Use of half-dose gadolinium-enhanced MRI and magnetization transfer saturation in brain tumors

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Abstract The aim of this study was to search if half-dose gadolinium (Gd)-enhanced MR imaging with magnetization transfer saturation (MT) can replace standard-dose T1-weighted spin echo (SE) without MT saturation in brain tumors. Thirty patients with a total of 33 brain tumors (14 gliomas, 13 meningiomas, 6 metastases) were prospectively studied using T1-weighted SE half-dose of Gd with MT, and T1-weighted SE standard-dose Gd without MT. The contrast-to-noise ratio (CNR) of the two sequences was calculated and four radiologists reviewed qualitatively the images of the two sequences. There was no significant difference between both techniques for quantitative analysis (Wilcoxon test). However, there was a good agreement between sequences to evidence an intraclass correlation coefficient ($r = 0.70$) of all lesions. In cases of meningioma, the agreement was better ($r = 0.84$). The results show a difference in the qualitative data between the two sequences, suggesting the use of the T1-weighted MR images with MT and half-dose of Gd with good results in the whole tested parameters except the lesional edema and the presence of artifacts. Half-dose T1-weighted SE with MT can replace standard-dose T1-weighted SE without MT with no loss of contrast enhancement in investigation of meningiomas and saving $50\%$ of the contrast material.

Keywords Brain MRI · Half-dose gadolinium · Meningioma · Inter-observer agreement

Introduction

In clinical use of MRI, gadolinium has the ability to demonstrate blood-brain-barrier abnormalities and is of benefit in diagnosis of tumors and in planning their treatment. Contrast agents shorten T1 relaxation time of tissues in which they accumulate and improve signal intensity on T1-weighted MR images. In current practice it is assumed that a dose of 0.1 mmol/kg gadolinium for MR imaging provides safe and effective enhancement of most intracranial tumors [1, 2]. Several studies have analyzed the utility of using a higher dose of contrast agent for the MR evaluation of primary and secondary brain lesions. It has been shown that using a double and triple dose of gadolinium would result in an improvement in the relative contrast of enhancing of the lesions [3, 4, 5].

Clinical trials were used to determine the effect of MR contrast dose and delayed scanning in the detection of cerebral diseases [4, 5, 6]. Further studies have revealed the relationship between the conspicuity of MR contrast enhancement and, not only the field strength, but also the MR pulse sequence applied. The conclusions regarding the field strength were that there is an improvement in detection of gadolinium enhancement when the field strength is increased [7]. Chappell et al. [8] have compared the lesion enhancement on spin-echo (SE) and gradient-echo images and found a subtle difference between the two techniques, especially for small lesions without sur-
rounding edema, in which case SE imaging seems better.

Among MR pulse sequences, the magnetization transfer (MT) technique has been shown to be a new method for tissue characterization [9, 10]. Tissue components are divided into pools according to their magnetic relaxation properties. The MT technique consists of applying an off-resonance pulse that saturates only the protons in the macromolecular pool and has no direct influence on those in free water. The saturation of the macromolecular pool is transferred to water molecules in the vicinity by means of dipol–dipol and chemical interaction altering relaxation time of the tissues, especially those rich in macromolecules. The number of molecules in the tissue determines the energy exchanged in this process and results in an increased relaxation of the tissue. It is assumed that the MT pulse does not influence the gadolinium enhancement because it acts mainly by means of a direct water–Gd$^{3+}$ ion interaction where macromolecules are playing no role. The MT technique reduces the signal intensity of normal tissue and increases the conspicuousness of gadolinium enhancement [9, 11, 12, 13].

Finelli et al. [11] and Knauth et al. [14] studied the possibility of using MT in order to increase the contrast-to-noise ratio (CNR) of enhancing intracranial lesions in T1-weighted spin-echo with gadolinium imaging. Comparing this technique with T1-weighted SE without MT, they concluded that the use of MT T1-weighted SE technique could give a CNR equivalent to triple-dose gadolinium technique, twice that obtained with single-dose gadolinium. Han et al. [15] assumed that using MT saturation technique they could increase the relative contrast of enhancing lesions in half-dose gadolinium MR imaging with MT to a degree comparable with that obtained with standard-dose Gd-enhanced SE MR imaging without MT. The results showed that half-dose-enhanced MR imaging with MT was comparable with that of standard-dose-enhanced SE MR imaging in less than 50% of cases; thus, the authors concluded that MT technique can replace the latter technique in only limited cases such as selected extra-axial tumors.

The aim of this study was to prove that half-dose-enhanced MR imaging with MT saturation could replace standard-dose T1-weighted SE without MT saturation in brain tumors.

Materials and methods

Study group

From January to August 1998, 30 patients (16 women and 14 men), age range 39–78 years (mean age 61 years), all presenting with a suspicion of cerebral tumor and prior CT studies, were included in the study. All subjects gave informed written consent. No patient had received medical treatment. There were 14 gliomas, 13 meningiomas, and 6 metastases. Twenty-nine tumors were histologically confirmed.

Imaging technique

All the patients were investigated with a 1.5-T imager (Signa, Horizon Echospeed, GE Medical Systems, Milwaukee, Wis.) using a circularized head coil. The axial T1-weighted SE sequence was performed with the following parameters: TR/TE = 640/20 ms; flip angle = 90°; slice thickness = 5 mm; gap = 1.5 mm; field of view = 25 × 18; matrix = 512 × 256; two signals averaged and acquisition time 3 min.

T1-weighted images with MT were obtained before and after administration of contrast material with the following parameters: TR/TE = 640/20 ms, flip angle = 90°, slice thickness = 5 mm; gap = 1.5 mm; field of view = 24 × 18; sample matrix = 256 × 192; two signals averaged; acquisition time 6 min 16 s. The MT pulse was centered 1600 Hz below the resonance frequency of water, with a duration of 8.2 ms repeated ten times during the TR interval and a power equivalent to 1000 degrees pulse.

The imaging protocol included sagittal spoiled gradient recalled (SPGR) T1-weighted sequence, an axial fast spin-echo T2-weighted sequence (TR = 6000 ms, TE = 102 ms), and an axial SE T1-weighted sequence with and without MT. All patients received a half dose (0.05 mmol/kg) of DOTA-Gd (Dotarem, Guerbet, Anulay-sous-Bois, France), and underwent axial MT T1-weighted SE imaging. An additional half dose of Gd was administered 7 min after this first injection (0.1 mmol/kg cumulative dose). Five minutes after the second injection, all patients underwent additional axial T1-weighted SE sequence without MT. Fifteen to 20 min after the first injection, the last sequence, T1-weighted SE with MT, was applied.

Data analysis

The quantitative analysis was performed by using an operator-defined region of interest (ROI) of 22 mm², and measuring the signal intensity of tumor tissue in the enhancing areas, normal white matter in the contralateral hemisphere, and the signal intensity of background noise in the phase-encoding direction.

Brain tumor’s CNR was calculated for all sequences with the following formula: $C/N = (S1 - S0)/N$, where $S1$ $wm$ = signal intensity of white matter, $S1$ $t$ = signal intensity of tumor, and $N$ = measured intensity of background noise. Mean CNR data were compared between the two sequences with a Wilcoxon signed-rank test and agreement was estimated by means of intraclass correlation coefficient (ICC).

In the qualitative analysis, four radiologists (two neuroradiologists and two general radiologists) compared all lesions on half-dose Gd DT T1-weighted SE and on standard-dose T1-weighted SE without MT, looking at the degree and extent of the enhancement. Lesion detectability, lesion enhancing, definition of tumor’s border, and distinction of edema at the two different doses of Gd were evaluated using a five-grade scale for scoring: −2, markedly inferior than standard dose T1-weighted SE images; −1, slightly inferior than standard dose T1-weighted SE images; 0, same as standard dose T1-weighted SE images; +1, slightly superior to standard-dose T1-weighted SE images; +2, markedly superior to standard-dose T1-weighted SE images. The degree of visible artifacts was subjectively evaluated using a three-grade scale: 3, non-interpretable; 2, moderate artifacts; 1, poor artifacts.

All evaluations were done independently by the observers, without knowledge of patient identity and final diagnosis.