Original Article

Agreement of Susceptibility-Weighted Imaging (SWI) for Detecting Metastatic Brain Lesions Compared to Gadolinium-Enhanced THRIVE MRI Technique

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Abstract

Introduction: To evaluate the sensitivity, agreement, and PPV of SWI for detecting metastatic brain lesions compared to Gadolinium-enhanced THRIVE MRI technique.

Methods: A retrospective review of the brain MRI of metastatic brain patients on SWI and Gadolinium-enhanced THRIVE MRI technique from January, 2016 to December, 2018 which interpreted by one radiologist with ten-year experience and one third-year resident-training radiologist. The sensitivity and PPV between the SWI and THRIVE techniques were calculated.

Results: A total of 17 patients with brain metastasis were enrolled. There were 11 patients (64.7%) with lung cancer, four (23.5%) with breast cancer, one (5.9%) with colon cancer, and one (5.9%) with lung and thyroid cancer. Among these 17 patients, the experienced radiologist detected 413 lesions, while the resident detected 401 lesions. According to the experienced radiologist's results, the sensitivity of the SWI for detecting metastatic brain lesions at different sites, compared to THRIVE, ranged from 0.20 - 0.36. The PPV at different sites ranged from 0.92 - 1.00. A high PPV was suggestive of a high chance of enhancement on THRIVE of microbleed area on SWI, which indicated metastatic brain lesions. Good to excellent inter-observer agreement regarding the ICC, and substantial agreement concerning the Kappa value, were noted. Therefore, both sequences for evaluating metastatic brain lesions can be confidently used by experienced radiologists and trainee-radiologist.

Conclusions: SWI has benefit for predicting hemorrhagic brain metastasis due to high PPV, especially when found coexisting with vasogenic brain edema or location at gray-white matter junction at cerebral hemisphere or cerebellar area.

Keywords: Susceptibility-Weighted Imaging (SWI), Metastatic brain lesion, Gadolinium-enhanced MRI brain

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Introduction

Brain metastases are the most frequent neurological complication of cancer and the most common brain tumor type.[1] Incidence about 20 - 40% of patients with cancer and their frequency increase over time.[2] The development of diagnostic procedure for early detection small metastatic lesions by using magnetic resonance imaging (MRI) and improvement of management of brain metastases such as technique of surgical resection and radiotherapy cause effective palliation and increase number of long-term survivors.[3, 4, 5]

In adults, the primary tumors are lung (19.9%), followed by melanoma (6.9%), renal (6.5%), breast (5.1%), and colorectal cancers (1.8%).[6] Brain metastasis may be found one or multiple sites and can occur at cerebral or cerebellar hemisphere by hematogenous dissemination. Metastatic brain lesions are usually located at the grey-white matter junction where the tumor microemboli lodge in the capillaries of the distal parts of superficial arteries.[7]

One of the most severe complications of brain metastasis is intracerebral hemorrhage. Clinical presentations are based on the size and site of the hemorrhage. Hemorrhagic metastatic brain tumors often occur at border of tumors and mechanisms of hemorrhage occur from intratumoral vascularization with dilated thin-walled vessels and tumor necrosis.[8] Primary tumors that can be found hemorrhage such as lung cancer, renal cell carcinoma, choriocarcinoma, thyroid cancer, hepatocellular carcinoma, colorectal cancer, and sarcoma.[9]

In the initial diagnostic workup for metastatic disease, the choice of imaging modality is dependent on the clinicians and situations, which can be contrast-enhanced MRI or contrast-enhanced CT scan of the brain. However contrast-enhanced MRI is the most sensitive tool to characterize and localize metastatic CNS tumors for initial diagnosis, preoperative and post-treatment evaluation, as compared with a non-enhanced MRI or a contrast-enhanced computed tomography.[10]

According to the Radiological Society of North America's (RSNA's) Statement on Gadolinium-Based MR Contrast Agents, most gadolinium-based contrast agents are contraindicated in patients with severe acute, or chronic renal failure or in patients with a glomerular filtration rate (GFR) below 30 mL/min/1.73 m^2, because of the risk of nephrogenic systemic fibrosis (NSF).[11] From this limitation of using Gadolinium-based contrast agent this study try to find benefit of SWI in detecting or predicting brain metastases by comparing with Gadolinium-enhanced MRI that using as gold standard for evaluating brain metastases nowsday.

SWI is a non-contrast magnetic resonance imaging (MRI) technique that uses the gradientecho sequence to detect paramagnetic substances such as deoxygenated blood or hemosiderin. These paramagnetic substances are found in hemorrhagic brain metastasis, intracranial hemorrhage, traumatic brain injury, stroke, multiple sclerosis, etc.[12]

Franceschi et al. studied the utility of Susceptibility Weighted Imaging (SWI) in the detection of hemorrhagic brain metastases from breast cancer and melanoma that found the benefit of SWI in detecting microhemorrhage inside metastatic brain lesions especially in macrometastatic brain lesions due to more frequently found hemorrhage inside tumor more than micrometastatic brain lesion or tumor size < 0.1 cm^3.[13]

At Siriraj Hospital, THRIVE, or the 3D T1-weighted high-resolution isotropic volume MRI sequence, has been used to detect metastatic brain lesions. THRIVE is a T1-weighted image with a Gadolinium-enhanced MRI technique; it employs a gradient-echo sequence and multiplanar reconstruction. These techniques have different names, depending on the companies which produce the technology. For example, Siemens' machine is called the VIBE (the Volumetric Interpolated Breath-hold Examination). THRIVE is made by Philips' and is reconstructed with 0.94 mm. in thickness. Such thin slices increase the chance of detecting small brain lesions.

In this study, we reviewed the correlations of imaging findings in patients with brain metastases who had both SWI and Gadolinium-enhanced THRIVE MRI brain technique. We hypothesized that the rate of detecting metastatic brain lesions using the SWI technique might be approximate to Gadolinium-enhanced MRI brain on the THRIVE technique.

The main objective of this study was to evaluate the sensitivity and positive predictive value (PPV) of susceptibility-weighted imaging (SWI) for detecting metastatic brain lesions,

compared with Gadolinium-enhanced THRIVE MRI brain technique. Two additional objectives were to find evidence of the usefulness of SWI in predicting metastatic brain lesions and evaluating inter-observer agreement between an experienced radiologist and a trainee-radiologist in detecting brain metastases by using SWI and Gadolinium-enhanced THRIVE MRI brain technique.

Methods

Study population

This retrospective study was approved by the Siriraj Institutional Review Board (SIRB) Project no. 801/2561(EC4).

The inclusion criteria:

1. The patients were at least 18 years old.
2. The patients who were suspected of brain metastases and underwent to perform brain MRI on both of the following sequences on a 1.5-Tesla or 3-Tesla machine from January, 2016 to December, 2018.

- Susceptibility-weighted imaging (SWI, Siemens) or T2 star-weighted angiography (SWAN, General Electric) or venous blood oxygen level-dependent (Ven_BOLD, Philips)
- A 3D T1-weighted high-resolution isotropic volume examination an MRI sequence (THRIVE, Philips) or a Liver Acquisition with Volume Acceleration (LAVA, General Electric)

All MRI studies used head coils. All MR images were retrieved for viewing on the PAC systems of the Department of Radiology at Siriraj Hospital, Mahidol University.

3. The patients planned to have further treatment, such as chemotherapy and/or radiation therapy and/or surgery after being diagnosed with brain metastases.

The exclusion criteria:

1. The patients who underwent surgery and/or radiation therapy before brain MRI.
2. The patients with a previous history of stroke.
3. MRI study with a severe motion artifact

The demographic data (sex, age, type of primary tumor, and type of further treatment) of all included patients were also recorded.

Image interpretation

The MRI images were retrospectively reviewed by ten-year experienced neuro-radiologist and one third-year radiologic resident. These two reviewers and two sequences were interpreted separately to prevent bias. Lesions with blooming artifact on the SWI sequence or a companion sequence were recorded as positive lesions. Enhancing lesions on the THRIVE sequence or a companion sequence were also recorded as positive lesions. These lesions were grouped by reviewers into three types: positive on the SWI and positive on the THRIVE technique (Figure 1), positive on the SWI and negative on the THRIVE technique (Figure 2), and negative on the SWI and positive on the THRIVE technique (Figure 3).

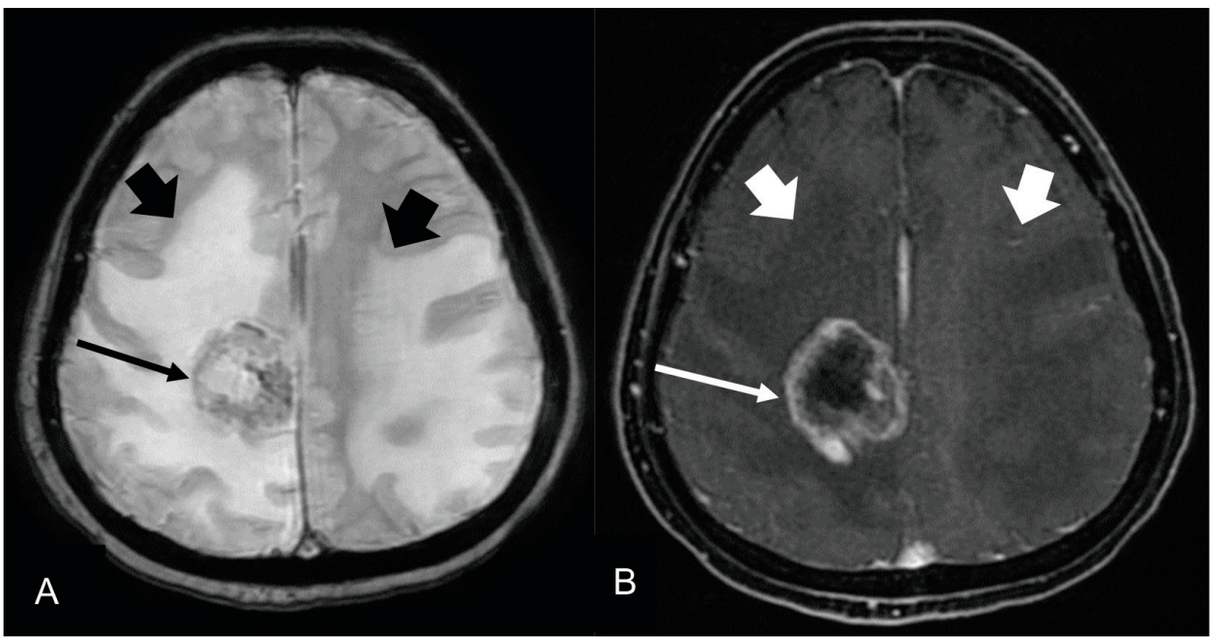

Figure 1 MR image "positive on SWI and positive on THRIVE technique". Axial MRI scan of a 39-year-old female with a history of breast cancer and a newly diagnosed brain metastasis in the right fronto-parietal region. **A.** Susceptibility-weighted imaging (SWI) demonstrates a blooming-signal void area at the right frontoparietal region (the long black arrow). Massive vasogenic brain edema in both cerebral hemispheres on the SWI were also detected. (the short black arrow) **B.** Post-contrast T1-weighted MRI sequence (THRIVE) demonstrates an abnormal, irregular, rim-enhancing lesion at the same area of positive SWI (the long white arrow). Massive vasogenic brain edema in both cerebral hemispheres on the THRIVE technique were also detected. (the short white arrow).

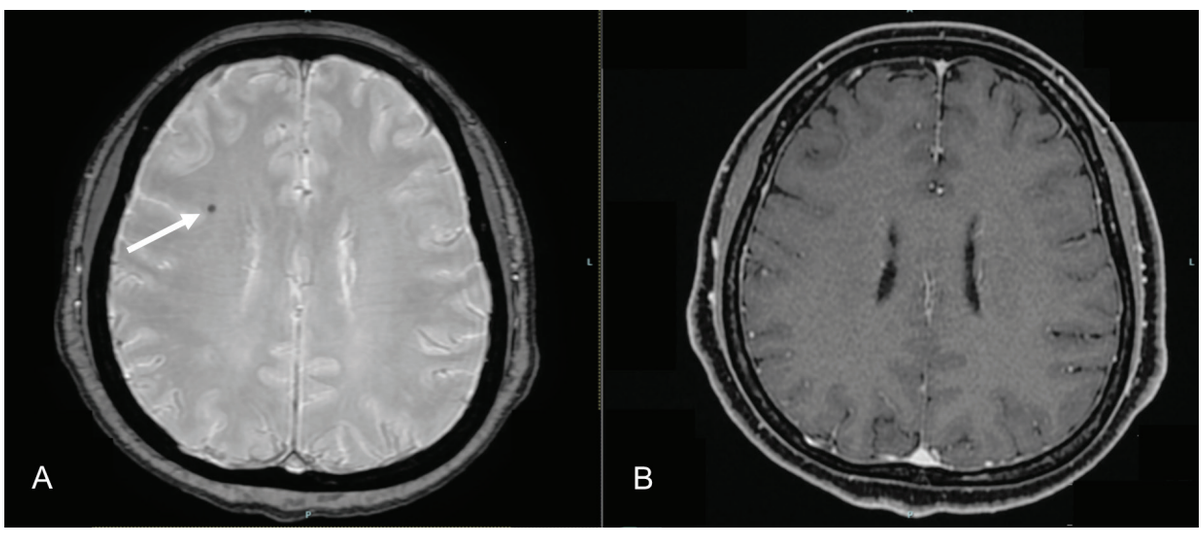

Figure 2 MR image "positive on SWI and negative on THRIVE technique". Axial MRI scan of a 53-year-old female with a history of thyroid and lung cancer, and with a newly diagnosed brain metastasis at the grey-white matter junction of the right frontal lobe. **A.** Susceptibility-weighted imaging (SWI) demonstrates a spot of blooming signal void area at the right frontal lobe. (arrow) **B.** Post-contrast T1-weigthed image demonstrates no abnormal contrast-enhancing lesion at the same area of SWI positive.

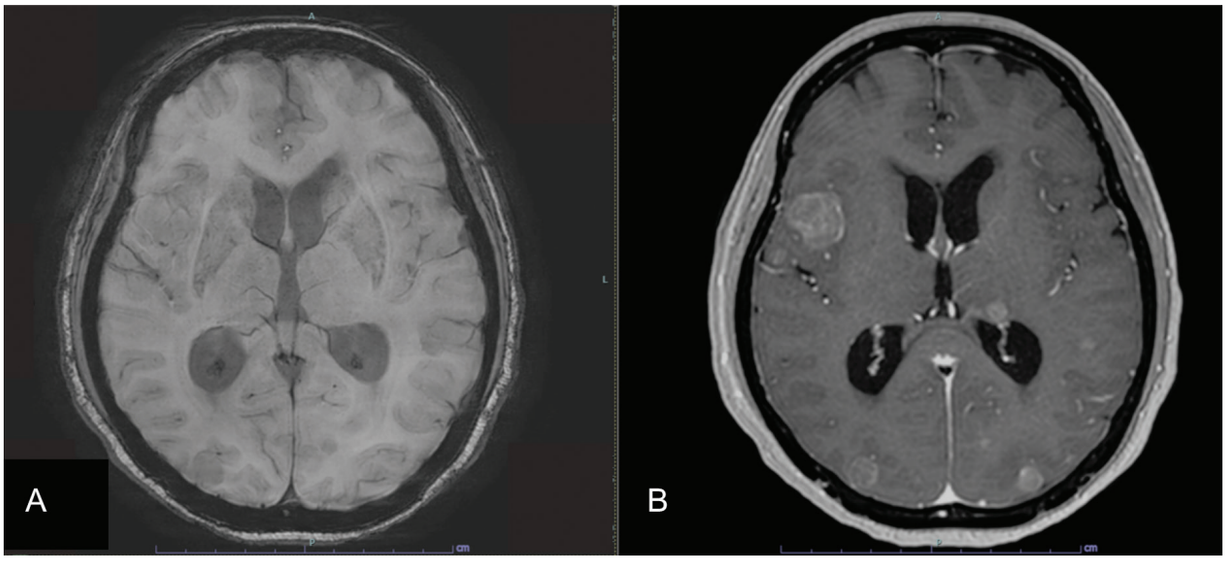

Figure 3 MR image "negative on SWI and positive on THRIVE technique". Axial MRI scan of a 53-year-old female with a history of lung cancer and newly diagnosed multiple brain metastases at both cerebral hemispheres. **A.** Susceptibility-weighted imaging (SWI) demonstrates no definite blooming signal void area at both cerebral hemispheres. **B.** Post-contrast T1-weighted image demonstrates multiple nodular enhancing lesion at the gray-white junction of both cerebral hemispheres and the left thalamus that suggestive multiple brain metastases.

Statistical analysis

Descriptive statistical analyses were used to analyse demographic data such as age, sex, type of primary tumor, and type of further treatment. The data were analyzed by using PASW Statistics 18 (SPSS Inc., Chicago, IL, USA)

An intraclass correlation coefficient (ICC) with a two-way random-effects model was used to evaluate the inter-rater reliability between an experienced radiologist and a trainee-radiologist regarding the number of lesions, with positive on the SWI and THRIVE techniques, and lesions with negative on the SWI and positive on the THRIVE techniques.

Interpretation of ICC was classified as follows: < 0.5 for poor; 0.5 - 0.75 for moderate; 0.75 - 0.9 for good; and > 0.90 for excellent reliability.[14]

Kappa statistical analysis was also used to evaluate inter-observer agreement between an experienced radiologist and a trainee-radiologist regarding the presence of lesions, with positive on the SWI and negative on the THRIVE techniques.

Kappa values were classified as follows: < 0.00 (poor); 0.00 - 0.20 (slight); 0.21 - 0.40 (fair); 0.41 - 0.60 (moderate); 0.61 - 0.80 (substantial); and 0.81 - 1.00 (almost perfect).[15]

The diagnostic value of the parameters were reported as having sensitivity and positive predictive value (PPV).

Results

Out of 330 studies, only 17 studies matched the inclusion criteria. There were 17 patients (23.5% male and 76.5% female), with a mean age of 60.0 years old (The range was 39 - 80 years old). There were 11 patients (64.7%) with primary lung cancer; four (23.5%) with primary breast cancer; one (5.9%) with primary colon cancer; and one (5.9%) with primary lung and thyroid cancer. There were 11 patients (64.7%) who received chemotherapy and radiation therapy; four (23.5%) who received chemotherapy alone; and one (5.9%) who received chemotherapy, radiation therapy and surgery. Only one patient (5.9%) was planned for chemotherapy, but she chose an alternative treatment.

The inter-rater reliability regarding the number of lesions with **positive on the SWI and THRIVE techniques** showed good agreement concerning the occipital lobe and left cerebellum, and excellent agreement concerning the frontal, temporal, and parietal lobes and the right cerebellum (Table 1).

Table 1 Inter-rater reliability of the lesions with positive on the SWI and THRIVE techniques

Lobe	**ICC (Intraclass Correlation Coefficient)**
Frontal	0.987 (0.965 - 0.995)
Temporal	0.971 (0.922 - 0.989)
Parietal	0.920 (0.794 - 0.970)
Occipital	0.837 (0.612 - 0.937)
Left cerebellum	0.813 (0.563 - 0.927)
Right cerebellum	0.965 (0.902 - 0.987)

Inter-observer agreement regarding the presence of lesions with **positive on the SWI and negative on the THRIVE techniques** was substantial with Kappa value at 0.638.

The inter-rater reliability regarding the number of lesions with **negative on the SWI and positive on the THRIVE techniques** showed good agreement concerning the temporal, parietal and occipital lobes with excellent agreement concerning the frontal lobe, left and right cerebellum (Table 2).

Table 2 Inter-rater reliability of the lesions with negative on the SWI and positive on THRIVE techniques

Lobe	**ICC (Intraclass Correlation Coefficient)**
Frontal	0.932 (0.827 - 0.975)
Temporal	0.893 (0.733 - 0.959)
Parietal	0.818 (0.563 - 0.930)
Occipital	0.867 (0.677 - 0.950)
Left cerebellum	0.987 (0.965 - 0.995)
Right cerebellum	0.990 (0.972 - 0.996)

From 17 patients, the experienced radiologist detected 413 lesions and the trainee-radiologist detected 401 lesions.

According to the experienced radiologist's results, we calculated the sensitivity, and PPV of susceptibility-weighted imaging (SWI) for detecting metastatic brain lesions, compared to using the Gadolinium-enhanced MRI brain on the THRIVE technique (Table 3).

Table 3 Sensitivity and PPV of SWI for detecting metastatic brain lesions, compared with the Gadolinium-enhanced MRI brain on the THRIVE technique

Lobe	SWI	THRIVE		Sensitivity	PPV
		Positive	Negative		
Frontal	Positive	38	1	0.34	0.97
	Negative	73	0#		
Temporal	Positive	20	0	0.36	1.00
	Negative	36	0#		
Parietal	Positive	19	1	0.30	0.95
	Negative	44	0#		
Occipital	Positive	12	1	0.20	0.92
	Negative	48	0#		
Left cerebellum	Positive	15	0	0.24	1.00
	Negative	47	0#		
Right cerebellum	Positive	15	0	0.26	1.00
	Negative	43	0#		

Lesions with negative on the SWI and THRIVE techniques, corresponding with normal brain parenchyma (n = 0)

Discussion

Brain metastases are the most common intracranial neoplasms. Imaging plays a crucial role in detecting tumor growth and staging for pretreatment planning.[16] Gadolinium-enhanced MRI is the best imaging tool for detecting brain metastases; it's more effective than using non-enhanced MRI or contrast-enhanced CT scan. Using thin slice of Gadolinium-enhanced MRI such as THRIVE technique may provide more sensitive for detecting brain metastases than the conventional brain MRI thickness of 3 - 5 mm. In this study, we found metastatic brain tumors developing from lung, breast, colon, and thyroid cancers. Most of them are hemorrhagic brain metastases and we hypothesized that SWI may be help to detect or predict brain metastases. If SWI can detect or predict metastatic brain lesion, we can use this benefit in patients that have limitations for Gadolinium-based contrast administration.

This study revealed low sensitivity of SWI for detecting metastatic brain lesions, compared with Gadolinium-enhanced THRIVE MRI brain technique ranging from 0.20 - 0.36. From these results strongly suggests using Gadolinium-enhanced MRI brain as gold standard for detecting metastatic brain lesion if no contraindication for using Gadolinium-based contrast agent due to metastatic brain lesion demonstrate enhancement more than demonstrate microhemorrhage on SWI.[17] However, SWI demonstrated a high positive predictive value (PPV) for detecting metastatic brain lesions, compared to Gadolinium-enhanced THRIVE MRI brain technique; SWI ranged from 0.92 - 1.00, that suggests positive lesions on SWI sequence at the same area of positive enhancing lesion on Gadolinium-enhanced THRIVE MRI brain technique which stand for metastatic brain lesions. This finding supports our hypothesis that SWI has benefit for predicting brain metastases especially in group of hemorrhagic brain metastases due to microhemorrhage as found by Zhang et al.[18]

From our inspection of the imaging datas we found other additional image findings that support positive SWI from metastatic brain such as location of positive SWI at the grey-white matter junction of cerebral hemisphere or cerebellar area or demonstrate perilesional vasogenic brain edema around positive SWI lesions (Figure 1) as found on Sehgal V et.al that suggested a combination of T2* and edema effects within a single image improves lesion detection, even without a contrast agent.[19, 20]

In the group of positive SWI and negative THRIVE as shown on figure 2 may be found in case of small lesions which size less than thickness of THRIVE technique about 0.9 mm., but SWI can demonstrate due to the blooming signal void of microhemorrhage from a susceptibility artifact of paramagnetic substances.[21] However, this finding

should be differentiated from a mimicking lesion such as small-vessel disease or cerebral amyloid angiopathy.[22, 23, 24]

In the group of negative SWI and positive THRIVE, found in case of no hemorrhage area inside tumor that cause negative SWI, but positive Gadolinium-enhanced THRIVE MRI technique (Figure 3) or metastatic disease that located near surface or area of air-bone-tissue interfaces, which cause limitations for interpretation by using SWI sequence due to susceptibility artifact (Figure 4).[25]

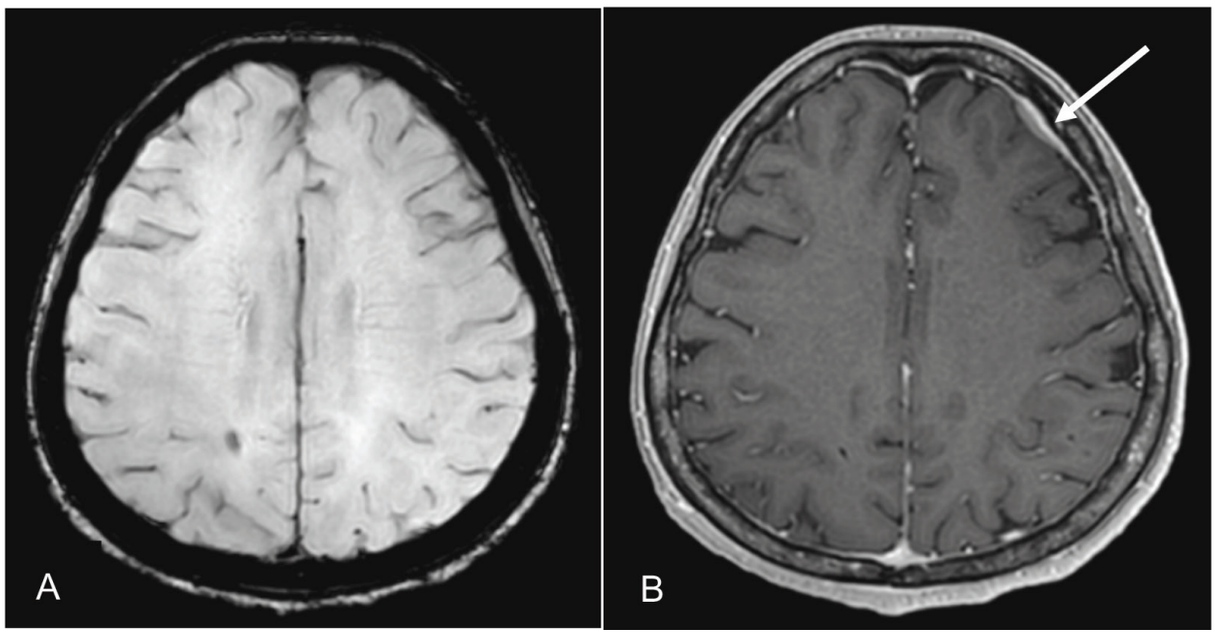

Figure 4 MR image "negative on SWI and positive on THRIVE technique". Axial MRI scan of a 53-year-old female with a history of breast cancer and newly diagnosed multiple brain metastases. **A.** Susceptibility-weighted imaging (SWI) demon-strates no blooming signal void area at brain parenchyma. **B.** Post-contrast T1-weighted MRI sequence (THRIVE) revealed an abnormal focal dural thickening and enhancement at cortical area of the left frontal lobe (the white arrow).

From this study shows good to excellent agreement of the ICC for inter-rater reliability and substantial agreement regarding the Kappa value for inter-observer agreement. These statistics suggest SWI can be confidently used by experienced radiologists and trainee-radiologists for detecting or predicting evidence of brain metastases.

Cerebral microbleed on SWI can be used as evidence for predicting of hemorrhagic brain metastases in case of limitation for using Gadolinium administration or additional use with Gadolinium-enhanced MRI for increasing confidence, especially in situation that exclude small vessels disease or other mimicking conditions and it will be strongly suggest brain metastases if it demonstrate coexisting with vasogenic brain edema or locate at the gray-white matter junction area of cerebral hemisphere or in cerebellar hemisphere.

Limitations

This study has limitation due to retrospective study design with selective bias in case diagnosed brain metastases and small sample size.

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