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Detection of small brain metastases at 3 T: comparing the diagnostic performances of contrast-enhanced T1-weighted SPACE, MPRAGE, and 2D FLASH imaging☆

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ABSTRACT

The aim of this study was to compare the diagnostic performance of contrast-enhanced T1-weighted sampling perfection with application-optimized contrasts using different flip angle evolutions (SPACE), magnetization-prepared rapid gradient-echo (MPRAGE), and two-dimensional (2D) fast low angle shot (FLASH) for the detection of small brain metastases. Twelve patients who had brain metastases less than 10 mm in diameter were enrolled. The diagnostic performance was evaluated using alternative free-response receiver operating characteristic analysis. Sensitivity and positive predictive value were also calculated. The mean A_z and sensitivities of SPACE for all observers were significantly higher than those of MPRAGE and 2D FLASH.

1. Introduction

Brain metastases are frequently encountered intracranial tumors in adults and occur in approximately 20% to 30% of patients with primary malignant tumors [1–3]. Accurate early diagnosis of brain metastases is essential for providing optimal therapy, and contrast-enhanced magnetic resonance imaging (MRI) is currently the best imaging modality for detecting brain metastases [4–9].

The two-dimensional (2D) spin-echo (SE) sequence has been considered the standard clinical protocol for T1-weighted imaging in routine intracranial examinations at 1.5-T MR. As the 3-T MRI system is increasingly being used for clinical practice, the application of 2D SE technique at 3 T has been limited because of the specific absorption rate (SAR) and flow-related artifacts. Consequently, 2D gradient-echo (GE) sequence is now available for T1-weighted imaging at 3 T due to its multiple advantages, including lower SAR, shorter acquisition time, higher gray–white contrast, and fewer flow-related artifacts [10–13].

The contrast-enhanced three-dimensional (3D) T1-weighted GE sequence [magnetization-prepared rapid acquisition of GE (MPRAGE)] is commonly used for detecting brain metastases at 3 T because it allows for higher detectability of small metastatic lesions than the 2D SE sequence [14,15]. However, when detecting small brain metastases located near the cortex of the brain on contrast-enhanced MPRAGE, it has been pointed out that normal enhancing blood vessels on the surface of brain or in the sulci can either obscure small metastatic lesions or be mistaken as the metastatic lesions [3,9,16].

Recently, a 3D fast spin-echo (FSE)-based sequence [sampling perfection with application-optimized contrasts using different flip angle evolutions (SPACE)] was introduced to contrast-enhanced T1-weighted imaging for the evaluation of brain metastases [1]. Several investigators have evaluated the clinical utility of contrast-enhanced T1-weighted SPACE for the detection of brain metastases [1,6,8].

The purpose of our study was to compare the diagnostic performance of three contrast-enhanced T1-weighted sequences for detecting small brain metastases at 3 T: 3D FSE (SPACE), 3D GE (MPRAGE), and 2D GE [fast low angle shot (FLASH)] imaging.

2. Materials and methods

2.1. Patient population

Our institutional review board approved this retrospective study and waived the requirement of written informed consent for all the study patients. Forty-one consecutive patients with known primary malignancy, who underwent cranial MRI examination for the evaluation of brain metastases, were enrolled in this study. Among these 41 patients,

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15 with intraparenchymal enhancing lesions, which were determined by one board-certified neuroradiologist (S.H.) who did not participate in the observer test, and with at least 1 follow-up MRI were selected. On follow-up imaging, the enhancing lesions that increased in size, decreased in size, or disappeared after treatment were decided to be brain metastases. The enhancing lesions having ambiguous change in size were determined as probable metastases. All precontrast MR images, including T1-weighted, T2-weighted, and diffusion-weighted images, were also reviewed to assist in identifying brain metastases by the nonobserver neuroradiologist (S.H.) on initial and follow-up MRI scans. We excluded three patients from this study because they had solitary brain metastases larger than 10 mm in diameter ($n=2$) or leptomeningeal metastasis ($n=1$). Consequently, 12 patients (9 men and 3 women; mean age, 62.4 years; age range, 50–77 years) who had small brain metastases less than 10 mm in diameter were examined retrospectively. The primary tumors of brain metastases were lung cancer ($n=11$) and breast cancer ($n=1$).

2.2. MR examination

All studies were performed using a 3-T whole body MR scanner (Magnetom Verio; Siemens, Erlangen, Germany) and a 12-channel head coil. After obtaining a routine precontrast imaging protocol with 2D T1-weighted (FLASH, axial and sagittal), T2-weighted (fast SE, axial), and diffusion-weighted (axial) images, contrast-enhanced T1-weighted SPACE (sagittal), MPRAGE (sagittal), and 2D FLASH (axial and coronal) images were obtained immediately after intravenous administration of the standard dose (0.1 ml/kg body weight) of Gadobutrol (Gadovist; Bayer Schering Pharma, Berlin, Germany). The scan parameters of postcontrast MRI were as follows: for SPACE imaging—repetition time (TR), 750 ms; echo time (TE), 10 ms; field of view (FOV), 256×256 mm; bandwidth, 781 Hz/pixel; matrix, 256×256×128; number of slices, 144; intelligent parallel acquisition technique (iPAT), 2; echo spacing, 3.3 ms; turbo factor, 52; slice thickness, 1.2 mm; scan time, 3 min 58 s; for MPRAGE imaging—TR, 1900 ms; TE, 2.5 ms; inversion time, 900 ms; FOV, 256×256 mm; bandwidth, 170 Hz/pixel; matrix, 256×256×144; number of slices, 144; iPAT, 2; echo spacing, 7.3 ms; slice thickness, 1.2 mm; flip angle, 9°; scan time, 4 min 26 s; and for 2D FLASH imaging—TR, 222 ms; TE, 2.9 ms; FOV, 199×220 mm; bandwidth, 340 Hz/pixel; matrix, 448×284; number of slices, 25 for axial and 29 for coronal planes; flip angle, 70°; slice thickness, 5 mm; scan time, 2 min 8 s for axial and 2 min 15 s for coronal planes. To reduce scan time, we obtained sagittal planes covering the whole brain for the SPACE and MPRAGE imaging modalities. To avoid timing bias, the postcontrast T1-weighted imaging sequence order was randomized for the patients. To analyze each image, we generated axial- and coronal-reformatted images with 1.2-mm slice thickness and no gap for the SPACE and MPRAGE imaging modalities.

2.3. Image analysis

Two board-certified neuroradiologists (19 and 7 years of experience in neuroradiology) were blinded to the patient information independently and separately reviewed the postcontrast images on a picture archiving and communication system. Both the axial and coronal postcontrast images of the whole brain were available for assessment. Each observer analyzed SPACE, MPRAGE, and 2D FLASH images in random order at three reading sessions. These three separate reading sessions were performed with at least a 4-week interval to minimize any learning bias. Each observer recorded the presence and location of the lesions, assigning each lesion a confidence level on a four-point scale: 1=probably not present, 2=possibly present, 3=probably present, and 4=definitely present.

2.4. Statistical analysis

To assess the diagnostic performance of all sequences with respect to the detection of brain metastases, an alternative free-response receiver operating characteristic (AFROC) curve analysis was performed on a lesion-by-lesion basis; this was based on the reviews submitted by the two observers. The diagnostic performance of each sequence and for each observer was assessed by calculating the area under the AFROC curve (A index, A_z). The differences among the three sequences, with respect to the area under the ROC curves, were statistically analyzed using a two-tailed Student's t test for paired data. The sensitivities and positive predictive values for each observer and for each sequence were also calculated. Lesions were classified as true-positive lesions based on the number of lesions assigned a confidence level of 3 or 4 from among all of the lesions. The sensitivity and positive predictive value of each sequence were then compared using the McNemar test. For all analyses, $P<.05$ was considered to indicate a statistically significant difference.

To assess the interobserver agreement for the evaluation of all sequences, we calculated a weighted kappa (κ) statistic for the blinded observers. The degrees of agreement were categorized as follows: $\kappa \leq 0.20$ indicated positive but poor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, good agreement; and ≥0.81, excellent agreement. All data were analyzed using the statistical software packages SPSS version 12.0 for Windows (SPSS, Chicago, IL, USA) and MedCalc version 12.3.0 for Windows (MedCalc Software, Ostend, Belgium).

3. Results

A total of 72 lesions (size, 2–9.5 mm; mean, 5.68 mm) were determined in the 12 patients. For the 12 patients, the actual imaging orders of the three sequences after gadolinium injection were as follows: 2D FLASH–SPACE–MPRAGE ($n=6$), 2D FLASH–MPRAGE–SPACE ($n=3$), SPACE–2D FLASH–MPRAGE ($n=1$), SPACE–MPRAGE–2D FLASH ($n=1$), and MPRAGE–SPACE–2D FLASH ($n=1$). For all 72 lesions, the calculated A_z values for the SPACE, MPRAGE, and 2D FLASH images, as determined by each observer, are shown in Table 1. For the detection of small brain metastases, the area under the AFROC curve (A_z) for all observers was highest for SPACE, followed by MPRAGE and 2D FLASH. The mean value of SPACE (mean $A_z=0.931$) was significantly higher than those of MPRAGE (mean $A_z=0.864$) and 2D FLASH (mean $A_z=0.783$) ($P<.05$) (Fig. 1).

The sensitivities and positive predictive values for each observer and sequence are shown in Table 2. The sensitivities of SPACE for all observers were significantly higher than those of MPRAGE and 2D FLASH ($P<.05$). The lesions that were simultaneously missed by all observers included 7 of 72 lesions on SPACE, 15 of the 72 lesions on MPRAGE, and 26 of the 72 lesions on 2D FLASH. No significant difference in positive predictive values was observed among the three sequences.

In terms of the positive predictive values, all sequences showed a similar value for each observer (mean value, 97.0% for SPACE; mean value, 97.3% for MPRAGE; mean value, 97.6% for 2D FLASH). For all observers, four false-positive lesions were identified with the use of SPACE, three false-positive lesions were identified with the use of MPRAGE, and two false-positive lesions were identified with the use of 2D FLASH. The presence of vascular structures caused the false-positive findings on SPACE (four lesions, 100%). On MPRAGE, the causes for the false-positive findings were vascular structures (two lesions, 67%) and artifacts (one lesion, 33%). On 2D FLASH, the causes for the

Table 1
Individual and mean A_z values with the use of SPACE, MPRAGE, and 2D FLASH for the detection of small brain metastases

Sequence	A_z values		
	Observer 1	Observer 2	Mean
SPACE	0.937 ± 0.025[a]	0.928 ± 0.027[a,b]	0.931 ± 0.019[a,b]
MPRAGE	0.886 ± 0.038	0.841 ± 0.042[a]	0.864 ± 0.028[a]
2D FLASH	0.824 ± 0.033	0.745 ± 0.050	0.783 ± 0.031

A_z values are mean ± 1 SD.
[a] The A_z value was significantly different from 2D FLASH ($P<.05$).
[b] The A_z value was significantly different from MPRAGE ($P<.05$).