High-resolution three-dimensional T₂-weighted sequence for neuronavigation: a new setup and clinical trial

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Object. Conventional imaging for neuronavigation is performed using high-resolution computerized tomography (CT) scanning or a T₁-weighted isovoxel magnetic resonance (MR) sequence. The extension of some lesions, however, is depicted much better on T₂-weighted MR images. A possible fusion process used to match low-resolution T₂-weighted MR image set with a referenced CT or T₁-weighted data set leads to poor resolution in the three-dimensional (3D) reconstruction and decreases accuracy, which is unacceptable for neuronavigation. The object of this work was to develop a 3D T₂-weighted isovoxel sequence (3D turbo–spin echo [TSE]) for image-guided neuronavigation of the whole brain and to evaluate its clinical application.

Methods. The authors performed a phantom study and a clinical trial on a newly developed T₂-weighted isovoxel sequence, 3D TSE, for image-guided neuronavigation using a common 1.5-tesla MR imager (Siemens Sonata whole-body imager). The accuracy study and intraoperative image guidance were performed with the aid of the pointer-based Medtronic Stealth Station Treon.

Conclusions. Three-dimensional TSE imaging broadens the spectrum of navigational and intraoperative data sets, especially for lesions that appear hyperintense on T₁-weighted images. The accuracy of its registration is very reliable and it enables high-resolution reconstruction in any orientation, maintaining the advantages of image-guided surgery.

KEY WORDS • neuronavigation • isovoxel sequence • glioma • three-dimensional turbo–spin echo magnetic resonance imaging

Abbreviations used in this paper: CT = computerized tomography; FOV = field of view; fMR = functional magnetic resonance; MPR = multplanar reconstruction; RMSE = root mean square error; SD = standard deviation; TSE = turbo–spin echo; WHO = World Health Organization; 3D = three-dimensional.

Computers-assisted neuronavigation for intraoperative viewing of anatomical landmarks is being increasingly used for surgical removal of intracranial lesions. High-resolution 3D data sets are therefore gaining importance in preoperative imaging. The standard imaging method for neuronavigation is the high-resolution CT scan and the T₁-weighted isovoxel MR sequence (T₁-weighted MPR), depending on the characteristics of the lesion and the need for an additional application of contrast agent. Other modalities, such as T₂-weighted or fluid-attenuated inversion recovery–weighted MR images, can also be integrated or fused using some navigational systems. These images can be fused automatically or semiautomatically by using anatomical landmarks to overlay images within the 3D data set. This procedure bears the risk of a fusion mistake and may therefore decrease the accuracy of such sequences. The use of poor-resolution images (usually in axial orientation with a 3- to 5-mm slab thickness) in MPR can compromise anatomical observation in the remaining orientations (Fig. 1). For some types of lesion, such as low-grade gliomas, cystic lesions, or the hemorrhagic rim surrounding cavernomas, T₁-weighted images provide much better delineation than T₂-weighted MPR images. Nevertheless, the neuronavigational approaches to these lesions have not yet been covered by an adequate 3D sequence.

The object of the study was to develop a 3D T₂-weighted isovoxel sequence, 3D TSE, for navigational purposes and to evaluate the feasibility of this sequence in an experimental study and a clinical trial. The advantages a 3D T₂-weighted isovoxel sequence has over conventional imaging techniques are discussed, and clinical indications for the neuronavigation it provides are highlighted.

Clinical Material and Methods

Systems and Sequences

All experiments were performed using a Sonata 1.5-tesla whole-body MR imaging unit (Siemens, Erlangen, Germany) equipped with a 40 mtesla/m (200 mtesla/m/ms) gradient system and a circularly polarized standard head coil. Syngo MR 2002B (VA21B) software was used (Siemens). The standard 3D-shimming procedure was performed automatically before each new sequence-loading step.

In addition to a single-shot echo-planar imaging sequence for fMR imaging studies, both a T₁-weighted 3D TSE sequence (FOV 204 × 256 mm², matrix 204 × 256, turbo factor 25) and a 3D-turbo fast–low angle shot with magnetization-prepared rapid gradient echo (FOV 224 ×
Three-dimensional T2-weighted imaging

![Image](image_url)

**Fig. 1.** Fusion of a high-resolution CT scan with axial T2-weighted MR images (5-mm slab thickness). The anatomical resolution in the axial orientation (left) is adequate, whereas 3D reconstructions in the sagittal (center) and coronal (right) orientations provide insufficient resolution for neuronavigational purposes. The boundaries separating cerebrospinal fluid from the tumor and from normal brain tissue in this case of a recurrent low-grade glioma are poorly identified.

256 mm², matrix = 224 × 256) for anatomical imaging were performed, each with an isotropic 1-mm³ voxel for the MPR, resulting in FOV of 256 mm after interpolation. The MPR type of sequence is characterized by the magnetization, which includes a nonselective inversion 180° radiofrequency pulse and the echo acquisition for the whole partition after an inversion time of 710 msec. The repetition time was set to 2000 msec and the echo time to 3.93 msec to guarantee enough relaxation between image acquisitions to avoid saturation effects. The 3D TSE sequence possesses two major advantages: minimization of susceptibility artifacts due to successive spin echoes and a high isotropic spatial resolution. The contrast and image quality is comparable to that of the conventional spin-echo technique. A turbo factor of 25 means that a corresponding number of phase-encoded echoes is acquired using a single shot, thus reducing the measurement time by a factor of M/N, where M is the matrix dimension (256) and N is the turbo factor. Saturation effects at the transitions of the slabs (in our experiments 15 slabs containing 10 slices each) can be avoided by selecting two concatenations. This means that the sequence steps to the next slice after acquiring two echoes and does not sample the remaining raw data lines for the previous slice position until a later time. With a repetition time of 2570 msec and an echo time of 106 msec, the measurement takes 12 minutes, 27 seconds depending on the size of the patient’s head.

The Neuronavigation Process

Intraoperative image guidance was achieved using a pointer-based navigation system (Stealth Station Treon, Mach 4.1 software; Medtronic, Inc., Louisville, KY). The disposable skin fiducial markers (Medtronic, Inc.) are easily identified in the 3D TSE sequence due to the T2-weighted hyperintense signal caused by the moisture of the fiducial. The navigation system calculates the registration accuracy, given as the RMSE, by using a matching algorithm after successful registration of six to 14 disposable skin fiducial markers. The algorithm is used to compare the relationship of the fiducial marker’s position on the images with that on the patient’s head during the preoperative registration procedure. The RMSE is therefore an indicator of registration accuracy, which needs to be verified by checking defined landmarks.

**Phantom Study**

Many MR sequences are prone to artifacts that may lead to distortion in the 3D geometry. To rule out these artifacts, which are unacceptable for neuronavigation, we performed a pilot study in which we used a 17-cm-diameter spherical phantom (Fig. 2).

To evaluate the distortion in the 3D geometry depending on the imaging modality, we used the accuracy check of the navigation system for the registration process. Three experimental trials were performed, in which seven, nine, and 14 disposable skin fiducial markers were placed in different attachment patterns. Three additional fiducial markers were applied in each trial as “artificial landmarks” and were not included in the registration procedure. Each trial involved a high-resolution CT scan as well as the 3D TSE and T2-weighted MPR sequences covering the entire phantom.

The nine data sets obtained from the three trials were integrated into the neuronavigation system and the registration procedure was performed by referencing the fiducial markers without any surface merging. The RMSE was recorded and a landmark check was made on the additional fiducial markers.

**Clinical Trial**

In the prospective clinical trial 25 patients underwent surgery in the initial prospective evaluation, by using the 3D TSE sequence. The patients ranged in age from 30 to 64 years (mean age 43 years). All patients had intracranial lesions that were better delineated on preoperative T2-weighted images than on T1-weighted images or CT scans. To make contrast-enhancing lesions visible, in some cases an additional T2-weighted MPR sequence was added. After registration of the eight to 10 skin fiducial markers, surface merging was performed. An accuracy of 2.5 mm or less is tolerated by the navigation system and is double-checked by identifying the landmark before starting surgery. In cases in which there is insufficient accuracy, the registration process has to be repeated or the navigation process terminated. The intraoperative setup for the navigation system within the operating room was not changed for this study. In selected cases, data from fMR images were integrated in the 3D TSE sequence.

Apart from neuronavigation, the 3D TSE sequence has
been routinely used for diagnostic imaging in more than 60 patients with various diseases thus far. The study design accords with the guidelines of our institute's ethics committee and was performed according to regulations outlined in the revised Declaration of Helsinki of 1998.

**Results**

**Phantom Study**

The high-resolution CT scanning as well as the T₁-weighted MPR and 3D TSE MR sequences had comparable registration accuracy in the phantom study. The mean RMSE was 1.1 mm (range 0.68–1.35 mm) for CT scanning, 1.4 mm (range 0.81–1.9 mm) for T₁-weighted MPR imaging, and 1.3 mm (range 0.9–1.6 mm) for 3D TSE imaging.

In each landmark checking trial, the distance from the landmark's calculated position in the navigational setup to its real position on the phantom (the center of additional fiducial markers) was less than 1.5 mm. The results confirmed that the 3D TSE sequence maintained the 3D geometry without major distortions.

**Clinical Application**

In clinical use (Table 1) the 3D TSE data set was easily integrated into the navigation process in 24 cases. In 21 cases neuronavigation was performed using 3D TSE imaging alone, and in four cases an additional T₁-weighted MPR sequence was integrated to make visible contrast-enhancing anatomical structures (for example, blood vessels or an accompanying developmental venous anomaly). The fusion result was controlled by the correspondence of the fiducial markers and landmarks in both 3D data sets. In one case, a technical malfunction of the navigation system unrelated to the use of 3D TSE imaging occurred after successful registration.

In 17 cases a neuronavigation-guided minimally invasive craniotomy was performed and the lesion resected. In one case of glioma a subtotal resection was obtained, and in five cases a stereotactic biopsy via a burr-hole trepanation was performed. The decision to perform a biopsy depended on the localization of the lesion near eloquent areas of the cortex and the expected histological characteristics of the lesion.

The calculated mean registration accuracy after surface merging for the 3D TSE sequence was sufficient in all cases (RMSE ≤ 2.1 mm, mean ± SD 1.62 ± 0.32 mm). Anatomical landmark checks confirmed absolutely satisfactory clinical accuracy in all cases.

The 3D TSE sequence provided in these selected cases a valid intraoperative delineation of the lesion combined with the advantages of neuronavigation, especially when used in patients with low-grade gliomas (15 cases), WHO Grade III astrocytomas without definite contrast enhancement (five cases), and cavernomas (three cases).

In the one patient harboring a glioblastoma multiforme, the coreferenced conventional T₁-weighted MPR sequence obtained after contrast enhancement had been used for stereotactic biopsy because it made visible a small contrast-enhancing area; the 3D TSE sequence had no significant influence on surgery in this case.

In a patient with an arteriovenous malformation the flow void appearing on T₂-weighted images delineated the extent of the lesion more precisely than the contrast enhancement with flow artifacts in the additional T₁-weighted MPR sequence.

The high resolution allowed precise visibility in the MPR image and in the different guidance mode of the navigation system, for example, illustration along the trajectory for a stereotactic biopsy. The cortical blood vessels could be easily identified by the flow void, which appeared hypointense on T₂-weighted images, and was made visible for planning of a craniotomy or burr-hole trepanation.

**Illustrative Cases**

**Case 1**

This 26-year-old patient presented with a 3-year history of complex partial seizures while receiving anticonvulsive multidrug therapy. A T₁-weighted MPR sequence in

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**TABLE 1**

**Patient population and histological findings**

<table>
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<tr>
<th>Characteristic</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>sex (no. of patients)</td>
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<td>male</td>
<td>14</td>
</tr>
<tr>
<td>female</td>
<td>11</td>
</tr>
<tr>
<td>mean age of patients (yrs)</td>
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<tr>
<td>female</td>
<td>41.3</td>
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<tr>
<td>histological diagnosis (no. of patients)*</td>
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<tr>
<td>astrocytoma Grades I &amp; II</td>
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</tr>
<tr>
<td>oligoastrocytoma Grade II</td>
<td>2</td>
</tr>
<tr>
<td>astrocytoma Grade III</td>
<td>5</td>
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</tr>
<tr>
<td>cavernoma</td>
<td>3</td>
</tr>
<tr>
<td>arteriovenous malformation</td>
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</tr>
</tbody>
</table>

* Tumor grades are based on the WHO classification.
Three-dimensional T₂-weighted imaging

![Fig. 3. Multiplanar reconstruction in a case of a left temporal cavernoma using T₁-weighted (T₁-weighted MPR, upper) and T₂-weighted (3D TSE, lower) data sets.]

three orientations (axial, coronal, and sagittal; Fig. 3 upper) and a 3D TSE sequence in the same three orientations (Fig. 3 lower) revealed a cavernoma in the right postcentral region. The hypointense rim surrounding the cavernoma on the T₂-weighted images represented a hemosiderin deposit caused by microhemorrhages. The 3D TSE sequence, which proved superior to the T₁-weighted data set in illustrating the region surrounding the cavernoma, was applied to the navigational setup (RMSE 1.8 mm). The cavernoma and its hemosiderin rim could be completely removed by minimal craniotomy. Neuropathological examination confirmed the expected cavernoma. No neurological deficits remained. The patient was seizure free during the early postoperative course and remained so at the 6-month follow-up examination.

Case 2

The 54-year-old patient presented with simple partial seizures without focal neurological deficits. Preoperative T₁-weighted images obtained in the axial and coronal (Fig. 4 upper left and center) orientations revealed no contrast enhancement of the invasive tumor in the left postcentral region. The extension of the lesion was better delineated in the 3D TSE images (Fig. 4 lower). The disposable skin fiducial markers were clearly displayed in the volume-rendering image created from the 3D TSE sequence for the registration procedure (Fig. 4 upper right). Given the tumor’s localization adjacent to eloquent cortex, we performed a frameless stereotactic biopsy based on the 3D TSE sequence (in axial, sagittal, and coronal orientations) for optimal assessment of tumor extension while maintaining a high accuracy for the stereotaxy (RMSE 1.2 mm). The neuropathological examination revealed an oligoastrocytoma (WHO Grade II). The patient’s postoperative course was uneventful and no neurological deficits were noted.

Discussion

Magnetic resonance images used for the navigational setup focus mainly on the established T₁-weighted isovoxel sequence for contrast-enhancing lesions. The alternative, high-resolution CT scans, provide low-contrast imaging of brain tissue, but precise depiction of bone; it is, therefore, the first choice for navigated skull-base surgery. Our aim was to develop and evaluate a T₂-weighted sequence applicable for neuronavigation to cover the spectrum of nonenhancing lesions that appear hyperintense on T₁-weighted images.

Principal Findings

The sequence can be used with common 1.5-tesla MR imaging units and is easily integrated into the navigational setup. Using the registration procedure of the navigational system to evaluate the accuracy of and rule out distortion in the 3D geometry on MR images is applicable and, from our point of view, acceptable because it simulates the clinical situation. Nevertheless, this measurement is influenced by other factors such as the preciseness of the registration procedure (finding the center of the fiducial marker) and a system error—the accuracy of the navigation system itself. Therefore, the absolute value of the imaging study is less important than its comparison with the results of conventional imaging modalities.

The registration accuracy of the 3D TSE images in the phantom study in which we used common disposable skin fiducial markers (mean RMSE 1.3 mm) was equal to the ac-
Curacy of conventional T$_1$-weighted MPR images and CT scans. Its high accuracy was confirmed by the additional landmark checks in the phantom study, which excluded geometric distortion within the sequence.

In the clinical trial, the registration accuracy (RMSE $\leq$ 2.1 mm [SD 0.32]) was sufficient and comparable to the results obtained using CT scans$^{16,33}$ and T$_1$-weighted MPR images reported in previous studies.$^{7,16,17}$ During the clinical trial the drop-out rate was very low; in one case a technical malfunction of the navigation system unrelated to the use of 3D TSE images occurred. Therefore, the clinical application of the sequence for neuronavigation was reliable. Compared with previous studies, the exclusive use of the 3D TSE sequence for neuronavigation rules out fusion mistakes and the isovoxel design allows 3D reformatting in any orientation.$^{10,14}$

**Clinical Indications**

In this first clinical trial, the new setup’s illustration and delineation were very convincing and the application of the 3D TSE sequence can be recommended for many pathological conditions.

Because T$_1$-weighted images are well equipped to depict low-grade gliomas, this new sequence provides an excellent data set for neuronavigation in treating these lesions. The extension and area of infiltration is well illustrated by the navigational use of the 3D TSE sequence. The exclusive registration of the 3D TSE image ensures a high registration accuracy for stereotaxy and a good delineation for multiple sampling, even near eloquent brain areas.

The value of the 3D TSE sequence for contrast-enhancing high-grade gliomas may lie in its capacity to make the infiltration zone visible. This area, however, is not clearly delineated by the hyperintense area appearing on T$_2$-weighted images, especially in cases of surrounding edema, and the possible visualization of infiltration is still subject to debate. From our point of view the navigation for these lesions should not be based on the exclusive use of the 3D TSE sequence; at least an additional integration of a Gd-enhanced T$_1$-weighted MPR sequence is necessary.

Cystic lesions with contents that appear hyperintense on T$_2$-weighted images (such as cystic craniopharyngioma and arachnoidal cyst) are precisely depicted and the boundary to the surrounding cerebrospinal fluid is illustrated.

Surgery on cavernomas, especially if they are deep seated, is a definite indication for neuronavigation.$^{3,6,8,9}$ In 40 to 60% of cases, the clinical presentation of cerebral cavernomas is characterized by seizures of various types. Seizure control is therefore one of the principal objectives of cavernoma surgery.$^{5,6}$ Since the surrounding gliosis scar and the hemosiderin deposition caused by microhemorrhages have been implicated in epileptic seizures,$^{14}$ resection of these areas should be attempted at surgery.

The cavernoma as well as the T$_2$-weighted hypointense hemosiderin rim can be observed much better on 3D TSE images than on conventional T$_1$-weighted MPR images, and the registration of the 3D TSE sequence is superior in depiction and delineation.

For these lesions and other T$_2$-hyperintense disorders (for example, ventricular lesions and a flow void accompanying vascular lesions), the 3D TSE sequence should prove to be advantageous for intraoperative MR imaging–guided resections and intraoperative updates of navigation. In general, additional preoperative fMR imaging data can be integrated into the 3D TSE data set and sulcal limitations or anatomical relationships between eloquent cortex and T$_2$-hyperintense lesions are emphasized.
Three-dimensional T2-weighted imaging

Limitations of the Sequence

The main disadvantage of the 3D TSE sequence is its longer acquisition time (12–27 minutes), compared with the standard T2-weighted data set in the axial orientation (for example, a 5-mm slab thickness whose acquisition time is 3–18 minutes). Nevertheless, differences concerning acquisition time are relative because an additional 3D data set for registration is necessary for the application of the sequence to search for very small lesions, for example, in cases of abscess or cavernoma with hemorrhage, or may lead to motion artifacts compromising image quality and registration accuracy.

The TSE design reduces susceptibility artifacts compared with conventional spin-echo T2-weighted imaging or gradient-echo imaging. This allows evaluation of the real extension of a hemosiderin deposition without overestimation but limits the application of the sequence to search for very small lesions, for example, in cases of multiple cavernomas. Generally T2-weighted images might not allow a precise differentiation of a hyperintense infiltration zone from surrounding edema, as found in high-grade gliomas and cerebral infections.

Study Limitations

In the present study we did not compare the extent of resection that was obtained using different 3D imaging modalities for different lesions. It remains for future studies to elucidate and quantify this expected benefit.

Conclusions

The introduced T2-weighted isovoxel sequence, which can be used on common 1.5-tesla MR imaging units, extends the spectrum of navigational data sets, particularly for T2-weighted hyperintense lesions. This allows the choice of an adequate sequence for neuronavigation or for intraoperative MR imaging—guided resection, depending on the signal characteristics of the pathological entity. This sequence maintains a high registration accuracy as well as the possibility of high-resolution reconstruction in any orientation.

References