Exploring linearity of deep neural network trained QSM: QSMnet

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Abstract

Recently, deep neural network-powered quantitative susceptibility mapping (QSM), QSMnet, successfully performed ill-conditioned dipole inversion in QSM and generated high-quality susceptibility maps. In this paper, the network, which was trained by healthy volunteer data, is evaluated for hemorrhagic lesions that have substantially higher susceptibility than healthy tissues in order to test “linearity” of QSMnet for susceptibility. The results show that QSMnet underestimates susceptibility in hemorrhagic lesions, revealing degraded linearity of the network for the untrained susceptibility range. To overcome this limitation, a data augmentation method is proposed to generalize the network for a wider range of susceptibility. The newly trained network, which is referred to as QSMnet∗, is assessed in computer-simulated lesions with an extended susceptibility range (−1.4 ppm to +1.4 ppm) and also in twelve hemorrhagic patients. The simulation results demonstrate improved linearity of QSMnet∗ over QSMnet (root mean square error of QSMnet∗: 0.04 ppm vs. QSMnet: 0.36 ppm). When applied to patient data, QSMnet∗ maps show less noticeable artifacts to those of conventional QSM maps. Moreover, the susceptibility values of QSMnet∗ in hemorrhagic lesions are better matched to those of the conventional QSM method than those of QSMnet when analyzed using linear regression (QSMnet∗: slope = 1.05, intercept = −0.03, R² = 0.93; QSMnet: slope = 0.68, intercept = 0.06, R² = 0.86), consolidating improved linearity in QSMnet∗. This study demonstrates the importance of the trained data range in deep neural network-powered parametric mapping and suggests the data augmentation approach for generalization of network. The new network can be applicable for a wide range of susceptibility quantification.

1. Introduction

Deep learning has been widely applied for MRI reconstruction and has demonstrated promising outcomes (Akcakaya et al., 2019; Bollmann et al., 2018; Cohen et al., 2018; Knoll et al., 2019; Quan et al., 2018; Ronneberger et al., 2015; Yoon et al., 2016). Recently, it has been observed that the performance of a deep neural network is highly dependent on the training dataset. One example is image SNR of a training set. If a network is trained with a specific range of training dataset (e.g., image SNR of around 80), the performance of the network is substantially degraded for an input outside of this range (e.g. a test image SNR of 20) (Hay et al., 2019; Knoll et al., 2019). These types of input data are referred to as “out-of-distribution data” for a given network and are of great importance in network generalization (Amodei et al., 2016; Goodfellow et al., 2015). Data augmentation approaches have been suggested as a potential solution to handle the out-of-distribution data (Li et al., 2019; Tellez et al., 2019).

One particular field of MRI that requires a special consideration for the out-of-distribution data is parametric mapping, which quantitatively measures MR parameters such as T1, T2, diffusion, susceptibility, etc. (Bertleff et al., 2017; Cohen et al., 2018; Lee et al., 2018; Yoon et al., 2018). When a network is trained for quantitative parametric mapping, it is often trained with a restricted range of parameter due to the limited availability of training data. However, input data for inference may fall outside of the training data range, potentially generating unexpected outcomes. Hence, it is necessary to develop an approach to compensate...
Quantitative susceptibility mapping (QSM) was introduced as a quantitative approach for measuring magnetic susceptibility using MRI (de Rochefort et al., 2008; Liu et al., 2009; Shmueli et al., 2009). Because of the sensitivity to susceptibility sources such as hemoglobin, myelin and ferritin, QSM has been applied for several brain disorders including brain hemorrhage, multiple sclerosis, and Parkinson’s disease (Chen et al., 2014; Kim et al., 2018; Liu et al., 2015; Lotfipour et al., 2012; Sung et al., 2019; Wang and Liu, 2015). However, the key process of QSM reconstruction, which is referred to as dipole inversion, is an ill-conditioned problem and is a source for significant artifacts (Salomir et al., 2003). Several methods that utilize regularization have been proposed to improve the quality of QSM maps (Bilgic et al., 2014; de Rochefort et al., 2010; Li et al., 2011, 2015; Liu et al., 2009, 2011; Schweser et al., 2012; Wharton et al., 2010). Despite these improvements, reconstruction errors such as streaking artifacts still pertain in QSM images. As an alternative approach, a method that utilized multiple head orientation data (COSMOS) generated a high-quality susceptibility map at the cost of a long scan time (three times or longer than a single orientation scan) and subject discomfort (Liu et al., 2009).

Recently, deep neural network-based methods have been proposed as a tool for QSM reconstruction (Bollmann et al., 2019; Chen et al., 2019a; Chen et al., 2019b; Liu and Koch, 2019a, b; Liu et al., 2019a; Liu et al., 2019b; Polak et al., 2019; Wei et al., 2019; Yoon et al., 2018; Zhang et al., 2019). When a deep neural network was trained using local field maps and COSMOS QSM maps, the network generated a COSMOS-quality QSM map from a single head orientation data (Yoon et al., 2018). This network, which is referred to as QSMnet, has been applied to patient data and demonstrated successful delineation of lesions despite the fact that the network was trained only by healthy volunteers (Yoon et al., 2018). However, no quantitative analysis was performed for the lesions with relatively large susceptibility values. Since the magnetic susceptibility range of healthy volunteers can be different from that of patients, the issue of out-of-distribution data may exist in the susceptibility mapping based on deep learning. Therefore, exploring the accuracy of the network-generated susceptibility estimations for out-of-distribution data is of importance. Finding this characteristic can be considered as a test of “linearity” in QSM since we are exploring a linear relationship between true susceptibility and network-generated susceptibility.

In this study, we investigate linearity of QSMnet for out-of-distribution data. Furthermore, we suggest a data augmentation method to enhance the linearity of previously developed QSMnet. The proposed augmentation method is validated using computer simulation and in-vivo patient data. The newly trained network, which is referred to as QSMnet*, is available at https://github.com/SNU-LIST/QSMnet.

2. Methods

2.1. Susceptibility distribution in healthy volunteers

As the first step of this work, we explored the magnetic susceptibility distribution of healthy volunteers using the training dataset of QSMnet. The dataset included five healthy volunteer scans. Each scan had five head orientation data, which were used for COSMOS QSM reconstruction. Non-brain regions were excluded using brain masks (BET, FSL, Oxford, UK; Smith, 2002). Then, the susceptibility values of the five brains were counted to generate a histogram of the susceptibility distribution, which was normalized by the total number of voxels.

2.2. Data augmentation for improvement of linearity

To improve linearity in the susceptibility range, a data augmentation method that expands the susceptibility range of the training dataset was developed (Fig. 1). The extended susceptibility range was generated as follows:

\[
\tilde{\chi} = \Lambda \cdot \chi \\
\tilde{\delta} = F D F^{-1} \tilde{\chi}
\]

where \(\tilde{\chi}\) is a susceptibility map (in ppm) generated by the data augmentation, \(\chi\) is an original susceptibility map (in ppm), \(\Lambda\) is a scaling map defined below, \(\cdot\) is a symbol for voxel-wise multiplication, \(\tilde{\delta}\) is a field map generated by the data augmentation, \(F\) is a Fourier transform matrix, and \(D\) is a dipole convolution matrix. The scaling map, \(\Lambda\), is:

\[
\Lambda(x) = \begin{cases} 
\lambda & \text{if } x \in P \\
1 & \text{if } x \notin P 
\end{cases}
\]

where \(x\) is a voxel, \(\lambda\) is a scaling factor, and \(P\) represents a set of voxels where \(\lambda\) is applied. In our method, \(P\) was defined for voxels with positive susceptibility values in the input susceptibility map, scaling only the

![Fig. 1. Summary of data augmentation: (a) data acquired by MRI, (b) scaled data where positive susceptibility values (\(\chi > 0\)) are increased by a scaling factor \(\lambda\) using the augmentation method, (c) sign-inverted data, and (d) scaled and sign-inverted data. (e) The susceptibility distributions of the acquired data (blue line) and total training data (sum of the four datasets; red line). The distribution of the acquired data shows asymmetry, whereas that of the total training data shows symmetry with a wider susceptibility range than that of the acquired data.](https://example.com/fig1.png)
positive susceptibility sources (Fig. 1b; see Discussion for other conditions of P tested). This study defined \( \lambda \) to be greater than or equal to 1 so that the augmentation increased the range of the original susceptibility map. For a symmetric susceptibility distribution (Fig. 1e), additional datasets were generated by inverting the sign of both the original and the scaled susceptibility maps (Fig. 1c and d).

This data augmentation process was applied to the COSMOS reconstructed susceptibility maps of the five healthy volunteers in the QSMnet training dataset. Additionally, four more susceptibility maps of different head orientations were generated in each subject by applying a rotation matrix to the COSMOS reconstructed susceptibility map in order to increase the diversity of head orientation in the training dataset. The rotation angle was randomly chosen between \(-30^\circ\) and \(30^\circ\) relative to \( B_0 \). Then, for each map, the proposed data augmentation process was applied, generating a total of 25 “scaled” susceptibility and corresponding local field map pairs. The same process was repeated for the sign inverted susceptibility maps, generating additional 25 “inverted” data pairs and 25 “scaled and inverted” data pairs.

In summary, we had four different types of training datasets: the original dataset from QSMnet, the scaled dataset, the inverted dataset, and the scaled and inverted dataset. The total training dataset included 100 susceptibility maps and corresponding local field maps. This dataset was used to generate a new neural network, which is referred to as QSMnet\(_{t}^\ast\), that has improved linearity in susceptibility range compared to that of QSMnet.

### 2.3. Deep neural network

For a deep neural network, the QSMnet structure, which is a 3D U-net architecture, was utilized with a modification of ReLU to leaky ReLU (Supplementary Fig. S1; Yoon et al., 2018). The encoder part of the network consisted of 5 blocks. Each block contained two 5 x 5 x 5 convolutional layers. Each layer was followed by batch normalization and leaky ReLU (slope = 0.1) (Maas et al., 2013). Then, a 2 x 2 x 2 max-pooling layer with strides of two was performed except for the last block. The number of channels was 32 in the first layer, and it doubled for each subsequent layer. The decoder consisted of 4 blocks. Each block contained a 2 x 2 x 2 deconvolutional layer, followed by two 5 x 5 x 5 convolutional layers. Batch normalization and leaky ReLU (slope = 0.1) were performed after each convolutional layer with compressing the number of channels by half. In order to forward the feature information from the encoder to the decoder, four feature concatenations were applied between the corresponding encoder block and decoder block. In the last layer, a 1 x 1 x 1 convolution was performed with reducing the number of output channels to 1.

The loss function in QSMnet, which included model loss (loss\(_{\text{model}}\)), L1 loss (loss\(_{\text{L1}}\)), and gradient difference loss (loss\(_{\text{Gradient}}\)) was modified by defining the model loss as follows:

\[
\text{loss}_{\text{model}} = ||M \cdot (\delta - d \ast \chi)||
\]

where \( M \) is a brain mask, \( \ast \) is a symbol for voxel-wise multiplication, \( \delta \) is an input local field, \( d \) is a dipole kernel, and \( \gamma \) is an output susceptibility map. The other two losses were unchanged:

\[
\text{loss}_{\text{L1}} = ||(\gamma - y)||
\]

\[
\text{loss}_{\text{Gradient}} = \sum_{x+y+z} ||\nabla \gamma |-|\nabla y||
\]

where \( y \) is a label. The total loss was defined as the weighted sum of the three losses with empirically determined weighting parameters of 0.5, 1, and 0.1 for the model loss, L1 loss, and gradient different loss, respectively.

The learning rate was exponentially decayed from \(10^{-3}\) at every 600 steps with a decay factor of 0.95. The training process was stopped at 25 epochs. All the other settings and hyper-parameters were the same as QSMnet: Xavier initializer (Glorot et al., 2011), RMSProp for optimization, and a batch size of 12. Tensorflow (Rampasek and Goldenberg, 2016) and an Nvidia GTX 1080Ti GPU (Nvidia Crop., Santa Clara, CA) were utilized for network training and inference.

### 2.4. Network training

The training dataset was normalized for efficient convergence of the gradient descent method (LeCun et al., 1998). For normalization, the mean and standard deviation were calculated in the training dataset of the 100 susceptibility maps. Then, the susceptibility maps were normalized to have a mean of 0 and a standard deviation of 1 (LeCun et al., 1998). The local field maps were also normalized using the same process. When generating an output susceptibility map, the outcome of the neural net was re-scaled using the normalization parameters to restore the susceptibility unit to ppm.

When training the network, the normalized input (local field map) and the normalized output (susceptibility map) were divided into 3D
patches with a size of 64 × 64 × 64 voxels. The patch was generated with a 66% overlap. Overall, a total of 33,600 patches were used for training. The training time was approximately 172 h.

To investigate the effect of λ in QSMnet, four different augmentation datasets were created using λ of 1, 2, 3, and 4. The maximum λ value of 4 was chosen such that the susceptibility distribution of the training dataset sufficiently covered the susceptibility value of the fully deoxygenated blood, which was approximately 1.4 ppm (see Discussion) (Chang et al., 2016; Haacke et al., 1997; Zborowski et al., 2003). The four different QSMnet networks were labeled as QSMnet$_{1}$, QSMnet$_{2}$, QSMnet$_{3}$, and QSMnet$_{4}$.

For comparison, QSMnet was re-trained using the new activation function, loss function, learning rate, and normalization process to avoid complications from the modifications in this study. Hence, differences between the results of QSMnet and QSMnet$_{1}$ were primarily from the difference in the data augmentation.

### 2.5. Datasets for network evaluation

The evaluation of QSMnet and QSMnet$_{1}$ was performed using the datasets of six healthy volunteers and fourteen patients with hemorrhage. The six healthy volunteer test sets were from Yoon et al. (2018). Each volunteer dataset consisted of five local field maps with different head orientations and a corresponding COSMOS QSM map. The dataset was scanned at 3T (Skyra, SIEMENS, Erlangen, Germany) with the following scan parameters: 3D single-echo gradient echo (GRE) data were acquired with voxel size $1.4 \times 1.4 \times 1.4$ mm$^3$, TR = 33 ms, TE = 25 ms, bandwidth = 100 Hz/pixel, and flip angle = 15°.

The fourteen healthy volunteer test sets were acquired to investigate the effects of the out-of-distribution data (i.e., high susceptibility values) in hemorrhagic lesions (3T, 12 patients using Skyra, SIEMENS, Erlangen, Germany; 2 patients using Ingenia, PHILIPS, Best, Netherlands). All scans were approved by the internal review board. The data scanned in SIEMENS were acquired with the same scan parameter as the healthy volunteer data except for FOV of 192 × 192 × 80 mm$^3$. The sequence parameters for PHILIPS were as follows: FOV = 220 × 220 × 144 mm$^3$, voxel size = 0.5 × 0.5 × 2 mm$^3$, TR = 36 ms, TE = 25 ms, bandwidth = 255 Hz/pixel, and flip angle = 17°. The resolution of the PHILIPS data was matched to that of the training data (i.e., 1 × 1 × 1 mm$^3$) by zero-padding in slice direction and truncating in-plane direction in the Fourier domain. For preprocessing, a brain mask was extracted from the magnitude image using BET (FSL, Oxford, UK; Smith, 2002). Within the brain mask, the phase image was unwrapped by Laplacian phase unwrapping (Li et al., 2011). Finally, a local field map was generated by removing a background field using V-SHARP (Wu et al., 2012).

### 2.6. Simulated lesion

To investigate linearity of QSMnet and QSMnet$_{1}$ for a wide susceptibility range, a simulated local field map was generated by combining the local field maps of a healthy volunteer and simulated lesions. The healthy volunteer data were chosen from the test sets. The field map of the simulated lesions was generated as follows: First, hemorrhagic lesions were manually segmented in the magnitude image of one of the patients. A susceptibility value was assigned to the lesions. Then, Gaussian noise with a mean of zero and a standard deviation of half of the assigned susceptibility value was added to the lesions. These simulated lesions were generated 15 times for lesion susceptibility values from −1.4 ppm to 1.4 ppm in the step size of 0.2 ppm. The maximum susceptibility of 1.4 ppm represented the susceptibility of fully deoxygenated blood. From the lesion susceptibility map, a local field map was generated by dipole convolution. After that, this local field map was added to that of the healthy volunteer.

From the final local field map, susceptibility maps were reconstructed using STAR-QSM (Wei et al., 2015), QSMnet QSMnet$_{1}$, QSMnet$_{2}$, QSMnet$_{3}$, and QSMnet$_{4}$. Note that QSMnet$_{4}$ is considered as the default network and is referred to as QSMnet if not noted. Reconstruction results were evaluated by averaging the susceptibility values in the lesions. Root mean square error (RMSE) between the assigned and reconstructed susceptibility values in the lesions was calculated.

### 2.7. Patients

The fourteen hemorrhagic patients were reconstructed using two model-based QSM (MEDI (Liu et al., 2011) and STAR-QSM (Wei et al., 2015)), QSMnet and QSMnet$_{1}$. The data from two patients, which showed diamagnetic susceptibility in the hemorrhagic lesions were excluded in the analysis. The resulting maps were visually inspected for reconstruction quality. For a region of interest (ROI) analysis, the largest hemorrhagic lesion in each patient was manually segmented in the GRE magnitude images. Linear regression was applied between STAR-QSM and QSMnet$_{1}$ (or QSMnet) for the mean susceptibility values of the

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**Fig. 3.** (a) Susceptibility maps from STAR-QSM (left column) and QSMnet (right column) in a hemorrhagic patient. The red circles in the STAR-QSM maps indicate streaking artifacts which are not noticeable in the QSMnet maps. (b) Scatter plot of the susceptibility values in the lesion (yellow circle in the inset) generated by STAR-QSM in x-axis and QSMnet in y-axis. The susceptibility values in the QSMnet map are underestimated when compared to those of the STAR-QSM map.
The mean susceptibility values of the lesions are varied from 0.2 ppm. The results of QSMnet, the simulated lesions with the susceptibility of approximately 1.40 ppm (Chang et al., 2016, also see Supplementary Fig. S2), are compared for the simulated lesions with the susceptibility of −1.4 ppm (left) and +1.4 ppm (right).

### 2.8. Healthy controls

To demonstrate that the proposed augmentation approach sustained the quality of QSM maps of healthy volunteers, the six healthy volunteer test sets were processed using the two networks. The quantitative metrics, peak signal-to-noise-ratio (pSNR), normalized root mean squared error (NRMSE), high-frequency error norm (HFEN), and structure similarity index (SSIM), were calculated with the COSMOS QSM map as a reference (Langkammer et al., 2018). In addition, ROI analysis was performed in caudate (CAU), globus pallidus (GP), putamen (PUT), red nucleus (RN), and substantia nigra (SN). A linear regression line and $R^2$ value were calculated between the mean ROI values of COSMOS QSM and QSMnet (or QSMnet+).

### 3. Results

The histogram of the magnetic susceptibility in the training data of QSMnet is plotted in Fig. 2. The brain susceptibility distribution of the healthy volunteers ranges from −0.41 ppm to 0.61 ppm, whereas 98% of the susceptibility values exist in a much narrower range (from −0.06 ppm to 0.10 ppm). The top 1% of the susceptibility values range from 0.10 ppm to 0.61 ppm, and the bottom 1% ranges from −0.41 ppm to −0.06 ppm, reporting a wider range and higher values of positive susceptibility than negative susceptibility (Fig. 2b). Compared to this distribution, the susceptibility value in the lesion of the QSMnet result shows little streaking artifacts when compared to that of STAR-QSM (red circles in Fig. 3a). However, the susceptibility value in the lesion of the QSMnet map is underestimated (Fig. 3b). This result suggests that QSMnet may fail to scale susceptibility values linearly when they are outside of the training data distribution (i.e., −0.41 to 0.61 ppm).

This issue of linearity and improvement using our data augmentation method are demonstrated in the simulated lesion study shown in Fig. 4. The plot in Fig. 4a shows the mean susceptibility values of the simulated lesions reconstructed by QSMnet (blue), QSMnet$^+_{λ=1}$ (green), QSMnet$^+_{λ=2}$ (yellow), QSMnet$^+_{λ=3}$ (purple), and QSMnet$^+_{λ=4}$ (red). The QSMnet results yield underestimated susceptibility estimation in both positive and negative susceptibility values with larger underestimation in negative susceptibility. This asymmetry might originate from the asymmetric training data distribution (Fig. 2). On the other hand, the results of QSMnet$^+$, which applied the proposed data augmentation, show less asymmetry. The estimated susceptibility values become closer to the assigned values as $λ$ increases from 1 to 4, demonstrating a successful improvement of linearity (RMSE in QSMnet: 0.36 ppm, QSMnet$^+_{λ=1}$: 0.19 ppm, QSMnet$^+_{λ=2}$: 0.12 ppm, QSMnet$^+_{λ=3}$: 0.07 ppm, and QSMnet$^+_{λ=4}$: 0.04 ppm). In Fig. 4b, exemplary susceptibility maps from STAR-QSM, QSMnet, and QSMnet$^+$ are shown for two different susceptibility values assigned to the lesions (left: 1.4 ppm; right: +1.4 ppm). Compared to the results of STAR-QSM and QSMnet, the QSMnet$^+$ maps show less noticeable artifacts, revealing a well-defined lesion boundary. Hence, QSMnet$^+$ improves not only the linearity of susceptibility values but also image quality.

The same trends as in the simulated results are observed when the networks are applied to the hemorrhagic patients. Fig. 5 shows magnitude images and four QSM maps (MEDI, STAR-QSM, QSMnet, and QSMnet$^+$) of four representative hemorrhagic patients. Significant streaking artifacts are observed in the MEDI and STAR-QSM maps, whereas much reduced artifacts are visible in the QSMnet and QSMnet$^+$ maps.

When the quantitative analysis is performed for lesions of the patients, the improved linearity in the QSMnet$^+$ results over those of QSMnet is confirmed (Fig. 6). Each dot in Fig. 6a represents the mean susceptibility value of the lesion in a hemorrhagic patient, reconstructed by STAR-QSM and QSMnet (blue dots) or by STAR-QSM and QSMnet$^+$ (red dots). The linearly fitted line of the red dots (slope = 1.05; intercept = −0.03; $R^2$ = 0.93) is closer to the line of unity than that of the blue dots (slope = 0.68; intercept = 0.06; $R^2$ = 0.86). When we focus on one lesion (black circles in Fig. 6a) and generate a scatter plot of the susceptibility values in the lesion, the plot illustrates that underestimated lesion susceptibility values in QSMnet are successfully corrected in QSMnet$^+$ (Fig. 6b). These results consolidate the improved linearity of QSMnet$^+$ in the areas with large susceptibility.
When the six healthy volunteer data are reconstructed by QSMnet and QSMnet\textsuperscript{+}, all the ROI measurements show a good agreement with those of COSMOS (see Supplementary Fig. S3 and Table S1). These results suggest that the proposed data augmentation method does not degrade the image quality of the healthy volunteers.

4. Discussion and conclusion

In this study, we demonstrate that the linearity of QSMnet is undermined in the high susceptibility region (e.g., hemorrhagic lesion). To solve this issue, this study proposed a new data augmentation method that scales the susceptibility values of the training data of the current QSMnet. The newly trained network, QSMnet\textsuperscript{+}, shows improved linearity when tested with computer-simulated lesions and in-vivo hemorrhagic patient data, validating the utility of the proposed data augmentation method.

Our data augmentation approach was designed to generate symmetric linearity for both positive and negative susceptibility as shown in Fig. 4.
Additionally, when compared to the original QSMnet in Yoon et al. (2018), the data augmentation method. In-vivo data and scaled data is an important consideration of the proposed inference outcomes of the in-vivo data. Therefore, a balance between the errors as shown in Fig. S4. Lastly, we tested the effects of training dataset when the scaling map was applied for both positive and negative susceptibility, varied by the different scaling maps despite the same training data range. The results suggest that the performance of the network can be maximized of the scaling factor. (data not shown), the new model loss conveys better physical meaning of the model. Lastly, the activation function was changed from ReLU to leaky ReLU. When tested using the simulated lesions, the leaky ReLU improved the linearity of QSMnet in the negative susceptibility values (Supplementary Fig. S7). The improvement may be explained by the preserved gradients for negative inputs in the leaky ReLU (Maas et al., 2013).

Recently, a few different approaches of deep neural network-powered QSM reconstruction have been proposed (Bollmann et al., 2019; Chen et al., 2019a; Chen et al., 2019b; Liu and Koch, 2019a, b; Liu et al., 2019a; Liu et al., 2019b; Polak et al., 2019; Wei et al., 2019; Yoon et al., 2018; Zhang et al., 2019). Among them, the method by Liu et al. combined the conventional QSM and deep neural network (Liu et al., 2019b); the method by Polak et al. combined the physical model of dipole and variational networks (Polak et al., 2019); and the work by Zhang et al. developed the loss function based on the physical model of dipole (Zhang et al., 2019). These methods may potentially have improved linearity when compared to QSMnet. However, no systematic test of linearity was performed in their works.

In conclusion, this study suggested a data augmentation method to improve linearity of susceptibility estimation in QSMnet. The improved deep neural network, QSMnet+, covers a wide range of susceptibility values, and, therefore, can be used as a tool for clinical studies.

CRediT authorship contribution statement

Woojin Jung: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization, Project administration. Jae Yeop Kim: Methodology, Data curation. Sooyeon Ji: Writing - review & editing. Jongho Lee: Writing - review & editing. Jae Myung Kim: Investigation, Writing - review & editing. Yoonho Nam: Resources, Writing - review & editing. Eung Yeop Kim: Resources, Writing - review & editing. Sooyeon Ji: Writing - review & editing. Joon Yul Choi: Writing - review & editing. Sooyeon Ji: Writing - review & editing. Joon Yul Choi: Writing - review & editing. Jae Myung Kim: Investigation, Writing - review & editing. Yoonho Nam: Resources, Writing - review & editing. Eung Yeop Kim: Resources, Writing - review & editing. Jongho Lee: Writing - review & editing. Supervision, Project administration, Funding acquisition.

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Appendix A. Supplementary data

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