Optimizing 3D EPI for rapid T₁-weighted imaging

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Purpose: To investigate the use of 3D EPI for rapid T₁-weighted brain imaging, focusing on the RF pulse’s influence on the contrast between gray and white matter.

Methods: An interleaved 3D EPI sequence use partial Fourier and CAIPIRINHA sampling was used to acquire T₁-weighted brain volumes with isotropic resolution, low echo times, and low geometric distortions. Five different RF pulses were evaluated in terms of fat suppression performance and gray–white matter contrast. Two binomial RF pulses were compared to a single rectangular (WE-rect) RF pulse exciting only water, and two new RF pulses developed in this work, where one was an extension of the WE-rect, and the other was an SLR pulse. The technique was demonstrated in three clinical cases, where brain tumor patients were imaged before and after gadolinium administration.

Results: A fat-suppressed 3D EPI sequence with a phase encoding bandwidth of around 100 Hz was found to exhibit a good trade-off between geometrical distortions and scan duration. Whole-brain T₁-weighted 3D EPI images with 1.2 mm isotropic voxel size could be acquired in 24 seconds. The WE-rect, its extension, and the SLR RF pulses resulted in reduced magnetization transfer effects and provided a 20% mean increase in gray–white matter contrast.

Conclusion: Using a high phase encoding bandwidth and RF pulses that reduce magnetization transfer effects, a fat-suppressed multi-shot 3D EPI sequence can be used to rapidly acquire isotropic T₁-weighted volumes.

Keywords
3D, binomial, brain, EPI, RF, T₁-weighted
1 | INTRODUCTION

Using EPI for MRI was suggested already in 1977 in the classical paper by Mansfield. Today, 2D single-shot EPI (ss-EPI) is routinely used for diffusion (DWI and DTI), functional (FMRI), and perfusion imaging because of its extremely high sampling speed. Recently, 2D ss-EPI has been used to acquire a full brain exam, producing six clinically relevant contrasts in ~1 minutes. Although EPI is typically acquired with 2D Fourier encoding using slice-selective RF pulses, applications of EPI with 3D Fourier encoding have been reported. 3D EPI is typically acquired as a gradient echo, where an additional phase encoding gradient before the EPI train is used to encode the slice direction. Interleaved acquisition (a.k.a. multi-shot) along the in-plane phase encoding direction, can be used to increase the effective phase encoding bandwidth along this direction to reduce geometric distortions and blurring. The bandwidth along the in-plane phase encoding direction is usually called phase encoding bandwidth and provides a good quantification of the geometrical distortions to be expected from an EPI train.

The fundamental SNR advantage of 3D over 2D Fourier encoding was described in the early days of MRI. Although the T1 saturation for 3D encoding is stronger because of the typically shorter TR, this is compensated for in most cases by the increased sampling time per voxel because of the volumetric excitation. Slice profile imperfections that occur in 2D imaging can be avoided, and parallel imaging can be applied in both phase-encoding directions yielding higher acceleration factors. In brain imaging, 3DEPI has been widely applied to fMRI where superior SNR efficiency compared to 2D simultaneous multislice EPI was demonstrated in Stirnberg et al. Moreover, in anatomic T2 brain imaging, 3DEPI achieved a significantly higher sampling efficiency in comparison to conventional GRE imaging at the cost of minor geometrical distortions.

Because of its typically low phase encoding bandwidth, EPI suffers not only from geometric distortions but also from a large chemical shift of the fat signal. Consequently, fat suppression techniques must be applied. Water-selective RF pulses such as spectral–spatial (SPSP) pulses are often preferred over a separate leading fat saturation pulse, because they are less sensitive to off-resonance excitation issues caused by B0 field inhomogeneities. For 3D acquisitions of the brain, non-spatially selective RF pulses may also be used, such as binomial pulses.

The T1-weighted imaging contrast is essential for most neurologic MRI exams and is well known for its excellent delineation of gray matter (GM) and white matter (WM). It is also well known for its contrast-enhancing effect following a post-gadolinium injection. Often, 3D sequences are used given their high SNR efficiency, and more importantly, an isotropic resolution is chosen to enable retrospective reformating of the image plane. Common isotropic T1-weighted imaging sequences include 3D inversion-prepared, spoiled gradient echo (IR-SPGR or MPRAGE), 3D T1-weighted turbo spin echo (T1wTSE), or simple 3D spoiled gradient echo (SPGR). High-resolution isotropic SPGR sequences can be acquired in ~2 minutes in clinical practice, whereas MPRAGE and T1wTSE typically require 3-5 minutes. Taking into account that T1-weighted sequences are often run twice, pre- and post-gadolinium, these scan durations may not only cause patients discomfort but also make the data acquisition prone to motion artifacts.

In this paper, we explore extremely fast isotropic T1-weighted imaging of the brain using a gradient echo 3D EPI sequence. Recently, 3D EPI has been used to acquire T1-weighted images that are distortion-matched with corresponding fMRI data. T1-weighted images for cerebral blood volume fMRI have also been acquired. We focus on clinical imaging, specifically imaging speed, minimizing distortions and the challenge of rapid fat suppression by comparing various types of water excitation pulses for 3D EPI. We also investigate the importance of magnetization transfer (MT) in T1-weighted imaging and quantify its impact on the GM–WM contrast. The drawbacks of EPI, such as geometric distortions, are analyzed and compared with conventional imaging techniques. The 3D EPI sequence is also applied in a clinical case to emphasize its use in time-critical situations, such as uncooperative patients that do not tolerate long scans, or as a backup to the conventional T1-weighted acquisition in case of motion corruption.

2 | METHODS

2.1 | Pulse sequence design

2.1.1 | Description of the pulse sequence

The 3D EPI pulse sequence was implemented using the KS Foundation framework. Multi-shot EPI and the echo-time-shift technique were used to minimize geometric distortions, blurring, and ghosting. A pulse sequence diagram is presented in Figure 1A. Ramp sampling was used to achieve a short echo spacing in the EPI train. The echo spacing was, however, limited by the relatively large blip area caused by the high number of shots used, which reduced the number of points sampled on the ramps significantly compared to single-shot EPI. To achieve the low TE needed for T1-weighted imaging, partial Fourier in the in-plane phase encoding direction was used. To prepare a T1 steady-state, 16 shots were used as dummy TRs. These shots were then also acquired, with both phase encoding gradients deactivated, and used as reference
The image reconstruction started with computing and applying zero and first-order phase correction coefficients for Nyquist ghost correction, followed by ramp sampling correction. Auto-calibrating reconstruction for Cartesian imaging (ARC) was used to synthesize missing k-space lines, using the fully sampled central k-space lines as calibration. Projections onto convex sets was used for partial Fourier reconstruction. A weighted sum of squares was used for coil combination, where the weights were computed from receiver noise measurements performed in the prescan.

2.1.2 | Calculations of flip angles

With approximate $T_1$ times and the relative proton density of WM and GM ($T_{1GM} = 1331$ ms and $T_{1WM} = 832$ ms, $k_{GM} = 1.0$ and $k_{WM} = 0.9$, respectively), the flip angle corresponding to the highest contrast-to-noise ratio (CNR) was estimated using the signal equation for a spoiled gradient echo, neglecting $T_2$ relaxation. For the 3D EPI scans performed in this work, the Ernst angle was $\sim 10^\circ$, and CNR was greatest around $15^\circ$.

2.2 | Radiofrequency pulse design

2.2.1 | Binomial pulses

A binomial pulse is a composite pulse consisting of rectangular sub-pulses with relative flip angles following a binomial distribution. The duration between sub-pulses ($\tau_{\text{bino}}$) is calculated with the following equation

$$\tau_{\text{bino}} = \frac{1}{2 |\Delta \omega|},$$

where $\Delta \omega$ is the frequency offset between fat and water. With the main fat peak at $-3.3$ ppm from the water peak, $|\Delta \omega|$ becomes $\sim 422$ Hz at 3T.

Two different binomial pulses were used in this work, the 1-1 and 1-2-1. The sub-pulse durations were set to 64 $\mu$s.

2.2.2 | Water exciting rectangular pulse

The water exciting rectangular pulse (WE-rect) is a rectangular or box-car shaped pulse with a specific duration such that one of the zero-crossings of its sinc-shaped frequency response matches the frequency of fat. The duration ($\tau_{\text{rect}}$) of the pulse is calculated using the following equation
\[ \tau_{\text{rect}} = \frac{\sqrt{(2\pi n^2 - n^2)}}{2\pi |\Delta\omega|}, \quad (2) \]

where \( \alpha \) is the flip angle in radians, and \( n \) is the order (specifying which zero-crossing that matches \( \Delta\omega \)). We only explored the case: \( n = 1 \), that is, the first zero-crossing coincides with the frequency of fat. Higher-order pulses have durations that are out of the useful scope of this work.

The WE-rect has comparable fat–water selectivity to a binomial 1-1 pulse but with much lower specific absorption rate (SAR) and reduced magnetization transfer (MT) effects.\(^{37,38} \) The reduced MT effect compared to binomial pulses is theorized to be a result of the sinc-shaped frequency response, with a single center frequency passband and decreasing sidebands around it.\(^{37} \) In contrast, a 1-1 pulse has many repeating passbands that excite the macromolecular (semi-solid) pool, thereby causing MT effects.\(^{39} \) The reduction of the MT effects of WE-rect pulses has been shown to increase the temporal SNR (tSNR) for 3D EPI fMRI acquisition of the MT effects of WE-rect pulses has been shown to increase the GM–WM contrast in T1-weighted imaging.\(^{40} \)

### 2.2.3 WE-rect 1-2-1

To obtain a pulse with a broader stopband (ie, improved fat suppression) while retaining the low SAR and reduced MT effects of the WE-rect, we combined the WE-rect with the binomial series.

The side lobes of a binomial pulse can be suppressed by multiplying its frequency response with the frequency response of the WE-rect. Under the small flip angle approximation, this corresponds to a convolution in the time domain. With the small flip angle approximation Equation (2) simplifies to

\[ \tau_{\text{rect}} = \frac{n}{|\Delta\omega|}, \quad (3) \]

which, for \( n = 1 \), is double the time between sub-pulses in a binomial pulse (\( \tau_{\text{bino}} \)). Therefore, a good approximation of the convolution between the WE-rect and a binomial pulse is a train of WE-rect sub-pulses overlapping by one \( \tau_{\text{bino}} \), creating a binomial pattern. For example, the convolution between the WE-rect and the binomial 1-1 would lead to a continuous 1-2-1 stair-shaped pulse with each plateau having a duration of approximately one \( \tau_{\text{bino}} \). We termed this new pulse, WE-rect 1-2-1. The duration of the WE-rect 1-2-1 will, because of the convolution, increase by \( \tau_{\text{rect}} \) compared to its base binomial pulse. For the convolution, the binomial pulse was represented by Dirac delta functions placed with a gap of \( \tau_{\text{bino}} \) and scaled by the binomial coefficients.

### 2.2.4 WE-SLR

We also created a Gaussian-shaped water excitation pulse with a duration of 4.0 ms. A minimum-phase Parks-McClellan optimal equiripple finite impulse response (FIR) filter and the inverse Shinnar-Le Roux (SLR) transform\(^{41} \) was used to calculate its envelope. The shape of the FIR filter depends on three input design parameters: the time-bandwidth product (TBW) and the ripple in the pass- and stopband (\( \sigma_1 \) and \( \sigma_2 \)). The TBW was set to 2.0, whereas the design parameters \( \sigma_1 = 0.001 \) and \( \sigma_2 = 0.009 \) were found heuristically. For this WE-SLR pulse, we chose this low TBW to get a passband narrow enough to only excite water while keeping the duration as short as possible.

### 2.3 Experiments

A total of six experiments were carried out. If not stated otherwise, the settings for the 3D EPI acquisitions were: FOV = 24 cm, 192 × 192 matrix, 1.2 mm isotropic voxels, sagittal scan orientation with frequency encoding direction superior-inferior, 160 z-segments in the left–right direction, phase encoding bandwidth per pixel = 93 Hz, echo spacing = 0.98 ms, readout plateau gradient strength = 24.5 mT/m, partial Fourier factor = \( \frac{2}{3} \), ETL = 8, \( R_y = 2 \), 16 shots per \( k_z \) plane, and 16 auto-calibration lines. The number of shots is stated as the number of shots it takes to fill an unaccelerated \( k_z \) plane. The different parameter settings of all experiments are summarized in Table 1. The blip-direction of the EPI train was in the anterior–posterior direction, hence also the direction of geometric distortions. Five volunteers and three patients were scanned under local ethical approval. One volunteer was imaged for experiment A, and five, including the previously mentioned subject, were imaged for experiment C. The three patients were imaged in experiment D. All experiments were performed on a GE 3T SIGNA Premier (GE Healthcare, Waukesha, WI), using a 48-channel head coil.

Because the 3D EPI acquisitions were performed with a superior–inferior frequency encoding direction, flow artifacts were mitigated, and the use of spatial saturation bands could be avoided. An additional experiment was performed to show these benefits, the results of which can be found in Supporting Information Figure S1.

#### 2.3.1 Experiment A

To show the geometrical distortions and chemical shift-related artifacts, five brain scans were performed with a decreasing number of shots (from 32 to 8), therefore, decreasing phase encoding bandwidth. The partial Fourier factor had to
be adjusted to ensure divisibility, resulting in ETLs ranging from 5 to 16. Each scan was run twice, once using a 0.1-ms hard pulse and once with the WE-rect pulse. Because the TR increased, the flip angle was adjusted to optimize the GM/WM CNR for each scan using the method described above.

For comparison, a sagittal 3D SPGR was acquired using the same 0.1-ms hard pulse, the same FOV, and voxel size as the 3D EPI, but with a circular \( k\)-space \((k_y, k_z)\) acquisition scheme. Other SPGR sequence parameters were TR = 5.5 ms, TE = 2.5 ms, and FA = 9°, resulting in a scan duration of 68 seconds.

### 2.3.2 Experiment B

Bloch simulations for all RF pulses were performed in MATLAB (The MathWorks, Natick, MA) with a flip angle of 20°. To compare the SAR of the different RF pulses, the B1 RMS area of the pulses was calculated and scaled relative to the binomial 1-1 pulse. The flip angle dependence of the WE-rect is negligible for excitation pulses, but because the WE-rect 1-2-1 was based on the small flip angle approximation, its flip angle-dependency was investigated. This was done by Bloch simulating flip angles between 1° and 90°.

For the interested reader, the simulated frequency responses of the RF pulses were experimentally validated using the method laid out in Block et al.

### 2.3.3 Experiment C

Next, the impact of RF pulses on the contrast between GM and WM was explored. Five volunteers were imaged five times using the five different RF pulses. Except for the choice of the excitation pulse, all parameters were kept identical. To encompass the WE-SLR, which is the longest of the RF pulses, the TR was set to 20 ms and the TE to 5.1 ms. This resulted in additional dead times both before and after the readout for all sequences not using the WE-SLR.

The contrast was measured by segmenting GM and WM using SPM12. First, the five-image volumes of each volunteer were coregistered and resliced to their mean volume. A new mean volume was then calculated from the coregistered images, and segmentation was done with that volume, using the default settings. The resulting probability maps for GM and WM were used to create binary masks containing only voxels with a probability higher than 95%. The Michelson contrast was calculated as the difference between the mean values of GM and WM in these masks.

### Table 1

| Figure reference | TR (ms) | TE (ms) | Flip angle (°) | ETL | Number of shots per \( k_z \) plane | Partial Fourier factor | Acquisition time (s) | RF pulse                  |
|------------------|--------|--------|----------------|-----|-----------------------------------|------------------------|----------------------|--------------------------|
| **Experiment A** |        |        |                |     |                                   |                        |                      |                          |
| 1A and 2A        | 5.5    | 2.5    | 9              | 1   | N/A                               | N/A                    | 68                   | Hard pulse               |
| 1 and 2B         | 9.7    | 2.9    | 12             | 5   | 32                                | 5/6                    | 29                   | Hard pulse               |
| 1 and 2C         | 10.5   | 2.8    | 13             | 6   | 24                                | 3/4                    | 24                   | Hard pulse               |
| 1 and 2D         | 12.3   | 2.7    | 14             | 8   | 16                                | 2/3                    | 19                   | Hard pulse               |
| 1 and 2E         | 20.0   | 4.7    | 18             | 16  | 8                                 | 2/3                    | 15                   | Hard pulse               |
| 1 and 2F         | 11.9   | 4.0    | 14             | 5   | 32                                | 5/6                    | 36                   | WE-rect                  |
| 1 and 2G         | 12.8   | 4.0    | 14             | 6   | 24                                | 3/4                    | 29                   | WE-rect                  |
| 1 and 2H         | 14.5   | 3.9    | 15             | 8   | 16                                | 2/3                    | 22                   | WE-rect                  |
| 1 and 2J         | 22.3   | 5.8    | 18             | 16  | 8                                 | 2/3                    | 17                   | WE-rect                  |
| **Experiment C** |        |        |                |     |                                   |                        |                      |                          |
| 5A               | 20     | 5.1    | 18             | 8   | 16                                | 2/3                    | 30                   | Binomial 1-1             |
| 5B               | 20     | 5.1    | 18             | 8   | 16                                | 2/3                    | 30                   | WE-rect                  |
| 5C               | 20     | 5.1    | 18             | 8   | 16                                | 2/3                    | 30                   | Binomial 1-2-1           |
| 5D               | 20     | 5.1    | 18             | 8   | 16                                | 2/3                    | 30                   | WE-rect 1-2-1            |
| 5E               | 20     | 5.1    | 18             | 8   | 16                                | 2/3                    | 30                   | WE-SLR                   |
| **Experiment D** |        |        |                |     |                                   |                        |                      |                          |
| 7A,C, 8A,C, and 9A,C | 6.9  | 2.8    | 12             | 1   | N/A                               | N/A                    | 230                  | Adiabatic inversion and minimum-phase excitation |
| 7, 8, 9B, and 9D | 15.7   | 4.5    | 16             | 8   | 16                                | 2/3                    | 24                   | WE-rect 1-2-1            |

Note: The number of shots is specified as the number of shots that it takes to acquire a fully sampled \( k_z \) plane.
GM compartment and the mean WM compartment, divided by their sum. This approach relies on prior receive coil sensitivity correction, which was performed on all volumes based on a separate coil sensitivity calibration scan for each volunteer (known as PURE on GE MR systems).

2.3.4 | Experiment D

Three patients were imaged pre- and post-gadolinium injection using the 3D EPI sequence. In this case, the 3D EPI used the WE-rect 1-2-1 pulse, with minimum TE = 4.5 ms, minimum TR = 15.7 ms, and an acquisition time of 24 seconds. As part of the clinical protocol, a T1-weighted 3D inversion recovery SPGR (IR-SPGR) sequence (BRAVO, GE Healthcare) was also acquired before and after gadolinium administration. The 3:50-min long IR-SPGR scan was acquired before the 3D EPI and had 1-mm isotropic voxels, TR = 6.9 ms, TE = 2.8 ms, and IR = 450 ms.

3 | RESULTS

3.1 | Experiment A

In Figures 2 and 3, a conventional SPGR image (Figures 2A and 3A) is compared to 3D EPI acquisitions (Figures 2B-I and 3B-I) using a hard water excitation pulse and a decreasing number of shots. Despite sharing the same hard pulse, the fat signal appears notably darker in 3D EPI images compared to SPGR, likely because of the self-interference of the different fat resonances during the echo train. The pure chemical-shift effect of fat applies only to the center of k-space (along the frequency encoding direction), whereas at the edges, the phase accrual of fat along the phase direction is no longer a simple phase ramp, which may lead to signal loss added to the chemical-shift displacement in the image domain. The fat signal causes some notable smearing artifacts (green arrow) even for the 32-shot acquisition where the phase encoding bandwidth per voxel is comparable to the SPGR acquisition.

FIGURE 2  (A) An SPGR acquisition using a hard pulse, for reference. (B-E) 3D-EPI scans with a decreasing number of shots per k-plane acquired with a hard pulse that excites both fat and water. (F-J) The same scans, but acquired with a WE-rect RF pulse, only exciting water. The sequence example described in Figure 1 corresponds to (H). The green arrows point to artifacts arising from unsaturated fat signal in the EPI acquisitions using the hard pulse. The bottom row shows axial reformats, where signal pileup above the nasal cavity is marked by orange arrows. The BW per pixel of the SPGR and the phase encoding BW (pBW) per pixel of the EPI acquisitions are also shown.
Figures 2F-I and 3F-I confirm that the aforementioned artifacts vanish if a water excitation pulse, in this case, the WE-rect, is used instead of a hard pulse. Figures 2F-I and 3F-I show axial reformats at the level of the basal frontal lobe. The image quality in the region close to the nasal cavity (orange arrow) deteriorates with fewer shots and the well-known signal pileup artifacts or geometric distortions start to form. For this work, we concluded that 16 shots or a phase encoding bandwidth of 93 Hz per voxel was the best compromise between image quality and acquisition time.

3.2 | Experiment B

The five water excitation pulses implemented for this work are depicted in Figure 4A-E and their corresponding frequency responses in Figure 4F. The frequency responses of the WE-rect and the WE-rect 1-2-1 show stopband ripples that rapidly diminish with the distance from the center frequency, unlike the binomial pulses. The WE-SLR causes a frequency response with lower and more constant amplitude ripples. The WE-rect and the binomial 1-1 both have similar passbands, and the WE-rect 1-2-1 and the WE-SLR have almost the same passband as the binomial 1-2-1.

Moreover, the low amplitudes of the WE-rect, WE-rect 1-2-1, and WE-SLR pulses result in largely reduced B$_1$ RMS (that is proportional to SAR) between 11% and 17% compared to the binomial 1-1 pulse.

In Figure 4G, the flip angle dependence of the WE-rect 1-2-1 can be observed. Below 20°, there is only a slight widening of the stopband, but above 30°, the stopband starts to split up into two frequency offsets straddling the fat resonance frequency, leading to less ideal fat suppression. However, the effect is small and negligible at flip angles around 15° used in this work.

The results of the experimental validation of the frequency responses are presented in Supporting Information Figure S2.

3.3 | Experiment C

In Figures 5A-E, the benefit of the pulses with decreasing sideband amplitude (the WE-rect, WE-rect 1-2-1, and WE-SLR pulse) can be identified. They provide superior fat suppression.
in cases where $B_0$ fluctuations shift the fat peak to lower frequencies. This effect appears in the neck region and is pointed out by purple arrows. The wider stopbands of the WE-rect 1-2-1 pulse with flip angles ranging from 1° to 90°. The computed flip angle on the vertical axis is the nominal flip angle at the frequency of water. The horizontal axis shows a frequency band centered around the main frequency of fat. The color map corresponds to the relative flip angle of each computed pulse, scaled to the flip angle at the frequency of water. The solid white lines indicate 1% of the flip angle of water. The stopband of the WE-rect 1-2-1 widens slightly as the flip angle increases and eventually splits in two. However, this effect is negligible for the ~15° flip angles used in this work.

**FIGURE 4**  (A-E) Plots of all five evaluated RF pulses. (F) Bloch-simulated frequency response curves at a flip angle of 20° for all RF pulses. The side lobe amplitudes of the WE-rect pulses and the WE-SLR are significantly lower than those of the binomial pulses. (G) Bloch simulations of the WE-rect 1-2-1 pulse with flip angles ranging from 1° to 90°. The computed flip angle on the vertical axis is the nominal flip angle at the frequency of water. The horizontal axis shows a frequency band centered around the main frequency of fat. The color map corresponds to the relative flip angle of each computed pulse, scaled to the flip angle at the frequency of water. The solid white lines indicate 1% of the flip angle of water. The stopband of the WE-rect 1-2-1 widens slightly as the flip angle increases and eventually splits in two. However, this effect is negligible for the ~15° flip angles used in this work.

The observations that were made in Figure 5 were quantified by the GM–WM contrast measurements presented in Figure 6. The WE-rect, WE-rect 1-2-1, and WE-SLR pulse, compared to those acquired using the binomial 1-1 and binomial 1-2-1.

Enlarged images of the cerebellum and lower brain are shown in Figure 5F-J, where a more clear GM–WM differentiation can be perceived in the images acquired with the WE-rect, WE-rect 1-2-1, and WE-SLR pulse, compared to those acquired using the binomial 1-1 and binomial 1-2-1.

The observations that were made in Figure 5 were quantified by the GM–WM contrast measurements presented in Figure 6. The WE-rect, WE-rect 1-2-1, and WE-SLR pulse result in a mean GM–WM matter contrast increase of 20%, 20%, and 19%, respectively, compared to the 1-1 binomial pulse. The binomial 1-2-1 achieves a slightly improved
contrast compared to the binomial 1-1, with a mean GM–WM matter contrast increase of 3% compared to the 1-1 binomial pulse.

3.4 | Experiment D

Figure 7 shows sagittal, axial, and coronal reformats of a 70-year-old patient with brain metastases from esophageal cancer, comparing pre- and post-gadolinium injection images acquired with conventional 3D IR-SPGR and 3D EPI. Figure 8 presents the same comparison for a 77-year-old patient operated for hemangiopericytoma and Figure 9 shows a 61-year-old patient with two metastasis. As expected, the 3D IR-SPGR provides better contrast and image sharpness owed to the inversion preparation, higher resolution and the far shorter readout, but at the cost of approximately ten times longer scan time. Overall, 3D IR-SPGR and 3D EPI show comparable features of the tumors and the gadolinium enhancement is visible on both.
We have optimized a 3D EPI sequence for T1-weighted brain imaging and have achieved scan times of ~24 seconds for an isotropic scan with a resolution of 1.2 × 1.2 × 1.2 mm³. A conventional SPGR acquisition with the same resolution took more than three times longer, providing similar image quality, whereas a clinical 3D IR-SPGR usually requires 3-4 minutes scan time, which is approximately ten times longer.

The short scan times of 3D-EPI are unattainable with conventional Cartesian GRE readouts. The SNR penalty for ultra-short TR 3D SPGR sequences is substantial because of the high readout bandwidth and the increased T1 saturation. On the contrary, 3D EPI achieves far higher SNR efficiency owing to the much longer sampling time per RF excitation pulse, therefore, using the $T_2^*$ decaying MR signal more efficiently. Alternatively, advanced parallel imaging techniques such as wave-CAIPI might be able to achieve similar scan times but at the expense of additional calibration.

![FIGURE 7](image_url)

**FIGURE 7** A 70-year-old patient with brain metastases, imaged before and after gadolinium injection with 3D IR-SPGR and 3D EPI. (A) Axial 3D IR-SPGR pre-gadolinium acquisition with sagittal and coronal reformats. (B) Sagittal 3D EPI pre-gadolinium acquisition with axial and coronal reformats. (C and D) Same acquisitions and reformats as (A) and (B) after gadolinium injection. The green arrows point to a small region of signal pileup in 3D EPI. The blue arrows point to one of the metastases in the cerebellar vermis, where the gadolinium enhancement is slightly less visible on the 3D EPI than on the IR-SPGR. The red arrow points to minor motion artifacts in the 3D IR-SPGR acquisition.

### Table: Scan Times Comparison

|          | Pre-Gadolinium | Post-Gadolinium |
|----------|----------------|-----------------|
| 3D IR-SPGR | Acq. = 3:50 min | Acq. = 3:50 min |
| 3D EPI    | Acq. = 24 sec  | Acq. = 24 sec   |
| 3D IR-SPGR | Acq. = 3:50 min | Acq. = 3:50 min |
| 3D EPI    | Acq. = 24 sec  | Acq. = 24 sec   |

**4 | DISCUSSION AND CONCLUSIONS**
and reconstruction effort. Unlike wave-CAIPI, we used only a parallel imaging factor of $R = 2$, making 3D EPI compatible with almost all head coils. Additionally, the Cartesian acquisition scheme and the conventional parallel imaging approach enables reconstruction times of a few seconds and is hence well suited for clinical use.

Axial $T_1$-weighted 3D EPI seemed very vulnerable to pulsation artifacts, for example, of the Carotids. A sagittal scan plane with frequency encoding in superior-inferior direction, as suggested for example in Mugler and Brookeman, reduced these artifacts to almost zero. Inferior saturation bands were also able to suppress pulsation artifacts for axial acquisitions but dramatically reduced the contrast between GM and WM because of MT effects.

The biggest concern about EPI is typically the geometrical distortions. However, with 16 shots per $k_z$ plane, a phase encoding bandwidth of 93 Hz per voxel was achieved, which sufficiently reduced the geometrical distortions. Only in the direct vicinity of large susceptibility gradients at air/tissue interfaces, minor signal pileups remain (Figure 7B,D). Furthermore, we found that fat suppression is needed, although the chemical-shift of fat should be only ~4.5 voxels, which might be tolerable for brain imaging. The fat signal did not only shift but also caused some smearing artifacts.

**FIGURE 8** A 77-year-old patient operated for hemangiopericytoma. (A) Axial 3D IR-SPGR pre-gadolinium acquisition with sagittal and coronal reformats. (B) Sagittal 3D EPI pre-gadolinium acquisition with axial and coronal reformats. (C and D) Same acquisitions and reformats as (A) and (B) after gadolinium injection. One remaining tumor recidive is marked with red arrows.
and ringing in the frontal lobe. We speculate that this may be caused by the multi-peak spectrum of fat and additionally by the odd-even readout of EPI, which also causes a smearing of the point spread function, especially at high off resonances. Therefore, efficient fat suppression is a requirement for T1-weighted 3D EPI.

It has been shown that the WE-rect RF pulse improves the tSNR of fMRI time series. This was attributed to lower MT effects because of less off-resonance excitation. In this work, we have shown that water excitation pulses with diminishing sidebands can notably improve GM–WM contrast by around 20% in T1-weighted imaging compared to a binomial 1-1 pulse. However, there was no significant difference in GM–WM contrast comparing the WE-rect and WE-rect 1-2-1 to the WE-SLR, even though the WE-SLR has slightly less off-resonance excitation (Figure 4F). When comparing the binomial 1-1 and 1-2-1, there is a slight increase in GM–WM contrast using the binomial 1-2-1. This can be explained by the more narrow passbands of the binomial 1-2-1 pulse, which reduces the overall area of the sidebands and the MT effect.

The WE-rect 1-2-1 and the WE-SLR did provide a more reliable water selectivity than the WE-rect. However, the fat suppression attained with the WE-rect seemed to be satisfactory for brain imaging. If 3D EPI were to be used in other parts of the body, for example, cervical spine or neck imaging, pulses with a wider stopband, such as the WE-rect 1-2-1.

**FIGURE 9** A 61-year-old patient with two metastasis, previously treated with gamma knife surgery. (A) Axial 3D IR-SPGR pre-gadolinium acquisition with sagittal and coronal reformats. (B) Sagittal 3D EPI pre-gadolinium acquisition with axial and coronal reformats. (C and D) Same acquisitions and reformats as (A) and (B) after gadolinium injection.
or the WE-SLR, may be beneficial. The WE-rect could also be convolved with any binomial pulse to create pulses that have superior water selectivity.

WE-rect pulses rely on the flip angle to achieve the correct nulling frequency. $B_1$ field imperfections cause a slight shift of the nulling frequency as well as an incorrect flip angle. At the flip angles used in this work, the effect is negligible. However, a disturbance in the $B_1$ field only impacts the flip angle (ie, no frequency shift) for the binomial pulses and the WE-SLR, giving the WE-SLR an advantage for high flip angle applications.

Concerning inhomogeneities in the $B_0$ field, the pulses with reduced sideband excitations (ie, the two WE-rect pulses and the WE-SLR) are advantageous. If a $B_0$ field fluctuation shifts the water and fat peaks to lower frequencies, the main fat peak is not subject to a large sideband excitation, as when using the binomial pulses. This effect can be seen in Figure 5. The binomial 1-1 and the WE-rect should be somewhat more resistant to causing erroneous flip angles because their passband is slightly wider.

The ultra-fast $T_1$-weighted 3D EPI sequence achieved an image quality that is competitive with a conventional 3D SPGR acquisition. The short acquisition time unlocks many possible uses for the $T_1$-weighted 3D EPI sequence.

The sagittal acquisition strategy allows for a large FOV in the SI direction with a minimal scan time penalty. This might enable, for example, simultaneous imaging of the cervical spine (Figure 7). The limiting factor for this approach is only the spatial uniformity of the fat suppression, and the WE-rect 1-2-1, or the WE-SLR might be best suited for this application.

A 24-s $T_1$-weighted sequence with isotropic resolution and full head and neck coverage would be an excellent addition to a single-shot EPI based multi-contrast sequence such as EPIMix. The drastically reduced geometric distortions and the ability to reformat the data increases the diagnostic value, making EPIMix a more standalone screening sequence.

For quantitative imaging, $T_1$ weighted 3D EPI seems well-suited for rapid multi-flip angle $T_1$ mapping techniques like DESPOT significantly shortening scan times.

Given the results so far, it is likely that $T_1$-weighted 3D EPI can be of value for gadolinium-enhanced imaging. We presented in this work an example of how 3D EPI compares to an almost ten times longer 3D IR-SPGR with encouraging results. Still, minor signal pileups (Figure 7B,D) in the 3D EPI may be confused with Gd enhancement at first glance but potential doubts can be eliminated by comparison with the pre-Gd image (that also includes the signal pileup). Gadolinium contrast is costly, and administering it may cause patient discomfort and potential long term retention in the brain. Therefore, it is essential to combine it with a high-resolution 3D SPGR or 3D RARE $T_1$-weighted scan. However, such sequences might not be successful for uncooperative, motion prone or claustrophobic patients because of motion corruption or premature termination of the scan. In this case, 3D EPI could be used as an ultra-short alternative or as a backup.

There is also the fact that inversion prepared $T_1$-weighted imaging, despite its superior dynamic range, may miss the gadolinium enhancement because of an unfavorable zero-crossing of the signal relaxation. In this case, 3D EPI could be used as a non-IR backup scan to resolve potential doubts.

With higher parallel imaging acceleration, scan times of less than 10 seconds are feasible, using the short WE-rect, for the given resolution or much less for lower image resolutions, provided a high channel count head coil is used. Therefore, $T_1$-weighted 3D EPI might be suitable for dynamic imaging of gadolinium enhancement. Additionally, the acquisition times could be further reduced using an existing external calibration to reconstruct the missing data instead of internal auto-calibration data that was used in this work.

In conclusion, there is a need for rapid $T_1$-weighted imaging, and 3D EPI is a strong contender given its sheer speed, fast and straightforward reconstruction. We have optimized the sequence for an isotropic resolution of 1.2 mm, most notably, using water exciting pulses with minimal MT effects, sagittal scan orientation and a very high phase encoding bandwidth of almost 100 Hz, achieving an image quality very similar to a conventional 3D SPGR sequence while taking only 24 seconds.

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

**FIGURE S1** Three scans were performed; one sagittal with frequency encoding direction superior-inferior and two axial with frequency encoding direction left–right, where the latter axial scan had a spatial saturation pulse applied inferior to the imaging volume. The sagittal scan used the WE-rect for excitation and the axial scans used a slab selective unipolar flyback SPSP pulse with three sub-pulses, retaining a low TE. The matrix sizes in slice direction were 110 and 160 for the axial and sagittal acquisitions, respectively. (A) Axial acquisition, sagittal reformat. (B) Axial acquisition with inferior saturation, sagittal reformat. (C) Sagittal acquisition. (D) Axial acquisition (same as a). (E) Axial acquisition with inferior saturation (same as B). (F) Sagittal acquisition, axial reformat. Green and purple arrows point to flow artifacts arising in the axial acquisitions. The saturation band causes magnetization transfer effects that dramatically reduce the contrast between GM and WM.

**FIGURE S2** Measured on phantom and Bloch simulated frequency responses of the RF pulses evaluated in this work. A constant Gy pulse was used to generate the spectral dimension across the FOV. The signal was acquired using an SPGR sequence and using the single-channel body coil for transmit and receive, to remove multi-channel coil non-uniformities. The images were then compared to Bloch simulations.

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