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Brain Imaging: Reduced Sensitivity of RARE-Derived Techniques to Susceptibility Effects

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Abstract

Objective: Our goal was to evaluate the decreased sensitivity of RARE-derived pulse sequences to susceptibility effects.

Materials and Methods: A variety of RARE-derived T2-weighted fast SE echo (FSE) sequences with echo trains from 6 to 16 were compared with conventional SE (CSE) sequences by means of MRI in phantoms (iron oxides), volunteers (n = 10), and patients (n = 13) with old hemorrhagic brain lesions. All experiments were performed on a 1.5 T clinical MR system (Magnetom SP 4000; Siemens AG, Erlangen, Germany) with constant imaging parameters. Contrast-to-noise ratios (CNRs) of tubes doped with iron oxides at different concentrations and brain areas with physiological iron deposition (red nucleus, substantia nigra) were calculated for CSE and FSE pulse sequences. Areas of old brain hemorrhage were analyzed for lesion conspicuity by blinded analysis with CSE as an internal standard.

Results: CNR of iron oxide tubes (TE 90 ms, CSE 45.0 ± 3.5, FSE 16 echo trains 28.5 ± 3.1; $p \leq 0.01$) and iron-containing brain areas decreased with increasing echo trains of FSE sequences. A significantly lower number of old hemorrhagic brain lesions was visible in patients scanned with FSE sequences (6 echo trains: n = 28; 16 echo trains: n = 26) than CSE (n = 40).

Conclusion: Our results demonstrate that the sensitivity of RARE-derived techniques to susceptibility effects is significantly decreased compared with CSE. CSE sequences or GE sequences should still be preferred in patients with a history of seizures or intracranial hemorrhage.

RARE (rapid acquisition with relaxation enhancement)-derived techniques such as fast SE (FSE) or turbo SE (TSE) MRI have the potential to provide heavily T2-weighted images in shorter acquisition times and at higher spatial resolution than conventional SE (CSE) sequences [1,2]. However, CSE sequences represent an imaging standard for MRI of the brain and have been proven to be valuable for the detection and characterization of brain lesions.

Signal intensity and contrast of MR images are based on a variety of factors including magnetic susceptibility, relaxation times, diffusion, flow, and proton density [2,3]. Magnetic susceptibility artifacts have been demonstrated to be reduced in RARE-derived images [3-5]. However, susceptibility effects are helpful in terms of discriminating anatomic structures like the red nucleus or substantia nigra or detecting areas of brain hemorrhage and form the basis of a whole class of contrast agents. The clinical relevance of differences in magnetic susceptibility of CSE and RARE-derived sequences has yet to be fully worked out [4-6].

Therefore, we evaluated a variety of FSE sequences with different echo train length (ETL) with respect to their sensitivity to susceptibility effects in phantoms, volunteers, and patients with old hemorrhagic brain lesions.

MATERIALS AND METHODS

MRI

All MRI studies were performed on a 1.5 T clinical imaging system (Magnetom SP 4000; Siemens AG, Erlangen, Germany) equipped with 10 mT/m gradients. Phantoms, volunteers, and patients were imaged using a protocol consisting of a T2-weighted CSE sequence and FSE pulse sequences with ETL ranging from 6 to 16 echoes with otherwise constant imaging parameters (effective TE 90 ms, bandwidth 130 Hz/pixel, and field of view 230 mm). Specific imaging parameters were as follows.

CSE

For phantom experiments, coronal T2-weighted single echo CSE images were acquired with a TR of 2,000 ms (4.56 min acquisition time), a TE of 90 ms, a 128 (phase) × 256 (frequency) matrix, section thickness of 10 mm with 20% gap, and a pixel bandwidth of 78 Hz/pixel. Only three sections were acquired per measurement, and all

measurements were performed with a circularly polarized head coil. In volunteers and patients, axial T2-weighted single echo CSE images were acquired with a TR of 2,700 ms, a TE of 90 ms, and a matrix of 192 × 256. Within 8.43 min, 21 sections with a section thickness of 6 mm and 20% intersection gap were measured.

RARE-Derived SE—FSE

FSE pulse sequences were acquired with 6-16 echoes per echo train,In volunteers axial FSE sequences were scanned with a TR of 2,700 ms constant echo spacing of 22.5 ms, and a pixel bandwidth of 130and a TE of 90 ms using a section thickness of 6 mm with 20% Hz/pixel. For phantoms coronal T2-weighted FSE sequences wereintersection gap and a 192 × 256 matrix. In patients axial FSE images acquired with a TR of 2,000 ms, TE of 90 ms, 10 mm section thickness,were acquired with a TR of 4,200 ms (TE 90 ms) to obtain the same 20% intersection gap, and a 128 × 256 matrix. Acquisition time (0.28-coverage as with CSE (section thickness of 6 mm with 20% intersection 1.39 min) and image matrix in the phase-encoding direction (120-132)gap and 192 × 256 matrix). Acquisition time (0.43-3.01 min) and the varied depending on the number of echoes per echo train, and again number of measurable sections [5-13] again varied depending on the three slices were scanned per measurement. number of echoes per echo train.

Phantom Experiments

Six plastic tubes containing different concentrations of superparamagnetic iron oxide (SPIO) (0.001, 0.005, 0.01, 0.05, 0.1, and 0.5 mg Fe/ml saline) were placed in an agarose (4%)-containing gel (Dubliplast; Dentaurum, Pforzheim, Germany) that was doped with 0.33 mmol Gd-DTPA/L gel (Magnevist; Schering AG, Berlin, Germany) for adapting relaxation times to human tissue (T1 ≈400-600 ms, T2 ≈40-80 ms) (see Fig. 1). The contrast medium utilized was a conventional, dextran-stabilized SPIO (AMI-25; R1 30 m$M^{-1}s^{-1}$ and R2 100 m$M^{-1}s^{-1}$) with a mean hydrodynamic diameter of 72 nm [7]. Quantitative analysis was provided by measurement of signal intensities. Signal intensity measurements were performed in iron oxide tubes and the agarose gel that was used as a reference tissue. Background noise was measured in the phase-encoding direction with region of interests (ROIs) as large as possible. Signal intensity (SI) measurements were performed by a single observer using ROIs drawn as large as possible. Contrast-to-noise ratio (CNR) was calculated using the following formula:

Equation 04B

Fig. 1

Volunteers

Signal intensity in brain areas with physiological susceptibility effects such as the red nucleus, substantia nigra, and internal capsule was measured in MR images of 10 volunteers (mean age 25.1 ± 1.9 years; 4 women, 6 men). White matter was used as a reference tissue for contrast calculations. Written informed consent was obtained from all volunteers.

Patients

Clinical MR studies were performed in 13 consecutive patients (mean age 49.0 ± 17.9 years; 8 women, 5 men) with a clinical history (10-36 months) of intracerebral hemorrhage (0.5-1.6 cm in diameter) to evaluate the influence of reduced sensitivity to susceptibility effects on lesion conspicuity. Written informed consent was obtained from all patients. Signal intensity was measured in areas of intracerebral hemorrhage with white matter as a reference tissue. Signal intensity measurements were performed by a single observer using ROIs drawn as large as possible. CNR was calculated using the following formula:

Equation 04C

Images of patients with intracerebral hemorrhage were qualitatively analyzed by counting hemorrhagic lesions comparing CSE images as an imaging gold standard and FSE images acquired with different ETL. Images were presented in random order with imaging parameters masked and evaluated by consensus of two board-certified radiologists.

Statistical Analysis

Repeated measures analysis of variance was performed on contrast parameters, and lesion conspicuity was analyzed with the χ^2 test [8]. A p value of ≤0.05 was considered significant.

RESULTS

Contrast between iron-containing tubes and simulated reference "tissue" showed highest values for the CSE sequence for all concentrations evaluated (Table 1). CNR values gradually decreased with increasing echo trains. Compared with CSE, CNR significantly ($p \leq 0.01$) decreased by almost 30% when a FSE sequence with 16 echoes was used (TE 90 ms: CSE 45.0 ± 3.5; FSE 16 ET 28.5 ± 3.1). MR images showed fewer apparent susceptibility effects and increased blurring on FSE images with increasing echo trains than CSE images (Fig. 1). The appearance and signal behavior of the FSE sequence with six echo trains were more comparable with CSE images than those of FSE sequences with an increasing number of ETL.

Table 1

Contrast of iron-containing brain structures in volunteers is summarized in Fig. 2. CNR of the substantia nigra and red nucleus significantly decreased with increasing numbers of echo trains. The

CSE sequence demonstrated a significantly higher contrast than all FSE sequences, for both the red nucleus and the substantia nigra. Differences among CNRs of FSE sequences were not significant; however, images acquired with longer echo trains also provided less contrast and more blurring than those measured with shorter echo trains (Fig. 2).

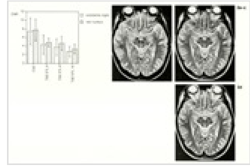
Fig. 2

Quantitative measurements of hemorrhagic brain lesions in 13 patients (median of three lesions/patient) showed a significant decrease in CNR when FSE sequences were used (CSE 20.5 ± 9.0, FSE 6 ET 13.3 ± 7.3, FSE 8 ET 11.4 ± 6.9, and FSE 16 ET 8.8 ± 6.1). Again, CNR significantly decreased with an increasing ETL. Qualitative analysis with CSE as an internal gold standard confirmed these measurements, allowing detection of 40 lesions. Relative to CSE, only 28 lesions (75%) were detected with an ETL of 6, 26 (65%) with an ETL of 8, and 26 (65%) with an ETL of 16 (Fig. 3). Thus, significantly ($p \leq 0.01$) more lesions were detected with CSE, while the difference among FSE sequences was not significant. These results demonstrate the clinical relevance of the reduced sensitivity of RARE-derived techniques in terms of identifying old hemorrhagic brain lesions (Fig. 3).

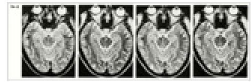
Fig. 3

DISCUSSION

RARE-derived techniques such as FSE provide high quality T2-weighted MR images either at higher spatial resolution or in significantly reduced acquisition time than required for CSE imaging. We evaluated the sensitivity of CSE and RARE-derived techniques to susceptibility effects by means of phantoms as an in vitro model system and subsequently in vivo in volunteers and patients. Our results demonstrate that the sensitivity of RARE-derived techniques to susceptibility effects decreases with increasing ETL, which is clinically relevant since the detectability of old hemorrhagic brain lesions decreases as well. Magnetic susceptibility effects of late phase resolving hematomas are attributed to ferritin in glial cells and macrophages as well as hemosiderin in macrophages around the lesion and typically depicted on T2- or $T2^*$-weighted MR images [3,9-11].

RARE imaging was proposed by Hennig et al. in 1986 with subsequent reports expanding the technique from a localizer sequence to myelographic studies and to three-dimensional volume acquisitions [1,12,13]. Since then, derivatives of this technique have been introduced by several authors and implemented into clinical scanners by different manufacturers [14,15]. The technique is currently expanding into different fields of clinical MRI, gradually replacing CSE sequences [2,16,17]. However, RARE-derived techniques have been predicted to exhibit a reduced sensitivity to magnetic susceptibility, which remains a major contributing factor to image contrast under certain circumstances such as the depiction of hemorrhagic lesions in the brain [3-6].

It has been hypothesized that the sensitivity to susceptibility effects is decreased by the use of multiple refocusing pulses that are inherent to RARE-derived pulse sequences [4,5]. Magnetic susceptibility can be described as a property of materials that causes a local field shift proportional to the main magnetic field. The local field at the boundaries between materials of different susceptibility may change dramatically, thus creating large magnetic field inhomogeneities. This causes distortions in the surrounding field, which vary according to the geometry of the object. The shortening of T2 and resultant signal loss due to diffusion of water through cellular field gradients have been established and are used in conventional T2-weighted MRI as an important signature of the evolution of hematoma [11,18,19]. The effect of signal loss in hematoma has been shown to be particularly useful to detect and stage brain hemorrhage [3,10,20-22]. Since the degree of dephasing depends on the time diffusing water spends in these inhomogeneous fields before refocusing, the time between refocusing pulses (or the TE in a single echo CSE sequence) is a critical determinant of this susceptibility contrast. RARE-derived sequences with reduced echo spacing and an increased echo train envelope may show a reduced sensitivity to diffusion weighting and thus to magnetic susceptibility, because diffusion-related dephasing is decreased compared with CSE. Gross susceptibility artifacts shall appear identical only when comparing RARE techniques with a CPMG (Carr-Purcell-Meiboom-Gill) sequence with equal echo spacing.

More recently, even more rapid acquisition schemes mixing SEs and GEs (GRASE) have been introduced [23-25]. Hypothetically, the GE content of the techniques might compensate for the decreased sensitivity of RARE techniques to susceptibility effects. Whether this holds promise remains to be investigated.

Our data demonstrate that there is a significant difference between CSE and RARE sequences in the ability to detect magnetic susceptibility artifact. Therefore, when patients with a history of seizures or intracranial hemorrhage are clinically evaluated, CSE sequences or GE sequences should still be preferred.

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