CHAPTER 7

Localisation of the central sulcus region in glioma patients with three-dimensional fluid-attenuated inversion recovery and volume rendering: comparison with functional and conventional magnetic resonance

Br J Neurosurg 2011; 25(2):210-7

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ABSTRACT

Purpose
Volume rendering (VR) of three-dimensional (3D) fluid-attenuated inversion recovery (FLAIR) magnetic resonance (MR) images shows regional intensity differences, reflecting the central sulcus (CS) region and occipital cortex. The purpose of this study was to determine whether 3D FLAIR with VR could be used as an alternative method to localize the CS region in comparison with functional and conventional MR-imaging in patients with perirolandic glioma.

Methods
Eleven patients with intracranial gliomas were studied with single-slab 3D FLAIR including VR and conventional T1-weighted imaging. In all patients preoperative fMRI was performed with a motor paradigm of the hand. The hypo-intense central gyri on 3D FLAIR with VR were interpreted as the CS area. Localization of the motor hand knob on anatomical images and fMRI results were used for identification of the primary motor cortex.

Results
Anatomical localization of the motor hand knob on T1-weighted images was possible in 91 % of both hemispheres. In 73 % of the affected (AH) and 91 % of the unaffected (UH) hemispheres the hand knob and CS region could be identified on 3D FLAIR axial and VR images respectively. With one exception, fMRI activation confirmed the CS region as observed with 3D FLAIR with VR.

Conclusions
Volume rendering of 3D FLAIR MR images shows central hypo-intensities frequently corresponding with the CS region. Two-dimensional localization of the CS region on conventional T1-weighted images and fMRI seems favourable compared to 3D FLAIR. However, in selected cases, especially where fMRI is not possible or feasible, volume rendering with 3D FLAIR may enhance the 3D visualization of gliomas in relation to the CS region which can be used as an alternative method in the presurgical structural and functional evaluation of neurosurgical patients.
INTRODUCTION

Structural magnetic resonance (MR) imaging is essential in the evaluation of patients with intracranial lesions, in whom a neurosurgical procedure is considered. Successful presurgical planning requires knowledge of the spatial relation between the lesion and eloquent cortex. Large interindividual differences between structural and functional neuroanatomy make it difficult to accurately assess this relation, especially in the presence of intracranial lesions with edema and brain shift (1; 2). For lesions near the central sulcus (CS) neuro-anatomical landmarks, such as gyral morphology on MR-imaging, can be used to locate the motor cortex of the hand (3), but can be unreliable in the presence of intracranial pathology (4). Direct cortical stimulation is widely accepted as the best means for identifying the primary motor cortex in humans but requires an operation and lacks the possibility of presurgical planning (5). Noninvasive preoperative functional information can be obtained with functional magnetic resonance imaging (fMRI) (6; 7), magnetoencephalography (MEG)(8; 9) or positron-emission tomography (PET) (10-12) , to locate quite reliably the primary motor and sensory cortex, which can be subsequently used for preoperative planning and intra-operative navigation. However, these methods have methodological and logistical drawbacks, are time-consuming, costly and mostly require adequate patient cooperation.

An alternative identification of the CS region is possible due to the lower signal intensities (SI) as observed on turbo fluid-attenuated inversion recovery (FLAIR) MR images in the normal population (13; 14). The FLAIR sequence is useful in detecting white matter abnormalities or subtle lesions in structures situated in the interface between the cerebrospinal fluid (CSF) and the cerebral parenchyma, because of suppression of the CSF signal. Recently, single-slab methods have been developed with T2 and FLAIR contrasts (15; 16). Using this sequence, 3D FLAIR images can be obtained with isotropic voxels. This allows reconstruction of the brain in all orientations as well as volume rendering (VR). Volume rendering of the 3D FLAIR dataset show hypo-intense cortical regions corresponding to the CS region and occipital cortex. The purpose of our study was twofold. First, we wanted to determine if the observed hypo-intense areas on 3D FLAIR is the result of lowered SIs or could be related to the volume-rendering process itself. Our second goal was to determine whether this single-slab 3D FLAIR MR imaging technique with VR could be used as an alternative method to localize the CS region in comparison with functional and conventional MR-imaging techniques in patients with perirolandic glioma. In case of reliable CS localization with the volume-rendered 3D FLAIR MR images, this imaging technique could be used as an alternative or complimentary method of CS localization, especially in cases where other functional imaging modalities are either not available or feasible due to patient cooperation or neurologic deficit.
MATERIALS AND METHODS

Patients
From the patients with intracranial lesions, referred to the department of Neurosurgery of the VU University Medical Centre (Amsterdam, The Netherlands), we retrospectively selected eleven consecutive patients with periorbital gliomas who had had surgery (four female and seven male, age range 35 - 63 years; mean: 45.0 years), a pre-operative Karnofsky Performance Status score ≥ 70, 3D FLAIR and fMRI data available.

Table 1 summarizes the clinical data of the patient group. Seven patients had an astrocytoma (four WHO grade II, three WHO grade III), one had an oligo-astrocytoma (WHO grade II) and three had an oligodendroglioma (one WHO grade II, two WHO grade III). The lesions were located in the right hemisphere in seven cases and in the left hemisphere in four cases. Ten patients had seizures and one (patient 6) had a neglect preoperatively. All patients had conventional T1-weighted imaging and fMRI data had been acquired in the context of a prospective functional imaging study. Functional MRI was performed with a motor paradigm of the contra- and ipsilateral hand in six cases. In five cases motor activation was only performed with the hand contralateral to the lesion. Intraoperative mapping of the CS was performed in 8 out of 11 patients. Postoperatively, two patients had a transient dysphasia and paresis, one patient had persistent dysphasia. The study was approved by the Medical Ethics Committee of the VU University Medical Centre and informed consent from the participants was obtained prior to inclusion.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age / Gender</th>
<th>Diagnosis</th>
<th>Location, Lateralization</th>
<th>Motor paradigm hand</th>
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<td>35 / F</td>
<td>astrocytoma, II</td>
<td>parietal, R</td>
<td>L + R</td>
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M, male; F, female; L, left; R, right
**MR acquisition**

Imaging was performed with a 1.5 T MR scanner (Siemens Sonata, Erlangen, Germany). A single-slab 3D FLAIR MR sequence was used, with slightly different parameters to obtain nearly isotropic voxels. Repetition time TR = 6500 ms, inversion time TI = 2200 ms, 191 echoes, with effective echotime TE = 355 ms. Whole brain coverage was obtained with a sagittal 3D slab of 156 – 166 mm, consisting of 120 – 128 partitions of 1.3 mm. Using a 190 x 256 matrix and 230 x 310 mm field-of-view, the in-plane resolution was 1.21 x 1.21 mm. No interpolation was used either in-plane or in the slab direction. Employing 75% partial Fourier in the slab direction, the acquisition time varied between 9 min 47 s and 10 min 15 s.

Functional MR imaging was performed using the blood oxygenation level dependent (BOLD) technique (echo-planar imaging, TR = 3000 ms, TE = 60 ms, 25 axial slices were obtained with slice thickness of 3 mm and 10 % gap, a 64 x 64 matrix and 211 x 211 mm field-of-view resulting in isotropic 3.3 x 3.3 x 3.3 mm³ voxels). The motor paradigm consisted of self-paced clenching and opening of the hand during 15 seconds alternated with rest periods of 15 sec, for a total of 10 epochs. Conventional 3D T1 (inversion recovery fast gradient echo) images (TR = 2700 ms, TE = 5 ms, TI = 950 ms, 176 coronal 1.5 mm slices with 1.0 x 1.0 mm² in-plane resolution) were obtained for anatomical labelling.

**Post processing**

Post processing and visualisation software (Siemens, Erlangen, Germany) was used to make VR images of the 3D FLAIR dataset. The visual properties of the volume images can be changed by optimizing the transparency, brightness and signal intensity. The result is a freely rotatable 3D volume image with three additional orthogonal cutting planes available. Modified parameters can be stored to be used for subsequent evaluations and individual adjustments of contrast.

After motion-correction of the fMRI volumes, activated areas were calculated with a t-test taking into account the delay of the hemodynamic response function. Voxels exceeding a t-value of 3.0 were colour-coded and considered as activated areas. The functional data-set was then transferred to the VR images to examine the activated areas in their anatomical context (Figure 1a).

**Signal Intensities**

The signal-to-noise ratio (SNR) of the 3D FLAIR images of all subjects was calculated in three cortical regions of interest (ROI), the CS-region, the parietal and occipital cortex. The ROIs were placed on a paramedian sagittal image with a visible marginal ramus of the cingulate fissure and parieto-occipital fissure in the unaffected hemisphere. The cortex anterior of the fissure was taken for the CS-region, the parietal cortex was taken between the cingulate fissure and the parieto-occipital fissure and the occipital cortex posterior from the parieto-occipital fissure. The SI of the cortex was obtained from the three locations described above. The standard deviation (SD) of the noise was obtained from a ROI outside and superior of the skull. The SNR was calculated as $\frac{SI_{ROI}}{0.654 \times SD_{noise}}$. 

taking into account a correction for underestimation of the noise in magnitude images (18). The SNR of the three regions were compared and tested statistically, using the paired t-test. Statistical significance was determined at an alpha level of 0.05 and data are presented as means ± SD.

**Identification of the central sulcus region**
The anatomical hand knob localization of the CS was identified on reformatted axial slices of the 3D T1 (Figure 1b) and the 3D FLAIR scan. Without the functional data available, an experienced neuroradiologist (F.B.) identified the presence of the hand knob on the posterior border of the precentral gyrus in both hemispheres. The hand knob was only identified in case of a typical inverted omega- or horizontal epsilon shaped cortex. Failure to identify the hand knob could be related to the presence of tumour or variations in the course of one of the fissures. Functional MR localization of the motor hand area was judged positive when a clear area of activation was found in the central region contralateral to the hand movement. The CS region was identified on 3D FLAIR with VR in case of regional hypo-intensity in the central area. Figure 2 demonstrates an example of 3D FLAIR with VR from a superior view in two patients. Figure 2a shows bilateral lowered SI in the CS region, whereas Figure 2b demonstrates only unilateral lowered SI around the CS region. The affected hemisphere lacks the presence of a visible CS region.

![Figure 1](image1.png)

*Figure 1.* A: Right-sided postero-lateral view of 3D FLAIR MR imaging with volume rendering of patient 8. Low signal intensities are visible in the area of the CS and the occipital cortex (arrowheads). Superimposed fMRI data (red) showing left hand motor activation in the CS region with two orthogonal planes and a right-sided parietal astrocytoma, WHO grade II (white). B: axial reformatted 3D T1 gadolinium-enhanced MR image with arrowheads pointing to the hand knob (L = left; R = right) in the same patient.
**RESULTS**

In 3D FLAIR images, the SNR of both the CS region (64.2 ± 9.9) and the occipital cortex (60.1 ± 8.0) was significantly lower ($p < 0.01$) than the SNR of the parietal cortex (72.9 ± 10.1). No significant difference in SNR was found between the CS region and the occipital cortex. The correspondence between the presence of the motor hand knob on anatomical axial slices, fMRI activation and the presence of a visible CS region on 3D FLAIR is shown in Table 2. Anatomical identification of the hand knob on axial reformatted 3D T1 images was possible in 10 out of 11 (91 %) of both the affected and unaffected hemisphere. The two failures (patient 2 and 9) were due to anatomical variance and not related to tumour presence. Hand knob identification on axial reformatted 3D FLAIR images was possible in 8 out of 11 (73 %) of the affected and in 10 out of 11 (91 %) of the unaffected hemispheres. Two failures were due to the presence of tumour (patient 6 and 11), the other two were identical to the failures of the 3D T1 scan.

The fMRI results were successful in 10 out of 11 (91 %) of the affected hemispheres and in 5 out of 6 (83 %) of the unaffected hemispheres. The two failures were in the same patient (patient 6) due to large tumour mass on the affected side and inadequate
performance of the motor task for the unaffected hemisphere. The 3D FLAIR VR show that the CS region could be visualized in 8 out of 11 (73 %) of the affected and 10 out of 11 (91 %) of the unaffected hemispheres. Failures in affected hemispheres were due to tumour presence.

In all twelve hemipheres with a visible CS region and corresponding fMRI data available, the fMRI results were located in the hypo-intense CS region, except for one fMRI due to inadequate patient performance. In three of the AHs and one of the UH the CS region was not visible on VR images, while fMRI was successful in three of the corresponding hemispheres. The absence of CS hypo-intensity in combination with posterior tumour invasion and succesful fMRI is demonstrated in the VR image of Figure 3a with corresponding sagittal projection of the FLAIR image. The unaffected hemisphere shows a clear hypo-intense CS in combination with successful fMRI (Figure 3b).

In five cases bilateral anatomical (hand knob) and functional localization (fMRI) was possible in combination with a visible CS region on 3D FLAIR with VR.

<table>
<thead>
<tr>
<th>Table 2. Correspondence of motor hand knob presence on axial MR images (3D T1 and 3D FLAIR), fMRI activation in motor hand area and hypo-intense CS region on 3D FLAIR with volume rendering (VR).</th>
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<tbody>
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<td>Patient</td>
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<td>11</td>
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<td>TOTAL</td>
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FLAIR, fluid attenuated inversion recovery; +, presence; -, absence; CS, central sulcus. Cause of failure due to: * anatomical variance; # tumour mass; ! inadequate performance; $ presumably structural cortical characteristics.
DISCUSSION

We demonstrated an isotropic single-slab 3D FLAIR MR imaging technique of the brain, which is suitable for VR. The images have no signal from CSF and low signal from skull and skin, which allows a reconstruction of the cortical surface without pre-processing steps like skull-stripping. We have shown that VR of the 3D FLAIR dataset has lowered SIs in the CS region and the occipital cortex and can be used to visualize the CS region in the large majority of cases. The data from fMRI confirmed the visible area of the CS in most cases, which offers new possibilities to use structural MR imaging with functional characteristics.

Hypo-intensity in 3D FLAIR volume rendering

The regional intensity differences in the VR images reflect differences in T1 relaxation time and have been described earlier for two-dimensional (2D) FLAIR, showing the lowest signal intensities along the CS (13; 14; 19). In our study, we also found significant lower SIs in the CS region and the occipital cortex as measured on sagittal 3D FLAIR images. Therefore, the regional hypo-intensity as seen on the VR images is an objective finding and seems not related to the VR process itself. The regional variations are possibly related to structural differences in cortical areas (20). Classic post-mortem studies have shown regional variability in cortical thickness across the cortex, with thickness varying between 1 and 4.5 mm (21). The most variable areas of the cortex are the pre- and post-central gyri, the primary visual areas and the anterior medial temporal lobes (22), reflecting...
different proportions of grey matter. Fischl et al. have used an automated method to accurately measure cortical thickness across the entire brain and demonstrated that the CS region and the visual cortex have the lowest average cortical thickness, which could be an explanation for the observed hypo-intensities on VR images (23). Others have used measurements of cortical thickness ratios on T2-weighted images in patients with brain tumours and vasogenic edema and showed a significant difference between the CS versus both frontal and parietal sulci (24). However, probably cortical thickness properties are not the only explanation for lower signal intensities. Cytoarchitectural factors in the different cortical layers influence relaxation time and other MR properties as well (25). In three hemispheres at the affected side the VR images failed to show a local hypo-intense CS region, possibly related to nearby tumour location with edema or tumour infiltration (as demonstrated on the sagittal FLAIR projection in Figure 3a). Remarkably, in one hemisphere the VR image did not show a rolandic hypo-intensity at the unaffected side, while it was present at the affected side. This finding seems not related to motion artefacts or other pathology and might be explained by cortical properties.

**Functional localization with 3D FLAIR volume rendering**

Intra-operative cortical stimulation is still considered the standard method to localize language and motor function in neurosurgical procedures. To date, an increasing number of non-invasive imaging modalities are used for preoperative functional localization. Gyral morphology on structural MR images can be used to localize the CS region. Yoursey et al. described the motor cortex hand knob as a potential neuro-anatomical landmark (3). The motor hand knob has a characteristic inverted omega or horizontal epsilon shape on axial anatomical images. Despite the presence of intracranial lesions, identification of the motor hand knob on axial reformatted 3D T1 images was still possible in the majority of cases and failures were only due to anatomical variance in the course of one of the fissures. Hand knob identification on axial reformatted FLAIR images was similar for the UHs. In the AHs two extra cases could not be identified due to lower resolution of the FLAIR scan in combination with tumour presence. In our series, identification of the CS region on VR images was possible in 73 % of the AHs, which is comparable with motor hand knob identification on axial FLAIR images. While hand knob identification on the 3D T1 sequence seems to be favourable compared to 3D FLAIR, the latter sequence has the advantage of 3D whole-brain visualization not only showing the tumour but also its relation to the CS in a freely rotatable manner. Others have used a brain surface reformatted imaging technique based on isotropic T1-weighted 3D data as an accurate and reliable technique to visualize superficial brain lesions in relation to the precentral gyrus. This technique may also provide useful additional information for preoperative surgical planning, but it only shows a part of the brain surface. In addition, anatomical variations in the CS region may lead to false localization (26).

Progress in non-invasive functional imaging modalities like fMRI, MEG and PET has made it possible to localize functions in the human brain. Functional MRI is the most widely
used modality and has shown successful localization of the motor hand area in more than 80% of the cases (27-30). Others have shown that cerebral structure-function correlation is possible with special structural MR techniques to localize different functional areas of the cortex (20; 24; 31), but these techniques are not very useful in daily neurosurgical practice.

Advantages of 3D FLAIR volume rendering
Conventional 2D imaging is not always sufficient to perceive the true spatial relationships between anatomical structures. Therefore, 3D datasets can be used to select images from any plane and visualize the lesion from any direction for better understanding. However, true 3D visualization can only be acquired with VR methods, showing realistic-looking brain surface images. Volume rendering of 3D FLAIR images can be performed without pre-processing steps like skull stripping which increases the possible use in daily routine. The VR image gives a good view of the localization of the tumour in the case of cortical extension, which can be viewed in all directions. In most cases the spatial relationship to the CS or occipital area can be viewed as well and by adding three orthogonal planes, the extension of the lesion in the white matter can easily be visualized simultaneously. Most unenhancing lesions are better visualized on T2-weighted or FLAIR sequences than on T1 sequences. Therefore, this technique is especially suitable for low-grade gliomas to assess the relation to the CS.

Identification of the sensorimotor cortex with 3D FLAIR renderings seems to be comparable with hand knob identification but has a lower success rate than the results of fMRI in our patient group. However, functional MRI with a motor paradigm, requires good patient cooperation and no severe motor deficits, conditions not necessary for 3D FLAIR imaging. Furthermore, the 3D FLAIR images can easily be imported into a neuronavigational system and automatically be fused with other modalities. In this way a registration accuracy as well as high-resolution reconstruction in any direction is possible.

Limitations of 3D FLAIR volume rendering
Because of differences in signal intensity between sessions and subjects, there is no single solution for optimal parameter settings to achieve the best VR. On an individual basis, the stored parameters sometimes need slight modifications in opacity and brightness. In the presence of edema, a strong contrast-enhancing lesion or a very large tumour with compression of the CS region the results can be difficult, making additional functional imaging necessary.

Because of signal intensity differences between the parietal lobe and the CS region, the CS region is frequently visible on 3D FLAIR, however delineation of the CS can be difficult because of lack of contrast between the pre- and post-central gyrus. Furthermore, in some cases there is a prefrontal extension of the hypo-intense area, which is not apparent in the parietal area. Therefore, a better delineation between the parietal lobe and the CS region is seen than between the premotor area and the CS region. This makes 3D FLAIR renderings more useful for parietal than premotor lesions.
Using a qualitative dependant variable (visibility of the CS region) requires further analysis with inter-observer agreement. However, our first objective was to evaluate the presence of the hypo-intense rolandic zone in AH and UH, found in 3D FLAIR VR for comparison with anatomical and functional imaging techniques. Finally, the concordance between VR images and fMRI was only studied for motor hand function, suggesting that the visible area on these images corresponds to the CS region. While this may be true for the motor cortex of the hand, we did not investigate the localization of other functions in the CS region such as sensory function or foot and tongue movements.

**Implications for the future**

Information from 3D FLAIR VR can be useful in the preoperative evaluation of patients with intracranial gliomas to assess the spatial relationship of the lesion to the CS region and may support additional functional imaging investigations. However, due to the preliminary character of this study, additional prospective studies should be performed to show the usefulness of 3D FLAIR with VR in the presurgical evaluation of neurosurgical patients. At the same time, the use of multi-channel phased-array coils and parallel imaging techniques will lead to an increased spatial resolution of 3D FLAIR images in similar or shorter acquisition times. This will presumably improve localization of the CS region.

**CONCLUSIONS**

We demonstrated an isotropic 3D FLAIR imaging sequence with VR to visualize important cortical areas in relation to intracranial gliomas. With this new non-invasive structural MR technique it seems possible to identify functional areas corresponding with the pre- and post-central cortex and possibly the primary visual cortex. Two-dimensional localization of the CS region on conventional axial T1-weighted images and fMRI seem favourable compared to 3D FLAIR with VR. In selected cases, especially where fMRI is not possible or feasible, VR with 3D FLAIR may enhance the 3D visualization of gliomas in relation to the CS region which can be used as an alternative method in the presurgical structural and functional evaluation of neurosurgical patients.
REFERENCES


