde{\mathbf{s}}_\ell), \text{Im}(\tilde{\mathbf{s}}_\ell)\}), \{\text{Re}(\mathbf{s}_\ell), \text{Im}(\mathbf{s}_\ell)\}), \quad (9)$$

where $\mathcal{L}$ measures the discrepancy between the vectorized estimates $\hat{\mathbf{s}}_\ell$ generated by the LEARN-IMG and the

ground-truth $\mathbf{s}_\ell$ on both imaginary and real channels. Common choices for $\mathcal{L}$ include the ℓ_1 and the ℓ_2 distances. This minimization problem can be solved by using stochastic gradient-based optimization algorithms such as Adam.^{33,34}

Our CNN architecture processes the 3D volumetric image of the whole brain by applying the model slice by slice. Once the optimal set of parameters θ^* are learned from minimizing the optimization problem on the training dataset, which consists of many slices, the trained network $\mathcal{I}_{\theta^*}$ can be applied to unseen data to perform motion-correction tasks. As illustrated in Figure 2A, the output of a LEARN-IMG network on the motion-corrupted images $\tilde{\mathbf{s}}_\ell$ is the motion-corrected complex mGRE data $\hat{\mathbf{s}}_\ell$, decomposed with its real and imaginary components. The unknown motion-free quantitative maps $\mathbf{p}_\ell$ of input signals $\tilde{\mathbf{s}}_\ell$ can then be obtained by feeding the output signals $\hat{\mathbf{s}}_\ell$ into the standard NLLS analysis, where both magnitude and phase images are needed to compute $F(t)$ values used during NLLS fitting. Notice this NLLS approach is only used for the quantitative maps computation during the test stage, not for the training of our CNN model.

2.2.2 | Method 2: LEARN-BIO

Let $\hat{\mathbf{p}}_\ell = \mathcal{B}_\eta(\text{Mag}(\tilde{\mathbf{s}}_\ell))$ denote our model LEARN-BIO, which computes the estimates $\hat{\mathbf{p}}_\ell$ of the unknown true values of $\mathbf{p}_\ell$ given the magnitude value of the mGRE signal $\tilde{\mathbf{s}}_\ell$. The operator $\text{Mag}(\cdot)$ denotes the magnitude of the complex data and vector η denotes the trainable set of weights in the CNN. The network takes absolute data

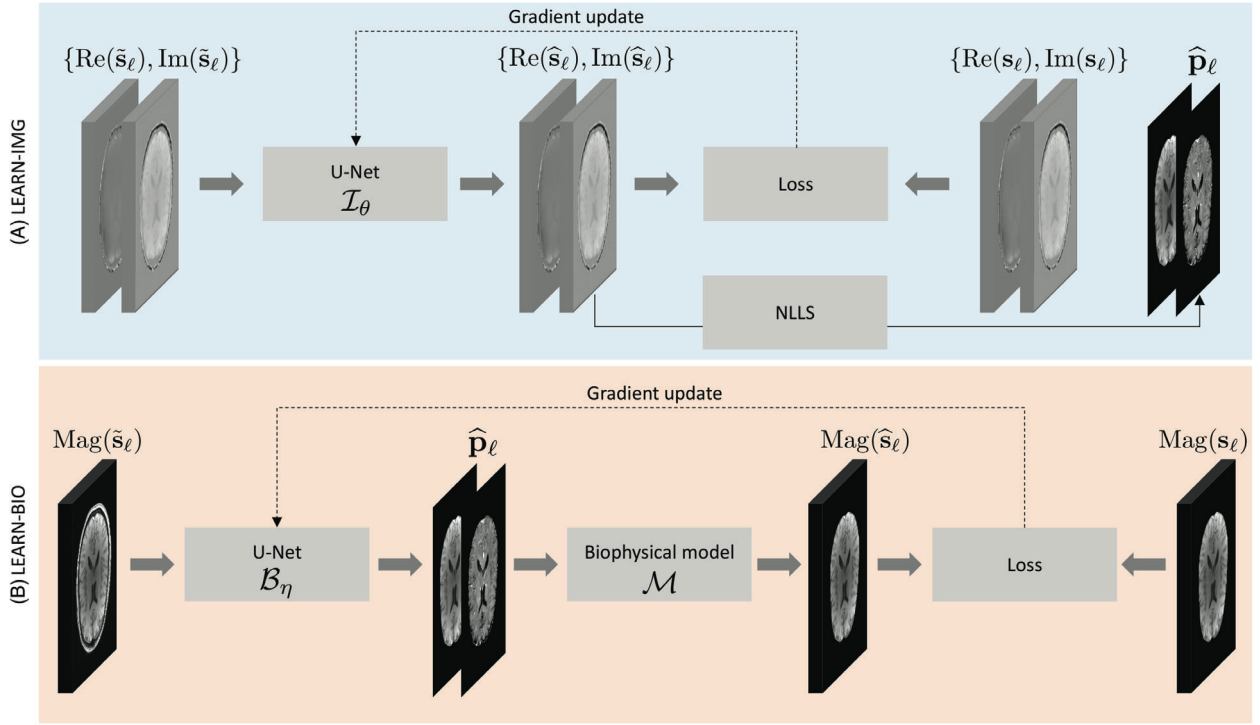


FIGURE 2 Comparison of two approaches for training the motion-correction models. (A) In LEARN-IMG, the model $\mathcal{I}_\theta$ is optimized so that $\{\text{Re}(\hat{\mathbf{s}}_\ell), \text{Im}(\hat{\mathbf{s}}_\ell)\} = \mathcal{I}_\theta(\{\text{Re}(\tilde{\mathbf{s}}_\ell), \text{Im}(\tilde{\mathbf{s}}_\ell)\})$ is close to the corresponding ground-truth multi-Gradient-Recalled Echo (mGRE) data $\{\text{Re}(\mathbf{s}_\ell), \text{Im}(\mathbf{s}_\ell)\}$. Standard nonlinear least squares approach is applied to the motion-corrected output $\hat{\mathbf{s}} = \{\text{Re}(\hat{\mathbf{s}}_\ell), \text{Im}(\hat{\mathbf{s}}_\ell)\}$ to estimate unknown motion-free quantitative maps $\mathbf{p}_\ell = (\mathbf{S}_0, \mathbf{R}_2^*)$. (B) In the self-supervised approach LEARN-BIO, the model $\mathcal{B}_\eta$ is trained to directly estimate motion-free quantitative maps $\mathbf{p}_\ell$ given measurement mGRE data $\text{Mag}(\tilde{\mathbf{s}}_\ell)$ and the biophysical model $\mathcal{M}$. The loss is formulated so that $\text{Mag}(\hat{\mathbf{s}}_\ell) = \text{Mag}(\mathcal{M}(\mathcal{B}_\eta(\text{Mag}(\tilde{\mathbf{s}}_\ell)); \mathbf{f}_\ell))$ is close to corresponding ground-truth mGRE data $\text{Mag}(\mathbf{s}_\ell)$

$\text{Mag}(\tilde{\mathbf{s}}_\ell)$ as its N -channel input and produces $\hat{\mathbf{p}}_\ell = (\hat{\mathbf{S}}_0, \hat{\mathbf{R}}_2^*)$ as its two-channel output. The major difference between LEARN-BIO and the previously described LEARN-IMG is that the former directly learns to predict motion-free quantitative R_2^* maps. LEARN-BIO is trained using a *self-supervised learning* strategy, illustrated in Figure 2B, where the model $\mathcal{B}_\eta$ is trained only using the mGRE data. We adopt a widely used definition of self-supervised learning where a model is trained using a *pretext* (or *auxiliary*) task, but tested on the actual *desired* task.^{30,35-40} In the context of our work, the *desired* task is the estimation of R_2^* maps, while the *pretext* task is the generation of high-quality mGRE images. In LEARN-BIO, self-supervised learning is enabled by using the analytical biophysical model $\mathbf{s}_\ell = \mathcal{M}(\mathbf{p}_\ell; \mathbf{f}_\ell)$ in Equation (1) to relate the mGRE images and the quantitative R_2^* maps into a loss function and solving the corresponding optimization problem on a training dataset $\{(\tilde{\mathbf{s}}_\ell, \mathbf{s}_\ell)\}_{\ell=1, \dots, L}$

$$\min_{\eta} \sum_{\ell=1}^L \mathcal{L}(\text{Mag}(\mathcal{M}(\mathcal{B}_\eta(\text{Mag}(\tilde{\mathbf{s}}_\ell)); \mathbf{f}_\ell)), \text{Mag}(\mathbf{s}_\ell)), \quad (10)$$

where $\mathbf{f}_\ell$ denotes matrices containing F-function values precalculated from the training mGRE images $\mathbf{s}_\ell$ using the VSF method. Therefore, the training of LEARN-BIO is *exclusively* reliant on the measurement data $\mathbf{s}_\ell$ instead of the ground-truth data $\mathbf{p}_\ell$, and is classified as a self-supervised method for using the supervision of measurements themselves through the signal model $\mathcal{M}$ and the prior induced by the CNN to solve the model-fitting and motion-correction problem together.

As illustrated in Figure 2B, the output of our LEARN-BIO network for the ℓ th data element yields the quantitative maps $\hat{\mathbf{p}}_\ell = \mathcal{B}_\eta(\text{Mag}(\tilde{\mathbf{s}}_\ell))$, which serve as an intermediate result for our optimization problem defined in Equation (10). The network is trained to find the best parameters η^* such that its prediction $\{\hat{\mathbf{p}}_\ell\}$ can well describe the measured mGRE signals and reduce the motion artifacts at the same time. The detailed network structures of LEARN-BIO and LEARN-IMG are illustrated in Figure S1. As described below, the training of our CNNs is done by simulating the motion artifacts.

2.3 | Motion correction with LEARN-IMG and LEARN-BIO

LEARN-IMG and LEARN-BIO are trained to remove motion artifacts from motion-corrupted mGRE data in order to produce high-quality R_2^* maps. This can be achieved by solving the optimization problem defined in Equations (9) and (10) using paired mGRE images $\{\tilde{\mathbf{s}}_\ell, \mathbf{s}_\ell\}$, where $\{\mathbf{s}_\ell\}$ are the images that are not contaminated by motion artifacts and $\{\tilde{\mathbf{s}}_\ell\}$ are the corresponding synthetic motion-corrupted images consisting of different levels of motion artifacts. We show below that our CNNs *only* trained on synthetic data can achieve excellent performance on previously unseen experimental data.

2.4 | In vivo brain dataset

For validating our method, we selected 20 different MRI scans with no visible motion artifacts (qualitatively inspected) from the previously published brain image data⁶ as the motion-free source to generate the synthetic motion-corrupted mGRE images. These brain image data are collected from 20 healthy volunteers (age range 26–76) using a Siemens 3T Trio MRI scanner and a 32-channel phased-array head coil. Studies were conducted with the approval of the local IRB of Washington University. All volunteers provided informed consent. The data was obtained using a 3D version of the mGRE sequence with $N = 10$ gradient echoes followed by a navigator echo¹⁷ used to reduce artifacts induced by physiological fluctuations during the scan. Sequence parameters were flip angle $FA = 30^\circ$, voxel size of $1 \times 1 \times 2 \text{ mm}^3$, first echo time $t_1 = 4 \text{ ms}$, echo spacing $\Delta t = 4 \text{ ms}$ (monopolar readout), repetition time $TR = 50 \text{ ms}$, and the total imaging time for each acquisition was around 10 min.

In addition, experimental brain mGRE image data of four volunteers (ages: 32, 67, 71, and 78 years) with clear visible motion artifacts were selected for evaluating the correction of real motions of our CNN models that trained on syntactic data.

2.5 | Data generation preprocessing

To obtain the paired motion-corrupted and motion-free images for training, brain mGRE images of 20 different MRI scans with no visible motion artifacts described above were selected to serve as the “motion-free” reference images for the training and quantitative evaluation of our CNNs. We split this data into 14 datasets (75%) for training, three for validation (15%) and three for testing (15%), and our aforementioned motion simulation procedure was

then applied to these datasets slice by slice to generate motion-corrupted images.

To generate a range of realistic motion artifacts for our training dataset, we select the total number of motions occurring during data acquisition as a random number in the range from 1 to 10. For each motion, we simulated random in-plane shifts within the range of 0–15 voxels followed by a combination of three random rotations along each axis relative to the center of a 3D mGRE data volume, where each rotation is within the range of 0° – 15° . While the simulation setting above yields excellent performance in our experimental data, it can be adjusted for different applications. The time at which each motion occurred and the duration it lasted were randomly generated as well. In particular, all motions were assumed to occur randomly throughout the whole examination process, and each of them is assumed to last for a random duration from about 3 to 30 s, which would be equivalent to disturbing about 1 to 10 k-space lines in a single 2D slice. All random numbers mentioned above were uniformly generated in the given range, introducing various levels of motion artifacts to our training and validation dataset. Those synthesized motion-corrupted data together with their motion-free origins were used for the training of our CNNs.

To quantitatively evaluate the performance of our trained CNNs across different levels of motion artifacts, we synthesized three motion types using our test dataset with motion settings such that the corresponding artifacts introduced by each can well represent the different levels of corruption that appear in our experimental data. In particular, we manipulate 8%, 16%, and 24% of the k-space data for each slice in our test dataset, respectively. We name the motions generated through each of these settings as *light*, *moderate*, and *heavy* motion, based on the levels of artifacts they introduced to our motion-free mGRE data. Those three settings were only applied to our test dataset to generate images at certain corruption levels for validating the robustness and capacity of our trained CNNs against different motion levels. Examples of these three motion type images are shown in Figure 3.

Prior to feeding the data into our CNNs, the top slices, that include slice oversampling images and the intracranial space images, and the bottom slices that include brain stem images or highly corrupted images due to the macroscopic field inhomogeneities, were discarded in each data volume. Specifically, we only used the middle *brain slices* corresponding to slice 25 through 55 of a 72-slice MRI data, 20 through 50 of a 60-slice MRI data, 30 through 60 of a 88-slice MRI data for all the experiments and numerical evaluation. This resulted in 4340 images for training, 930 for validation, and 930 for testing in the simulation. Each dataset was also normalized to improve compatibility of our CNNs with different scanners, parameters, and

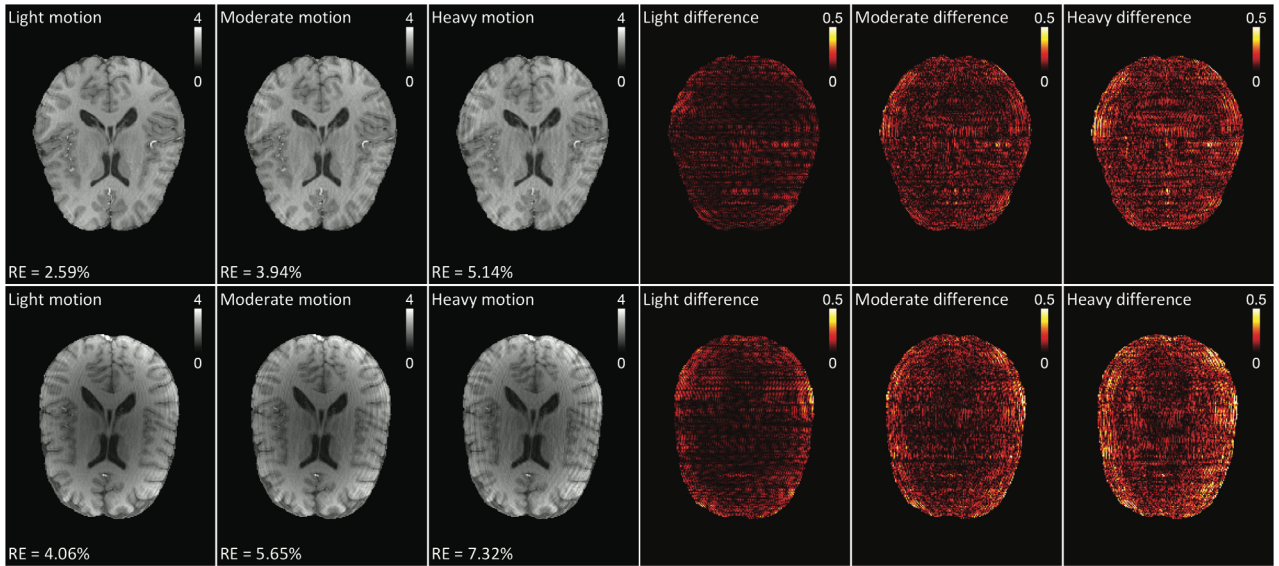


FIGURE 3 Illustration of synthetic motion-corrupted images. The background and skull voxels are masked out for better visualization. The left three columns show the magnitude of the first of 10 echoes of multi-gradient-recalled echo images corrupted with *light*, *moderate* and *heavy* motions, respectively. The relative error (RE) of each image is shown in its bottom left corner. The right three columns show the absolute differences between the motion-corrupted images and the motion-free images used to synthesize them

intensity values following the strategy introduced in Reference 30, where the signal intensity of each given data volume was divided by the mean of the signal intensity of its middle slice in the first echo. Consequently, the estimations from different approaches on S_0 maps were scaled accordingly, while R_2^* maps were not affected.

2.6 | Performance evaluation

We trained our neural networks on a GeForce RTX 2080 GPU (NVIDIA Corporation), and implemented in TensorFlow,⁴¹ using the Adam optimizer to minimize the Euclidean distance. LEARN-BIO was trained for about 400 epochs (4 h) and LEARN-IMG for 200 epochs (24 h) in order to achieve the best performance on the validation set. Additional details on training are provided in the Supporting Information Appendix S1. In the training of LEARN-BIO, the $F(t)$ function defined in Equation (1) was used in the loss function to account for the macroscopic magnetic field inhomogeneities, which is essential in the estimation of R_2^* maps free from B_0 inhomogeneity artifacts. This $F(t)$ function was precomputed using the VSF approach¹ on the corresponding ground-truth images. Note that this $F(t)$ function was *only* used during the training stage, and is *not* required for testing purpose once the CNN is trained. This means our LEARN-BIO model is able to directly generate both motion- and inhomogeneity-corrected R_2^* maps from the magnitude mGRE images.

We used the traditional voxel-wise NLLS approach on the output of LEARN-IMG to produce corresponding motion-corrected R_2^* maps. NLLS is a standard iterative fitting method for computing R_2^* based on Equation (1). The $F(t)$ function computed using the VSF method on motion-corrected output of LEARN-IMG was also used before running NLLS in order to account for the effects of macroscopic magnetic field inhomogeneities. At each iteration, the regression is conducted by combining the data from different echo times t with their $F(t)$ values voxel by voxel. Prior to the NLLS fitting procedures, a brain extraction tool, implemented in the Functional Magnetic Resonance Imaging of the Brain Library, was used to mask out both skull and background voxels in all MRI data,⁴² where the signal model defined in Equation (1) does not apply. NLLS, implemented in MatLab R2020a (MathWorks), was run over only the set of unmasked voxels, optimizing for 400 iterations at each spatial point. Similarly, we applied the same brain masks in the loss functions Equations (9) and (10) for the training of our neural networks. Note for LEARN-BIO, those masks were *only* used during the training and were *not* needed for testing. All the visual results presented in this paper were also processed by these masks for better comparison.

To demonstrate the performance of our proposed CNNs, the predicted R_2^* results were compared with the ones computed from motion-corrupted mGRE data using the NLLS approach with a corresponding $F(t)$ function. In the synthetic scenario, the R_2^* maps computed from the motion-free mGRE images through NLLS can be thought

of as a reference, which we only use at test time to quantitatively evaluate the R_2^* results of different approaches. We use the *relative error (RE)* metric and *structural similarity index (SSIM)*⁴³ as two means to quantitatively compare the estimated result $\hat{\mathbf{x}}$ with its reference $\mathbf{x}^*$. We define RE as

$$RE = \frac{\|\mathbf{x}^* - \hat{\mathbf{x}}\|}{\|\mathbf{x}^*\|} \times 100\%, \quad (11)$$

where $\hat{\mathbf{x}}$ and $\mathbf{x}^*$ represent the vectorized image estimation and its ground-truth reference, respectively, and $\|\cdot\|$ denotes the standard Euclidean norm. In the synthetic scenario, to evaluate the performance of different approaches on motion-free R_2^* estimation, we regarded R_2^* computed using NLLS on motion-free mGRE data as the reference. To evaluate the motion correction performance of

LEARN-IMG on mGRE signals, we use the motion-free mGRE images as references. Both RE and SSIM are computed on the brain voxels indicated by the aforementioned brain mask for each slice. In the experimental scenario, where the motion-free references are not available, we applied the models trained on the synthetic data and provided a qualitative visual comparisons of the different approaches.

3 | RESULTS

Figure 4 shows example R_2^* maps calculated by NLLS, LEARN-IMG and LEARN-BIO for two simulated motion-corrupted slices in two different corruption scenarios (one is with moderate motions and the other is

FIGURE 4 Motion correction results from LEARN-IMG and LEARN-BIO on the synthetic data. Images represent two sets of results obtained from the synthetic datasets with different motion levels (*moderate* in rows 1 and 2 and *heavy* in rows 3 and 4). The Reference R_2^* maps computed using nonlinear least squares on motion-free multi-gradient-recalled echo (mGRE) images and the magnitude of the first of 10 echoes of motion-free mGRE images are shown in the first column. Columns 2–4 show the R_2^* maps and their absolute differences from the R_2^* references for different methods. The relative error of each R_2^* map is shown in the bottom left corner. Representative regions with 2× zoom are shown on the bottom right of each R_2^*

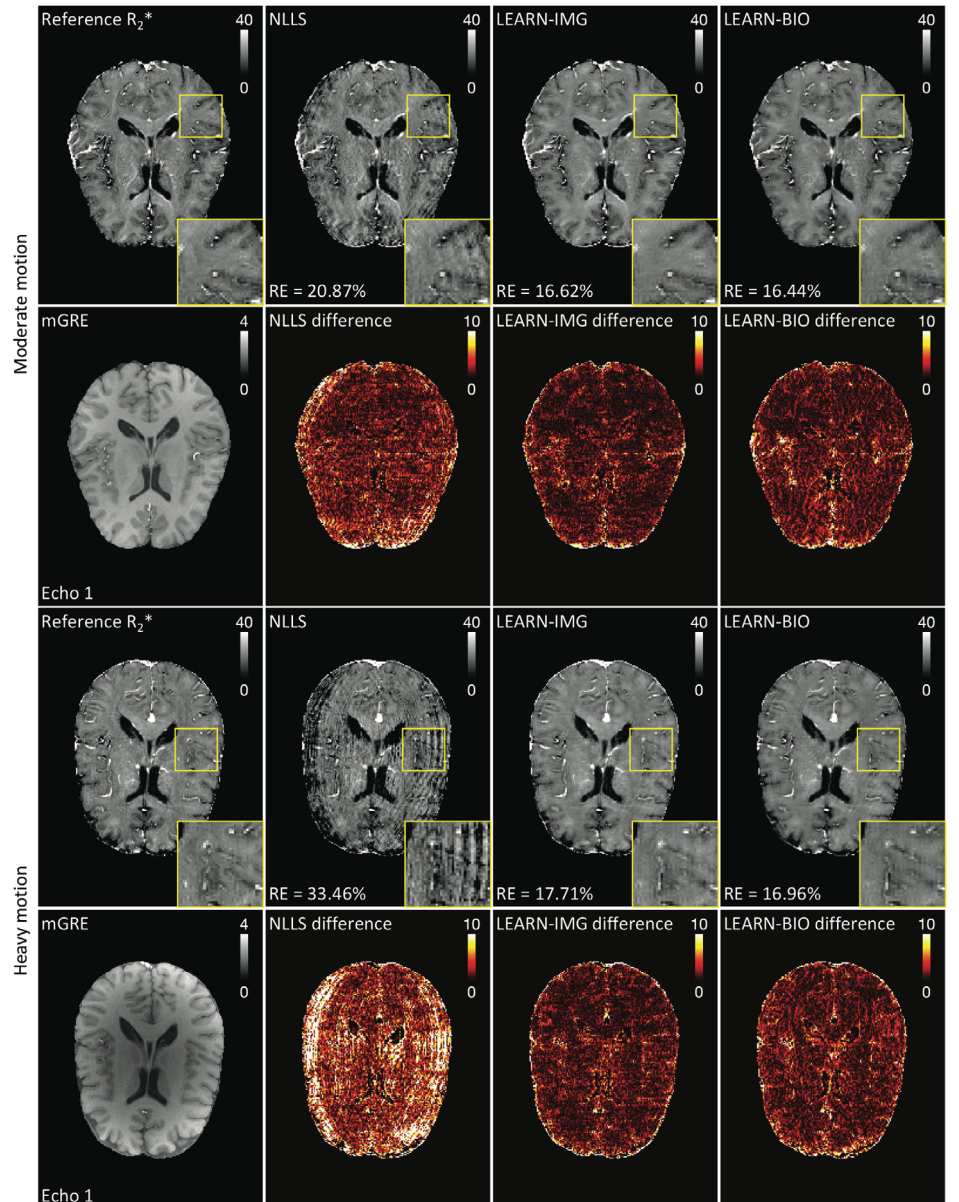


TABLE 1 Average relative error (RE) and structural similarity index (SSIM) values for the R_2^* estimation on the synthetic test data. Results here summarize the performance of each approach at different levels of motion artifacts. We additionally provide the RE and SSIM values for the motion-corrupted mGRE input data and the output of LEARN-IMG averaged on 10 echoes

	Method	Light		Moderate		Heavy	
		RE	SSIM	RE	SSIM	RE	SSIM
mGRE	Input	5.02%	0.96	7.31%	0.93	9.19%	0.90
	LEARN-IMG	3.86%	0.98	4.91%	0.96	5.82%	0.95
R_2^*	NLLS	22.52%	0.90	28.53%	0.86	33.55%	0.82
	LEARN-IMG	20.02%	0.94	22.04%	0.91	23.92%	0.90
	LEARN-BIO	20.28%	0.93	21.76%	0.90	23.08%	0.89

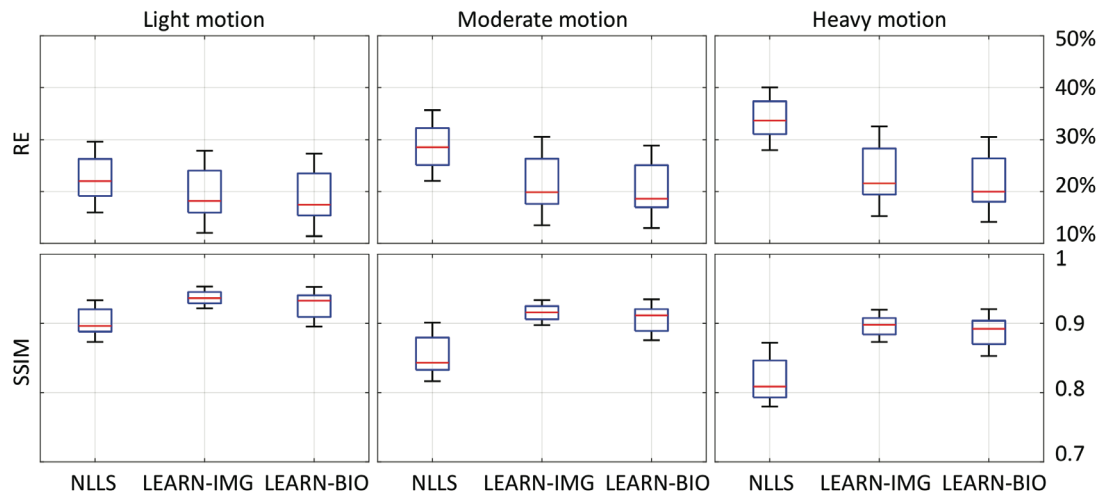


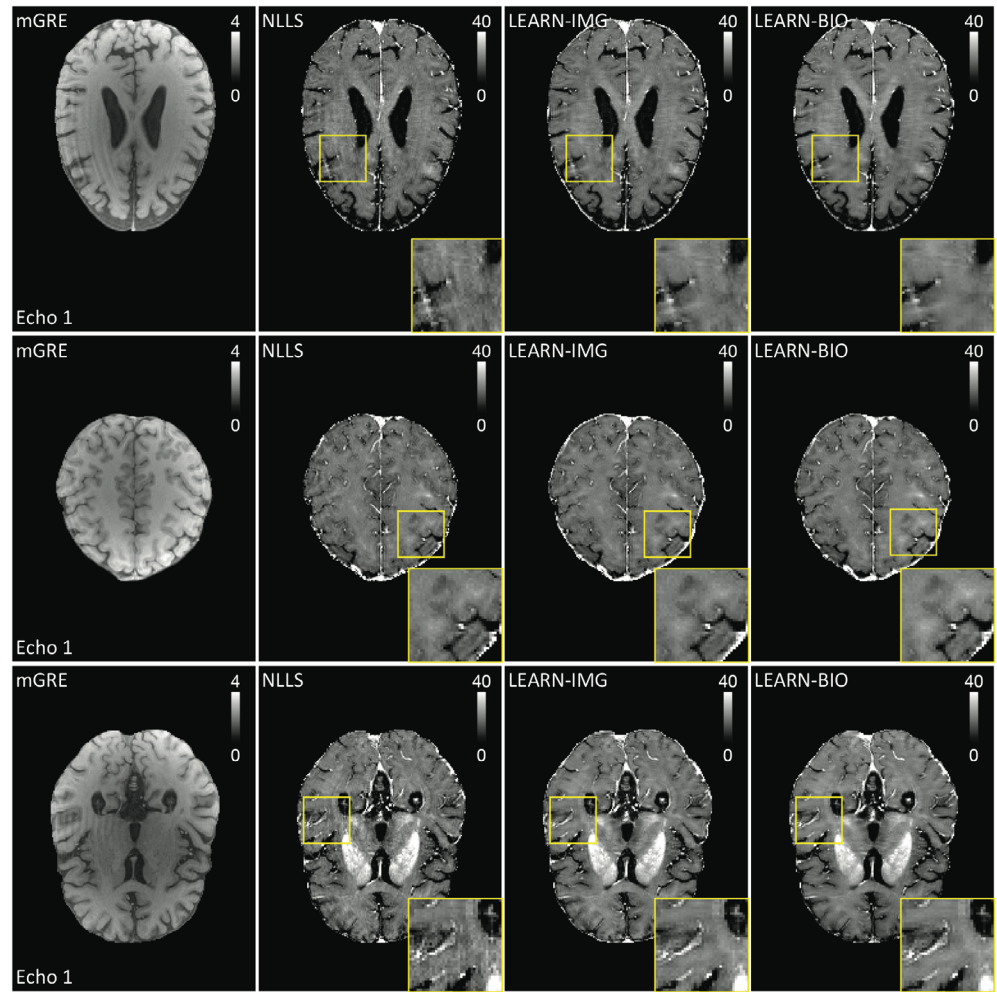
FIGURE 5 The statistical analysis of nonlinear least squares, LEARN-IMG and LEARN-BIO on the synthetic test data. Results visualize the performance of R_2^* reconstruction from each approach in dealing with different levels of motion artifacts

with heavy motions, as shown in Figure 3). Reference mGRE images without motion artifacts are shown for each example. It is clear that all the R_2^* maps from NLLS contain strong motion artifacts, while the ones from LEARN-BIO and LEARN-IMG are of significantly higher quality with no obvious artifacts remaining. We also notice that while removing the artifacts, our approaches can also preserve important microstructure details of the R_2^* maps, as can be seen from the exemplar zoomed regions in Figure 4. Numerical RE results in each figure quantitatively corroborate that our methods provide better estimation of R_2^* compared to NLLS, with LEARN-BIO providing similar performance with LEARN-IMG in all examples. Note that the RE numbers in our results should be interpreted with care since the reference R_2^* maps were computed using NLLS on motion-free in vivo data. Thus, despite the very similar RE performance compared to LEARN-IMG, LEARN-BIO usually achieves better motion-artifact removal as corroborated by visual evaluation (see zoomed details in Figures 4 and 6). The difference

maps ($|\text{estimated} - \text{reference}|$) that illustrate the absolute value of the deviation from their reference are also visualized for each result. It can be seen that difference maps of NLLS are much brighter compared to LEARN-IMG and LEARN-BIO, especially in the heavy motion scenario where NLLS estimations are contaminated by severe motion artifacts.

Table 1 and Figure 5 summarize the average RE and SSIM over the whole test dataset on three motion corruption scenarios for all methods. We note that LEARN-IMG and LEARN-BIO share very similar performance across all corruption scenarios by providing much lower RE than NLLS. It is also worth noting that our proposed approaches are robust, showing about only 2% gain of RE along with the increase of motion levels from light to moderate, and again from moderate to heavy. While the performance of the results from NLLS is dramatically affected by the motion levels, showing about 6% gain of RE along the increase of motion levels each time. As a results, the quality gap between our approaches and

FIGURE 6 Motion correction results obtained using the experimental data from *three* different subjects. The magnitude of the first of 10 echoes of motion-corrupted multi-gradient-recalled echo (mGRE) images of the method inputs are shown in the first column and R_2^* maps of different methods are shown in columns 2–4. Representative regions with 2× zoom are shown on the bottom right of each R_2^*



NLLS enlarges noticeably as inputs get more and more corrupted: from around 2% at light to around 10% at heavy. In addition to the R_2^* , the motion-corrupted mGRE inputs of the neural networks and the image predictions from LEARN-IMG are also evaluated and presented in the table. Here, the references for measuring the image predictions are the motion-free mGRE data and the numbers are computed on the magnitude of the complex data. The corresponding numerical results align with the conclusion over R_2^* , showing that LEARN-IMG is effective in removing motion artifacts in the spatial domain.

Figure 6 visualizes examples of the R_2^* calculated by NLLS, LEARN-IMG, and LEARN-BIO for *three* in vivo slices of *different* subjects from the experimental data with real motion. While the motion artifacts in this data might not follow our simulation model, we do observe similar results to our synthetic experiments. It can be seen that the R_2^* maps produced by our methods are much better than the ones from NLLS, showing that our methodology is capable of handling the real motion artifacts while still keeping detailed structural information. While our networks are trained on the middle slices, they can perform

motion correction across the whole brain volume (including the very top and bottom slices). As shown in Figure 7, our networks that were trained on middle slices can remove the motion artifacts across different brain regions, including the top (columns 1 and 2), middle (columns 3 and 4), and bottom (columns 5 and 6) slices in the experimental data with real motion. Our networks outperform the baseline method NLLS which suffers from high motion artifacts in the estimated R_2^* maps across the whole brain. We hypothesize that the ability of our networks to generalize across different brain regions is due to their ability to capture similarity in the motion artifacts.

4 | DISCUSSION AND CONCLUSIONS

In this manuscript we proposed two CNN approaches, namely LEARN-IMG and LEARN-BIO, for the robust motion correction of R_2^* maps from mGRE Echo MRI data. LEARN-IMG is based on a supervised deep neural network that conducts the motion correction on complex

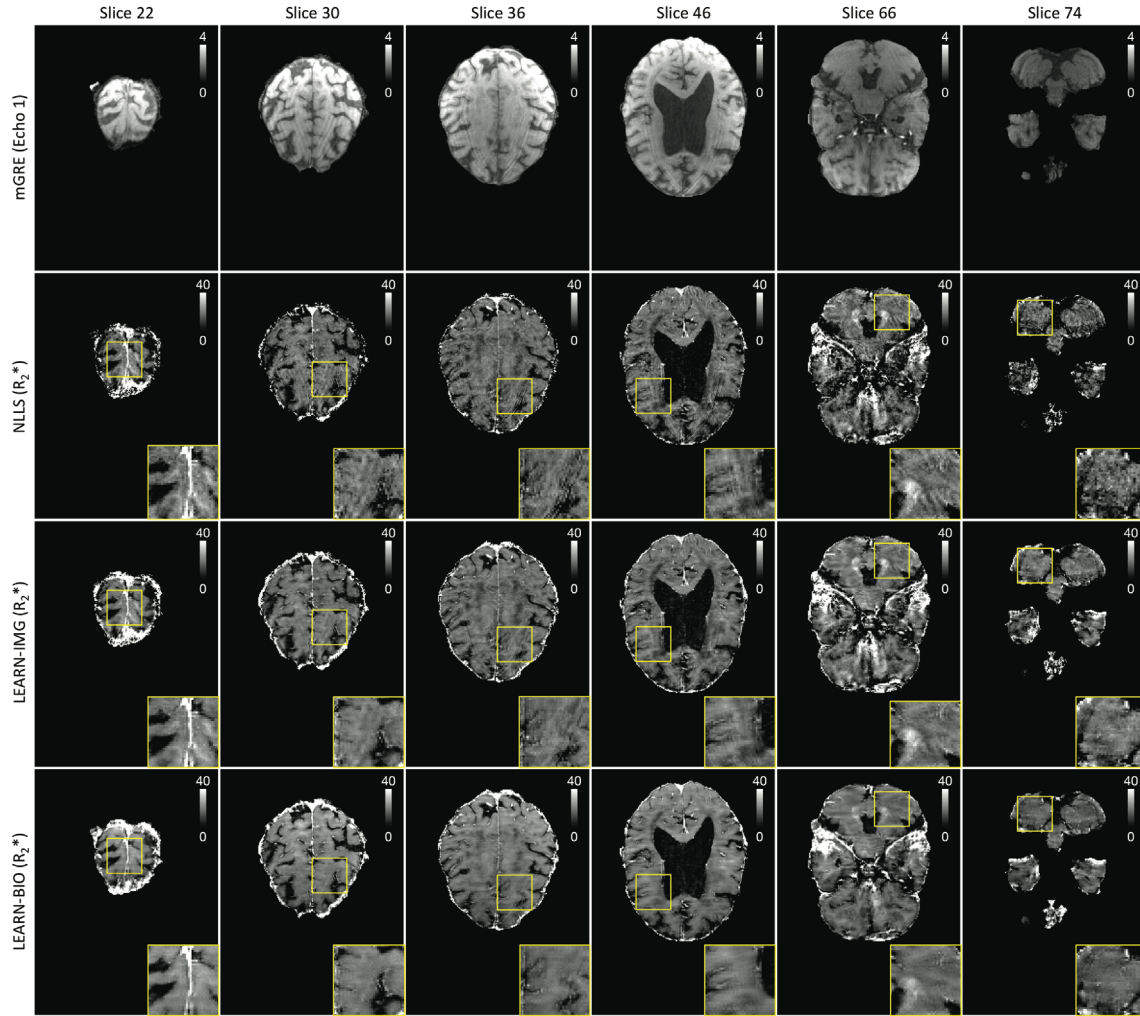


FIGURE 7 Motion correction results obtained using the experimental data from one subject across different brain slices. The representative top, middle, and bottom slices of a three-dimensional data volume are illustrated in columns 1-2, 3-4, and 5-6, respectively. The magnitude of the first of 10 echoes of motion-corrupted multi-gradient-recalled echo (mGRE) images are shown in row 1 and corresponding R_2^* maps of different methods are shown in rows 2-4. Representative regions with 2 $\times$ zoom are shown on the bottom right

mGRE images, followed by the standard NLLS fitting approach. It decomposes the motion correction and quantitative maps estimation into two procedures, bringing more flexibility to various potential applications of quantitative mapping. In this approach, the training of CNN simply relies on the paired MR images. In testing, it only takes 30 s for CNN to process the full brain data (using a GeForce GTX 1080 Ti GPU), while NLLS fitting together with the computation $F(t)$ functions take about 120 min on a modern PC (using eight cores). On the other hand, LEARN-BIO is based on a self-supervised deep neural network that uses a biophysical model connecting mGRE MRI signal with underlying biological tissue microstructure. It integrates the motion correction and quantitative mapping procedures together within one single CNN. During the training (but not application), both paired MR images and the $F(t)$ functions as well as the knowledge of

the biophysical model are needed. This allows our CNN to recognize the contribution of macroscopic magnetic field inhomogeneities to the mGRE signal only from the magnitude data. Therefore, at testing time, the information of $F(t)$ functions is not required, which saves a great amount of time compared with the LEARN-IMG approach. Specifically, it takes only 3 s for LEARN-BIO to predict the motion- and B_0 -corrected R_2^* maps for the full brain data.

Both of our methods, LEARN-IMG and LEARN-BIO, show great performance in producing motion- and B_0 -corrected R_2^* maps that are of the same quality as NLLS-based voxel-by-voxel analysis from motion-free mGRE data. As shown in Figure 4 and Table 1, LEARN-BIO and LEARN-IMG consistently gives the best performance over the synthetic data in our different corruption scenarios. Figures 6 and 7 further elaborates the capability of our CNN models on experimental data,

showing a practical application of our approaches on removing real-world motion artifacts and keeping feature details. Our approaches constantly outperform NLLS both qualitatively and quantitatively, thanks to the power of our deep neural networks.

While both of our proposed methods enable the estimation of high-quality motion-corrected R_2^* maps, they have distinct trade-offs that can lead to different applicability in practical scenarios. LEARN-BIO is suitable for applications where one directly requires motion-correction quantitative R_2^* maps with low computational time. In this paper, we used LEARN-BIO with a specific biophysical model in Equation (1) to produce R_2^* maps, but the same approach can potentially be applied to any biophysical model. LEARN-IMG, on the other hand, provides motion-corrected mGRE images that can be used in a combination with any previously developed model that did not account for motion in the data. For example, motion-corrected mGRE images can be used for generating quantitative tissue-cellular-specific (R_{2t}^*) and Blood-Oxygen-Level-specific ($R_{2'}^*$) maps,^{4,31} which have proved useful in studying healthy aging,³ brain neuronal content⁶ and its relationship to brain functional connectivity,⁴⁴ Alzheimer Disease,^{5,8} Multiple Sclerosis,⁴⁵⁻⁴⁷ and psychiatric disease.⁴⁸ mGRE sequences are also used to study brain tissue multicompartiment structure,⁴⁹⁻⁵¹ mapping of cerebral metabolic rate of oxygen by combining quantitative susceptibility mapping and quantitative blood oxygenation level-dependent imaging,⁵² etc. Therefore, LEARN-IMG can be generalized to various applications and different quantitative map computation. Nevertheless, this generalization capability requires applying additional quantitative-map-oriented fittings to the motion-corrected mGRE outputs of the network, which consequently increases the computation time compared to LEARN-BIO. Therefore, LEARN-IMG fits applications where different quantitative maps are required under less-restrictive time constraints.

In this work, we have accounted for the macroscopic magnetic field inhomogeneity effects by including in the biophysical model the F-function term (Equation 1) computed using the the VSF approach¹ that accounts for the presence of magnetic field inhomogeneities in the imaging object. Since magnetic field inhomogeneities are induced mostly by the air cavities (e.g. sinuses) inside the head, they change with head motion, thus affecting MRI data. This effect is not accounted for in our current motion-correction implementation. While detail analysis of this effect is beyond the scope of this paper, we can estimate a potential error resulting from this effect by recalling that only a projection (ΔB) of the magnetic susceptibility-induced inhomogeneous magnetic field ($\Delta \mathbf{B}$) on the main magnetic field B_0 actually

affects MRI signal. Hence, if the object in the MRI scanner is rotated by an angle θ , the ΔB would not change by more than $\cos^2\theta$. For example, for θ about 10° , this change is only about 3% and can potentially cause about 3% error in R_2^* estimation in the brain regions strongly affected by the magnetic field inhomogeneities (see figure A2 in Reference 44). However, in a typical MRI session, 3D mGRE data are acquired over about 6-min scan while motion usually does not last for more than a few seconds, affecting only small portion of 3D dataset, and consequently resulting in R_2^* estimation error significantly smaller than 3%.

It worth mentioning that while 3D motion is considered in the simulation, our network architectures takes as its input a sequence of 2D images at different echo times. The key benefit of using our architectures, instead of more complex ones that consider sequences of 3D images, is the lower computational and memory complexity. However, it conceivable that by using more complex architectures one can better capture the 3D motion and thus improve the final performance. Similar to all image restoration methods, our method exhibits a common trade-off between artifact-removal and smoothing on some images. In future work, it might be worth exploring the potential of obtaining sharper images by replacing the Euclidean loss used in our training with other common functions (e.g., ℓ_1 loss).

In conclusion, we introduced LEARN-IMG and LEARN-BIO as two fast and robust learning-based methods that can utilize motion-corrupted mGRE data to produce high-quality R_2^* maps which are free from B_0 -inhomogeneity and motion artifacts. This validates the representation power of our CNNs in quantitative map estimation as well as motion correction. The good motion-reduction performance on experimental data demonstrates a potential clinical usage of our trained models.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

Appendix S1. Supporting information

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