Accelerating quantitative susceptibility and R2* mapping using incoherent undersampling and deep neural network reconstruction

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A B S T R A C T
Quantitative susceptibility mapping (QSM) and R2* mapping are MRI post-processing methods that quantify tissue magnetic susceptibility and transverse relaxation rate distributions. However, QSM and R2* acquisitions are relatively even, with parallel imaging. Incoherent undersampling and compressed sensing reconstruction techniques have been used to accelerate traditional magnitude-based MRI acquisitions; however, most do not recover the full phase signal, as required by QSM, due to its non-convex nature. In this study, a learning-based Deep Complex Residual Network (DCRNet) is proposed to recover both the magnitude and phase images from incoherently undersampled data, enabling high acceleration of QSM and R2* acquisition. Magnitude, phase, R2*, and QSM results from DCRNet were compared with two iterative and one deep learning methods on retrospectively undersampled acquisitions from six healthy volunteers, one intracranial hemorrhage and one multiple sclerosis patients. As well as one prospectively undersampled healthy subject using a 7T scanner. Peak signal to noise ratio (PSNR), structural similarity (SSIM), root-mean-squared error (RMSE), and region-of-interest susceptibility and R2* measurements are reported for numerical comparisons. The proposed DCRNet method substantially reduced artifacts and blurring compared to the other methods and resulted in the highest PSNR, SSIM, and RMSE on the magnitude, R2*, local field, and susceptibility maps. Compared to two iterative and a one deep learning methods, the DCRNet method demonstrated a 3.2% to 9.1% accuracy improvement in deep grey matter susceptibility when accelerated by a factor of four. The DCRNet also dramatically shortened the reconstruction time of single 2D brain images from 36-140 seconds using conventional approaches to only 15-70 milliseconds.

1. Introduction
Quantitative susceptibility mapping (QSM) is an MR phase post-processing technique developed to quantify the magnetic susceptibility distribution of the human brain (Liu et al., 2015; Wang & Liu, 2015). It has shown significant clinical potential for studying multiple neurological disorders, including multiple sclerosis (Elkady et al., 2019), Alzheimer’s disease (Acosta-Cabronero et al., 2013), Parkinson’s disease (Acosta-Cabronero et al., 2017), alcohol use disorders (Juhász et al., 2017), and intracranial hemorrhage (Sun et al., 2018), as well as healthy aging (Bilgic et al., 2012). QSM scans are generally acquired with a three-dimensional (3D) gradient-recalled-echo (GRE) sequence (Deh et al., 2019; Haacke et al., 2004), while other sequences such as ultra-short TE (UTE) (Lu et al., 2019), multi-echo MP2RAGE (Caan et al., 2019; Metere et al., 2017; Sun et al., 2020), and water saturation shift referencing (WASSR (Lim et al., 2014)) have also been proposed. These acquisition methods are relatively slow (usually 5-10 minutes with parallel imaging) since large areas of k-space need to be traversed, with

Abbreviations: QSM, quantitative susceptibility mapping; ME-GRE, multi-echo gradient-echo; SWI, susceptibility-weighted imaging; UTE, ultra-short TE; FOV, field of view; ROI, region-of-interest; DGM, deep grey matter; FWM, frontal white matter; RESHARP, regularization enabled sophisticated harmonic artifact reduction for phase data; CS, compressed sensing; CSpr, CS with periodic regularizations; CSps, CS with phase cycling algorithm; CNN, convolutional neural network; AUTOMAP, automated transform by manifold approximation; Mag-Unet, U-net trained on magnitude images; Phase-Unet, U-net trained on phase images; DCRNet, Deep Complex Residual Network; BET, brain extraction tool; FSL, FMRI Software Library; AF, accelerating factor; COSMOS, Calculation Of Susceptibility through Multiple Orientation Sampling; GP, globus pallidus; PU, putamen; CN, caudate nucleus; TH, thalamus; SN, substantia nigra; RN, red nucleus; PSNR, peak signal to noise ratio; SSIM, structural similarity; SSE, sum of squared errors; MS, multiple sclerosis; ppb, part-per-billion.
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each sampling line accumulating scan time (Liu et al., 2015; Wang et al., 2018). Gradient-echo EPI sequences (Langkammer et al., 2015; Sun & Wilman, 2015) can significantly shorten the QSM acquisition time to seconds; however, they come with the compromise of substantially increased image distortion and reduced image resolution.

Incoherent k-space undersampling strategies combined with compressed sensing (CS) reconstruction techniques have been used to accelerate magnitude-based MRI scans substantially. Since the early work of Lustig et al. (Lustig et al., 2007), an increasing number of approaches, such as sparsity-based CS-MRI models (Feng et al., 2017; Feng et al., 2014; Jung et al., 2009; Lustig et al., 2008; Ye, 2019), Low-Rank models (Hong et al., 2011; Jin et al., 2016; Ye et al., 2016; Yu et al., 2014), and deep learning frameworks (Hammernik et al., 2018; Han et al., 2018; Han et al., 2019; Hyun et al., 2018; Lee et al., 2018; Ravishankar et al., 2019; Schlemper et al., 2018; Yang et al., 2018; Zhu et al., 2018), have been established to recover magnitude images from sparsely sampled k-space data. However, MR images are inherently complex-valued with an equally important phase component essential for phase-based contrasts such as QSM. The image sparsity assumption commonly used in previous CS-MRI methods does not apply to the phase since it is periodic and wraps, making it inherently non-convex problem. More advanced reconstruction methods have recently been proposed to reconstruct both magnitude and phase images by extending traditional CS-MRI frameworks. For instance, Zhao et al. (Zhao et al., 2012) designed a phase regularization that is periodic and effective against phase wraps. Ong et al. (Ong et al., 2018) developed a phase cycling technique invariant to the phase wraps by shifting the wrap positions in each iteration; this was successfully applied to accelerate mouse brain QSM in a recent work (Wang et al., 2018). However, these phase regularization methods lead to blurring in the reconstruction results, and the algorithms are computationally expensive and slow, which makes them impractical for high-resolution 3D MRI volumes.

Deep learning has received increasing attention in various imaging research areas (McCann et al., 2017; Ravishankar et al., 2019) as an alternative to conventional iterative algorithms. One method, named Automated Transform by Manifold Approximation (AUTOMAP) (Zhu et al., 2018), can directly recover the magnitude and phase maps from the k-space signals (sensor-domain data). However, this network only works for small-size images due to the memory-consuming fully connected layers. Another study (Lee et al., 2018) proposed two separate convolutional neural networks (CNN) for magnitude and phase reconstruction, respectively. However, the phase wraps in the reconstructed images are disrupted, making it problematic for quantitative phase imaging results. Furthermore, these methods only showed limited results on 2D phase reconstructions, and their feasibility and robustness on the QSM reconstruction pipeline have not been investigated.

In this study, a Deep Complex Residual Network (DCRNet) is designed, by incorporating the complex convolutions (El-Rewaidy et al., 2020; Virtue et al., 2017; Wang et al., 2020) into a deep residual network backbone to recover both MR magnitude and quantitative phase images, thus enabling the acceleration of QSM from undersampled multi-echo GRE acquisitions. The apparent transverse relaxation rates, i.e., R2* maps, which correlate significantly with QSM in iron-rich regions (Sun et al., 2015), can also be generated from the same multi-echo GRE scans. The DCRNet processes the real and imaginary images with complex convolutions inspired by the multiplication of complex numbers, which may better exploit the correlation between real and imaginary parts of a complex image (Wang et al., 2020). Qualitative and quantitative comparisons are performed among different iterative and deep learning algorithms on the magnitude, R2*, and QSM images from healthy subjects and patients with intracranial hemorrhage and multiple sclerosis. The undersamplings are performed both retrospectively on existing 3T datasets and prospectively at 7T. The performance of the proposed DCRNet under different accelerating factors (i.e., 2 ×, 4 ×, 6 ×, 8 ×) is also investigated.

2. Theory

2.1. General forward model

The general forward model of CS undersampled MRI (Ong et al., 2018; Zhao et al., 2012) can be formulated as:

\[ y = AF(m \odot \exp(i\phi)) \]

where \( i = \sqrt{-1} \); \( F \) is the discrete Fourier transform matrix; \( m \) and \( \phi \) represent the magnitude and phase images to be reconstructed; \( \odot \) represents the elementwise multiplication; \( \exp(\cdot) \) denotes the element-wise exponential operator; \( A \) is the CS undersampling matrix from a designed subsampling mask; \( y \) is the CS undersampled k-space data.

2.2. Conventional method for magnitude-only reconstruction

In the conventional CS reconstruction method for MR magnitude images (Lustig et al., 2007), a sparsifying transformation regularization (e.g., total variation, wavelet transform) is usually incorporated into the cost function to derive an optimized solution:

\[ \arg\min_{m} \frac{1}{2} ||y - AF(m \odot \exp(i\phi))||_2^2 + \lambda R(m), \]

where \( \cdot \) \( \cdot \) is the vector l2 norm; \( R(\cdot) \) represents the sparsifying regularization function; \( \lambda \) is the regularization parameter. In this scheme, the phase signal is estimated from the fully-sampled low-frequency k-space region, which can be used to correct low-order phase variation and better sparsify the MR magnitude image be reconstructed (Lustig et al., 2007). Although this method can obtain fairly robust magnitude images and has been widely adopted for accelerating magnitude-based scans, it is not feasible to restore high-resolution GRE phase images for QSM.

2.3. Iterative approaches with phase regularizations

To reconstruct both magnitude and phase, some previous methods (Ong et al., 2018; Zhao et al., 2012) added magnitude and phase regularizations, respectively:

\[ \arg\min_{m, \phi} \frac{1}{2} ||y - AF(m \odot \exp(i\phi))||_2^2 + \lambda_1 R_m(m) + \lambda_2 R_\phi(\phi), \]

where \( \cdot \) \( \cdot \) is the vector l2 norm; \( R_m \) and \( R_\phi \) are regularization functions for magnitude and phase, respectively; \( \lambda_1 \) and \( \lambda_2 \) are empirical regularization parameters. However, it is reported (Ong et al., 2018; Zhao et al., 2012) that using conventional CS regularizers (e.g., wavelet transform and finite differencing matrix) on the phase component leads to significant reconstruction errors and artifacts at phase wraps because the phase image \( \phi \) appears as an exponential term in the cost function, making the optimization process inherently non-convex. Zhao et al. (Zhao et al., 2012) suggested using periodic regularizations in the complex exponential form to solve this problem:

\[ \arg\min_{m, \phi} \frac{1}{2} ||y - AF(m \odot \exp(i\phi))||_2^2 + \lambda_1 ||Wm||_1 + \lambda_2 \sum_{k=1}^{K} \psi \left( \left| |Cexp(i\phi)|_m \right| \right), \]

where \( \cdot \) \( \cdot \) is the vector l1 norm operator; \( W \) is the wavelet transform matrix; \( C \) is the finite differencing matrix; \( K \) is the number of rows of \( C \); \( \psi(x) = \delta^2 \sqrt{1 + (\frac{x}{\delta})^2} - 1 \) is an edge-preserving potential function, and \( \delta \) (empirically set as 0.005) is the parameter to tune the edge-preserving weight. However, this method is not general and cannot be applied to phase-based water-fat or flow imaging (Ong et al., 2018). Alternatively, a more generalized algorithm (Ong et al., 2018) named phase cycling was developed, which is equivalent to an inexact proximal gradient
method applied to the following cost function:

\[
\arg\min_{m, \varphi} \frac{1}{2} \| y - AF(m \odot \exp(ij)) \|^2 + \lambda_1 \| W m_1 \|^2 + \lambda_2 \frac{1}{|P|} \sum_{p \in P} \| W (q + p) \|_1,
\]

where \( P \) is a collection of phase-shifting matrices generated from the zero-filling reconstruction to shift the phase wraps. The phase cycling technique achieves the reconstruction robustness against the phase wraps by randomly shifting the phase wraps in each iteration and effectively averaging the artifacts spatially to a low level. This algorithm has been applied to accelerate mouse brain QSM in previous work (Wang et al., 2018); however, it is slow (i.e., around 40 seconds for a single 2D slice) and has not been investigated using high-resolution 3D human brain QSM data.

In this study, the above two iterative methods Eqs. (4) and (5) referred to as CS_pq (periodic regularizations) and CS_pc (phase cycling) were implemented and compared with the proposed new method, detailed below.

3. Methods

3.1. Quantitative susceptibility and R2* mapping acceleration framework

The proposed deep learning-based QSM and R2* acceleration framework is shown in Supp. Fig. 1, which consists of two parts: (i) the MRI magnitude and quantitative phase reconstruction from the CS undersampled k-space data using the proposed DCRNet, (ii) QSM and R2* processing pipelines, including brain mask generation with BET (Smith, 2002) from the FMRI Software Library (FSL) (Jenkinson et al., 2012), R2* mono-exponential fitting (Lebel et al., 2012), phase unwrapping with a best path method (Abdul-Rahman et al., 2007), magnitude-weighted fitting of multi-echo phase with echo times, background field removal with RESHARP (Sun and Willman, 2014), and dipole inversion (single-orientation: LSQR (Li et al., 2015), multiple orientations: Calculation Of Susceptibility through Multiple Orientation Sampling (COSMOS) (Liu et al., 2009)).

3.2. DCRNet for complex-valued MRI reconstruction

The proposed DCRNet architecture is shown in Fig. 1(a), specifically designed for complex-valued MR images, adding complex-valued operations to a deep residual network backbone. Although QSM is reconstructed from 3D phase images, the proposed network is a 2D residual neural network to save GPU memory. It is straightforward to apply this 2D network to 3D MRI reconstruction in a slice-by-slice manner. As shown at the top of Fig. 1(a), the 3D subsampled k-space data are first converted into 2D k-space slices after a 1D Fourier Transform along the fully-sampled \( k \) (frequency-encoding) direction. These 2D k-space slices are then reconstructed into real and imaginary images after 2D Fourier Transforms and are fed into the DCRNet. A data consistency operation is appended to the end of the network using the 2D k-space slices (details below). The proposed DCRNet is a fully convolutional neural network, enabling it to process complex images of any size. The details of each building block, i.e., the input layer, residual blocks, the output layer, and the data consistency layer, are described as follows:

First, an input layer, consisting of a complex convolution followed by a batch-normalization operation and an activation function, is used to extract the high-dimensional features from the complex input \( x_0 \) (i.e., the initial zero-filling reconstruction):

\[
y_0 = ReLU \left( BN \left( W_0 \ast x_0 + b_0 \right) \right),
\]

where \( W \in \mathbb{C}^{64 \times 1 \times 3 \times 3} \) and \( b_0 \in \mathbb{C}^{64 \times 1} \) are the complex convolutional kernel and bias of this input layer, and \( \mathbb{C} \) is the complex number set; \( BN \) and \( ReLU \) represent the conventional batch-normalization operation and the Rectified Linear Unit activation function, which are applied separately to the real and imaginary components of the complex feature maps; \( x \) is the complex convolution operation (detailed in the following section); \( y_0 \) represents the output features of this layer.

The DCRNet then cascades the middle residual block five times, with each block consisting of two complex convolutions and one addition:

\[
F_m = ReLU \left( BN \left( W_m \ast x_m + b'_m \right) \right) \quad A_m = x_m + y_m = ReLU \left( BN \left( W_m \ast A_m + b'_m \right) \right),
\]

where \( x_m \) and \( y_m \) are the input and output of the \( m \)th residual block, with \( x_1 = y_0; W_i \in \mathbb{C}^{64 \times 64 \times 3 \times 3} \) and \( W_i \in \mathbb{C}^{64 \times 64 \times 3 \times 3} \) are the complex convolutional kernels, and \( b'_i \in \mathbb{C}^{64 \times 3} \) and \( b'_i \in \mathbb{C}^{64 \times 3} \) are the bias terms; \( F_m \) and \( A_m \) are intermediate feature maps.

An output layer is applied to generate an image of the same size as the input by aggregating the high-dimensional features from previous blocks. Additionally, a skip connection between the input and result of this output layer is added, forming a whole residual block, which helps network training converge faster (Kim et al., 2016) and mitigates the gradient vanishing problem (He et al., 2016). The corresponding output image \( y_2 \) can be formulated as:

\[
y_2 = x_0 + W_0 \ast x_0 + b_0,
\]

where \( x_0 = y_1 \) is the output of the 5th middle residual block and \( W_0 \in \mathbb{C}^{1 \times 64 \times 3 \times 3} \) and \( b_0 \in \mathbb{C}^{1 \times 3} \) correspond to the complex convolutional kernel and bias term in the output layer, respectively.

Finally, a data consistency layer is adopted at the end of the DCRNet to generate the final reconstruction image \( y_{rec} \) from \( y_0 \) and the network input \( y_0 \), which can be expressed as:

\[
y_{rec} = \begin{cases} \ Y (i) & \text{if } k \notin \Omega \\ \ a X_0 (k) + (1 - a) Y (k) & \text{if } k \in \Omega \\ \end{cases},
\]

where \( Y (i) \) and \( X_0 (k) \) are the corresponding k-space representations of \( y_2 \) and \( y_0 \), the size of the collection of the sampling positions determined by the subsampling masks; \( \alpha \) is a weighting parameter depending on the noise levels (Schlemper et al., 2018; Wang et al., 2020) and is set as learnable in the current work. The final reconstruction of the DCRNet, \( Y_{rec} \), is obtained from the inverse Fourier Transform of the k-space signal \( Y_{rec}(k) \).

3.3. Complex convolutional operations

In this study, the complex convolutional layer is developed based on the multiplication rules of complex numbers (El-Rewaidy et al., 2020; Wang et al., 2020). The diagram of the proposed complex convolution is shown in Fig. 1(b). The complex convolution between a complex input \( X = X_R + i X_I \) and a complex convolutional kernel \( W = W_R + i W_I \) is represented as:

\[
Y = X \ast W,
\]

\[
\begin{align*}
Y &= Y_R + i Y_I \\
Y_R &= X_R \ast W_R - X_I \ast W_I \\
Y_I &= X_R \ast W_I + X_I \ast W_R
\end{align*}
\]

Here \( \ast \) represents the complex convolution and \( \ast \) represents the conventional real-valued convolution operation in traditional CNNs; in summary, a complex convolution can be split into four traditional real-valued complex convolutions and two addition operations.

Other conventional operations, such as the batch-normalization and \( ReLU \) function on a complex feature map \( X = X_R + i X_I \) are separately applied to the real and imaginary components:

\[
BN (X) = BN (X_R) + i \cdot BN (X_I) \\
ReLU (X) = ReLU (X_R) + i \cdot ReLU (X_I)
\]

3.4. In vivo experiments and data preparation

Institutional ethics board approval was obtained and all subjects gave informed consent. Whole-head 3D multi-echo GRE (ME-GRE) raw
k-space data (8 unipolar echoes, first TE: 3 ms, echo spacing: 3.3 ms, TR 29.8 ms, FOV: 256 × 256 × 128 mm³, voxel size: 1mm isotropic, 12-channel head coil with ASSET acceleration factor of 2, 3/4 partial Fourier with POCs reconstruction (Haacke et al., 1991) applied in both phase and slice directions) from ten healthy volunteers were acquired at 3T (Discovery 750, GE Healthcare, Milwaukee, WI) and used to generate training labels. The coil-combined magnitude and phase images exported from the scanner were transferred into the Fourier domain to simulate the fully-sampled k-space data of these scanner reconstructed images.

These simulated single-channel 3D fully-sampled k-space datasets were retrospectively subsampled using a 2-D variable density k-space sampling mask in the k_y,k_z plane, generated with the probability density function (Wang et al., 2018) formulated as:

\[ PDF = \exp \left(-P_u \times \sqrt{\frac{k_y^2}{n_y^2} + \frac{k_z^2}{n_z^2}}\right), \]

where \( P_u \) and \( P_d \) are two experimental parameters, \([n_y, n_z] \) is the k-space matrix size, and \( k_y, k_z \) are the k-space coordinates. Fig. 2(a) shows the undersampling masks generated for training of the proposed networks (\( P_u=7, P_d=1.8 \) for 2 ×, \( P_u=12, P_d=1.8 \) for 4 ×, \( P_u=12, P_d=1.8 \) for 6 ×, and \( P_u=22, P_d=1.8 \) for 8 × accelerations). The undersampling aliasing artifacts from the zero-filling reconstructions are demonstrated in Fig. 2(b) in three orthogonal views in both magnitude and phase images. These initial zero-filling results, reformatted as real and imaginary images, are used as the training inputs for DCRNet.

Next, these 3D zero-filling image volumes were sliced into 2D complex images along the k_x direction and were normalized (i.e., divided by the maximum intensity of the 3D complex image volume) before network training. A total of 16800 complex GRE images (size: 256 × 128) retrospectively undersampled from 10 healthy subjects were used for network training.

To compare the performance of the proposed DCRNet with other methods, another fourteen fully-sampled 3D ME-GRE MRI scans from six healthy volunteers were acquired and undersampled retrospectively using the subsampling mask at AF = 4. Two of these subjects were scanned at five different head orientations, while another four subjects were obtained with a single head orientation. Two more ME-GRE datasets, one intracranial hemorrhage and one multiple sclerosis patients, were also fully-sampled and retrospectively undersampled to validate the performance of the proposed DCRNet in the presence of pathology.

To implement and test the proposed QSM acceleration framework, including both acquisition and reconstruction, one healthy volunteer was scanned with modified GRE sequences at 7T (Magnetom Classic, Siemens Healthcare, Erlangen, Germany). The acquisitions were prospectively undersampled by AFs of 4 and 8, using the pre-designed sampling masks shown in Fig. 2(a). A single transmit 32 channel head coil (Nova Medical, Wilmington, USA) was used for signal reception. The GRE scan parameters were as follows: 8 unipolar echoes, first TE 3.4 ms, echo spacing 3.5 ms, TR 31 ms, BW 480 Hz/pixel, FOV 256 × 192 × 128, voxel size 1mm isotropic, scan time 3 mins 10 seconds for 4 × AF and 1 min 35 seconds for 8 × AF. Zero-filling reconstruction was first performed for each receiver channel. Coil sensitivity maps were estimated using the POEM method before properly combined for phase (Sun et al., 2020). For the DCRNet method, the combined zero-filling images were first fed into the deep neural network without the data consistency module. The reconstructed images were multiplied by the estimated coil sensitivities before converting them into a 32-channel k-space. Data consistency was then performed to obtain the magnitude and phase images for each coil channel. Finally, these multi-channel images were re-combined using the POEM method (Sun et al., 2020). The modified DCRNet reconstruction pipeline for the multi-channel data was illustrated in Supp. Fig. 2. For the CSQc reconstruction method, raw k-space measurements from individual channels and estimated coil sensitivity maps were used according to the original paper (Gong et al., 2018).
3.5. Network training

The mean squared error loss function was adopted to train the proposed DCRNet. An extra noise adding layer detailed in one recent work (Gao et al., 2021) was applied to improve the network’s robustness against noise. $\alpha$ in Eq. (9) was initialized as 1 and all other trainable network parameters were initialized with normally distributed random numbers with a mean of zero and a standard deviation of 0.01. The training process was optimized using the adaptive moment estimation (Adam optimizer (Kingma and Ba, 2014)) with a mini-batch size of 32. The networks were trained for 100 epochs, and the learning rate was set to $10^{-3}$, $10^{-4}$, and $10^{-5}$ for the first 40 epochs, 40-80 epochs, and the final 20 epochs, respectively. It took around 8 hours for network training on 2 Nvidia Tesla V100 GPUs (32 GB). The networks were implemented using Pytorch 1.8, and the source codes and trained networks are available at https://www.github.com/sunhongfu/deepMRI/tree/master/DCRNet.

3.6. Quantitative performance evaluation

The proposed DCRNet was compared with two iterative algorithms (i.e., CS$_{QR}$ (Zhao et al., 2012) and CS$_{PC}$ (Ong et al., 2018)) and one deep learning method with separate magnitude and phase Unets (Lee et al., 2018) (referred to as Mag-Unet and Phase-Unet) at accelerating factors (AFs) of 4 and 8. The Mag-Unet and Phase-Unet were retrained using the same datasets and optimizer settings as for DCRNet. The reconstructions of deep learning methods were computed on a high-performance computing cluster using one Tesla V100 GPU (32 GB), while the reconstructions of the iterative methods were accomplished with 5 Intel Xeon E5-2680V3 2.5Ghz CPU (12 core processors) on a high-performance computing cluster.

For quantitative assessment of different QSM accelerating methods, peak signal-to-noise ratio (PSNR), structural similarity (SSIM) (Wang et al., 2004), and root-mean-squared error (RMSE) (Langkammer et al., 2018) were calculated as follows:

\[
\text{PSNR}(x, x_{\text{ref}}) = 20 \log_{10} \left( \frac{\|x_{\text{ref}}\|_m}{\|x-x_{\text{ref}}\|_2} \right).
\]

\[
\text{RMSE}(x, x_{\text{ref}}) = \left( \frac{\|x-x_{\text{ref}}\|_2^2}{\|x_{\text{ref}}\|_2^2} \right) \times 100%.
\]

where $\| : \|_m$ and $\| : \|_2$ are the vector infinity and L2 norm operators; $x$ and $x_{\text{ref}}$ denote the reconstruction image and the ground truth, respectively.

\[
\text{SSIM}(x, x_{\text{ref}}) = \left( \frac{2\mu_x\mu_{x_{\text{ref}}} + C_1}{\mu_x^2 + \mu_{x_{\text{ref}}}^2 + C_1} \right) \left( \frac{2\sigma_{x_{\text{ref}}} + C_2}{\sigma_x^2 + \sigma_{x_{\text{ref}}}^2 + C_2} \right),
\]

where $\mu_x$ is the average of $x$, $\sigma_x^2$ is the variance of $x$, $\sigma_{x_{\text{ref}}}^2$ is the covariance of $x$ and $x_{\text{ref}}$; $C_1 = (k_1L)^2$ and $C_2 = (k_2L)^2$ are two variables to stabilize the division, where $L$ is a dynamic range of the pixel intensities (set as 1 by default for images of class single/double); $k_1$ and $k_2$ are constants and set as their default values ($k_1 = 0.01$ and $k_2 = 0.03$) in the current work.

Susceptibility and R2* measurements of one frontal white matter (FWM) region and six deep grey matter (DGM) regions (i.e., globus pallidus (GP), putamen (PU), caudate nucleus (CN), thalamus (TH), substantia nigra (SN), red nucleus (RN)), which were drawn manually using ImageJ (National Institutes of Health, Bethesda, MD), were measured for quantitative comparison using data from the 6 healthy volunteers. The hemorrhage susceptibility measurements were reported for the intracranial hemorrhage patient, and voxel-wise linear regressions were carried out to compare different QSM accelerating methods. Visual inspection was performed to assess the QSM image quality and the delineation of white matter lesions in the multiple sclerosis patient. Different subsampling reconstruction methods were applied to restore the full magni-

Fig. 2. (a) shows the subsampling masks of different acceleration factors (AFs). Each dot in the $k_x$-$k_y$ plane (the first 4 masks) represents a fully-sampled readout line in the $k_x$ direction, as shown in the $k_x$-$k_y$ plane (the last mask). (b) illustrates the aliasing artifacts from zero-filling reconstructions in three orthogonal views in both magnitude and phase images from AF = 4.
Fig. 3. Comparison of different MRI phase accelerating methods (at 4 × AF) on one healthy subject acquired with a single head orientation. The top four rows compare the reconstructions of magnitude and $R^2^*$ images, while the bottom four rows show the local field and QSM reconstructions from different methods. PSNR, SSIM, and RMSE relative to the ground truth (fully-sampled data) on the whole brain slices displayed are reported under the error maps. Red arrows point to the overwhelming artifacts introduced in CS$_{PR}$ and Phase-Unet methods.

4. Results

4.1. QSM undersampling reconstruction for healthy subjects

The magnitude, $R^2^*$, local field, and susceptibility maps reconstructed at 4 × and 8 × AFs from different methods were compared...
on one healthy volunteer. As shown in Fig. 3, at the acceleration of 4 × , the proposed DCRNet led to the best PSNR, SSIM, and RMSE (e.g., 41.64/0.97/34.76 for QSM reconstructions) in all image contrasts. CS\(_{\text{PR}}\) and Phase-Unet exhibited severe artifacts (red arrows) in some of the R2\(^*\), local field, and QSM images near the strong susceptibility sources (e.g., sinuses) absent in other methods. Moreover, as shown in Supp. Fig. 3, at the acceleration of 8 × , DCRNet is the only method that did not introduce substantial artifacts in the local field and susceptibility maps. The reconstruction time on one brain slice (size: 256 × 128) of this simulated brain subject for the deep learning methods (around 15 milliseconds for DCRNet and 35 milliseconds for Mag/Phase-Unet) is substantially shorter than the traditional iterative methods (around 36 and 49 seconds for CS\(_{\text{PC}}\) and CS\(_{\text{PR}}\), respectively).

Susceptibility and R2\(^*\) measurements of one FWM and six DGM regions, as shown in Fig. 4(a), using different reconstruction methods from a total of 14 scans were compared in Fig. 4. Paired t-test found that all methods except DCRNet showed significant difference in QSM images (Fig. 4(b)) relative to the fully-sampled ground truth in GP, with average QSM deviations of 5.8% (P = 0.01), 6.2% (P = 0.02), 4.4% (P = 0.04), 10.3% (P = 0.01), and 1.2% (P = 0.09) in zero-filling, CS\(_{\text{PR}}\), CS\(_{\text{PC}}\), Phase-Unet, and DCRNet, respectively. Furthermore, the Phase-Unet reconstructions showed the largest standard deviations in all region-of-interest (ROI) susceptibility measurements (e.g. 154% and 162% larger than other methods in RN and FWM) due to the overwhelming artifacts from corrupted phase wraps recovery. As shown in Fig. 4(c), DCRNet also resulted in the most accurate R2\(^*\) measurements in all brain ROIs, with only 0.7% deviation from the fully-sampled ground truth in RN, compared with 5.2%, 2.3%, 5.0% and 4.3% in zero-filling, CS\(_{\text{PR}}\), CS\(_{\text{PC}}\), and Mag-Unet reconstructions, respectively. No significant difference was found in R2\(^*\) measurements from different methods.

The COSMOS results (at 4 × AF) from DCRNet with zero-filling and CS\(_{\text{PC}}\) methods on two healthy subjects (five head orientations acquired for each) were compared in Fig. 5. Overall, the proposed deep residual network DCRNet led to higher PSNR, SSIM, and RMSE (47.57/0.99/32.39) than CS\(_{\text{PC}}\) (44.75/0.97/41.45) and zero-filling reconstruction (44.54/0.97/51.52). Significant image smoothing was found in the CS\(_{\text{PC}}\) method, while the DCRNet preserved fine details as seen in the zoomed-in regions in Fig. 5. Substantial artifacts near the cortex were observed in zero-filling results (red arrows). According to the table at the bottom of Fig. 5, the CS\(_{\text{PC}}\) method exhibited the highest susceptibility deviation from fully-sampled reconstruction in GP (5.1%), SN (10.3%), and RN (23.9%) regions. In contrast, the smallest deviations were found in the DCRNet results for all seven brain regions measured.

4.2. QSM undersampling reconstruction in the presence of pathology

Accelerated QSM acquisition results from the intracranial hemorrhage patient (at 4 × AF) were compared between the proposed DCRNet and CS\(_{\text{PC}}\) methods in Fig. 6. QSM from DCRNet appeared similar to the fully-sampled result from visual inspection, with the highest PSNR, SSIM, and RMSE (37.79/0.98/40.83). In contrast, zero-filling results showed severe artifacts and CS\(_{\text{PC}}\) exhibited over-smoothness. A hemorrhage ROI was drawn on a sagittal slice (blue contour) in Fig. 6(a), and the susceptibility of each voxel was compared with ground truth through linear regression in Fig. 6(b)-(d). It confirmed that the proposed DCRNet (R\(^2\): 0.75, SSE: 1.40) led to the most accurate hemorrhage susceptibility measurements, compared with zero-filling (R\(^2\): 0.74, SSE: 1.55) and CS\(_{\text{PC}}\) (R\(^2\): 0.71, SSE: 1.66) methods.

The proposed DCRNet and CS\(_{\text{PC}}\) QSM accelerating methods were applied to the multiple sclerosis patient in Fig. 7. All QSM acceleration reconstruction methods successfully detected the brain lesions, as indicated by the red arrows. However, the zero-filling reconstruction method suffered from significant artifacts, and the CS\(_{\text{PC}}\) method led to an apparent over-smoothing effect compared to DCRNet and full-sampled QSM results.

4.3. QSM Reconstruction for the prospectively undersampled acquisition

The zero-filling, CS\(_{\text{PC}}\), and DCRNet methods for the prospectively undersampled subject at 4 × AF were compared in Fig. 8. The in vivo acquisition was performed with a subsampled GRE sequence at 7T. The coil-combined magnitude images from the zero-filling method displayed apparent aliasing artifacts similar to retrospectively undersampled results. The CS\(_{\text{PC}}\) method exhibited residual artifacts in the magnitude and R2\(^*\) reconstructions, while the aliasing artifacts were removed after DCRNet reconstruction. Local field and susceptibility maps from zero-filling showed poor SNR, significantly degraded the image qualities, while the CS\(_{\text{PC}}\) and DCRNet methods substantially decreased the noise level and increased SNR in the local field and susceptibility maps, as evident in the zoomed-in images. The reconstruction time for one slice (matrix size: 192 × 128 × 32(receivers)) of this in vivo subject for the DCRNet (around 70 milliseconds) is substantially faster than the CS\(_{\text{PC}}\) method (about 140 seconds).

Fig. 9 compares the zero-filling, CS\(_{\text{PC}}\), and DCRNet methods for the prospectively undersampled in vivo subject at 8 × AF. Similar to the 4 × AF case (shown in Fig. 8), zero-filling results in aliasing artifacts in the magnitude, R2\(^*\), local field, and QSM images. By contrast, the
Fig. 5. Comparison of the proposed DCRNet with zero-filling and CS$_{PC}$ methods on COSMOS results at 4 × AF from two healthy volunteers, each acquired in 5 different head positions. COSMOS maps, zoomed-in regions and error maps from one subject were shown in three orthogonal views, with PSNR, SSIM, and RMSE relative to the fully-sampled ground truth displayed below the images. Red arrows point to the apparent artifact in the error map. The table reports the susceptibility measurements (mean and standard deviation) in one FWM region and six DGM regions from the two COSMOS subjects. The best measurements closest to full-sampled are highlighted in bold.

CS$_{PC}$ and DCRNet methods substantially decreased the noise level and increased the image SNR, as evident in the zoomed-in images. However, both CS$_{PC}$ and DCRNet exhibited apparent smoothing effects and blurred some fine details of brain structures at this high acceleration factor (i.e., 8 × AF).

4.4. Evaluation with different accelerating factors

The reconstruction results of the proposed DCRNet under different AFs (2 × , 4 × , 6 × , and 8 × ) were demonstrated in Fig. 10 on one healthy subject, undersampled retrospectively. None of the images
Fig. 6. Comparison of the proposed DCRNet and CSpc (at 4 × AF) on the subsampled MRI data from an intracranial hemorrhage patient. QSM images are illustrated in (a) along with PSNR, SSIM, and RMSE reported underneath. (b)-(d) demonstrate the scatter plots of susceptibility values in the brain lesion (blue contour in (a)) of different reconstruction methods (x-axis) against the ground truth (y-axis). Linear regression results are reported in the bottom-right corner for each plot. The red circle in (b) highlights some of the hemorrhage measurements in zero-filling results highly deviated from the fully-sampled references.

Fig. 7. Comparison of different QSM accelerating reconstruction methods (at 4 × AF) on one multiple sclerosis (MS) patient. The first column shows fully-sampled GRE magnitude images in two orthogonal slices, while the corresponding QSM results from different methods are illustrated from the second column. Red arrows point to the MS lesions that are identified by visual inspection.
showed visually apparent artifacts, and the overall QSM contrast was adequately preserved in all AFs. However, some fine details were gradually blurred out with higher AFs, as evident in the zoomed-in images. Supplemental Table 1 summarized the evaluation of the numerical metrics of DCRNet using 14 scans from 6 healthy subjects. It can be seen that PSNR and SSIM decreased, and RMSE increased with higher AFs for all image contrasts (i.e., magnitude, R2*, local field, and QSM).

5. Discussion

In this work, we demonstrated the feasibility of using deep neural networks to accelerate the QSM acquisition. Specifically, we developed a DCRNet method to recover the GRE phase from the CS undersampled k-space acquisition, thus enabling the phase-based QSM acceleration. The proposed method was compared with two iterative algorithms (i.e., CSPC, CSPR) and one previous deep learning-based phase reconstruction method (i.e., Phase-Unet). The results on healthy volunteers and patients with multiple sclerosis and intracranial hemorrhage showed that the proposed deep learning QSM accelerating framework resulted in more accurate QSM reconstructions (substantially improved PSNR, SSIM, RMSE, and susceptibility ROI measurements) with fewer artifacts and over-smoothness than conventional CS and the Phase-Unet approaches.

Although many previous deep neural networks (Bollmann et al., 2019; Bollmann et al., 2019; Chen et al., 2020; Gao et al., 2021; Jung et al., 2020; Liu and Koch, 2019; Polak et al., 2020; Wei et al., 2019; Yoon et al., 2018) have been proposed for solving QSM reconstruction problems, most of them focused on solving the QSM dipole inversion; this work is the first to investigate how to use deep neural networks accelerating 3D QSM acquisition with incoherent subsampling strategies. To the best of our knowledge, only one previous work (Wang et al., 2018) studied compressed-sensing accelerated QSM, reconstructed with the conventional iterative method CSPC on super-high-resolution mouse brains. This paper compares the proposed method with existing literature on QSM CS-undersampling acceleration.

The deep learning-based DCRNet QSM accelerating framework has two main advantages over the iterative CSPC and CSPR methods. Firstly, it does not need to manually design feature representations (regularizations) based on top-down mathematical modelling since it can learn more effective ones from the training datasets and, therefore, potentially
Fig. 10. Performance evaluation of the proposed QSM accelerating framework against varying acceleration factors (AFs). Magnitude, R2*, local field, and susceptibility maps are displayed from top to bottom rows, with corresponding PSNR, SSIM, and RMSE relative to the fully-sampled ground truth below the images. The first column shows the reconstruction of fully-sampled data, and the results of different AFs (from left to right: 2 × , 4 × , 6 × , 8 × ) are displayed from the second column. Error maps from the zoomed-in regions are amplified to illustrate differences in structural details better.

improve the reconstruction results. Secondly, the proposed method is much more computationally efficient than conventional iterative methods. Our test results on both retrospectively (at 3T) and prospectively (at 7T) undersampled human brain data confirmed that the proposed deep learning method substantially shortened the reconstruction time.

We also compared DCRNet with one previous deep learning-based MRI phase reconstruction method (Phase-Unet). It was found that the phase wraps in the reconstructed images were disrupted by Phase-Unet, making it problematic for the phase unwrapping process of the QSM pipeline. Our results showed that compared with DCRNet, Phase-Unet introduced severe artifacts near phase wraps in the field and susceptibility maps. In addition, the Mag-Unet and Phase-Unet reconstruct magnitude and phase images independently. On the other hand, the DCRNet method exploits the intrinsic relationship between magnitude and phase components through the complex convolution, leading to more accurate reconstructions for both.

The DCRNet neural network was trained on retrospectively undersampled GRE datasets from simulated single-channel MRI data. For the prospectively undersampled GRE acquisitions at 7T, a 32-channel head coil was used for signal reception. To reconstruct these data, the coil
sensitivities were first estimated, and complex signals from individual channels were properly combined before de-aliasing with the DCRNet. A modified data consistency operation was also applied, which significantly reduced the image blurring of the initial DCRNet results as shown in Supp. Fig. 4. Compared to training with a fixed multi-channel coil setup (Wang et al., 2020), the current approach of retrospectively undersampling and training on coil-combined images (i.e., single-channel input and single-channel-output) is less sensitive to variations in coil configuration. As pointed out by (Wang et al., 2020), among others, networks trained on multi-channel data generally require re-training for different coil configurations, which significantly limits their use in practice. Nevertheless, the proposed DCRNet is readily adaptable to the multi-channel-input structure. Future work could explore the possible benefits of leveraging these coil-sensitivity profiles to achieve even higher acceleration factors.

The DCRNet method's performance as a function of the acceleration factor was also studied, and the results showed that no substantial errors or artifacts were introduced at all tested AFs (from 2 × 8 × 8) using the proposed DCRNet framework. However, image quality gradually degraded with higher accelerations, showing increased blurring, which obscures structural details. For example, although the DCRNet successfully removed the aliasing artifacts in the zero-filling reconstruction at AF × 8, it led to reduced cortical contrast as shown in Figs. 9 and 10. This study adopted deep neural networks for GRE phase undersampling reconstruction (i.e., DCRNet). However, the QSM processing steps (e.g., phase unwrapping, background field removal, and dipole inversion) were still using traditional algorithms. Future work may develop a single or cascaded neural network that can directly reconstruct QSM from the undersampled phase acquisition. This strategy may minimize error propagation and amplification in each intermediate step and improve final results.

6. Conclusion

This study proposed a deep learning-based MRI accelerating framework, DCRNet, to accelerate data acquisition and reconstruction for QSM and R2*. The experimental results showed that the DCRNet method led to QSM and R2* images with fewer reconstruction errors and more accurate susceptibility and relaxation measurements than the state-of-the-art iterative methods with the same accelerating factors. In addition, the DCRNet substantially reduced the reconstruction time of single 2D brain images from 36-140 seconds using conventional approaches to only 15-70 milliseconds. The trained DCRNet model from healthy subjects can also be generalized to patients, as demonstrated in intracranial hemorrhage and multiple sclerosis cases.

Credit authorship contribution statement

Yang Gao: Conceptualization, Methodology, Software, Formal analysis, Writing – original draft, Writing – review & editing, Visualization.
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Stuart Crozier: Writing – review & editing. G. Bruce Pike: Data curation, Writing – review & editing, Funding acquisition.
Hongfu Sun: Conceptualization, Methodology, Data curation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Data and code availability statements

Data are available on request due to privacy/ethical restrictions. Source codes and trained networks are available at https://github.com/sunhongfu/deepMRI/tree/master/DCRNet.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2021.118404.

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