LOW RESOLUTION SUSCEPTIBILITY MAPPING IN THE ESTIMATION OF IRON CONTENT IN DEEP GREY MATTER OF BRAIN AT 3 TESLA

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ABSTRACT

Objective: The objective of this study is to determine the effect of low resolution in the estimation of iron content in deep grey matter of brain using quantitative susceptibility mapping.

Methodology: Six females with mean age 43.16, S.D= 20, age range (23-66) and 13 males with mean age 28.92 $\pm$ 8.14 were scanned with 3D SWI sequence at 3 Tesla (Trio-Seimens, Erlangen, Germany). The caudate nucleus, red nucleus, globus pallidus, putamen, white matter, thalamus and substantia nigra of brain were drawn manually based on their anatomical locations in Signal Processing in Nuclear Magnetic Resonance (SPIN). Magnitude and phase images of high resolution (HR) (0.5x0.5x2 mm^3) were processed in *SPIN* using collapsing parameter to generate the low resolution (LR) (1x1x2 mm^3) susceptibility mapping. Data was analyzed using paired t-test.

Results: A strong linear correlation (R^2=0.99, $p \leq 0.05$) was found between the susceptibilities of Deep Grey Matter (DGM) at low resolution versus high resolution which showed the consistency of susceptibility at both resolution. When the susceptibilities in ppb of DGM were correlated with iron content (mgFe/100g), a positive correlation was found with R-saqure (R^2=0.67, $p \geq 0.05$ at HR, R^2=0.66, $p \geq 0.05$ at LR). The slope of the above linear correlation was consistent with the equivalent susceptibility trend at low and high resolution QSM.

Conclusion: Linear correlation between susceptibility and iron content at HR and LR has demonstrated that low resolution QSM holds the consistency of susceptibility and does not affect the estimation of iron content in deep grey matter of brain.

Keywords: Susceptibility, Deep grey matter, Resolution

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INTRODUCTION

Susceptibility mapping has a remarkable clinical application in the estimation of the concentration of contrast agents as well as exploring the relationship between iron content and the progression of many neurodegenerative diseases like Parkinson disease and multiple sclerosis[1, 2].

Susceptibility weighted imaging and mapping (SWIM) is executed with magnitude and phase images to identify the local susceptibility changes between tissues due to iron deposition and induces field shifts that can be determined on phase images which are more directly related to iron concentration[3, 4].

Spatial resolution plays a significant role in anatomical contrast in MRI to assess the visualization of brain arteries, MS lesions, differentiation between grey and white matter (WM)[5-7]. As high resolution (HR) images produce high signal changes without partial volume effect than the low resolution images[8]. However, the importance of low resolution (LR) in medical imaging cannot be ignored due to its higher signal to noise ratio and short acquisition time. Kornprobst et al presented that

all the super resolution images are the result of larger voxel sizes in magnetic resonance images[9]. Ying et al has described the methodology using two orthogonal low resolution volumes into a single volume for better tissue segmentation on magnetic resonance images[10]. Greenspan et al merged several LR images in the slice direction to produce the best resolution for better signal to noise ratio and contrast to noise ratio in tissue[11].

Previous resolution based research demonstrated the quality of images in MRI at the expense of signal to noise ratio, the acquisition time and partial volume effect but work on low resolution using QSM was not explored well[12, 13]. The objective of this study is to evaluate the effect of low resolution in the estimation of iron content in deep grey matter of brain using quantitative susceptibility mapping (QSM).

METHODOLOGY

This study was approved by the local ethics committee and informed consent was obtained from each individual**.** Total 19 healthy subjects underwent study in MRI research facility center, WSU, Detroit, MI, USA. Six females with mean age 43.16, SD= 20, range of age (23-66) and 13 males with mean age 28.92, SD=8.14, age range (21-45) were scanned at 3 Tesla (Trio Siemens, Erlangen, Germany).

Data Acquisition

Magnetic resonance images of high resolution (HR) (0.5x0.5x2 mm^3) were acquired 3D SWI sequence, TE=20 ms, TR =30 ms, matrix size 512 x 384, bandwidth pixel=100, flip angle (F.A) =15° at 3T.

Data processing

Signal Processing in NMR (SPIN) homemade software (MRI Institute for Biomedical Research, Detroit, MI, USA) was used to generate the susceptibility mapping using magnitude and phase images. It is based on visual C^{++}. SPIN is a powerful tool in MRI that can measure structural measurements in 3D, susceptibility, micro hemorrhage quantification and calcification. SPIN has the ability to show the number of pixels, mean, standard deviation, maximum intensity and minimum intensity within the ROI and copy these values to an excel sheet for analysis. The key feature of SPIN is to perform anti-aliasing and processing of high pass filtered phase images. The collapsing parameter in SPIN was used to construct the low resolution images from high resolution during the post processing[14].

A high pass filter of size (64x64) was selected to delete the unnecessary background frequencies due to air or sinuses effect[15]. The iron content was estimated in DGM and WM using the B. Hallgren and P. Sourader equation[16].

Region of Interest (ROI)

ROIs were drawn manually by the author and coauthor of this work in SPIN based on their anatomical locations of deep grey matter of brain; caudate nucleus (CN), red nucleus (RN), globus pallidus (GP), putamen (PUT), thalamus (THA), substantia nigra (SN) and white matter (WM). GP, PUT and CN were drawn on same slices and homogeneous region were selected more than three slices. SN and RN were drawn on same two slices. THA and WM were also drawn choosing the most homogeneous region. These all ROIs were observed twice by author and coauthor to evaluate the SD within structures.

Statistical analysis was performed by using software (OrgionPro.8, china). Paired *t*- test was applied to find the variation in susceptibility of deep grey matter of brain. Linear correlation was made between the iron content (Fe mg/100) and susceptibility (χ) in ppb of DGM/WM structures of brain and demonstrated the equivalent results on slope line with the subtle changes in susceptibility. A $P \leq 0.05$ was used to assess the significant results.

RESULTS

In order to investigate the effect of low resolution (LR) versus high resolution (HR), the linear correlation was developed between the susceptibility and iron content of DGM structure (GP, PUT, SN, RN, WM and THA) of brain. Susceptibility mapping of CN, GP and PUT was presented in Figure1A at high resolution (0.5x0.5x2 mm^3) and at LR (1x1x2 mm^3) shown in Figure 1-B. Susceptibility mapping of RN and SN was presented in Fig 2A at high resolution (0.5x0.5x2 mm^3) and at LR (1x1x2 mm^3) shown in Figure 2B. Figure 1 and 2 hold the image quality at both resolutions without partial volume effect. Susceptibility (X) with standard deviation (SD) in DGM/WM of brain assessed at both resolutions was mentioned in Table 1.

A P-value presented that all values of susceptibilities were in normal distribution. There was no significant difference in SD of susceptibility at HR and LR. The linear correlation between the susceptibility of DGM/WM was found positive on linear equation y=0.12+0.94*X at HR versus LR and it was presented on Figure 3. The R-square (R^2=0.99) with slope (0.94*x) was found in DGM /WM of brain in all 19 healthy subjects.

The empirical formulae reported by Hallgren and Sourander, the iron concentration in PUT, CN, GP and WM were calculated for 19 healthy subjects using the following equations:

Globus pallidus

$$y = 21.41\{1 - \exp(-0.09x)\} + 0.37 \text{ ---- (1)}$$

Figure.1: Axial images showing susceptibility mapping of CN, GP, PUT: (A) HR (0.5x0.5x2) (B) LR (1x1x2) with TE=20 ms, TR=30 ms, F.A=150 at 3 T.

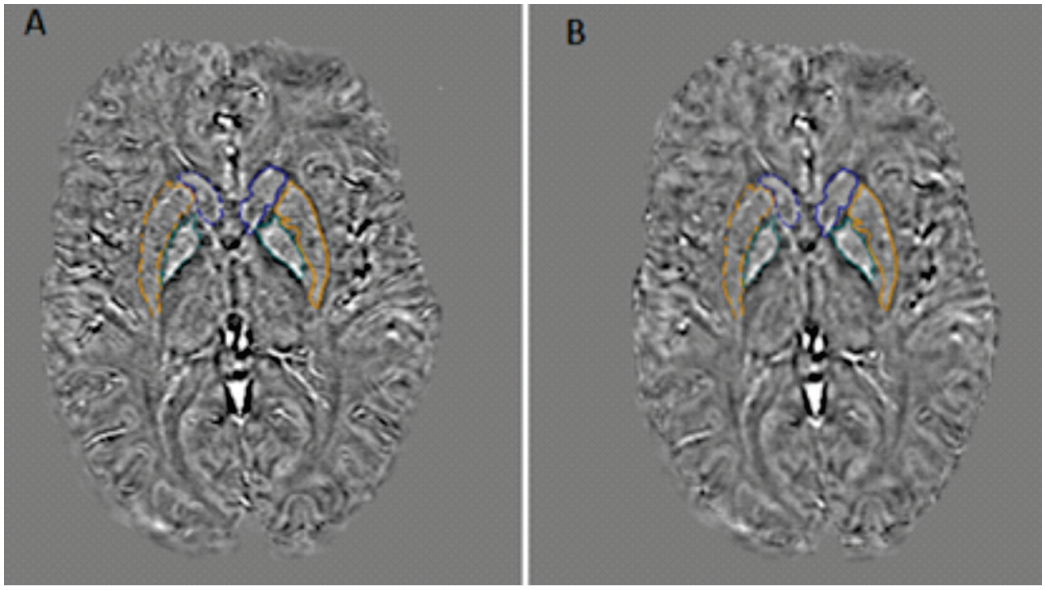
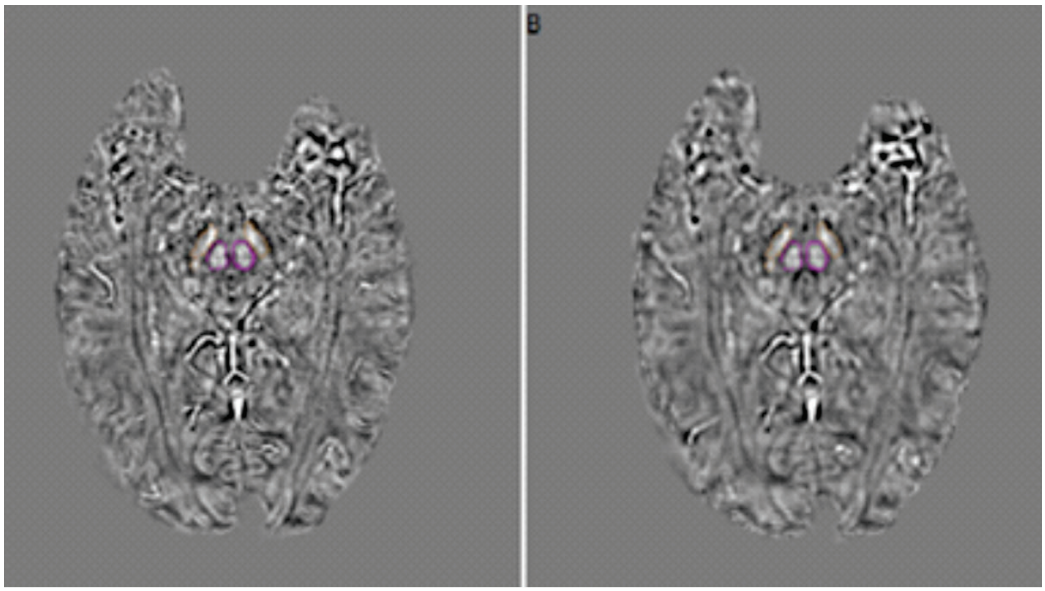


Figure.2: Axial images showing susceptibility mapping of SN and RN (A) HR (0.5x0.5x2) (B) LR (1x1x2) with (TE=20 ms ,TR=30 ms , F.A=150 at 3 T.



White matter

$$y = 3.95 \{1 - \exp(-0.10x)\} + 0.31 \text{ -------- (2)}$$

Caudate nucleus

$$y = 9.66 \{1 - \exp(-0.05x)) + 0.33 \text{ ---- (3)}$$

Putamen

$$y = 14.62\{1 - \exp(-0.04x)\} + 0.46 \text{ ---------- (4)}$$

Where y is the nonheme iron in parts per billion (ppb) and x is the subject's age in years. For RN and SN specific nonheme iron values are referred from Hallgren and Sourander equation[16].

When the susceptibilities of DGM at high resolution and iron content (mg/100g) were correlated, a positive correlation was found with R-square (R^2=0.67) shown

Figure 3: LR susceptibility versus HR suceptibility of DGM shows a positive correlation

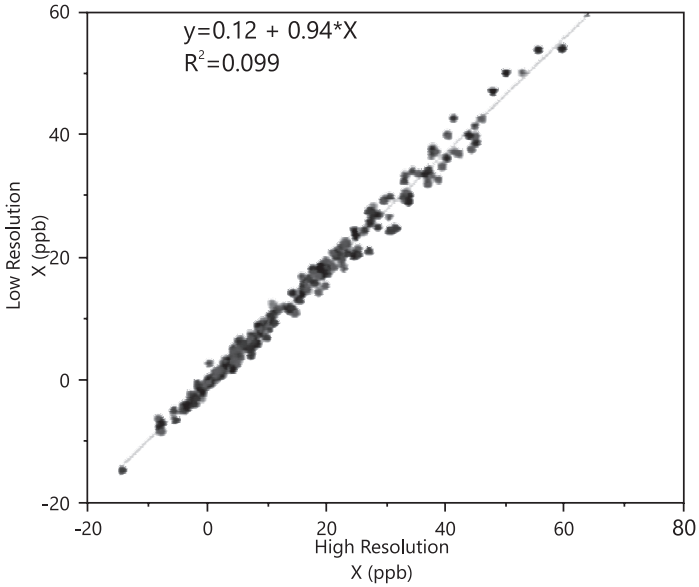
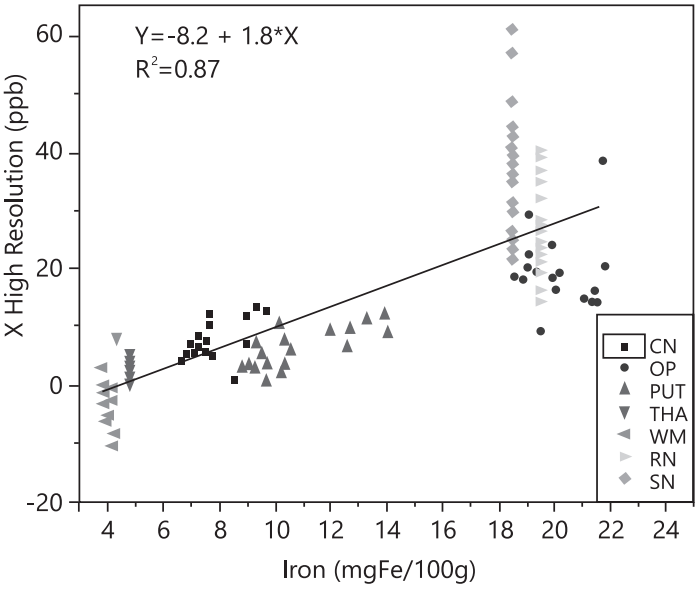


Figure 4: High resolution susceptibilities versus iron content in DGM showing a positive correlation



in Figure 4. Similarly, the linear correlation between the susceptibility of DGM versus iron content (mg/100g) at low resolution presented the positive correlation with R-saqure (R^2=0.66) with equation y=7.5+1.7*X shown in Figure 5. The R–square value (R^2=0.66) of LR was found equivalent to the R-saqure (R^2=0.67) of HR. The difference in susceptibility of CN = 2.15 %, GP= 5.52 %, PUT= 3.08 %, THA= 6.5 %, WM= 6.3 %, RN=6.3 %, SN=4.5 % at high and low resolution using quantitative susceptibility mapping (QSM) showed subtle changes due to iron concentration of DGM/WM.

Table 2 presented the negligible difference in iron content in DGM and white matter of brain in healthy subjects at both resolutions.

Figure 5: low resolution susceptibilities versus iron content in DGM shows a positive correlation

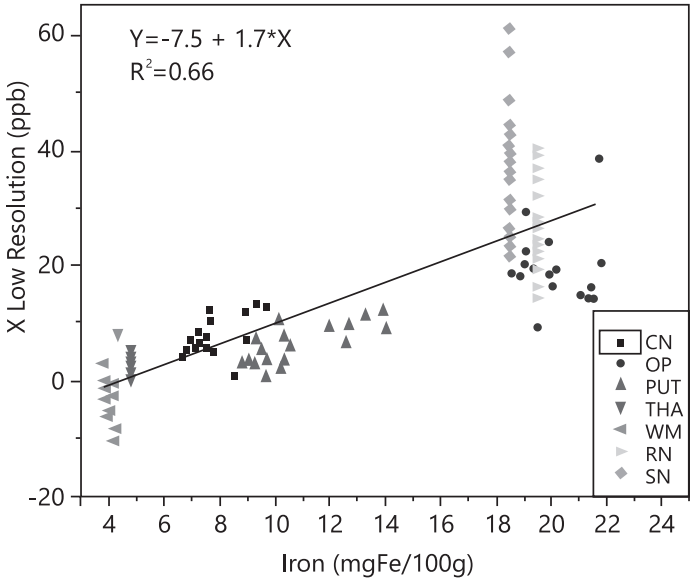


Table 1: Susceptibility(X) in DGM measured at HR and LR

ROI	(χ)ppb	S.D	Sum	Max	p-value
CN	8.36	4.02	158.87	18.33	0.45
CN'	8.54	4.17	162.28	18.10	
GP	19.57	6.23	371.77	38.57	0.40
GP'	18.49	5.59	351.31	35.35	
PUT	6.42	3.33	122.07	12.00	0.38
PUT'	6.17	2.97	117.27	11.88	
THA	2.15	1.76	40.76	5.77	0.25
THA'	2.01	1.78	38.25	5.58	
WM	-2.86	3.16	-54.31	3.20	0.27
WM'	-2.68	3.05	-51.00	3.34	
RN	27.30	7.51	518.73	40.14	0.39
RN'	25.19	7.44	478.64	38.84	
SN	36.68	11.14	696.93	61.04	0.01
SN'	34.93	10.42	663.65	56.65	

Prime ROIs values measured at LR,
S.D: Standard deviation,
ppb: parts per billion

DISCUSSION

This study demonstrated the effect of low resolution susceptibility maps on the susceptibility of underlying brain tissue and its contribution in the estimation of iron content in deep grey matter. As iron is considered a main source of variation in susceptibility in grey and white matter of normal brain tissue, therefore magnetic susceptibilities (χ) have subtle variation due to the iron concentration in normal brain tissue[17-19].

When the magnetic susceptibility of high resolution (0.5x0.5x2 mm^3) was correlated with low resolution (1x1x2 mm^3), a positive correlation was found in deep grey matter and white matter of the brain. The slope line showed that there was no significant change of suscep-

Table 2: Iron content (mgFe/100g) estimated using B. Hallgren and P. Sourader equation at HR and LR

ROI	HR	LR	(D)	%D(HLR)
CN	7.84	7.82	0.028	0.61
GP	20.12	20.10	0.026	4.0
PUT	10.78	10.75	0.05	1.15
THA	4.76	4.76	0	0
WM	4.02	4.04	0.008	0.16
RN	19.48	19.48	0	0
SN	18.46	18.46	0	0

D: difference of iron content,
%; percentage

tibility at both resolutions (0.5x0.5x2 mm^3) and (1x1x2 mm^3). It was assumed that these two low resolutions produced approximately same trends on regression line. Moreover, partial volume effect was not seen in CN, RN, GP, PUT, THA, and SN on susceptibility mapping.

Both resolutions (0.5x0.5x2 and 1x1x2 mm^3) presented the equivalent R-square in results. Haacke et al studied resolution (1x1x2) and reported that slice thickness of 2mm yielded the better images on susceptibility weighted images[20]. This study revealed that resolution (1x1x2) using susceptibility mapping reflected better images and same effect in the estimation of susceptibility and iron content in DGM of brain. Deistung et al studied the voxel aspect ratio equal or larger than 2mm at 3 T which displayed better contrast on susceptibility weighted images[21].

In this study, we demonstrated low resolution (1x1x2 mm^3) compatibility in the estimation of iron content for radiological purposes. We also estimated the iron content in DGM/ WM of healthy subjects using Hallgren and Sourander at HR and LR. The iron concentration of DGM/ WM in healthy subjects found a regression (R^2=0.67) at LR that was in agreement with the regression (R^2= 0.67) for iron concentration of brain studied by Langkammer et al[22]. Similarly regression of both resolutions was in accordance to the regression (R^2=0.83) of Bing Y. et al. study who measured iron content in healthy subjects using susceptibility mapping[23].

The plot of Figure 4 and 5 depicted the iron distribution of DGM structures at HR and LR. The study elaborated that susceptibility difference of DGM showed a negligible percentage difference with respect to low resolution. White matter in brain has less value of susceptibility than the susceptibility of DGM of brain due to structural and functional difference between white matter and grey matter structures. Therefore, white matter showed less amount of iron content in our study as it is documented in reference[22]. Duyn et al also demonstrated that the contrast between the grey and white matter phase images of the brain at high resolution is variable[24]. This study found negligible variability of susceptibility at both resolutions. Susceptibility of DGM/ WM assessed by quantitative susceptibility mapping presented the distribution as SN > RN > GP that was similar to the study of iron content estimation in susceptibility imaging of human brain by Grabner et al[25]. This work revealed the higher susceptibility in SN, RN and GP as Shmueli et al also demonstrated higher susceptibility in SN, RN and GP structures of brain[26].

The study of quantitative susceptibility mapping at low resolution in the estimation of iron content in deep grey matter structures of brain are equivalent to high resolution QSM in its finding. We have made an effort to assess the susceptibility in tissue of brain in healthy subjects at low resolution without anatomical effect on susceptibility mapping. Further research is needed using the lowest resolution so that magnetic susceptibility effect could be optimized in the estimation of iron content in brain for biomedical and radiological purpose at the cost of short acquisition time.

CONCLUSION

Linear correlation between susceptibility and iron content at HR and LR has demonstrated that low resolution QSM holds the consistency of susceptibility and does not affect the estimation of iron content in deep grey matter of brain.

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CONTRIBUTORS

MAJ conceived the idea, planned and wrote the manuscript of the study. MAK, ZL, JHB and AS helped in the results interpretation, data analysis and write up of the manuscript. All the authors contributed significantly to the research that resulted in the submitted manuscript.