Clinical application of functional magnetic resonance imaging in presurgical identification of the central sulcus

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Object. The authors sought to evaluate the advantages and limitations of functional magnetic resonance (fMR) imaging when it was used regularly in the clinical context to identify the central sulcus.

Methods. A 1.5-tesla MR system comprising a spoiled gradient recalled acquisition in the steady-state functional sequence and a cross-hand cancellation analysis method were used to evaluate 50 surgical candidates with centrally located space-occupying lesions in the brain. Three-dimensional (3-D) models of the patient’s head and brain showing the relative position of the tumor and the eloquent cortex were obtained in each case. A selective and reproducible focal activation was found, indicating the probable central sulcus position in 41 patients (82%). Direct cortical stimulation confirmed the fMR findings in 100% of 22 intraoperatively assessed patients. Failure to identify the central sulcus occurred in 18% of cases and was mainly a consequence of intrinsic damage in the primary sensorimotor region that resulted in severe hand paresis.

Conclusions. Although specific factors were identified that contributed to reduced sensitivity of fMR imaging in the clinical context, the present study supports functional assessment and 3-D representation of specific surgical situations as generally feasible in common practice.

Key Words • sensorimotor cortex • functional magnetic resonance imaging • cortical mapping • brain tumor

The central sulcus is a major anatomical and functional reference in neurosurgery, and its identification is required for surgery aimed at removing centrally located lesions. Magnetic resonance (MR) imaging now provides tools to recognize the central sulcus functionally and to visualize its location preoperatively in relation to the surgical target.13,14

By means of functional sequences, we are able to detect primary sensorimotor cortex activation on MR imaging. Extensive research conducted in healthy volunteers has yielded a comprehensive knowledge of the normal motor response.10,12,16,18 In addition to these studies, other authors have reported their initial experience with the application of functional (f)MR imaging in selected patients and have suggested its potential use in surgical planning.1,17,20,21 Furthermore, researchers have recently added a three-dimensional (3-D) image representation to the functional study to provide a preview of the operative field that greatly facilitates understanding of the spatial relationship between the eloquent region and the patient’s tumor.3,6,11

Current MR imaging methods seem to facilitate planning of surgical strategy. Nevertheless, the challenge now involves establishing the applicability of fMR imaging in common clinical practice. The specific condition of patients suffering from distorting cerebral lesions and dramatic neurological deficits may often interfere with examinations that detect subtle physiological changes and require active patient cooperation. On the other hand, the use of fMR imaging will depend largely on the adoption of procedures capable of assessing brain function within a reasonable acquisition and image-processing time.

We conducted a study aimed at establishing the potential and limitations of this MR imaging method when it was routinely used in patients with centrally located lesions. We report the usefulness and reliability of a functional imaging protocol to identify the central sulcus in the clinical setting and describe the use of 3-D MR imaging in surgical planning.

Clinical Material and Methods

Patient Population

Fifty consecutive surgical candidates presenting with a space-occupying lesion involving the central region of the brain (above the sylvian fissure and extending posteriorly beyond the coronal suture) were included in this study. All patients gave written informed consent prior to assessment, and the study was approved by the research committee of Bellvitge Hospital.

The patients included 19 females and 31 males with a mean age of 44.3 ± 15.1 years (range 17–76 years). The
pathological diagnoses included low-grade astrocytoma (19 patients), high-grade astrocytoma (five patients), glioblastoma multiforme (seven patients), oligodendroglioma (three patients), meningioma (three patients), single metastasis (three patients), arteriovenous malformation (five patients), cavernoma (four patients), and epithelial cyst (one patient). Forty patients suffered seizures in the course of the disease, and 24 developed a progressive motor deficit, which was mild (that is, the muscles were still capable of contracting against resistance) in 19 cases and moderate to severe in the remaining five. Thirty-nine patients were receiving antiepileptic drugs and 26 were being treated with dexamethasone at the time of assessment.

Activation Task and Testing Procedure

Patients were required to make repetitive self-paced opening and closing motions of the hand. Instructions were given to force both the flexion and extension phases of the cyclic movement at an approximate rate of one per second. The use of a similar task had been shown previously to produce notable sensorimotor activation with little propagation of motion in the patient’s head.14 Each patient was positioned supine in the MR imaging apparatus and motion was minimized by using two standard cervical collars as head holders. One of them was placed around the patient’s neck without pressure and the other was positioned around the patient’s forehead and fixed to the coil with a Velcro band.

An activation trial consisted of four 1-minute periods in which patients performed the specified motor task alternately with their left and right hands (two 1-minute periods per hand) without taking a rest. Patients began the trial by moving the hand corresponding to the lesion side. The order to change the active hand was given at the end of each period via a system intercom.

Functional MR Imaging

A 1.5-tesla Signa system (GE Medical Systems, Milwaukee, WI) with a standard quadrature head coil was used. The functional sequence consisted of spoiled gradient recalled acquisition in the steady state (TR 73 msec, TE 60 msec, pulse angle 30˚) with a 256 × 64–pixel matrix, within a field of view of 24 cm, and with a section thickness of 4 mm. First-order flow compensation gradients were used. Field homogeneity was adjusted in each patient at the level of the functional slice by automated shimming on the three axes. Each image in this protocol lasted 5 seconds. The functional time series consisted of 48 consecutive images obtained in 4 minutes.

Oblique–axial projections were selected from a T1-weighted sagittal view with the aim of including the sensorimotor strip at the hand level in Penfield’s map. In the absence of sulcal distortion, this region can usually be found midway between the superior border of the brain and the cingulate sulcus (15 ± 2 mm from the cerebral vertex).14 When anatomical distortion was present or when initial activation attempts were unsuccessful, we acquired consecutive functional sequences above and below this location to cover a wide region. The number of trials depended on activation success and patient tolerance.

Image Analysis

Functional sequences were analyzed immediately after each acquisition on an auxiliary workstation connected to the main system unit (SPARCstation 20; Sun Microsystems, Mountain View, CA). This practically on-line analysis allowed us to restrict the number of functional sequences to the minimum necessary for each patient.

Images that we intended to analyze by means of Student’s t-test were obtained using specific image analysis software (FuncTool; GE Medical Systems, Buc, France) and adapting previously described procedures.14,15 The activation image resulted from the pixel-by-pixel calculation of “t” statistics, comparing right- versus left-hand activation, and vice versa. This “cross-hand” comparison increases selectivity of the activation results by canceling activity outside the primary sensorimotor cortex (that is, bilateral changes occurring in premotor areas).14 Using

Fig. 1. Three-dimensional imaging approach to surgery. A: The tumor is superimposed on the patient’s head surface rendering. B: Computer-simulated craniotomy of the same patient providing a preview of the operative field. C: Transparency images used to help visualize the relative position of subcortical lesions (simulated craniotomy of a different patient). Note wide marks on neck and forehead made by the holders used. R = central sulcus at the level at which hand activation was observed in the functional assessment.
Identification of the central sulcus with functional MR imaging

Fig. 2.  A: Superior (left) and lateral (right) 3-D views of brain surface rendering images obtained in two different patients presenting with a tumor.  B: Tailored craniocerebral topography may be obtained by using transparent superimposition of head and brain rendering images.  R = mass effect and central sulcus displacement on the cerebral surface.

In this analysis, primary sensorimotor activation appears to be the most relevant finding of the functional image, with relative independence of the statistical threshold. However, in this study we considered only clusters larger than 13 pixels with t values greater than 2 and clusters larger than three pixels with t values greater than 4.14,15

We considered only selective and reproducible activation foci as presumptive primary sensorimotor cortex activation. We established that an activation focus was selective and reproducible when activity surrounding a single sulcus showed at least twice the number of pixels activated than in any other single region and when such an activation was observed in at least two different functional sequences (that is, in four 1-minute periods of activation).

Three-Dimensional MR Imaging Approach

Three-dimensional spoiled gradient recalled acquisition in the steady-state sequences (TR 40 msec, TE 4 msec, pulse angle 30°, section thickness 2.3 mm, field of view 26 cm, and matrix size 256 × 192 pixels) were obtained in each patient to aid in building 3-D models by using the SPARCstation and commercially available software (Version 1.2; GE Advantage Windows, GE Medical Systems).

Our 3-D image-guided approach to surgery consists of three different representations of each patient’s head. First, the tumor is superimposed on head surface rendering images on which the position of the central sulcus is also indicated (Fig. 1A). This representation may be useful in planning scalp incisions because it allows the location of surgical targets in relation to external landmarks. Second, in each case we perform a computer-simulated craniotomy (Fig. 1B and C), which involves removing the scalp and bone on the computer model to expose the gyral pattern of the operative field and display the relative position of the lesion in relation to the eloquent area. The third step consists of building surface-rendering images of the brain to provide an overall view of the spatial configuration (Fig. 2).

Intraoperative Cortical Mapping

Twenty-two patients underwent direct intraoperative electrical stimulation to validate fMR imaging results. This group of patients was selected according to two criteria: 1) successful fMR imaging; and 2) a tumor located one gyrus or less from the presumptive central sulcus (that is, patients at high risk for postoperative motor deficits).

As in our previous work, we used a mapping technique fully described by Berger and Ojemann,2 which involves performing surgery in awake patients and administering a local anesthetic and propofol as a transient hypnotic drug. Bipolar electrodes spaced 5 mm apart were used to stimulate the motor and sensory cortices. A constant-current generator was used to produce a train of biphasic square-wave pulses with a frequency of 50 Hz and a 1-msec single-phase duration. The maximum train duration was 3 seconds. Stimulation was initiated with a low current (2 mA), which was increased 0.5 to 1 mA each time until the desired responses were observed.

The tumor served as a landmark to compare the results obtained with fMR imaging and intraoperative electrical stimulation. The identification of the central sulcus on MR imaging was considered validated when the position of the activated cortex in relation to the tumor (in anteroposterior, superoinferior, and mediolateral directions) coincided in both functional methods. The amount of normal tissue located between the tumor and the activated cortex was also estimated.

Statistical Analysis

Statistical significance was calculated based on Student’s t-test and the chi-square test.
Results

In 41 patients in our series, focal functional activity in and around a single sulcus was distinguishable from that of other regions in at least two activation sequences. Therefore, a selective and reproducible activation allowed probable identification of the central sulcus in 82% of cases.

The central sulcus could not be identified using functional criteria alone in the remaining nine patients (18%). One of these patients showed no signal increase above the established threshold; in five patients, evident but not selective activation was observed; and in the remaining three cases, selective but not reproducible activation was obtained.

Validation Study

Successful fMR imaging results were obtained in 22 patients with a lesion very close to the presumptive primary cortex who then underwent intraoperative cortical stimulation. This group included the patients in whom central sulcus identification presented the greatest difficulty because of anatomical distortion. Intraoperative cortical stimulation confirmed the findings obtained with fMR imaging in 100% of cases; the structure identified as the central sulcus on fMR imaging corresponded to the sulcus located between the sensory and motor hand strips in intraoperative mapping.

The point at which direct cortical stimulation produced the most consistent responses, however, differed systematically from the main activation focus in fMR imaging. Imaging findings were often in deeper locations than the electrically excitable cortical points. Nevertheless, the correspondence was complete in terms of establishing the relative positions of the central sulcus and tumor and assessing the amount of apparently normal tissue existing between both structures.

The specificity of fMR imaging in our study was very high. In no case did we find that the most prominent activation in the functional images corresponded to an area other than the primary sensorimotor cortex. Indeed, the most evident imaging finding in the validated cases was always closely related to the central sulcus. These data indicate that, when rigorous activation criteria are used, the nominal sensitivity of the test may be 100%. However, larger series should be assessed to provide definitive specificity figures.

We cannot accurately assess the sensitivity of the imaging method, because intraoperative functional localization was not systematically achieved in the patients in whom fMR imaging had failed. Nonetheless, the real sensitivity of our fMR imaging method must be greater than 82%, because the intraoperative mapping may also provide negative findings when the sensorimotor cortex is severely damaged. In one patient (Fig. 3A), both imaging and intraoperative methods failed to activate the sensorimotor cortex at the hand level.

Factors Related to fMR Imaging Failure

Table 1 presents clinical and imaging features in patients in whom the poorest results were achieved. As a group, these patients were older than those in the rest of

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Pathological Diagnosis</th>
<th>Preop Neuro</th>
<th>SM</th>
<th>CS Displaced</th>
<th>Abnormal Vessels</th>
<th>Tissue Blood</th>
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<tr>
<td>4</td>
<td>54, M</td>
<td>low-grade astro</td>
<td>M–S</td>
<td>S1</td>
<td>yes</td>
<td>yes</td>
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<tr>
<td>9</td>
<td>76, M</td>
<td>low-grade astro</td>
<td>M–S</td>
<td>M1 &amp; S1</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>56, M</td>
<td>single metastasis</td>
<td>M–S</td>
<td>M1</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>68, F</td>
<td>glioblastoma</td>
<td>M–S</td>
<td>M1 &amp;</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>48, F</td>
<td>high-grade astro</td>
<td>M–S</td>
<td>M1</td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>49, M</td>
<td>glioblastoma</td>
<td>Mild</td>
<td>M1</td>
<td>yes</td>
<td>no</td>
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<tr>
<td>27</td>
<td>61, F</td>
<td>low-grade astro</td>
<td>M–S</td>
<td>M1</td>
<td>yes</td>
<td>no</td>
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<tr>
<td>31</td>
<td>44, F</td>
<td>AVM</td>
<td>none</td>
<td>none</td>
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</tr>
<tr>
<td>42</td>
<td>43, F</td>
<td>low-grade astro</td>
<td>M–S</td>
<td>M1</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td></td>
</tr>
</tbody>
</table>

* Astro = astrocytoma; AVM = arteriovenous malformation; CS = central sulcus; M1 = primary motor hand area; M–S = moderate to severe; neuro = neurological; S1 = primary sensory hand area; SM = sensorimotor cortex.
the series (aged 55.4 ± 11.2 compared with 41.8 ± 14.9 years; \( t = 2.57 \) and two-tailed \( p = 0.013 \)). Failure to obtain a selective and reproducible activation focus was closely related to relevant sensorimotor deficits in patients exhibiting invasion and displacement of the primary sensorimotor region. All patients in our series who showed moderate-to-severe motor deficits at assessment (five patients) can be found in this group, as can two additional patients who exhibited only mild hand paresis but showed severe sensory loss and pseudathetosis movements.

Other causes of central sulcus identification failure were insufficient cooperation to execute commands adequately and avoid head motion during activation attempts, in a patient presenting with a large tumor and severe mass effect (Case 26); and the presence of signal changes in abnormal vessels (lack of activation selectivity), in a patient with an arteriovenous malformation (Case 31).

The effort to move the affected hand was closely related to excessive movements of the patient’s head. In the nine patients showing the poorest activation results, 56.2% of the functional sequences were not considered as a consequence of head motion. This figure exceeds the 27.9% found in the whole series. Sequences with head motion were 27 of a total of 48 in the small group and 58 of 208 in the whole series (\( \chi^2 = 14.1, p = 0.0004 \)).

Our data indicate that poor fMR imaging results were associated with severe damage in the primary sensorimotor cortex. In the whole group, however, most patients with lesions involving the primary region, but without severe motor function impairment, showed a selective and reproducible activation. Certainly, in 17 (89.5%) of the 19 patients suffering from mild hand paresis, fMR imaging results were adequate. In contrast, in 14 (63.6%) of 22 patients with tumor invasion or edema at the hand level of the primary cortex, functional assessment was satisfactory (Fig. 3B). Similarly, in 15 (65.2%) of 23 patients showing central sulcus displacement in relation to the corresponding position in the normal hemisphere, activation in this region was sufficiently selective and reproducible (Fig. 4). The same result occurred in nine (81.8%) of 11 cases exhibiting abnormal vessels near the central sulcus (Fig. 5) and in seven (63.6%) of 11 patients showing signs of extravasated blood on MR imaging.

**Discussion**

Functional MR imaging consecutively applied to identify the central sulcus in patients with a centrally located space-occupying lesion was feasible in most cases. Nevertheless, the failure rate in the clinical use of this technique was not negligible, occurring in 18% of patients studied.

The main clinical factor associated with poor functional results was the presence of moderate-to-severe paresis in the involved hand. Common imaging alterations observed in these cases were sensorimotor cortex invasion by the tumor or edema and central sulcus displacement. Accordingly, extensive damage in the primary region was the major impediment to functional identification of the central sulcus. This type of limitation, however, is not unique to fMR imaging. Berger and Ojemann\(^2\) have stated that patients with a dense hemiparesis are not optimal candidates for intraoperative stimulation mapping.
In contrast, fMR imaging was generally useful in patients at risk for further functional loss during tumor removal. Indeed, in patients showing distortion of the primary sensorimotor region and suffering from only mild motor deficits, we were able to identify the central sulcus reliably by using functional criteria alone. In our study, as in previous reports, intraoperative mapping validated the accuracy of the imaging results. We stress that qualitative rather than quantitative criteria were used to assess the correspondence between intraoperative and imaging methods. Thus, we verified in each case that the relative position between the tumor and the central sulcus fully coincided and that the apparent tumor invasion of the pre- and postcentral gyri had occurred. Absolute distances in millimeters cannot be provided unless stereotactic procedures are adopted.

We emphasize some procedural aspects that may be decisive in obtaining high quality functional studies. The method used to fix the patient’s head may be very relevant. Ideally, holders should minimize motion without reducing patient comfort. Such a requirement may be better achieved if the holders are wide and soft as is the case with some standard cervical collars. The type of activation task used is also important. Complex tasks produce widespread activation in the motor system, whereas simpler tasks produce weak activation. A task requiring patients to force flexion and extension phases of movement may strike a good balance between activation sensitivity and selectivity. Similarly, cross-hand comparison, which cancels nonprimary cortex activation, may be necessary to identify the central sulcus by using only functional criteria.

Because prolonged examinations and complex image analyses could greatly limit the clinical use of fMR imaging, we stressed optimization of procedures to suit patient tolerance and the radiologist’s availability. Our patients underwent a mean of four functional sequences (16-minute acquisition time). Thus, including time for optimizing imaging parameters and 8 minutes for acquiring a 3-D sequence, studies were regularly acquired in little more than 30 minutes. Likewise, 3-D models can currently be built in the time it takes to perform conventional MR angiography studies.

Functional changes in our study depend in part on blood velocity in cortical veins and reflect relatively poorly localized, albeit task-related, functional activity. Nevertheless, this apparent handicap may be an advantage because venous changes notably increase the sensitivity of the method. Indeed, because venous drainage of the primary sensorimotor cortex is located deep in the central sulcus, the large venous signal change contributes to identification of this sulcus.

We modified our previous protocol to potentiate this effect and found an increase in sensitivity without reducing the selectivity of the activation.

The main limitation in our study is the use of a single-section method that cannot encompass a large brain volume and include, with certainty, the eloquent cortex when anatomical distortion occurs. Echo-planar imaging with multiple sections or volume acquisition is advantageous in this respect. We observed, however, that this limitation did not produce a significant reduction in our success rate. We failed to obtain a selective activation or to reproduce activation in some instances, but focal activity was absent in only one case in repeated activation attempts. We acknowledge, nevertheless, that single-section fMR imaging in patients with complications may notably prolong the MR examination.

An issue under ongoing discussion is the proper method of statistical analysis for use in fMR imaging studies. Although we used a statistical threshold, we emphasize that a thresholding method is not crucial when adopting our procedures, because the results are based on the qualitative criterion of demonstrating sensorimotor cortex activation that exceeds activations observed in other regions. Three-dimensional reconstructions of the brain and head of individual patients substantially enhance the usefulness of the functional data. A 3-D representation of structure and function may facilitate the surgeon’s task of visually assessing a patient’s specific situation. As previously stated, 3-D models may be useful for risk assessment and for planning surgical strategies. Increasingly, 3-D images may simplify the task of providing prognostic information to patients and their relatives. In practice, fMR imaging and 3-D reconstructions of the brain may decrease operating time. We currently use these procedures to replace direct cortical mapping in cases in which the central sulcus is located at one gyrus or more from the tumor and to direct intraoperative mapping in high-risk patients.

Conclusions

Functional and 3-D MR imaging, together with other emerging functional methods such as magnetoencephalography, provide tools to assist surgical planning. We have reported our experience with the clinical use of fMR imaging to identify the central sulcus. Although our imaging procedures have limitations, we have observed that fMR imaging is feasible in the majority of clinical situations. The most relevant application of our work may be optimization and validation of an imaging protocol sufficiently simple and rapid to be routinely applied in surgical candidates with centrally located space-occupying lesions.

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