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Preoperative fMRI in tumour surgery

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Abstract Minimally invasive resection of brain tumours aims at removing as much pathological tissue as possible while preserving essential brain functions. Therefore, the precise spatial relationship between the lesion and adjacent functionally essential brain parenchyma needs to be known. Functional magnetic resonance imaging (fMRI) is increasingly being used for this purpose because of its non-

invasiveness, its relatively high spatial resolution and the preoperative availability of the results. In this review, the goals of fMRI at various key points during the management of patients with a brain tumour are discussed. Further, several practical aspects associated with fMRI for motor and language functioning are summarised, and the validation of the fMRI results with standard invasive mapping techniques is addressed. Next, several important pitfalls and limitations that warrant careful interpretations of the fMRI results are highlighted. Finally, two important future perspectives of presurgical fMRI are emphasised.

Keywords Functional MRI · Presurgical planning · Motor cortex · Language cortex

Introduction

Minimally invasive resection of brain tumours aims to remove as much of the affected tissue as possible, while preserving essential brain functions. Therefore, the precise spatial relationship between the lesion and adjacent, functionally essential brain parenchyma needs to be known. Identification of eloquent cortex often cannot be obtained from anatomical landmarks alone; mass effect can distort the normal topography, or disease processes can induce relocation of functions due to brain shift or plasticity.

Functionally essential cortex has traditionally been localised by invasive mapping techniques (IMT), i.e.

cortical stimulation mapping (CSM) or the recording of sensory-evoked potentials [1]. Determination of language dominance can be attempted with the intra-arterial administration of barbiturates [2] or the dichotic listening test [3]. Each of these has its limitations. Although these 'gold standard' methods have proven valid, they are, except for the dichotic listening test, highly invasive, carry significant morbidity and are often highly demanding for the patients. All have limited use in children or cognitively impaired subjects. With IMT and CSM, only limited cortical areas can be tested, as the grey matter along the depth of the sulci is poorly accessible to stimulation. As the preoperatively available information thus remains incomplete, IMT has limited contribution for choosing the

optimal, function-preserving treatment modality and for planning the surgical procedure itself.

The advent of non-invasive mapping of brain areas with functional MRI (fMRI) [4] helps to overcome these issues. fMRI is a widely available and fast-evolving imaging technique that has been increasingly used in a presurgical setting since its introduction in the early 1990s [5, 6]. fMRI is mainly used to localise the primary sensory and motor cortex, determine essential language areas and their hemispherical dominance.

Structural and functional information can be acquired in the same imaging session. This structural–functional co-registration allows assessment of the risk of causing a potential post-surgical neurological deficit. Unlike IMT, fMRI provides information before a commitment to perform surgery has been made, in turn allowing the opportunity to better plan the surgical approach or biopsy trajectory and to improve the patient information.

fMRI has been extensively validated against current gold-standard techniques [6, 7]. A large number of studies also reported an excellent concordance between fMRI and the Wada test for the lateralisation of language [8, 9].

Although fMRI has proven useful at several key-points during the management of patients with brain tumours, including the assessment of the potential surgical risk of causing a neurological deficit, selecting patients who require IMT and planning the surgical procedure [11, 14], several technical issues are only partially resolved. These include the effects of tumour-induced phenomena on the measurable BOLD signal [10–13], signals from larger draining veins, the lack of standardisation in fMRI paradigms and statistical analysis, variations in MR sequences and field strengths and the effects of brain shift during surgery. Because fMRI measures phenomena related to neural activation indirectly, the validity of the assumption that the BOLD-related signals are indeed indicating the brain area responsible for the studied function will always have to be interpreted with caution. Experience, knowledge and common sense are essential skills for all involved with this technique in presurgical evaluation. Also, fMRI only shows the cortical involvement of the functional brain. White-matter connections are as essential as the cortex, and combining diffusion tensor imaging (DTI) with fMRI will allow a more complete risk estimate before neurosurgery.

In summary, the cautious use of fMRI for the presurgical assessment of brain function is justified, but the knowledge of local brain function is imperative for risk and outcome evaluation. There is now enough direct and circumstantial evidence that major functions can be localised and regional plasticity due to focal brain lesions can be studied with fMRI. The non-visualisation of an expected function or the unexpected displacement of functional regions should ring the alarm-bell though and be interpreted with great caution. In these cases, IMT is still indicated.

Goals of presurgical fMRI

In an early study, Lee et al. [14] retrospectively evaluated how often and in what ways the results of preoperative sensorimotor fMRI exams had influenced the treatment of 46 neuro-oncology or epilepsy surgery patients. The fMRI results could be used for patient management at three key stages: (1) *assessment of the risk associated with, and thus the feasibility of the surgical resection*, (2) *selection of patients for IMT* and (3) *guidance of the surgical planning*. In tumour patients, fMRI results helped to assess the feasibility in 55%, influenced the planning in 22% and helped to select patients for invasive mapping procedures in 78%. Recently, Petrella et al. prospectively evaluated the effect of preoperative fMRI localisation of language and motor areas on therapeutic decision-making in 39 patients with resectable brain tumours [11]. The fMRI results altered the therapeutic plan in 49% and enabled a more aggressive approach in 45%. Of the 30 patients who underwent surgery, fMRI helped to shorten the surgical time in 60%, increased the extent of surgical resection in 16% and decreased the craniotomy size in 15%.

Risk assessment

Many papers have shown that the risk of causing a neurological deficit depends on the distance between the tumour margin and the eloquent area [50]. No deficit was induced when this distance exceeded 2 cm, a motor deficit occurred in 33% of the patients with a distance between 1 and 2 cm, and this increased to 50% when the distance was less than 1 cm. More recently, Haberg et al. [15] showed that the risk of post-operative loss of function was significantly reduced when the distance between tumour boundary and functional cortex was 10 mm or more. Krishnan et al. [16] reported that a lesion-to-activation distance of less than 5 mm was associated with a significantly higher risk of neurological deterioration when using fMRI-integrated neuronavigation in patients with lesions around the motor strip. They suggested that within a 10-mm range, IMT should be performed and that a complete resection can be achieved safely for a lesion-to-activation distance of more than 10 mm.

However, one should be aware of the exact measurement of the distance being highly dependent on various factors, such as the statistical threshold used for the evaluation of fMRI results and the effect of brain shift during craniotomy. The spatial extent of the fMRI activations increases when the statistical threshold is decreased and vice versa. However, fMRI can precisely localise the centre of the functional areas within the relevant gyrus during surgery [17].

Selecting patients for IMT

As mentioned above, IMT is still needed to validate the fMRI results intraoperatively when an eloquent area is located immediately adjacent to a brain lesion. Even then, fMRI is a valuable adjunct to IMT because it speeds up the IMT procedure itself and limits the extent of the craniotomy. A major limitation that precludes current replacement of CSM by fMRI is the inability of fMRI to distinguish 'essential' or 'critical' from 'non-essential' or 'expandable' functional areas. fMRI tasks induce activation in many cortical and subcortical structures, but not all of these are necessary for the execution of the behaviour in question [18]. For instance, damage to the SMA and the PMC can cause a transient motor deficit but will not usually result in a permanent deficit [19–21].

Guidance of the surgical procedure

If a decision for surgical removal of a lesion is made, fMRI maps can assist in the appropriate choice of the surgical approach, site and extent of the trepanation, and the extent of surgical excision in order to maximise the functional integrity.

During surgery itself, the fMRI findings facilitate orientation at the site of operation. Furthermore, the preoperative fMRI data can be co-registered into a frameless neuronavigation system and interactively employed during the neurosurgical procedure [16].

However, this functional neuronavigation can be seriously hampered by the occurrence of brain shift after the craniotomy flap and opening of the dura. Several groups have recently proposed solutions to correct for this brain shift, thus allowing more accurate intraoperative information [22–24].

Practical aspects of presurgical fMRI and validation

Principles of BOLD-fMRI

fMRI measures neuronal activity indirectly by measuring metabolic and/or vascular changes associated with neural activity changes (Fig. 1). The most commonly used method is based on the blood oxygenation level-dependent contrast [25–27]. This technique takes advantage of the inherent magnetic properties of deoxyhaemoglobin (deoxyHb): the iron in deoxyHb is paramagnetic and perturbs the main magnetic field, resulting in a local reduction in main field homogeneity. This is usually measured by means of T2*-weighted sequences, most often by means of echoplanar imaging (EPI). In resting brain, there is a close correlation among regional cerebral blood flow [28, 29], regional cerebral blood volume and the regional metabolic rate of oxygen. Activation of a neuronal cell population results in

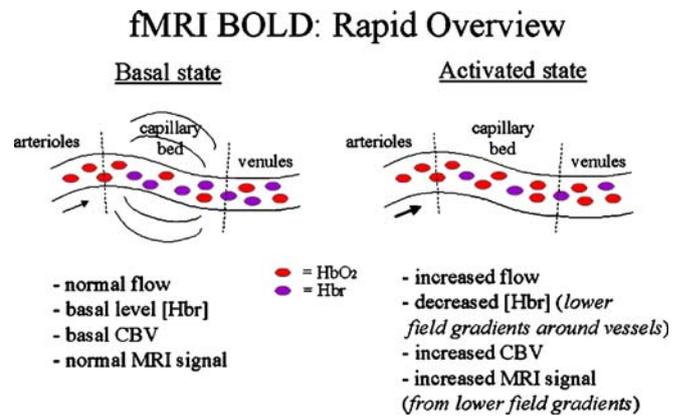


Fig. 1 Schematic depiction of the blood oxygenation level-dependent contrast. The *left panel* depicts the 'baseline' or 'rest' situation. The *right panel* shows the 'activated' state: upon neural activation, the local increase in blood flow and blood volume results in an increased oxygenation and a decrease in paramagnetic deoxyhaemoglobin in the capillaries and venules, leading to an increased T2*-weighted MR signal. Courtesy of Peter Jezzard, FMRIB Centre, Oxford, UK

an increase in these three parameters. Secondary to the activation of a neuronal cell population, rCBF may increase as much as 50%, which far exceeds the oxygen metabolism demands. This mismatch results in an overall increase in oxyhaemoglobin and a relative decrease in deoxyHb concentration in the capillary and venous beds of the activated cortex. The net decrease in deoxyHb concentration then induces a decrease of local susceptibility, and the MR signal, measured with a T2*w pulse sequence, will thus increase in the activated cortex.

Presurgical motor mapping

The brain activation network involved in voluntary movement includes the premotor area (PMA), the superior parietal lobe (SPL), the supplementary motor area (SMA), the primary somatosensory cortex (S1) and the primary motor cortex (M1) [30, 31]. M1 and S1 are located immediately anterior and posterior to the central sulcus respectively. In fMRI, they often co-activate as one big 'blob', which is referred to as the primary sensorimotor cortex (SM1) (see Fig. 2 for risk assessment in a patient with a Rolandic tumour). M1 and S1 are organised according to a somatotopic order [32], which is easily reproduced with fMRI using a block design. Alternating rest and movement of mouth muscles (lip pouting) results in lateral Rolandic activation. Finger tapping, finger-thumb opposition or fist clenching movements will activate the Rolandic region higher up, at the so-called hand area, and extension-flexion of the toes will result in medial Rolandic activation. These uni- or bilateral movements can be performed at a self-paced rate or guided by a visual or auditory cue (e.g. one per second). Self-triggered move-

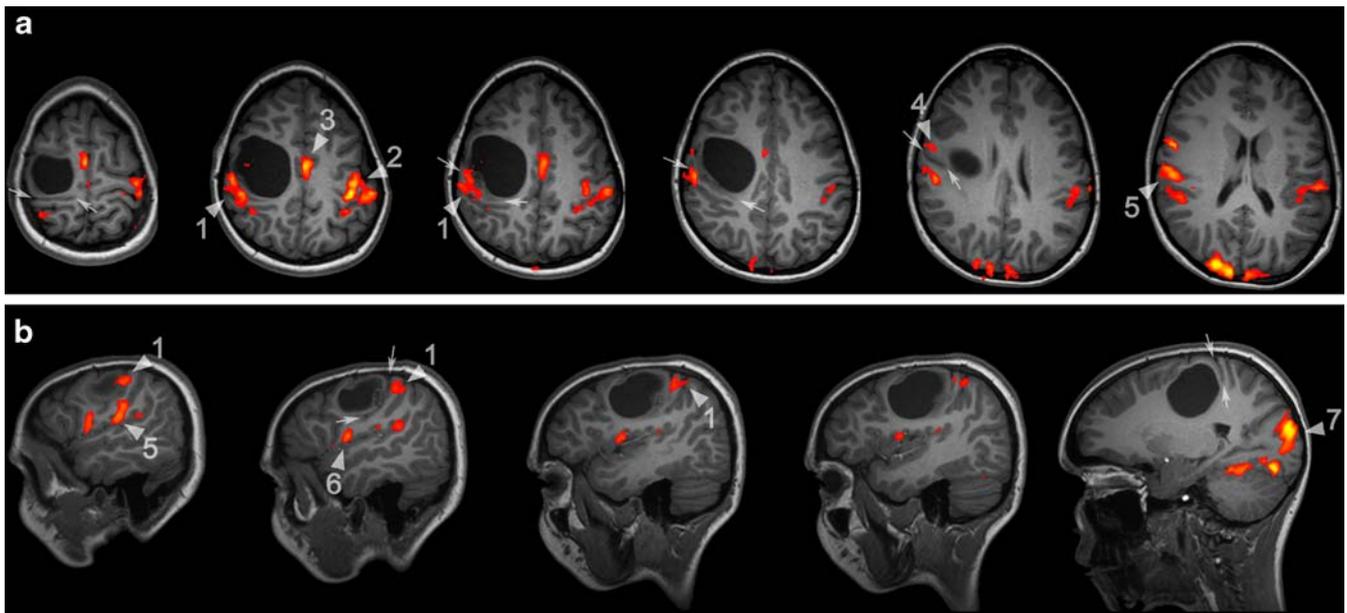


Fig. 2 Statistical parametric map contrasting bilateral finger tapping versus rest overlaid onto transverse (**a**) and sagittal (**b**) non-contrast-enhanced T1W slices in a 16-year-old patient with a histologically proven pilocytic astrocytoma in the right frontal lobe. The central sulcus is delineated by an *arrow*. Activity can be seen in the hand area of the right and left primary sensorimotor (SM1) cortices (1 and 2 respectively). The right SM1 is displaced laterally and posteriorly

by the mass effect of the lesion. The hand representation in the right SM1 is adjacent to the lesion and located just posterior and above the solid part of the tumour. Other regions of activity include the supplementary motor area (3), the right premotor cortex (4), the right (5) and left secondary sensory cortex, the subcentral gyrus (6) and the visual cortex (7)

ments are more suitable for presurgical fMRI, as they can be performed according to the patient's proper capability [33]. The experimental set-up is in favour of block designs over event-related designs because the sensitivity for detection of activation is much higher for block designs. At 1.5T, not more than four cycles of 16-s blocks of movement and rest will result in very robust activation in normal subjects. For patients, it is wise to extend the block

time to about 30 s to compensate for lesser compliance and sometimes compromised movement (in house experience).

While in normal subjects the resulting activation can be attributed unequivocally to the SM1 area, in patients with distorted anatomic landmarks, undesirable co-activation of secondary motor areas, such as the SMA, PMA and SPL, can sometimes interfere with a reliable identification of the primary motor cortex. Papke et al. have suggested a partic-

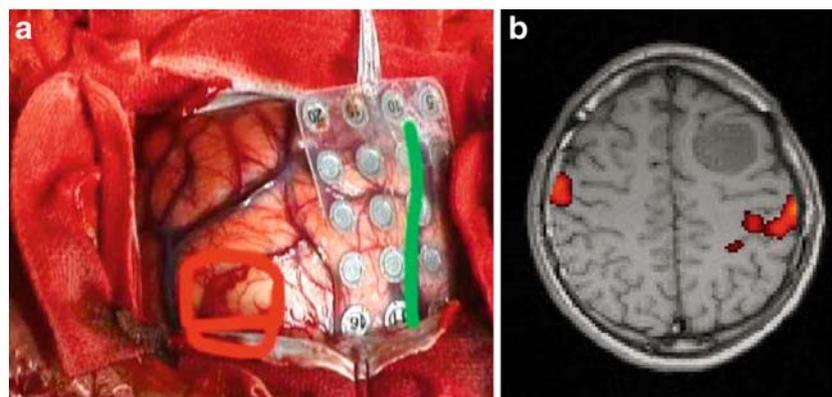


Fig. 3 Correlation between intraoperative cortical stimulation (ICS) and fMRI. The agreement in the location defined by the two methods for motor centres was found to be 93% in a group of women, 73% in a group of men and 84% in the whole group. This figure shows patient MS, with a metastasis ad cerebri. **a** ICS during

somatosensory-evoked potentials. *Red* Tumour, *green* central sulcus. **b** fMRI during sensory task. Activation is seen in the primary sensory cortex contralaterally and in the sensorimotor cortex. Reproduced from [47] with permission

ular experimental design or paradigm set-up by contrasting voluntary movements of the affected side with the normal side. This accentuates activation of the primary motor area and suppresses undesirable co-activations [34].

Voluntary motor paradigms sometimes have to be adjusted to the patient's particular situation. For instance in patients with hand paresis, finger tapping can be replaced by simpler hand clenching. In the case of total motor paralysis with intact sensation, the affected limb can be sensory stimulated and the location of the primary motor cortex can be derived from the location of the primary sensory cortex. Brushing, stroking or rubbing the body part under investigation can be used to map the S1 cortex. Plantar vibrotactile stimulation and electrical stimulation of the median and tibial nerves with dedicated devices have also been used to activate the sensorimotor network [35, 36]. In paralysed patients, even imaginary movement has been shown to produce activation in the primary motor cortex [37].

In terms of validation, several studies reported a good correlation between fMRI and IMT [6, 38–40]. Majos et al. [47] compared preoperative fMRI with ECS in 33 patients with Rolandic brain lesions (Fig. 3). They found 83% agreement for the motor cortex and 83% agreement for the somatosensory cortex between the two techniques. The agreement increased to 98% when both types of activation were taken into account. Recently, Roessler et al. compared preoperative fMRI at 3T with ECS in patients with gliomas in the motor cortex [42] and reported a 100% agreement between fMRI and ECS motor foci within 10 mm.

Presurgical language mapping

The language function can be subdivided into several components, including orthography, phonology, syntax and lexical semantics [44, 57], and relies on a frontal expressive language area (Broca's area), two posterior receptive language areas (Wernicke's and Geschwindt's areas), the dorsolateral prefrontal cortex, the SMA and the interconnecting white matter tracts of which the arcuate fasciculus is the most important. Broca's area is located in the pars triangularis and opercularis of the inferior frontal gyrus. The Wernicke's and Geschwindt's areas are less circumscribed and involve a series of regions in the posterior temporal lobes, including parts of the posterior superior and middle temporal lobe, the angular gyrus, and the supramarginal gyrus.

Language organisation is lateralised. Approximately 95% of right-handed and 70% of left-handed healthy volunteers are left-hemispheric language dominant [45].

Lesions in Broca's area, Wernicke's area or the communicating pathway within the dominant hemisphere can cause severe aphasia. Damage to other language regions may result in transient difficulties, but rarely produces marked aphasia (Fig. 4). It is advisable to use

several different types of language paradigms within the same imaging session, so that different linguistic sub-components can be mapped and to provide for some redundancy in the acquisition of the language network. Therefore, in a preoperative setting, language mapping generally involves paradigms assessing language comprehension or reception on the one side and language production on the other. Language expression or production tasks include verb generation tasks, verbal fluency tasks and picture-naming tasks [46, 48, 49]. These tasks routinely give rise to activation in Broca's area, but secondarily require language comprehension and often co-activate Wernicke's area. Language comprehension or reception can be mapped by means of semantic or grammatical judgment tasks [48], which activate Wernicke's and Geschwindt's areas and to lesser extent also Broca's area. In the case of language impairment (aphasia), in cognitively impaired patients or in children, passive listening tasks can be used as a—far less appropriate—alternative.

For the assessment of language dominance, several studies report a greater than 90% agreement between fMRI and the invasive Wada test [9, 45]. A few case reports urge caution however because of lesion-induced neuro-vascular uncoupling (see below). Word generation tasks (with frontal region-of-interest analysis) generally yield the best results [51]. Good within-test and test–retest intra-subject reproducibility for language lateralisation with fMRI was reported in patients with epilepsy [52]. There is by now enough evidence that language fMRI is a reliable, non-invasive substitute for the Wada test for the assessment of language lateralisation.

In terms of validation of fMRI language mapping by means of ECS, the situation is more problematic than for motor mapping because of a naturally high degree of functional heterogeneity in Broca's and Wernicke's areas [53–55], which is aggravated in patients with brain tumours because of associated language impairment, deformation or plasticity. We would like preoperative fMRI to have a high predictive power in showing the essential language areas. In that respect, a number of studies compared fMRI with IOM and reported different results. This difference in results depends in part on the type and number of tasks used and the applied statistical threshold. Most studies that validate fMRI against ECS for the localisation of the tentative Broca's and Wernicke's areas reported a high sensitivity and specificity, both usually significantly lower for the identification of Wernicke's area. Hirsch demonstrated that sensitivity can be increased by the use of multiple tasks [41]. Others similarly found that specificity increased when multiple tasks were used in combination without sacrificing sensitivity in true positive areas [5, 57]. On the other hand, Roux et al. confusingly reported relatively low sensitivity but high specificity, particularly when the tasks were combined [49].

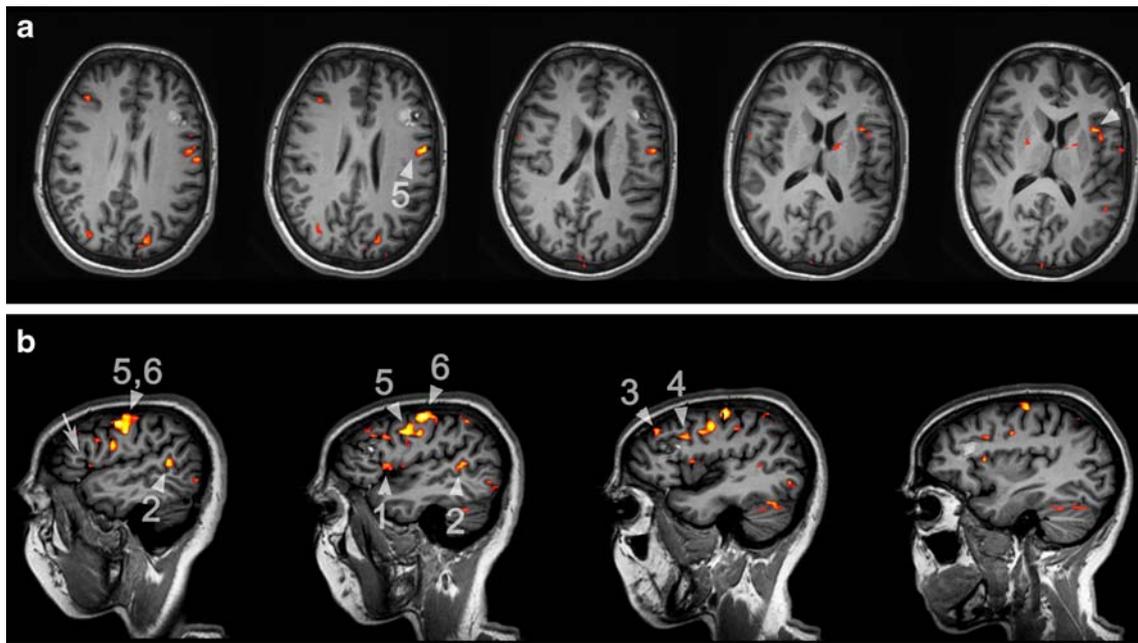


Fig. 4 Statistical parametric map contrasting a verbal fluency task with a counting task overlaid onto transverse (a) and sagittal (b) non-contrast-enhanced T1w slices in a 40-year-old right-handed patient with a cavernous haemangioma in the triangular part (arrow) of the left inferior frontal gyrus. Activity can be seen in the opercular part of the inferior frontal gyrus (1) corresponding to Broca's proper

area. Other expressive language regions are found in the middle frontal gyrus (3 and 5). The receptive language area (Wernicke's) is located in the middle temporal gyrus (2). Additional regions of activation can be seen in the precentral sulcus (5) and gyrus (6) corresponding to the premotor cortex (5) and primary motor cortex (6) respectively

Pitfalls and limitations of presurgical fMRI

fMRI relies on many assumptions and the validity of these have to be checked for each exam: normal vascular reactivity, compliance of the patient (e.g. attention, performance, capacity), stability of the MRI hardware, etc. When all of these conditions are fulfilled, the fMRI results have to be weighted against the expected activation pattern for the paradigm under study. When unexpected findings are present, IMT may still be mandatory. The technical issues described below have to be assessed.

Accuracy of fMRI localisation

BOLD-fMRI is sensitive not only to signal changes in the capillaries and small post-capillary venules in the immediate vicinity of the neuronal electrical activity, but is also sensitive to the signal arising from larger draining veins located at a distance downstream from the actual site of electrical activity.

Several authors [58] suggested the use of spin-echo sequences that greatly reduce the disturbing signal contributions from the macrovasculature, resulting in a superior spatial localisation. However, as SE sequences are less sensitive to magnetic susceptibility effects, the BOLD

contrast is significantly lower, resulting in longer acquisition times or penalty in brain coverage.

The small parenchymal venules are estimated to be maximally 1.5 mm apart from the site of neuronal activation, whereas the spatial uncertainty originating from the larger draining veins was estimated to be no larger than 5 mm. This suggests that although the accuracy of fMRI is sufficient for pre-surgical fMRI, invasive mapping is still mandatory.

Influence of tumours on BOLD effect

BOLD fMRI is critically dependent on an intact functioning of the neurovascular coupling. However, the BOLD response in the cortex surrounding certain brain tumours, especially infiltrative gliomas, does not reflect the electrical neuronal activity as accurately as it does in healthy brain tissue [10, 12, 13]. A disturbed BOLD effect has been reported both in the immediate vicinity of a tumour and in distant "normal" vascular territories. A number of physiological and/or metabolic factors have been invoked, of which abnormal vessel proliferation in the immediate vicinity of high-grade gliomas seems important [59]. This tumour neovasculature does not respond adequately to an increase in neuronal activity because there is loss of

autoregulation and vasoactivity, resulting in false-negative results.

Several case reports illustrated that the absence of activation caused by tumour-induced uncoupling (Fig. 5) could wrongfully be interpreted as brain plasticity or atypical hemispheric language dominance [10, 12, 60].

Head motion artefacts

Head movements, both gradual and abrupt, can induce significant MR signal changes that may wrongfully be interpreted as true activation. Hajnal et al. showed that these movement artefacts are difficult to distinguish from 'real' [61, 62]. Krings et al. found significantly more head motion artefacts in paretic patients, which seemed to be induced by co-innervation of shoulder movements for tasks involving the upper limbs and muscles from the trunk in tasks involving the lower limbs [63].

Susceptibility artefacts

Susceptibility artefacts can be problematic in fMRI acquired with EPI sequences. They are often found at air-tissue interfaces, such as in the medial and basal parts of the temporal lobes and at the orbitofrontal cortex, causing drop-outs in signal intensity and geometric distortions [61, 64]. Vascular lesions, tumour, haemorrhages or prior neurosurgery (presence of titanium plates, surgical clips, haemorrhagic products, residual metal dust from a skull drill) can increase susceptibility artefacts, making it difficult or even impossible to obtain sufficient signal from the surrounding cortex [65]. In the extreme case this may lead the neurosurgeon to resect functionally important cortex. The habit of overlaying the statistical fMRI images onto high-resolution T1-weighted images can be misleading because the susceptibility artefacts are then no longer visible. Therefore, it is advisable to assess the presence of artefacts on the raw T2*-weighted images and to keep in mind that a negative fMRI does not preclude electrical activation.

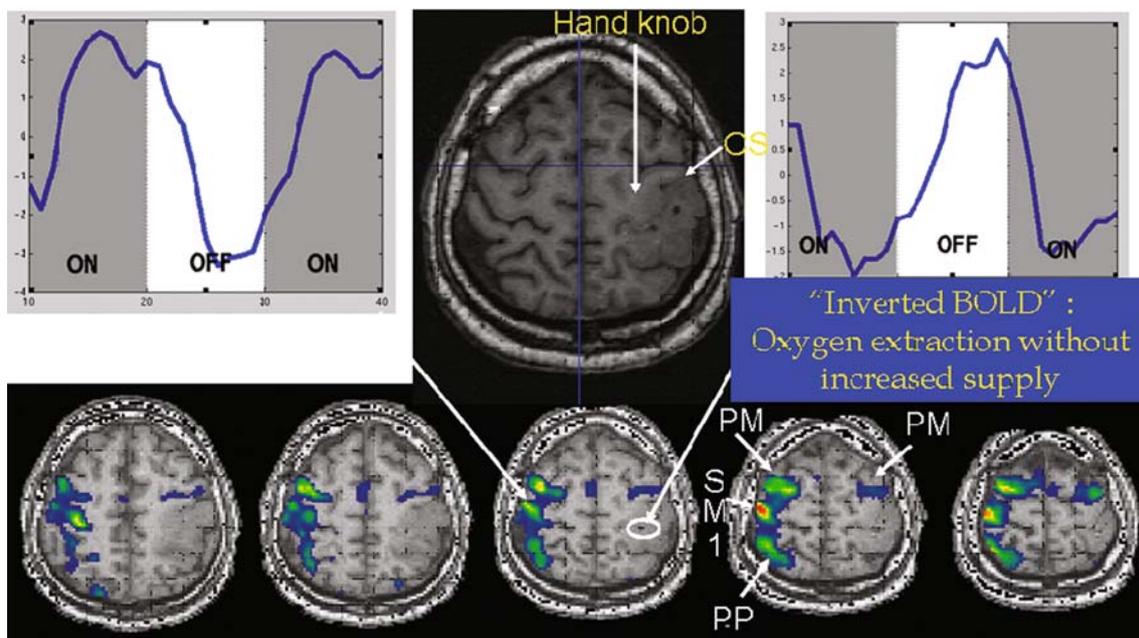


Fig. 5 fMRI activity during bilateral finger-tapping versus rest in a patient with a Rolandic tumour (glioma grade 2) within the post-central gyrus, but extending within the “hand knob” of the precentral gyrus. In the non-lesioned right hemisphere, fMRI activity is observed within the right sensorimotor cortex (SM1; pre- and post-central gyri), the right premotor cortex (PM) and right parietal cortex (PP). In contrast, in the lesioned left hemisphere, activation is only observed anterior from the tumour in the left premotor cortex (PM). While this fMRI activation map might be interpreted as an absence of electrical neuronal activity within the left SM1 and PP areas (e.g. because of plastic changes and the take-over of motor function

within the ipsilateral non-lesioned hemisphere), the time traces of the MR signal changes clearly show that this is a false conclusion. Within the left, tumour-invaded hand area in SM1, the MR signal decreases during performance of the motor task, and increases during the rest or baseline condition, i.e. a BOLD MR signal that changes inversely compared with that expected in normal volunteers. This phenomenon can be explained as a lesion-induced neurovascular uncoupling, where oxygen extraction occurs without increase in regional cerebral blood flow and volume, resulting in a steady decrease in the MR signal during the increased electrical neuronal activity. Reproduced from [54] with permission

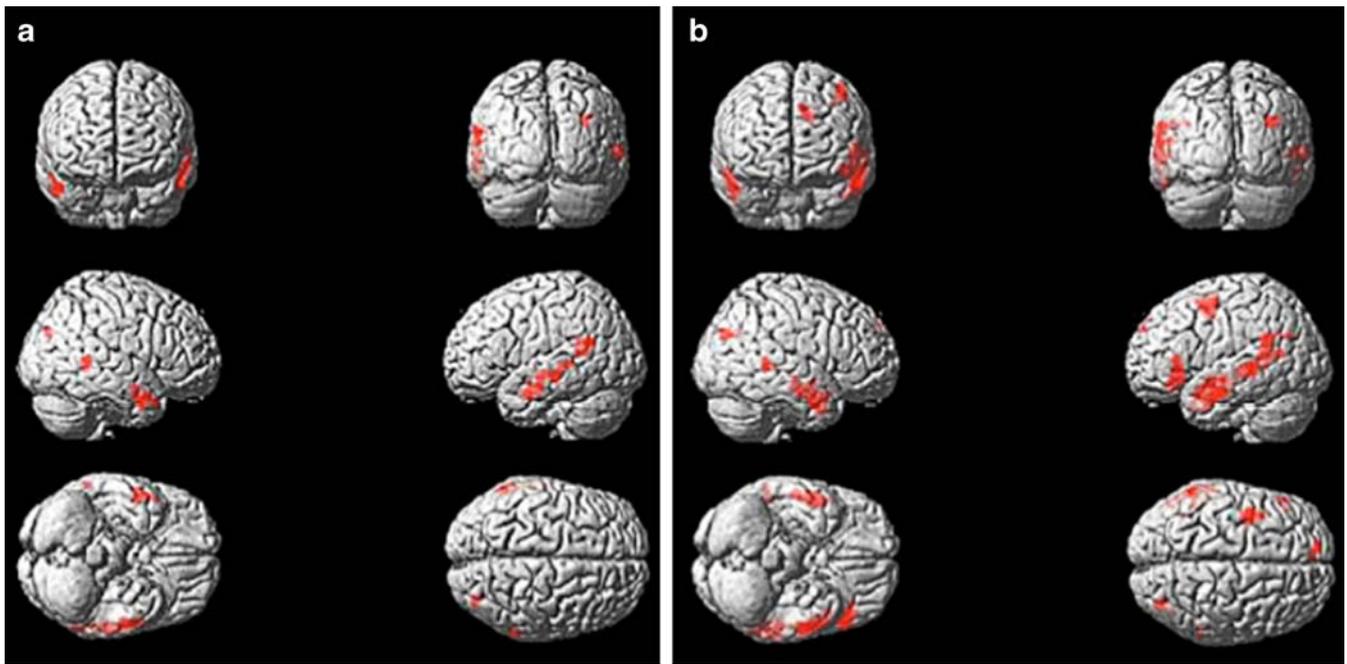


Fig. 6 Areas of significant cerebral activation related to a reading task at 1.5T (a) and 3T (b). Areas of significant activation are shown according to neurological convention in a 3D rendering. Both figures show mainly left lateralised activations in the anterior-posterior part of the middle temporal gyrus, the posterior part

superior temporal gyrus and the inferior parietal lobe. Interestingly, at 3T compared with 1.5T, the activation in several language-related areas is not only increased, but additional areas can also be observed, mainly in the left lateral inferior and middle frontal gyri. Reproduced from [71] with permission

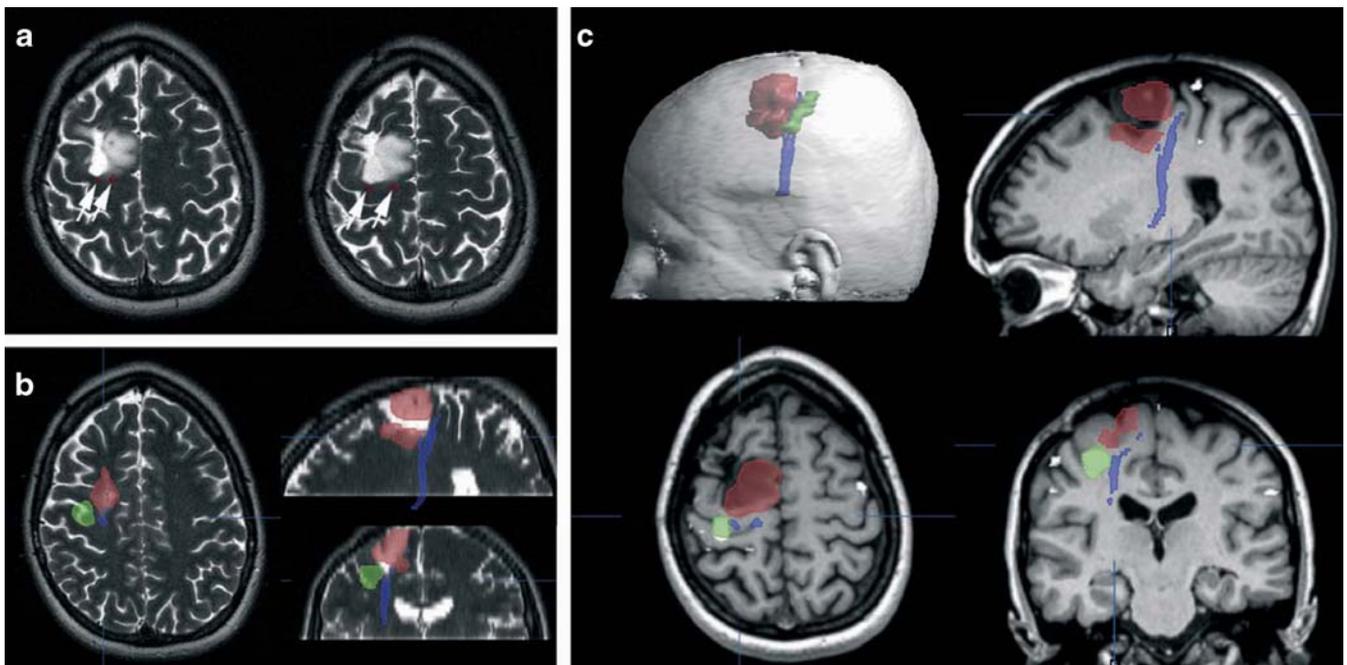


Fig. 7 Generation of a 3D object representing the whole fibre tract bundle of the pyramidal tract (blue). fMRI activation in the hand motor area is shown in green, the tumour in red. Reproduced from [76] with permission

Future perspectives

Influence of higher field strengths in preoperative fMRI

The use of higher field strengths results in improved sensitivity primarily related to BOLD changes in capillary beds, as changes in the relaxation rate R_2^* for a given vascular deoxyhaemoglobin concentration scale linearly with the static magnetic field (B_0) for water protons within or near large vessels ('vein') and quadratically with field strength (B_0^2) for water protons near capillaries ('tissue') [66–68]. Hence, several studies have demonstrated an increased detection of activation at higher field strengths during voluntary movement, visual processing and language processing [68–71] (Fig. 6).

The increased BOLD effect at 3T has several potential benefits in clinical fMRI: it allows reduced imaging time for a given (higher) resolution (and hence better patient compliance, indicated for ill or less cooperative subjects), and reduction of the false negative rate or a combination of both. The advantage of 3T may not hold for cortex affected by susceptibility artefacts, which increase with field strength, so that signal losses in regions of the brain near air–tissue interfaces worsen. This hampers BOLD signal detection in areas such as medial temporal and inferior orbitofrontal regions [67]. To further maximise the beneficial effects of higher fields, future technological improvements are required to cope with these problems. For this purpose, the benefit of more advanced sequences has recently been suggested, such as spin-echo sequences

[72], parallel imaging [73, 74], usage of B_0 field maps, and advanced spiral imaging [75].

Diffusion tensor imaging (DTI)

fMRI provides no or only limited information about the relation of the tumour to white-matter fibre tracts. Interruption of these fibre tracts can lead to major disruptions in neurological function, e.g. conduction aphasia. Evaluation of the relationship of the lesion to these white-matter tracts is sometimes mandatory and can be achieved with other imaging techniques, mainly DTI (Fig. 7).

Conclusions

Most of the studies reviewed here conclude that fMRI has great potential to assist with function-preserving treatment in patients with brain tumours and to substantially reduce the number of invasive measures needed during surgery. A sufficient spatial correlation between fMRI and other mapping techniques seems to exist, especially for the motor areas. However, one should always be aware of the methodological shortcomings of fMRI in a clinical setting, such as tumour-induced neuro-vascular uncoupling, susceptibility artefacts and head motion artefacts. Ultimately, the success of presurgical fMRI will depend on its capability to reduce complication rates, improve clinical outcome and quality of life, as well as survival time, facts that still warrant further study.

References

- Ojemann JG, Ojemann GA, Lettich E (2002) Cortical stimulation mapping of language cortex by using a verb generation task: effects of learning and comparison to mapping based on object naming. *J Neurosurg* 97:33–38
- Desmond JE, Sum JM, Wagner AD, Demb JB, Shear PK, Glover GH et al (1995) Functional MRI measurement of language lateralization in Wada-tested patients. *Brain* 118:1411–1419
- Hund-Georgiadis M, Lex U, Friederici AD, von Cramon DY (2002) Non-invasive regime for language lateralization in right- and left-handers by means of functional MRI and dichotic listening. *Exp Brain Res* 145:166–176
- Atlas SW, Howard RS 2nd, Maldjian J, Alsop D, Detre JA, Listerud J et al (1996) Functional magnetic resonance imaging of regional brain activity in patients with intracerebral gliomas: findings and implications for clinical management. *Neurosurgery* 38:329–338
- FitzGerald DB, Cosgrove GR, Ronner S, Jiang H, Buchbinder BR, Belliveau JW et al (1997) Location of language in the cortex: a comparison between functional MR imaging and electrocortical stimulation. *AJNR* 18:1529–1539
- Lehericy S, Duffau H, Cornu P, Capelle L, Pidoux B, Carpentier A et al (2000) Correspondence between functional magnetic resonance imaging somatotopy and individual brain anatomy of the central region: comparison with intraoperative stimulation in patients with brain tumors. *J Neurosurg* 92:589–598
- Jack CRJ, Thompson RM, Butts RK, Sharbrough FW, Kelly PJ, Hanson DP et al (1994) Sensory motor cortex: correlation of presurgical mapping with functional MR imaging and invasive cortical mapping. *Radiology* 190:85–92
- Binder JR, Swanson SJ, Hammeke TA, Morris GL, Mueller WM, Fischer M et al (1996) Determination of language dominance using functional MRI: a comparison with the Wada test. *Neurology* 46:978–984
- Deblaere K, Boon PA, Vandemaele P, Tieleman A, Vonck K, Vingerhoets G et al (2004) MRI language dominance assessment in epilepsy patients at 1.0 T: region of interest analysis and comparison with intracarotid amytal testing. *Neuroradiology* 46:413–420

10. Holodny AI, Schulder M, Liu WC, Wolko J, Maldjian JA, Kalnin AJ (2000) The effect of brain tumors on BOLD functional MR imaging activation in the adjacent motor cortex: implications for image-guided neurosurgery. *AJNR* 21:1415–1422
11. Petrella JR, Shah LM, Harris KM, Friedman AH, George TM, Sampson JH et al (2006) Preoperative functional MR imaging localization of language and motor areas: effect on therapeutic decision making in patients with potentially resectable brain tumors. *Radiology* 240:793–802
12. Ulmer JL, Krouwer HG, Mueller WM, Ugurel MS, Kocak M, Mark LP (2003) Pseudo-reorganization of language cortical function at fMR imaging: a consequence of tumor-induced neurovascular uncoupling. *AJNR* 24:213–217
13. Schreiber A, Hubbe U, Ziyeh S, Hennig J (2000) The influence of gliomas and nonglial space-occupying lesions on blood-oxygen-level-dependent contrast enhancement. *AJNR* 21:1055–1063
14. Lee CC, Ward HA, Sharbrough FW, Meyer FB, Marsh WR, Raffel C et al (1999) Assessment of functional MR imaging in neurosurgical planning. *AJNR* 20:1511–1519
15. Haberg A, Kvistad KA, Unsgard G, Haraldseth O (2004) Preoperative blood oxygen level-dependent functional magnetic resonance imaging in patients with primary brain tumors: clinical application and outcome. *Neurosurgery* 54:902–914, discussion 914–5
16. Krishnan R, Raabe A, Hattingen E, Szelenyi A, Yahya H, Hermann E et al (2004) Functional magnetic resonance imaging-integrated neuronavigation: correlation between lesion-to-motor cortex distance and outcome. *Neurosurgery* 55:904–914, discussion 914–5
17. Stippich C, Hofmann R, Kapfer D, Hempel E, Heiland S, Jansen O et al (1999) Somatotopic mapping of the human primary somatosensory cortex by fully automated tactile stimulation using functional magnetic resonance imaging. *Neurosci Lett* 277:25–28
18. Desmond JE, Annabel Chen SH (2002) Ethical issues in the clinical application of fMRI: factors affecting the validity and interpretation of activations. *Brain Cogn* 50:482–497
19. Nelson L, Lapsiwala S, Haughton VM, Noyes J, Sadrzadeh AH, Moritz CH et al (2002) Preoperative mapping of the supplementary motor area in patients harboring tumors in the medial frontal lobe. *J Neurosurg* 97:1108–1114
20. Zentner J, Hufnagel A, Pechstein U, Wolf HK, Schramm J (1996) Functional results after resective procedures involving the supplementary motor area. *J Neurosurg* 85:542–549
21. Krainik A, Lehericy S, Duffau H, Capelle L, Chainay H, Cornu P et al (2003) Postoperative speech disorder after medial frontal surgery: role of the supplementary motor area. *Neurology* 60:587–594
22. O'Shea JP, Whalen S, Branco DM, Petrovich NM, Knierim KE, Golby AJ (2006) Integrated image- and function-guided surgery in eloquent cortex: a technique report. *Int J Med Robot* 2:75–83
23. Jannin P, Fleig OJ, Seigneuret E, Grova C, Morandi X, Scarabin JM (2000) A data fusion environment for multimodal and multi-informational neuronavigation. *Comput Aided Surg* 5:1–10
24. Rasmussen IAJ, Lindseth F, Rygh OM, Berntsen EM, Selbekk T, Xu J et al (2007) Functional neuronavigation combined with intra-operative 3D ultrasound: initial experiences during surgical resections close to eloquent brain areas and future directions in automatic brain shift compensation of preoperative data. *Acta Neurochir (Wien)* 149:365–378
25. Turner R, Le Bihan D, Moonen CT, Despres D, Frank J (1991) Echo-planar time course MRI of cat brain oxygenation changes. *Magn Reson Med* 22:159–166
26. Ogawa S, Lee TM, Kay AR, Tank DW (1990) Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc Natl Acad Sci USA* 87:9868–9872
27. Bandettini PA, Wong EC, Hinks RS, Tikofsky RS, Hyde JS (1992) Time course EPI of human brain function during task activation. *Magn Reson Med* 25:390–397
28. Fujiwara N, Sakatani K, Katayama Y, Murata Y, Hoshino T, Fukaya C et al (2004) Evoked-cerebral blood oxygenation changes in false-negative activations in BOLD contrast functional MRI of patients with brain tumors. *Neuroimage* 21:1464–1471
29. Leybaert L (2005) Neurobarrier coupling in the brain: a partner of neurovascular and neurometabolic coupling? *J Cereb Blood Flow Metab* 25:2–16
30. Alkadhi H, Kollias SS, Crelier GR, Golay X, Hepp-Reymond MC, Valavanis A (2000) Plasticity of the human motor cortex in patients with arteriovenous malformations: a functional MR imaging study. *AJNR* 21:1423–1433
31. Rizzolatti G, Luppino G, Matelli M (1998) The organization of the cortical motor system: new concepts. *Electroencephalogr Clin Neurophysiol* 106:283–296
32. Penfield W, Rasmussen T (1950) *The cerebral cortex of man*. MacMillan, New York
33. Tieleman A, Seurinck R, Deblaere K, Vandemaele P, Vingerhoets G, Achten E (2005) Stimulus pacing affects the activation of the medial temporal lobe during a semantic classification task: an fMRI study. *Neuroimage* 26:565–572
34. Papke K, Reimer P, Renger B, Schuierer G, Knecht S, Schulz M et al (2000) Optimized activation of the primary sensorimotor cortex for clinical functional MR imaging. *AJNR* 21:395–401
35. Golaszewski SM, Siedentopf CM, Koppelstaetter F, Fend M, Ischebeck A, Gonzalez-Felipe V et al (2006) Human brain structures related to plantar vibrotactile stimulation: a functional magnetic resonance imaging study. *Neuroimage* 29:923–929
36. Gasser TG, Sandalcioglu EI, Wiedemayer H, Hans V, Gizewski E, Forsting M et al (2004) A novel passive functional MRI paradigm for preoperative identification of the somatosensory cortex. *Neurosurg Rev* 27:106–112
37. Stippich C, Ochmann H, Sartor K (2002) Somatotopic mapping of the human primary sensorimotor cortex during motor imagery and motor execution by functional magnetic resonance imaging. *Neurosci Lett* 331:50–54
38. Yetkin FZ, Mueller WM, Morris GL, McAuliffe TL, Ulmer JL, Cox RW et al (1997) Functional MR activation correlated with intraoperative cortical mapping. *AJNR* 18:1311–1315
39. Dymarkowski S, Sunaert S, Van Oostende S, Van Hecke P, Wilms G, Demaerel P et al (1998) Functional MRI of the brain: localisation of eloquent cortex in focal brain lesion therapy. *Eur Radiol* 8:1573–1580

40. Achten E, Jackson GD, Cameron JA, Abbott DF, Stella DL, Fabinyi GC (1999) Presurgical evaluation of the motor hand area with functional MR imaging in patients with tumors and dysplastic lesions. *Radiology* 210:529–538
41. Hirsch J, Ruge MI, Kim KH, Correa DD, Victor JD, Relkin NR et al (2000) An integrated functional magnetic resonance imaging procedure for preoperative mapping of cortical areas associated with tactile, motor, language, and visual functions. *Neurosurgery* 47:711–721, discussion 721–2
42. Roessler K, Donat M, Lanzenberger R, Novak K, Geissler A, Gartus A et al (2005) Evaluation of preoperative high magnetic field motor functional MRI (3 Tesla) in glioma patients by navigated electrocortical stimulation and postoperative outcome. *J Neurol Neurosurg Psychiatry* 76:1152–1157
43. Naidich TP, Hof PR, Gannon PJ, Yousry TA, Yousry (2001) Anatomic substrates of language: emphasizing speech. *Neuroimaging Clin N Am* 11:305–341
44. Noppeney U, Josephs O, Hocking J, Price CJ, Friston KJ (2008) The effect of prior visual information on recognition of speech and sounds. *Cereb Cortex* 18:598–609
45. Lurito JT, Dzemidzic M (2001) Determination of cerebral hemisphere language dominance with functional magnetic resonance imaging. *Neuroimaging Clin N Am* 11:355–363
46. Rutten GJ, van Rijen PC, van Veelen CW, Ramsey NF (1999) Language area localization with three-dimensional functional magnetic resonance imaging matches intrasulcal electrostimulation in Broca's area. *Ann Neurol* 46:405–408
47. Majos A, Tybor K, Stefanczyk L, Goraj B (2005) Cortical mapping by functional magnetic resonance imaging in patients with brain tumors. *Eur Radiol* 15:1148–1158
48. Deblaere K, Backes WH, Hofman P, Vandemaële P, Boon PA, Vonck K et al (2002) Developing a comprehensive presurgical functional MRI protocol for patients with intractable temporal lobe epilepsy: a pilot study. *Neuroradiology* 44:667–673
49. Roux FE, Boulanouar K, Lotterie JA, Mejdoubi M, LeSage JP, Berry I (2003) Language functional magnetic resonance imaging in preoperative assessment of language areas: correlation with direct cortical stimulation. *Neurosurgery* 52:1335–1345, discussion 1345–7
50. Mueller WM, Yetkin FZ, Hammeke TA, Morris GL 3rd, Swanson SJ, Reichert K et al (1996) Functional magnetic resonance imaging mapping of the motor cortex in patients with cerebral tumors. *Neurosurgery* 39:515–520, discussion 520–1
51. Benson RR, FitzGerald DB, LeSueur LL, Kennedy DN, Kwong KK, Buchbinder BR et al (1999) Language dominance determined by whole brain functional MRI in patients with brain lesions. *Neurology* 52:798–809
52. Fernandez G, Specht K, Weis S, Tendolkar I, Reuber M, Fell J et al (2003) Intrasubject reproducibility of presurgical language lateralization and mapping using fMRI. *Neurology* 60:969–975
53. Amunts K, Schleicher A, Burgel U, Mohlberg H, Uylings HB, Zilles K (1999) Broca's region revisited: cytoarchitecture and intersubject variability. *J Comp Neurol* 412:319–341
54. Amunts K, Weiss PH, Mohlberg H, Pieperhoff P, Eickhoff S, Gurd JM et al (2004) Analysis of neural mechanisms underlying verbal fluency in cytoarchitectonically defined stereotaxic space—the roles of Brodmann areas 44 and 45. *Neuroimage* 22:42–56
55. Price CJ (2000) The anatomy of language: contributions from functional neuroimaging. *J Anat* 197:335–359
56. Rutten GJ, Ramsey NF, van Rijen PC, Noordmans HJ, van Veelen CW (2002) Development of a functional magnetic resonance imaging protocol for intraoperative localization of critical temporoparietal language areas. *Ann Neurol* 51:350–360
57. Rutten GJ, Ramsey NF, van Rijen PC, van Veelen CW (2002) Reproducibility of fMRI-determined language lateralization in individual subjects. *Brain Lang* 80:421–437
58. Abduljalil AM, Kangarlu A, Yu Y, Robitaille PM (1999) Macroscopic susceptibility in ultra high field MRI. II: Acquisition of spin echo images from the human head. *J Comput Assist Tomogr* 23:842–844
59. Hou BL, Bradbury M, Peck KK, Petrovich NM, Gutin PH, Holodny AI (2006) Effect of brain tumor neovascularity defined by rCBV on BOLD fMRI activation volume in the primary motor cortex. *Neuroimage* 32:489–497
60. Sunaert S (2006) Presurgical planning for tumor resectioning. *J Magn Reson Imaging* 23:887–905
61. O'Doherty J, Rolls ET, Francis S, Bowtell R, McGlone F, Kopal G et al (2000) Sensory-specific satiety-related olfactory activation of the human orbitofrontal cortex. *Neuroreport* 11:893–897
62. Hajnal JV, Myers R, Oatridge A, Schwieso JE, Young IR, Bydder GM (1994) Artifacts due to stimulus correlated motion in functional imaging of the brain. *Magn Reson Med* 31:283–291
63. Krings T, Reinges MH, Erberich S, Kemeny S, Rohde V, Spetzger U et al (2001) Functional MRI for presurgical planning: problems, artefacts, and solution strategies. *J Neurol Neurosurg Psychiatr* 70:749–760
64. Devlin JT, Russell RP, Davis MH, Price CJ, Wilson J, Moss HE et al (2000) Susceptibility-induced loss of signal: comparing PET and fMRI on a semantic task. *Neuroimage* 11:589–600
65. Kim MJ, Holodny AI, Hou BL, Peck KK, Moskowitz CS, Bogomolny DL et al (2005) The effect of prior surgery on blood oxygen level-dependent functional MR imaging in the preoperative assessment of brain tumors. *AJNR* 26:1980–1985
66. Ugurbil K, Hu X, Chen W, Zhu XH, Kim SG, Georgopoulos (1999) A functional mapping in the human brain using high magnetic fields. *Philos Trans R Soc Lond B Biol Sci* 354:1195–1213
67. Kruger G, Kastrup A, Glover GH (2001) Neuroimaging at 1.5 T and 3.0 T: comparison of oxygenation-sensitive magnetic resonance imaging. *Magn Reson Med* 45:595–604
68. Krasnow B, Tamm L, Greicius MD, Yang TT, Glover GH, Reiss AL et al (2003) Comparison of fMRI activation at 3 and 1.5 T during perceptual, cognitive, and affective processing. *Neuroimage* 18:813–826
69. Yang Y, Wen H, Mattay VS, Balaban RS, Frank JA, Duyn JH (1999) Comparison of 3D BOLD functional MRI with spiral acquisition at 1.5 and 4.0 T. *Neuroimage* 9:446–451
70. Hoenig K, Kuhl CK, Scheef L (2005) Functional 3.0-T MR assessment of higher cognitive function: are there advantages over 1.5-T imaging? *Radiology* 234:860–868

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71. Tieleman A, Vandemaele P, Seurinck R, Deblaere K, Achten E (2007) Comparison between functional magnetic resonance imaging at 1.5 and 3 Tesla: effect of increased field strength on 4 paradigms used during presurgical work-up. *Invest Radiol* 42:130–138
 72. Jovicich J, Norris DG (1999) Functional MRI of the human brain with GRASE-based BOLD contrast. *Magn Reson Med* 41:871–876
 73. Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P (1999) SENSE: sensitivity encoding for fast MRI. *Magn Reson Med* 42:952–962
 74. Weiger M, Pruessmann KP, Osterbauer R, Bornert P, Boesiger P, Jezzard P (2002) Sensitivity-encoded single-shot spiral imaging for reduced susceptibility artifacts in BOLD fMRI. *Magn Reson Med* 48:860–866
 75. Preston AR, Thomason ME, Ochsner KN, Cooper JC, Glover GH (2004) Comparison of spiral-in/out and spiral-out BOLD fMRI at 1.5 and 3 T. *Neuroimage* 21:291–301
 76. Nimsy C, Ganslandt O, Merhof D, Sorensen AG, Fahlbusch R (2006) Intraoperative visualization of the pyramidal tract by diffusion-tensor-imaging-based fiber tracking. *Neuroimage* 30:1219–1229