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Tools and techniques

Preoperative navigated transcranial magnetic stimulation and tractography in transparietal approach to the trigone of the lateral ventricle

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ABSTRACT

Objective: Eloquent neural structures including white matter tracts surround the trigone of the lateral ventricle. Surgical resection of trigonal tumors via the transparietal approach may cause neurological deterioration depending on the trajectory.
Methods: The authors retrospectively reviewed patients with trigonal tumors that underwent combined preoperative navigated transcranial magnetic stimulation (nTMS) and optic radiation tractography to guide a transparietal approach towards the trigone.
Results: Five patients underwent preoperative nTMS motor mapping, rTMS language mapping, nTMS-derived corticospinal tract tractography, and optic radiation tractography. The information was used to select the optimal trajectory for a transparietal approach and for intraoperative neuronavigation. Four patients underwent surgical resection. None of them experienced a new permanent deficit.
Conclusion: Combination of preoperative nTMS and optic radiation tractography facilitates the identification of the optimal parietal trajectory towards the trigone. It allows for sparing of visual and motor pathways as well as cortical language areas.

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1. Introduction

The lateral ventricle of the ventricular system resembles a C-shape structure made up of an anterior (frontal), a posterior (occipital) and an inferior (temporal) horn. The trigone of the lateral ventricle is at the junction of the posterior and inferior horns. This area represents the floor of the atrium of the lateral ventricle [1,2].

Tumors located within the trigone, such as intraventricular meningiomas or choroid plexus papillomas, are rare [3,4]. Parenchymal tumors located adjacent to the trigrone like gliomas and metastases are much more frequent [5]. Selection of the optimal surgical trajectory can be challenging. Depending on tumor entity, size, location and extension, and size of the ventricles, various surgical approaches have been proposed including the supracerebellar, transtentorial, transcollateral sulcus approach [6,7], the contralateral transfalcine, transprecuneus approach [8,9], and the distal Sylvian, lateral transtemporal, or subtemporal approaches [1,2]. Every approach inherits specific benefits and risks. The transparietal approach is another option to approach the trigone (Fig. 1). The cortical incision is performed within or in proximity of the intraparietal sulcus (IPS) or nearby sulci. This approach is referred to as transsulcal, intraparietal, or parietal intrasulcal approach. Transsulcal dissection was described by Yasargil with the intention to minimize damage of white matter tracts by using the shortest possible distance to deep seated tumors [10]. The IPS separates the medially located superior parietal and laterally located inferior parietal lobes (IPL). The parietal transsulcal approach has been used to operate on both vascular malformations and cerebral neoplasms. This approach allows avoidance of the visual pathway, speech areas, and sensorimotor areas. However, the reach of the transparietal approach to the trigone is long and incautious dissection and retractor placement may cause significant

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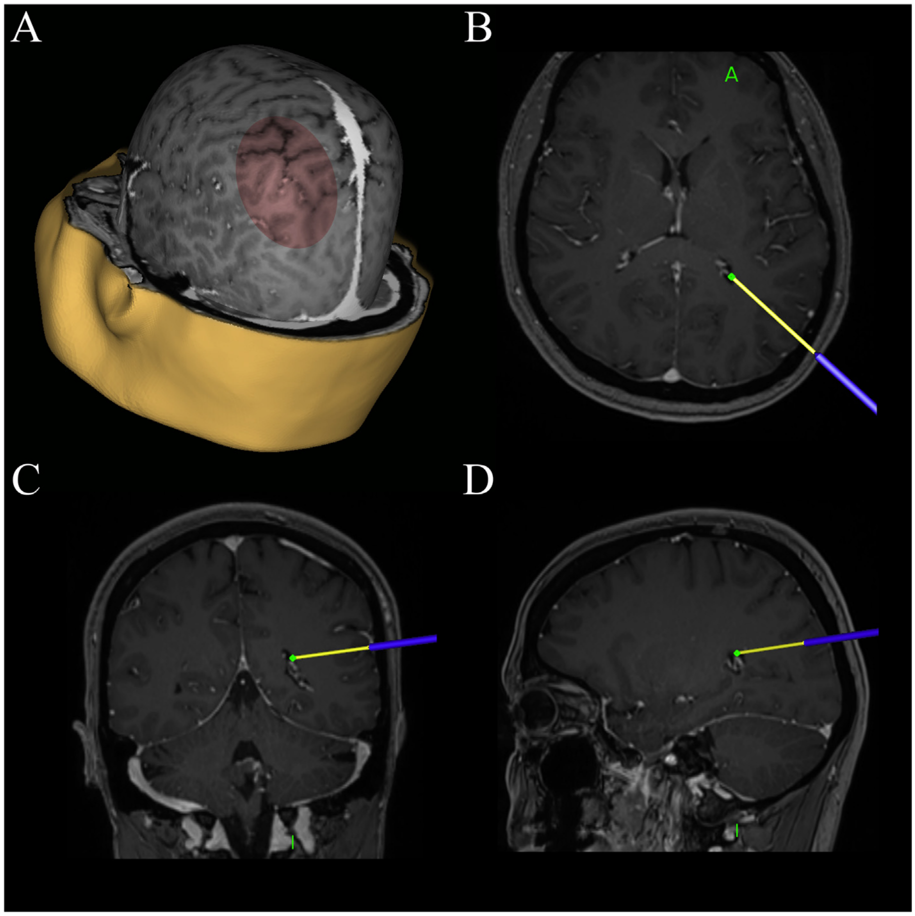

Fig. 1. Potential trajectory for a transparietal approach to the trigone. Panel A illustrates the entry zone on a pseudo-3D-model. Panel B, C, and D illustrate the trajectory in 2D.

brain injury including speech disturbance, particularly, when the lesion is located within the dominant hemisphere [1,2,11–14]. While this approach can be purely based on neuroanatomical landmarks [15,16], neuronavigation is routinely used these days [17,18].

Here, we retrospectively reviewed patients with trigonal tumors undergoing preoperative nTMS and tractography to select the optimal trajectory for a transparietal approach to the trigone of the lateral ventricle.

2. Methods

We retrospectively reviewed all consecutive patients that underwent nTMS and tractography for presurgical workup of a trigonal tumor between January 2014 and September 2016. For the present analysis, the following criteria were defined: left-sided trigonal lesion in right handed patients or right-sided trigonal lesion in left-handed patients, preoperative nTMS motor mapping, preoperative rTMS language mapping, nTMS-based corticospinal tract tractography, optic radiation tractography, export of nTMS datasets and tractography to neuronavigation, preoperative identification of an optimal trajectory towards the trigone via neuronavigation-based planning modell, scheduling of surgery guided by neuronavigation under general anesthesia.

2.1. Data collection

Data collection on patients undergoing nTMS and tractography was prospective. Neurological condition was assessed preoperatively, at hospital discharge (approximately one week after surgery), and at follow-up visit in the outpatient clinic. The Medical Research Council scale (MRC) grade 0–5 was applied to report motor strength of the limbs [19]. Diagnosis was confirmed by histopathology.

2.2. Preoperative MRI

Preoperative MRI scans were performed on a 1.5 or 3 T scanner (Magnetom Skyra 3.0 T; Magnetom Symphony-TIM 1.5 T, Siemens, Erlangen, Germany). Patients underwent contrast-enhanced T1-weighted MRI for intraoperative neuronavigation (MP RAGE in axial plane: TR = 1.9; TE = 3.52; FLIP-angle 15; slice thickness 1 mm). For diffusion tensor imaging (DTI) fiber tracking, diffusion weighted imaging was acquired (TR = 5.6; TE = 100; FLIP-Angle 90; slice spacing 3.6; slice thickness 3 mm).

2.3. Navigated transcranial magnetic stimulation (nTMS)

The eXimia NBS system with NEXSPEECH® was used to perform nTMS motor and language mapping. All mappings were performed by the first and second authors (P. H., S. S.), both experienced operators. Motor mapping was conducted according to Picht et al. [20,21]. For nTMS language mapping, a protocol published by Krieg et al. was followed [22–26]. Briefly, patients underwent baseline assessment using an object-naming task performed twice (inter-picture interval 2500 ms, display time of presented object 700 ms) recorded on a video camera. Correctly and fluently identified baseline objects were re-displayed to the patient in a random manner with simultaneous application of a repetitive nTMS stimulus (picture to trigger interval 0 ms, 7 Hz/7 pulses with 110 % of the individual RMT of the abducens pollicis brevis muscle – identified in the nTMS motor mapping session) and recorded on a video camera. Language mapping was performed by moving the stimulation coil from one spot to another after every object-presentation/repetitive nTMS stimulus-application. In this manner, the whole hemisphere was examined. Additionally, same spots were randomly mapped repeatedly up to three times. On average, a total of 200–350 repetitive nTMS stimuli were applied to cover the hemisphere. Finally, baseline object-naming and repetitive nTMS-linked object-naming were compared and analyzed for errors. Errors were classified either: no response, hesitation, phonological error, semantic error, neologism, or performance error. Finally, every spot that delivered a positive MEP on nTMS motor mapping (i.e. motor map) and every spot that was linked to an error on repetitive nTMS language mapping (i.e. language map) was fused with the MRI for neuronavigation.

2.4. Tractography

Diffusion-tensor-imaging fiber tracking of optic radiation and corticospinal tract was performed according established protocols [27–31]. The DWI images and the MRI for neuronaviation with nTMS motor and language maps were imported into a StealthStation S7 neuronavigation system (Medtronic Inc., Surgical Technologies, Neurosurgery, Coal Creek Circle Louisville, Colorado). Tractography was performed using StealthViz software system (Medtronic Inc., Surgical Technologies, Neurosurgery, Coal Creek Circle Louisville, Colorado) after coregistration of DWI images with MRI for neuronavigation and DTI tensor computation.

First, nTMS-derived corticospinal tract tractography was performed. Placement of the first region-of-interest (ROI) was guided by the nTMS motor map [28]. A second ROI was placed at the ipsilateral anterior cerebral peduncle [30]. The tracking algorithm we used was: fractional anisotropy threshold 0.20; vector step length 1 mm; minimum fiber length 20 mm; seed density 3.0; maximum directional change 45 for arm and leg tractography and 90 for face tractography.

Then, optic radiation tractography was performed. Multiple protocols are available to improve quality and allow illustration of the different optic radiation fiber bundles [27,29,31]. For the parietal approach, illustration of the anterior portion of the optic radiation (i.e. Meyer's loop) is of minor importance. In contrast, the center and posterior bundles coursing to the superior aspect of the calcarine fissure are of great relevance as these fibers are in proximity of the parietal trajectory towards the trigone. We performed optic radiation tractography by placement of the first ROI at the lateral geniculate nucleus and a second ROI at the calcarine fissure. The directionally encoded color map provided by the software was used to support anatomic ROI placement. The tracking algorithm was: fractional anisotropy threshold 0.20; vector step length 1 mm; minimum fiber length 20 mm; seed density 3.0; maximum directional change 60.

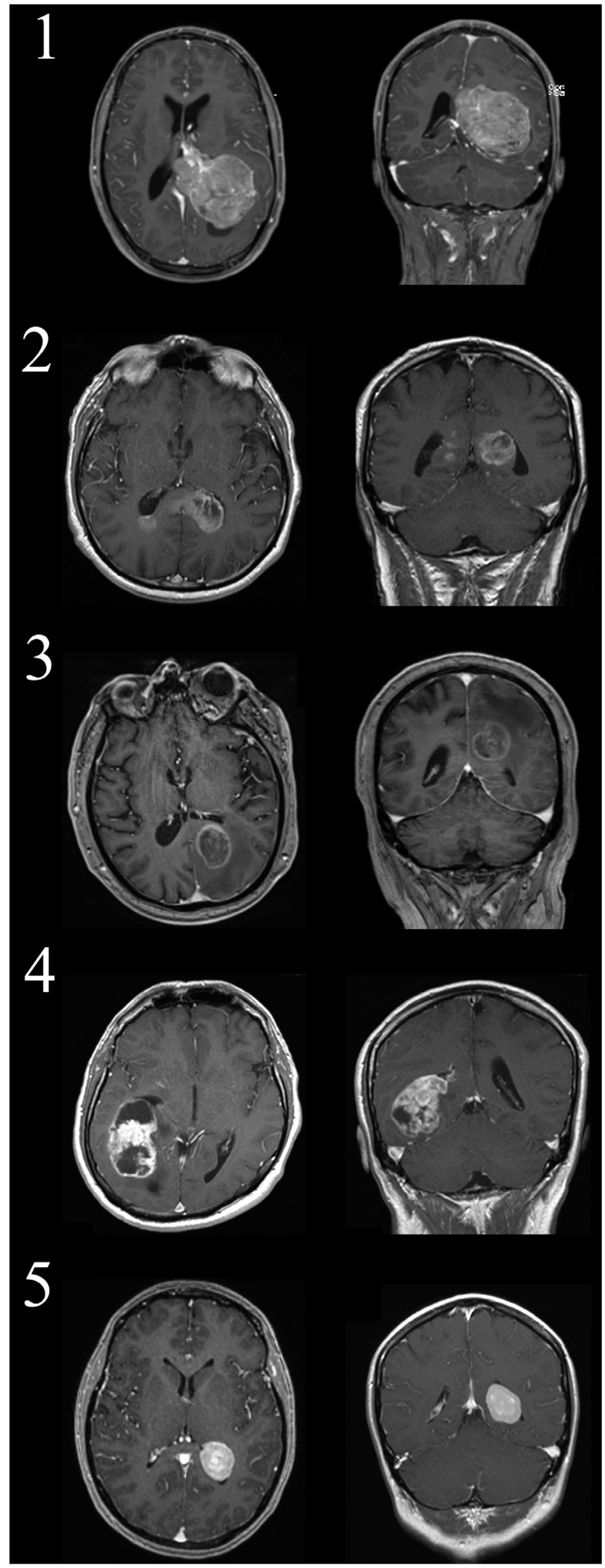

Fig. 2. Preoperative imaging of patients that underwent preoperative nTMS and tractography.

3. Results

3.1. Patient cohort

A total of five patients with trigonal tumors underwent preoperative nTMS mapping and tractography (Fig. 2). Surgery was performed in four patients, one patient (case 5) refused surgery after preoperative work-up was completed (Table 1). All patients were right-handed with left-sided lesions with exception of Case 3 which was left-handed patient suffering from a right-sided contrast-enhancing lesion and presented amnesic aphasia.

Table 1
Patients with trigonal lesions undergoing preoperative combined nTMS and tractography.

Case	Gender	Age	Entity	Location	Side	Procedure	Preoperative status	Postoperative status (1 week)	Follow-up (6 weeks)
1	Male	16	Choroid plexus papilloma	Intraventricular	Left	Resection	Syncope, incomplete hemianopia	Mild dysarthria, incomplete hemianopia	Incomplete hemianopia
2	Male	72	Glioblastoma	Parenchyma	Left > right	Subtotal resection	Amnesic aphasia, hemiparesis MRC 3/5	Slight improvement of deficits	Recurrence
3	Male	56	Glioblastoma	Parenchyma	Right	Resection	Amnesic aphasia	No deficits	No deficits
4	Male	63	Melanoma metastasis	Parenchyma	Left	Resection	Amnesic aphasia, hemiparesis MRC 3/5	No aphasia, persistent MRC 3/5 paresis	Improved hemiparesis MRC 4/5
5	Female	27	Choroid plexus papilloma*	Intraventricular	Left	Refused surgery	No deficits	–	–

* Most likely diagnosis based on MRI appearance. Patient refused surgery so no tissue was available for histopathology.

3.2. Preoperative nTMS and tractography

All patients underwent preoperative nTMS motor and language mapping. Motor mapping was performed to precisely identify the primary motor cortex (M1) and subsequently guide nTMS-derived corticospinal tractography. In all cases nTMS motor mapping lead to adequate delineation of M1. Language mapping was performed routinely to identify language positive and language negative areas. For the parietal approach, potential sites of corticotomy in proximity of the intraparietal sulcus harbored language positive sites were analyzed. In all patients, the site for corticotomy was

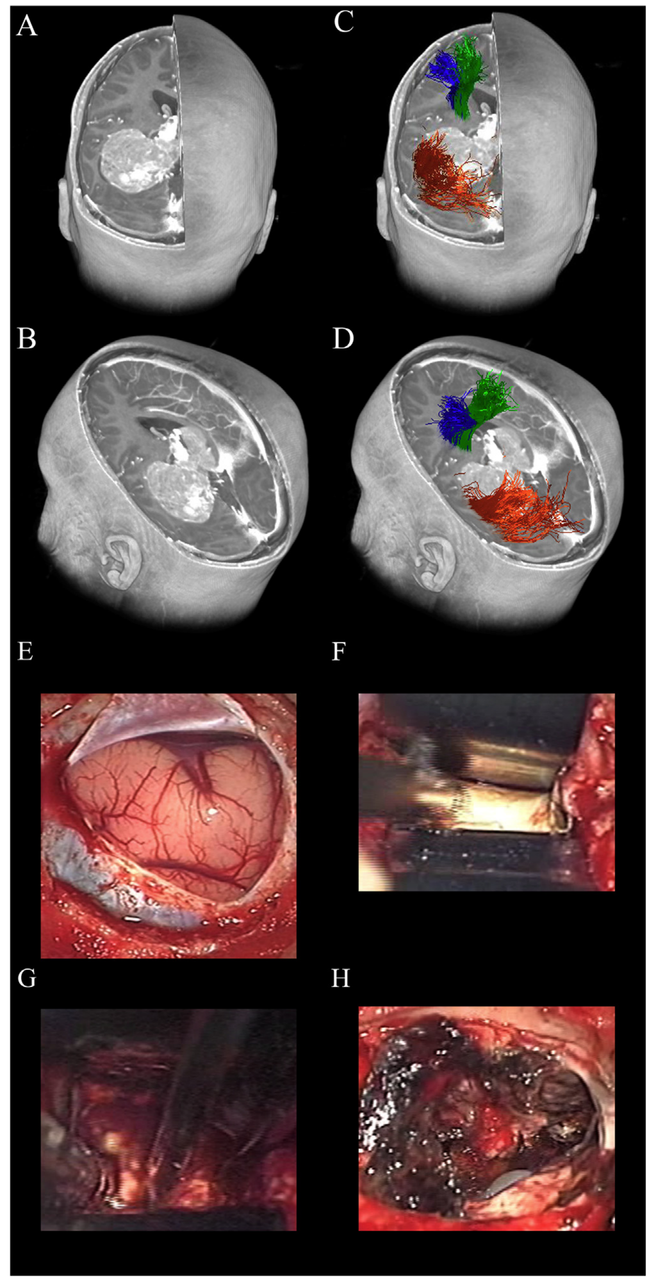

Fig. 3. Preoperative nTMS and tractography of Case 1. Panel A and B show the pseudo-3D-model without tractography. Panel C and D show optic tractography (red fibers) and corticospinal tract tractography (green fibers = lower limb, blue fibers = upper limb). Panels E-H show intraoperative microscopic images. Cortical surface after dura opening (E). After corticotomy, two spatula are inserted to support dissection towards the trigone (F). Tumor resection is performed via bipolar and suction device (G). At the end of the operation, the meningioma had completely been removed (H).

chosen at language negative areas. Distance to language positive sites was >10 mm.

3.3. The transparietal approach towards the trigone

In all patients, preoperative nTMS mapping and tractography were used to select the optimal surgical corridor sparing eloquent brain structures (Figs. 3 and 4). One patient (case 5) refused surgery. Cases 1–4 underwent surgical resection via the transparietal approach. Surgery was performed under general anesthesia. Corticotomy and subcortical dissection were cautiously performed using bipolar and suction device. Surgery has been performed by the senior author (J. O.). In all operated cases, identification of the optimal trajectory was facilitated by preoperative nTMS mapping and tractography. In none of the cases the surgical strategy of performing a transparietal approach was abandoned. In contrast, preoperative nTMS mapping and tractography information encouraged the subjective confidence of the operating surgeon follow this strategy.

3.4. Neurological outcome

None of the patients suffered from visual deterioration. Postoperatively, Case 1 (Fig. 5) suffered from new mild dysarthria due to edema and postoperative changes. The surgery was complicated by significant intraoperative blood loss and operation time. However, within six weeks the dysarthria had completely resolved. Follow-up imaging showed complete tumor resection at six months after surgery. Due to multifocality, surgical treatment in Case 2 was limited to a left-sided subtotal resection. Despite adjuvant radio- and chemotherapy, the patient suffered from significant tumor progression and deterioration of general health six weeks after surgery.

Case 3 was a 56-year-old male, left-handed patient suffering from a right-sided glioblastoma. Preoperatively, he presented mild amnesic aphasia most likely due to involvement or displacement of right-sided language eloquent brain areas. After surgical resection, the language impairment completely resolved within one week after surgery.

Preoperatively, case 4 suffered from a right-sided hemiparesis MRC 3/5 and mild amnesic aphasia. One week after surgery aphasia complete resolved. Paresis improved to MRC 4/5 within six weeks.

Case 5 suffered from an incidentally diagnosed trigonal lesion. Outpatient MRI was performed due to unspecific headache episodes for several months. After outpatient clinic presentation, the patient was scheduled for surgery and underwent preoperative workup routine including nTMS and tractography. However, she finally refused to undergo surgery and wished to postpone surgery.

4. Discussion

The transparietal approach has been applied to operate on vascular and tumorous brain lesions. The ideal trajectory for a parietal transsulcal approach towards the trigone allows sparing of visual pathways, speech areas, and sensorimotor areas [1,2,11–14]. To achieve this goal, knowledge on neuroanatomical relationships of the corticospinal tract, of the optic radiation and of language negative cortical brain areas is of high relevance. This knowledge may even allow performing surgery purely based on neuroanatomical landmarks in selected cases [15,16]. However, tumor entity, size, location and extension as well as shape of the ventricles may hamper selection of an optimal transparietal trajectory towards the trigone.

Navigated transcranial magnetic stimulation and tractography are established techniques in current neurosurgical care. They

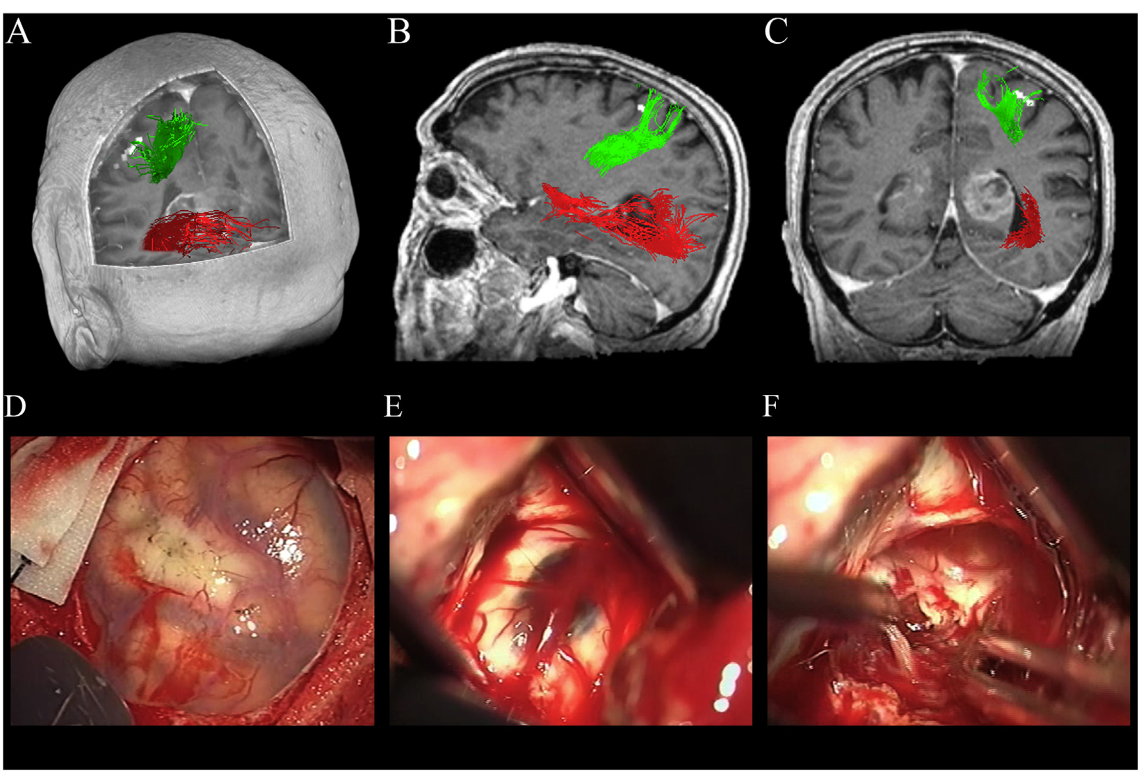

Fig. 4. Preoperative nTMS and tractography of Case 2. Panel A shows the pseudo-3D-model with tractography. Panels B and C show the optic radiation fibers (red) and corticospinal tract fibers (green) in 2D. Panels D-F show intraoperative microscopic images. After craniotomy, dura opening is performed to expose cortical surface (D). Corticotomy is then performed at language negative sites. White matter dissection is performed along the optimal trajectory with two spatula insitu (E). Tumor resection is performed with bipolar and suction device (F).

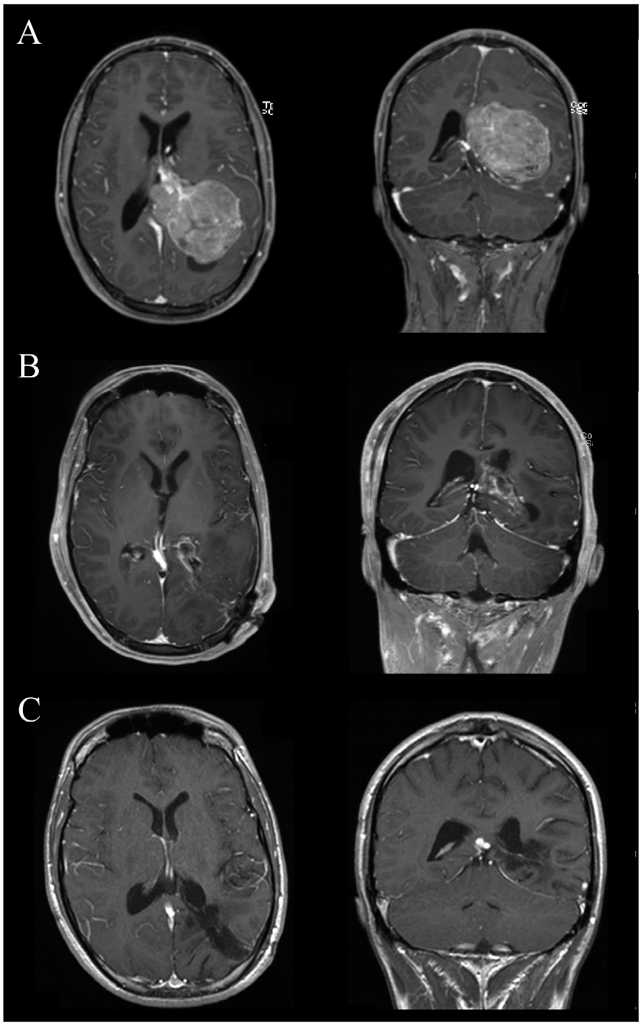

Fig. 5. Radiological course of Case 1: Preoperative (Panel A), one week after surgery with edema and postoperative changes at surgical corridor (Panel B), and at six month follow-up (Panel C).

both provide neurosurgeons with preoperative, individual information on eloquent cortical motor areas (nTMS motor mapping), subcortical motor pathways (nTMS-derived corticospinal tract tractography), visual white matter pathways (optic radiation tractography) and eloquent cortical language areas (rTMS language mapping). We raised the question whether the combination of these modalities facilitates decision making on selecting the optimal trajectory for a transparietal approach towards the trigone. Therefore, we retrospectively analyzed five consecutive patients that underwent this extensive presurgical workup. Preoperative identification of an optimal trajectory was feasible in all cases. It was used for surgical resection in four cases and provided a favorable outcome in all of these patients.

4.1. Optic radiation tractography

The anatomy of visual pathways has intensively been studied in cadavers using white matter dissecting techniques. Optic radiation tractography is capable of illustrating these white matter bundles in vivo [27,29,31]. Fibers leaving the upper lateral geniculate nucleus (LGN) (central and posterior bundles) terminate in the superior part of the calcarine fissure. In contrast, fibers from the lower LGN form Meyer's loop at the tip of the temporal horn and are destined for the lower aspect of the calcarine fissure [1,2,32]. Due to anatomical vicinity, fibers from the upper LGN projecting to the superior calcarine fissure are at higher risk when performing a transparietal approach towards the trigone. Optic radiation tractography has been widely used for preoperative planning and intraoperative guiding of surgery for lesions affecting visual pathways. It has been shown very helpful and resulting in good neurological outcome [33–35]. Comparably, it also allowed sparing of visual pathways in our cohort. None of the patients experienced deterioration of vision or new visual field impairments. Hence, optic radiation tractography may contribute to reduce the risk for visual deterioration in the transparietal approach towards the trigone.

4.2. Corticospinal tract tractography

The risk for motor function deterioration with the transparietal approach is of subordinate dimension compared to deterioration of vision or language. However, large tumors or tumors extending ventrally towards the corticospinal tract may significantly alter the setting. Visualization of the corticospinal tract facilitates targeting of the trajectory as additional anatomical landmarks are available. Before nTMS was established, seed placement for tractography was based on anatomical landmarks by the individual tractography operator. Lately, preoperative nTMS has been implemented into the tractography process of the corticospinal tract. This enables operator-independent seed placement at individual functional areas of the primary motor cortex. Additionally, nTMS motor mapping allows computation of somatotopic tractography. This allows for separate illustration of white matter bundles within the corticospinal tract. Fibers carrying motor information for the upper limb, lower limb and face area can be distinguished [28,30,36]. In our cohort, information on eloquent motor pathways helped for finding an optimal angle towards the trigone due to availability of another eloquent landmark. Intraoperatively, specifically while operating deep seated at the level of the trigone, neuronavigation with motor pathway information helped to envision anatomical relationships.

4.3. Language mapping

Traditionally, Broca and Wernicke are considered speech eloquent areas. Studies of individual cortical language sites, however, during intraoperative language mapping procedures in patients undergoing epilepsy or brain tumor surgery have overhauled this traditional concept [37–39]. The inferior parietal lobule is critically involved in processing of attention, action and language [40]. Specifically, its two major subdivisions, the supramarginal and angular gyri, are profoundly involved in language domains. Whereas the angular gyrus is involved in semantic processing, word reading, and comprehension [41], the supramarginal gyrus is deeply involved in visual word recognition [42]. Cortical language areas can be studied via direct cortical stimulation (DCS), functional MRI, and magnetoencephalography. Whereas the latter two are noninvasive functional neuroimaging modalities, DCS is an invasive procedure requiring surgery for cortical surface exposure with subsequent electrical stimulation of the brain surface. Still, DCS represents the goldstandard for the identification of cortical language sites [39,43,44]. A lately evolving modality for precise noninvasive functional investigation of cortical language areas is the use of repetitive nTMS. Application of a nTMS impulse evokes an electrical field on the brain surface which is capable of modulating cortical neuronal networks. Repetitive nTMS application (also referred to as rTMS) to speech eloquent areas may induce a temporary neuronal modulation that is capable of provoking errors on an object-naming task. Various studies on preoperative rTMS for language mapping in brain tumor patients have recently been published [22–24,45,46]. In 2008, Sanai et al. reported an alteration in their awake craniotomy procedure. Their resection strategy was directed by identification of DCS-negative language sites and did not require DCS-positive language sites as controls. Hence, they performed smaller, tailored craniotomies for intraoperative mapping and still had favorable functional outcomes [39]. Correlating DCS language mapping with rTMS has shown good concordance, particularly for identification of areas that are language negative [23,26]. During a transparietal approach to the trigone under general anesthesia, knowledge of language negative cortical sites are of high relevance to avoid postoperative language impairments. We performed preoperative rTMS language mapping in our cohort. For selection of the optimal trajectory, language positive cortical sites were avoided. Instead language negative sites provided information on potential cortical entry points when performing the transparietal approach towards the trigone. None of the patients developed persisting speech disturbances even though the lesion was most likely located within the speech dominant hemisphere.

4.4. Limitations

The herein presented retrospective study has its limitation due to sample size. Larger cohorts are needed to elucidate whether the preoperative work-up performed here decreases risk for neurological deterioration in complex cases or for surgeons with less experience. Whereas tractography of white matter bundles has been widely applied and investigated, research on mapping language function via rTMS is a yet evolving modality. Even though recent studies have shown the benefits of rTMS, we still cannot definitely exclude language function of a cortical area by a simple rTMS-linked object-naming task. We expect to gain more insight into this field with future research and the development of more sophisticated protocols. We believe progressive implementation of nTMS into the preoperative work-has the potential to contribute to favorable surgical outcomes.

5. Conclusion

The transparietal corridor towards the trigone is surrounded by eloquent structures. Combination of preoperative nTMS and tractography facilitates the identification of the optimal surgical trajectory. It allows for sparing of visual and motor pathways as well as cortical language areas.

Disclosure

None of the authors have any conflicts of interest to report.

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