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Enhancing Gray-to-White Matter Contrast in 3T T1 Spin-Echo Brain Scans by Optimizing Flip Angle

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BACKGROUND AND PURPOSE: **Compared with MR imaging at 1.5T T1-weighted spin-echo imaging at 3T shows up with reduced gray-to-white matter contrast. The purpose of the present study was to show the effects of alterations of different flip angles as an easily accessible parameter to increase gray-to-white matter contrast.**

METHODS: **Spin-echo T1 sequences of 6 healthy volunteers were acquired in a 3T head scanner with 5 different flip angles. Observer-independent contrast-to-noise ratios for gray versus white matter from different flip angles, as well as subjective ratings of image quality from 2 blinded neuroradiologists, were compared statistically.**

RESULTS: **Gray-to-white matter contrast increased significantly with decreasing flip angle. No artifacts were introduced by decreasing flip angles, and T1 contrast characteristics were robust and stable at lowered flip angles. Also, specific absorption ratios significantly decreased with decreasing flip angles.**

CONCLUSION: **Using a flip angle of 50° significantly increases gray-to-white matter contrast in T1 spin-echo brain scans at 3T B0 field strength.**

To an increasing extent, 3T high-field-strength scanners have entered clinical routine (1, 2). In addition to the theoretical doubling in signal intensity, there are some limitations (3) associated with going to higher field strengths that, in turn, are mainly due to the doubling of spin resonance frequencies when compared with 1.5T.

One of the major changes of brain imaging at higher magnetic fields is the rather low gray-to-white matter contrast in spin-echo T1 sequences. These sequences are widely used in clinical imaging, and neuroradiologists' diagnostic decisions frequently rely heavily on this usually robust technique; however, the contrast reduction in spin-echo T1 sequences has already led to doubts on the usefulness of these sequences at higher field strengths in routine clinical brain imaging (4).

Moreover, increasing resonance frequency at higher fields often causes problems with limits in individual specific absorption rates (SARs). In contrast to the linear increase in signal intensity with increasing B0 field strength, SAR increases with the square of the B0 field strength, or resonance frequency (5). The frequently experienced problems with SAR limitations in T1 spin-echo sequences, as well as the contrast reduction in T1 imaging, motivated the present study.

From a theoretical perspective (see "Material and Methods," below), we hypothesized that altering the flip angle as a single and easily accessible parameter has the potential to target both increasing contrast-to-noise ratios (CNRs) and decreasing SARs (5–8).

To test empirically the effects of varying flip angles on CNRs from T1-weighted spin-echo sequences upon 3T head imaging, an observer-independent method to measure gray-to-white matter contrasts reliably and objectively was introduced. Subjective ratings by 2 experienced neuroradiologists were used to test the practical gain of the above approach. Finally, we empirically investigated the relationship between SAR and different flip angles to determine whether decreasing flip angles might represent a possible and easily accessible parameter to compensate for SAR problems at higher field strengths.

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Materials and Methods

Theoretical Considerations

With T1 and T2 relaxation times for gray and white matter known (9), signal intensity (I) for gray and white matter can be predicted for given TRs and TEs and different flip angles according to the following formula (5):

$$I = \frac{N(H) \cdot \sin(\theta) \cdot \exp(-TE/T2)}{1 + \cos(\theta) \cdot \exp(-TR/T1)} \cdot (1 + \exp(-TR/T1) - 2 \cdot \exp[(TE/2 - TR)/T1])$$

Here, N(H) is the hydrogen attenuation, θ denotes the flip angle, T1 and T2 are the relaxation times of the gray and white matter, and TR and TE are repetition time and echo time, respectively. Solving the equation above, signal intensities for gray and white matter at different flip angels can be calculated and gray-to-white matter contrast can be predicted in terms of differences between signal intensities of both types of tissue. Theoretically, from the relationships it can be shown that a lowering of flip angles with TR and TE kept constant leads to a reduction of signal intensities while there is an increase of gray-to-white matter contrast. This relationship, however, is of practical use only until a certain lower bound of flip angles is reached, beyond which gray and white matter no longer yield reasonable amounts of absolute signal intensity. Within this framework, we empirically tested the effects of different flip angles on gray-to-white matter contrast. It is noteworthy, however, that technical restrictions on the commercially available software did not permit us to test flip angles <50° empirically.

With respect to the relationship between flip angle and the SAR it is of relevance that deposition of radio-frequency (RF) power is related to the square of excitation pulse at 90° $(\theta/90°)^2$ (5). Again, by computing SAR for different flip angles, the exponential increase of depositing RF power with increasing flip angles can be demonstrated.

Subjects

Six healthy volunteers (1 woman and 5 men; mean age, 28.8 years; SD, 1.7) gave written informed consent before the study. The subjects' heads were fixed by means of foam pads within the head coil, and the subjects were instructed not to move during MR acquisition.

Imaging Protocol

MR brain scanning was performed by use of 3T dedicated head scanner (Magnetom Allegra; Siemens, Erlangen, Germany) with the following parameters: TR, 700 ms; TE, 10 ms; matrix, 256 × 256; field of view, 220 × 220; section thickness, 5 mm; 19 transversal sections oriented parallel to the hypophysis-fastigium line. Within each subject, this sequence was repeated with flip angles of 50°, 70°, 90°, 110°, and 130°; all other imaging parameters were kept constant.

In addition, for purposes of coregistration, a necessary prerequisite to compute fully automated CNR measurements described below, each subject was scanned with a 3D-MPRAGE (magnetization-prepared rapid acquisition of gradient echo) sequence (10). Section orientation was equivalent to the T1 spin-echo sequence, while covering the whole brain.

Calculation of Gray-to-White Matter Contrast

Gray-to-white matter contrasts were calculated in an observer-independent, objective manner. All images were transferred to a workstation running SPM 2 (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, London) under Matlab 6 (Mathworks, Natick, MA). The MPRAGE volume was segmented into gray and white matter probability maps (11, 12) by using SPM 2. To correct for head movements between the acquisition of the spin-echo T1 sequences with different flip angles and the MPRAGE sequence, the MPRAGE volume image was coregistered to each of the T1 spin-echo sequences by using a rigid body algorithm, and the coregistration was applied to the gray and white matter segments.

To ascertain exclusive masking of gray and white matter in further computations, probability maps were thresholded at a probability of >95%, to create gray and white matter masks. These masks were applied to the spin-echo images, which resulted in matrixes containing the individual gray and white matter intensity values. Means and SDs of these matrices were calculated. To account for differences in general scanner signal intensity, values were scaled to the overall mean signal intensity of each individual sequence. CNRs were calculated as differences between intensity means of gray and white matter divided by the mean of their SDs (13). In addition, signal intensity–to-noise ratios (SNR) were calculated in the same manner as intensity means and divided by the means of their SDs.

Other Dependent Variables

In addition to the method described above, image quality was rated independently, on a scale of 1–10, by 2 experienced neuroradiologists blinded to the imaging parameters. For each of the different flip angles, observer-related scoring differences were tested by means of 5 separate unpaired t tests. Because none of the tests revealed any significant difference between observers (all P values >.15), scores from both observers were averaged for further analysis.

Individual SARs, in units of watt per kilogram body weight, and estimated for the whole body according to the manufacturer's algorithm were tabulated for each measured sequence.

Statistical Analysis

For each of the various dependent variables (CNR, mean observer scores, SAR, and SNR) differences were tested on significance by means of separate multivariate analyses of variance (MANOVA) for repeated measures with the within-subjects factor flip-angle (5 levels). In cases of a significant main effect of this factor, post hoc comparisons (Fisher LSD, $P <$ .05) were calculated to further locate differences between factor levels.

Results

All acquired images were free of artifacts and were suitable for statistical analysis. Visual inspection of the calculated gray and white matter masks, as well as visual control of the coregistration, showed optimal fitting of the different volumes.

Observer-Independent Parameters

Comparing CNR for gray versus white matter revealed a highly significant effect of the different flip angles (F [4, 2] = 207.86; P = .0048). Post hoc comparisons showed significant differences between all CNR values for the different flip angles (Fig 1*A*). CNR was greatest for a flip angle of 50°.

Comparing SNR values, a MANOVA for repeated measures demonstrated a significant effect of the factor flip angle (F [4, 2] = 104.75; P = .009). Post hoc tests revealed significant differences between all SNR values for the different flip angles.

A MANOVA for repeated measures on individual SAR values demonstrated highly significant differences (F [4, 2] = 2290.04; P = .00044). Here, post hoc

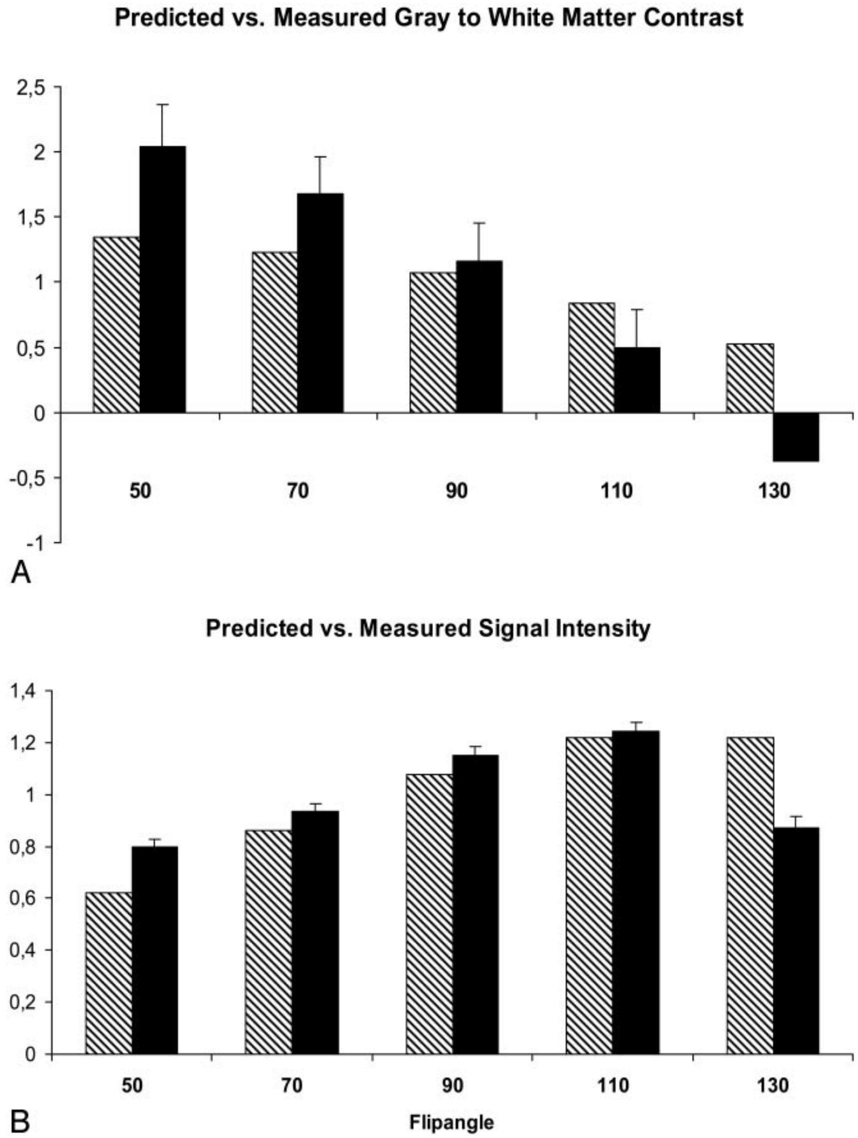

FIG 1. *A,* Black bar charts represent measured mean gray-to-white matter CNR at increasing flip angles. (Values were scaled to their grand mean to scale with predicted signal intensity.) Error is in SD. Striped bar charts represent predicted gray-to-white matter contrast.

B, Black bar charts represent measured SNR at increasing flip angles. (Values were scaled to their grand mean to scale with predicted signal intensity.) Error is in SD. Striped bar charts represent predicted mean signal intensity for gray and white matter.

comparisons were significant when SAR values from the 50° flip angle were compared to SAR values from all the other flip angles. In addition, SAR values from a 70° flip angle were significantly lower than from a 90° flip angle, whereas the latter was still significantly lower than the SAR value for a flip angle of 130°.

Observer-Dependent Parameters

Subjective image reading by the 2 neuroradiologists also showed a significant effect of the different flip angles (F [4, 2] = 30.04; P = .032). Again, post hoc comparisons showed significant differences between all observer scores for the different flip angles (Fig 1*B*).

Although low flip angles resulted in a robust and stable—even improved—T1 contrast characteristic, flip angles >90° introduced additional artifacts that even inverted the contrast of the basal ganglia region (Fig 2).

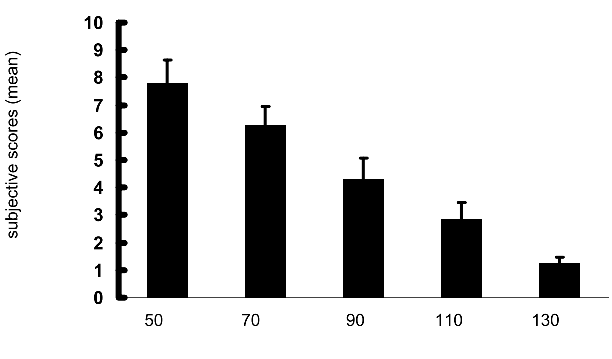

FIG 2. Bar charts represent mean subjective observer scores on image quality at increasing flip angles. Error is in SD. Observers were 2 experienced neuroradiologists.

Discussion

Brain imaging at 3T high field strength is prone to a substantial reduction of gray-to-white matter contrast in T1 spin-echo sequences (4). The present study showed a highly significant effect of different flip

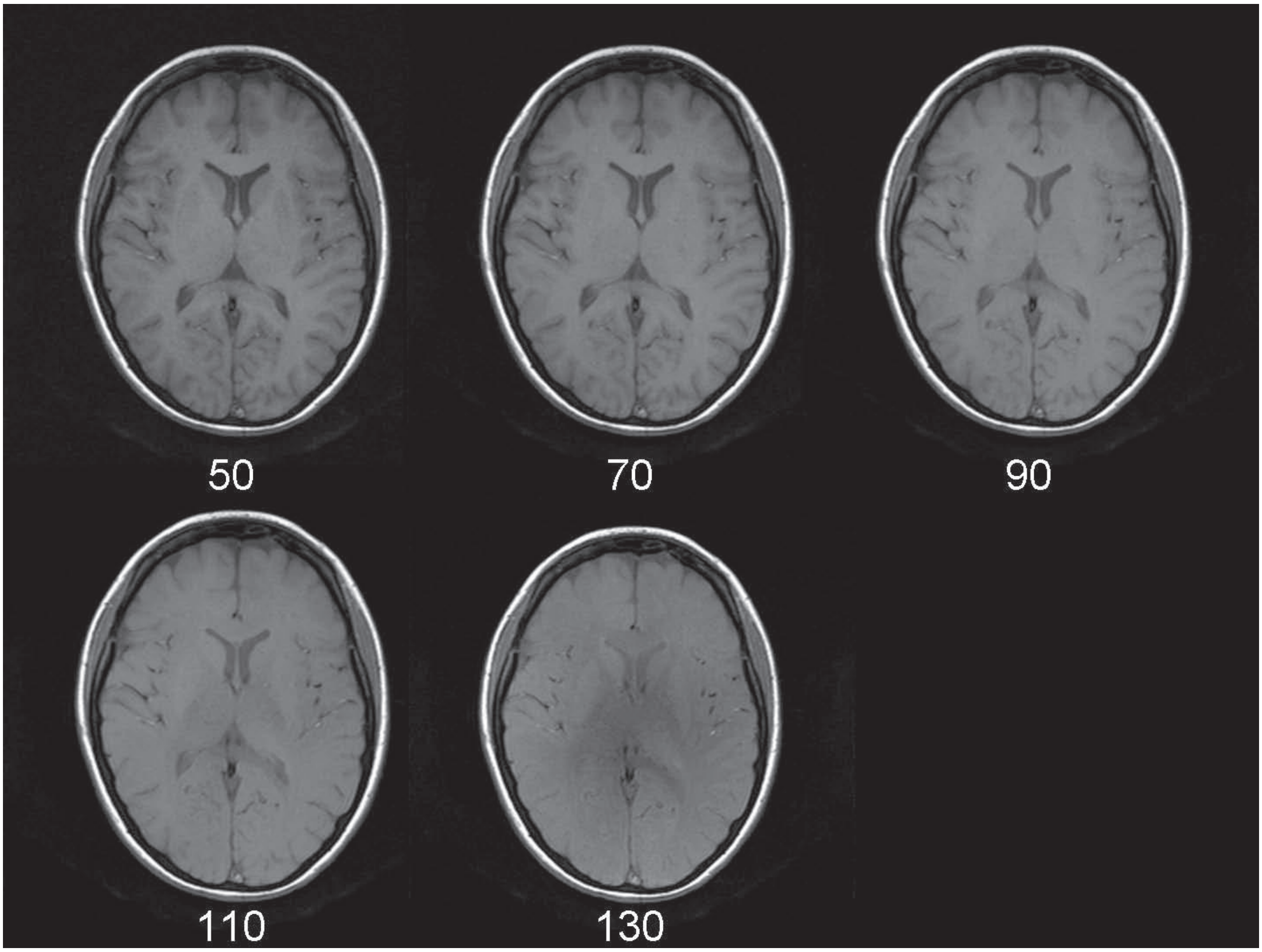

FIG 3. Transversal sections of a prototypical subject scanned at different flip angles during a spin-echo T1 sequence at 3T B0 field strength to demonstrate the obvious decrease of gray-to-white matter contrast with increasing flip angle. Also noteworthy is the inverted T1 contrast in the basal ganglia region at a flip angle of 130°.

angles on gray-to-white matter contrast in 3T imaging, with the best CNR at the lowest flip angle of 50°. The variance in contrast was more pronounced than theoretically predicted, which indicates that other factors—such as, for example, magnetization transfer or shielding effects—contribute to the contrast reduction with higher flip angles.

SNR was lowest for a flip angle of 50°, but this effect was less pronounced than theoretically predicted, probably because of more uniform signal intensity distribution at lower flip angles. Moreover, flip angle reduction led to a significant decrease of SAR.

CNR measurements in MR data sets to compare gray and white matter most frequently involve an expert defining regions in which to find exclusively gray or white matter (9, 14); however, the small cortical band is especially prone to partial volume effects, which ultimately might bias the computation toward erroneously higher gray-to-white matter contrasts because every expert must define gray and white matter areas on the images to judge. Therefore, gray and white matter intensities are already implied in defining the regions, leading to a bias toward higher gray-to-white matter contrast.

In our present method, gray and white matter of the images could be defined independently by automatically segmenting an additional MPRAGE sequence with high resolution into gray and white matter probability maps (11, 12, 15). The MPRAGE sequence with high isotropic resolution was aligned to the lower resolved T1 images, to avoid introduction of partial volume effects from rotation or translation of these anisotropic images. Moreover, thresholds for defining gray and white matter were set at a high level, 95%, to further increase robustness of voxel selection. As a result, and in contrast to the standard region of interest-based analysis, the present method is able to include gray and white matter intensities from the entirely scanned brain and is no longer confined to subjectively selected brain areas.

Certainly, image quality is not solely affected by CNR. To account for other factors that cannot be objectively measured, subjective observer ratings based on clinical expertise were included. These subjective ratings by 2 independent neuroradiologists blinded to the sequence parameters confirmed the results of the automated process, and the high overlap of the results of both methods was seen as indicative for the robustness and reliability of the automated, and observer-independent, method.

Conclusion

Within the context of clinical routine diagnostics, the data presented here strongly suggest low flip angles of 50° for T1 spin-echo brain imaging at a B0 field strength of 3T to increase gray-to-white matter contrast. As a side product, considerable reduction in SAR can also be gained by means of this approach.

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