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FULL PAPER

Improved motion-sensitized driven-equilibrium preparation for 3D turbo spin echo T_1 weighted imaging after gadolinium administration for the detection of brain metastases on 3T MRI

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Objective: To evaluate the clinical usefulness of an improved motion-sensitized driven-equilibrium (iMSDE) preparation for three-dimensional turbo spin echo (TSE) T_1 weighted imaging after gadolinium administration in 3.0-T MRI for the detection of brain metastases compared with conventional gradient echo (C-GRE) T_1 weighted imaging with gadolinium.

Methods: 40 patients with suspected brain metastases underwent MR studies, including two contrast-enhanced sequences, iMSDE-TSE and C-GRE. Post-enhancement images of 14 patients with suspected metastatic brain lesions were retrospectively analyzed, and comparisons between iMSDE-TSE and C-GRE were made using the Wilcoxon signed-rank test.

Results: C-GRE detected 86 metastatic lesions, whereas iMSDE-TSE detected 97, including one false-positive lesion on both sequences. 11 of 96 metastases were detected on iMSDE-TSE only. On C-GRE, 15 of 85

metastases were equivocal. There was a significant difference between C-GRE and iMSDE-TSE in terms of the number of detected lesions ($p = 0.024$). Notably, the interobserver agreement for diagnosing metastases and identifying non-metastases was nearly identical. Overall, iMSDE-TSE achieves higher detectability of metastatic brain lesions, especially equivocal lesions.

Conclusion: Compared with C-GRE, iMSDE-TSE detected more brain metastases. This method is especially helpful in discerning equivocal metastases.

Advances in knowledge: Previous studies have offered limited clinically useful information because they have all been preliminary studies such as comparing the contrast-to-noise ratio of each sequence without evaluating iMSDE-TSE. This study, however, is unique because we evaluate the clinical usefulness of iMSDE-TSE for the detection of brain metastases, and we compare these results to C-GRE.

INTRODUCTION

The presence of brain metastases is a poor prognostic factor, which predicts a shortened life expectancy. Early diagnosis of brain lesions and determination of the number of metastases are important for the treatment plan and to help maintain the quality of life. The number of brain metastases detected by radiologists is important to the clinician, guiding decisions between conservative and surgical treatment options.^{1–3}

Using an improved motion-sensitized driven-equilibrium (iMSDE) preparation is a technique for black blood imaging that suppresses enhanced blood vessel signals and improves the contrast-to-noise ratio (CNR) between the blood vessel lumen and adjacent tissues,⁴ and it compensates the signal loss probably due to the limitation of motion-sensitized

driven-equilibrium (MSDE) such as inherent T_2 decay, the diffusion effect and instrumental factors by adding extra 180° refocusing pulse.⁵ Although broadly used, the black blood technique is based on double inversion–recovery preparation sequence; iMSDE pre-saturation pulse was based on the motion-sensitized gradient echo to dephase all moving blood spins before imaging.⁶ With fast-acquired three-dimensional (3D) turbo spin echo (TSE), iMSDE could achieve appropriate blood signal suppression during the scan time.⁷ Specifically, iMSDE improves the ability to differentiate small-sized tumours. On the other hand, the inherently long acquisition time of iMSDE-TSE leads to artefacts easily, and residual blood vessel signal can produce false-positive result.

Several authors^{4,8} have assessed iMSDE technique for carotid wall imaging, coronary MR angiography in their studies.

Figure 1. Schematic of improved motion-sensitized driven-equilibrium (iMSDE) pre-pulse sequence. iMSDE pre-pulse consists of 90° excitation pulse, two 180° refocusing pulses and 90° excitation pulse with motion-sensitized gradients between the radiofrequency (RF) pulses. It was based on the motion-sensitized gradient echo to dephase all moving blood spins before imaging. G, gradient; S, spoiler gradient; TSE, turbo spin echo.

In addition, there have been several studies evaluating the difference between iMSDE-prepared sequences and conventional sequences, but no study has evaluated the TSE sequence with iMSDE preparations, which would offer more information that could be used clinically.^{9,10} Thus, this study aimed to evaluate the clinical usefulness of an iMSDE 3D TSE T_1 weighted imaging after gadolinium administration on 3.0-T MRI for the detection of brain metastases, and we compared this technique to conventional gradient-echo (C-GRE) T_1 weighted imaging after gadolinium administration.

METHODS AND MATERIALS

Patients

Institutional review board at Hanyang University Guri Hospital approved this study. A total of 40 patients with known primary malignant tumours other than brain tumours underwent MRI to rule out brain metastases, which is routinely used in our hospital for patients suspected to have brain metastases clinically. Post-enhancement MR images of 14 patients with suspected metastatic brain lesions were retrospectively reviewed. 10 patients were diagnosed with non-small-cell lung cancer, 2 patients with malignant melanoma, 1 patient with follicular lymphoma, 1 patient with stomach cancer and 1 patient with urothelial cancer of the urinary bladder. 9 patients were male and 5 were female. The mean patient age was 64.5 years (range: 37–87 years). Among the 14 patients with suspected metastases, 7 underwent follow-up imaging studies.

MRI

MRI was performed with a 3.0-T MR scanner (Philips Healthcare, Best, Netherlands). C-GRE was performed with a 10-ms TR, 5-ms TE and 2-mm slice thickness. iMSDE-TSE was scanned with 407-ms TR, 6-ms TE and 2-mm slice thickness, and iMSDE pre-pulse consists of 90° excitation pulse, two 180° refocusing pulses and 90° excitation pulse with motion-sensitized gradients between the radiofrequency pulses. The duration between the two 90° pulses, which means TE_{prep} , was 15 ms, and the flow velocity encoding was 2 cm s^{-1} for the gradient pulses (Figure 1). We set the duration between the two 90° pulses as short as possible to minimize T_2 contamination, then we chose the low flow velocity-encoding

value to maximize gradient echo for the signal suppression of slow flow.¹⁰ Gadopentetate meglumine 0.1 mmol kg^{-1} was injected as a bolus intravenously in all patients. C-GRE was obtained about 2.5 min after injection. iMSDE-TSE was obtained about 9 min after injection. Other sequences such as routine spin echo, gradient echo and fluid-attenuated inversion-recovery was also scanned by the brain tumour protocol of Hanyang University Guri Hospital.

Imaging analysis

Post-enhancement iMSDE-TSE and C-GRE imaging of 14 patients with suspected metastatic brain lesions on MR were retrospectively analyzed and compared, focusing on each technique's ability to detect metastatic brain lesions. Two radiologists, with 20 and 5 years' experience, performed a randomized, independent and blinded review. The two readers were not informed of the study conditions, except that all of the patients had brain metastases. First, the readers were asked to read C-GRE imaging of 14 patients and to indicate metastatic nodules in each patient. Then, after a month, the readers were asked to read the iMSDE-TSE and indicate metastatic nodules in each

Figure 2. Flow chart of the process for determining metastatic lesions. C-GRE, conventional gradient echo; iMSDE, improved motion-sensitized driven-equilibrium; TSE, turbo spin echo.

patient. After the readers read both C-GRE and iMSDE-TSE and indicated that nodules were metastases, the readers reviewed the other sequences together and excluded other non-metastatic possibilities for the lesions. The gold standard was defined radiologically. The diagnostic imaging criteria for metastatic lesions included definite enhancement of nodular lesion, rim-enhancing necrotic nodule with necrotic core and increased diffusivity, peritumoural oedema and size change in response to treatment on follow-up imaging (7 of 14 patients). Nodular or rim-enhancing lesions, visually compared with surrounding grey and white matter in C-GRE and iMSDE-TSE. When the response to treatment was concordant with other metastatic nodules on follow-up imaging, it was defined as metastasis. Peritumoural oedema or increased diffusivity was additionally evaluated on T_2 weighted imaging. When there was discordance between the two readers, both readers reviewed the cases together and explored the reason for the disagreement and then reached a consensus. Additionally, equivocal metastases that could not be detected on C-GRE scan alone were reviewed because they were not easily distinguishable from other high-signal structures, such as vessels, or they had unclear increases in signal intensity, which brought into question their definition as metastases on the C-GRE scan. With additional information characterizing the lesions in other sequences, we were able to identify and define the lesions as metastases.

Therefore, all metastatic lesions were determined and counted *via* imaging analyses after referring to clinical records and with the consensus of observers, and all patients had primary cancer lesions other than primary brain tumours.

Statistical analysis

The metastatic lesions in each patient were counted and evaluated in each C-GRE and iMSDE-TSE sequence, and the value differences in each sequence were compared for statistical significance using the Wilcoxon signed-rank test. Because two different radiologists performed the imaging analyses and because this study was designed to qualitatively analyze and to

compare the clinical usefulness of iMSDE-TSE and C-GRE, the reproducibility of diagnosis in this study is essential. Therefore, we estimated the interobserver agreement in each sequence. The significance was set at $p < 0.05$, and SPSS® software (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) was used for statistical analyses.

RESULTS

We detected 86 lesions as metastases in C-GRE, and 85 detected lesions were defined as metastases by mentioned imaging criteria (Figure 2). One lesion was found to be false positive. On the C-GRE sequence, 70 of the 85 metastases were definitely identified (Figure 3), and 15 of the 85 metastases were equivocal lesions (Figure 4). The median value of lesions detected as metastases in each patient was 3 and interquartile range was 6 (upper quartile 7, lower quartile 1) (Table 1). In addition, on iMSDE-TSE, we detected 97 lesions as metastases and 96 lesions were defined as metastases; one lesion was found to be false positive. Also, 11 of the 96 metastases were only detected in the iMSDE-TSE sequence and were not detectable in the C-GRE sequence (Figure 5). In addition, we analysed the characteristics of metastases only detected in iMSDE-TSE (Table 2). The median value of lesions detected as metastases in each patient was 4 and the interquartile range was 6.25 (upper quartile 7.25, lower quartile 1).

Overall, there was a significant difference between C-GRE and iMSDE-TSE sequences in terms of the number of detected lesions ($p = 0.024$). Notably, all 85 detected metastatic lesions on C-GRE were also detected on iMSDE-TSE. Two false-positive lesions were found during the imaging analysis. One lesion was found on C-GRE, and the other lesion was found on iMSDE-TSE.

Additionally, we reviewed the equivocal metastases seen on C-GRE (Table 3). As mentioned, the equivocal lesions indicate that we could not diagnose brain metastases based on C-GRE scan alone. On C-GRE, 15 total equivocal metastases were

Figure 3. Metastatic nodule determined on both conventional gradient-echo T_1 weighted imaging (a) with improved motion-sensitized driven-equilibrium preparation on three-dimensional turbo spin echo T_1 weighted imaging (b) after gadolinium administration. A 78-year-old male patient with small-cell-lung cancer underwent MRI to rule out brain metastases. MRI showed multiple brain metastases, and two metastatic nodules were seen (arrows) in the left mid frontal cortex in the corticomedullary junction area.

Figure 4. Equivocal lesion on conventional gradient-echo (C-GRE) T_1 weighted image after gadolinium administration and clearly detectable nodule with the improved motion-sensitized driven-equilibrium (iMSDE) preparation on three-dimensional turbo spin echo (TSE) T_1 weighted image after gadolinium administration that was later diagnosed as a metastasis. A 43-year-old female patient with non-small-cell lung cancer underwent initial MRI to rule out brain metastases. She had an equivocal left frontal lesion (arrow) on C-GRE (a), but iMSDE-TSE revealed a clearly detectable metastatic nodule (arrow) (b). The left frontal lesion mimics a vessel structure on the contralateral side. This patient had follow-up MRI 1 month later, and the left frontal lesion was found to be a discrete and more brightly enhancing nodule (arrow) on iMSDE-TSE (d). This nodule (arrow) was also definitely revealed to be a metastasis on C-GRE (c). Additionally, she had other metastatic nodules in the cerebellum (a) and left occipital lobe (d). Of note, you can see different structures at the posterior portion in each sequence due to differences in axial angle for each sequence, but the paramedian frontal cortex and vessels adjacent to the lesion of interest are the same.

detected in 14 patients. Of these equivocal lesions, 11 of the 15 lesions underwent follow-up studies, and on follow-up, all 11 lesions were defined to be metastases. All 4 of the 15 lesions that did not undergo follow-up study were defined as metastases in other sequences. Notably, all 15 lesions were clearly defined as metastases on iMSDE-TSE (Figure 4).

Of note, the interobserver agreement for the diagnosis of metastases and non-metastases was nearly identical between the two readers. There was just one lesion that was differently identified by the two readers (Figure 4a). Because of this high level of agreement, there was no need to analyze interobserver agreement statistically.

DISCUSSION

In one previous study exploring iMSDE-prepared sequences, it was revealed that using an iMSDE preparation before

low-refocusing flip-angle TSE suppressed enhanced blood vessel signal, reduced the number of visualized blood vessels in a single slice and improved the CNR between white matter and brain tumours.⁹ Another study demonstrated that iMSDE-prepared 3D TSE sequences after gadolinium administration results in better T_1 -contrast than 3D TSE sequences alone.¹⁰ However, as mentioned above, the literature has not yet offered information that will be clinically applicable.

According to our results, iMSDE-TSE achieved higher detectability of metastatic brain lesions than C-GRE but not superior for false-positive results, although there was just one false-positive case in each sequence. 11 metastases were detected only on iMSDE-TSE and most of them were nodular-enhancing cortical or subcortical lesions <3 mm in diameter. More than half of the lesions were adjacent to the cortical vessels, and this is

Table 1. Detecting brain metastases on 3-T MRI using conventional gradient echo (C-GRE) vs improved motion-sensitized driven-equilibrium (iMSDE) turbo spin echo (TSE)

Descriptive statistics	C-GRE ^a	iMSDE-TSE ^b
Number of metastases ^c	85	96
Number of equivocal metastases	15	0
Number of patients	14	14
Median	3	4
IQR	6	6.25
False-positive lesions	1	1

IQR, interquartile range.

^aC-GRE T_1 weighted image after gadolinium administration.

^biMSDE in 3D TSE T_1 weighted images after gadolinium administration.

^cNumber of metastasis, including equivocal metastases.

because of the characteristics of the iMSDE preparation investigated in the previous studies. Additionally, our results revealed that iMSDE-TSE sequences offer the ability to make

more clear-cut clinical decisions about brain metastases. All the metastases detected on C-GRE were also detected on iMSDE-TSE. In addition, all the 15 equivocal metastases were adjacent to the enhancing vessels or venous sinuses and clearly defined as metastases on iMSDE-TSE. With these results, iMSDE-TSE would be useful to detect early brain metastases for staging of other primary cancer without suspicious symptoms of brain tumour.

According to the study by Kato et al¹¹ in 2009, lesion detectability was significantly higher on TSE than on C-GRE, so this difference between TSE and C-GRE might contribute to the higher detectability on iMSDE-TSE than on C-GRE. But in another study by Yoneyama et al⁹ in 2012, they revealed significantly higher CNR on MSDE-TSE than on TSE or C-GRE and showed similar CNR on TSE and C-GRE although it was not statistically analyzed.

Both C-GRE and iMSDE-TSE resulted in two false-positive findings, but by using both imaging tools, these false positives

Figure 5. No visible metastatic lesions on conventional gradient-echo (C-GRE) T_1 weighted imaging after gadolinium administration are noted. However, a metastasis is seen with the improved motion-sensitized driven-equilibrium (iMSDE) preparation on three-dimensional turbo spin echo (TSE) T_1 weighted imaging after gadolinium administration and was ultimately confirmed to be a metastasis. An 87-year-old male patient with squamous-cell lung cancer had no visible enhancing lesions (arrow) except for one vessel at the right insula on C-GRE (a). However, a well-defined enhancing metastatic nodule (arrow) with suppressed vessel signal was noted with iMSDE-TSE (b). The lesion was demonstrated as a brightly enhancing lesion (arrow) on T_2 -fluid-attenuated inversion-recovery with enhancement sequence (c), and slightly increased signal intensity (arrow) was seen with the T_2 TSE sequence (d).

Table 2. Characteristics of metastases only detected in improved motion-sensitized driven-equilibrium (iMSDE) turbo spin echo (TSE)^a (total 11 lesions)

Characteristics		Number of metastases
Size (mm)	<3	11
	4	0
Location	Cortex	8
	Subcortex	2
	Convexity dura	1
Enhancement	Nodular	11
	Rim	0
Adjacent enhancing structure	Cortical vessel	6
	Venous sinus	0
	–	5
C-GRE ^b	Subtle enhancement	4
	No enhancement	7

C-GRE, conventional gradient echo.

^aiMSDE preparation in three-dimensional TSE T_1 weighted images after gadolinium administration.

^bC-GRE T_1 weighted image after gadolinium administration.

may be properly classified. False-positive lesions were found during the imaging analyses. One lesion was an enhancing small vessel signal, mimicking a tiny nodule on C-GRE, and the other lesion was a focally enhancing superior sagittal sinus signal that was not suppressed enough to be differentiated from

a meningeal metastasis on iMSDE-TSE. Each false-positive lesion mimicked metastases in one sequence but could be ruled out in the other sequence. The enhancing small vessel signals in the C-GRE sequences were sufficiently suppressed, and there was no evidence of brain metastases in the other sequences. The focally enhancing superior sagittal sinus signals in the iMSDE-TSE sequence were not found in the C-GRE sequence, and there was also no evidence of brain metastases in the other sequences such as routine spin echo, gradient echo and fluid-attenuated inversion–recovery.

In addition, our false-positive lesion results were different than the results from previous studies, in which black blood images were created using a MSDE preparation for the TSE, which increased the false-positive rate compared with C-GRE imaging.¹² This difference may be due to improved tissue–blood CNR and tissue SNR without the loss of flow suppression capabilities of the iMSDE-prepared sequence when compared with the traditional MSDE-prepared sequence.⁵ Also, because it is known that the black blood effect can increase false-positive rate, our results may have been influenced by our efforts to avoid false-positive results.

In this current study, a 53-year-old female with visual changes showed a clival and a sphenoid meningioma on MRI. However, with conventional MR sequences using a 3.0-T MR scanner, we could not determine whether the tumour was invading the cavernous sinus because it was impossible to distinguish the signals of the enhancing mass from the enhancing cavernous sinus. On additional iMSDE-TSE sequences, which suppressed the enhanced blood vessel signal as previously mentioned, we were able to discern that the tumour was near but did not invade the cavernous sinus. As seen in this case, iMSDE-TSE scans not only help distinguish brain metastases from tumour-mimicking vessel signals but also show more accurate views of the extension of the tumour, particularly into vessels. Thus, iMSDE-TSE may be helpful in surgical planning.

There were some limitations in this study. First, because of the short study period, the diagnosis of several brain metastases was confirmed only with single MRI without any follow-up imaging studies. Nevertheless, the interobserver reliability was nearly perfect, and 11 of the 15 equivocal metastatic lesions on C-GRE were all confirmed as metastases with follow-up imaging. Thus, the radiological diagnoses of metastatic brain nodules in each sequence were quite reliable. Second, each metastatic nodule was assessed by our imaging-based criteria, but the nodules were not confirmed histologically. Third was the risk of bias in classifying and counting metastases. In our study, two readers reviewed C-GRE sequences first, followed by the iMSDE-TSE sequences. We could decrease risk of bias by one reader reviewing GRE and the other reviewing iMSDE-TSE. But, we thought evaluating interobserver agreement is very important for the clinical significance for clinical usefulness, so every reader reviewed GRE and iMSDE-TSE separately. For decreasing the risk of bias, we reviewed all the GRE sequences of 14 patients then iMSDE-TSE sequences.

Table 3. Characteristics of equivocal metastases on conventional gradient echo (C-GRE)^a (total 15 lesions)

Characteristics		Number of metastases
Size (mm)	<3	14
	4 ^b	1
Location	Cortex	13
	Convexity dura	1
	Corpus callosum ^c	1
Enhancement	Nodular	14
	Rim ^b	1
Adjacent enhancing structure	Cortical vessel	13
	Venous sinus	1
	Pericallosal artery ^c	1

^aC-GRE T_1 weighted image after gadolinium administration.

^b4-mm metastasis with rim enhancement.

^cMetastasis at corpus callosum nearby pericallosal artery.

Fourth, the false-positive rate on iMSDE-TSE sequences, especially for the lesions equivocal on conventional imaging, was not evaluated statistically because of the small patient population. One previous study suggested that, owing to the occasional difficulty in differentiation between residual blood vessels and small brain metastases, the higher potential risk for false positivity should not be ignored.¹² Although iMSDE-prepared sequences are more effective than conventional MSDE preparations, more accurate evaluations regarding the clinical usefulness of the iMSDE-TSE sequences and the false-positive rate should be performed.

CONCLUSION

In conclusion, the iMSDE preparation in 3D TSE T_1 weighted images after gadolinium administration detected more metastases than C-GRE T_1 weighted images after gadolinium administration. iMSDE-TSE is especially helpful in equivocal findings of metastases but still has inherent limitation of black blood image. The iMSDE preparation in 3D TSE T_1 weighted images after gadolinium administration could be used in combination with conventional sequences for tumour analysis to improve the diagnosis of brain metastases.

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