Impact of the combined use of tractography, functional magnetic resonance imaging and brain neuronavigation on high grade glioma extent of resection

Abstract

Introduction: Maximal surgical resection of brain high grade glioma, involves the risk of damaging either eloquent cortical areas or efferent subcortical white matter tracts. Identification of the anatomical and functional relation between the tumor and adjacent functional cortical areas or eloquent white matter bundles may provide critical information to guide tumor resection and prevent surgical morbidity. The main objective of this study was to assess the combined use of diffusion tensor (DT) tractography and functional magnetic resonance (fMR) imaging to assist in the extent of resection of brain high grade glioma (HGG) with preservation of eloquent areas. Material and methods: 42 consecutive patients harboring brain HGG underwent surgery with the purpose of maximal resection. Patients were randomly divided in two groups: Group A (22 cases): control group, and group B (20 cases), where surgery was performed with navigation and combined use of DT imaging and fMR imaging. Results: Extent of resection in group A was 81.5% and 90.5% in group B (ANOVA's test p=0.03). We did not observe differences in postoperative neurological deficit and surgical time between both groups. Conclusion: The combined use of tractography, functional MRI and neuronavigation may provide critical information to guide brain high grade glioma resection without increasing surgical morbidity or surgical time.

Resumen

Introducción: La resección radical de los gliomas cerebrales de alto grado (GCAG) comporta el riesgo de afectación tanto de áreas corticales elocuentes como de los tractos subcorticales de sustancia blanca. La identificación de la relación anatómica y funcional entre el tumor y las áreas corticales o los tractos de sustancia blanca elocuentes, puede proporcionar una información fundamental para guiar la resección quirúrgica y contribuir a reducir la morbilidad postquirúrgica. El principal objetivo del estudio es el análisis del uso combinado de la tractografía y la resonancia magnética funcional (RMf) en el grado de resección de gliomas cerebrales de alto grado con preservación de áreas elocuentes. Material y métodos: Presentamos 42 pacientes con diagnóstico de GCAG y localización próxima a córtex motor o áreas del lenguaje, que fueron intervenidos quirúrgicamente con el objetivo de llevar a cabo una resección radical de la lesión. Los pacientes se distribuyeron de forma aleatoria en 2 grupos: el grupo A (22 pacientes) fue el grupo control y el grupo B (20 casos) fue también intervenido pero utilizando la neuronavegación y el uso combinado de tractografía y RMf. Resultados: El grado de resección en el grupo A fue de un 81,5% y del 90,5% en el grupo B (test de ANOVA p=0,03). No observamos diferencias en la incidencia de morbilidad postquirúrgica o del tiempo de cirugía entre ambos grupos. Conclusiones: El uso combinado de la tractografía, RMf y neuronavegación proporciona una información funcional que facilita la cirugía de los GCAG sin incrementar la morbilidad o el tiempo de cirugía.

Keywords: Diffusion tensor; functional magnetic resonance; high grade glioma; neuronavigation; surgery; tractography.
Introduction
Management of brain high grade glioma depends on a multidisciplinary treatment that includes surgery, radiotherapy and chemotherapy. Although is a pathology not curable with neurosurgical procedures, the extent of resection might have an influence on the further course of the disease. Nevertheless, maximal surgical resection of brain high grade glioma, involves the risk of damaging either eloquent cortical areas or efferent subcortical white matter tracts.

Diffusion tensor (DT) tractography is a noninvasive magnetic resonance (MR) technique that can provide subcortical localization of motor pathways, whereas functional magnetic resonance (fMR) imaging has been proved to be useful in the localization of eloquent cerebral cortex. These techniques are complimentary and allow both the identification of the eloquent areas of the brain, and the connections between them.

Identification of the anatomical and functional relation between the tumor and adjacent functional cortical areas or eloquent white matter bundles may provide critical information to guide tumor resection and prevent surgical morbidity.

This functional neuronavigation allows the preoperative planning of patients with mass lesions affecting functionally important brain regions as well as to visualize intraoperatively eloquent white matter bundles or gray matter tissue with relationship to brain tumor. The main objective of this study was to assess the combined use of DT and fMR imaging to assist in the increase of resection of high grade glioma with improved preservation of eloquent regions during surgery.

Materials and Methods

42 consecutive patients operated of high grade glioma in two years were included in the study. All of them underwent surgery with the purpose of maximal resection, being excluded brain biopsies. Patients were randomly divided in two groups: Group A (22 cases): control group, surgery with navigation without combined use of DT imaging and fMR imaging, and group B (20 cases), surgery with navigation and combined use of DT imaging and fMR imaging. Data sets of DT imaging, magnetic resonance imaging, and functional magnetic resonance imaging were acquired preoperatively during the same investigation in 22 patients harboring brain high grade glioma. Off-line processing of DT imaging data was performed to visualize the corticospinal tract (CST), superior longitudinal tract, corpus callosum fibers and uncinate fascicule. The target region of interest for the CST was placed in the cerebral peduncle of the midbrain, where a high density of fibers of the descending motor pathway is found. fMR imaging cortical activation maps of motor and somatosensory regional activation were obtained. Then this information was transferred to the neuronavigation system (Brainlab) to initiate functional neuronavigation. (Fig.1)

A control MRI was performed not later than 48h after surgery. The extent of resection observed in these control MRI was assessed by regular team of neuroradiologists of our hospital and by an external independent neuroradiologist. As well as extent of resection, data sets of age and sex, tumoral volume, tumoral localization, surgical postoperative neurological deficit and surgical time were recorded. Univariate and multivariate analysis were performed and a level of signification < 0.05 was established to determine differences between both groups in terms of extent of resection, postoperative neurological deficit, and surgical time.

Results

Twenty-two patients, 19 male and 3 female, formed the control group in which the mean age was 59.9 years old with a minimum of 28 and a maximum of 79. In the studied group of twenty patients, 15 male and 5 female, the mean age was...
57.9 with a minimum of 22 and a maximum of 78 years old.

In group A 14 patients out of 20 harbored tumor in eloquent areas, whereas in group B were 14 patients out of 22. Pathology showed 18 glioblastoma multiform (GBM) and 4 anaplastic astrocytoma (AA) in group A and 15 GBM, 4 AA and 1 anaplastic ependymoma in group B.

Tumoral volume in group A was less than 20cc in 8 patients, from 20 to 40 cc in 7 patients and superior to 40 cc in 7 patients. In group B we found tumoral volume less than 20cc in 8 patients, from 20 to 40 cc in 6 patients and superior to 40 cc in 6 patients.

The extent of resection in group A was 60-70% in 4 patients, 70-80% in 5 patients, 80-90% in 1 patient and 90-100% in 12 patients. In group B 60-70% of resection was achieved in 2 patients, 70-80% in 2 patients, and 90-100% in 16 patients.

Overall, the extent of resection in group A was 81, 5% and 90, 5% in group B (ANOVA test p=0, 03). In a multivariate analysis, sex, age, pathology or tumoral volume were found not to affect the different extent of resection between both groups.

Despite not being statistically significant, we found a trend of a higher extent of resection in eloquent areas in group B (87.3% compared to 79.1% in group A). In non eloquent areas a significant increase of resection was found in group B (100%) compared to group A (85.2%) (ANOVA test p=0, 017). Resections observed in eloquent areas in patients of group B were superior to those obtained in non eloquent areas in group A.

We did not observed differences in terms of postoperative neurological morbidity between both groups (around 10% of patients), but those patients without neurological complications belonging to group B had a significant higher extent of resection that those of group A. (ANOVA test p=0, 01). Surgical time was found to have no differences between groups.

Discussion

Preoperative assessment provided by DT tractography and fMR about the location of functional fiber tracts and expressive cortical areas in patients with brain tumor, cannot be obtained by conventional imaging methods. Nevertheless, knowledge of those critical areas and their relationship to the tumor is of major interest for reducing operative morbidity [19, 33].

Accuracy of DTI and fMR

To establish the accuracy of both techniques is of great value in order to rely on the information provided to take intraoperative surgical decisions. In that way, several studies have addressed this problem verifying the estimated course of a specific tract after direct intraoperative subcortical stimulation. The mean distance between the stimulation sites and the DT-imaged fiber tracks varies from 2mm to 1cm in the pyramidal tract [3, 16, 18, 24] and to visualize language-related subcortical connections, such as the arcuate fasciculus (AF) distances between the stimulus points and the AF were within 6 mm [10]. In these studies motor evoked potential (MEP) response has been documented to be consistently absent at distances beyond 10 to 13 mm of the estimated pyramidal tract [11, 18].

Intraoperative diffusion-weighted imaging using an intraoperative MR scanner of low magnetic field strength (0.3 Tesla) has been developed demonstrating clinical usefulness and efficacy in detecting the pyramidal tract and its relationship with tumor borders [26]. Comparing with other techniques, DT tractography appears to be more accurate than functional magnetic resonance imaging and somatosensory evoked magnetic fields in detecting primary motor area, with rates of successful detection between 92 to 100% [5, 12]. Several series conclude that tractography imaging is consistent with anatomical and functional intraoperative references and is useful in neurological surgery [2, 4].

Several studies have focused on the functional accuracy of fMR imaging findings, evaluating the correlation between fMR findings and the results of intraoperative direct cortical stimulation in patients who harbor tumors in eloquent areas. Correlation is high, from 82 to 100% in different series, mainly in the evaluation of motor function [8, 9, 27]. Nevertheless, in language cortical areas, brain mapping additional to fMR is advised to make surgical decisions [30].

Limitations of the technique

Major limitations of the combined use of DT tractography and fMR in the resection of HGG include a possible shifting of the tracts after major tumor parts are removed, the acquisition technique that usually relies on subjective identification of anatomical landmarks of a tract of interest and the length of time required for the procedure [1, 6, 22, 23, 24, 31, 39]. Shifted positions of the brain structures after tumor removal have been compensated usually with intraoperative updates by using motor evoked potentials with intraoperative fiber stimulation [11], intraoperative high-field magnetic resonance imaging [20, 23] including intraoperative tractography [22] and intraoperative three-dimensional ultrasound neuronavigation system [7]. In some cases it has been observed that the images of fiber-tracking technique failed to present the disposition of the fiber bundles [1, 13] due to the acquisition technique or vicinity of areas with elevated water content (edema), tissue compression or fiber degeneration [31]. To avoid fiber distortion it has been proposed to use the seed region of interest for DT tractography based on fMR, instead of anatomical landmarks [31] and to apply...
an automated approach of tract reconstruction to reduce potential subjective variability due to manual procedure [39]. As regards to the length of time required for the procedure in our experience is not significantly increased and has been quantified to amount to up to 10 minutes of added time. [21]

Clinical and operative results

Only one prospective, randomized controlled study has been carried out in patients with cerebral glioma to study the effect of tractography over the extent of resection, postoperative morbidity and Karnofsky Performance Scale, and mean survival time [38]. Compared to the control group, the use of DT tractography associated increased extent of resection in HGG (gross total resection of 74.4 versus 33.3% in control group), significantly higher 6-month Karnofsky Performance Scale score and significantly lower postoperative motor deterioration. Mean survival after surgery in HGG was also significantly longer.

Different studies have focused on the safety of the tractography guided surgery of tumors near the motor tract, based on lower postoperative morbidity mainly when associated with intraoperative brain stimulation [2,11,16,17,18,25]. Preoperative planning by using combination of fMR and DT tractography appears to improve surgical results in terms of function preservation [9]. Nevertheless, the increase of the extent of resection due to that preoperative combination has been infrequently addressed with only 27% of complete resections being reported. These data were improved by using intraoperative MRI up to 40% of patients with complete resections. Despite extended resections the low postoperative morbidity remained being frequently transient deficits [20]. More frequently, experiences with fMR guided neuronavigation have been reported with gross total resection (more than 95%) of gliomas in 83% to 91% of the patients and postoperative neurological deterioration in 16% to 31% of patients [15,29].

It has been demonstrated in DT tractography studies that despite tumor infiltration, swelling, apparent necrosis, and gross distortion, anatomically intact fibers may remain located inside the tumor mass [2,14,32,34,35,36,37]. This fact implies a modification of the surgical strategy in terms of avoiding postoperative neurological deterioration. An interesting experience has focused of the impact of tractography on the surgical procedure in terms of modification of surgical approach and extent of resection during surgery and has quantified it to appear in 80% of cases [28].

Our results in terms of extent of resection are consistent with those of the literature. Even though our series include patients harboring tumor in presumably non eloquent areas, the extent of resection of 87.3% in eloquent areas compares favorably with those of the majority of larger series, mainly given the fact that no intraoperative method was used to correct brain shift or verify eloquent cortical or white matter areas. The only prospective, randomized controlled study performed to assess the usefulness of tractography in surgical resection of gliomas found a significantly clinical improvement in terms of Karnofsky performance scale, neurological deficit and survival [38]. Our study does not include survival analysis, but patients of the studied group did not differ from those of the control group in number of postoperative neurological deficit. With regard to this fact, it should be taken into consideration the higher rate of motor deterioration observed 32.8% in the control group of the randomized controlled study compared to 10% detected in the present study. Even though we did not reduce the rate of neurological deterioration, we significantly increased the extent of resection in patients without neurological postoperative complications.

Conclusions

The combination of fMRI with DT tractography allows for assessment of eloquent cerebral cortex and visualization of functional white matter fibers and ensures higher extent of resection during surgery of high grade glioma. Three dimensional visualization of the white matter fibers such as corticospinal tract, optic radiation and arcuate fasciculus with relationship to high grade gliomas is helpful, and when used routinely in neuronavigation surgery of high grade glioma does not increase the length of surgery neither increase the neurological deficit rate despite the increased resection in both eloquent and non eloquent areas. The main drawbacks of the technique are the intraoperative shift of the tracts after tumor removal and the subjective procedure of selection of fiber tracts during the acquisition of DT tractography.
References


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Trabajo presentado de forma preliminar en el Congreso de la Sociedad Española de Neurocirugía celebrado en Valencia en 2008.