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Original research article

Surgical treatment of adult patients with thalamic tumors with the aid of tractography, fMRI, transcranial electrical stimulation and direct electrical stimulation of the subcortical white matter

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ABSTRACT

The aim of investigation was to assess treatment outcomes in adult patients with thalamic tumors, operated on with the aid of tractography (DTI) and monitoring of motor evoked potentials (MEPs) generated due to transcranial electrical stimulation (TES) and direct electrical stimulation (DES) of the subcortical white matter.

38 subsequent patients with thalamic tumors were operated on using tractography (DTI)-integrated neuronavigation, transcranial electrical stimulation (TES) and direct electrical stimulation (DES). The volumetric method was used to calculate pre- and postoperative tumor volume.

Total tumor resection (100%) was performed in 18 (47%) patients, subtotal in 9 (24%) (mean extent of resection −89.4%) and partial in 11 (29%) patients (mean extent of resection −77.18%). The mean extent of resection for all surgical patients was 86.5%.

Two (5.2%) patients died postoperatively. Preoperative hemiparesis was present in 18 (47%) patients. Postoperative hemiparesis was observed in 11 (29%) patients of whom only in 5 (13%) new paresis was noted due to surgical intervention. In patients with hemiparesis significantly more frequently larger tumor volume was detected preoperatively. Low mean normal fractional anisotropy (nFA) values in the internal capsule were observed statistically significantly more frequently in patients with preoperative hemiparesis as compared to the internal capsule of the unaffected hemisphere. Transcranial electrical stimulation helps to predict postoperative paresis of extremities. Direct electrical stimulation is an effective tool for intraoperative localization of the internal capsule thus helping to avoid postoperative deficit.

In patients with tumor grade I and II the median time to tumor progression was 36 months. In the case of patients with grades III and IV it was 14 months. The median survival time in patients with grades I and II it was 60 months. In patients with grades III and IV it was

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18 months. Basing on our results, patients with glioma grade I/II according to WHO classification are the best candidates for surgical treatment of thalamic tumors. In this group of the patients more often resection is radical, median time to progression and survival time are longer than in patients with gliomas grade III and IV. Within a 7-year follow-up none of the patients with GI/GII grade glioma died.

1. Introduction

Thalamic gliomas are extremely rare brain tumors [1–4]. Such gliomas are the most prevalent among children or adolescents and after the age of 40 as WHO grade III or IV tumors. Surgical treatment of thalamic tumors is associated with the risk of hemiparesis and/or hemianopia [5–9]. Furthermore, patients whose tumors are located within a dominant hemisphere may suffer from postoperative speech disorders.

Children and adolescents present with thalamic glial tumors of different nature than those found in adults [5,7,9,10,11]. Pilocytic astrocytoma is the most common thalamic glial tumor diagnosed in children. This tumor is well demarcated from the surrounding tissues and causes distortion of adjacent anatomical structures. The prognosis is favorable provided that total resection of the lesion is performed. Pilocytic astrocytoma does not usually infiltrate the surrounding neural structures [10–12]. The most common types of thalamic glial tumors diagnosed in adults are anaplastic astrocytoma and glioblastoma multiforme [5,9,11]. Due to infiltration of the surrounding anatomical structures and rapid progression, prognosis in patients with these tumors is generally poor [5,9,11].

Low-grade gliomas of the thalamus are considerably less common in other locations, e.g. in the insula [9]. The thalamic lesion frequently involves also posterior and mesencephalic peduncles (as the so-called thalamopeduncular tumor) [9,12]. Total resection of such tumor may be hindered due to the presence of the corticospinal tract fibers within the mass [13]. In order to minimize the risk of severe postoperative disability in pediatric patients operated for pilocytic astrocytomas, Moshel et al. [7] used a diffusion tensor imaging (DTI)-based fibertracking and intraoperative neuronavigation. It resulted in markedly lower incidence of postoperative motor deficits. Hou et al. [8] described eight different types of tumors based on their location within the thalamus or subcortical nuclei and relation to the surrounding anatomical structures, documented on DTI. It enabled them to accurately identify the posterior limb of the internal capsule and its relation to the thalamic mass. The use of this approach was reflected by markedly lower incidence of postoperative limb hemiplegia and hemiparesis [8]. Also transcranial electrical stimulation (TES) and intraoperative mapping of the internal capsule based on direct electrical stimulation (DES) were shown to prevent postoperative hemiparesis in patients with thalamic tumors [14–17].

The aims of this study were: (1) to explore if preoperative hemiparesis results from neoplastic infiltration of the corticospinal tract fibers (manifesting as decreased nFA) and is associated with the size of thalamic tumor, (2) to verify if the outcome of intraoperative TES and the result of intraoperative DES of the subcortical white matter may be used to predict the risk of postoperative hemiparesis, (3) to assess whether the extent of resection has a significant influence on progression and survival time of patients with thalamic tumors.

2. Material and methods

38 subsequent patients with thalamic tumors, including 17 women (mean age 38 years, range 20–60 years) and 21 men (mean age 35.7 years, range 30–65 years) were treated surgically at the Department of Neurosurgery between 2007 and 2014. The patients were operated under general anesthesia with the aid of a neuronavigation system (BrainLab AG, Munich, Germany) used to visualize the eloquent areas of the cortex identified on the basis of fMRI (i.e. sensorimotor cortex, Wernicke's and Broca's areas) and tractography of the white matter tracts (i.e. corticospinal tract and optic tract) with a diffusion tensor imaging (DTI-MRI) and monitoring of motor evoked potentials (MEPs). Mapping of the Broca's and the Wernicke's areas was done so that postoperative speech disorders could be maximally limited during surgical procedure, especially in the case of left-sided tumors.

Monitoring of MEPs included application of transcranial electrical stimulation (TES) and direct electrical stimulation (DES) to visualize the course of the corticospinal pathway within the internal capsule. The MEPs obtained by means of TES were classified according to Neuloh et al. [18], i.e. as stable, reversibly deteriorated, irreversibly deteriorated or completely lacking. The MEPs obtained during the subcortical white matter DES were grouped as positive (in cases of a high-amplitude recording from the upper and lower limbs contralateral to the tumor) or missing (if the intraoperative stimulation resulted in no electromyographic response).

The extent of resection was assessed according to Sawaya et al. [19], i.e. based on the results of pre- and postoperative (up to 72 h post-surgery) FLAIR-MRI. The extent of resection was classified as: (1) gross total resection (GTR, >95%), (2) subtotal resection (STR, 85–95%), or (3) partial resection (PTR, <85%). The extent of resection was determined as percentage in particular groups and the mean value of the extent of resection was also determined for the whole study group of patients.

Follow-up MRI spectroscopy and perfusion MRI were carried out 6 months after surgery and then at 6-month intervals. At the same time neurological examination was performed postoperatively. We examined whether new transient or permanent neurological deficits, such as hemiparesis, homonymous hemianopia and speech disorders appeared. The deficits were considered transient if they resolved within six months after surgery, or permanent if persisted longer than six months after surgery. The assessment of paresis was done by an independent neurologist and was carried out using the NIHSS scale [20].

The prognosis was analyzed in terms of: (1) median time to progression (TTP), (2) median survival time (OS).

MRI of the brain was performed with a 1.5-T Magnetom Avanto (Siemens AG, Erlangen, Germany) and 3-T Achieva (Philips Medical Systems, Best, Netherlands) scanners with standard coils for the examination of the head. Tumor volumes were measured on FLAIR MRI scans. Measurements of hyperintense regions were made in three orthogonal dimensions. The volume of the tumor was extrapolated to ellipsoid. Mean diffusivity (MD) maps, fractional anisotropy (FA) maps in a gray scale, color-coded FA maps and tractography were obtained using a software provided by the MRI system manufacturers. Resolution (~2 mm) mentioned in the paper concerns DTI sequence.

MEPs were obtained with a 16-channel ISIS apparatus (Inomed, Teningen, Germany). TES was performed with the electrodes screwed or inserted into the points C3 and C4 (eventually M3 and M4) of the scalp skin. DES was conducted with a bipolar Galanda probe and double-needle receiver electrodes placed in the muscles. The receiver electrodes for the MEP recording in contralateral limbs were placed in the thenar and hypothenar of the upper extremity and interior tibial muscle and triceps surae muscle of the lower extremity. The control electrode was placed in the thenar of the upper limb ipsilateral to the tumor. Monitoring of MEPs requires verification of control TES recordings from the ipsilateral limb; this ensures that a potential loss of MEP from the contralateral limb results from an injury to the corticospinal tract rather than from problems with anesthesia or technical drawbacks. In the case of DES, transcranial stimulation needs to be performed periodically in order to ensure whether a potential lack of MEP after the direct stimulation is truly a consequence of the corticospinal tract injury rather than an effect of stimulating the white matter that lacks motor fibers.

Stimulation parameters were used during the MEP recording – a train stimulation: impulses applied every 2–3 s, each containing 4–6 pulses of 0.5 ms at 3–4 ms intervals, 300–700 V voltage and 100–150 mA (max. 220 mA) current (in the case of TES) or 120–180 V voltage and 3–30 mA current (DES). Typically, a 10–15 mA current in DES was used. The MEP recordings were considered stable if no more than a 50% increase in the baseline 100–150 mA current was required to maintain the response. Also a decrease in the amplitude down to 50% was considered a stable recording. A deterioration of MEP corresponded to more than a 50% decrease in the amplitude of electromyographic recording in relation to the baseline recording. The loss of recording was defined as the lack of MEP at the highest current. Other researchers also used bipolar electrical stimulation [14–16,21–23]. The intensity of the stimulating current which these authors used ranged from 2 to 16 mA. It is more difficult to obtain a response from the corticospinal tract using bipolar electrical stimulation as compared to the monopolar electrical stimulation. Higher electrical current is necessary in patients with general anesthesia as compared to patients recovered from anesthesia. The use of anesthetic gases, barbiturates and relaxants is contraindicated during the MEP monitoring. An optimal protocol of anesthesia includes propofol and opioids in continuous infusion.

2.1. *Statistical analysis*

Statistical analysis was performed using the STATISTICA 10 software. Distributions of quantitative variables were checked using the Shapiro–Wilk test. The Mann–Whitney *U* test was used to evaluate differences between the variables. Probability of survival and tumor progression over time were calculated according to the Kaplan–Meier method and Kaplan–Meyer curves for patients with particular clinical features (i.e. mode of treatment or grade of tumor malignancy) were tested with the log rank test.

The study was reviewed and approved by the Bioethics Committee of Medical University of Silesia. Our Bioethics Committee approved the study concerning surgical treatment of adult patients with thalamic tumors (March 2008). Written informed consent was obtained from all study participants.

3. Results

38 patients underwent surgical treatment of thalamic tumors. In 30 cases (79%) the tumor was located on the right side and in 8 (21%) on the left side. In 25 (66%) patients the tumors involved solely the thalamus, and in 13 (34%) both the thalamus and mesencephalic peduncles. The mean follow-up of the group was 3.02 years.

The following approaches were used for surgical procedures: postero-inferior temporal approach in 16 (42%) patients; pterional, transcortical, transventricular approaches in 8 (21.1%) patients; posterior interhemispheric parasplenial approach in 4 (10.5%) patients; pterional, transsylvian, transinsular approach in 4 (10.5%) patients; superior parietal gyrus approach in 2 (5.3%) patients; postero-inferior transchoroidal fissure approach in 2 (5.3%) patients; transfrontal stereotactic biopsy in 2 (5.3%) patients.

The choice of a surgical approach was based on the tumor location within the anterior, posterior, dorsal or ventral thalamus and topography of the internal capsule. Anterior (via the anterior horn of the lateral ventricle), superior (via the superior parietal lobule) and posterior (via the interhemispheric fissure and precuneus) approaches were used only if the internal capsule was located laterally from the thalamic mass. Lateral approaches (via the middle temporal gyrus behind the sublenticular portion of the internal capsule or via the choroidal fissure or insula) were used only when the internal capsule was located anteriorly or medially from the mass.

Below are two examples of qualifications to a particular surgical approach, depending on the location of the internal capsule (Fig. 1).

Magnetic resonance images of a patient with a large right-sided tumor in the thalamus and in the mesencephalic peduncle. The sagittal and axial magnetic resonance scans show that the internal capsule (yellow arrow) is located posteriorly from the tumor. The transinsular approach

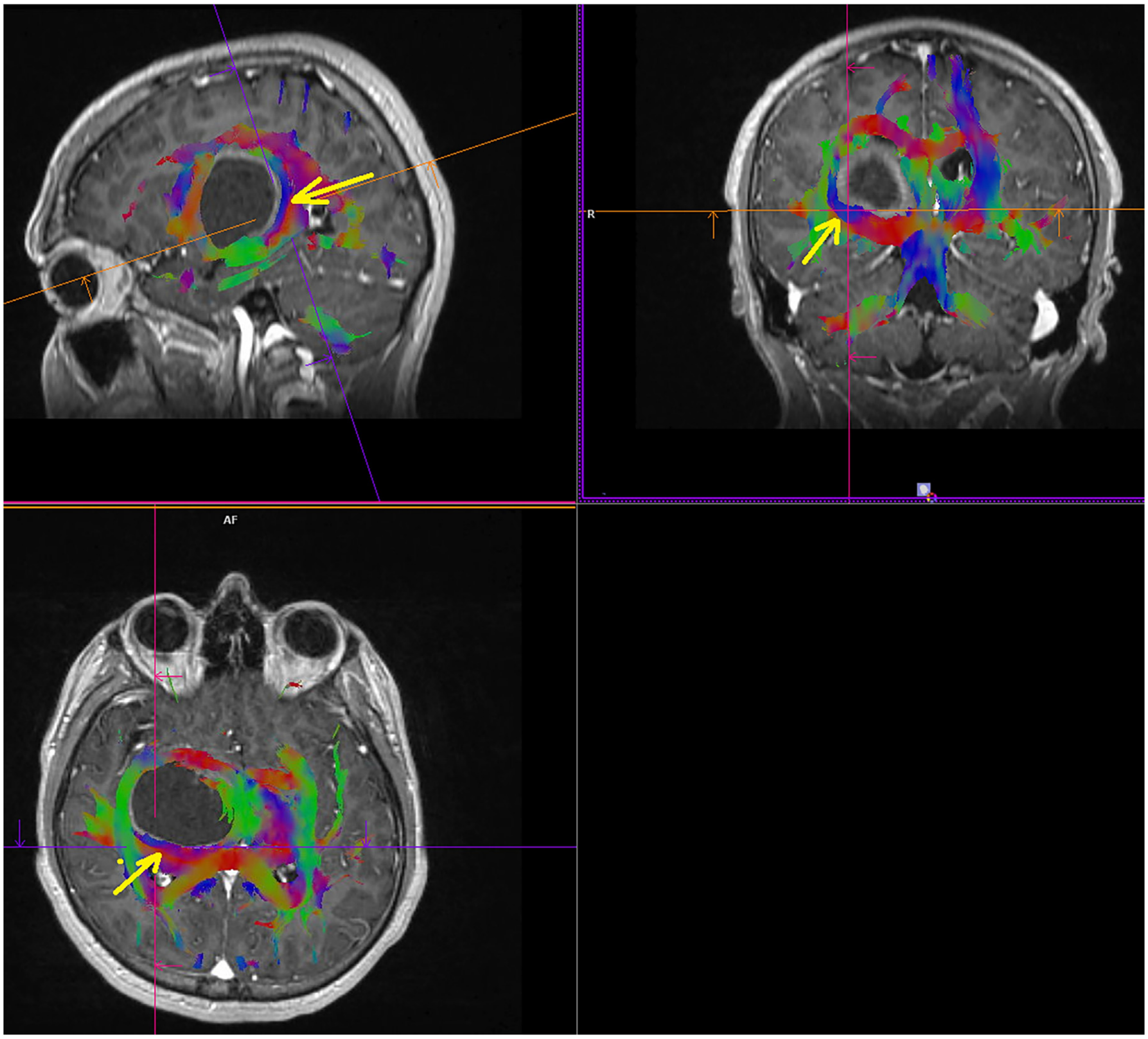

Fig. 1 – Magnetic resonance images of a patient with a large right-sided tumor in the thalamus and in the mesencephalic peduncle. The sagittal and axial scans show that the internal capsule is located posteriorly from the tumor. The transinsular approach through the lenticular nucleus was adopted with the intention to spare the internal capsule (yellow arrow).

through the lenticular nucleus was adopted with the intention to spare the internal capsule (Fig. 2).

Postoperative magnetic resonance scans of a patient. Total tumor resection. The internal capsule (yellow arrow) is spared. Histopathological investigation revealed pilocytic astrocytoma (Fig. 3).

Magnetic resonance images of a patient with a right-sided posterior thalamic tumor. The internal capsule is located medially and anteriorly from the tumor. Interhemispheric parasplenial approach was adopted. As a result, the patient did not present with postoperative paresis or hemianopia. Histopathological investigation revealed anaplastic astrocytoma.

In order to confirm the presence of conduction within the corticospinal tract and to identify the localization of the posterior limb of the internal capsule, we recorded MEPs obtained during intraoperative TES and DES of the subcortical white matter. In patients who did not present with postoperative hemiparesis, stable MEP recordings were obtained both prior to and after surgery. In contrast, irreversible deterioration of MEP recordings was documented intraoperatively in patients who presented with NIHSS grade 2 postoperative hemiparesis, despite the presence of normal preoperative MEP recordings from the operated hemisphere (Fig.4).

Preoperative motor evoked potential (MEP) response to transcranial electrical stimulation (TES) in a patient who developed postoperative hemiparesis (Fig.5).

Irreversible deterioration of motor evoked potential (MEP) response to transcranial electrical stimulation (TES) in a patient who developed permanent postoperative hemiparesis.

As seen in the figures, irreversible deterioration of the electromyographic recording was documented intraoperatively, which eventually was associated with the development of contralateral hemiparesis postoperatively.

Relationships between the type of MEP recording obtained during TES and DES and the incidence of postoperative hemiparesis in 35 patients surgically treated for thalamic tumors are shown in Table 1. Intraoperative MEP examination was not done in 3 patients.

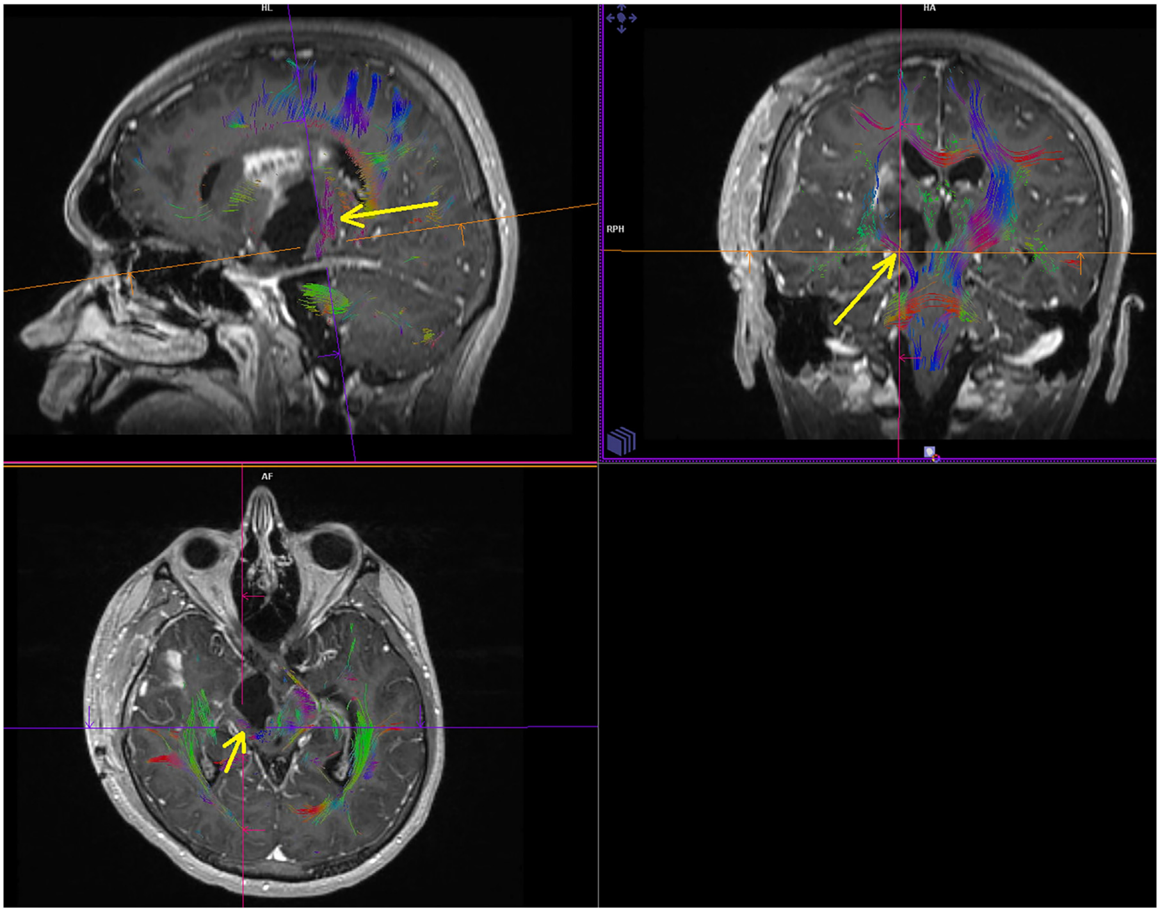

Fig. 2 – Postoperative magnetic resonance images of a patient. Total tumor resection. The internal capsule is spared. The patient presented with postoperative paresis grade I (NIHSS).

As shown in the table, stable MEP recordings were documented in 49% of the patients who did not develop postoperative hemiparesis. A reversible deterioration of MEPs was typical of patients with transient hemiparesis (17%) and irreversible deterioration was observed virtually only in individuals with permanent postoperative hemiparesis (28%).

During the stimulation of the subcortical white matter (DES), positive MEPs corresponding to close proximity of the internal capsule were recorded in 15 (43%) patients. Only one of these patients presented with permanent hemiparesis, 2 (6%) experienced transient hemiparesis and 9 (26%) presented without evidence of postoperative hemiparesis. It enabled us to spare the internal capsule in 14 of 15(93%) patients thus preventing permanent hemiparesis.

We compared neurological status of our patients on admission and postoperatively. The results are presented in Table 2.

Table 2 shows that preoperative hemiparesis was observed in 18 (47%) patients of whom 11 patients presented with paresis grade 1 and 7 with grade 2, according to the NIHSS classification. After 6 months paresis was still present in 11 (29%) patients. Four patients presented with paresis grade 1 (NIHSS), which allowed the patients to walk without assistance. Among patients with permanent hemiparesis (grade 2, NIHSS) 6 of 7 (86%) patients presented with postoperative hemiparesis, which was of the same intensity as prior to the surgery.

Preoperative hemianopia was documented in 1 patient, and newly-developed postoperative hemianopia in 3. In all these cases, hemianopia did not resolve during follow-up and was permanent.

1 patient presented with preoperative speech disorders. In 4 patients aphasia was still observed 6 months after surgery. In all of them, thalamic tumors were located in the left, dominant hemisphere. Preoperative and postoperative disorders of superficial and deep sensation were observed in 4 and 5 patients, respectively, with no tendency to resolve. A total of 4 patients reported headaches of marked severity prior to the surgery. In 3 of these patients headache resolved after surgery. Hydrocephalus was observed prior to surgery in 11 patients. After a 6-month follow-up only 2 patients presented with symptoms of hydrocephalus. Bleeding from the postsurgical site was observed in 4 patients. In two of them, bleeding was controlled successfully with surgical evacuation of hematoma.

Two patients died after surgical procedure for thalamic tumors (5.2%). One patient died postoperatively after the occurrence of hematoma located in the postoperative site. The cause of hematoma was disseminated intravascular coagula-

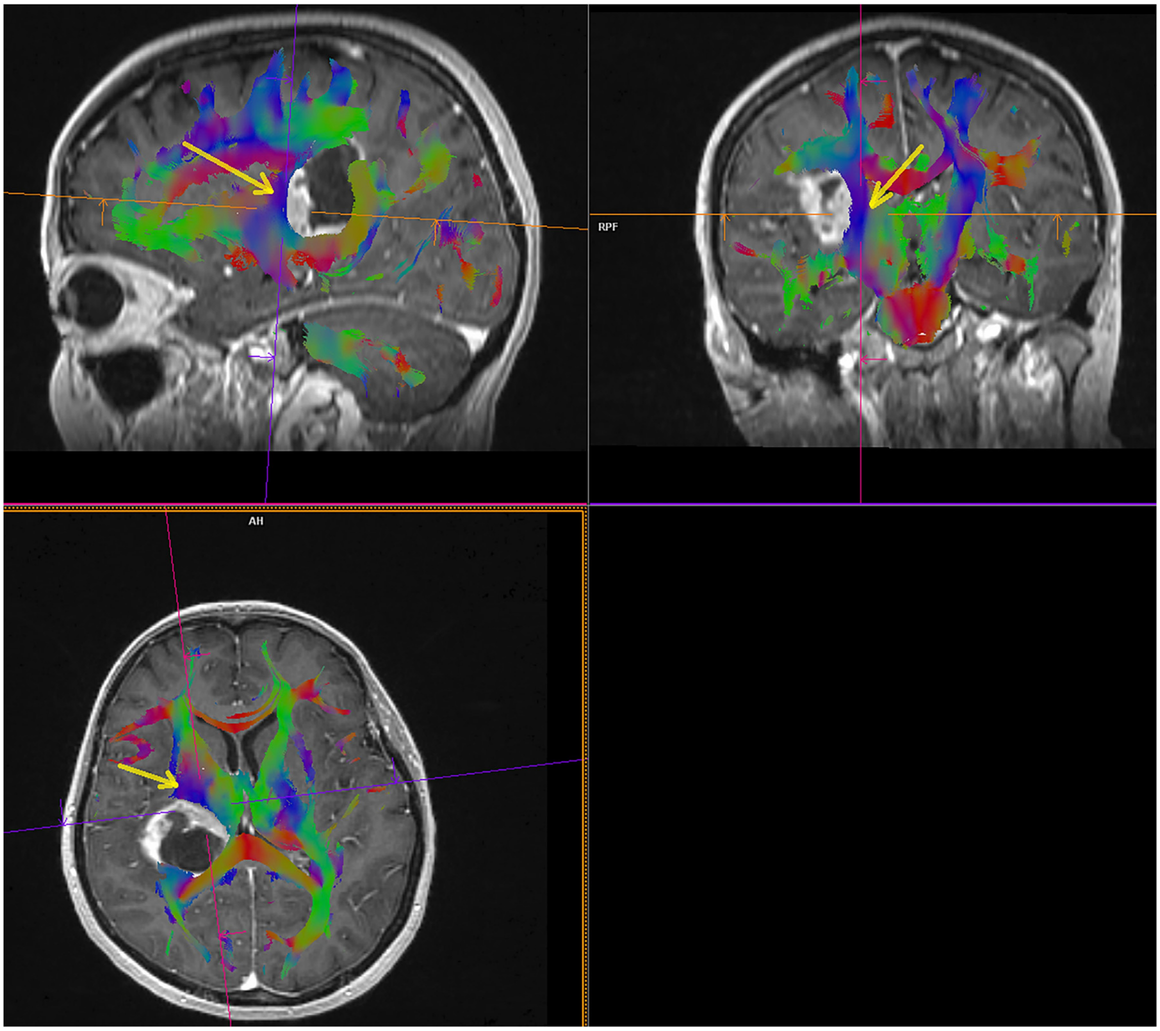

Fig. 3 – MRI of a patient with a right-sided posterior thalamic tumor. The internal capsule is located medially and anteriorly from the tumor. Interhemispheric parasplenial approach was adopted. As a result, the patient did not present with postoperative paresis or hemianopia.

tion (DIC). Despite urgent surgical procedure and treatment the patient died due to complications. Pulmonary embolism was the cause of death of the other patient despite antithrombotic treatment.

We verified if the volume of the thalamic tumor was associated with the risk of preoperative hemiparesis (Table 3).

The study was related only to patients with glial tumors (36 patients). A statistically significant difference was observed in the tumor volume (MRI-FLAIR) between patients with and without hemiparesis before operation ($p < 0.05$). The tumor volume was larger in a group of 16 patients with hemiparesis before operation.

Moreover, we analyzed if the preoperative hemiparesis observed in patients with thalamic tumors resulted from the partial damage to the corticospinal tract fibers associated with neoplastic infiltration, calculating normal fractional anisotropy (nFA) in the posterior limb of the internal capsule ipsilaterally and contralaterally to the tumor (16) (Table 4).

The subset of patients with preoperative hemiparesis showed significantly lower nFA in the posterior limb of the internal capsule ipsilaterally to the mass than in the intact hemisphere ($p < 0.05$). This phenomenon most likely corresponded to the neoplastic infiltration of the internal capsule [24].

Histopathological examination of surgical specimens revealed the following histological types of thalamic tumors: anaplastic astrocytoma ($n = 16$), multiform glioblastoma ($n = 1$), anaplastic oligoastrocytoma ($n = 1$), malignant ependymoma ($n = 1$), PNET ($n = 1$), pilocytic astrocytoma ($n = 7$), fibrillary astrocytoma ($n = 4$), oligoastrocytoma ($n = 4$), polymyxoid astrocytoma ($n = 1$), metastatic breast cancer ($n = 1$) and lymphoma ($n = 1$).

The relationship between the prognosis and the histopathological type of thalamic tumors according to the WHO classification is presented in Table 5. The table does not contain the data for patients with non-glial thalamic tumors.

Among the patients with grade I/II progression was observed in 3/13 (23%). In the group with grade III/IV it was 19/23 (83%). Median TTP was 36 months for patients with grade I/II, and 14 months with grade III/IV. The differences are

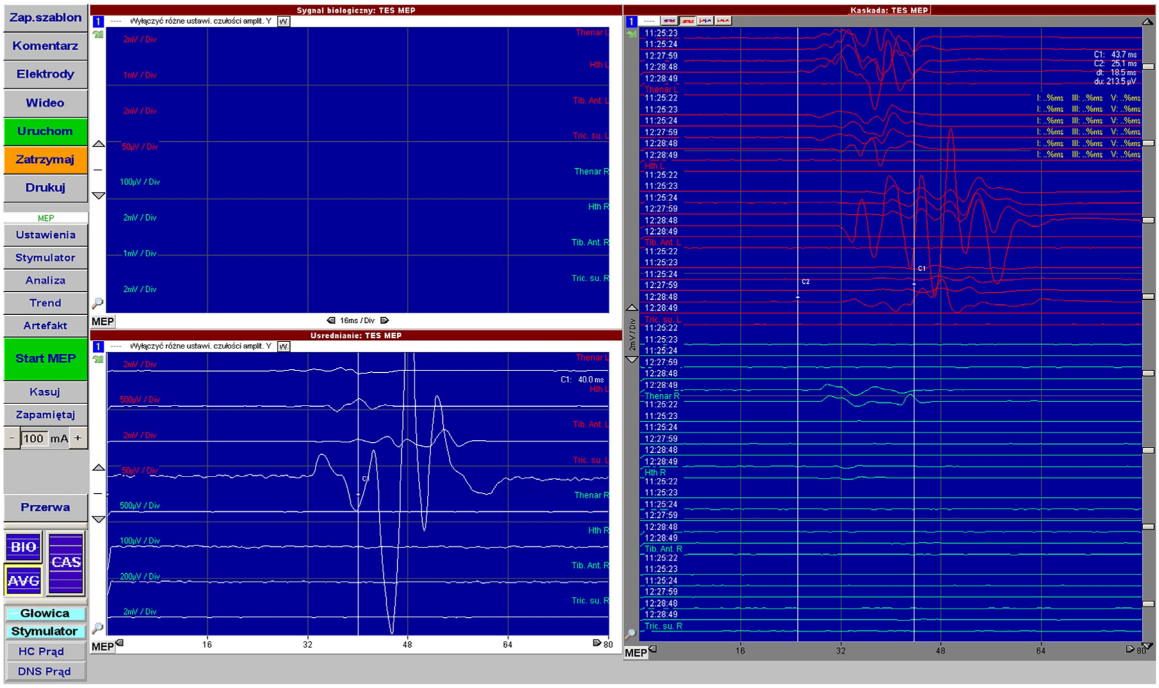

Fig. 4 – Preoperative motor evoked potential (MEP) response to transcranial electrical stimulation (TES) in a patient who developed postoperative hemiparesis.

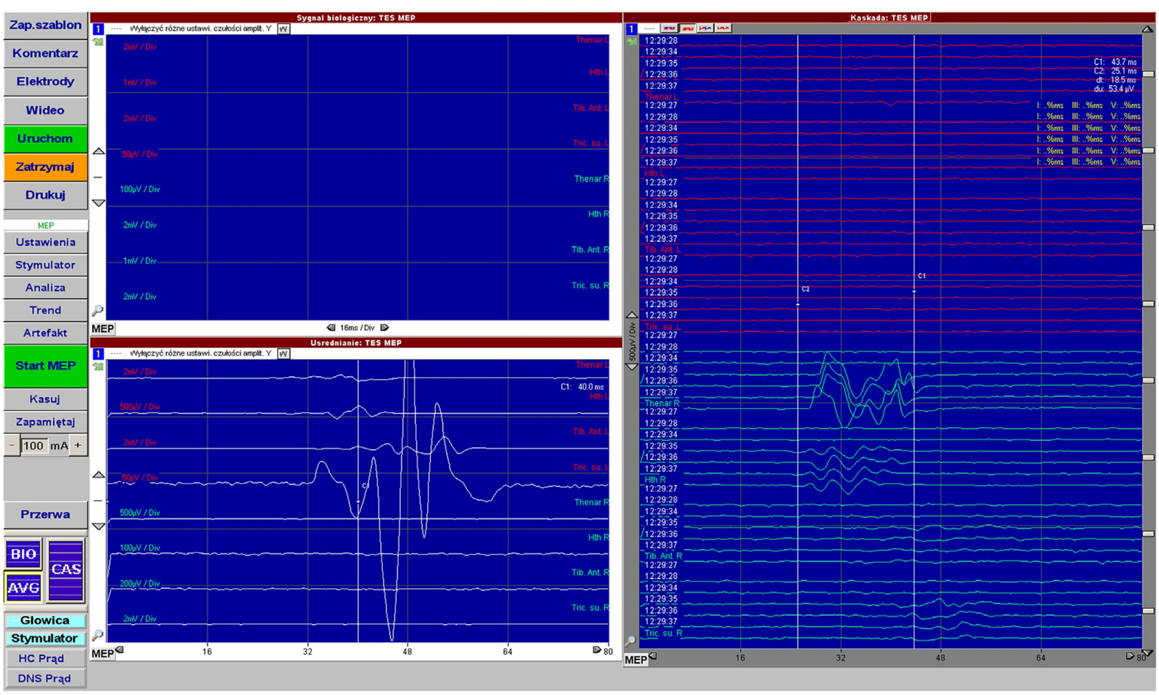

Fig. 5 – Irreversible deterioration of MEP response to TES in a patient who developed permanent postoperative hemiparesis.

statistically significant (log-rank test, $p = 0.0002$). The shortest median time to progression concerned the patients with malignant tumors of the thalamus.

None of the patients with grade I/II died. Among the patients with grade III/IV 11 of 23 (48%) died. Median OS was 60 months for patients with grade I/II and 18 months with grade III/IV. It is a statistically significant difference (log-rank test, $p = 0.002$). Worse prognosis was observed for patients classified as III/IV grade glioma.

The analysis of the extent of resection showed that GTR, STR and PTR were achieved in 18 (47%), 9 (24%) and 11 (29%) patients. Mean extent of resection was 100% in the group with

Table 1 – Prognostic value of transcranial electrical stimulation (TES) and direct electrical stimulation (DES) in prediction of transient and permanent postoperative hemiparesis.

Stimulation	Outcome	Transient hemiparesis	Permanent hemiparesis	Lack of hemiparesis	*p*-Value
TES	Stable	0 (0%)	0 (0%)	17 (49%)	<0.05
	Reversible deterioration	6 (17%)	1 (3%)	0 (0%)	–
	Irreversible deterioration	1 (3%)	10 (28%)	0 (0%)	–
DES	Positive response	5 (14%)	1 (3%)	9 (26%)	–
	Missing response	2 (6%)	10 (28%)	8 (23%)	–

Table 2 – Incidence of neurological symptoms in patients with thalamic tumors scheduled for surgical treatment.

Symptom	Prior to surgery	6 months post-surgery
Mean age, years(range)	37 (20–65)	
Male/female	Male 36/female 38	
Hemiparesis	18 (47%)	11 (29%)
- NIHSS grade 1	11 (29%)	4 (10.5%)
- NIHSS grade 2	7 (18%)	7 (18.5%)
Hemianopia	1 (3%)	4 (10.5%)
Speech disorders	1 (3%)	4 (10.5%)
Paresthesia	4 (10.5%)	5 (13%)
Headache	4 (10.5%)	1 (3%)
Hydrocephalus	11 (29%)	2 (5%)

Table 3 – Relationship between tumor volume and the incidence of hemiparesis in patients with thalamic tumors before surgery.

Parameter	No.	Mean V flair [cm^3]	Median V flair [cm^3]	Minimum V flair [cm^3]	Maximum V flair [cm^3]	Std deviation
All patients	36	35.2	26.5	6.8	150.2	29.1
Lack of hemiparesis before operation	20	21.2	13.1	6.8	63.6	17.8
Hemiparesis before operation	16	52.7	45.3	18.8	150.2	31.5

$p < 0.05$.

Table 4 – Relationship between the incidence of hemiparesis and mean nFA in the posterior limb of the internal capsule ipsilaterally and contralaterally to the tumor before operation.

Parameter	Hemiparesis (n = 16)	Lack of hemiparesis (n = 20)	*p*-Value
nFA ipsilaterally	0.838 ± 0.0904	0.951 ± 0.084	<0.05
nFA contralaterally	1	1	–

Table 5 – Progression and median survival time of the patients with WHO classification of glioma tumors.

Pathological grade	Cases	Mean age Years (range)	Progression		Median TTP	Median survival time
	n		*n*	%	mths	mths
WHO grade I/II	13	32 (20–65)	3	23	36	60
WHO grade III/IV	23	39 (20–62)	19	83	14	18

Time to progression ($p < 0.05$).
Survival time ($p < 0.05$).

total resection and 89.4 % in the group with subtotal resection, and 77.18% in the case of partial resection. The mean extent of resection was 86.5% for all operated patients.

GTR was achieved in 6 of 7 (85.7%) patients with pilocytic astrocytoma, 4 of 8 (50%) subjects with fibrillary astrocytoma or oligoastrocytoma, and 8 of 23 (35%) with anaplastic astrocytoma or multiform glioblastoma.

The relationship between the prognosis and the extent of tumor resection is presented in Table 6. The table does not contain the data for patients with non-glial thalamic tumors.

Among the patients with GTR progression was observed in 7/18 (39%), in a group with STR in 4/7 (57%) and in PTR in all 11 patients (100%). A statistically significant difference is observed between the extent of tumor resection and time to progression (p = 0.0004).

The mortality rates were as follows: GTR – 2/18 (11%), STR – 1/7 (14%) and PTR – 8/11 (72%). There is a statistically significant difference between patients with different extent of resection with respect to survival time ($p < 0.05$). Worse prognosis was related to patients with partial tumor resection (PTR).

Table 6 – Effect of extent of resection on progression and survival.

	Cases	Progression		Median TTP	Median survival time
	n	N	%	mths	mths
GTR (mean range of resection – 100%)	18	7	39	24	31
STR (mean range of resection – 89.4%)	7	4	57	26	32
PTR (mean range of resection – 77.18%)	11	11	100	9	12

4. Discussion

A tendency to conservative treatment of thalamic gliomas existed for many years. In 1995 Krouwer and Prados published a study on 70 patients with thalamic astrocytoma who had brain biopsy and underwent radio and chemotherapy [25]. The mean time to progression was 11.7 months and the mean survival time was 18 months. Sometime earlier Kelly et al. reported satisfactory surgical treatment results of patients with thalamic pilocytic astrocytoma [11]. Based on conservative treatment results of patients with thalamic astrocytoma and the thymidine labeling index in the cancer tissue, Franzini et al. tried to search for indications for surgical treatment. Forty three percent of patients with thalamic tumor died within 3 years. The mortality rate was 100% in a group of patients with the thymidine label index $>$5% and only 20% in patients with the index $<$5. Therefore, surgical treatment should be considered in the first group [26].

A number of surgeons use MEPs at the time of surgery of low-grade and high-grade gliomas in order to prevent postoperative hemiparesis [14–16,27]. The presence of conduction within the corticospinal tract fibers was verified on the basis of TES. This test accurately reflects the risk of postoperative hemiparesis associated with the conduction disorders. None of the patients with stable MEP responses developed postoperative hemiparesis, and an irreversible deterioration of MEP turned out to be associated with the incidence of postoperative hemiplegia in 90% of cases. Zhou and Kelly [28] analyzed MEPs in a group of 50 patients and showed that an irreversible deterioration of the response, namely a 50% decrease in the amplitude, is associated with higher incidence of permanent hemiplegia. According to these authors, transcranial mapping of MEPs is a safe and valuable method for the detection of the corticospinal tract conduction disorders in patients operated on for the brain tumors. Neuloh et al. [18] did not observe postoperative hemiparesis in any of the patients with insular tumors and stable MEP responses, and documented the presence of hemiparesis in most individuals presenting with an irreversible deterioration of MEP response.

Moreover, we used bipolar DES of the subcortical white matter to identify the posterior limb of the internal capsule. Direct stimulation of the subcortical white matter enabled us intraoperative identification of the internal capsule in 43% of cases. We classified the MEP recordings as positive responses from the contralateral limb. Electrical current used for the stimulation in our patients ranged between 10 mA and 15 mA. We did not apply lower current as bipolar stimulation used in this study is less likely to induce a response from the upper and lower extremity muscles as compared to the monopolar stimulation [27]. Surgical procedure was more cautious whenever a positive response was obtained from the white matter tracts located in the vicinity of the internal capsule. Resection was performed at a slower pace and that stimulation was constantly repeated. Identification of the internal capsule at surgery enabled us to save internal capsule thus preventing hemiparesis in 14/15 (93%) patients.

Eighteen patients included in our series (47%) presented with hemiparesis prior to the surgery. Similarly high incidence of hemiparesis in patients with thalamic tumors was previously reported by Nishio et al. [29]. Also other authors confirmed that the incidence of preoperative hemiparesis in patients with thalamic tumors is quite high, ranging between 33% and 87% [5,7,9,10]. Hemiparesis was significantly more frequent among patients with large thalamic tumors and turned out to be associated with lower mean nFA in the internal capsule ipsilaterally to the mass. All the patients with preoperative evidence of hemiparesis showed its exacerbation during the postoperative period. Six months following surgery 11 patients (29%) presented with the permanent disability. However, this group included four patients with minor hemiparesis (corresponding to NIHSS grade 1), thus being capable of relatively independent functioning. In 6 of the 7 remaining patients paresis was observed preoperatively mainly in patients with anaplastic astrocytoma. According to Sai Kiran et al. [9], preexisting hemiparesis in patients with anaplastic astrocytoma never resolves postoperatively, as opposed to patients with pilocytic astrocytoma. According to these authors, preoperative hemiparesis does not resolve after surgery if the internal capsule is infiltrated by cancer cells [9]. In our series, preoperative hemiparesis did not usually resolve in patients who presented with lower mean nFA in the posterior limb of the internal capsule at the baseline. Also the incidence of permanent postoperative hemiparesis was the highest in this group. Therefore, the risk of permanent postoperative hemiparesis does not seem to be associated solely with the histopathological type of thalamic tumor. One previous study showed that the risk of the permanent hemiparesis is greater in patients in whom anaplastic astrocytoma infiltrates the internal capsule, while similar phenomenon is not observed in patients with pilocytic astrocytoma [31].

Planning surgery, we aimed at sparing the optic radiation. We achieved this objective due to preoperative identification of the optic tract topography by means of DTI and further intraoperative visualization in the neuronavigation system. As a result, only 8% patients from our series developed permanent postoperative hemianopia. This likely reflected the fact that the topography of the optic radiation was visualized intraoperatively with the neuronavigation system. According to Baroncini et al. [6], hemianopia constitutes the most common complication of surgery for thalamic tumors in children. It occurred in 7 (44%) of 16 operated patients. Steiger et al. [5] reported postoperative visual impairment in 20% of adult patients undergoing thalamic tumor resection.

The prognosis in patients with thalamic tumors is determined, to a large extent, by histopathological diagnosis. None of our 13 patients with WHO grade I or II gliomas died during a 7-year follow-up, as compared to 55% mortality among those with WHO grade III or IV gliomas. None of the patients with malignant astrocytomas included in another series survived three years post-surgery [31]. In another study, the 16-year mortality rate of children operated on for WHO grade III or IV thalamic gliomas amounted to 73%. However, three patients from this group survived at 2, 3 and 16 years post-surgery, respectively [30]. According to Kelly [11], patients with grade IV astrocytoma may survive, on average, up to 1.5 years post-surgery. Steiger et al. [5] reported progression or recurrence in 60% of their patients diagnosed with WHO grade III or IV gliomas. According to Sai Kiran et al. [9], grade III or IV thalamic gliomas have a worse prognosis than their equivalents arising in other parts of the CNS. In turn, Cuccia and Monges [32] reported that the outcomes in patients operated on for anaplastic astrocytomas of the thalamus are better than in individuals subjected to biopsy and irradiation. Similar findings were reported by Kelly [11] who analyzed the group of patients with glioblastoma multiforme. Favorable prognosis in patients with low-grade thalamic gliomas was confirmed by Puget et al. [12] and Albright [30]. It substantiates the surgery of patients with thalamic astrocytoma, which we performed with good results in 6 patients.

In contrast, Waqar et al. [33] showed that median survival of patients with low-grade gliomas arising from the cerebral midline structures, including the thalamus, was shorter than in the case of lobar low-grade gliomas.

The extent of tumor resection constitutes a significant prognostic factor. In our series, the longest survival was documented in the case of individuals who achieved GTR. Sai Kiran et al. [9] achieved total or subtotal resection in 64% of patients with WHO grade I tumors, as well as in 100% and 41% of individuals with WHO grade II and III gliomas, respectively. We achieved GTR in 47% of patients from our cohort, whereas STR and PTR were achieved in 24% and 29% of the subjects, respectively. The number of GTRs in patients with grade I and II gliomas was significantly higher than in individuals with the grade III and IV tumors. In the study conducted by Steiger et al. [5], the extent of resection assessed on the basis of postoperative MRI corresponded to 80–100% in 11 (78.5%) cases. During a 4-year follow-up, a progression or recurrence of malignant glioma was observed in 60% of the cases [5]. In another study, more than 90% resection was achieved in 83% of pediatric patients [29]. Also Moshel et al. [7] reported achieving GTR in 80% of children with thalamic pilocytic astrocytomas. A significant role of the extent of resection as a determinant of prognosis in patients with thalamic tumors was also emphasized by French authors [12].

In our study we demonstrated that none of the patients with WHO grades I and II gliomas died in the follow-up period. Tumor progression was observed only in 3 of 13 (23%) patients. Radical resection was the most frequently done in these patients and mildly expressed hemiparesis occurred only in 2 patients. It seems that these patients should first undergo surgical treatment with the use of brain mapping and neuromonitoring.

Time to progression in patients with grades III or IV gliomas was 14 months, which, to some extent, would substantiate the performed surgical procedures. The median survival time was 18 months.

5. Conclusions

1 The preoperative volume of tumor in patients with hemiparesis is significantly larger than in patients with lack of hemiparesis. Hemiparesis is the result of the neoplastic infiltration of the posterior limb of the internal capsule (decreased mean nFA).
2 Transcranial electrical stimulation (TES) helps to predict postoperative paresis of extremities.
3 Direct electrical stimulation (DES) is an effective tool for intraoperative localization of the internal capsule thus helping to avoid postoperative deficit.
4 The extent of resection heavily influences the prognosis of patients with thalamic tumors. Progression of patients with WHO grades I and II is substantially longer than gliomas grade III/IV. Median survival time was 60 months for grade I/II and 18 months for grade III/IV.
5 Basing on our results, the patients with grade I/II (WHO classification) are the best candidates for surgical treatment of thalamic tumors. More often resection is radical, median time to progression and survival time are longer than in patients with gliomas grade III and IV. Within a 7-year follow up none of the patients with GI/GII grade glioma died.

Conflict of interest

None declared.

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References

[1] Beks JWF, Bouma GJ, Journée HL. Tumours of the thalamic region. A retrospective study of 27 cases. Acta Neurochir 1987;85:125–7.

[2] Cheek WR, Taveras JM. Thalamic tumors. J Neurosurg 1966;24:505–13.

[3] McKissock W, Paine KWE. Primary tumours of the thalamus. Brain 1958;81:41–63.

[4] Tovi D, Schisano G, Liljeqvist B. Primary tumors of the region of the thalamus. J Neurosurg 1961;18:730–40.
[5] Steiger HJ, Gotz C, Schmid-Elsaesser R, Stummer W. Thalamic astrocytomas: surgical anatomy and results of a pilot series using maximum microsurgical removal. Acta Neurochir (Wien) 2000;142:1327–37.
[6] Baroncini M, Vinchon M, Minéo JF, Pichon F, Francke JP, Dhellemmes P. Surgical resection of thalamic tumors in children: approaches and clinical results. Childs Nerv Syst 2007;23:753–60.
[7] Moshel YA, Elliott RE, Monoky DJ, Wisoff JH. Role of diffusion tensor imaging in resection of thalamic juvenile pilocytic astrocytoma. J Neurosurg Pediatr 2009;4:495–505.
[8] Hou JZ, Chen XL, Xu BN. Prediction of the location of the pyramidal tract in patients with thalamic or basal ganglia tumors. PLOS ONE 2012;7(11):e48585.
[9] Kiran NAS, Thakar S, Dadlani R, Mohan D, Furtado SV, Ghosal N, et al. Surgical management of thalamic gliomas: case selection, technical considerations, and review of literature. Neurosurg Rev 2013;36:383–93.
[10] Moshel YA, Link MJ, Kelly PJ. Stereotactic volumetric resection of thalamic pilocytic astrocytomas. Neurosurgery 2007;61:66–75.
[11] Kelly PJ. Stereotactic biopsy and resection of thalamic astrocytomas. Neurosurgery 1989;25(2):185–94.
[12] Puget S, Crimmins DW, Garnett MR, Grill J, Oliveira R, Boddaert N, et al. Thalamic tumors in children: a reappraisal. J Neurosurg Pediatr 2007;106:354–62.
[13] Broadway SJ, Ogg RJ, Scoggins MA, Sanford R, Patay Z, Boop FA. Surgical management of tumors producing the thalamopeduncular syndrome of childhood. J Neurosurg Pediatr 2011;7(6):589–95.
[14] Duffau H. Intraoperative cortico-subcortical stimulations in surgery of low-grade gliomas. Expert Rev Neurother 2005;5:473–85.
[15] Kamada K, Todo T, Ota T, Ino K, Masutani Y, Aoki S, et al. The motor-evoked potential threshold evaluated by tractography and electrical stimulation. J Neurosurg 2009;111:785–95 [Clinical article].
[16] Keles GE, Lundin DA, Lamborn KR, Chang EF, Ojemann G, Berger MS. Intraoperative subcortical stimulation mapping for hemispherical perilonandic gliomas located within or adjacent to the descending motor pathways: evaluation of morbidity and assessment of functional outcome in 294 patients. J Neurosurg 2004;100:369–75.
[17] Majchrzak K, Bobek-Billewicz B, Tymowski M, Adamczyk P, Majchrzak H, Ładziński P. Chirurgiczne leczenie guzów wyspy z wykorzystaniem traktografii (DTI), stymulacji elektrycznej przezczaszkowej (TES) oraz bezpośredniej stymulacji istoty białej podkorowej (DES). Neurol Neurochir Pol 2011;45:1–12.
[18] Neuloch G, Pechstein U, Schramm J. Motor tract monitoring during insular glioma surgery. J Neurosurg 2007;106:582–92.
[19] Sawaya R, Hammoud M, Schoppa D, Hess KR, Wu SZ, Shi WM, et al. Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. Neurosurgery 1998;42:1044–55.
[20] Meyer BC, Hemmen TM, Jackson C, Lyden PD. Modified National Institutes of Health stroke scale for use in stroke clinical trials. Stroke 2002;33:1261–6.
[21] Bertani G, Fava E, Casaceli G, Carrabba G, Casarotti A, Papagno C, et al. Intraoperative mapping and monitoring of brain functions for the resection of low-grade gliomas: technical considerations. Neurosurg Focus 2009;27:4. Page E4.
[22] Duffau H, Taillander L, Gatignol P, Capelle L. The insular lobe and brain plasticity: lessons from tumor surgery. Clin Neurol Neurosurg 2006;108:543–8.
[23] Hentschel SJ, Lang FF. Surgical resection of intrinsic insular tumors. Neurosurgery 2005;57(1):176–83.
[24] Jellison BJ, Field AS, Medow J, Lazar M, Salamat MS, Alexander AL. Diffusion tensor imaging of cerebral white matter: a pictorial review of physics, fiber tract anatomy, and tumor imaging patterns. AJNR Am J Neuroradiol 2004;25:356–69.
[25] Krouwer HGJ, Prados MD. Infiltrative astrocytomas of the thalamus. J Neurosurg 1995;82:548–57.
[26] Franzini A, Leocata F, Servello D, Allegranza A, Broggi G. Low grade glial tumors in basal ganglia and thalamus: natural history and biological reappraisal. Neurosurgery 1994;35(5):817–20.
[27] Szelenyi A, Senft C, Jardan M, Forster MT, Franz K, Seifert V, et al. Intra-operative subcortical electrical stimulation: a comparison of two methods. Clin Neurophysiol 2011;122:1470–5.
[28] Zhou HH, Kelly PJ. Transcranial electrical motor evoked potential monitoring for brain tumour resection. Neurosurgery 2001;48:1075–81.
[29] Nishio S, Morioka T, Suzuki S, Takeshita I, Fukui M. Thalamic gliomas: a clinicopathologic analysis of 20 cases with reference to patient age. Acta Neurochir 1997;139:336–42.
[30] Albright AL. Feasibility and advisability of resections of thalamic tumors in pediatric patients. J Neurosurg Pediatr 2004;100:468–72.
[31] Ischii R, Suzuki Y, Watanabe A, Mouri Y, Ishii N, Yoshii I. Gross total removal of gliomas in the pulvinar and correlative microsurgical anatomy. Neurol Med Chir (Tokyo) 2002;42:536–46.
[32] Cuccia V, Monges J. Thalamic tumors in children. Childs Nerv Syst 1997;13:514–21.
[33] Waqar M, Hanif S, Rathi N, Das K, Zakaria R, Brodbelt AR, et al. Diagnostic challenges, management and outcomes of midline low-grade gliomas. J Neurooncol 2014;120(2):389–98.