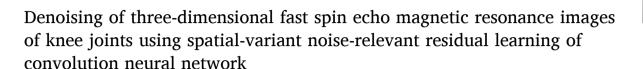


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Shutian Zhao <sup>a</sup>, Dónal G. Cahill <sup>a</sup>, Siyue Li <sup>a</sup>, Fan Xiao <sup>a</sup>, Thierry Blu <sup>b</sup>, James F. Griffith <sup>a</sup>, Weitian Chen <sup>a,\*</sup>

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#### ABSTRACT

*Purpose*: Two-dimensional (2D) fast spin echo (FSE) techniques play a central role in the clinical magnetic resonance imaging (MRI) of knee joints. Moreover, three-dimensional (3D) FSE provides high-isotropic-resolution magnetic resonance (MR) images of knee joints, but it has a reduced signal-to-noise ratio compared to 2D FSE. Deep-learning denoising methods are a promising approach for denoising MR images, but they are often trained using synthetic noise due to challenges in obtaining true noise distributions for MR images. In this study, inherent true noise information from two number of excitations (2-NEX) acquisition was used to develop a deep-learning model based on residual learning of convolutional neural network (CNN), and this model was used to suppress the noise in 3D FSE MR images of knee joints.

*Methods*: A deep learning-based denoising method was developed. The proposed CNN used two-step residual learning over parallel transporting and residual blocks and was designed to comprehensively learn real noise features from 2-NEX training data.

Results: The results of an ablation study validated the network design. The new method achieved improved denoising performance of 3D FSE knee MR images compared with current state-of-the-art methods, based on the peak signal-to-noise ratio and structural similarity index measure. The improved image quality after denoising using the new method was verified by radiological evaluation.

Conclusion: A deep CNN using the inherent spatial-varying noise information in 2-NEX acquisitions was developed. This method showed promise for clinical MRI assessments of the knee, and has potential applications for the assessment of other anatomical structures.

### 1. Introduction

The knee is the largest joint in the human body, with a complex and frequently injured anatomical structure [1]. It is a synovial hinge joint, and its stability is maintained by ligaments, tendons, a joint capsule, and menisci. Magnetic resonance imaging (MRI) is the most prominent non-invasive diagnostic modality, and its excellent visualization of soft tissue characteristics means it provides optimal imaging of the knee joint [2]. Fast spin echo/turbo spin echo (FSE/TSE) [3], the commercial

implementation of rapid acquisition with relaxation enhancement (RARE) [4], plays a central role in clinical knee MRI. Current knee MRI protocols often consist of two-dimensional (2D) FSE sequences repeated in multiple planes to observe overall anatomical structure. However, this process is time-consuming and its low through-plane resolution results in partial volume effects. Compared to 2D FSE, three-dimensional (3D) FSE can be used to generate thinner sections due to its volumetric acquisitions and thus reduced partial volume effects. Consequently, 3D FSE can be acquired with high isotropic resolution and reformatted into

<sup>&</sup>lt;sup>a</sup> CU Lab for AI in Radiology (CLAIR), Department of Imaging and Interventional Radiology, the Chinese University of Hong Kong, Hong Kong Special Administrative Region of China

b Department of Electronic Engineering, the Chinese University of Hong Kong, Hong Kong Special Administrative Region of China

Abbreviations: 3D, three-dimensional; FSE, Fast Spin Echo; NEX, number of excitation; CNN, convolutional neural network; RL, residual learning; SNR, signal-to-noise ratio; PSNR, peak signal-to-noise ratio; SSIM, structural similarity index.

<sup>\*</sup> Corresponding author. Room 15, Sir Yue Kong Pao Centre for Cancer, Prince of Wales Hospital, Shatin, NT, Hong Kong.

E-mail addresses: shutian@link.cuhk.edu.hk (S. Zhao), donalcahill@cuhk.edu.hk (D.G. Cahill), 1155105213@link.cuhk.edu.hk (S. Li), freidaxiao@gmail.com (F. Xiao), thierry.blu@gmail.com (T. Blu), griffith@cuhk.edu.hk (J.F. Griffith), wtchen@cuhk.edu.hk (W. Chen).

an arbitrary plane to visualize complex anatomical structures. The application of 3D isotropic FSE in clinical practice may therefore markedly decrease the total time required for MR imaging examination [5]

Commercial 3D FSE sequences typically use long echo trains with variable flip angles to achieve a reasonable scan time without excessive blurring [6]. As short T2 tissues are dominant in knee joints, image blurring often remains in 3D FSE MR images of the knee if long echo trains are used. The approaches used to reduce image blurring without increasing scan time, such as reducing the minimum flip angle of the echo train, are often accompanied by a reduced signal-to-noise ratio (SNR) [7]. In addition, high isotropic resolution in 3D images is often obtained at the cost of the SNR. Therefore, denoising is desirable when 3D FSE is used for clinical MR imaging of the knee.

Traditional denoising methods have been commonly used for decades and include bilateral filtering [8], total variation (TV)-based regularization [9], nonlocal means (NLM) [10], and K-singular value decomposition (K-SVD) [11]. Block-matching 3D collaborative filtering (BM3D) [12] is a state-of-the-art denoising method [13] with a substantial number of applications in the MRI domain [14–16]. However, this denoising method's long calculation time and requirement for a carefully designed prior [17] have prevented its routine use in clinical MRI settings.

Convolutional neural networks (CNNs) [18] use a series of convolution and non-linear activation operations, and thus show good flexibility and capability for learning a hierarchy of features, which makes them useful in image denoising. However, when a CNN goes to a certain depth, its gradient tends to vanish, causing a degradation in performance. To address this problem in deep CNNs, He et al. developed a residual learning (RL) approach that involves adding skip connections to a convolution block to connect low-level features directly to high-level representations [19]. RL allows for considerable increases in the depth and width of a network, and it has been shown to be efficient at image processing including classification [20], single image super-resolution [21], and denoising [22].

It is easier to predict the residual difference between the desired output and the input for a given stack of nonlinear layers in deeplearning models than to directly optimize the original mapping [19]. Many existing image denoising networks attempt to apply RL to approximate residual noise [22-28], based on the assumption that a noisy observation may be expressed as a combination of a clean image and noise. Zhang et al. [22] were the first to use RL with batch normalization (BN) in neural networks to generate denoising DnCNN, which are capable of blind Gaussian denoising of natural images. The application of DnCNN in the MRI field has also achieved remarkable results, such as removing artificial Rician noise [23] and real noise in diffusion-weighted brain MR images [24]. In addition to DnCNN, various other RL-based denoising CNNs have been developed for MRI applications. Xie et al. [25] improved denoising performance in arterial spin labeling (ASL) MRI by preserving the spatial resolution of input images during model learning. Li et al. [26] used Rician denoising to process synthetic and clinical brain MR images. RL combined with a fully convolutional network (FCN) by Ulas et al. [27], and an encoder-decoder structure by Tripathi et al. [28] were also used to denoise MR images.

Given the limited amount of available data, many MRI denoising networks have been trained using synthetic data with a given noise variance over an entire image. However, the noise distributions in actual MR images are often more complicated than those in these synthetic data-based approaches. For example, reconstruction methods such as sensitivity encoding (SENSE) and generalized autocalibrating partial parallel acquisition (GRAPPA) contribute to the non-stationarity of the noise variance. In this study, we explored deep learning-based methods for denoising 3D FSE MR images based on real noise distributions.

It is a common practice to increase the SNR (i.e., denoise) of MR images using time integration methods [29], such as by adjusting the

number of excitations (NEX). As SNR is calculated as the mean signal over the standard deviation of the noise [30], the SNR of MR images is generally proportional to the square root of the NEX ( $\sqrt{NEX}$ ). Although higher-quality images are obtained by increasing the NEX, a time penalty results. Thus, to restrict imaging time within reasonable ranges, typical NEX values need to be adjusted to obtain an acceptable tradeoff between time and image quality [31].

In this study, we assumed that spatial-varying noise information can be extracted from 2-NEX acquisitions. This enabled us to use 2-NEX acquisitions to achieve denoising that generated a much higher SNR gain than that generated by the standard method, which uses the time integral of 2-NEX images. The scan time penalty was controlled by replacing a 1-NEX acquisition protocol with rapid low-SNR 2-NEX acquisitions with protocol optimization. We also developed a CNN model to make use of the inherent noise map embedded in these 2-NEX acquisitions, and thereby achieved significantly improved denoising performance compared to that without the CNN model. Overall, under the framework of RL designed for 2-NEX images, we demonstrated that our developed CNN model outperformed state-of-the-art denoising methods in the 3D FSE MRI of knee joints.

#### 2. Methods

### 2.1. Spatial-varying noise distribution in 3D FSE MRI

It is commonly accepted that both the real and imaginary parts of the original signal from a single-coil MR acquisition are corrupted with uncorrelated zero-mean and equal-variance Gaussian noise in the frequency domain. After complex Fourier transform, a linear transformation method, the Gaussian characteristics of noise in real and imaginary images, denoted by  $N(0,\sigma_0^2)$ , are preserved. Consequently, if the MR acquisition is repeated, a second complex-valued image is obtained; then, arithmetic can be performed on the two complex-valued images, as their signals can be assumed to be the same. Specifically, a complex-valued signal-strengthened map, also referred as the 2-NEX image in this paper, can be obtained by summing MR image data and a complex-valued noise map can be obtained by subtracting MR image data. The real and imaginary components of this signal-strengthened map and the noise map continue to exhibit a Gaussian distribution, denoted by  $N(0,\sigma^2)$ , where  $\sigma=\sqrt{2}\sigma_0$ .

The magnitude image of the signal-strengthened map therefore follows a Rician distribution and approximates a Gaussian distribution when the signal is sufficiently high [32]. In contrast, the magnitude image of the noise map follows a Rayleigh distribution, with the mean and variance given by Eq. (1), as follows.

$$\mu_R = \sigma \sqrt{\frac{\pi}{2}}$$
 and  $\sigma_R^2 = \left(2 - \frac{\pi}{2}\right)\sigma^2$  (1)

Phased array coils with multiple coil elements, in which the complex Gaussian assumption of noise is valid in each coil in the frequency domain, are commonly used in MRI. If the k-space is fully sampled, the final composite magnitude image will follow a Rayleigh distribution in the background noise-only region, or a noncentral chi  $(nc - \chi)$  distribution, which take the signal intensities, but not the noise correlations, into consideration [30].

However, in addition to the non-negligible correlations in phased array systems, the commonly employed k-space undersampling and reconstruction algorithms used in fast MRI increases the complexity of noise distributions [33]. To illustrate this in 3D FSE MRI, we used an eight-channel knee coil with a SENSE acceleration factor of 2 to acquire 3D FSE images. Fig. 1 shows two signal-strengthened magnitude images and the corresponding noise maps calculated using the aforementioned method. We generated the histograms of noise and fitted them with a Rayleigh distribution. If the noise follows an  $nc - \chi$  distribution, its square will follow a noncentral chi-squared  $(nc - \chi^2)$  distribution [34]. It

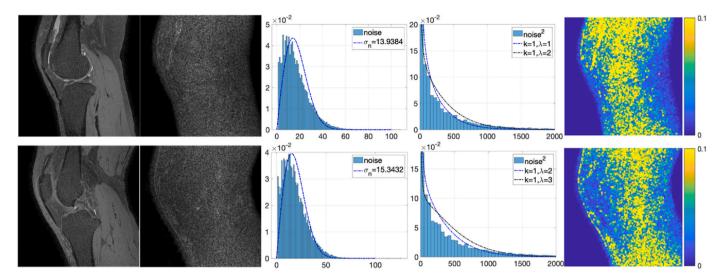


Fig. 1. Two typical slices of 2-NEX images. From left to right: signal-strengthened images, noise maps, histograms of the noise with corresponding fitted Rayleigh probability density functions, histograms of the noise squared with noncentral chi-squared distribution probability density functions, and local variance maps of noise.

can be seen in Fig. 1 that the noise showed a non-stationary pattern and did not exactly follow either a simple Rayleigh distribution or an  $nc-\chi$  distribution. We also calculated the local variance of the noise maps in patches of  $3\times 3$  pixels (Fig. 1), which revealed an obvious spatial variation in the noise variance. Thus, based on the assumption that noise is non-stationary in a given set of MR images, we considered that it would be more appropriate to use real MR images with a true noise distribution than simple synthetic noise to train a denoising network.

### 2.2. Network architecture

A key aspect in the development of our proposed network was to use

RL to learn the inherent real noise distribution in a dual-NEX acquisition, and thereby realize denoising of MR images that was superior to that obtainable with existing methods. The overall pipeline of our method, with some intermediate features of a typical slice, is illustrated in Fig. 2.

The CNN consists of three modules: a feature extraction module, a bridge module, and an assembly module. The whole network has about 1.6 M trainable parameters.

 Feature extraction module. The first six 128-kernel convolutional layers serve as the feature extraction module, which extracts certain

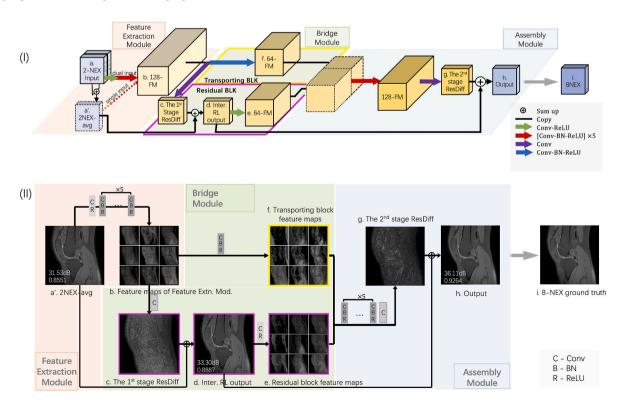


Fig. 2. Our novel convolutional neural network (CNN) architecture (I) and an illustration of some of the channel features at some layers of a typical slice (II). Our CNN can manage both dual-input (solid line (a)) and single-input (dashed line (a')) data.

low-level features (b) of the noise from the 2-NEX input (a). Our CNN is able to handle both dual-input (a) and single-input data (a').

- Bridge module. This module further optimizes the noise features using two parallel blocks: a transporting block and a residual block. The transporting block uses a 64-kernel convolutional layer with BN to maintain the flow of the original 2-NEX input information. The residual block provides a coarse evaluation of the denoised image by implementing the first stage of RL on the original 2-NEX inputs. An intermediate RL output (d) is then obtained by summing the first-stage residual difference (c) and a skip connection from the average of the 2-NEX input (a'). The residual filter feature maps (e) show features from the preliminary denoised intermediate RL output (d), while the transporting block feature maps (f) mostly inherit noise features from the feature extraction module.
- Assembly module. In this module, another convolutional layer is applied to consolidate the concatenated residual block feature maps (e) and transport the block feature maps (f). The remaining five convolution layers employ 128 kernels to generate high-level noise features. A sophisticated evaluation of the noise is then generated as the second residual difference (g). This residual difference and the previous coarsely denoised intermediate RL output (d) are summed to obtain the final denoised output (h).

#### 2.3. Two-step residual learning for 2-NEX images

The noise map for 2-NEX images may be calculated as the difference between two individual NEX images, and thus we assumed that keeping each NEX image separated in the network would facilitate the determination of the inherent noise information. General RL models used for denoising requires the consistency of format between the input and the target output due to direct application of skip connections. Some variants of RL models, such as DL-ASL [25], does not have this limit after adding convolution to skip connections. These methods, however, are initially proposed for single input. In our network we designed RL to process two independent NEX images as input to use the inherent noise information in 2-NEX data for residual difference prediction and used their average for the skip connection.

We implemented RL in two stages in our network. The first stage of RL calculated a coarse residual difference and built its skip connection on the average of 2-NEX inputs, with its output denoted as the intermediate RL output. The second stage of RL generated a more sophisticated second-stage residual difference using features from both the 2-NEX input and the intermediate RL output. The final output was obtained from the second-stage residual difference with a skip connection to the intermediate RL output. This RL design ensured that the network made full use of both the strengthened signal and the inherent noise information from 2-NEX images.

### 2.4. Loss function

The mean squared error,  $l_2$ , is probably the most widespread and convenient error measure used in image processing. However, it is widely accepted that  $l_2$  does not correlate well with human perception of image quality [35]. The structural similarity index measure (SSIM) [36] is a commonly used reference-based index that evaluates images while accounting for the fact that the human visual system is sensitive to changes in local structure [37]. We thus combined  $l_2$  loss and SSIM loss to generate an output with sharper edges and clearer details than either loss alone, as described in Eq. (2) below.

$$argmin_f ||f(I_{2NEX}) - I_{8NEX}||_2^2 * (1 - SSIM(f(I_{2NEX}), I_{8NEX}))$$
 (2)

### 2.5. Evaluation methods

The image denoising performance of our method was measured using the peak signal-to-noise ratio (PSNR) and the SSIM value. The

PSNR describes the denoising quality, and the SSIM is determined by modeling any image distortion as a combination of brightness, contrast, and structure correlation [38].

Given a reference image f and a test image g, with mean luminance  $\mu_f$  and  $\mu_g$ , respectively, standard deviation  $\sigma_f$  and  $\sigma_g$ , respectively, and covariance  $\sigma_{fg}$  between f and g, the PSNR and SSIM between f and g are defined by Eqs (3) and (4), as follows:

$$PSNR(f,g) = 10 \log_{10} \left( \frac{255^2}{MSE(f,g)} \right)$$
 (3)

$$SSIM(f,g) = \frac{\left(2\mu_f \mu_g + C_1\right) \left(2\sigma_{fg} + C_2\right)}{\left(\mu_f^2 + \mu_g^2 + C_1\right) \left(\sigma_f^2 + \sigma_g^2 + C_2\right)} \tag{4}$$

where MSE is the mean square error between f and g, and  $C_1$  and  $C_2$  are constants used to avoid division by zero. A higher PSNR indicates a higher image quality, and the closer that the SSIM value of two images is to 1, the more similar are the two structures. In our experiments, the SSIM is locally calculated by an  $11 \times 11$  Gaussian window and the mean value is used as the final measure. Matlab R2021a (Mathworks, Natick, MA, USA) was used for image analysis.

The quality of the patient datasets was independently reviewed for perceived SNR, overall image quality, and structure visibility by a radiologist with specialty fellowship training in musculoskeletal radiology. The key anatomical structures of the knee that were evaluated were the cartilage, anterior cruciate ligament, posterior cruciate ligament, medial collateral ligament, lateral collateral ligament, medial meniscus, lateral meniscus, extensor tendons, and bone.

#### 2.6. Methods for comparison and training settings

The performance of our method was evaluated and compared with the following state-of-the-art methods: BM3D [12], DnCNN [22], DL-ASL [25], and RicianNet [26]. For the 2-NEX input, the concatenation of two individual complex-valued images was denoted as dual-input, while the use of their average as the input was denoted as single-input. The real noise distribution was inherently present in the dual-input scenario but was absent from the single-input scenario. Because BM3D and DnCNN can only process single inputs, dual-input results were not obtained for these two methods. The paired *t*-test was applied to compare the difference. The p-value of less than 0.05 indicated a significant difference. We also trained separated networks on three different imaging planes; i.e., the axial, coronal, and sagittal planes. We performed slice-by-slice denoising in 2D instead of direct 3D denoising for all denoising methods compared in this study, including our novel method.

Our CNN has 14 layers, and each convolution has filter size of  $3\times 3$ , stride 1, and padding 1. In addition, it employs BN and the rectified linear unit (ReLU) [39] activation function. We used the Adam optimizer and the ReduceLROnPlateau monitor with an initial learning rate of 0.0001, which is decayed by a factor of 0.2 when the loss stops decreasing for 10 epochs. The entire  $214\times 214$  images were used as inputs, with a batch size of eight. All of the models were optimized using the loss function, as described in Eq. (2). As more kernels allow the CNN to capture more features [40,41], we doubled the number of convolution filters in each layer in the DnCNN (from 64 to 128) to enable a fair comparison of these methods. All experiments were implemented in Python 3.9.7 with Pytorch 1.10.0 on four NVIDIA TITAN V GPUs (12 GB).

### 2.7. Data acquisition

The datasets were collected using a 3D proton density-weighted FSE/TSE VISTA™ pulse sequence on a Philips Achieva TX 3.0 T MRI instrument (Philips Healthcare, Best, Netherlands) with an eight-channel receiver knee coil (Invivo, Gainesville, FL, USA). All MRI examinations

were conducted under the approval of the Institutional Review Board. The MRI parameters were as follows: a repetition time/echo time of 900/33.6 ms; excitation flip angle 90; spectral attenuated inversion recovery (SPAIR) for fat suppression; FOV  $160 \times 160 \times 120 \text{ mm}^3$  [3]; 150 slices with an isotropic resolution of  $0.8 \times 0.8 \times 0.8 \text{ mm}^3$ ; an echo train length of 42; and a SENSE acceleration factor of 2. The imaging acquisition time per NEX was approximately 2.9 min. We collected high-SNR images (which served as the target images) from the 8-NEX acquisition, and the first 2-NEX provided the input of the network. Datasets including 8-NEX 3D FSE MRI data were collected from 67 healthy volunteers. 50 of these datasets were used for training and 17 were used for testing. An additional 40 3D FSE MRI datasets with 2-NEX were collected from 40 patients (categorized into the four Kellegren and Lawrence (KL) grades for the classification of osteoarthritis, with KL4 being the most severe) exhibiting various stages of osteoarthritis, and these datasets were used for testing. The subjects recruited in MRI exams include 51 males (age  $36.9 \pm 17.9$ ) and 56 females (age  $43.4 \pm 19.5$ ).

#### 3. Results

#### 3.1. Network performance with single-input and dual-input data

Table 1 shows the average PSNR and SSIM results for the sagittal plane testing of healthy volunteer datasets. We denoted 2NEX-avg as the standard results after averaging two complex-valued images of 2-NEX acquisitions. The four deep-learning models were superior to the traditional denoising method, BM3D, and our novel model using dual-input images achieved the best performance.

Although the single-input and dual-input training data were from the same batch, with equal acquisition times, the denoising performance with the dual-input data was always superior to that with the single-input data. This was because our RL method for 2-NEX images was designed to take advantage of the noise information from 2-NEX images, which enabled our model to process dual-input data with better denoising ability than single-input data. Results of the paired samples t-test demonstrate a statistically significant improvement (p < 0.05) in the performance of all three models (DL-ASL, RicianNet, and our model) using dual-input data compared to using single-input data. Also note our model shows a statistically significant improvement in performance (p < 0.05) compared to DL-ASL and RicianNet when using dual-input data.

**Table 1**Mean PSNR and SSIM values indicating the performance of denoising methods in the sagittal plane. The BM3D and DnCNN methods only process single inputs.

	PSNR		SSIM			
	Single- input	Dual- input	p <sup>b</sup>	Single- input	Dual- input	p <sup>b</sup>
2NEX- avg	31.4114 ±	2.2761	-	$0.86612 \pm$	0.03834	-
BM3D <sup>a</sup>	$32.2920 \\ \pm \ 2.3124$	_	-	$0.88810 \pm 0.03103$	-	-
DnCNN <sup>a</sup>	$\begin{array}{c} 34.0181 \\ \pm \ 2.2646 \end{array}$	-	-	0.91976 ± 0.02026	-	-
DL-ASL	$34.0692 \\ \pm 2.2068$	$\begin{array}{c} 34.4133 \\ \pm \ 2.1456 \end{array}$	0.000	0.92052 ± 0.02125	$0.92367 \pm 0.02047$	0.000
RicianNet	$34.0455 \pm 2.2154$	$34.5632 \\ \pm 2.2042$	0.000	0.92055 ± 0.02066	$0.92388 \pm 0.02031$	0.000
Our Model	$\begin{array}{c} {\bf 34.1432} \\ {\bf \pm \ 2.2244} \end{array}$	$\frac{34.7233}{\pm 2.2108}$	0.000	$0.92054 \pm 0.02123$	0.92459 ± 0.02047	0.000

<sup>&</sup>lt;sup>a</sup> BM3D and DnCNN only process single input.

Fig. 3 shows the results from a representative test subject and the corresponding 8-NEX ground truth. The use of the dual-input data resulted in greater similarity to the 8-NEX ground truth than the use of the single-input data. Of all the methods tested, our model with dual-input data suppressed noise most uniformly, even in regions with high noise levels. Facilitated by the separation and concatenation operations of the parallel transporting and residual blocks, the RL design for 2-NEX images ensured that the final output used both original and residual features.

### 3.2. Network performance for denoising in 3D datasets

Table 2 shows the mean PSNR and SSIM denoising results from healthy volunteer testing datasets in the axial, coronal, and sagittal planes. Fig. 4 shows the result of denoising the data of one healthy test subject in these three planes. The noise level and the distribution of 2NEX-avg images differed in each plane, even for the same knee, which is consistent with the spatially variant characteristics of noise. As we trained our model using MR images containing real noise, our method achieved denoising performance in all three planes that was superior to that achieved by standard averaging methods. Moreover, our denoising method clearly denoised MR images of critical structures, including bone, cartilage, menisci, and the anterior cruciate ligament.

The patient cohort group comprised 40 patients with varying severities of osteoarthritis of the knee. The implementation of our denoising approach afforded MR images of all anatomical structures that had superior perceived SNR and improved overall image quality relative to standard averaging method. The result from a representative patient test dataset is shown in Fig. 5. This subject had KL4 osteoarthritis, and the characteristic radiological findings seen in osteoarthritis, such as cartilage thinning, osteophytosis, bone marrow cysts, bone marrow edema, joint effusions, and para-labral cysts, were all clearly identifiable following noise suppression using our method.

The performance of our method using data from both healthy volunteer and osteoarthritis patient datasets implies that our CNN is able to simultaneously denoise and retain anatomical structures. The beneficial reduction in overall patient scan time in three planes combined with improved image quality highlights its potential clinical utility.

### 3.3. Ablation study

The feature extraction module and the assembly module constitute the nonremovable skeleton in our CNN. Thus, ablation studies were used to investigate the design of the bridge module. The modified network structure and the corresponding denoising results on the same test datasets are shown in Fig. 6. Model-Tra represents our CNN with only a transporting block in the bridge module, and Model-Res corresponds to the CNN with only a residual block. Table 3 shows the mean PSNR and SSIM values of the three models for the healthy volunteer test datasets. Our model showed increased denoising performance compared to both the Model-Tra and Model-Res models. In particular, the transporting block preserved the overall noise information from the original 2-NEX input, and the residual block extracted more subtle noise information from the already coarsely denoised intermediate residual output. The parallel block structure thus provided sufficient information for our novel CNN, contributing to its improved performance in both PSNR and SSIM metrics.

### 3.4. Network performance for denoising synthetic noise

To further illustrate that our proposed network can learn nonstationary noise, we synthesized MR images with known spatial noise distribution and performed denoising on these synthetic images. Fig. 7 shows the comparison of the given and the predicated noise distribution using the proposed method. The predicted noise distribution is calculated as the difference between the images after denoising and the input. Note the proposed method can learn the spatial noise distribution.

<sup>&</sup>lt;sup>b</sup> The p value is the significance level of Paired Sample *t*-Test comparing the means between models' performance with single-input and dual-input. All p values here are less than 0.05, indicating a significant difference of the data.

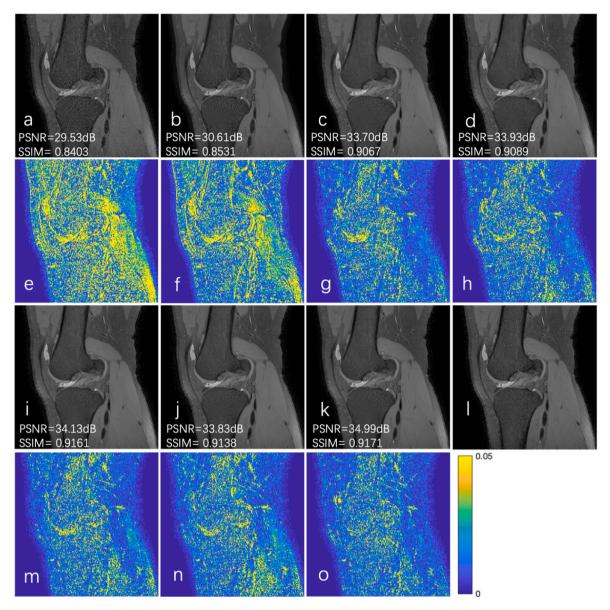


Fig. 3. Denoising results of a typical slice of the volunteer test dataset. The first row shows (a) the single-input 2NEX-avg and its corresponding denoised output using (b) BM3D, (c) DnCNN, and (d) our model. The third row shows the denoised outputs from a dual-input 2-NEX using (i) DL-ASL, (j) RicianNet, (k) our model, and (l) the ground truth. The second and fourth rows are residual differences between corresponding images and the 8-NEX ground truth. 2NEX-avg = the standard results after averaging two complex-valued images of 2-NEX acquisitions.

**Table 2**Mean PSNR and SSIM values of the test datasets denoised in the axial, coronal, and sagittal planes.

	PSNR		SSIM	
	2NEX-avg	Our Model	2NEX-avg	Our Model
axial	31.1043 ± 2.6417	33.4544 ± 2.4321	0.86473 ± 0.05759	$\begin{array}{c} 0.91581 \; \pm \\ 0.03581 \end{array}$
coronal	$33.2752 \pm 2.2388$	$35.8279 \pm 2.3827$	$\begin{array}{c} 0.91528 \pm \\ 0.02548 \end{array}$	$\begin{array}{c} 0.94977 \; \pm \\ 0.01524 \end{array}$
sagittal	$\begin{array}{c} 31.4160 \pm \\ 2.2530 \end{array}$	$\begin{array}{c} 34.7236 \; \pm \\ 2.1836 \end{array}$	$\begin{array}{c} 0.86614 \pm \\ 0.03823 \end{array}$	$\begin{array}{c} 0.92463 \pm \\ 0.02046 \end{array}$

### 4. Discussion

3D FSE shows clinical potential for MRI-based assessments of articular cartilage, menisci, ligaments, tendons, and nerves [42,43]. To further utilize 3D FSE high-through-plane resolution to visualize

complex anatomical structures, we developed a method for 3D FSE knee joint MR image denoising.

Prior knowledge of a noise distribution facilitates denoising; however, real noise distributions of typical 3D MR images often have spatial variations and are difficult to characterize. Li et al. [6] obtained a 3D FSE MRI noise map using additional noise-only acquisition with radiofrequency (RF) excitations switched off and by following a routine reconstruction pipeline. Instead, we used 2-NEX acquisition to provide a network with inherent noise information. As the traditional denoising methods often compromise the image details, a deep learning denoising method was employed in this experiment to minimize such side effects by its data-driven feature exaction. Our CNN was specifically designed for dual-input data, and it contains feature extraction, bridge, and assembly modules to extract, integrate, and transfer the features of the 2-NEX input. Assisted by the L2 norm and SSIM loss, our CNN's two-step RL parallel transporting and residual block design ensured that it can learn real noise information from the 2-NEX input and the high-SNR training target data. The experimental results suggest that our method

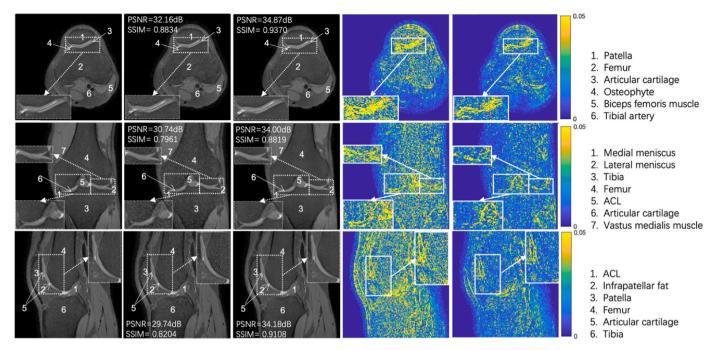


Fig. 4. Results of denoising typical slices from different planes of the volunteer test dataset. From top to bottom row: the axial, coronal, and sagittal planes. From left to right: a ground truth 8-NEX image, an input 2NEX-avg image, an image denoised using our model, the residual difference between the 2NEX-avg input and the ground truth, and the residual difference between the denoised image and the ground truth. 2NEX-avg = the standard results after averaging two complex-valued images of 2-NEX acquisitions.

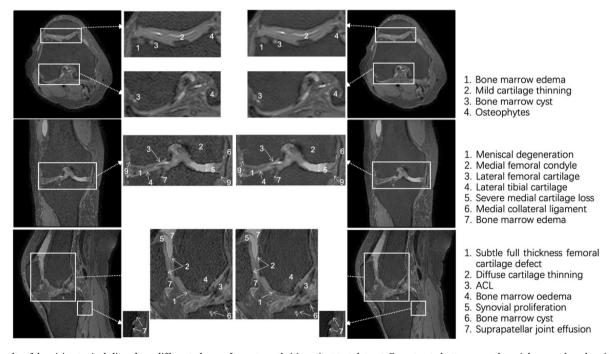


Fig. 5. Results of denoising typical slices from different planes of an osteoarthritis patient test dataset. From top to bottom row: the axial, coronal, and sagittal planes. From left to right: an input 2NEX-avg image and the image denoised using our model. The image in the white box is enlarged to highlight the fine structural information. 2NEX-avg = the standard results after averaging two complex-valued images of 2-NEX acquisitions.

was superior to state-of-the-art denoising networks. Specifically, the overall improvement in the quality of 3D FSE MR images of osteoarthritis patients' knees processed by our method compared with the quality of images processed with standard averaging methods demonstrates the clinical potential of our approach.

FSE acquisition plays a central role in clinical MRI and is used for various anatomical structures. In this study, we focused on denoising 3D

FSE MR images of knee joints. This method may be extended to 3D FSE imaging of other anatomical structures and imaging applications based on 3D FSE acquisitions. Moreover, quantitative analysis based on 3D FSE may also benefit from image denoising. Magnetization-prepared 3D FSE has been used for fast 3D quantitative parametric MRI [44,45] due to its high SNR efficiency and insensitivity to T1 relaxation effects during FSE readout under the Carr–Purcell–Meiboom–Gill condition. As accurate

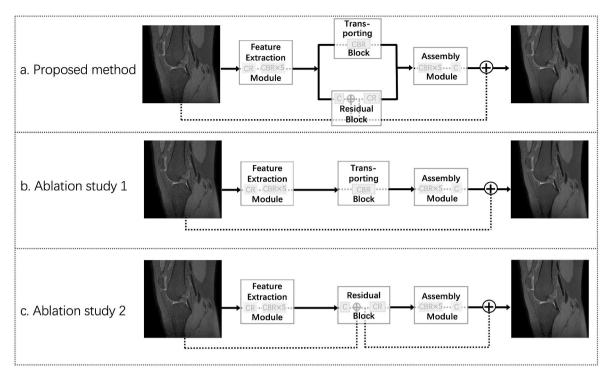


Fig. 6. Our convolutional neural network (a) and its variants, Model-Tra (b) and Model-Res (c).

**Table 3**Mean PSNR and SSIM values of the ablation study models used to test the performance of the models in the sagittal plane.

	PSNR	SSIM
Model Model-Tra Model-Res	$\begin{array}{c} 34.7233 \pm 2.2108 \\ 34.5816 \pm 2.2452 \\ 34.6493 \pm 2.1935 \end{array}$	$\begin{array}{c} 0.92459 \pm 0.02047 \\ 0.92308 \pm 0.02157 \\ 0.92320 \pm 0.02115 \end{array}$

MRI quantification depends on the noise characteristics in quantification models, our method is potentially beneficial to quantitative MRI based on 3D FSE acquisitions. In addition, our deep-learning denoising CNN is likely to be generalizable to other MRI pulse sequences using the

multi-NEX acquisition method, such as 2D FSE.

For protocols that use multi-NEX during FSE acquisition, there is no scan time penalty when applying our method for denoising. For protocols with 1-NEX acquisition, a 2-NEX scan of simply two repeated 1-NEX scans doubles the scan time. For 3D FSE, there is the flexibility of adjusting the pulse sequence parameters to achieve a tradeoff between scan time and SNR. The scan time can be reduced by increasing the echo train length (i.e., the number of refocusing RF pulses in one train). However, increasing the echo train may also increase image blurring. The flip angle train can be designed (i.e., by reducing the minimum refocusing flip angle) to reduce blurring. The train duration can also be reduced by increasing the readout bandwidth, thus reducing image blurring resulting from the increased echo train length. In addition, the

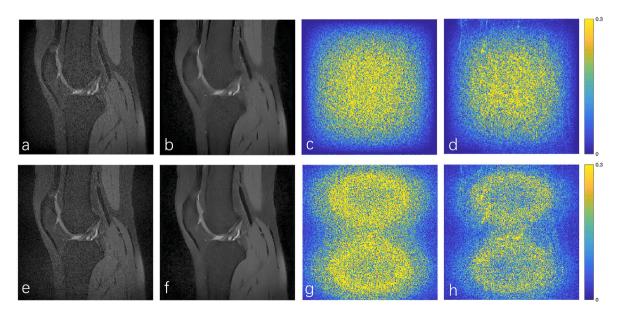


Fig. 7. An illustration of the denoising performance on the synthetic images with two non-stationary noise patterns (c) (g). (a) (e) are the original synthetic images, (b) (f) correspond to the denoised output of our proposed model, and (d) (h) are the corresponding predicted noise distributions using our proposed model.

scan time can be reduced by performing greater undersampling of the k-space. However, the scan time reduction for such a protocol adjustment comes at the cost of the SNR. Thus, the scan time penalty of a 2-NEX scan involves a tradeoff with an SNR penalty. A final denoised image obtained by our method therefore has a much higher SNR than the sum of the 2-NEX acquisitions which is expected to have SNR similar to 1-NEX acquisition with comparable scan time.

There are several limitations to this study. First, our method was a supervised approach. Thus, if the imaging protocol is changed, resulting in a substantial change in the real noise distribution, the network may need to be retrained with target images acquired using the corresponding protocol. It is thus important to investigate approaches that require few target images to train the network, under the same principle proposed in this work; namely, using the inherent real noise in a dualinput complex-valued image. Second, our training data were all from healthy subjects, and thus our method may be relatively weak at processing real patient data. That is, except for the reconstruction methods, dielectric and inductive losses in a sample may also influence the noise distribution [46]. Tissues with different water content may contribute differently to noise [47]. This emphasizes the need to use real MR images of different anatomical structures and inhomogeneous dielectric properties for network training. Third, we used 8-NEX 3D FSE images as the ground truth for training. The acquisition of these images requires a long scan time, and thus it should be investigated whether images obtainable via other shorter acquisitions can be used as the ground truth. Fourth, we performed denoising slice-by-slice using a 2D network. Given the redundancy of 3D data, it should be explored whether our CNN can be extend to 3D complex-valued CNN [48], as this would enable exploration of the 3D noise features of complex-valued MRI data and the development of more convenient applications.

### 5. Conclusion

We developed an RL-based CNN that uses the spatial-variant noise information from dual-NEX acquisition to denoise MR images. This approach achieved significantly improved SNR gain compared to standard methods of averaging multi-NEX acquisition. Our method also outperformed existing methods in the denoising of 3D FSE MR images of knee joints. The results from patients exhibiting various stages of osteoarthritis show that our method has potential clinical utility for knee joint MR imaging and provides a new perspective for MRI denoising tasks.

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