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Contrast-enhanced Magnetic Resonance Imaging of Brain Metastases at 7.0T versus 1.5T: A Preliminary Result

Sun Ha Paek¹, Jhi-Hoon Kim², Sung-Hong Choi², Tae-Jin Yoon²,
Young Don Son³, Dong Gyu Kim¹, Zang-Hee Cho³, Chul-Ho Sohn²

¹Department of Neurosurgery, Seoul National University Hospital, Cancer Research Institute, Ischemic/Hypoxic Disease Institute, Seoul National University College of Medicine, Seoul, Korea

²Department of Radiology, Seoul National University College of Medicine, Seoul, Korea

³Neuroscience Research Institute, Gachon University of Medicine and Science, Incheon, Korea

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Correspondence to:

Chul-Ho Sohn, M.D., Ph.D.
Department of Radiology, Seoul National University College of Medicine, 28 Yeongeong-dong Jongno-gu, Seoul 110-744, Korea.
Tel. +82-2-2072-3072
Fax. +82-2-747-7418
Email: neurorad63@gmail.com

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Purpose: To compare the depiction of brain metastases on contrast-enhanced images with 7.0 tesla (T) and at 1.5T MRI.

Materials and Methods: Four consecutive patients with brain metastases were scanned on 7.0T whole-body scanner and 1.5T MRI. A 3D T1-weighted gradient echo sequence (3D T1-GRE) at 1.5T (voxel size = $0.9 \times 0.9 \times 1.5 \text{ mm}^3$ after double-dose, gadoterate meglumine, Gd-DOTA) was compared to a 7.0T 3D T1-GRE sequence (voxel size = $0.4 \times 0.4 \times 0.8 \text{ mm}^3$, single-dose Gd-DOTA) in four patients after a 5 minute delay. The number of contrast-enhancing metastases in MPRAGE images was compared in each patient by two radiologists in consensus. We measured contrast ratio of enhancing brain metastases and white matter in 1.5T and 7.0T.

Results: In all four patients 7.0T 3D T1-GRE images after single-dose Gd-DOTA and 1.5T after double-dose Gd-DOTA depicted 11 brain metastases equally. In the quantitative analysis of contrast ratios of enhancing brain metastases and white matter, the 1.5T 3D T1-GRE after double-dose showed an increased contrast ratio compared to 7.0T 3D T1-GRE after single-dose (0.961 ± 0.571 versus 0.885 ± 0.494 ; $n = 11$ metastases). But this difference was not statistically significant ($P = 0.711$).

Conclusion: Our preliminary results indicate that 7.0T single-dose Gd-enhanced images were not different to 1.5T double-dose Gd-enhanced images for the detection of brain metastases.

Keywords: Brain metastasis; Magnetic resonance imaging; 7T MRI

INTRODUCTION

Brain metastases are the most common intracranial tumors, and this rapidly growing incidence is likely due to the growing effectiveness of therapies for primary malignant tumors and improved detection with new CNS imaging modalities. Brain metastases occur in 20-40% of patients with systemic cancer (1, 2). The diagnosis and determination of the number of brain metastases influence staging as well as therapy (3). The median survival time of patients with one or only two brain metastases in non-

eloquent brain areas can be prolonged up to 14 months by stereotactic radiotherapy or by operation followed by radiotherapy (3, 4). Multiple or inoperable brain metastases are mostly decisive for the prognosis of metastatic cancer. In patients with multiple brain metastases, the therapeutic possibilities are currently limited to whole-brain radiation and/or chemotherapy without surgery. The resulting median survival time rarely exceeds 6 months. Hence, the detection and identification of brain metastases with respect to number, size, and location are indispensable for optimal therapeutic management.

MRI with contrast administration has been shown to be the most sensitive imaging modality for detecting brain metastases noninvasively (5-7). Several strategies to improve the detection rate of brain metastases by MRI have been reported: the use of a higher dose of contrast agent (8, 9), the use of magnetization transfer contrast (10), and MR examinations with higher field strength (11, 12). With an increased magnetic field, the signal-to-noise ratio (SNR) increases almost linearly. Hence, ultra high field MRI allows improvement of the spatial resolution without sacrificing the SNR and contrast-to-noise ratio compared to MRI at lower field strengths (13, 14). Ultra high field MR whole-body scanners at 7.0T to 9.4T are currently being tested for clinical application in humans. Several studies have already proved the superior sensitivity and specificity of 3.0T versus 1.5T MR systems for imaging brain tumors and brain metastases (15-17). 3.0T MRI allows a reduction in the contrast media dose to half of the standard dose while still rendering similar contrast compared to 1.5T (15, 17).

The purpose of this study was to evaluate depiction of brain metastases after intravenous administration of the clinically established single-dose of gadolinium-based contrast media at 7.0T compared to double-dose 1.5T.

MATERIALS AND METHODS

Patients

We received the permission from the Korean Food and Drug Administration and the Institutional Review Board of Seoul National University Hospital and the Neuroscience Research Institute of Gacheon Medical Center, and we obtained written informed consent from all subjects. Adult (>20-year-old) patients with brain metastasis of histologically proven primary tumors at 1.5T MRI were included. Prior to enrollment, all study participants were informed of the scientific nature of 7.0T MR examination.

At present, 7.0T MR examination is not yet allowed for diagnostic use. Therefore, the results of 7.0T MR studies had no influence on oncological therapies of all study participants. All MR examinations were supervised by an experienced radiologist capable of treating allergic reactions, seizures, and other emergencies. The medical staff at the 7.0T site avoided fast table movements in the ultra-high magnetic field in order to prevent vertigo.

Over a period of 12 months, four consecutive patients with brain metastases (3 women and 1 man) were included in the study. The mean age of the patients was 53.5 years (age range, 46-58 years). The primary cancer types were three lung cancers (2 adenocarcinomas, 1 small cell) and one malignant melanoma.

MR Imaging Techniques

Ultrahigh field MR examinations were performed on a 7.0T whole-body MR system (Magnetom 7.0T, Siemens Healthcare, Erlangen, Germany). The 7.0T magnet, with a clear bore of 90 cm, is equipped with a water cooled gradient and RF coils. The gradient system operates at 2000 V/650 Amp with gradient amplitude of 40 mT/m, a maximum slew rate of 200 mT/m/ms, and a minimum gradient rise time of 200 microseconds. A birdcage TX/RX single channel coil was used. The 1.5T system was a Signa Excite whole-body scanner (GE Healthcare, Milwaukee, WI, USA) with a birdcage head coil.

The time elapsed between the 1.5T and 7.0T MR examinations of each patient ranged from 1 to 10 days (mean interval, 4.5 days). A contrast-enhanced 3D T1-weighted gradient echo sequence with magnetization preparation (3D T1-GRE; MP-RAGE at 7.0T and FSPGR at 1.5T) at 1.5T was compared to a 7.0T MR sequence. For coronal T1-weighted 3D GRE at 7.0T, the acquisition parameters were: TR, 3200-4000 ms; TE, 3.4-4.4 ms; TI, 1000 ms; FA, 100; section thickness, 0.7-0.8 mm; matrix, 256-448 x 256-448; NEX, 1; and acquisition time, 13 min 29 sec. For axial T1-weighted 3D T1-GRE at 1.5T, the acquisition parameters were: TR, 8.6-11.9 ms; TE, 3.6-5.3 ms; FA, 200; section thickness, 1.5 mm; matrix, 256 x 256; NEX, 2; and acquisition time, 7 min 26 sec.

At 7.0T gadolinium-enhanced 3D T1-GRE images were obtained after injection of a single dose (SD) (0.1 mmol/kg body weight) of gadopentetate dimeglumine (Gd-DTPA) (Magnevist®, Bayer Healthcare Pharmaceuticals Inc., Leverkusen, Germany) in all patients with a 5 minutes delay. The 1.5T 3D T1-GRE sequence was performed with an initial double dose (DD) (0.2 mmol/kg body weight) of Gd-DTPA

mine after a 5 minutes delay. For comparison with 1.5T, we generated axial-reformatted T1-GRE images with 1.5 mm slice thickness at 7.0T.

Imaging Analysis

Image analysis was performed by two radiologists in consensus. The number of contrast-enhancing metastases on axial T1-GRE images was counted at both field strengths. In four patients the number of brain metastases on 3D T1-GRE images was compared after administration of SD Gd-DTPA at 7.0T with DD Gd-DTPA administration at 1.5T with a delay of 5 minutes.

Quantitative image assessment was performed subsequently. Signal intensities of individual types of tissue and lesions were assessed by region of interest (ROI) measurements with ROI values placed identically on both series of images using the same sized circular ROI from the software available on both scanners. Lesion-to-brain-contrast for the lesion was evaluated as follows.

Numerical tumor-to-brain-contrast after gadolinium administration (TB contrast ratio) is defined as:

$$\text{TB contrast ratio} = (\text{TB} - \text{NW})/\text{NW}$$

With TB taken as the signal intensity of an ROI assessed over a lesion after contrast agent administration and NW taken as the signal intensities assessed over the normal appearing deep white matter. The signal intensity of a lesion was measured within an enhanced area. In

inhomogeneously enhanced tumors, the area of maximum uptake was chosen for measurement.

Statistical Analysis

The signal intensity values in the quantitative measurements were expressed as mean \pm standard deviation. The paired t test was used to compare the tumor-to-brain contrast ratio between 7.0T and 1.5T. For all tests, significance was set at $P < 0.05$, and SPSS software package (SPSS 16.0, Chicago, IL, USA) was used for statistical analyses.

RESULTS

No allergic reactions were observed after intravenous application of Gd-DTPA at both field strengths. Among four patients, a total of 11 brain metastases were detected by two radiologists at the 1.5T 3D T1-GRE sequence after DD of Gd-DTPA and 7.0T 3D T1-GRE sequence after SD of Gd-DTPA (Fig. 1).

In the quantitative analysis of contrast ratios of enhancing brain metastases and white matter, the 1.5T 3D T1-GRE after DD showed an increased TB contrast ratio compared to 7.0T 3D T1-GRE after SD (0.961 ± 0.571 versus 0.885 ± 0.494 ; $n = 11$ metastases). But this difference was not statistically significant ($P = 0.711$) (Fig. 2).

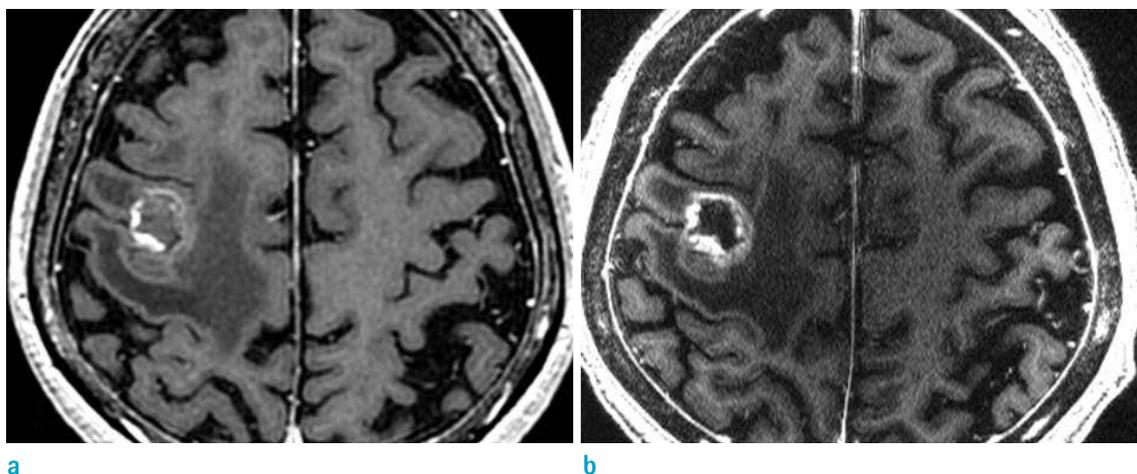


Fig. 1. 63-years-old woman with single brain metastasis from lung adenocarcinoma.

Double-dose Gd-enhanced axial 3D T1-GRE image shows a ring like enhancing lesion at the right precentral gyrus at 1.5T (a), and single-dose Gd-enhanced 3D T1-GRE image clearly demonstrates the peripheral enhancing rim portion of the metastasis at 7.0T (b).

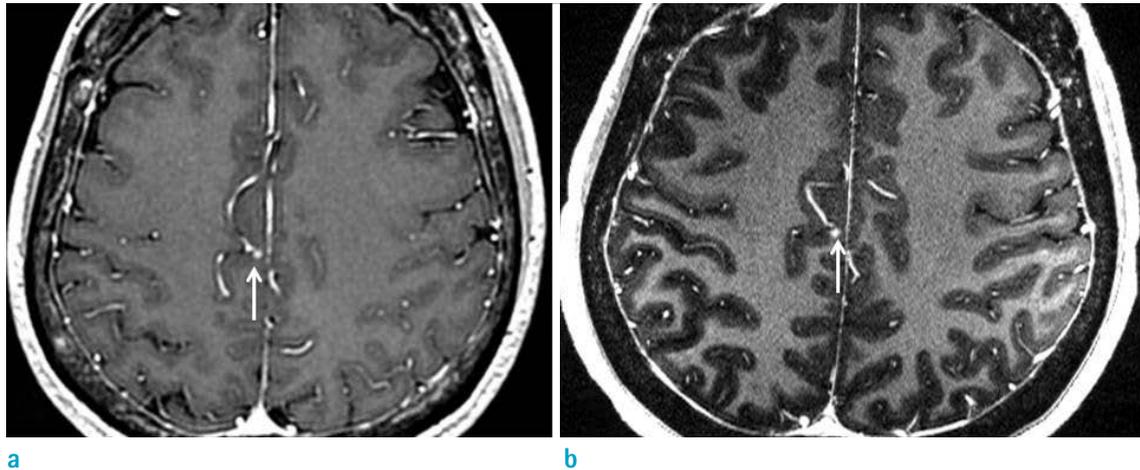


Fig. 2. 56-years-old woman with five brain metastases from lung adenocarcinoma.

A right paracentral lobule metastasis (white arrow) has similar signal intensity at 1.5T double-dose (a) and 7.0T single-dose (b) Gd-based axial T1-GRE images (mean tumor-brain contrast ratio $0.604/0.611 = 1.5T/7.0T$).

DISCUSSION

Limiting the easy clinical implementation of ultra-high field MRI ($\geq 7.0T$) is the fact that human dimensions are no longer a negligible fraction of the wavelength of radiofrequency radiation, leading to radiofrequency field (B1) inhomogeneity that compromises image quality. In addition, magnetic field (B0) inhomogeneities produced by air/water interfaces or mineralization become amplified at 7.0T compared to lower field strengths. Higher energy absorption (measured by the specific absorption ratio, or SAR) constrains sequence development. Nevertheless, the most dominant benefit of high magnetic field strengths in MR imaging is the approximately linear enhancement of image signal-to-noise ratio (SNR).

Ultra-high field 7.0T MRI offers superior SNR relative to any other noninvasive imaging technique. The higher signal-to-noise ratio can be used to increase scan speed and/or to obtain a higher resolution (18, 19) and where the higher spectral resolution (20) and the increased sensitivity for various contrast mechanisms such as blood oxygenation level-dependent (BOLD) (21) have proven useful. The increased SNR leads to a higher contrast-to-noise ratio (CNR) between enhancing and non-enhancing tissues. In addition, with the longer baseline relaxation times brought about by the higher magnetic field strength, the T1-shortening effect of Gd-based contrast agents should be greater and the contrast enhancement of the lesions on T1-weighted images should generally be stronger at 3.0T than they are at 1.5T (22). The significantly enhanced sensitivity

at 7.0T may prove to be a decisive advantage for the diagnosis of tumorous entities (23). In a preliminary study, the detection of metastases of bronchial carcinomas in single-dose gadolinium contrast-enhanced MRI at 7.0T was almost equivalent to the sensitivity at double-dose 1.5T (198 versus 238 brain metastases) (24). Our results are similar to this study.

The standard dose of contrast for 1.5T MR imaging systems is 0.1 mmol/kg body weight. It has been shown that greater sensitivity can be achieved when higher doses, up to 0.3 mmol/kg gadolinium are administered (8-10). In a larger series specifically evaluating brain metastasis, it was shown that triple-dose gadolinium MRI increases mean lesion contrast, increases qualitative conspicuity of lesions, detects additional small lesions and, in a subset of patients, would have changed choice of therapy (25). Lesions greater than 10 mm will be seen at all dose levels. The utility of higher dose gadolinium mainly lies in the ability to reveal smaller lesions, especially less than 5 mm (25, 26). However, the use of a higher dose of contrast medium not only increases the potential side effects, but also represents a substantial increase in cost, compared to a standard 0.1 mmol/kg dose. Since early 2006 evidence has accumulated that some gadolinium based contrast agents, particularly gadodiamide (Omniscan, GE Healthcare, Chalfont St. Giles, UK), may cause a potentially devastating or even fatal scleroderma-like, fibrosing condition called nephrogenic systemic fibrosis (NSF) in patients with renal failure (27-29). Recently, it has been shown that gadopentetate dimeglumine (Magnevist, Bayer Schering, Berlin, Germany) may also trigger NSF,

but apparently not with the same high frequency as gadodiamide. Therefore, we concern to use high dose gadolinium based contrast agents.

There are two limitations in this study. First limitation of this study is that the number of patients in our study was too small, making the sensitivity data less robust than the specificity data. Second limitation is different spatial resolution in each contrast-enhanced MRI protocol.

In conclusion, we suggest that assessment of possible brain metastases using 0.1 mmol/kg Gd-DTPA with a 7.0T MR imaging system is comparable to 0.2 mmol/kg Gd-DTPA at 1.5T.

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REFERENCES

1. Klos KJ, O'Neill BP. Brain metastases. *Neurologist* 2004;10:31-46
2. Arnold SM, Patchell RA. Diagnosis and management of brain metastases. *Hematol Oncol Clin North Am* 2001;15:1085-1107, vii
3. Sanchez de Cos J, Sojo Gonzalez MA, Montero MV, Perez Calvo MC, Vicente MJ, Valle MH. Non-small cell lung cancer and silent brain metastasis. Survival and prognostic factors. *Lung Cancer* 2009;63:140-145
4. Smalley SR, Schray MF, Laws ER Jr, O'Fallon JR. Adjuvant radiation therapy after surgical resection of solitary brain metastasis: association with pattern of failure and survival. *Int J Radiat Oncol Biol Phys* 1987;13:1611-1616
5. Davis PC, Hudgins PA, Peterman SB, Hoffman JC Jr. Diagnosis of cerebral metastases: double-dose delayed CT vs contrast-enhanced MR imaging. *AJNR Am J Neuroradiol* 1991;12:293-300
6. Engh JA, Flickinger JC, Niranjan A, Amin DV, Kondziolka DS, Lunsford LD. Optimizing intracranial metastasis detection for stereotactic radiosurgery. *Stereotact Funct Neurosurg* 2007;85:162-168
7. Jena A, Taneja S, Talwar V, Sharma JB. Magnetic resonance (MR) patterns of brain metastasis in lung cancer patients: correlation of imaging findings with symptom. *J Thorac Oncol* 2008;3:140-144
8. Runge VM, Kirsch JE, Burke VJ, et al. High-dose gadoteridol in MR imaging of intracranial neoplasms. *J Magn Reson Imaging* 1992;2:9-18
9. Sze G, Johnson C, Kawamura Y, et al. Comparison of single- and triple-dose contrast material in the MR screening of brain metastases. *AJNR Am J Neuroradiol* 1998;19:821-828
10. Hawighorst H, Debus J, Schreiber W, et al. Contrast-enhanced magnetization transfer imaging: improvement of brain tumor conspicuity and delineation for radiosurgical target volume definition. *Radiother Oncol* 1997;43:261-267
11. Komada T, Naganawa S, Ogawa H, et al. Contrast-enhanced MR imaging of metastatic brain tumor at 3 tesla: utility of T(1)-weighted SPACE compared with 2D spin echo and 3D gradient echo sequence. *Magn Reson Med Sci* 2008;7:13-21
12. Trattinig S, Pinker K, Ba-Ssalamah A, Nobauer-Huhmann IM. The optimal use of contrast agents at high field MRI. *Eur Radiol* 2006;16:1280-1287
13. Paek SH, Son YD, Chung HT, Kim DG, Cho ZH. Clinical application of 7.0 T magnetic resonance images in Gamma Knife radiosurgery for a patient with brain metastases. *J Korean Med Sci* 2011;26:839-843
14. Yuh WT, Christoforidis GA, Koch RM, et al. Clinical magnetic resonance imaging of brain tumors at ultrahigh field: a state-of-the-art review. *Top Magn Reson Imaging* 2006;17:53-61
15. Nobauer-Huhmann IM, Ba-Ssalamah A, Mlynarik V, et al. Magnetic resonance imaging contrast enhancement of brain tumors at 3 tesla versus 1.5 tesla. *Invest Radiol* 2002;37:114-119
16. Schwandt W, Kugel H, Bachmann R, et al. Magnetic resonance imaging protocols for examination of the neurocranium at 3 T. *Eur Radiol* 2003;13:2170-2179
17. Krautmacher C, Willinek WA, Tschampa HJ, et al. Brain tumors: full- and half-dose contrast-enhanced MR imaging at 3.0 T compared with 1.5 T--Initial Experience. *Radiology* 2005;237:1014-1019
18. Pfeuffer J, van de Moortele PF, Yacoub E, et al. Zoomed functional imaging in the human brain at 7 Tesla with simultaneous high spatial and high temporal resolution. *Neuroimage* 2002;17:272-286
19. Vaughan JT, Garwood M, Collins CM, et al. 7T vs. 4T: RF power, homogeneity, and signal-to-noise comparison in head images. *Magn Reson Med* 2001;46:24-30
20. Ugurbil K, Adriany G, Andersen P, et al. Ultrahigh field magnetic resonance imaging and spectroscopy. *Magn Reson Imaging* 2003;21:1263-1281
21. Gizewski ER, de Greiff A, Maderwald S, Timmann D, Forsting M, Ladd ME. fMRI at 7 T: whole-brain coverage and signal advantages even infratentorially? *Neuroimage*

- 2007;37:761-768
22. Biswas J, Nelson CB, Runge VM, et al. Brain tumor enhancement in magnetic resonance imaging: comparison of signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) at 1.5 versus 3 tesla. *Invest Radiol* 2005;40:792-797
 23. Lupo JM, Banerjee S, Hammond KE, et al. GRAPPA-based susceptibility-weighted imaging of normal volunteers and patients with brain tumor at 7 T. *Magn Reson Imaging* 2009;27:480-488
 24. Monninghoff C, Maderwald S, Theysohn JM, et al. Imaging of brain metastases of bronchial carcinomas with 7 T MRI - initial results. *Rofo* 2010;182:764-772
 25. Yuh WT, Tali ET, Nguyen HD, Simonson TM, Mayr NA, Fisher DJ. The effect of contrast dose, imaging time, and lesion size in the MR detection of intracerebral metastasis. *AJNR Am J Neuroradiol* 1995;16:373-380
 26. Akeson P, Larsson EM, Kristoffersen DT, Jonsson E, Holtas S. Brain metastases--comparison of gadodiamide injection-enhanced MR imaging at standard and high dose, contrast-enhanced CT and non-contrast-enhanced MR imaging. *Acta Radiol* 1995;36:300-306
 27. Broome DR, Girguis MS, Baron PW, Cottrell AC, Kjellin I, Kirk GA. Gadodiamide-associated nephrogenic systemic fibrosis: why radiologists should be concerned. *AJR Am J Roentgenol* 2007;188:586-592
 28. Sadowski EA, Bennett LK, Chan MR, et al. Nephrogenic systemic fibrosis: risk factors and incidence estimation. *Radiology* 2007;243:148-157
 29. Thomsen HS. Nephrogenic systemic fibrosis: A serious late adverse reaction to gadodiamide. *Eur Radiol* 2006;16:2619-2621