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In accordance with the resolution of the Higher Attestation Commission of the Ministry of Education and Science of the Russian Federation, the Problems of Neurosurgery named after N.N. Burdenko was included in the List of Leading Peer-Reviewed Journals and Periodicals issued in the Russian Federation where the main results of Candidate and Doctor Theses are recommended to be published.
Surgical Management of Patients with Pathological Deformation of Carotid Arteries

D.YU. USACHEV, V.A. LUKSHIN, A.D. SOSNIN, L.V. SHISHKINA, A.V. SHMIGEL’SKII, I.A. NAGORSKAYA, V.V. VASIL’CHENKO, A.YU. BELYAEV, A.D. AKHMEDOV, E.V. BATISHCHEVA

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Surgical management of pathological deformation of the internal carotid arteries, a cause of chronic cerebral ischemia, is discussed. This pathology is very common and is found in 25% of all individuals who underwent preventive medical examination according to the ultrasonography data. Most deformations do not pose any threat to patients, while some of them may cause ischemic stroke and chronic cerebral ischemia. The study included 165 patients with the known follow-up history who have been operated on at the Burdenko Neurosurgical Institute since 2001. A total of 196 reconstructive interventions of carotid arteries were analyzed. The indications for surgical management of pathological deformation based on clinical symptoms and identification of the signs of vessel wall dysplasia are thoroughly discussed. The local and cerebral hemodynamics during the pre- and postoperative period are analyzed. The results of pathomorphological examination of the resected fragments of the deformed arteries are presented; they show that the changes are identical to those in patients with fibromuscular dysplasia. The follow-up history of the patients showed a sustained regression of transient ischemic attacks and cerebral symptoms in most cases (69%). For proper indications for surgical management, reconstructive surgical interventions are a reliable and effective method for treating chronic cerebral ischemia and preventing recurrent ischemic strokes in patients with deformation of carotid arteries.

Keywords: carotid arteries, pathological deformation, cerebral ischemia, reconstructive surgery.
groups of patients who had been operated on and the improved neurological status in patients after surgical intervention. However, no comprehensive multicenter studies devoted to surgical treatment of pathological deformation that would be methodologically correct have been conducted yet. When making attempts to prove the effectiveness of ICA reconstruction in patients with ICA deformation, surgeons often jointly evaluate the outcomes of surgical treatment of patients with isolated deformation and the combination of critical stenosis in the bifurcation area and distal deformation, which is totally incorrect. There is no unified approach to classification of deformations; the indications for surgical treatment differ as well. Thus, in North America, Australia, Great Britain, and most European Union countries, surgical intervention for pathological deformation is performed only in exceptional situations in patients who experienced ischemic circulatory disorders, while surgical resection and redressment of the ICA are also widely used in asymptomatic patients in Russia, Italy, and Western European countries.

The advanced diagnostic methods (in particular, the wide use and availability of Doppler ultrasonography) resulted in higher detection rate of pathological deformation in population. According to ultrasonography data [14], the detection rate of ICA tortuosity is as high as 25—30% in adults and 43% in children. Most patients obviously do not require surgical management; however, they are erroneously referred to vascular surgeons and neurosurgeons. So it is extremely important to properly determine the indications for reconstruction. Various types of pathological deformations, degrees of their hemodynamic significance and effect on cerebral hemodynamics, as well as the necessity for differential diagnosis between pathological deformations and other neurosurgical and neurological pathologies make selecting the optimal strategy for managing patients with pathological deformation of carotid arteries extremely difficult. In this publication, we propose an approach to determining the indications for surgical management of patients with pathological deformations, which is based on clinical presentation, deformation classification, and detections of signs of vessel wall dysplasia. The local and cerebral hemodynamics is studied depending on the deformation types. The outcomes of surgical management are evaluated according to the follow-up data.

Material and Methods

The study included 165 patients who had been operated on at the Burdenko Neurosurgical Institute in 2001—2013 for isolated pathological deformation of the ICA; the postoperative follow-up data were available. The male:female ratio was 62:63. In 27 (16.3%) cases, surgical interventions for ICA deformation were performed to pediatric patients (younger than 18 years of age). Patients’ age varied from 6 to 85 years (median age, 48±19 years). The age and gender structure of patients is shown in Fig. 1.

The somatic risk factors revealed most frequently in this patient group included hypertension (86 patients, or 54.3%) and ischemic heart disease (41 patients, or 25%). Obesity (8%), pulmonary risk factors (7.2%), diabetes mellitus (4%), and renal pathology (3.7%) were detected much less frequently.

The diagnostic algorithm in patients with pathological deformation of carotid arteries included complex clinical examination (neurological, neuro-ophthalmologic, and oto-neurological examination). Patients with an underlying pathology were followed up by a cardiologist, a general practitioner, and an endocrinologist.

The clinical manifestations in patients with pathological deformation of the ICA can be subdivided into three large groups:

— non-focal neurological symptoms (headache, chronic fatigue syndrome, concentration problems, and delayed intel-
Prior to that, all patients underwent comprehensive ultrasound scanning including duplex scanning of the brachiocephalic arteries and transcranial Doppler ultrasound examination of intracranial vessels. Various angiographic procedures (SCT/MR angiography; less frequently, conventional selective angiography) were used to verify the ultrasound data if indicated (in 71 (43%) patients).

Duplex scanning was performed on a SONOS 2500 (Hewlett Packard) instrument, 7 MHz, with a linear sensor in the continuous and pulsed modes of operation; the volumetric blood flow in the brachiocephalic arteries was determined. In addition to detecting the deformation, the examination aimed at measuring the linear blood flow velocity (LBFV) before and after deformation, as well as in the maximum bend area (Fig. 3). The deformation type was revealed and concomitant symptoms of carotid artery dysplasia (septal tortuosity (kinking), diverticulae or microaneurysms, 180—360° torsion of the artery, distal hypoplasia of the ICA) were identified. To evaluate the contribution of ICA in the total cerebral blood flow, we measured the volumetric blood flow velocity using a hardware procedure.

To assess cerebral hemodynamics, all patients underwent transcranial Doppler ultrasound examination of intracranial vessels using an Angiodin-2 Doppler system (Bioss, Russia) with a 2 MHz frequency sensor [2, 12]. The location of the anterior, middle and posterior cerebral arteries was identified; the asymmetry of LBFV parameters in them was assessed; and peripheral resistance indices were calculated.

Seventy-one patients underwent angiographic examination. Branches of the aortic arch (brachiocephalic arteries), skull base and the circle of Willis arteries were visualized regardless of the procedure selected. The indications for angiographic examination were as follows:

- verification of deformation, especially for high-lying deformations that were located in the distal one-third of the extracranial ICA segments and could not be adequately imaged using duplex scanning;
- imaging of dysplasia signs in the deformation area: hourglass-like torsion of the artery, septal stenosis, diverticulae and microaneurysms, regions of distal artery hypoplasia or artery dissection;
- ruling out the underlying stenosing pathology of the skull base and cerebral arteries;
- evaluation of the condition of the circle of Willis to determine the risks of the main stage of reconstruction.

SCT angiography was performed most frequently; this method can be regarded as a gold standard for diagnosis of stenosing and deforming pathology of brachiocephalic arteries (in 41 patients). MR angiography was carried out in 19 cases. Bolus-chase and phase contrast angiography are the most informative MR angiography procedures. Time of flight angiography also allows visualization of deformations; however, their information capacity decreases significantly when imaging vessels with turbulent blood flow (which is typical of pathological deformation). This fact limits their use for diagnosis of this pathology. The conventional direct puncture angiography of the branches of the aortic arch was used in 11 cases: mostly

Identification and classification of the pathological deformation, determining the extent of its effect on local and cerebral hemodynamics and severity of dysplasia symptoms were the key stage of diagnosis.
in the early 2000s when other angiographic modes were not commonly used. Today, the conventional angiography is not used in diagnosis of pathological deformation, except for the accidental detection of tortuosity during angiographic examination in patients with combined intracranial vessel pathologies.

According to the classification proposed by J. Weibel and W. Fields [28], all the deformations revealed were subdivided into tortuosities (C- and S-shaped) and U-shaped loops (Fig. 4b). Kinks are located in the same plane for tortuosities, while being located in two planes for loops.

The prognosis of clinical course of deformation depends on whether there are signs of vessel wall dysplasia (septal stenosis, signs of 180—360˚ torsion of the artery around its axis, diverticulae and microaneurysms, signs of distal hypoplasia and ICA dissection) or not. The presence of dysplasia symptoms gives grounds for regarding the deformation as a sign of pathology (“pathological deformation”).

**Septal stenoses** are caused by an abrupt kink of the artery in the deformation area. The severity of dysplastic changes of the vessel wall in septal stenosis depends on its geometry. The method proposed by Metz [19] is used to classify septal stenoses:
- type 1: artery kinking by over 60˚;
- type 2: artery kinking by 30—60˚ (Fig. 4d);
- type 3: abrupt kinking of the artery by less than 30˚.

**Torsion of the artery** is rotation of the artery around its axis by 180—360˚ in the deformation area. A local narrowing is formed in the torsion area, resulting in severe hemodynamic shifts. The torsion area can be diagnosed during imaging according to its characteristic hourglass shape (Fig. 4a).

**Diverticulae and microaneurysms** are represented by abnormal vessel contour in the deformation area and formation of small protrusions. These pathologies result from severe morphological changes in vessel wall and impose a significant risk of artery dissection and acute arterial occlusion (Fig. 4c).

---

**Fig. 4. Pathological deformation according to the duplex scanning data with rough local hemodynamic significance.**

a — bilateral S-shaped tortuosities with torsion (hourglass-shaped); b — loop-shaped tortuosities according to SCT angiography data; c — severe S-shaped deformations with signs of a microaneurysm; d — type 2 septal stenosis according to the classification proposed by Metz.
**Distal hypoplasia** is represented by arterial luminal narrowing in the distal direction from a pathological deformation. It usually accompanies septal stenosis or torsion of the artery. Distal hypoplasia significantly reduces the volumetric blood flow in the deformed artery, so the concomitant septal stenosis can be of less significant in terms of local hemodynamics.

Hemodynamic significance (local gain in LBFV in the deformation area due to its local narrowing) is another key parameter of deformation. First and foremost, hemodynamic significance is indicative of the severity of septal stenosis and artery torsion when there are no signs of distal hypoplasia and reduction of volumetric blood flow in the deformed artery. Tortuosity was considered to be hemodynamically significant when the gain in LBFV in the deformation area was more than 170 cm/s (moderate significance). The gain in LBFV over 250 cm/s was regarded as pronounced hemodynamic significance, while the gain in LBFV over 300—350 cm/s and presence of turbulent noise was regarded as severe one.

The study group included only isolated pathological deformations of the ICA with hemodynamically insignificant atherosclerotic lesions (less than 50%).

The indications for surgical management of isolated pathological deformations were determined according to clinical symptoms and deformation type (including the presence of possible dysplastic changes in the vessel wall), its hemodynamic significance, and risks of reconstructive surgical intervention.

**Absolute indications** for surgical treatment of pathological deformations were as follows:

- past medical history of disruption of cerebral blood flow and any type of deformation combined with any dysplasia symptom (hemodynamically significant septal stenosis, torsion, diverticulae or distal hypoplasia);
- non-focal neurological symptoms and presence of aneurysms or diverticulae of the vessel wall in the deformation area regardless of its hemodynamic significance;
- non-focal neurological symptoms and severe septal stenosis (LBFV higher than 300—350 cm/s);
- non-focal neurological symptoms and type 2—3 septal stenosis with signs of distal hypoplasia and reduced volumetric blood flow in the deformed artery (local hemodynamic significance is unimportant in this case).

First and foremost, surgical treatment was offered to patients with absolute indications for it to prevent ischemic disruption of cerebral blood flow, development of ICA dissection and ICA occlusion.

**Relative indications** for surgical management included:

- non-focal neurological symptoms and presence of septal stenosis with pronounced hemodynamic significance (LBFV over 200—250 cm/s) if conservative treatment proved to be ineffective or the patient made a decision to undergo surgical treatment;
- deformations of carotid arteries impeding the endovascular approach to the concomitant pathology of cerebral vessels. This group includes patients with cerebral aneurysms and arteriovenous malformations that can be treated endovascularly. Severe deformations of carotid arteries technically impede catheter insertion into the intracranial vessels and stent placement. These procedures require performing ICA reconstruction at the first stage, followed by planning the primary endovascular intervention.

Surgical interventions for relative indications aimed at improving patient’s quality of life. Hence, prior to making a decision whether to conduct surgery or not, the risks of surgical intervention were meticulously assessed. In particular, surgical management for relative indications was considered unreasonable in patients having high-lying deformations (under the skull base), disrupted circle of Willis, and combined somatic pathology. The patients with non-focal neurological symptoms underwent conservative therapy for 4—6 months under dynamic monitoring by neurologists. A decision regarding surgical intervention was made only if the symptoms persisted or were aggravated.

General **contraindications** for surgical treatment of pathological deformations include severe neurological or somatic status, severe cardiac arrhythmia, cardiac aneurysms, severe coagulopathy, demyelinating disease, dementia, and poor prognosis for survival in patients with combined cancer pathology.

In all cases, the ICA was resected and redressed according to the conventional procedure to eliminate the pathological deformation. Surgical intervention was carried out under general endotracheal anesthesia in 153 (92.7%) patients. Locoregional anesthesia was used only in 12 (7.3%) cases, mostly in elderly patients with concomitant somatic pathology or for the proximally situated ICA deformations. The regional anesthesia when separating the middle and the distal one-thirds of the ICA often proves to be ineffective, since sensory fibers of the mandibular branch of the trigeminal and glossopharyngeal nerves are involved in innervation of these structures.

A 5—6 cm long linear skin incision along the transverse fold was made in the projection of the upper one-third of the anterior edge of the sternocleidomastoid muscle. A neurovascular bundle was isolated: the common, external and internal carotid arteries were separated within the bundle and fixed. The carotid body was coagulated and dissected in all cases to mobilize the ICA. ICA was isolated along the entire extracranial segment, including the deformation area. To isolate the distal third of the ICA, we coagulated and transected the muscular branches of the external carotid artery (ECA) and branches of the internal jugular vein and mobilized the hypoglossal nerve. If needed, the anterior belly of the digastric muscle was coagulated and transected. The ICA was not separated distally from the styloid process as there was a high risk of damaging the facial nerve.

When separating the ICA, we dissected the tortuosity-forming commissures together with tunica adventitia (redressement).

Special care is needed when dissecting commissures in the deformation area and possible ICA diverticulae: they are eliminated by hydrodilatation at the main stage of reconstruction (**Fig. 5a**).

Prior to compression of the common carotid artery (CCA) and the beginning of the main reconstruction stage, we evaluated patients’ tolerance to compression according to
multimodal neuromonitoring, which was performed in 162 (82.6%) cases. Transcranial Doppler ultrasound examination with detection of the middle cerebral artery ipsilaterally to the operated area using a transcranial Doppler system (Rimed) and cerebral oximetry were used. No monitoring was performed in 34 (17.4%) cases due to technical difficulties (absence of an acoustic window).

If patients showed any signs of intolerance to ICA compression, the question regarding intraluminal shunt placement was solved. After the CCA, ECA, and ICA had been compressed, the ICA was separated from the bifurcation. The ICA was rotated along its axis in case of its torsion and hydrodilatation was performed: a cannula was placed into the arterial lumen through which normal saline solution was injected with a syringe and diffusely dilated the narrowed ICA (Fig. 5b). The excessive length of ICA was resected (Fig. 5c). End-to-side anastomosis with the CCA was created using Prolene 6.0 suture in adult patients and resorbable monofilament suture in pediatric patients (to prevent narrowing of the anastomosis region as children grow and develop). Fig. 5d shows the appearance of the ICA after its reconstruction and deformation correction.

In patients with pronounced signs of dysplasia (diverticulae, thinning of the artery wall in the commissure area), the aim of reconstruction was to make a pathological deformation hemodynamically insignificant (physiological).

In patients with extremely severe dysplasia, pathological deformations are accompanied by the formation of aneurysms of the extracranial segment of the ICA (Fig. 6).

When performing resection of a pathological deformation with an aneurysm of the extracranial segment of the ICA, one needs to isolate the aneurysm while the ICA is compressed to reduce possible cerebral embolism induced by thrombotic masses. An end-to-end anastomosis is created after the dysplastic segment was dissected. Fragments of the resected artery, especially in the deformation area, were subjected to pathomorphological examination of the vessel wall structure.

All patients were postoperatively subjected to neurological examination, disaggregation and vascular therapy.

Fig. 5. Stages of ICA resection and redressment involving elimination of pathological deformation of the ICA.

a — isolated looping of the ICA in the wound; b — hydrodilatation of ICA involving widening of its stenosed segment; c — resection of the excessive ICA; d — appearance of the common carotid artery bifurcation after reconstruction.
In patients with severe bilateral pathological deformation of the ICA, reoperations were performed at least 3 months after the first reconstruction if clinical signs persisted. Patency of the operated artery in the absence of negative dynamics was monitored 2—3 months after surgery because of the edema of the adjacent tissues and the high risk of incorrect interpretation of the examination data. Regular (every 8—10 months) clinical examination of the operated patients was performed subsequently using control Doppler ultrasound examination and other neuroimaging procedures. Thorough assessment of the neurological and neuropsychological status was performed. The longest follow-up duration was 10 years.

**Results**

A total of 165 patients with pathological deformation of the ICA were treated. The most common pathological deformations included tortuositities of the internal carotid artery (121 (62%) patients), mainly the S-shaped tortuosity — in 86 (44%) cases. C-shaped tortuositities were diagnosed in 35 (18%) cases. Looping was the reason for surgical intervention in 75 (38%) patients.

The pathological deformations were accompanied by symptoms of vessel wall dysplasia in 89% of cases (Table 1). Septal stenosis (44%) and torsion of arteries (21%) combined with distal hypoplasia were revealed most commonly (22%).

When studying the cerebral hemodynamics during the preoperative period, blood flow asymmetry (the blood flow being decreased ipsilaterally) was observed only in 10 (6%) cases. Bilateral decrease in blood flow in the middle cerebral artery (the lower limit of the normal range) was observed in 14 (8%) patients. Regardless of deformation type, significant blood flow asymmetries were observed in the remaining patients (86%) neither at rest nor in association with head turning. Reduced ipsilateral blood flow was typically revealed in patients with type 3 septal stenosis combined with distal hypoplasia of the ICA and in patients with reduced volumetric blood flow in the deformed ICA (Table 2). Type 3 septal stenosis was associated with the most severe dysplastic changes and was combined more often with distal hypoplasia and reduced volumetric blood flow. The strongest local hemodynamic shift in the deformation area was observed in patients with type 1 septal stenosis; the least severe one, in patients with type 3 septal stenosis.

A total of 196 reconstructive interventions were performed. Unilateral resection and redressem were per-

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**Fig. 6.** Extremely severe form of dysplasia in pathological deformation of the ICA: aneurysms of the extracranial segment of the ICA. a — SCT angiography data; b — appearance of an aneurysm in the wound.

**Table 1.** Revealed signs of dysplasia of pathological deformation and the extent of their effect on clinical presentation and outcomes of surgical treatment

<table>
<thead>
<tr>
<th>Dysplasia type</th>
<th>Improvement, %</th>
<th>Total number of cases revealed, abs. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torsion of artery</td>
<td>54</td>
<td>35 (21)</td>
</tr>
<tr>
<td>Kinking:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>type 1</td>
<td>73</td>
<td>30 (18)</td>
</tr>
<tr>
<td>type 2</td>
<td>86</td>
<td>25 (15)</td>
</tr>
<tr>
<td>type 3</td>
<td>94</td>
<td>18 (11)</td>
</tr>
<tr>
<td>Diverticulae</td>
<td>—</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Distal hypoplasia</td>
<td>80</td>
<td>36 (22)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>149 (89)</td>
</tr>
</tbody>
</table>
formed in 134 patients; bilateral surgeries were performed in 31 (19%) patients. A temporary intraluminal shunt was applied in 12 (6%) cases during the main stage of reconstruction.

An analysis of the morphological structure of the vessel wall revealed typical signs of dysplasia. Microscopic examination showed microruptures of the intima in the deformation area and microdissections with the formation of local intramural dissections in a number of patients (Fig. 7b).

Despite the fact that the extracranial regions of the ICA typically consist of arteries with mixed structure, an analysis of the fragments of deformed arteries showed that elastic arteries with heterogeneous wall thickness (areas of hypertrophic and thinned muscular walls and subendothelial fibrosis phenomena) predominated. Signs of disorganization of layers of the arterial wall, such as elastic fiber tear, non-uniform thinning of the muscular layer and foci of degenerative changes with phenomena of lipidosis and necrotic changes in the thickened intima, were often detected in the deformation area (Fig. 7a, 1, 2). Near-wall thrombus formation took place in the area of aneurysmal widening of the ICA adjacent to the deformations (Fig. 7a, 3).

In the septal stenosis area, the arterial wall was also characterized by non-uniform thickness with regions of atrophic and hypertrophic middle tunica presenting as expression of smooth muscle fibers in the form of intimal thickening with foci of intimal detachment and lipidosis; there were regions characterized by sclerosis and adventitial cell outgrowth between the tortuous arterial walls (Fig. 8d).

Various pathological deformations are characterized by a common pathomorphologic change, subintimal fibrosis surrounded by hyalinized collagen fibers (Fig. 8a), atheromatous masses (Fig. 8b), and calcifications (Fig. 8c).

The detected morphological changes in the arterial wall structure in the deformation area were similar to those of the carotid form of the conventional fibromuscular dysplasia.

All patients in the study group were followed up (the maximum duration was 10 years; the mean duration was 2.7 years). The evaluation of postoperative outcomes showed positive dynamics: regression of headache and dizziness, improvement of memory and cognitive function in 115 (69%) cases. Complete regression of transient disruption of cerebral circulation was observed in all patients with past history of impaired cerebral blood flow. Meanwhile, there was almost no significant positive dynamics of focal neurological deficit: the improved arm range of motion, reduced spasticity, and reduced ataxia symptoms (score 1—2 according to the NIHSS scale) were observed only in four patients.

Table 2. Parameters of cerebral and local hemodynamics depending on type of septal stenosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Septal stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>type 1</td>
</tr>
<tr>
<td>Volumetric blood flow, ml/min</td>
<td>310±34</td>
</tr>
<tr>
<td>Local LBFV, cm/s</td>
<td>294±47</td>
</tr>
<tr>
<td>Ipsilateral decrease in blood flow, %</td>
<td>3.3</td>
</tr>
<tr>
<td>Distal hypoplasia, %</td>
<td>3.3</td>
</tr>
<tr>
<td>Total, abs. (%)</td>
<td>30 (19)</td>
</tr>
</tbody>
</table>

Fig. 7. Microscopic presentation of dysplastic changes in the deformation area.

a — arterial wall at the site where the deformation becomes an aneurysm bulge (1 — intact arterial wall, 2 — wall where the deformation becomes an aneurysm with dysplasia signs and thinning of arterial tunics, 3 — thrombotic masses in the aneurysm lumen); b — dysplastic signs typical of fibromuscular dysplasia (1 — microdissections, 2 — microtears in the intima).
According to the clinical examination data and subjective feelings in patients, no significant postoperative dynamics was observed. It is noteworthy that 3 months after surgical intervention, symptoms were improved in 133 (79.8%) patients; however, 18 patients reported that the clinical symptoms (vertebrobasilar insufficiency, headache and vertiginous attacks) had returned after one-year follow-up. This group also included 3 patients in whom reconstruction of the ICA was performed as the first stage of endovascular treatment of intracranial aneurysms.

The follow-up showed aggravation of clinical symptoms in 12 (7%) patients, usually after reconstructive reoperations. The main complaints included aggravation of signs of vertebrobasilar insufficiency, syncope, and vertigo. Significant arterial blood pressure instability and a tendency toward systemic hypotension were observed in all cases.

Five patients developed persistent complications. The mortality rate was 0.6%.

One patient died of massive cerebral air embolism caused by using a temporary intraluminal shunt.

Four (2.4%) patients developed ischemic disorders of cerebral circulation; extensive ischemic stroke was caused by acute thrombosis of the reconstructed ICA in one patient. Three patients had partial strokes presenting as minor limb weakness and ataxia that had completely regressed by the time of the first follow-up examination (3 months). Insufficiency of cranio-cerebral nerves was detected in 5 (3%) patients.

Despite the fact that no negative clinical dynamics were observed postoperatively, the outcomes of surgical treatment were regarded as unsatisfactory in two more cases. In one patient, ICA ligation had to be performed as it was damaged throughout its length. In another patient, an ostial restenosis (deformation) was formed after the reconstruction of a severe ICA deformation, thus requiring endovascular angioplasty with stenting to be performed at the second stage.

**Discussion**

The treatment strategy for pathological deformation of carotid arteries is one of the most controversial problems of...
modern neurology and vascular neurosurgery. Carotid artery tortuosity was first reported more than 100 years ago [25] and were considered to be a variant of norm for a long time. As reconstructive surgery of carotid arteries was actively developed in the 1960s, pathological deformations and carotid artery stenosis started to be regarded as one of the reasons for ischemic impairment of cerebral blood flow [22, 25]. A series of successful reconstructive interventions for this pathology have been reported: the patients had complete regression of transient impairment of cerebral blood flow [3, 5, 19, 22, 26]. In all cases, the presence of dysplastic changes in the deformation area was mentioned when defining the indications for surgical treatment [25]. The classification of pathological deformations proposed by Weibel and Metz in 1965 [19, 28] also included the list of possible dysplasia signs presenting as septal stenosis. However, surgical management of all types of ICA tortuositities, in particular in patients with asymptomatic course of the disorder, proved ineffective [9, 10]. Many experts currently regard simple deformations not complicated by dysplasia as a variant of norm or the mechanism of adaptation to arterial hypertension [9]. They report benign clinical course of this type of deformation, which makes treating them unreasonable, as opposed to deformations complicated by vascular dysplasia signs [8, 9, 25].

When determining the absolute indications of surgical treatment in our group of patients, we relied on the presence and severity of dysplastic changes in ICA in combination with the clinical presentation. The tortuosity was visualized ultrasonographically and angiographically; its hemodynamic significance was determined.

Postoperative morphological examination of the resected artery fragments revealed changes typical of fibromuscular dysplasia [25], non-uniform muscular layer with thinned and thickened regions, retrotinal fibrosis, degeneration of elastic elements of vessel wall, intimal microdissections and microtear in the deformation area. All these findings can certainly be a reason for the impaired cerebral blood flow due to cerebral microemboli, dissection and thrombosis of the deformed artery and require preventive surgical correction [25].

Meanwhile, the study of cerebral hemodynamics in patients with deformed carotid arteries showed no significant cerebrovascular insufficiency. Thus, blood flow asymmetry in the middle cerebral artery was observed only in 6% of cases; in 8% of cases, the cerebral hemodynamics lay in the lower limit of the norm. The reasons behind this fact include the retained normal values of volumetric blood flow in moderately deformed arteries (except for type 3 septal stenosis) and the extensive collateral network (the circle of Willis). The latter fact can also be used to explain why temporary intraluminal shunts are used relatively rarely at the primary reconstruction stage. These results coincide completely with the views of foreign experts [9, 21] who have also revealed no cerebrovascular insufficiency in patients with various types of deformations (including the use of rotation tests).

After ICA reconstruction, the patients with all types of deformations showed a tendency toward increased volumetric blood flow; however, statistically significant difference was revealed only for type 3 septal stenoses.

The properly defined indications for surgical treatment of pathological deformations of ICA guarantee that there will be a good outcome and the clinical status of patients will improve. 69% of patients showed sustained improvement of non-focal neurological symptoms and regression of TIA. Meanwhile, almost no dynamics of focal neurological deficit were observed. It is difficult to determine what was the key mechanism that improved the clinical symptoms in patients after surgical elimination of pathological deformations. The volumetric blood flow in the reconstructed artery basin was increased, but not in all patients; furthermore, cerebral blood flow was initially compensated for well in most patients. Another mechanism that has been described is the reduced possible platelet damage in turbulent blood flow in the deformation area, resulting in enhanced platelet aggregation and development of cerebral microemboli. The possible arterial bends in certain head positions causing significant rearrangement of the cerebral hemodynamics are also eliminated. However, the key mechanism is most likely to be desympatization of the carotid basin performed during redressement. Such interventions were proposed by R. Leriche [17] in 1931 to treat obliterated iliac and femoral arteries and were subsequently used to treat ICA occlusion with the positive clinical outcome. This mechanism is indirectly confirmed by the fact that 80% of patients had an improvement during the first 3 months, while 11% of patients subsequently observed the initial clinical symptoms.

Patients who underwent bilateral reconstruction deserve special mention. This problem is particularly relevant, since bilateral deformations occur in 48% of all patients with carotid artery deformation. Bilateral reconstructions were performed in 31 patients. After the first stage, all patients observed moderately positive dynamics; however, clinical symptoms aggravated in 12 (37%) patients after the second stage due to the development of systemic hypotension and unstable arterial pressure. These symptoms undermined the positive effect of reconstructive interventions. The main reason for the development of this condition is deinnervation of carotid bodies and baroreceptors involved in the cycle of neurogenic regulation of systemic arterial pressure as ICA was separated [27]. We believe that special care is needed when defining the indications for the second reconstruction stage. When performing bilateral reconstructive interventions, one should do his/her best to preserve the carotid body and the innervating branches of the glossopharyngeal nerve to prevent development of the denervation syndrome.

Conclusions

1. Comprehensive ultrasonographic examination and non-invasive angiography (SCT/MR-AG) are methods of choice for diagnosis of pathological deformation of ICA. They make it possible to thoroughly study the pathological tortuosity of ICA, to evaluate its shape and spatial arrangement, to reveal dysplasia signs, and to evaluate hemodynamic significance.
2. A decision regarding surgical treatment is made based on clinical symptoms and signs of dysplasia. The local hemodynamic significance of deformation is taken into account when evaluating the severity of arterial dysplasia.

3. Surgical treatment is recommended for symptomatic patients with past history of impaired cerebral blood flow and ICA deformations in combination with dysplasia symptoms (septal stenosis, torsion, diverticulae) and low hemodynamic significance.

4. A decision regarding surgical treatment in patients with non-focal neurological symptoms is made for each individual case with allowance for the severity of dysplastic changes, hemodynamic significance of deformations and the absence of the effect of conservative therapy. It is also made in case of negative dynamics during dynamic follow-up.

5. Pathological deformation of carotid arteries is typically accompanied by insignificant reduction of blood flow in the basin of the affected artery and signs of good collateral compensation for cerebral hemodynamics. The signs of cerebrovascular insufficiency are most frequently caused by type 3 septal stenoses and distal hypoplasia of ICA.

6. Pathological deformations have morphological signs typical of fibromuscular dysplasia.

7. The second stage of reconstruction may cause severe instability of systemic arterial pressure in patients with bilateral deformation of carotid arteries. When separating the arteries, one should preserve carotid bodies and branches of the glossopharyngeal nerve that innervate baroreceptors of the carotid sinus area.

8. Provided that indications have been defined properly, the method of surgical treatment of pathological deformation of carotid arteries can reduce the risk of ischemic cerebral disorders, result in regression of non-focal neurological symptoms, and improve patients’ quality of life.

REFERENCES


Commentary

The present article analyzes treatment of 165 patients with pathological deformation of carotid arteries. The data presented are of significant fundamental and practical interest, since no unified approach to treatment strategy for this group of patients currently exists in the world. A thorough classification of pathological deformations of carotid arteries has been provided. Close attention has been paid to clinical manifestations; clear indications for surgical treatment based on deformation type and local changes in hemodynamics according to duplex scanning and CT angiography data, as well as neurological symptoms, have been provided. Thus, most patients (68%) experienced problems with cerebral circulation; 65% of those were operated on for S- or U-shaped tortuosity of the internal carotid artery. Postoperative follow-up data showed aggravation of the neurological status in 78% of cases. It should be emphasized that patients with prior history of transient ischemic attacks had no recurrent episodes of cerebral circulatory disorders. The histological analysis of the resected artery fragments made it possible to find that the morphological changes in the vessel wall structure in the deformed area are similar to those of fibromuscular dysplasia.

V.N. Dan (Moscow, Russia)
Trapping of Large and Giant Paraclinoid Aneurysms Based on Intraoperative Flowmetry Test

O.D. SHEKHTMAN, SH.SH. ELIAVA, YU.V. PILIPENKO

Burdenko Neurosurgical Institute, Moscow, Russia

Four cases of giant or large paraclinoid aneurysms of the internal carotid artery successfully trapped after assessing blood flow using a flowmeter are presented. In all cases, the initial plan for clipping was changed to aneurysm trapping due to various reasons. The collateral blood flow was assessed using the flowmetry test, the original procedure of measuring volumetric blood flow in the middle cerebral artery using an ultrasonic flowmeter. We analyze the reasons for clipping refusal, the procedure of measuring blood flow, treatment outcomes, and catamnetic data. The risks of reconstructive surgeries involving the internal carotid artery are discussed and the literature data are analyzed. Conclusions. Ultrasonic flowmetry is a simple and safe method for intraoperative control over blood circulation, which may play the key role in complicated surgical cases.

Keywords: ultrasonic flowmetry, paraclinoid aneurysms, aneurysm trapping.

Abbreviations: BOT — balloon occlusion test, IAB — intravascular aspiration of blood; ICA — internal carotid artery; PCA — posterior communicating artery; CT — computed tomography, MRI — magnetic resonance tomography, ACerA — anterior cerebral artery, ACA — anterior communicating artery, MCA — middle cerebral artery, GOS — Glasgow outcome scale.

Paraclinoid aneurysms are aneurysms of the internal carotid artery (ICA) that are formed in a segment between the distal dural ring and the ostium of the posterior communicating artery (PCA). The term “paraclinoid aneurysm” was proposed by S. Nutik [18], who used it for the first time in his paper (1978) reporting 5 cases of ICA aneurysms with cavernous spread.

The incidence rate of paraclinoid aneurysms is 0.5—5.4%. Aneurysms of this location are more frequently diagnosed in women and typically manifest themselves at an age of 40—50 years. Paraclinoid aneurysms are characterized by large size (75% of them are larger than 1 cm in diameter), combination with aneurysms of other locations, and high rate of ophthalmic disturbances developing soon after onset [1, 15].

The natural course of this pathology is unfavorable. According to Peerless et al., among 31 patients with giant aneurysms (25 saccular and 6 fusiform ones), 68% of patients with saccular aneurysms died within 2 years of follow-up; 85% of patients died within 5 years. In patients without hemorrhage, 2-year mortality was also high (62%) [9]. According to the data of the International Study of Unruptured Intracranial Aneurysms (ISUIA) published in 2003 in Lancet, the annual risk of rupture of large (13—24 mm) and giant (larger than 25 mm) aneurysms is 14.5 and 40%, respectively [21].

Hunter’s ligation (proximal exclusion of an aneurysm-carrying artery) received its name from the Scottish surgeon John Hunter and was the first method for surgical management of aneurysms. As experience has been accumulated, it became obvious that ICA ligation surgeries are associated with high mortality and persistent disability; the tolerance to exclusion is determined by the capabilities of the collateral circulation (accurately evaluation of these capabilities became possible later) [17]. V.A. Lazarev [1] demonstrated that after the balloon occlusion test (BOT) has been put into practice and the surgery involving placement of the extracranial-to-intracranial bypass Anastomosis has been elaborated, the surgeons broadened the range of indications for ICA exclusion in treatment of complex ICA aneurysms. Nevertheless, the advance in microsurgical procedures during the 1980s has made clipping of paraclinoid aneurysms the main treatment method characterized by relatively low mortality (3.7—6.4%) and complication rates (3.6—17.3%) [1, 12, 14]. The advance in surgical approaches, anesthesiological support of surgeries, development of the procedure of retrograde intravascular aspiration of blood, etc. made it possible to achieve high radicality in paraclinoid aneurysm surgery, which reaches 90—92% [2, 3, 12].

Nevertheless, deconstructive interventions for large and giant ICA aneurysms remain the method of choice; it often becomes clear that this procedure needs to be used only during the surgery when an aneurysm cannot be clipped. We report four cases when in situ trapping of a paraclinoid aneurysm was performed based on intraoperative assessment of blood flow using a flowmeter.

Material and Methods

Four patients with large (1—1.5 cm) and giant (>2.5 cm) paraclinoid aneurysms were singled out from the database of patients who had been operated on in 2006—2011. In these patients, it became clear during an intervention that an aneurysm cannot be clipped, so aneurysm trapping was performed. The aneurysms were diagnosed after a hemorrhage in three patients (in two of those, after a recurrent hemorrhage) and were associated with headache in one patient. No neurological...
disorders have been detected; one patient (K., 38 years old) had an ophthalmic defect unrelated to the aneurysm (macular dystrophy). The clinical characterization of the patients is presented in Table 1.

<table>
<thead>
<tr>
<th>Patient, age (years)</th>
<th>Gender</th>
<th>Aneurysm</th>
<th>Side</th>
<th>Size</th>
<th>Clinical signs</th>
<th>Neurological status</th>
</tr>
</thead>
<tbody>
<tr>
<td>B., 51</td>
<td>F</td>
<td>Saccular, lateral</td>
<td>Left</td>
<td>Large</td>
<td>Headache</td>
<td>No functional deficit</td>
</tr>
<tr>
<td>V., 32</td>
<td>F</td>
<td>Fusiform</td>
<td>Right</td>
<td>Large</td>
<td>SAH</td>
<td>No functional deficit</td>
</tr>
<tr>
<td>K., 38</td>
<td>F</td>
<td>Fusiform, eccentric</td>
<td>Left</td>
<td>Large</td>
<td>Recurrent SAH (2)</td>
<td>Reduced visual acuity OS (macular dystrophy)</td>
</tr>
<tr>
<td>E., 44</td>
<td>M</td>
<td>Saccular, medial</td>
<td>Left</td>
<td>Giant</td>
<td>Recurrent SAH (2)</td>
<td>No functional deficit</td>
</tr>
</tbody>
</table>

**Footnote.** SAH — subarachnoid hemorrhage.

**Fig. 1. CT and spiral CT angiography of patient E.**
The images show the medially located giant aneurysmal sac. Approximately 1/3 of aneurysm volume is contrasted. The aneurysm neck is “low” but sufficiently narrow, which was the main argument in favor of the attempt at clipping.

The aneurysm was trapped by exclusion of neck ICA and exclusion of the distally located intracranial aneurysm neck. Stationary trapping was carried out by placing temporary clips after the vessels had been excluded; the volumetric blood flow in the M1 segment of the middle cerebral artery (MCA) was...
measured using a flowmeter. A universal HT313/323 ultrasonic flowmeter (Transonic Systems Inc., USA) was used to assess the volumetric blood flow. This device performs real-time measurement of the volumetric blood flow in a vessel under study (in ml/min or L/min).

### Results

The preoperative preparation involved selective angiography with clipping of the contralateral ICA to assess the collateral blood flow; magnetic resonance imaging (MRI) and computed tomography (CT) of the brain to detect thrombosed aneurysm and atherosclerosis of the vessel walls; electroencephalography including the Matas’ test; as well as ophthalmological, neurological, and anesthesiological examination. Aneurysm clipping using intravascular aspiration of blood was planned for all four patients. The aneurysms were accessed using the standard pterional approach. The common and internal carotid arteries were exposed through a linear neck incision. The surgical procedure was described in detail in our previous publications [2, 3, 11]. If the aneurysm spread into the cavernous sinus, or the vessel walls were dense and atherosclerotic, or no reliable aneurysm clipping could be performed with preservation of the blood flow in the ICA, an operating surgeon made a decision about trapping. The blood flow was measured in the M1 segment of the MCA before and 3—4 min after test trapping of the aneurysm using temporary clips. Stationary aneurysm trapping was performed if blood flow was reduced by less than 20% of the initial blood volume. After the surgery the patients were transferred to the intensive care unit, where special attention was paid to adequate cerebral perfusion and stability of the hemodynamics. Table 2 lists the reasons for refusal of clipping and the blood flow measurement results.

Three patients had signs of poor blood circulation and development of a hemisindrome (hemiparesis and hemi-hypoesthesia), aphasia (patients B. and V.), and cerebral symptoms (headache, reduced vigilance level, lethargy, aspontaneity, etc.). Dynamic CT imaging of the brain revealed hemispheric edema as a response to rearrangement of circulation (smoothening of the subarachnoid fissures, blurring of the gray and white matter borders on the side of trapping), which gradually regressed after treatment in all patients. No ischemic foci were formed. The treatment regimen included i.v. infusion of colloidal and crystal solutions to maintain arterial blood pressure (+10—20% of the individual normal level), antiedemic, metabolic, and analgesic agents. Only patient B. received vasopressors to maintain her hemodynamics. All patients were transferred to the intensive care unit on day 2—3 after surgery. Neither aggressive critical care measures against ischemia (hypothermia, barbiturates, hyperventilation, etc.) nor external cranial decompression were required.

In two patients, rehabilitative treatment was carried out in combination with aid from a logopedist, a motor rehabilitation specialist, and a neuropsychologist. The patients were discharged in satisfactory condition, without any pronounced neurological deficit. An analysis of the catamnestic data (filling out a questionnaire), the condition of all four patients has improved subsequently (+1 point according to the Glasgow Outcome Scale (GOS)), which made it possible for them to perform household and workplace tasks (Table 3).

### Clinical case

Male patient E., 44 years old. The patient was examined at the community-based neurosurgical department after a recurrent subarachnoid hemorrhage (SAH) on May 7, 2011 (the first episode of SAH was in 2003). Spiral CT angiography de-

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### Table 2. Reasons for refusal of aneurysm clipping and flowmetry test results

<table>
<thead>
<tr>
<th>Patient, age (years)</th>
<th>Reason for refusal of aneurysm clipping</th>
<th>V&lt;sub&gt;b&lt;/sub&gt; before trapping, mL/min</th>
<th>V&lt;sub&gt;b&lt;/sub&gt; after trapping, mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>B., 51</td>
<td>Fusiform-eccentric shape, atherosclerotic walls, spreading into the cavernous sinus</td>
<td>70/70</td>
<td></td>
</tr>
<tr>
<td>V., 32</td>
<td>Fusiform aneurysm affecting the cavernous sinus</td>
<td>65/60</td>
<td></td>
</tr>
<tr>
<td>K., 38</td>
<td>Atherosclerotic walls, unsuccessful attempts at clipping (clips were displaced and the ICA was stenosed after the blood flow had been restored)</td>
<td>140/120</td>
<td></td>
</tr>
<tr>
<td>E., 44</td>
<td>Dense walls and fusion with the adjacent structures, partial thrombosis of the aneurysm, poor aneurysm relaxation during intravascular aspiration of blood</td>
<td>50/45</td>
<td></td>
</tr>
</tbody>
</table>

---

### Table 3. Postoperative neurologic deficit, length of stay, outcomes, and vocational rehabilitation

<table>
<thead>
<tr>
<th>Patient, age (years)</th>
<th>Neurologic status at discharge</th>
<th>Length of stay, days</th>
<th>Follow-up, months</th>
<th>GOS, score (at discharge/follow-up)</th>
<th>Disability group and employment status</th>
</tr>
</thead>
<tbody>
<tr>
<td>V., 32</td>
<td>Memory impairment. Chronic asthenia</td>
<td>15</td>
<td>22</td>
<td>4/5</td>
<td>Disability group II, unemployed</td>
</tr>
<tr>
<td>K., 38</td>
<td>Elements of sensory aphasia. Mild VII nerve paralysis. Mild paresis of hand</td>
<td>18</td>
<td>29</td>
<td>4/5</td>
<td>Disability group III, employed</td>
</tr>
<tr>
<td>E., 44</td>
<td>No aggravation of symptoms</td>
<td>8</td>
<td>16</td>
<td>4/5</td>
<td>No disability status, unemployed</td>
</tr>
</tbody>
</table>
detected a giant aneurysm of the left ICA; the patient was transferred to the N.N. Burdenko Neurosurgical Institute for care. The angiography data showed that there was a giant paraclinoid ICA aneurysm on the left side, of medial location, contrasted by 1/3 of its volume (Fig. 1). Clipping of the ICA demonstrated that the carotid basins were communicating through the anterior communicating artery (ACA) (Fig. 2a,b). An ophthalmologic examination revealed a right-sided homonymous hemianopsia; no other focal disorders were detected. With allowance for the fact that the aneurysm neck was sufficiently narrow (Fig. 2), the method of choice was clipping using intravascular aspiration of blood.

Surgery. The internal and common carotid arteries were exposed through a linear neck incision and ligated. The standard pterional craniotomy on the left side was performed. The approach towards the left optic nerve was used; the carotid and chiasmal cisterns were dissected. The cortex of the frontotemporal region was yellowish and had a thickened arachnoid sheath with signs of old hemorrhagic lesions. A large aneurysm was visualized under the optic nerve and the ICA. The Sylvian fissure was dissected; the supraclinoid ICA region, ICA bifurcation and the MCA displaced anteriorly by the aneurysm were isolated. The aneurysm was ~4 cm in diameter, partially thrombosed and virtually not pulsating; it had dense whitish walls. The aneurysm sac was tightly connected with the dura mater of the skull base, ran under the optic chiasm, into the diencephalon, posteriorly replacing the temporal lobe. Temporal exclusion of the ICA in the neck region had a negligible effect: being thrombosed and tightly attached to the surrounding tissues, the aneurysm was slightly. Intravascular aspiration of blood is ineffective under these conditions. The aneurysm neck started from the dural ring

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*Fig. 2. Preoperative left-side carotid angiography; the lateral and frontal projection views.*

a, b — the portion of giant paraclinoid aneurysm of the left ICA accumulates contrast and is visualized. The control right-side carotid and vertebral angiography, frontal projection views (c, d): the basin of the left MCA is filled through the ACA and PCA. The arrow shows a clip placed on the supraclinoid segment of the left ICA.
and reached the ostium of the PCA. Aneurysm isolation and clipping were extremely challenging under these conditions and were associated with a high risk of traumatic injury. The volumetric blood flow in the M1 segment of the MCA on the left side was measured (50 ml/min). Temporary aneurysm clipping (clipping the ICA proximally from the ostium of the PCA + exclusion of the ICA on the neck) was then performed. The blood flow in the M1 segment after 3 min was 43—45 ml/min. The collateral circulation was regarded as adequate; stationary aneurysm trapping was performed. The hemostatic system was used and the wound was closed layerwise.

The control angiography detected no aneurysm. The carotid basin was adequately filled on the left side from the right ICA and the vertebral artery (Fig. 2c,d).

Discussion

Proximal occlusion of the aneurysm-carrying artery (Hunter’s ligation) and exclusion of the artery above and below the aneurysm neck together with the vessel (trapping) are among the first vascular surgeries that were used at the dawn of neurosurgery. Olivecrona [10] is considered to be the first surgeon to successfully perform trapping followed by dissection of a large aneurysm of the posterior inferior cerebral artery back in 1932. Both surgery variants belong to the so-called deconstructive interventions: an aneurysm is excluded at the expense of occlusion of a large artery. The exclusion of a paraclinoid aneurysm along with ICA, which supplies the major part of the hemispheric blood flow, is associated with a high risk of cerebral ischemia and is used only when no other treatment alternatives are available for some reasons. Elective ICA occlusion is currently performed endovascularly using detachable balloons provided that a patient has successfully passed the balloon occlusion test with venous phase timing or CT/MRI perfusion. Prognostic significance of BOT with venous phase timing is sufficiently high (98% according to W. van Rooij [20]). However, BOT is not performed in acute SAH because of the high risk of recurrent hemorrhage and disturbance of the cerebral circulatory reserve caused by vasospasm and cerebral edema.

Ultrasonic flowmetry as a method for measuring the volumetric blood flow in surgeries for aneurysms was first described by F. Charbel et al. [4—6] in 1998. The procedure was used as an alternative to contact Doppler ultrasonography and allowed one to intraoperatively assess the blood flow in arteries before and after aneurysm clipping. The correctness of flowmetry data is almost independent of the angle of insonation, atherosclerosis of the artery wall, and other factors distorting the Doppler ultrasonography measurements. The key advantage of flowmetry is that the volumetric blood flow (ml/min) is measured, as opposed to the linear velocity (cm/s) recorded by Doppler ultrasonography. Thus, as previously demonstrated by F. Charbel [7, 8], intraoperative flowmetry can become a valuable diagnostic tool in aneurysm surgery as it allows one to solve the problems related to intervention tactics in situ. Meanwhile, flowmetry has certain technical limitation: the large size of sensors makes it possible to examine only the arteries that are sufficiently large and completely isolated.

In our study, we reported 4 cases of changing the course of surgery when the original plan of aneurysm clipping using intravascular aspiration of blood turned out to be infeasible due to a number of factors. A flowmetry test measurement allowed us to verify the adequate circulation in the MCA under conditions of test aneurysm trapping and to complete the surgery with stationary occlusion. We found no description of this test in the analyzed literature. The reliability of the procedure remains disputable. The flowmetry test is not an equivalent of BOT as it is definitely inferior to it in terms of informativeness, since the blood flow was measured intraoperatively and no allowance was made for the critical condition of patients in response to exclusion of the ICA, which is a significant and fine diagnostic indicator of intolerance of ICA occlusion. Furthermore, question related to the risk of delayed ischemia also remains open. In patients who gave positive results for the BOT test, this risk is 5—10%; ischemia can develop within 1—3 days after ICA occlusion [13].

All patients had clinical signs of cerebral ischemia in early postoperative period, which were caused by circulation rearrangement and were verified by CT scanning of the brain. In all the cases conservative methods were used to cope with these phenomena. The early postoperative and delayed treatment outcomes were favorable in 3 patients operated on (GOS score=4/5); mild leg paresis (GOS score=3/4). All four patients remained capable for work, although only two of them were employed at the moment of filling out the questionnaire.

ICA deconstruction to treat an aneurysm is associated with the risk of de novo aneurysm formation or growth of the existing aneurysm (1.4—4% according to M. Niiro et al. [16]). Aneurysms are typically formed in the region of the contralateral ICA or ACeA—ACA, which is attributed to the increased hemodynamic stress in these areas. In this connection, control follow-up examination (spiral CT angiography) is recommended to be performed every 3—5 years for patients subjected to trapping of paraclinoid aneurysm; in case of multiple aneurysms, they should be excluded from circulation during the multi-stage treatment. Furthermore, a number of authors [19] reported that ICA exclusion may induce essential hypertension, which requires special therapy and is an independent risk factor of aneurysm formation.

Integrated preoperative examination of patients using the modern diagnostic radiology and electrophysiological techniques plays a key role in successful surgical management. Intraoperative flowmetry is a simple noninvasive method to perform ultrasonic diagnosis of the blood flow, which may play a decisive role in a number of cases when selecting the surgical strategy for paraclinoid aneurysms.
Due to the topographic anatomy of paraclinoid aneurysms, their treatment still remains a challenging task. According to different authors, the mortality rate in patients with symptomatic giant aneurysms of this location can be as high as 70—100%. A tremendous growth in development of endovascular techniques for arterial aneurysm exclusion of using microsurgical application and stent assistance has recently been increasing the chances for preserving the carotid artery lumen in patients with small aneurysms. The endovascular procedures for managing giant paraclinoid aneurysms of pseudotumor course now include the use of flow-directed small-mesh stents to thrombose aneurysm cavity and preserve the carotid artery lumen. However, thrombolytic and antiaggregant therapy is required, which sometimes is impossible in the acute phase of aneurysm rupture. The authors have reported four cases of performing intraoperative trapping of large/giant paraclinoid aneurysms of the internal carotid artery (ICA) in a situation when the elective clipping surgery turned out to be infeasible. The contralateral blood flow was intraoperatively assessed using a flowmeter, which shows the volumetric blood flow in the arteries under study. It is a way out of an extremely difficult situation a neurosurgeon may face when clipping an aneurysm of this type, sometimes even using intravascular aspiration of blood, when circulation in the ICA cannot be preserved.

The paper is rather useful and interesting; it can be published in specialized journals. However, it would have been more original if wide-lumen anastomosis had been used along with forced intraoperative trapping of giant paraclinoid aneurysms.

V.A. Lazarev (Moscow, Russia)
Experience of Surgical Management of Trigeminal Schwannomas Simultaneously Spreading to the Middle and Posterior Cranial Fossae


Burdenko Neurosurgical Institute, Moscow, Russia

Trigeminal schwannomas account for 0.07—0.36% of all intracranial tumors and 0.8—8% of all intracranial schwannomas. Different surgical approaches are used depending on the topographic anatomical variant of the tumor. Dumbbell-shaped tumors that spread both to the middle and posterior cranial fossae are the most challenging ones in terms of their resection.

Material and Methods. Five patients with dumbbell-shaped trigeminal schwannomas were operated on at the Burdenko Neurosurgical Institute in 2011—2013. In four cases, tumor resection comprised two stages using the retrosigmoid suboccipital approach (RSA) and lateral extended transphenoidal endoscopic approach (LETEA): in one case, the tumor was resected in a single session through the LETEA. If there were pronounced symptoms affecting the brainstem and/or corebellum, the tumor was resected from the posterior cranial fossa through RSA at the first stage (3 cases). If no symptoms were observed, tumor resection from the middle cranial fossa through LETEA was used as the first stage (2 cases).

Results and Discussion. After two surgical stages, total, subtotal, and partial tumor resection was performed (one case each). Total tumor resection from the middle cranial fossa was achieved through LETEA in two cases. Aggravation of ipsilateral paresis of the cranioencephal nerve VI was observed postoperatively in two cases. No cases of nasal liquorrhoea were observed after transnasal surgery. In one case, the cavernous segment of the internal carotid artery was damaged during LETEA, thus requiring endovascular occlusion of the damaged vessel to be performed.

Conclusions. LETEA is an effective approach that allows resection of tumors from the middle cranial fossa and the cavernous sinus. Combined with RSA, this approach can be used for two-stage resection of dumbbell-shaped trigeminal schwannomas.

Keywords: trigeminal nerve, schwannoma, dumbbell-shaped tumor.

Abbreviations: ICA — internal carotid artery, PCF — posterior cranial fossa, CS — cavernous sinus, LETEA — lateral extended transphenoidal endoscopic approach, RSA — retrosigmoid suboccipital approach, MCF — middle cranial fossa, DM — dura mater.

Trigeminal schwannomas account for 0.07—0.36% of all intracranial tumors and 0.8—8% of all intracranial schwannomas [6—8, 10, 14, 18, 19].

According to the classification by G. Jefferson [7] 1953, trigeminal schwannomas are divided into three types:
— type A — schwannomas that are located in the middle cranial fossa (MCF) and develop from the Gasser’s ganglion;
— type B — schwannomas that are located in the posterior cranial fossa (PCF) and develop from the trigeminal nerve root;
— type C — hourglass tumors located both in the MCF and in the PCF.

In this case, 50% of trigeminal schwannomas are located in the MCF, 25% of the tumors are localized in the PCF, and 25% are hourglass tumors. In some cases, tumors spread extracranially along the peripheral branches of the trigeminal nerve [6, 7, 9, 11].

In the MCF, a trigeminal schwannoma is located interdurally (between the layers of the lateral wall of the cavernous sinus (CS)) and is surrounded by the meningeal perineural capsule. According to A. Goel [10, 12, 13], none of 73 cases had evidence of tumor invasion into the CS cavity. In this case, the cavernous segment of the internal carotid artery (ICA) and the cranioencephal nerves located in the CS are shifted by the tumor. In the PCF, tumors that arise from the trigeminal nerve root are located subdurally.

M. Samii et al. [18], describing their experience in resection of 27 schwannomas, note that invasion of the tumor into the CS cavity was observed in 8 patients. Two cases of tumor recurrence in the MCF with spread into the CS cavity have also been reported.

Various transcranial microsurgical approaches are suggested depending on the tumor type. The retrosigmoid suboccipital approach (RSA) is convenient to resect schwannomas located in the PCF. A presigmoid approach can be used in the case of hourglass schwannomas. Pterional or subfrontal craniotomy provides an approach to trigeminal schwannomas located exclusively in the MCF. A frontotemporal orbitozygomatic approach is indicated when the tumor spread along the distal portions of the first and second branches of the trigeminal nerve. The infratemporal extradural approach is indicated if the tumor spreading along the third branch of the trigeminal nerve [6].

In the early series of observations by A. Goel [12, 13], dumbbell schwannomas were resected in two stages (pterional craniotomy and RSA). In more recent observations, resection was performed in a single session through a lateral presigmoid approach.

There are publications with single observations devoted to one stage resection of hourglass schwannomas. In one case, the pterional approach was used in a 6-year-old child to resect the tumor from the cavity of both the MCF and PCF [9]. In
another case, a combined infratemporal transmandibular approach was used in a patient with a dumbbell schwannoma with infratemporal spread [11].

A. Kassam et al. [16, 17] have described 6 cases of resection of trigeminal schwannoma from the Meckel’s cavity through a lateral extended transsphenoidal endoscopic approach (LETEA). It was carried out through the quadrangular foramen that was confined on the posterior surface of the sphenoid sinus by the ICA inferiorly and medially, by the second branch of the trigeminal nerve laterally, and by the abducent nerve superiorly.

### Material and Methods

Thirty-four patients diagnosed with trigeminal schwannoma were operated on at the Burdenko Neurosurgical Institute between 2011 and 2013. Of them, 5 (14.71%) patients with dumbbell schwannomas were operated on using LETEA. All main information on the patients is presented in Table.

According to brain MRI, all patients were detected with an hourglass tumor located both in the PCF and in the MCF.

The main disease symptoms were hypesthesia, paresthesia, pain in the innervation area of the respective branches of the trigeminal nerve, and a reduction/loss of the corneal reflex. Upon a significant amount of the tumor in the PCF, symptoms of VI—VIII cranio cerebellar nerve lesions on the tumor growth side and cerebellar symptoms were observed (see Table).

All patients were scheduled for two stage surgery. The tumor portion located in the MCF was resected through LETEA; the tumor portion located in the PCF was resected through RSA. The order of surgery stages depended on clinical symptoms. In 3 cases with predominance of the stem and cerebellar symptoms, resection of a tumor node from the PCF was performed at the first stage with the purpose of, as a minimum, decompression of the brain stem, as a maximum, total resection of the tumor from the PCF (see Table). In 2 cases with the minimal PCF symptoms (small size of a node in the PCF), endoscopic transsphenoidal resection of a tumor node located in the MCF was carried out at the first stage. The interval between surgery stages ranged from 4 to 9 months.

RSA was used to resect the tumor from the PCF [5]. The vertical incision line was made 1 cm medial to the mastoid notch and perpendicular to the projection line of the transverse sinus. A bur hole was made in the asterion region, and either osteoplastic or resection trepanation of the squama of the occipital bone was performed. The trepanation window borders were as follows: superiorly, at the level of the lower margin of the transverse sinus; superiorly and laterally, at the junction level of the transverse sinus and the sigmoid sinus; inferiorly and laterally, at the level of air mastoid cells; medially, until the external occipital crest; inferiorly, at the level of the foramen magnum, before reaching its bone margin. After opening the tumor capsule, tumor resection from the PCF cavity was carried out by fragmentation with mainly an ultrasound (US) aspirator and tumor forceps [5].

In one case (case 1, see Table), was possible to partially remove the tumor through RSA from the posterior portions of the Meckel’s cavity.

Implementation of LETEA can be divided into nasal, sphenoidal, and parasellar phases [1—3]. A bilateral endoscopic approach (through both halves of the nasal cavity) is performed during the nasal phase. In some cases, resection of the middle turbinate on the tumor side was carried out, and dislocation of the middle turbinate was performed laterally on the opposite side (contralateral side of the nose). Frontal sphenoidectomy using an intranasal micro drill was performed at the sphenoidal phase. Posterior portions of the nasal septum (1—2 cm from the anterior wall of the sphenoid sinus) were resected concomitantly with resection of the anterior wall of the sphenoid sinus. After removal of the sinus septa (one or more), the key anatomical structures of the sphenoid sinus came into view (Fig. 1a). Trepanation of the posterior wall of the sphenoid sinus in the CS projection was performed using a micro drill (Fig. 1b). The localization of the ICA relative to the midline and the depth of its occurrence were determined using an US aspirator through the dura mater (DM) in the projection of the CS anterior wall (Fig. 1c).

The parasellar phase (laterosellar phase): resection of the tumor was performed after opening the DM and tumor capsule. In all cases, the tumor was partially cystic, soft, of elastic consistency, and with moderate blood supply. Resection of the tumor was performed by its fragmentation using an US aspirator under control of 0°, 30°, and 45° endoscopes. After resection of the medial portion of the tumor, gradual separation of the tumor from the DM was carried out using curved suction and curettes (Fig. 1d—f).

Upon implementation of LETEA, the anatomical landmarks of the posterior wall of the sphenoid sinus were partially modified by the tumor (Fig. 2a). In any case, no evidence of tumor invasion into the CS cavity was found. The cavernous ICA segment was separated from the tumor with a thin inner layer of the lateral wall of the sinuses in all cases (Fig. 2b). In this case, the cavernous ICA segment and the CS cavity were displaced medially and upward.

For the purpose of hemostasis and prevention of nasal liquorhea, the resected tumor cavity was covered with Tachocomb plates and sealed with Tissucol Kit glue (Baxter). The entrance to the resected tumor cavity was closed with bone fragments of the nasal septum, TachoComb, and Tissucol Kit glue (Fig. 3). The sphenoid sinus cavity was filled with autofat taken from the patient’s hip. At the end of surgery, all patients were placed with an inflated flexible tube (Foley catheter) into the nasal cavity at the entrance to the sphenoid sinus in order to support multilayer plasty. The tube was removed on day 7 after surgery.

Before endoscopic transsphenoidal surgery, all patients were placed with an external lumbar drainage to reduce intracranial pressure during surgery and to prevent nasal liquorhea at the postoperative period. The drainage was removed on day 5—7 after surgery.

### Results

The results of treatment are presented in Table.

In one case (case 4), the tumor was resected in one session using LETEA (Fig. 4). The tumor was intraoperatively found to be clearly separated from the PCF by the dural sheath.
<table>
<thead>
<tr>
<th>Case</th>
<th>Initial neurological status</th>
<th>First stage</th>
<th>Neurological status dynamics</th>
<th>Time before the second stage of surgery</th>
<th>Second stage</th>
<th>Neurological status dynamics</th>
<th>Completeness of resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Insufficiency of the V craniocerebral nerve, left (numbness and pain in the left face side, a reduction in the corneal reflex)</td>
<td>RSA</td>
<td>Paresis of the facial nerve (House-Brackmann scale, grade 3) that regressed by the second stage of surgery</td>
<td>3 months</td>
<td>LETEA</td>
<td>Insufficiency of the V craniocerebral nerve. Neurogenic keratopathy of the left eye developed</td>
<td>Complete resection</td>
</tr>
<tr>
<td>2</td>
<td>Insufficiency of the V craniocerebral nerve, left (a reduction in the corneal reflex, hypoesthesia of the left face side). Insufficiency of the III craniocerebral nerve (hemiphtosis, pupils OD&lt;OS, JS photosponse is sluggish, OD is satisfactory). Exophthalmos is 1.5—2 mm</td>
<td>LETEA</td>
<td>Paresis of the VI craniocerebral nerve, left, developed (grade 3—4) that regressed 3 months after surgery. Trophic neurogenic keratopathy of the left eye</td>
<td>9 months</td>
<td>RSA</td>
<td>Paresis of the facial nerve, left, developed (House-Brackmann scale, grade 5)</td>
<td>Subtotal resection</td>
</tr>
<tr>
<td>3</td>
<td>Insufficiency of the V craniocerebral nerve (sensation impairment on the right face side, a reduction in the right corneal reflex, neurotrophic keratopathy). Insufficiency of the VI craniocerebral nerve, right (grade 1). Postcranial symptoms: insufficiency of the VIII—X and XII craniocerebral nerves right</td>
<td>RSA</td>
<td>Did not change</td>
<td>8 months</td>
<td>LETEA</td>
<td>Did not change</td>
<td>Partial resection</td>
</tr>
<tr>
<td>4</td>
<td>Insufficiency of the V craniocerebral nerve, right (sensation impairment on the right face side, a reduction in the right corneal reflex). Insufficiency of the VI craniocerebral nerve, right (limitation of eyeball motion outwards) (grade 2—3). Right-sided exophthalmos</td>
<td>LETEA</td>
<td>Paresis of the VI craniocerebral nerve, right, developed (grade 4) that partially regressed 3 months after surgery</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td>Complete resection</td>
</tr>
<tr>
<td>5</td>
<td>Hypertensive symptoms (optic disc swelling, headache). Insufficiency of the V—VIII craniocerebral nerves right. Cerebellar ataxia</td>
<td>RSA</td>
<td>Insufficiency of the V craniocerebral nerve, right (a reduction in the corneal reflex, pain hyperesthesia in the region of the second and third branches). Insufficiency of the VI craniocerebral nerve, right (limitation of eyeball motion outwards, grade 1—2). Postcranial symptoms: insufficiency of the VIII craniocerebral nerve</td>
<td>3 months</td>
<td>LETEA</td>
<td>Rough paresis of the VI craniocerebral nerve, right, developed (the nerve function recovered to the preoperative level after 3 months)</td>
<td>First stage: the tumor was resected from the PCF. Second stage: no tumor resection</td>
</tr>
</tbody>
</table>
Fig. 1. Stages of tumor resection (intraoperative images).

a—c — sphenoid phase of surgery: a — the posterior wall of the sphenoidal sinus (1 — the floor of the sella turcica, 2 — projection of the left cavernous sinus); b — DM in the projection of the anterior wall of the left cavernous sinus after trepanation of the posterior wall of the sphenoidal sinus; c — identification of the location of the cavernous ICA segment using an ultrasonic probe before opening DM; d—f — parasellar phase of surgery: d — resection of the central portion of the tumor; e — isolation of the peripheral portion of the tumor from the inner layer of the lateral wall of the CS; f — a cavity formed after resection of the tumor from the MCF (arrow indicates the projection of the cavernous ICA segment).
Total resection of the tumor was achieved in one case after two stages of surgery (case 1, see Table). Subtotal resection of the tumor was achieved in one patient who underwent LETEA at the first stage and RSA at the second stage (Fig. 5). Partial resection of the tumor after two stage surgery was in the case 4.

In the case 5, massive arterial bleeding developed during LETEA that was stopped by means of Tachocomb plates and tamponade of the nasal cavity with gauze turundas. Without recovering from sleep anesthesia, the patient underwent carotid angiography that revealed a defect in the anterior segment of the cavernous knee of the right ICA. Given the availability of adequate collateral circulation, the patient underwent endovascular occlusion with ICA microcoils at the developed defect level (Fig. 6). Following the endovascular treatment, paresis of the right abducent nerve up to grade 4 developed. Any other focal neurological symptoms were not observed. The patient was discharged on the 12th day after ICA occlusion.

In the postoperative period, transient paresis of the VI cranioencephalic nerve with its full recovery after 3 months was observed in 3 cases (see Table). Aggravation of inefficiency of the trigeminal nerve function with the development of persistent neurogenic keratopathy was observed in 2 patients after surgery.

There were no cases of nasal liquorrhea and meningitis in this series of observations.

Discussion

Hourglass trigeminal schwannomas are of special challenge for surgical treatment. Spreading into the laterosellar region, they compress the CS and neurovascular structures localized there [12, 13]. Spreading into the PCF may result in rough compression of the brain stem and be a cause of occlusive symptoms.

One stage microsurgical resection of these tumors is enabled by the use of a basal presigmoid approach, which is quite traumatic and carries a high risk of complications.

The advantage of the lateral (presigmoid) approach is a broad approach both to the MCF and to the PCF. However, the disadvantage of this approach is the need of temporal lobe traction upon resection of the tumor from the MCF as well as the risk of damage to the vein of Labbe, the inner ear structures, and the facial nerve.

Another variant is to use a combination of the low-traumatic LETEA and classic RSA. Resection of a tumor node from the PCF is performed to reduce decompression of the stem using the well-established and generally available for practicing neurosurgeons RSA (in the presence of pronounced postcranial symptoms, this is the first stage of surgery). This approach is traditionally used to localize the process in the cerebellopontine angle and lower portions of the clivus as well as in the pyramid of the temporal bone and Meckel’s cavity.

LET EA provides a direct approach to the cavernous sinus, anterior-medial portions of the MCF, and Meckel’s cavity. In this case, resection of the tumor is performed through the quadrangular foramen (Fig. 7).

Fig. 2. Intraoperative images.

a — the posterior wall of the sphenoidal sinus; 1 — the floor of the sella turcica; 2 — changed (increased) bony prominence of the anterior wall of the cavernous ICA segment; 3 — resected posterior cells of the ethmoid bone; 4 — the posterior wall of the maxillary sinus; 5 — the pterygopalatine fossa; b — the ICA separated from the resected tumor cavity by a thin shell is seen; * — an ultrasound device for navigation (identification of the ICA location).
Fig. 3. Stages of hemostasis and postoperative defect plasty.

a — resected tumor cavity is covered with Tachocomb plates; b — Tachocomb is impregnated with Tissucol Kit thrombin-fibrin glue (Baxter); c, d — entrance to the resected tumor cavity is closed with a bone fragment and sealed with Tissucol Kit glue.

Fig. 4. One stage resection of a hourglass trigeminal schwannoma.

a — brain MRI prior to surgery; b — postoperative brain CT on the 1st day after surgery.
In cases where LETEA was used as the first stage, the portion of the tumor located in the PCF was usually not removed. This is due to the subdural (under DM) location of the tumor in the PCF. After resection of tumor nodes from the PCF through the transsphenoidal approach, an extensive DM defect can develop that increases the risk of postoperative liquorrhea. It should be noted that in some cases a node of the PCF located tumor is coated by a capsule and isolated from the PCF. According to A. Goel et al. [12], this may be due to protrusion of the tumor backward from the MCF. This situation was observed in the case 4 that allowed removing the tumor in a single session.

The advantage of LETEA is that there is no need for traction of the brain. Resection of the tumor is performed from “inside”, within the meningeal perineural sheath. The main risk of this approach is the close proximity of the ICA. In our cases, the tumor partially destroyed the bone structures of the posterior wall of the sphenoid sinus, with the bony prominence in the projection of the anterior CS wall being changed (enlarged and deformed) in all cases. All this generally changes

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**Fig. 5.** An example of subtotal two stage resection of an hourglass schwannoma using LETEA and RSA.

a — brain MRI. An hourglass schwannoma of the V cranio cerebroal nerve is identified; b — control brain MRI after the first stage of surgery using RSA (tumor residue in the MCF is identified); c — MRI after the second stage of the operation using LETEA.

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**Fig. 6.** Attempt to resect trigeminal schwannomas from the MCF through LETEA.

a — brain MRI with contrast enhancement before the first stage of surgery for resection of a tumor from the PCF through the RSA. The hourglass trigeminal schwannoma is identified; b — brain MRI with contrast enhancement before the second stage of the surgery for resection a schwannoma node from the MCF using LETEA; c — angiography after attempt to implement LETEA and endovascular occlusion of the cavernous ICA segment with micro coils (the red arrow indicates a defect in the ICA wall, the black arrow indicates occlusion with micro coils).
the main anatomical landmarks, thus leading to difficulties in determining the location of the ICA and CS. In this case, the position of the ICA can be identified at initial steps of surgery by US locating as well as a frameless navigation system [4]. This technique provides safe and quick identification of the location of the cavernous ICA segment relative to the place of DM incision and an approximate depth of location. In the case 5, an area in the DM incision place was located. The tumor was found after DM incision. Before removing the tumor, it was decided to continue the incision 3 mm longitudinally upward to the area, where additional locating of the carotid artery was not conducted that ultimately resulted in injury to the artery. This example illustrates that it is necessary to carry out US monitoring all over the place, where it is planned to cut the DM.

**Conclusions**

LETEA is effective and allows resection of tumors from the medial portions of the MCF and CS. This approach in combination with RSA can be used for two stage resection of trigeminal hourglass schwannomas. During manipulations in the CS cavity, there is a risk of injury to the ICA. To perform these operations safely, the control of the ICA location is required using modern neuroimaging methods (navigation systems, Dopper ultrasonography).
Endoscopic transsphenoidal surgery of tumors of the chiasmatal sellar region has been one of the most rapidly developing fields of neurosurgery in the past 20 years.

An endoscopic endonasal transsphenoidal approach is the most common approach in removing tumors of the sellar region. With accumulating experience, indications for the use of this approach in surgery of both pituitary adenomas and other basal extracerebral tumors have significantly been extended in recent years. This is also associated with accumulating experience in standard endoscopic techniques, developing new approach techniques, and improving the endoscopic technique. The so-called extended endoscopic transsphenoidal approaches have successfully been used in many international and Russian clinics to resect tumors of the parasellar localization. The experience of the Basal Brain Tumors Department of the Burdenko Neurosurgical Institute in this field is absolutely unique. At the Institute, the technique of resecting tumors of the chiasmatal region through the extended transsphenoidal endoscopic approach has been introduced and extensively used.

This work is devoted to the very interesting and, at the same time, complex topic of surgical treatment for trigeminal schwannomas with simultaneous spread into the middle and posterior cranial fossae. Just a few years ago, treatment of these patients was exclusively based on quite traumatic basal transcranial approaches, which had a significant number of disadvantages. The emergence of the opportunity to use for this purpose a minimally traumatic procedure in the form of extended transsphenoidal approach is of great importance for neurosurgeons.

The indication for using the lateral extended transsphenoidal approach is a massive tumor ingrowth into the cavernous sinus cavity, especially if the intracavernous portion of the internal carotid artery (ICA) is displaced medially, as well as the presence of tumors with the laterosellar location in the cavernous sinus projection.

The article describes in detail the surgical tactics, the clear algorithm is provided for choice of a certain approach as a first or second stage of surgery. The authors describe the lateral extended transsphenoidal approach procedure and skull base plasty methods. The article contains diverse and informative illustrations. The publication provides an analysis of the causes and structures of complications as well as factors affecting the risk of their occurrence.

One of the most dangerous complications of the extended lateral transsphenoidal approach is the risk of injury to the intracavernous ICA segment. The article describes the surgical and anesthetic tactics in intraoperative injury to the ICA. It provides the comprehensive description of the ways to prevent this complication by using intraoperative dopplerography and analyzes possible errors associated with identification of the ICA location.

In general, the authors findings indicate that two stage resection of dumbbell schwannomas using a combination of lateral extended transsphenoidal endoscopic and retrosigmoid suboccipital approaches is an effective and low traumatic technique capable of ensuring both complete resection of the tumor and relatively low rates of post-operative complications.

The article structure is fully consistent with the generally accepted principles for presentation of scientific data. The literature review describes the relevance and status of the problem accepted principles for presentation of scientific data. The references are provided with a sufficient amount of references to the a number of domestic and foreign sources.

The conclusions are fully consistent with the aim and findings of the study.

**Commentary**

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**REFERENCES**


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New Software for Objective Evaluation of Brain Glioblastoma Resection Extent

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It is still difficult to perform visual evaluation of the extent of GB resection based on postoperative enhanced MRI. It is explained by the intricate complex of tumor residual fragments, blood cells, hemostatic tissues and perifocal edema that are located in the postoperative area. We introduce the new software-based method for objective estimation of postoperative brain MRI data. Five independent specialists had examined the MRI data of 16 patients (including 12 GB and 4 patients with non-infiltrative intracerebral tumors) and tested the method’s specificity and sensitivity against the enhanced residual tumor (ERT). Our software determines the 100% sensitivity and specificity against hemostatic agent Surgicel, the high reproducibility of results while estimating the volume of ERT (0.14±0.02 cm³) and low considerable time (5.21±0.14 min). The software can be used both daily practice and research of malignant glioma management.

Keywords: glioblastoma, medical software, surgical efficacy.

Glioblastoma (GB) is the most common (65% of all glial tumors) and, at the same time, aggressive primary tumor of the brain in adults that has the poorest prognosis. The average annual incidence rate is 4—10 cases per 100,000 people [9, 11]. The GB treatment standard is the combination of tumor surgery followed by adjuvant radiotherapy and chemotherapy. Despite the significant progress of basic sciences over the recent decades in the field of neurobiology and neuro-oncogenes- is as well as considerable advances in the field of microneurosurgery, improvement in hardware for radiotherapy and radiosurgery, and introduction of new chemotherapeutic agents, at least 75% of patients die within 18 months after the diagnosis [11, 13]. This is primarily due to the infiltrative nature of tumor growth, the high proliferative potential of the tumor, and the variety of molecular mechanisms of tumor cell protection against therapy. Tumor resection in most cases is the first step in treatment and determines the efficacy of subsequent adjuvant therapy. A direct relationship between the GB resection extent and overall survival of patients has been proved. For example, the lifespan after the diagnosis is 1.5 times less in patients with subtotal tumor resection compared to patients after total resection [1, 10].

Contrast-enhanced magnetic resonance imaging (MRI) of the brain is a standard for the diagnosis and preoperative planning in GB. However, even modern high-field MRI scanners do not allow visualization of the true spread of tumor infiltration into the brain structures. At least 80% of GBs uptake a contrast agent to a large amount. However, according to MRI, the tumor always spreads beyond the contrast area. In modern neuro-oncology practice, this is the GB area accumulating a contrast agent that is regarded as an object of the efficacy of surgical treatment and subsequent adjuvant therapy techniques.

In order to determine the amount of resection of the contrast enhanced area of GB, MRI of the brain should be conducted within 72 h after surgery. The examination performed at a later time significantly reduces the information value of the neuroimaging data due to the development of the effect of benign contrast enhancement, reactive edema of the brain tissue, and changes in MRI signals from the hemoglobin degradation products in the resected tumor bed. At the same time, it should be noted that interpretation of MRI of the surgical intervention area within the indicated time is also often a complex task for an experienced neurosurgeon and an expert in neuroimaging for several reasons. An oxidized cellulose-derived hemostatic material, Surgicel (Ethicon), has been extensively used worldwide in surgery for malignant gliomas. To stop bleeding, a certain amount of the material is applied to the resected intracerebral tumor bed providing a reliable hemostatic effect within a short time. The MRI signal intensity from Surgicel is comparable, upon subjective evaluation, with that from contrast enhanced tumor portions that provides a significant error during interpretation of postoperative MRI data [2]. The error weight especially increases upon a small amount of contrast enhanced residual fragments of malignant glioma and, conversely, upon a large amount of a hemostatic agent in the tumor bed. The presence of the hemoglobin degradation products in the resected tumor bed and the edematous perifocal changes in the surgery area in a combination with a hemostatic material and true contrast enhanced residual tumor fragments form a pathomorphologic complex whose objective interpretation is very difficult. The situation is even more complicated in the case of GB progression after previous combination therapy. In this case, the presence of the area of postoperative glial changes and the radiation necrosis area, which often accumulate extensively a contrast agent, further complicates the situation. Currently, the extent of GB resection is determined subjectively by a MRI diagnostician and/or neurosurgeon based on the results of MRI with contrast. It is clear that at the present state of medical science, along with a sub-

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jective evaluation method, there should be a method providing objective information about the resection extent of malignant glioma.

The aim of this study was to define the contrast boundary between residual malignant glioma fragments and the hemostatic material Surgicel in the tumor bed based on brain MRI data.

To calculate the preoperative and postoperative volume of contrast agent uptake sites using software for processing of brain MR images of GB patients at the early postoperative period (within 72 h after surgery). Therefore, to develop an objective software method for evaluation of the resection extent of the contrast enhanced portion of malignant glioma.

**Material and Methods**

Two groups of patients were formed to analyze preoperative and postoperative brain MRI scans. The 1st group consisted of 12 patients diagnosed with brain GB. Four of them were operated on for recurrent GB after previous combined treatment that involved a surgical stage followed by radiochemotherapy/radiotherapy. The hemostatic material Surgicel (Ethicon) was used in 10 patients and Tachocomb (Nycomed Austria GmbH) was used in 2 patients. The 2nd group consisted of 4 patients with benign brain tumors (one patient with meningioma and 3 patients with acoustic schwannoma). The hemostatic material Surgicel (Ethicon) was used in 4 patients.

All patients underwent surgical treatment at the Center of Angioneurology and Neurosurgery of the Meshalkin Research Institute of Blood Circulation Pathology, the Ministry of Health of the Russian Federation.

One day before surgery and within 72 h after it, all patients were examined with brain MRI with contrast on General Electric Signa Infinity 1.5 T magnetic resonance scanners.

Each protocol of a standard brain MRI procedure included the following pulse sequences: T1 SE H in the sagittal plane, TE/TR=9/500 ms, slice thickness of 5 mm; DWI in the axial plane at b=1000, TE/TR=81.8/7,000 ms, slice thickness of 5 mm; T2 FRFSE in the axial plane TE/TR=85.4/4,240 ms, slice thickness of 5 mm; 3DT1 SPGR S in the axial plane, TE/TR=9/30 ms, slice thickness of 1.5 mm without and with contrast enhancement.

The basis for developing the mathematical algorithm.

The DICOM data packet uses a standardized algorithm for packing images with the JPEG Lossless extension [10, 14]. For the analysis, images in this format were imported into the software from a DICOM file to avoid data loss. Each tomogram was presented as a sequence of two-dimensional images (slices) that, taken together, provided a three-dimensional image. Each element of the two-dimensional image (pixel) corresponds to its element of the three-dimensional image (voxel).

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Pixels of each image are assigned X and Y coordinates, and different images (slices) are assigned different Z coordinates. The MRI signal intensity in resulting images is displayed with the grayscale (from 0 to 255, the RGB additive color model), with the 0 value corresponding to the zero intensity and 255 corresponding to the maximum intensity of the MRI signal. The reality is that several disjoint areas of the MRI signal intensity can be identified on any image, each of which comprises different types of the brain tissue (Fig. 1).

We developed software that allows a semi-automatic comparison of two tomograms of the same patient before and after contrast enhancement. The algorithm’s key idea is that the contrast enhanced tumor portion has a higher intensity upon the second examination than upon the first. Other portions of tomograms have the same relative intensity in both examinations.

Prior to a voxel-by-voxel comparison of tomograms, the brightness and spatial arrangement of two image sets should be compared, because actual tomograms differ greatly. A brightness change is related to the peculiarities of the MRI signal intensity normalization during the formation of a MRI slice sequence. Fixation of the patient’s head in a MRI scanner may result in substantial differences, which raises the need for matching the spatial coordinates of two MRI examinations.

Let us first consider spatial matching of two image sets. Planning of a MRI examination using a workstation enables a high repeatability of MRI slices along the Z axis. Therefore, the user needs only to specify once a single image in the first examination and its corresponding image in the second study, so the software can automatically match the Z coordinates of all voxels. Let us call these images reference ones. To match X and Y coordinates is sufficient to select a pair of points of one reference image and a corresponding pair of points of the other reference image. Two linear equations allow easy calculating the rotation and shear parameters that match one reference image to the other. The same shear and rotation parameters should be used to compare other pairs of images.

After defining the spatial transformation of one three-dimensional voxel array to another, the brightness level of two tomograms should be matched. To do this, the user should select a rectangular area on one of the reference images that

Fig. 1. Presentation of the MRI signal intensity from various brain structures on the linear grayscale of 256 tones.
comprises the intact brain tissue image only. In a tomogram, this area is colored in gray tones with values significantly different from the 0 and 255 limits, i.e. far from saturation. As mentioned earlier, pixels in the selected area should have the same MRI signal intensity in both tomograms. The software automatically finds the lightest and the darkest colors in the user-selected rectangle on one reference image and then finds similar colors on the other reference image. By matching pairs of colors on obtained images, it is easily to calculate the linear transformation of the pixel brightness that includes two coefficients – the shift coefficient and multiplication coefficient.

After calculating the spatial and brightness transformation coefficients, the software converts all voxels of a tomogram before contrast enhancement to a new three-dimensional image that fully complies with a tomogram after contrast enhancement.

Next, the user should specify the “region of interest”, within which the software will compare tomograms. Because the brightness of the contrast enhanced tumor portion is always higher than that of the intact brain tissue, it is sufficient to subtract the voxel brightness value for a tomogram before contrast enhancement from the brightness value for the corresponding voxel of a tomogram after contrast enhancement. The resulting difference should be increased several times (to increase the visibility of changes) and colored in red to emphasize the residual contrast enhanced area in the tumor. The software allocates the hemostatic material Surgicel in bright blue. The intact brain tissue is close to the black color (Fig. 2). The residual volume of a region with the disturbed blood-brain barrier is calculated at the last stage.

Based on the algorithm, the software to computerize the entire analysis process was developed. For the analysis purpose, the user opens relevant MRI images, for example in the SPGR pulse sequence, before and after contrast agent introduction. Two matching points are selected on the displayed images for calculation and automatic compensation of the displacement of the region of interest in the image plane on two matching images (button 2, Points). Then, the region of intact brain tissue and the region of brain tumor are selected, followed by pressing button 3 (Get Report) to calculate automatically the contrast enhanced residual mass lesion portion (Fig. 3).

**Study design.** To determine the performance of the developed algorithm and algorithm-based software, it is necessary to conduct a series of tests that clearly demonstrate parameters such as the software sensitivity and specificity to the contrast enhanced GB portion and to the hemostatic material Surgicel and the adequacy of defining the boundary between them; to evaluate the extent of software dependence on the user and to determine the standardization extent of results of MRI scan processing with the software by independent experts.

So far, evaluation of the radicalness of resection of the contrast enhanced GB portion has been performed visually and there are no standardized methods that would be the “gold standard” of this evaluation. To determine how correctly the

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Fig. 2. The results of the mathematical algorithm implementation.

a — brain MRI with contrast (SPGR method), axial slice, a patient with GB of the left frontal lobe of the brain. Condition after microsurgical resection. The red box denotes the “region of interest”. Right to the images, the analysis result is shown (Surgicel is in blue, residual tumor, dura mater, and vessels are in red); b — brain MRI with contrast (SPGR method), axial slice, a patient with GB of the right parietal, temporal, and occipital lobes of the brain. Condition after microsurgical resection. The blue box denotes the “region of interest”. Right to the images, the analysis result is shown (Surgicel is in blue, residual tumor, dura mater, and vessels are in red); c — brain MRI with contrast (SPGR method), axial slice, a patient with meningioma of the fronto-temporal region, right. Condition after total resection. The red box denotes the “region of interest”. The yellow arrow indicates the vessel location. This picture is compatible with intraoperative one; d — analysis of the intact brain tissue. The blue box denotes the “region of interest”.

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software defines the boundary between residual contrast enhanced fragments of malignant glioma and the hemostatic material Surgicel located in the tumor bed, the software processed MR images were offered for visual evaluation to 5 independent experts (3 experienced neurosurgeons and 2 neuroradiologists).

The experts were instructed how to use the developed software, after which they evaluated in percentages, using the software, the resection extent of the contrast enhanced portion of malignant glioma. Then, a comparative evaluation of the values provided by each expert was conducted. Thereby, the absolute values of differences in the experts’ conclusions were calculated, and the extent of algorithm performance dependence on the user and the standardization extent of processing results were determined.

The algorithm specificity with respect to the hemostatic material Surgicel was evaluated as follows: the software task was to define, based on the MRI data, the contrast boundary between the residual GB fragments and the hemostatic material Tachocomb (Nycomed Austria GmbH) located in the tumor bed. The latter has a hypointense signal on T1 WI and, unlike Surgicel, is easily distinguished from the contrast enhanced residual tumor fragments.

In another study that evaluated the sensitivity and specificity of the developed algorithm for identification of the contrast enhanced residual tumor fragments, the software task was to define the boundary, based on the MRI data, between the contrast enhanced residual fragments of focal tumors with a non-infiltrative growth pattern (meningiomas and acoustic neuromas) and the hemostatic material Surgicel situated in the surgical field. The study included tumors with no signs of infiltrative growth, whose extent of the resection radicalness was not in doubt and interpretation of preoperative and postoperative MRI scans was unambiguous.

Also, the protocol of software operation included the time spent by the expert for processing data from one patient, the residual volume of the contrast enhanced tumor portion, and the volume of the hemostatic material Surgicel. The numerical values that determine the residual volume of the contrast enhanced tumor portion and the volume of the hemostatic material Surgicel were compared among experts to determine the result repeatability in the analysis of an individual case.

**Results**

Five independent experts who conducted the visual analysis of software processed MRI scans concluded that the software defines adequately the boundaries between the contrast enhanced tumor portion and the hemostatic material Surgicel. The absolute difference in the independent expert conclusions on the software-based determination of the residual volume of the contrast enhanced GB portion was 0.14±0.02 cm³, on average, the range was 0.48 cm³, and the variation coefficient was 0.89.

In all cases, upon non-radical resection of brain GBs, the software visualized the contrast enhanced residual tumor fragments, differentiating them from the hemostatic material Surgicel.

The software-based analysis of totally removed tumors in patients of the 2nd group did not reveal abnormal foci, but the vessels and brain meninges, which also well uptake a contrast agent, were identified by the software as tumor fragments, which introduced an error to calculations. However, this error does not exceed 3% of the total volume of the residual contrast enhanced portion upon analysis of GB, because the lumen diameter can not be less than the side length of 1 voxel (0.5 mm).
for identification on a contrast MRI scan, and only when a contrast agent is situated in this vessel, and these requirements are met by just great vessels and tumor afferents, whose fraction is small. And occurrence of the meninges in the “region of interest” was excluded by the user based on the instruction of the software user manual.

The analysis of cases with the interoperative use of the hemostatic material Tachocomb demonstrated that the software visualizes only the hemostatic material Surgicel with the 100% sensitivity and specificity. This is related to the fact that a hypointense signal from Tachocomb has a lesser color value on the grayscale compared to the intact brain tissue. This is the reason why the calculated Tachocomb to intact brain tissue color ratio is less than 1 (equation 1), and its conversion into the RGB color model gives the black color that is insignificant to the software user.

The mean time required to process the data from one patient was 5.21±0.14 min (from the time of data input to the software to result output).

In examined patients of the 1st group, the mean software-based residual volume of contrast enhanced sites was 5.55±1.64 cm³. The volume of Surgicel relative to a contrast-enhanced focus was between 7.28 and 40.91% (Fig. 4).

**Discussion**

Primary malignant tumors of the brain have infiltrative growth, the tumor boundaries fall beyond the scope of increasing the signal intensity upon MRI examination with contrast, and to date there is no “gold standard” for defining the true tumor boundaries. This situation occurs for several reasons: the lack of uniform approaches and methods of volume estimation and limited resolution capabilities of neuroimaging equipment. In clinical trials, it is rather difficult to determine the true volume of a diffusely spreading tumor by means of various methods and to compare their accuracy. Despite this, signal amplification on the basis of contrast MRI results is used to evaluate the tumor volume and has a prognostic value [4, 8]. The surgical tactics is such that it is a contrasted focus that is affected for maximum safe resection. O. Dewitte et al. [5] in their analysis reported on a correlation between the residual volume and recurrence for 6 months. In 80% of cases, recurrence develops from unresected macroscopic tumor residuals [4, 5]. In this context, evaluation of the volume of the unresected tumor portion during an early period after surgery is an extremely important moment in developing further treatment tactics. It is logical to assume that the higher technique accuracy is, the more effective additional treatment will be.

Descriptions of a method for calculating the resection extent of primary malignant brain tumors are rare in modern literature. The literature analysis reveals two methods.

1. Ellipsoid volume calculation. In this case, three orthogonal diameters are measured, followed by calculation of the volume using the formula: $S=\frac{4}{3}\pi abc$, where $a, b, c$ are three radii (half the diameter). This method has the ease of use and a high rate, but an expectedly low accuracy, since mass lesion has a complex shape and sometimes diffuse growth into the brain tissue. Based on this method, it is very difficult to assess the radicalness of surgery, especially in the case of marginal residual tumor after surgery. Also, this method has a low repeatability, which is, of course, its drawback. Nevertheless, this is the method that has been used in many studies on the efficacy of treatment of malignant gliomas.

2. Volume calculation with the tracing method. In this case, the boundaries of contrast uptake in the tumor are defined in a manual or semi-automatic mode, followed by calculating the volume based on the number of voxels in the “region of interest”. The method has a low dependence on the

![Fig. 4. Dependence of the Surgicel volume percentage on the residual volume of the contrast-enhanced tumor portion.](image)
user and, correspondingly, a high repeatability, the variation coefficient is 1.0—1.3. The average time required to process data from one patient is 21.2 min in the manual mode and 16.6 min in the semi-automatic mode. This method has a good accuracy in the analysis of tumors before surgery; however, according to the results of post-operative MRI control, it does not allow defining the boundary between the hemostatic material Surgicel and the residual tumor [3]. In this regard, the conclusion of K.V. Shashkov [2] is valid that MRI within early 24—48 h, when Surgicel is used as an intraoperative hemostatic, has a low information content due to the appearance of a high MRI signal from the hemostatic in the T1 mode [2].

Our original software combines all positive aspects of the two methods of determining the surgery radicalness and eliminates the problem associated with a hyperintense signal from a hemostatic material. According to the users’ feedback, the software is simple to use, requires minimal user attention in the “region of interest”, and has a high analysis rate for each case (3.2 times faster compared to the use of the second method in the semi-automatic mode), but, at the same time, retains a high accuracy of determining the volume of the contrasted tumor portion and repeatability of results (low dependence on the user). The variation coefficient is comparable with that of the second method and is 0.89. The developed software provides the opportunity to clearly define the boundary between the hemostatic agent Surgicel and the contrast enhanced tumor portions that significantly increases the analysis accuracy. Previously, we already mentioned that the Surgicel volume relative to the contrast enhanced site accounts for 7.28 to 40.91% in the “region of interest”.

Conclusions

1. The developed software increases the accuracy of evaluation of the resection radicalness of malignant gliomas of the brain.
2. The software was developed for daily neurosurgeon activity and can also be used for research of the efficacy of malignant glioma treatment.

REFERENCES

Commentary

The problem of visualization and objective evaluation of residual malignant gliomas of the brain in the early postoperative period is an important task in neuroradiology. The diagnosis methodology — when to examine and which method is the best to solve these problems — is already developed and understood. The effects of Tachocomb and Surgicel hemostatic agents, commonly used in neurosurgery, on the MRI signal intensity are defined and known. In this case, neuroradiologists at the majority of neurosurgical centers evaluate residual tumor in the manual mode. Different approaches are used for this purpose — two-dimensional and three-dimensional measurements, or, less often, semi-automatic measurements are used on specialized and not widespread workstations supplied separately by diagnostic equipment manufacturers. This process of measuring and calculating residual tumor is either inaccurate in linear measurements due to a complex configuration of residuals or time-consuming in three-dimensional measurements. In this regard, the presented method to analyze images before and after surgery and the technology to calculate the amount of residual glioblastoma on the background of hyperintense regions caused by the paramagnetic effect of Surgicel deserve special attention and further development. Furthermore, automation of measurements without participation of the researcher enables objectifying of the process of residual tumor evaluation. The great advantage of the method is, worthy of note, a short time factor required for the entire measurement process. The study is supported by appropriate statistical estimates in the standardization of measurements among experts. The only drawback of the study is a small number of observations that limits the accuracy and reliability of determining the efficacy of the presented automated method for evaluation of postoperative MRI scans.

I.N. Pronin (Moscow, Russia)

Commentary

The study is devoted to evaluation of the radicalness of resection of malignant glial brain tumors on the basis of software for processing brain MRI scans in the early postoperative period. Given the prevalence of glial tumors, this issue is important, and evaluation of the surgical radicalness is of great significance for future assessment of the outcomes of combined treatment of malignant brain gliomas. The authors propose a totally new approach for determining the radicalness based on evaluation of the contrasted residual tumor portion with allowance for hemostatic materials that are left intraoperatively for hemostasis and that often complicate the true evaluation of residual tumor. The principle is based on evaluation of changes in MRI signal with respect to different densities of the postoperative changes in tissues. A postoperative MRI examination within the first 72 h after surgery is of great importance. The authors demonstrated that this method can be used to evaluate the radicalness of other tumors, in particular meningiomas and neuromas, although the study presents single observations. Ease to use this software shows that several independent experts demonstrate identical results of the radicalness evaluation. One of the requirements of this software is high-resolution MRI. The radicalness of resection of not only malignant but also benign tumors is of crucial importance for recurrence free survival, and therefore affects survival and prognosis. Given importance of the presented work and convincing results, it would be great if its results would soon be implemented in routine practice for evaluation of the radicalness of tumor resection.

D.I. Pitskhelauri (Moscow, Russia)
The Use of Intravascular Hypothermia to Correct Intracranial Hypertension in Patients with Severe Traumatic Brain Injury


Burdenko Neurosurgery Institute, Moscow, Russia

**Objective:** To assess the impact of hypothermia on the mean arterial pressure (MAP), cerebral perfusion pressure (CPP), intracranial pressure (ICP), and cerebral autoregulation. **Material and methods.** 14 patients with traumatic brain injury (TBI) (GOS score <9) underwent hypothermia by a Thermogard system within 32—35 °C (Zoll, USA). ICP was measured intraparenchymally by a Codman sensor. Cerebral autoregulation was estimated with the correlation coefficient Prx (Soft ICM Plus, Cambridge, UK). Temperature was measured in the urinary bladder. Five time periods were selected: 1 — phase of the initial state, 2 — phase of hypothermia induction, 3 — phase of hypothermia, 4 — phase of rewarming, 5 — phase after finishing hypothermia. All data are presented as a median (min; max). Statistical analysis was performed using Soft Statistica 10.0. **Results.** Phase 1 lasted nearly 7 (2; 12) h, MAP 94 (81; 102), CPP 73 (52; 87), ICP 27 (16; 45) mm Hg, Prx 0.25 (–0.15; 0.7), temperature 38.2 °C (37; 39.8). Phase 2: 5 (2; 12) h, MAP 95 (85; 114), CPP 80 (65; 96), ICP 18 (10; 22) mm Hg, Prx –0.055 (–0.15; 0.7), temperature 35.2 °C (34.5; 35.5). Phase 3: 55 (20; 100) h, there were no significantly changed MAP, CPP, Prx, ICP 15 (10; 18) mm Hg, temperature was 33.5 °C (32; 34.7). Phase 4: 17 (8; 24) h, ABP 90 (70; 100), CPP 77 (55; 85), ICP 15 (9; 27) mm Hg and Prx 0.2 (0.2; 0.32). Temperature 36.9 °C (35.9; 38.5). Phase 5: 20 (6; 24) h, MAP 87(53; 110), CPP 72 (47; 107), ICP 17 (10; 32) mm Hg and Prx 0.2 (0.2; 0.6). Temperature 37.7 °C (36.7; 39.0). **Conclusions.** 1. Hypothermia is an effective method for correction of intracranial hypertension. 2. Hypothermia can be used as an additional option of intensive care in refractory intracranial hypertension. 3. The rewarming phase is the most dangerous time for the re-development of intracranial hypertension and disruption of autoregulation.

**Keywords:** intravascular hypothermia, Thermogard system, intracranial hypertension, autoregulation coefficient Prx.

Intracranial hypertension (ICH) is one of the important factors of an adverse outcome in patients with traumatic brain injury (TBI) [1—3, 5]. High intracranial pressure (ICP) prevents adequate cerebral blood flow, promotes the development of brain ischemia, can cause dislocation and herniation of the brain structures and brainstem [1, 2, 5]. Timely diagnosis and correction of ICH as well as providing adequate perfusion of the brain are the priorities of intensive therapy upon treatment of patients with brain injury [2, 3, 6]. Hypothermia has proved itself to be an effective method of cerebroprotection in patients with cardiac arrest [7, 8] and in infantile asphyxia [9]. Hypothermia, both in experiment and in clinical practice, reduced neuroinflammation, permeability of the blood-brain barrier, brain edema, and ICP [10]. A large number of publications are devoted to the use of hypothermia in treatment of ischemic stroke and for correction of ICH associated with malignant cerebral edema. In this case, the efficacy of hypothermia is discussed for its use both alone and in combination with thrombolysis and decompression [11, 12]. Currently, hypothermia is extensively used as a part of intensive therapy for correction of ICH in patients with traumatic brain edema [13—15]. An analysis of studies conducted over the past two or three decades did not reveal the effect of hypothermia on injury outcome but suggested that hypothermia may improve the outcome of traumatic brain injury only under certain conditions. These conditions include rapid induction to hypothermia, early start and duration of hypothermia as well as target temperature values [16—18]. In addition, it is possible that the efficacy of hypothermia will depend on the gender and age peculiarities. The Eurotherm 3235 multicenter study, which should be completed in 2014, will probably help confirm or refute these assumptions [18]. Various methods of non-invasive contact cooling are used in routine practice of critical care. They include, for example, Blanketrol (Cincinnati Sub-Zero, USA) and Tropicool (Seabrook, USA) water mattresses, Arctic Sun (Bard Medical, USA) self-adhesive plates with a special gel coat (ArcticGel) that provides the maximum contact with the skin and good heat transfer. Furthermore, craniocerebral cooling helmets (ATG-01, Russia) [4] as well as various intranasal cooling systems [19] are used. The Thermogard intravascular cooling system (Zoll, USA) is gaining popularity in neurointensive therapy [20]. To conduct hypothermia, a cooling system with a roller pump is used for quick circulation of a cold saline through a closed system via cuffs of a special venous catheter. This system provides rapid cooling and quality control of the target temperature and also enables implementation of controlled normothermia. According to some authors [21], controlled normothermia allows using all advantages of hypothermia and minimizes all hypothermia associated complications. Controlled normothermia allows control of ICP, relief of hyperthermia, and control of the body temperature. In the present study, we demonstrate the effect of hypothermia on the parameters of arterial pressure (AP), cerebral perfusion pressure (CPP), ICP, and the autoregulation coefficient Prx.
Material and Methods

A retrospective analysis of the multi-parameter monitoring data was performed in 14 patients hospitalized to the Critical Care Department of the Burdenko Neurosurgical Institute with the diagnosis of severe TBI (Glasgow Coma Scale (GCS) score <9) for the period of 2010–2013. The method of intravascular hypothermia using the Thermogard (Zoll, USA) system as part of intensive care was used in all the patients in connection with the development of refractory ICH. Previously, the system was called Coolgard and was owned by Alsus (USA). Refractory ICH was considered as persistent episodes of increased ICP >20 mm Hg upon failure of conservative methods of ICP correction and their maximum aggressiveness when continued use of conservative therapy methods will inevitably lead to complications. Under the maximum therapy aggressiveness, the maximum dose of sedative and narcotic drugs, deepening of hyperventilation P CO₂ to 26 mm Hg, the mannitol overdose of more than 3 g/kg per day, and hypernatremia of more than 160 mM/L were understood. The mean ICP values in refractory ICH amounted to 38.4±16.3 mm Hg.

All the patients underwent invasive measurement of ICP and AP. CPP was calculated as the difference between the mean arterial pressure (MAP) and ICP. The causes for invasive monitoring of ICP and CPP in all the patients were as follows: comatose condition, brain computed tomography (CT) detected focal or diffuse changes in the brain substance (edema, contusion foci) and intracranial hematomas as well as CT signs of intracranial hypertension (compression of the basal cisterns and ventricular system, displacement of the midline structures of more than 5 mm). ICP was measured by a Codman Microsensor ICP sensor (Codman, Raynham, USA) placed into the white matter of the brain at the Kocher point to the depth of 2—2.5 cm. The sensor was placed to the premotor area of the non-dominant hemisphere upon diffuse injury and on the side of the major injury upon focal injury. The duration of ICP monitoring was 9±5.5 days. Invasive AP was measured through a catheter placed into the radial artery. The ICP, AP and CPP parameters were recorded using Philips MP40 and Philips MP60 bedside monitors and averaged over a 5-second interval using ICM Plus waveform processing software (UK).

At the Critical Care Department, all the patients received mechanical ventilation. P CO₂ was maintained at 30—35 mm Hg, P O₂ was maintained not lower than 100 mm Hg, sedation and analgesia (1—3 mg/kg/h of propofol or 10—30 μg/kg/h of midazolam, 10 μg/kg/h of fentanyl) were performed. CPP was maintained above 60 mm Hg. At admission to the Critical Care Department, all the patients underwent CT with a slice thickness of 2.5—5 mm on a CereTom device (Neurologica Corporation, USA). The condition of patients was assessed according to the classification of L. Marshall et al. [22]: 1 — no visible intracranial pathology; 2 — parenchymal injuries of the high and mixed density <25 cm³, the mesencephalic cisterns are observable, displacement of the midline structures <5 mm; 3 — parenchymal injuries of the high and mixed density <25 cm³, an increase in the brain volume with compression or lack of the cisterns, displacement of the midline structures <5 mm; 4 — parenchymal injuries of a different density >25 cm³, displacement of the midline structures >5 mm; 5 — any resected pathological substrates (hematomas, contusion lesions, a depressed fracture fragment, foreign bodies); 6 — unresected abnormal substrates. Outcomes were assessed using the Glasgow Outcome Scale (GOS): 1 — death; 2 — vegetative state; 3 — severe disability; 4 — moderate disability; 5 — good recovery.

Assessment of cerebral vessel autoregulation was performed using the correlation coefficient Prx. The latter was calculated using ICM Plus software (Cambridge, UK) and was a correlation coefficient between ICP and MAP. The Prx coefficient was calculated automatically on 40 consecutive averaged values of ICP and AP; this calculation was repeated within a sliding window every 5 s. The Prx values of [0.2; 1] were regarded as completely lost autoregulation.

A Thermogard intravascular hypothermia device (Zoll, USA) was used to provide hypothermia modes. Hypothermia was conducted until the temperature of 32—35 °C. The hypothermia mode was used for treatment of 14 patients. The temperature (of the body core) was measured in the urinary bladder through a thermistor, which was located in the Foley catheter (Smiths, USA).

To compare changes in the parameters in hypothermia phases, 5 time intervals were selected: 1 — initial state phase prior to hypothermia onset; 2 — hypothermia induction phase (from onset of the cooling procedure until the temperature reaches 35 °C); 3 — hypothermia phase from 35 to 32 °C; 4 — phase of rewarming from 35 to 36.5 °C; 5 — phase after finishing hypothermia.

A statistical analysis was performed using the Statistica 10.0 package. The measured parameters are presented as a median of the (minimum, maximum) values. To assess the reliability of repeated changes of the monitoring parameters at all stages of hypothermia, methods of nonparametric statistics were used: the χ² Friedman ANOVA test and the Kendall’s coefficient of concordance. Differences were considered significant at p<0.05.

Results and Discussion

The characteristics of 14 patients with severe TBI who underwent hypothermia with the Thermogard system are presented in Table 1.

The neurosurgical activity in the study group was (79%): 11 of the 14 patients needed neurosurgical assistance. Neurosurgical intervention was not performed in 3 (21%) patients due to the lack of indications. One patient underwent external ventricular drainage only, and 3 patients underwent craniectomy resection of meningeal hematomas.

Decompressive craniectomy was performed in 9 (64%) of 14 patients: in 2 patients after hypothermia in connection with the development of repeated ICH; in 7 prior to hypothermia, immediately at admission to the Burdenko Neurosurgical Institute. They received hypothermia in the early postoperative period in connection with fever and development of ICH.

It was found that in the phase 1 with the duration of 7 (2; 12) h, MAP was 94 (81; 102) mm Hg (Fig. 1a), and CPP was
73 (52; 87) mm Hg (Fig. 1b). CPP in all the patients was provided by means of catecholamines and infusion therapy. The ICP median was 27 (16; 45) mm Hg (Fig. 1c). Most of the patients in this phase manifested impaired autoregulation of the cerebral vessels, as evidenced by the Prx coefficient of 0.25 (—0.15; 0.7) (Fig. 2). As discussed earlier, the indication for hypothermia was the development of refractory ICH. The temperature median in this phase was 38.2 °C (37; 39.8).

The phase 2 (Fig. 2) with the duration of 5 (2; 12) h was characterized by a tendency to an increase in MAP, but this phenomenon was observed not in all the patients and did not reach a reliable significance upon the statistical analysis. The MAP median was 95 (85; 114) mm Hg, and the CPP median amounted to 80 (65; 96) mm Hg. In this phase, all the patients showed a distinct tendency to reduce ICP as their body core temperature reached 35 °C. This ICP decrease reached the statistical significance (Table 2). The ICP median was 18 (10; 22) mm Hg. A significant decrease in the Prx autoregulation coefficient values was observed together with reduction of temperature and ICP. The Prx median was —0.055 (—0.15; 0.7). The temperature median was 35.2 °C (34.5; 35.5).

The phase 3 (Fig. 2) is one of the longest-lasting ones. The duration of this phase varied from 20 to 100 h, the median was 55 h. The MAP, CPP, and Prx parameters were not significantly changed. A further decrease in ICP to 15 (10; 18) mm Hg was observed in this phase. The temperature median was 33.5 °C (32; 34.7).

The phase 4 (Fig. 2), which lasted 17 (8; 24) h, can be called the phase of destabilization of monitoring parameters. A tendency to a reduction in MAP to 90 (70; 100) mm Hg was observed during rewarming; on this background, a tendency to a decrease in CPP to 77 (55; 85) mm Hg was detected. Despite the fact that the ICP median (15 (9; 27) mm Hg) did not change in comparison with that of the previous phase, an increase in the spread and maximum values of ICP were observed (Fig. 1c). Some patients developed ICH already at the stage of rewarming. As can be seen (Fig. 1d), autoregulation of the cerebral vessels begins to suffer during rewarming, as it is confirmed by an in-

### Table 1. Characteristics of patients who underwent hypothermia using the Thermogard system

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Onset of hypothermia, days</th>
<th>Patient age, years</th>
<th>Gender</th>
<th>GCS, scores</th>
<th>GOS, scores</th>
<th>Marshall CT</th>
<th>Surgery</th>
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<td>51</td>
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<td>4</td>
<td>1</td>
<td>4</td>
<td>DCT, EVD</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>42</td>
<td>M</td>
<td>5</td>
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<td>6</td>
<td>DCT, SDH</td>
</tr>
<tr>
<td>12</td>
<td>2</td>
<td>29</td>
<td>M</td>
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<td>1</td>
<td>5</td>
<td>RCT, SDH, DCT</td>
</tr>
<tr>
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<td>54</td>
<td>M</td>
<td>4</td>
<td>2</td>
<td>5</td>
<td>RCT, SDH, DCT</td>
</tr>
<tr>
<td>14</td>
<td>1</td>
<td>26</td>
<td>M</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>DCT, SDH</td>
</tr>
</tbody>
</table>

Footnote: GCS — Glasgow Coma Scale; GOS — Glasgow Outcome Scale; Marshall CT — brain CT-based classification according to [22]; DCT — decompressive craniectomy; EVD — external ventricular drainage; SDH — subdural hematoma; RCT — resection craniectomy.

### Table 2. Assessment of the significance of a change in the neuromonitoring parameters in hypothermia phases

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Friedman’s $\chi^2$</th>
<th>Kendall’s coefficient of concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\chi^2$</td>
<td>$p$</td>
</tr>
<tr>
<td>MAP</td>
<td>3.87</td>
<td>0.42</td>
</tr>
<tr>
<td>CPP</td>
<td>8.56</td>
<td>0.07</td>
</tr>
<tr>
<td>ICP*</td>
<td>28.41</td>
<td>0.00001</td>
</tr>
<tr>
<td>Prx*</td>
<td>12.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Footnote. * — $p<0.05$. 

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crease in the Prx coefficient to 0.2 (−0.2; 0.32). Despite the relatively short duration of this phase, that is where destabilization of the CPP, ICP and Prx parameters is observed. The presented dynamics of monitoring parameters may probably be explained by the variability of temperature at this stage of rewarming that promoted the development of ICH and significantly worsened Prx in some patients. The temperature median was 36.9 °C (35.9; 38.5).

The phase 5 (Fig. 2) started after complete rewarming and turning off the Thermogard system. Its duration was 20 (6; 24) h. The duration of the phase 5 was “artificially” increased for complete acquisition of the monitoring data in patients with high fever and unstable MAP, CPP, ICP, and Prx. As seen in Fig. 1, the variability of all parameters increased during this phase. The temperature was 37.7 °C (36.7; 39.0).

Based on the statistical analysis results, MAP did not differ significantly at different stages of hypothermia. However, some tendency to an increase in MAP was observed during the phase of hypothermia induction, and, in contrast, a decrease in MAP was observed in some patients during the phase of rewarming. To our opinion, the increase in MAP during the phase 2 was due to an enhanced release of catecholamines to blood and an increase in the peripheral vascular resistance with a consequent increase in AP. This phenomenon is described in the literature. It is noted that lowering the temperature by 0.7 °C from the initial value promotes a four-fold increase in the concentration of circulating norepinephrine, and a decrease by 1.2 °C promotes a seven-fold increase [23]. A decrease in MAP, which was observed in phases 4 and 5, may be explained by a reverse phenomenon — vasodilatation and a decrease in the peripheral vascular resistance occurred [10, 18, 23, 27]. In addition, a tendency to hypotension during rewarming may be the consequence of hypovolemia, which is typical of patients with hypothermia. A cause of hypovolemia may be cold diuresis and a reduction in production of the antidiuretic hormone in response to hypothermia [24].
The dynamics of CPP parameters in all phases of hypothermia generally followed the dynamics of MAP but in contrast to the MAP parameters had a clearer statistical tendency ($p=0.07$). In phases 4 and 5, significant variations of CPP occurred on the background of rewarming and hyperthermia. The ICP parameters significantly changed in all phases of hypothermia. Starting with the phase of hypothermia induction, a significant decrease in ICP occurred in all cases ($p<0.01$), with this decrease occurring when the temperature reached 35 °C.

In this study, refractory ICH developed in 2 patients after completion of hypothermia, which required decompressive trepanation of the skull. On the background of additional conservative treatment, the mean ICP in 5 patients remained at the level of 20 mm Hg, and this situation was regarded as controlled, but it required symptomatic therapy in the form of controlled normothermia, hyperventilation, and introduction of hyperosmolar solutions. After completion of hypothermia, ICP in 7 patients remained within normal limits and did not require additional therapeutic interventions (hyperventilation, sedation, controlled normothermia).

Few publications are devoted to the autoregulation state during hypothermia [25, 26]. One of these studies was performed by a research team from the University of Cambridge [27]. Assessment of autoregulation using the Prx coefficient allowed the authors [27] to reveal the phenomenon of autoregulation failure at the stage of rewarming. According to the authors, decompensation of autoregulation occurred at elevating the brain temperature over 37 °C. Upon analysis of our results, it was interesting to monitor the autoregulation coefficient dynamics. Improvement of the autoregulation status in the form of Prx coefficient decrease occurred during the induction phase and the hypothermia phase. An increase in the Prx coefficient occurred during rewarming and hypothermia completion phases (Fig. 1d; Fig. 3a), which might indicate vasodilation of the cerebral vessels [24, 26, 27]. The negative dynamics of the Prx autoregulation coefficient coincided in time with the development of intracranial hypertension (Fig. 3). These stages are the most important in the context of early detection and elimination of factors of secondary brain injury [2, 5, 6, 8, 10]. The conducted analysis revealed that the brain is vulnerable to secondary ischemic injury during the rewarming phase and the phase of hypothermia completion. In this study, the Prx coefficient was >0.2 in 6 patients after hypothermia completion (Fig. 3a) that indicated the loss of cerebral vessel autoregulation. At this stage, these patients were detected with an increase in ICP in association with a decrease in CPP. The probability of secondary brain injury is known to increase, if autoregulation of cerebral blood flow is lost [2—6, 27]. All patients with this dynamics of the parameters had an adverse outcome: GOS scores 1 and 2 (see Table 1).

Early studies published in the 1990s indicated improvement in outcomes when hypothermia was used in treatment of severe TBI [20, 21]. The more recent studies could not confirm these results [16, 17, 29, 30]. In this study, we did not evaluate the effect of hypothermia on outcome of patients with severe TBI. 5 patients had a favorable outcome (GOS scores 4 and 5), the remaining 9 patients had an unfavorable outcome (GOS scores 1—3), of which 4 patients had the fatal outcome (GOS score 1). As indicated in the Material and Methods section, hypothermia in these patients was the only available and, as demonstrated by our analysis, effective method of ICH correction. ICH was successfully relieved in all cases. The positive effect of hypothermia on intracranial pressure is not in doubt, and this method can be regarded as effective in correction of ICH.

**Conclusions**

1. The method of intravascular hypothermia is an effective method of ICH correction.
2. Hypothermia can be considered as an additional therapeutic option of intensive care for refractory ICH.
3. The phase of rewarming after hypothermia is the most dangerous one due to the development of repeated ICH and failure of cerebral autoregulation.
The use of hypothermia in critical care medicine has been practiced for a long time. The highest level of methodology development was reached in cardiac anesthesia, cardiac critical care, management of patients with the postresuscitation disease as well as in neonatal intensive care.

In the presented article, a team of authors discusses the issue of intracranial hypothermia use efficacy for treatment of uncontrollable intracranial hypertension in patients with severe traumatic brain injury (TBI).

This study used modern software (ICM Plus, Cambridge, UK) that enabled acquisition of the parameters of blood pressure, intracranial pressure (ICP), and cerebral perfusion pressure with a high discreteness frequency and assessment of the state of cerebral vessel autoregulation. The study design is a retrospective analysis of prospectively collected data. The data are analyzed for similar periods of time that ensures a correct comparison of the hypothermia effects. The study used a modern method of hypothermia, endovascular cooling, that enables precise titrated cooling and rewarming of the body. The authors note that achieving hypothermia of 35–32 °C (temperature was measured in the urinary bladder) in all cases was accompanied by a decrease in initially high ICP. Indeed, the method of hypothermia is effective enough. However, a pathological increase in ICP was detected in the phase of rewarming and at the end of hypothermia. This is reminiscent of the recoil effect. Interestingly, in these same time intervals, some patients (6 of 14) were detected with autoregulation failure, coil effect and at the end of hypothermia logical increase in ICP was detected in the phase of rewarming accompanied by a decrease in initially high ICP temperature was measured in the urinary bladder) in all cases was

**REFERENCES**

blood vessels in response to rewarming and body temperature elevation.

To our opinion, this phenomenon of loss of autoregulation should probably be highlighted and emphasized, because vasodilation of the cerebral vessels may be one of the causes for brain hyperemia and ICP rise. This phenomenon was confirmed by a clinical observation: decompensation of two patients in the phase of rewarming with the development of repeated ICP rise, which required decompressive trepanation of the skull.

Despite the convincing efficacy of hypothermia provided in the study, hypothermia is not a panacea in treatment of intracranial hypertension. Hypothermia should be considered as an aggressive method for correction of ICP that is comparable with barbiturate coma and decompressive craniectomy. It is important to understand that the efficacy of hypothermia can be limited by its duration. We hope that future prospective studies of colleagues will help in more detail to determine the place of hypothermia in comprehensive treatment of patients with TBI.

In general, the study is of practical interest and will be useful for doctors of different specialties: neurosurgeons, neurologists, and intensivists.

D.N. Protsenko (Moscow, Russia)
Rare Cases of Reflex Epilepsy in Patients with Left Hemisphere Gliomas

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Burdenko Neurosurgical Institute, Moscow, Russia

We present the cases of symptomatic reflex epilepsy in patients with left hemisphere tumors. The first case: a 23-year-old man has had tonic-clonic seizures of the tongue with rare secondary localization over the past several months. The seizures were caused by intense tongue movements, in particular rightward and leftward (when having chewing gum or a candy in his mouth), but not during speech production or eating. MRI detected a small tumor in the lower segments of the central gyrus. It was found during the surgery under electrophysiological control that the tumor (Grade II astrocytoma) resided in the zone corresponding to the right half of the tongue and included this zone. The tumor was partially resected. The second patient, a 52-year-old man, has been suffering from generalized seizures since 1998. The seizures were caused by intense verbal load, in the beginning of spontaneous speech and subsequently when the patient was listening to others’ speech or was writing. Spontaneous seizures emerged when the patient stopped taking his anti-seizure medications unilaterally. MRI showed glioma in the posterior segments of the left temporal lobe. The patient underwent radiation and chemotherapy. In 2013, the patient’s condition worsened (right-sided hemiparesis and severe speech impairment emerged); the tumor was partially resected and an extensive cyst was opened. The third patient, a 38-year-old man with Grade III astrocytoma in the left insula with past medical history of spontaneous vegetative seizures, had only a seizure anticipation caused by strong smells. All the patients were prescribed chemo-, radiation, and antiseizure therapy. Literature data are reviewed.

**Keywords:** symptomatic reflex epilepsy, brain tumors.

Reflex epilepsy is characterized by epileptic seizures that are triggered by sensory, cognitive, or other stimuli remaining constant for a certain patient (known as triggers). It is believed that seizures in reflex epilepsy are always triggered and never occur spontaneously. However, patients have both spontaneous and reflex seizures much more frequently [1, 2, 4, 31, 38].

A distinction is made between simple and complex triggering factors. Seizures caused by simple triggers include photosensitive and TV-induced epileptic seizures, as well as those precipitated by eye closure and those caused by various somatosensory and proprioceptive stimuli (e.g., movement or fright), and seizures occurring in response to various external sensory stimuli, such as olfactory, gustative, audio-genic, and vestibular ones [1, 2, 4, 11, 15, 28, 31, 34, 36].

Complex triggers induce reading epilepsy (primary and secondary forms), praxis-induced seizures, eating epilepsy, hot-water epilepsy, water-immersion epilepsy, tooth-brushing epilepsy (when seizures are triggered as one observes this activity or even thinks about it) or seizures in response to various complex musical stimuli (e.g., music-induced seizures caused by listening to certain melodies or music of a certain composer, sometimes even when one recollects this music, and listening to certain voices (e.g., those of news readers)). This group also includes complex visual stimuli inducing seizures, sometimes being quite unexpected (e.g., the one’s own hand, certain paintings or faces, etc.) [1—4, 10, 14, 19, 22]. Types of seizures caused by various cognitive activities (e.g., writing, speech production, arithmetic calculation, decision making, playing chess, etc.) should be singled out as an individual group. A number of authors [1, 13, 21] currently regard the seizures induced by counting, playing chess, and performing complex tasks as praxis-induced ones, since most of them are observed when a patient performs tasks involving hand movements. However, “pure” cases of counting epilepsy have also been reported, when seizures were induced as one performed arithmetic calculations, especially complex ones, while automatic counting caused no seizures [3]. Extremely rare cases have also been reported, such as the cases verified by video-EEG monitoring when epileptic seizures were triggered by thoughts or questions about the parental home but were not caused by the sight of it or the patient’s relatives [25]. The seizures could also be triggered by the sight of moving water even in the absence of bright sunlight [6], micturition or orgasm [27, 33, 37], or sometimes by walking or sudden movements [18]. However, it has been suggested that these cases should be differentiated from non-epileptic paroxysmal kinesigenic dyskinesia according to the video-EEG monitoring data.

Some patients with reflex epilepsy have a pleasant feeling during partial seizures when they remain conscious and self-induce seizures (e.g., by inducing light flashes as they wave their fingers in front of eyes or by changing the temperature of water falling on their head in the shower). These cases have been reported for photosensitive epilepsy and for the so-called hot water epilepsy [7, 8].

Reflex photosensitive epilepsy when seizures are triggered by intermittent light, including the flickering image of TV screen (television epilepsy) is the best-studied form. The second most frequent form of reflex epilepsy is auditory epilepsy (usually music-induced) when seizures are triggered by a certain auditory stimulus. Other epilepsy forms (e.g., calculation-induced seizures, eating epilepsy, etc.) are much less common [3].
Reflex photosensitive epilepsy, as well as reading epilepsy and calculation-induced seizures, is almost always observed in patients with idiopathic generalized epilepsy, and juvenile myoclonic epilepsy in particular [3]. Meanwhile, eating, music-induced, proprioceptive, and hot water epilepsy can be symptomatic and focal in very rare cases [13].

Single cases of surgical treatment for reflex epilepsy have been reported. Some authors have emphasized that eating epilepsy is drug-resistant; hence, surgical treatment is used in exceptional cases when epileptic focus can be accurately localized (most frequently according to the video-EEG monitoring and magnetoecephalography data, because MRI shows no pathology). Since epileptic foci are located in the temporal lobe and the insula in this epilepsy form, either temporal lobectomy and amygdalohippocampectomy [16] or resection of the insula [9] were performed. The authors reported that the postoperative incidence of seizures was significantly reduced. N. Gomes et al. [15] reported the absence of seizures during one-year follow-up after callosotomy (no well-defined epileptic focus was detected) in a female patient with the so-called fright epilepsy.

The data on total incidence rate of reflex epilepsy reported by different authors vary. Thus, U. Kokes et al. [20] found only 6 (0.067%) patients with reflex epilepsy among 8,996 epilepsy patients; in all of them epileptic seizures were induced by eating. Reflex epilepsy is observed in 5% of all epilepsy patients according to V.A. Karlov et al. [3] and in 6% of patients according to J. Salas-Puig et al. [31]. However, the incidence rate of reflex epilepsy (especially eating epilepsy) in South Asian countries (e.g., India and Sri Lanka) is several hundred times higher than the worldwide statistics [16]. Such a high incidence rate of this pathology is caused by genetic and ethnic factors. For example, European authors have reported isolated cases of eating epilepsy, while 120 patients with eating epilepsy as a component of idiopathic generalized epilepsy have been revealed in several Sri Lankan hospitals within 9 months [32].

There have been sporadic case reports of patients with symptomatic focal reflex epilepsy caused by organic brain pathology. Thus, cases of complex partial seizures induced by thinking in patients with bacterial meningitis or focal cortical dysplasia of the left temporal lobe [25, 26] or a case of reflex hot water epilepsy in a patient with pineal cyst and the fifth ventricle [35] have been reported.

We have found only six case reports of reflex epileptic seizures in patients with gliomas of different degrees of malignancy in the available literature published over the past 35 years. It is noteworthy that those tumors affected the left hemisphere in all six cases. Three of those case reports were cases of reflex eating epilepsy [12, 13, 30]. Among those, a female patient with glioblastoma of the opercular region developed partial and generalized seizures after she had thought about food or felt its smell [12]. It should be mentioned that in these three patients with reflex eating epilepsy, glioma either directly affected the opercular and insular regions or was adjacent to them. There are case reports (one per each form) of music-induced epilepsy in a patient with frontotemporal tumor [5] and kinesigenic reflex epilepsy in a patient with astrocytoma in the central gyri [17]. The past medical history of a patient with an extensive glioblastoma in the left hemisphere who had compulsive weeping of epileptic genesis induced by speech but not any other movements of facial muscles unrelated to speech has also been reported [24].

Since reflex epilepsy in patients with brain tumors is extremely rare, we would like to report our own cases.

Case 1.

A 23-year-old patient T. was admitted to the Burdenko Neurosurgical Institute. He complained of seizures that developed 8 months prior to admission. In November 2012, the patient noted that his tongue “was suddenly cramped, displaced rightward and jerked involuntarily” during spitting. This condition lasted less than a minute; the patient remained conscious but was unable to speak at that moment. In early December 2012, during intensive tongue movements (the patient was moving chewing gum in his mouth), “the tongue was cramped again and displaced rightward”; jerking of the right cheek started, and short-term unconsciousness developed. After the patient quickly recovered after seizure, he could understand speech addressed to him well but could not produce speech as “he was unable to control his tongue.” The next several clonic seizures in the tongue, while the patient remained conscious, were triggered by dental work (when the patient was intensively spitting disinfectant solution). The most severe seizure developed in February 2013 as the patient was sucking a candy. Compulsive tongue displacement rightward and clonic spasms of the tongue emerged, followed by unconsciousness and development of generalized seizure. The seizure lasted several minutes and was longer than the previous ones. It should be mentioned that the seizures were never induced by eating or speaking. The patient received depakine-chrono (500 mg twice daily); seizures occurred 2—3 times per month.

After contrast-enhanced MRI had shown a tumor, the patient was admitted to hospital.

Clinical examination showed no focal neurologic signs. While in the hospital, the patient developed a clonic spasm of his tongue after making an attempt at dry-swallowing a pill.

Neuropsychological test: dextral patient (the coefficient of the right ear in dichotic listening test was 53%). The patient has a degree in humanities and is employed as a manager in a private enterprise. No focal-type psychologic disorders have been revealed.

MRI scans (Figs. 1—3) showed a small-sized left-sided tumor in the inferior portion of the precentral gyrus.

Functional MRI showed activation in Broca’s area located posteriorly and inferiorly from the pathological area.

EEG showed slow brain waves combined with sharp spikes in the anterior portions of the left hemisphere.

Surgery was performed on June 24, 2013: the tumor of the left posterofrontal region was resected using frameless navigation and electrophysiological control.

An arc-shaped incision of skin and soft tissues in the left posterofrontal-temporal region was made to a patient in lying position under intubation anesthesia (Fig. 4). Osteoplastic
Trepanation was performed in the left posterofrontal region. The SonoWand (frameless + untrasonic) neuronavigation system was used to precisely define tumor location. The dura mater was not tense; it was opened using an X-shaped incision. A tumor of gray-pink color affecting the cortex was detected. The cortex was stimulated electrically: the motor area of the right-side portions of the face was identified in the regions located anteriorly and inferiorly from the tumor. The motor area of the right half of the tongue was detected around the tumor and above it. Despite this fact, the tumor-infiltrated cortex was incised and started to be removed by bipolar coagulation using fenestrated forceps and a suction device. The tumor was soft, moderately supplied with blood and had small-size cystic contents. The tumor was removed under permanent electrophysiological control. Subcortical electrostimulation revealed a motor area corresponding to the right half of the tongue in the posteroinferior portions of the tumor bed, in the superior portions, and in its bottom as well. In this connection, the tumor was resected partially. The large cortical vein located above the tumor was preserved. Hemostasis was achieved using bipolar coagulation and hemostatic gauze. The dura mater was tightly sutured. The bone was returned to its original position and fixed with interrupted sutures. Soft tissues were sutured layerwise.

Emergency biopsy showed that the neoplasm was an anaplastic astrocytoma (WHO Grade III).

No negative dynamics of the neurological status were observed postoperatively. Neuropsychological test showed isolated perseverations during writing and an increased slowdown of the traces of auditory-verbal memory.

Several seizures with clonic spasms of the tongue and one generalized seizure developed postoperatively as the patient failed to administer depakine-chrono on time. Most of the spasms were spontaneous; only one of them was caused by intense tongue movements (the patient made an attempt to swallow water). However, the seizures stopped after he started receiving depakine-chrono (750 mg twice daily); the postoperative follow-up period lasted 3 months. The patient was referred for radio- and chemotherapy.

Thus, it was confirmed anatomically and physiologically that the tumor was located in the motor area corresponding to the right half of the tongue. The patient had both partial and

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Fig. 1. T2-weighted MRI of patient T. in the projection of cortical regions with involvement of adjacent white matter shows a small area of pathologically altered MR signal propagating to the inferior portions of the precentral gyrus on the left side along the cortex. The neoplasm does not accumulate the intravenously injected contrast agent.

Fig. 2. MRI scan of patient T.
The arc-shaped section parallel to the convexal surface of the left hemisphere and further located in the sagittal plane. 1 — the Broca’s area detected by fMRI; 2 — tumor; 3 — distal regions of the left precentral gyrus.

Fig. 3. fMRI of patient T. subjected to verb-generation task according to the pictures shown.
The Broca’s area located in a characteristic place anteriorly and inferiorly from the tumor. 1 — tongue activation zone; 2 — tumor; 3 — Broca’s area; 4 — Wernicke’s area.
secondarily generalized seizures. Spontaneous seizures were observed along with the postoperative induced seizures after the patient failed to administer depakine on time and postoperative edema. The seizures were induced only by active tongue movements (most often, side-to-side ones) but not by eating or talking.

**Case 2.**

A 52-year-old patient M. was admitted to the Burdenko Neurosurgical Institute. He complained of seizures, left-sided hemiparesis and speech impairment. Since 1995, the patient has been observing episodes of exhaustion when he was unable to collect his thoughts after intensive verbal or intellectual load. He had to stop working or talking and rest for 20—30 min. The incidence of these episodes increased gradually. Since 1998, he started experiencing difficulties with finding the right words during intense verbal load (e.g., when delivering a report). In 1998, after a 15—20-minute-long professional conversation, the patient suddenly experienced problems with understanding others’ speech. He suddenly saw a “frightening bomb” at the right and ran rightward. The patient did not remember the subsequent events. According to the information provided by the surrounding people, a generalized seizure developed. Severe more generalized seizures developed within several months; all of them were triggered by intensive verbal load. Seizures were stopped by using finlepsin. However, the patient stopped therapy unilaterally in 2003 and the generalized seizures returned. Both spontaneous and speech-induced seizures were observed. In 2004, MRI detected an intracranial massive neoplasm in the left temporal lobe (suspected benign astrocytoma). With allowance for the suspected tumor type, its location in the language zone and the absence of neurological deficit, the patient was left to be monitored at the Burdenko Neurosurgical Institute. MRI performed on July 25, 2006 showed a slight increase in tumor volume and severity of peritumoral edema compared to the previous MRI scans (made in 2004). Stereotactic biopsy of intracranial tumor in the left temporal lobe was performed on September 15, 2006. An astrocytic glioma with nuclear polymorphism was detected. The patient received several courses of radio- and chemotherapy. Within the subsequent several years he had rare (approximately once per three months) seizures caused by emotional intensive verbal load. However, the number of episodes when “everything started to get blurry” during conversation and the patient had to go to the room and lie down increased significantly. In these periods, the patient tried to quickly administer Seduxen or Relanium sublingually to stop seizure development. The time between the beginning of conversation and the seizure episode decreased. The difficulties in finding the right words and rare paraphasias became more evident; the patient was very quickly forgetting the text that he had read. The condition has rapidly aggravated since early 2013, when further progression of speech production disorders and paresis in right limbs were observed. Since that time, the patient had several seizures and seizure anticipation caused not only by patient’s own speech but also by writing, watching TV with loud sound, and loud speech of the surrounding people. When anticipating the onset of seizures, the patient demanded silence and tried to administer Relanium; otherwise, a generalized seizure developed. MRI performed on November 1, 2013 showed a large tumoral cyst in the left temporal lobe with a small solid portion of the tumor that mostly occupied the lateral margin of the cyst. The patient was admitted to the Burdenko Neurosurgical Institute for surgical management.

Neurological signs at admission included right-sided hemiparesis (score up to 3).

The neuropsychological test showed that M. was a retrained left-hander; he used the cell phone in his left ear and had left-handers among his relatives. The patient had a degree in mathematics and was a Candidate of Technical Sciences. He presented with pronounced acoustic-mnestic aphasia and literal gnosia; hence, the writing and reading abilities were disrupted. The elements of primary parietal acalculia were observed. Significant slowdown of the traces of auditory-verbal memory was observed. The patient retained criticism about his defects.

EEG recorded on April 16, 2013 showed that focal disruption of biopotentials in the left temporal-parietal-posterofrontal-frontal region was retained. The focal disruption zone expanded due to the involvement of the temporal-frontal regions of the left hemisphere. Individual epileptiform sharp waves were still recorded in the left parietal-temporal region.

MRI performed in November 2013 (Fig. 5) showed a large intracranial tumor with cystic structure in the projection of dorsal regions of the superior and middle temporal gyri.

Surgery was performed on November 12, 2013: the lateral portion of the cystic tumor in the left temporal lobe was resected; the tumoral cyst was opened and its anastomosis with the cavity of the left lateral ventricle was formed. The tumor occupied the posterior region of the left temporal lobe (the area of the middle and inferior temporal gyri) and spread deeper, up to the ventricle. The biopsy data showed that the
tumor was an astrocytic glioma with nuclear polymorphism, focal necrosis and hemorrhage, and low Ki-67 labeling index (<5%), WHO Grade II.

The postoperative period was characterized by positive dynamics: right limbs became stronger and speech production improved (although aphasia still remained pronounced). No recurrent seizures were observed as the patient postoperatively received 750 mg of depakine in the morning, Clonazepam (1/4 tablet twice daily), and Seduxen and avoided intensive verbal load. The patient was referred for radiotherapy.

Thus, the patient had an astrocytoma in the language zone in the left temporal lobe. The seizures were induced both by his own speech, as well as others’ speech and writing. Furthermore, spontaneous seizures were observed most recently.

Case 3.

A 38-year-old patient K. During one year prior to his admission to the Burdenko Neurosurgical Institute, the patient presented with vegetative seizures (unmotivated fear, a sudden “wave” spreading bottom-upward followed by facial blushing and sweating), one of which ended with a generalized seizure. Furthermore, the patient noted the development of pronounced olfactory hyperesthesia; he started being intolerant to strong smells, including food smells. The strong smell of “burned diesel fuel” (the patient was a heavy truck driver) repeatedly induced seizure anticipation. However, the seizure was prevented as the patient walked away from the source of the strong specific odor. An astrocytoma residing in the insular zone and the adjacent portion of the frontal lobe in the left hemisphere was detected upon admission.

R. Hoque et al. [17] reported a case very similar to our Case 1. A 67-year-old patient with Grade III astrocytoma affecting the lateral portions of the perirolandic region of the left hemisphere had tonic-clonic seizures of the tongue and mandible induced by movements in this area: eating, tongue movements (most often, side-to-side ones) and talking. Some seizures occurred spontaneously. The authors called them kinesigenic focal motor seizures and raised a question concerning their pathogenesis. It is still subject to debate whether these seizures should be regarded as a part of eating epilepsy (no unanimous opinion exists regarding what factors trigger seizures in this epilepsy form: movements of oral or pharyngeal muscles during chewing and swallowing) or as a part of proprioceptive-induced reflex epilepsy (to which most movement-induced cases are classified).

As for Case 1 reported, the patient developed seizures only after intense tongue movement that were related neither to eating nor to conversation. The tumor was located in the motor zone corresponding to the right half of the tongue, which seemingly gave grounds for classifying our case as “kinesigenic reflex epilepsy” as it has been done by R. Hoque et al. [17]. However, the need for singling out kinesigenic reflex epilepsy from the total group of proprioceptive-induced reflex epilepsy remains controversial, since proprioception is involved upon any movement.

C. Marchini et al. [24] reported cases of speech-induced seizures. A 62-year-old patient with a large glioblastoma in the left hemisphere presented with epileptic seizures as a first manifestation of the disease (in form of compulsive weeping induced by the patient’s own speech). The patient’s face had a grimace expression typical of weeping; however, the patient experienced no emotions.

Seizure triggering by speech rather than by movements of oral muscles in patients without tumors was described by S. Lee et al. [21]. A 48-year-old patient subjected to extra-, intracranial left-side microanastomosis developed partial motor seizures induced by his own speech, reading aloud, and writing. Meanwhile, seizures were not triggered by any movements of oral and pharyngeal muscles unrelated to speech or calculation. EEG showed that the main changes occurred in the left central region when provoked by speech and writing, while reading induced changes in the left temporal lobe.

When the accurate lesion location is known, the case reports of reflex symptomatic epilepsy can broaden our knowledge about the functions of different brain structures. For example, the insular and opercular zones are involved in the tumor processes during eating-induced reflex seizures [12, 23, 30]. K. El Bouzidi et al. [12] reported a case of a female patient with glioblastoma in the left opercular zone, who developed seizures in the right half of the face with possible secondarily generalized seizures when she was either thinking about food, or seeing, or smelling, or eating it. In Case 3 reported by us, the patient with an astrocytoma in the insular region had olfactory hyperesthesia. Curious data have been reported by K. Porubska et al. [29]: they used functional MRI in food-
deprived volunteers who were shown pictures of served food. The brain was activated bilaterally in the insular region, in the left opercular zone, and in the right putamen. It is clear that eating behavior is extremely complex, associated with a large number of stimuli. But the clinical findings suggest that the insular and the opercular zones are involved in eating behavior at different levels.

The pathogenesis of development of reflex seizures, as well as spontaneous ones, involves increased seizure excitability of various neural networks. However, unlike spontaneous seizures, the reflex ones require the cumulative effect of stimuli, which activates the sufficient critical mass of neurons resulting in a seizure discharge. More extensive activation of neural networks of the cortical-cortical and cortical-reticular levels is required for generalized seizures to develop [13, 22].

In patients having a tumor, it acts as a factor that increases seizure excitability of the surrounding tissue, especially taking into account the fact that in all cases reported by us and found in the available literature, the tumors affected the temporal lobe and the opercular zone or less frequently affected the frontal lobe (i.e., were located in the areas with potentially the highest rate of epileptogenesis).

REFERENCES

Commentary

In recent years, interest in epilepsy among neurosurgeons has been increasing. It is mostly caused by clinical manifestations of some nosological forms of brain pathologies presenting as various epileptic seizures (tumors, arteriovenous malformation, cortical dysplasia, etc.). The level of diagnostics of focal brain pathology is currently undergoing significant changes (high-field MRI, positron emission tomography, video-EEG monitoring). It is now possible to widely use intraoperative mapping of the functional areas of the brain and electrocorticography. These methods allow neurosurgeons to manage the brain tissue in a careful manner and improve the intraoperative possibilities.

The authors of this article report several cases of reflex epilepsy in patients with gliomas. It may appear that epilepsy in a patient with glioma located in the epileptogenic brain region is a rather common situation for neurosurgeons; however, there have been only anecdotal reports of reflex epilepsy. These seizures are triggered by various somatosensory and proprioceptive stimuli: olfactory, gustative, audiogenic, visual ones, etc. The authors have found only 6 case reports in patients with gliomas of different degrees of malignancy in the available literature. They reported three patients with intracranial tumors in the left temporal and opercular brain regions who had been operated on at the Burdenko Neurosurgical Institute.

I consider this manuscript to be rather interesting and beneficial for neurosurgeons; it can be published in the neurosurgical journal.

V.A. Lazarev (Moscow, Russia)
A Rare Clinical Case of Giant Hemangiopericytoma

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The authors provide an example of successful treatment of a patient with a giant intracranial hemangiopericytoma. Hemangiopericytomas are aggressive tumors characterized by a high rate of recurrence and delayed metastasis. Despite the malignant nature of these tumors, they often reach a large size with minor clinical signs. Surgical removal of the tumor is still the primary treatment method.

Keywords: hemangiopericytoma, surgery of intracranial hemangiopericytoma.

Meningeal hemangiopericytomas (HPCs) are aggressive tumors characterized by a high rate of recurrence and delayed metastasis. Despite the malignant nature of these tumors, they often reach a large size with minor clinical presentations. To date, surgical treatment still remains the primary treatment of these tumors.

HPC is a malignant tumor arising from pericapillary cells or Zimmerman pericytes. These tumors usually occur in the lower extremities, pelvis, and retroperitoneum.

Intracranial HPCs are rare, as they amount to 2—4% of all meningeal tumors and less than 1% of all intracranial tumors. According to the latest 2013 WHO classification of tumors of soft tissue and bone [25, 26], HPCs are included, as a histological variant, to a single nosological form — extrapleural solitary fibrous tumor called “solitary fibrous tumor with predominance of a hemangiopericytoma-like vascular component”. The term hemangiopericytoma is regarded as an obsolete synonym.

Despite this fact, taking into account the process localization and based on the current 2007 WHO classification of CNS tumors and a retrospective analysis of the literature on tumors previously diagnosed as HPCs, we reserve the right to use this term in the present study.

Clinical case

A 40-year-old male patient P. was admitted to the Central Clinical Military Hospital of the Russian Federal Security Service on March 13, 2009 with complaints of bilateral visual impairment, double vision, and pronounced persistent headache localized mainly in the fronto-parietal regions.

According to the medical records and the patient, the disease started in December 2008, when headache appeared. Later on, visual impairments (diplopia and tunnel vision) developed within 1 month. In January 2009, a medical examination by an ophthalmologist revealed congestion in the fundus of both eyes.

Ophthalmological examination: VIS OS = 0, VIS OD = 1.0. Visual fields: concentric narrowing of the visual field to 20—30° on the right of the fixation point and to 30—40° on the left of the fixation point, absolute paracentral scotomata of both eyes. Ocular fundus: the optic discs had increased, there was anisoreflexia with an increase in the tenodesis reflexes and extension of the reflexogenic zones.

There were patellar and foot clonuses, right more than left. Positive Oppenheim’s and Gessell’s signs on the left side. The Marronesco–Radvocix reflex on both sides. Distal hyperhidrosis. Ophthalmological examination: VIS OS = 0.9, VIS OD = 1.0. Visual fields: concentric narrowing of the visual field to 20—30° on the right of the fixation point and to 30—40° on the left of the fixation point, absolute paracentral scotomata of both eyes. Ocular fundus: the optic discs were hyperemic and edematous with blurred boundaries and protruded into the vitreous body; peripapillarily — edema, small hemorrhages, exudates, significantly narrowed and spastic arteries; dilated veins with ruptures and exudation. The crowded optic discs of both eyes.

Total selective carotid angiography (SCA) revealed a hypervascularized mass in the anterior and middle cranial fossae, left, with a size of 7×7 cm, fed by the branches of the left middle cerebral artery (MCA), left external carotid artery (ECA), and left intracranial segment of the internal carotid artery (ICA). The venous sinuses were without obstruction and thrombosis signs (Fig. 1).

Brain CT revealed a large mass lesion characterized by sufficiently distinct nodular contours, sized 78×76×64 mm, presumably meningioma of the anterior clinoid process region of the left wing of the sphenoid bone. The patient was hospitalized to the Neurosurgical Department of the Central Clinical Military Hospital of the Russian Federal Security Service for further examination and treatment, where the diagnosis was confirmed during further examination. Decongestant and dehydration therapy with corticosteroids was started.

Examination revealed no splanchnopathy. The patient was conscious and cooperative. The patient’s criticism to his condition and the surrounding was reduced. The patient answered questions adequately, but occasionally, with elements of prolalia. Neurological status: the patient did not bring his eyeballs laterally to the left, upgaze paresis, no accommodation, asymmetric face, descended right corner of the mouth. Muscle strength of the patient’s arms and legs was sufficient and amounted 5 points on both sides. The tendon reflexes were increased, there was anisoreflexia with an increase in the tendon reflexes right and extension of the reflexogenic zones.

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Brain CT revealed a large mass lesion characterized by sufficiently distinct nodular contours, sized 78×76×64 mm,
located predominantly in the left fronto-temporo-parietal region, with basal areas adherent to the right frontal lobe by 10—12 mm. The mass was intimately adjacent to the left carotid siphon, floor of the anterior cranial fossa, and anterior tubercle of the sella turcica. The bones forming the floor of the anterior cranial fossa were corroded. The mass compressed the anterior parts of the left lateral ventricle and likely extended to its lumen. When intravenous contrast enhancement was used, the mass accumulated a contrast agent somewhat unevenly (up to +60 — +85 Hounsfield Units). The mass was fed by numerous arterial vessels with a diameter of up to 2—3 mm, which were located primarily on the middle and anterior sides of the mass. Minor perifocal edema was observed (up to 7 mm, at the lateral margin of the mass in the left temporal region) (Fig. 2).

The surgery was carried out on 25.03.09. The arcuate incision was performed in the left fronto-parieto-temporal region. The extended pterional approach was performed. Resec-
tion of the external part of the left wing of the sphenoid bone was performed extradurally. The dura mater (DM) was severely tense, bulging, no brain pulsation was observed. DM was opened along the lateral margin of the basal parts of the left frontal lobe. An operating microscope and microsurgical instruments were used for further surgery. The frontal lobe was drawn aside the skull base. A bright pink undulating tumor separated from the brain substance was found. It was soft, readily bleeding, and looked more like a paraganglioma rather than a meningioma. There was heavy bleeding (bright red blood), and hemostasis was performed by pressing the tumor using cotton rolls with hydrogen peroxide. Acute swelling and bulging of the brain developed with its fungus bulging to the DM defect. Decongestant measures were undertaken. Microsurgical manipulations were renewed after a persistant decrease in the tension and bulging of the brain. The tumor was easily fragmented and removed using conventional vacuum suction. A tumor portion was sent to urgent histologic examination, the preliminary result of which was a mixed type meningioma. The tumor was mainly homogeneous and bleeding. Only medial-basal regions of the tumor structurally resembled a nodular cellular meningioma with a dense stroma, with more distinctly developed vessels in the stroma and a higher density. Blood supply of the tumor was carried out mainly through the transitional pial vessels that resulted in very intense bleeding when the tumor was resected along the boundary with the brain substance. The tumor matrix was found in the medial segments of the sphenoid bone wing at the boundary with the anterior clinoid process, where the tumor stromal structure was the most pronounced. DM in this area was eroded, bleeding, and thoroughly coagulated. The tumor was completely removed. The left supraclinoid ICA segment, the ICA bifurcation, and the initial segments of the MCA and anterior cerebral artery were visualized. Final hemostasis was achieved using Surgicel hemostatic cotton. Distinct brain pulsation appeared. The brain smoothened and partially retracted. No anatomical damage to the brain matter due to brain traction occurred. DM was continuously sutured without tension using an atraumatic suture. The bone flap was laid on the place and fixed with a bone suture. Layered wound closure. Intraoperative blood loss was about 3,500 mL.

Histological diagnosis: the examination carried out at the Central Clinical Military Hospital of the Russian Federal Security Service revealed the mixed-type meningioma with a dense cell arrangement. No necrosis foci or mitotic figures were found. An immunohistochemical examination in the laboratory of neuromorphology at the Burdenko Neurosurgical Institute of the Russian Academy of Medical Sciences revealed: hemangiopericytoma, pronounced focal expression of Vim, CD 34, Factor XIII, and the Ki-67 proliferation marker >5%, Grade III (Fig. 3).

The postoperative period was complicated by right-sided pleuropneumonia, formation of epidural hydroma at the surgical area, and persisting cephalgic syndrome. The patient received combined therapy, including replacement of postoperative blood loss (transfusion of packed red cells, in the total amount of 1,745 mL, and fresh frozen plasma – 4,900 ml), antibacterial therapy, sanitation lumbar punctures, and decongestant therapy. Cerebrospinal fluid cultures were sterile, with no growth. The wound healed by primary intention. Regression of general cerebral and focal neurological symptoms and regression of mental disorders were observed in the immediate postoperative period.

Fig. 3. Tumor slides. ×400.

a — hemangiopericytoma of the typical structure with few mitoses, b — CD 34 expression in hemangiopericytoma cells, c — nuclear Ki-67 expression in the tumor. Stained with hematoxylin and eosin.
Fig. 4. Contrast-enhanced CT. First day after surgery.
a — axial view; b — frontal view. The tumor is radically removed. There are no hemorrhagic complications in the removed tumor bed.

Fig. 5. Contrast-enhanced CT in the axial plane (a). Contrast-enhanced MRI in the axial (b) and frontal (c) planes. Five months after surgery (no signs of tumor recurrence).
Contrast-enhanced CT on the 1st postoperative day revealed no areas of pathological uptake of a contrast agent. The tumor was completely removed (Fig. 4).

Control contrast-enhanced CT and MRI 5 months after surgery revealed no signs of recurrence (Fig. 5).

However, given the histologic pattern, radiologists of the Neurosurgical Institute recommended radiotherapy, at the place of residence, of the resected tumor area at the total focal dose (TFD) of 56 Gy.

Five-year follow-up of the patient showed no tumor recurrence.

**Discussion**

The term hemangiopericytoma was first used by A. Stout and M. Murray [23] in 1942 to describe a tumor located in the retroperitoneal space and consisted predominantly of proliferating pericytes.

Meningeal HPCs were first described in 1928 by R. Bailey et al. [2] and were considered as an angioblastic type of meningioma. Later, immunohistochemical, ultrastructural and genetic studies demonstrated a fundamental difference between HPC and all other types of meningiomas [12, 18]. The latest WHO classification (2007) of CNS tumors classifies HPCs as mesenchymal non-meningioma tumors and assigns them two grades: II and III, according to their proliferative potential [14]. HPC consists of small oval cells with a large number of thin-walled vessels of various calibers and has the characteristic antler-like vascular pattern [18]. Many authors indicate the characteristic neuroradiological and angiographic features of HPCs. Unlike meningiomas, the majority of HPCs have the multilobar structure with indistinct boundaries and infiltration of the surrounding brain tissue without hyperostosis, bone erosions, and calcifications. The presence of perifocal edema is also observed. HPCs are predominantly supplied by the branches of the ICA and posterior cerebral artery, unlike meningiomas, that are mainly supplied by the meningeal branches of the ECA. Some authors [10, 16] indicate the presence of a large number of small corkscrew-like vessels in the stroma and pronounced vasculature, which is the distinctive feature of HPCs.

According to the literature [11], preoperative embolization of the tumor-feeding vessels is an effective method to reduce blood supply. However, given the features of HPC blood supply, it is not always possible.

Surgery is currently regarded as the primary method of treatment for meningeal HPCs [10, 13, 15]. The frequency of local recurrences is high even after radical resection of HPC. According to some authors [15], this indicator amounted up to 50%. Postoperative radiation therapy reduces the frequency of HPC recurrence [19—21, 24]. In the case of a hard-to-reach location of tumors, sparing surgery combined with postoperative radiation therapy is advisable [22]. According to most authors [8, 9, 19, 20], the most efficient TFD was 50—60 Gy.

Chemotherapy was ineffective in treatment of patients with meningeal HPCs [8]. According to E. Galanis et al. [8], only 1 of 7 patients had the positive dynamics during chemotherapy with doxorubicin. However, some authors [1] report on the efficacy of a combination of ifosfamide and epirubicin.

Intracranial HPCs are aggressive tumors with a high rate of recurrence and delayed metastasis [7, 17]. N. Mena et al. [16] who observed 94 cases of HPC reported on the recurrence rate of 70% and the metastasis rate of 27%. The bones, lungs, and liver are the most frequent metastasis localizations, but there are reports on other metastasis localizations [5, 20]. According to the literature [6], metastases were most frequently observed 63—99 months after the diagnosis. A case of HPC metastasis after 20 years was also described. Bone metastases appear as osteolytic lesions on plain radiographs. In most cases, tumor recurrence tends to precede the emergence of delayed metastasis [3].

**Conclusions**

The analysis of the present clinical case and world literature indicates the efficacy of surgical removal of meningeal HPCs as the first and primary treatment.

The specific feature of this clinical case is that the tumor reached a giant size with minimal clinical manifestations. Despite a careful additional examination, it was extremely difficult to establish the correct clinical diagnosis prior to surgery.

Given high vascularization of HPC, radical tumor resection is the main requirement for successful surgical treatment and elimination of postoperative hemorrhagic complications. Radiation therapy is auxiliary treatment after surgery. In cases of doubts in a histological diagnosis based on light microscopy, an immunohistochemical study is the essential prerequisite for the correct diagnosis.

**REFERENCES**

Hardly detectable and quite rare brain hemangiopericytomas (HPCs) are malignant tumors with main characteristics often resembling those of cerebral meningiomas. However, they have a high rate of recurrence and delayed metastasis.

The paper provides an interesting clinical case of giant intracranial HPC at the Neurosurgical Department of the Hospital of Federal Security Service. The clinical case is discussed in details, both patient's complaints and the dynamics of clinical manifestations are analyzed, the results of objective neurological examination are presented. In this case, the clinical syndrome resembled that occurring in patients with basal meningiomas with initial growth from the clinoide process region. The results of objective neuroimaging examinations are provided, including contrast-enhanced CT and total selective carotid angiography. The paper is well illustrated with photographs.

Next, stepwise surgery for tumor resection is described in detail (and it is very instructive), including selection of an adequate surgical approach, its details and the implementation technique, peculiarities of dura mater (DM) opening, imaging characteristics of the central nervous system, and its structure, which is non-uniform in different tumor portions. The tumor blood supply sources identified during the surgery and successful hemostasis methods are described in details. Nevertheless, hemostasis was assiduous, and blood loss was 3 L. The relation between the tumor and the great vessels, including the supraclinoid internal carotid artery (ICA), ICA bifurcation, and system of the middle and anterior cerebral arteries, is fundamentally clarified. Everything is convincingly and thoroughly described, but it would be desirable to see illustrative images of the surgery stages that are lacking in the article. The postoperative period proceeded with moderate complications that were timely and successfully stopped.

Control examinations (contrast-enhanced CT), conducted in the postoperative period, demonstrate success of the surgery. The immunohistochemical study conducted at the Neurosurgical Institute clarified the diagnosis and tumor grade (Grade III). Later, radiation therapy was conducted, and the patient was followed up for 5 years, no tumor recurrence was observed.

A brief discussion of the problem and the analysis of the literature in a historic context are provided at the end of the article. It is emphasized that, unlike brain meningiomas, main blood supply is provided by the branches of the ICA and posterior cerebral artery, rather than through the meningeal arteries. Due to pronounced vascularization of HPC, the feeding vessels should be preoperatively embolized when possible.

In conclusion, the authors emphasize the undoubted significance of surgical treatment of these tumors as the basis of the treatment process, complemented by radiation therapy, if necessary.

The article is very interesting and informative, especially for modern practicing neurosurgeons. It reflects the important tendencies in the search for appropriate ways to improve the technique of microsurgical operations for resection of such complex tumors as hemangiopericytomas.

V.L. Puchkov (Moscow, Russia)
Letter to the Editor about the article by P.L. Kalinin et al. “Injury to the cavernous segment of internal carotid artery upon transsphenoidal endoscopic removal of pituitary adenomas” (2013, no. 6)

Dear editors of the Journal “Problems of Neurosurgery named after N.N. Burdenko”,

The article by P.L. Kalinin et al. devoted to a relatively rare but rather severe complication of transsphenoidal surgery — injury to the internal carotid artery (ICA) — has been published in your journal (issue no. 6, 2013) [1]. The publication is well-illustrated, presents an acceptable analysis of the incidence rate and outcomes of the complication in similar case reports in the existing literature. However, some rather important aspects of managing these patients have remained beyond the authors’ focus. Furthermore, I find some conclusions drawn by the authors groundless and incorrect. Hence, I would like to return to this problem and case report no. 2 in particular, since I was an anesthesiologist in this case and remember the situation very well. Let us start from the very beginning.

In case report no. 2 presented in the article by P.L. Kalinin et al., the ICA injury was diagnosed rapidly and stopped rather promptly and effectively by tamponade. In other words, the risk of patient’s death from massive uncontrollable arterial bleeding was eliminated. Nevertheless, the patient, while under general anesthesia, was emergently transferred to an endovascular operating room. Cerebral angiography verified the fact that the ICA wall was injured but blood flow in the ICA was not affected (!). It means that there was no risk of cerebral ischemia at that moment, although the risk of recurrent bleeding from the injured ICA still persisted. Indeed, such cases have been reported in literature [5, 6, 8, 11–13].

There were several alternatives for solving the problem: placement of a stent graft into the site of ICA rupture while preserving the blood flow in the ICA [10, 14, 16], ICA occlusion in the rupture site with simultaneously performed vascular anastomosis of any type [7, 12, 16]. The variant of endovascular ICA occlusion in the site where it had been ruptured by a balloon was selected; no measures for increasing cerebral blood flow in the basin of the occluded carotid artery were taken.

Acute ICA occlusion (non-gradually developing atherosclerotic occlusion when there are temporary conditions for the formation of collateral circulation) always imposes a serious risk for a patient. It is unclear why this rather risky treatment option has been selected and how the possibilities of collateral circulation have been assessed. The degree of filling of collateral cerebral vessels in patients subjected to balloon test occlusion of the ICA is not a quantitative method for assessing cerebral circulation. I used cerebral oximetry in this patient, which showed that the rSO2 index significantly decreased from the initial values close to the normal ones (64–65% in patients subjected to normoxic ventilation) to 40–42%. This reduction was strongly pronounced and demonstrated that collateral circulation was decompensated or at least subcompensated. Nevertheless, the patient underwent stationary balloon occlusion of the ICA at its rupture site and was transferred to the intensive care unit.

While at the intensive care unit, patient’s condition remained serious but not critical. After sedation, the patient was capable of making contact and following simple instructions. However, MRI performed within 24 h after surgery confirmed the formation of an ischemic focus in the basin of the middle cerebral artery ipsilaterally to ICA occlusion. The patient was subjected to controlled arterial hypertension (i.v. infusion of sympathomimetic drugs and volemic support) with the target systolic blood pressure of 160–180 mm Hg and sedation; however, their effect seems to be insufficient.

The catastrophe occurred on day 3 after surgery. The patient became comatose and developed brain dislocation and herniation, which was an evident reason for the fatal outcome (no postmortem examination was performed upon the request of patient’s relatives).

I find this case report rather instructive. Was it a correct decision to exclude the ICA from circulation in a patient with temporally stopped bleeding? Were there reasons to do it without making sure that collateral blood flow was effective? What was to be done in this case: did neurosurgeons need to make a vascular anastomosis? What was the reason for patient’s decompensation on day 3 after the surgery, although it would be reasonable to expect decompensation earlier. I think that we need to answer these questions before proceeding to treatment of our patients.

Finally, I would like to comment on statements made by the authors of the article regarding the features of anesthesiological support in these patients.

Concerning the volume of intraoperative blood loss, it follows from table presented in the article that the maximum volume of blood loss was estimated by the anesthesiologist and the neurosurgeon to be 2500 ml (ranging from 1.5 to 2.5 ml). It is a very important aspect, since this volume is less than 50% of the reference circulating blood volume. For a patient having at least one peripheral venous catheter inserted and receiving background infusion therapy that can be forced, such blood loss volume is not a problem with respect to both stability of systemic hemodynamics and preservation of the oxygen-transport function of blood (where FiO2 can be easily shifted to 1.0). Taking into account the incidence rate of this complication (4 per 3000 surgeries), recommendations to insert a catheter into the central vein and radial artery in all patients appear absurd.
It is very expensive and is associated with the risk of further complications [2, 4, 9, 15]. The same can be said about the recommendations regarding prophylactic use of blood-saving techniques (acute isovolemic hemodilution and hardware reinfusion). In my opinion, it would be reasonable to isolate a group of patients with high risk of intraoperative injury to the ICA and then contemplate about using specialized, more complex and expensive, approaches within this cohort. The prognostic risk factors for this complication have been formulated:

1) acromegaly; 2) previous surgery (repeated intervention); 3) previous radiotherapy; 4) bromocryptin therapy [1, 16].

In sum, the article by P.L. Kalinin et al. is rather useful. Physicians who share their problems in managing patients (instead of telling only about their success) undoubtedly deserve respect from their colleagues. But it should be done more accurately and thoroughly, without omitting any details that can be the most crucial ones. In this case, there would be a chance that such publications will actually improve our daily practice or even save our patients’ lives.

A.Yu. Lubnin

REFERENCES


The Long Association Pathways of the White Matter: the Modern Neuroscience View


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Summary. This review presents basic information about the white matter pathways of the human brain, with a special emphasis being placed on the long association fibers (superior and inferior longitudinal fascicles, inferior fronto-occipital fascicle, arcuate fascicle, and uncinate fascicle). Their structure, history of discovery, functions, and methods of preoperative and intraoperative identification during neurosurgical operations are provided. Neurological symptoms caused by damage to each of the described long association fibers are described. A detailed description of methods of neuropsychological testing and neurophysiological identification for mapping of these pathways in focal brain lesions is given.

Keywords: long association pathways, superior longitudinal fascicle, inferior longitudinal fascicle, inferior fronto-occipital fascicle, arcuate fascicle, uncinate fascicle, MRI tractography, traumatic brain injury, intracerebral tumors, neurophysiological mapping.

Abbreviations:
SLF — superior longitudinal fascicle
ILF — inferior longitudinal fascicle
IFOF — inferior fronto-occipital fascicle
UF — uncinate fascicle
AF — arcuate fascicle
DT MRI — diffusion tensor magnetic resonance imaging
CST — corticospinal tract

I. The history of brain white matter pathways research

According to modern concepts, there are three groups of pathways, with each of them containing several structures. Interhemispheric interactions are mediated by the commissural fibers that connect topographically identical regions of the right and left cerebral hemispheres. These include the corpus callosum, anterior commissure, and fornixcommissure. Intra-hemispheric connections are provided by the association pathways, including short U-shaped and long ones (neurofibre associationis longae). The largest long association pathways are represented by the superior and inferior longitudinal fascicles and the inferior fronto-occipital and uncinate tracts. Projection connections are provided by various ascending and descending pathways.

In 1906, Camillo Golgi and Santiago Ramon y Cajal were awarded by the Nobel Prize for describing the cytoarchitectonics of various regions of the human brain. Three years later, K. Brodmann (Germany) described 11 regions in the cerebral cortex that included 52 cytoarchitectonic fields. Later, in the 1930s, W. Penfield (Canada) described the correct spatial projection of skeletal muscles onto the primary motor cortex of the cerebral hemispheres. Based on these findings, a concept was developed that allowed neurosurgeons to perform brain surgeries with allowance for the physiologic anatomy of the cortex [41].

Neurosciences had paid much less attention to investigation of the cerebral white matter pathways, interest to which increased significantly in recent decades. The history of discovery of some brain pathways is provided below (see Table).

V.M. Bekhterev [1] who trained under Prof. P. Flechsig in Leipzig in the 1890s, played a significant role in investigation of brain pathways. Later, this allowed V.M. Bekhterev to write the fundamental guideline on the brain and spinal cord pathways in two volumes.

In 1935, Joseph Klinger (1888—1963) described a fiber dissection technique that included freezing of the brain preliminarily fixed in a 10% formalin solution for 3 weeks. In the 1950s, M. Yasargil [96] was the first who used the knowledge of white matter fiber anatomy and fiber dissection technique during neurosurgical operations. In the 1990s, U. Tyge [91] used this technique for neurosurgical training. In recent years, a number of researchers have described the role and function of the long association pathways in surgery with intraoperative awakening in patients with brain tumors [29, 41, 72].

Implementation of diffusion tensor magnetic resonance imaging (DT MRI) has opened up new opportunities for quantitative and qualitative assessment of damages to the brain pathways and for their three-dimensional imaging both under normal and under various pathological brain conditions [3—6, 10, 21]. Based on DT MRI, new data on the dynamic status of the commissural and projection pathways in patients with severe traumatic brain injury have been obtained at the Burdenko Neurosurgical Institute [3—6, 97].

The DT MRI method evaluates diffusion properties of the investigated medium as well as the direction of water diffusion (anisotropy) and thus provides information on the integration extent of the white matter tracts [75]. Diffusion anisotropy is
not uniform in different areas of the white matter and reflects the difference in myelination, diameter and orientation of the fibers. Pathological processes that alter the white matter microstructure, such as disorganization and disconnection of the fibers or their disruption combined with myelin damage, retraction of neurons, and an increase or a decrease in the extracellular space, have a significant effect on diffusion and anisotropy parameters [35, 94, 97].

Fig. 1—4 show the results of MRI tractography with reconstruction of various associative, commissural and projection fibers that was carried out at the Burdenko Neurosurgical Institute one time or over time, including the calculation of fractional anisotropy indices along the tract fibers.

In particular, it was found that a change in the DT MRI parameters reflects the sequence of degenerative processes in axons and myelin sheaths of the pathways that lead to their destruction and atrophy several months or even years after diffuse axonal injury in patients with tumors and other brain lesions [13—15, 97].

2. Anatomical and functional features of the long association pathways

According to modern concepts, the main role of the long pathways is to provide the verbal function that is represented by a wide brain network, including the cortical speech centers and the fascicles (tracts) connecting them [71, 78]. A diagram of the topographo-anatomical position of some long association pathways is shown in Fig. 5.

2.1. The superior longitudinal fascicle

The superior longitudinal fascicle (superior longitudinals fasciculus, SLF) is a large tract connecting the cortex of the frontal, parietal and temporal lobes as well as the area around the Sylvian fissure. It was first described by Reil and Autenrieth in 1809—1812. Later, the tract structure was described by Burdach (1819—1826) and Dejerine (1895). Based on the MRI tractography and dissection data, Y. Fernandez-Miranda et al. described three segments of the superior longitudinal fascicle. Neuroimaging studies in primates demonstrated that SLF consists of the horizontal segment (fronto-parietal portion), vertical segment (temporo-parietal portion), and fronto-temporal segment (arcuate portion) [27, 45, 62]. The main function of SLF is to provide signal transmission for speech and language functions [95].

According to another classification, SLF consists of three parts: 1) a superficial anterior segment connecting the supramarginal gyrus and superior temporal gyrus with the precentral gyrus and lateral frontal cortex; 2) a superficial posterior segment connecting the posterior portion of the middle temporal gyrus and the supramarginal gyrus; 3) a deep long segment (arcuate fascicle) connecting the middle and inferior temporal gyri with the precentral, inferior and middle frontal gyri. In a study by J. Martino et al. [69], these portions of SLF were identified separately using postmortem dissection of brain specimens. Each component of the tract was found to connect specific cortical fields of the frontal, parietal and temporal lobes.

Intraoperative electrical stimulation of SLF results in speech disorders, syntactic and phonemic disorders (paraphasias), especially in injury to the dominant side [39]. There are reported cases of alexia and agraphia as well as spatial orientation disorders and development of dysgraphia when the inferior parietal region of SLF in the dominant hemisphere was affected [84, 86]. According to MRI tractography, anatomical representation of the tract exceeds its functional zones compared to the results of an intraoperative neurophysiological examination. This means that the tumor infiltrating a tract portion can be removed without augmentation of neurological symptoms [19, 24].

2.2. The arcuate fascicle

The arcuate fascicle (arcuatus fasciculus, AF) was described in studies of Burdach (1819—1826) and Dejerine (1895). They thoroughly studied the fibersystem and the connection between the inferior and middle temporal gyri and the lateral frontal cortex through AF. These researchers believed AF to be a part of the superior longitudinal fascicle. This tract connects the Broca’s and Wernicke’s speech centers. According to M. Glasser and J. Rilling (2008), this tract occurs in the left hemisphere in 100% of cases, while it occurs in the right hemisphere in 50% of cases. Intraoperative electrical stimulation of AF results in speech disruptions, speech disorders and development of dysphasia when the inferior parietal region and the AF are affected [84, 86].

<table>
<thead>
<tr>
<th>Author</th>
<th>Years of life</th>
<th>Discovery</th>
</tr>
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<tbody>
<tr>
<td>Andreas Vesalius</td>
<td>(1514—1564)</td>
<td>The first description of the corpus callosum</td>
</tr>
<tr>
<td>Raymond Vieuussens</td>
<td>(1641—1715)</td>
<td>Description of the brain internal structures from the anatomical viewpoint (semiolateral, radiant, internal capsule, pyramidal tract)</td>
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<tr>
<td>Domenico Misticelli</td>
<td>(1675—1715)</td>
<td>Description of the decussation of the pyramidal fibers</td>
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<tr>
<td>Johann Reil</td>
<td>(1759—1813)</td>
<td>The discovery of a method of alcohol fixation of the brain</td>
</tr>
<tr>
<td>Franz Joseph Gall</td>
<td>(1758—1828)</td>
<td>Description of the pyramidal tract fibers</td>
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<tr>
<td>Luigi Rolando</td>
<td>(1773—1831)</td>
<td>Description of the olfactory pathway</td>
</tr>
<tr>
<td>Bartholomeo Panizza</td>
<td>(1785—1867)</td>
<td>Description of the optic pathway fibers</td>
</tr>
<tr>
<td>Johann Christian Reil et coa.</td>
<td>(1759—1813)</td>
<td>Description of the superior longitudinal fascicle (1809—1812)</td>
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<tr>
<td>Johann Heinrich Ferdinand von Autenrieth</td>
<td>(1772—1835)</td>
<td>Description of the superior longitudinal fascicle (1809—1812)</td>
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<tr>
<td>Louis Pierre Gratiolet</td>
<td>(1815—1865)</td>
<td>Description of the arcuate fascicle (1819—1826, 1895) and inferior longitudinal fascicles (1822)</td>
</tr>
<tr>
<td>Karl Friedrich Burdach et coa.</td>
<td>(1776—1847)</td>
<td>Description of the inferior frontal-occipital tract (1909)</td>
</tr>
<tr>
<td>Edward Joseph Curran</td>
<td>(1885—1928)</td>
<td>Description of the arcuate fascicle (1819—1826, 1895) and inferior longitudinal fascicles (1822)</td>
</tr>
</tbody>
</table>
In addition, an indirect link between speech centers through the cortex of the inferior parietal region was described [48]. Fig. 6 demonstrates the topography of AF in the brain white matter and a clinical example of SLF reconstruction in the intact hemisphere in a patient with intracerebral tumor of the left cerebral hemisphere (Fig. 7).

AF lesion often occurs when a focus is located in the white matter of the inferior parietal lobule in the projection of the angular gyrus (the distance between the insular lobule and AF is 11—25 mm) [70]. This brain region is the “strategic” one and its injury leads to more serious disorders than the same size injury to another brain region. Correspondingly, the neurosurgeon operating near this white matter region should identify this tract portion by electrostimulation [66]. AF lesion leads to conduction aphasia due to impaired impulse transmission between speech centers as well as to articulatory, phonemic and syntactic speech disorders (phonemic paraphasia) and, more rarely, to semantic and phonological paraphasia [23, 47, 64]. A prominent impairment in phrase repeating after the doctor and in reading aloud is the main clinical sign of conduction aphasia. The development of dyslexia, optical spatial coordination deficit (spatial agnosia), and acalculia after radionecrosis with bilateral lesion of the arcuate fascicles in a patient with a brain tumor was reported [78].
2.3. The inferior fronto-occipital fascicle

The inferior fronto-occipital fascicle (inferior fronto-occipitalis fasciculus, IFOF) is a ventral associative pathway connecting the frontal lobe with the occipital and parietal ones through the temporal region and insula. This is one of the most important tracts in the brain, whose importance was underestimated [57]. In 1909, Curran was the first who described IFOF fibers in a corpse during anatomical dissection. The anatomy and functional role of IFOF still remain poorly studied [81]. Fig. 8 shows a photograph of dissection of the tract fibers adopted from the publication of M.V. Putsillo et al. [9].

According to the data of anatomical dissection of the fibers and intravital MRI tractography, IFOF consists of two layers: superficial and deep ones. The deep layer is in turn divided into the anterior, middle and posterior portions. The posterior component connects the middle frontal gyrus and dorsolateral regions of the prefrontal cortex, while the middle portion connects the middle frontal gyrus and lateral part of the orbitofrontal cortex. The anterior segment of the tract conducts impulses between the orbitofrontal cortex and the frontal pole. The superficial layer and posterior portion of the deep layer of IFOF are involved into semantic processing of information. The middle component of the deep layer may play some role in mixed sensory-motor integration. Finally, the anterior portion of the deep layer may be involved in emotional and behavioral reactions. Therefore, the inferior fronto-occipital fascicle is multifunctional and each its component is involved in a certain function of the brain. Fig. 9 shows a clinical example of inferior fronto-occipital fascicle reconstruction in a patient with intracerebral tumor of the left cerebral hemisphere. According to A. Castellano et al. [24], DT MRI is a highly specific method for identifying IFOF.

Intraoperative electrical stimulation of the inferior fronto-occipital fascicle can result in semantic paraphasia (lexical-sematic speech component), sensory-motor integration disorder, and emotional and behavioral disorders [81].

2.4. The inferior longitudinal fascicle

The inferior longitudinal fascicle (inferior longitudinalis fasciculus, ILF) was described by Burdach in 1822. It connects the visual cortex with the anterior frontal region via the posterior temporal region. In the temporal lobe, this fascicle connects the temporal pole, parahippocampal gyri, hippocampus, and amygdala. MRI tractography confirms a close relationship between the occipital and anterior frontal regions through the inferior longitudinal fascicle [26].

No speech disorders were observed upon direct stimulation of this tract during neurosurgery with intraoperative awakening, as evidenced by a study by E. Mandonnet et al. [67]. Based on 12 operations for intracerebral tumors of the left temporal lobe performed under local anesthesia, the authors demonstrated the existence of two alternative pathways involved in the speech function that are combined under the name of the semantic ventral stream: a direct pathway through the inferior IFOF, supporting semantic speech processes, and an indirect pathway through ILF.
which is not important under normal condition but can participate in compensation of speech disorders after tumor resection [67].

Research has demonstrated that damages to this tract can lead to problems with naming objects [44, 87, 88], while interruption of this pathway can result in the development of alexia [43] and visual memory deficits [87].

2.5. The uncinate fascicle

The uncinate fascicle (uncinatus fasciculus, UF) connects the temporal pole with the orbitofrontal region [25]. The function of this tract is not fully understood. Conducting a subject search, we found scarce data on the functional significance of
this tract. Direct subcortical stimulation of this pathway in the dominant hemisphere did not lead to speech disorders during surgery, as evidenced by standard speech tests [37]. The authors describe the semantic ventral stream involving the direct pathway through ILF, which provides semantic speech processes, and the indirect pathway through UF, which is not important under normal condition but can participate in compensation of speech disorders after tumor resection. Fig. 9 shows the results of MRI tractography with construction of IFOF (blue), ILF and UF that was performed at the Burdenko Neurosurgical Institute.

3. Intraoperative identification of the functional cortical areas and brain pathways

First attempts to identify the localization of functional cortical organization in the course of neurosurgery [46, 76] were taken as early as in the 1930s. Only direct stimulation of the cortex during resection of tumors and epileptogenic zones in conscious patients was initially used. This enabled assessment of the relationships of consciousness, motor actions and language production at various stages of surgery. Later on, in the 1970s, monitoring of somatosensory evoked potentials (SSEPs) [73] was introduced in neurophysiological practice, and quite recently, in the 1990s, motor evoked potentials were put into practice, which enabled a more precise localization of the functional cortical areas and pathways.

The phenomenon of phase reversion of the SSEP cortical component in the area of the central gyri and identification of the central sulcus were described in 1978 [51], which have extensively been used in surgery of intracerebral tumors [28, 59, 63]. In 1937, W. Penfield [76] described a technique of direct cortical stimulation using periodic (50—60 Hz) bipolar pulses. This approach has mainly been used to map the sensory and motor speech areas in conscious patients, but it has also been used in patients under general anesthesia [63]. A method of stimulation with trains of 4—5 pulses is also currently used.
Surgery with awakening and direct electrical stimulation of the cortex and pathways are the “gold standard” for resection of gliomas located close to the speech areas and other functionally important structures [36, 38, 42, 74]. Functional mapping of the brain during these operations is performed by the neurosurgeon together with the neurophysiologist and neuropsychologist, with the latter adjusting the stimulation parameters while concomitantly monitoring the state of spontaneous cortical activity using an electrocorticogram (ECoG) to detect the epileptic activity. This approach prevents the development of convulsive disorder during long-term rhythmic electrical stimulation. At the first stage, the localization of cortical

Fig. 6. A diagram of the arcuate, uncinate and inferior fronto-occipital fascicles [9].

Fig. 7. Preoperative MRI tractography with reconstruction of the superior longitudinal fascicle of the right (intact) hemisphere in a patient with intracerebral tumor of the left hemisphere of the brain. The shots were taken at the Burdenko Neurosurgical Institute.

Fig. 8. Topographic and anatomical relationships between the inferior fronto-occipital fascicle, arcuate fascicle, and external capsule [9].
areas related to verbal functions is identified by electrical stimulation, with each functionally important area being marked [2, 11, 12].

A stimulated zone is considered to be functionally significant when speech disturbances are observed thrice after consecutive impulses, with speech (language) function recovery being observed after stimulation completion. The type of speech disorders is verified by the neuropsychologist, and severity of speech disorders is evaluated using the National Institutes of Health Stroke Scale [92]. At the next stage, the tumor is resected based on the mapping data. In this case, periodic subcortical stimulation is performed to identify functionally significant pathways of the white matter [2].

Therefore, the use of intraoperative mapping and electrophysiological monitoring allows surgeons to remove the maximum amount of the tumor with minimal disturbance of neurological functions [31, 54, 61].

4. Neuropsychological methods of intraoperative examination

Dynamic examination of cognitive functions (before and after surgery) is performed using an appropriate set of neuropsychological tests that should match several criteria:

1) tests should allow assessment of several cognitive functions, while they should be sensitive enough to determine the tumor and treatment effect; 2) a test procedure should be standardized to allow a comparison of the results of patient’s examination over time; 3) availability of the testing standards will provide objective evaluation of patient test performance; 4) tests should be sufficiently reliable and insensitive to re-testing to obtain accurate data during a dynamic examination; 5) tests should have alternative forms for re-testing; 6) the total test time should not exceed 30—40 min to prevent fatigue.

The complex of neuropsychological testing is selected individually for each patient. Since tumors are often associated with impairments of memory, attention, information processing rate, executive functions and speech, appropriate tests should mandatorily be used during testing. As an example, tests for verbal associations (associations to a given letter of the alphabet and a certain semantic category), finding similarities between two items (e.g., “what is a common feature of an apple and a banana”), a test to follow the path from A to B (evaluates visual attention and attention dividing and switching) [65], memorizing a list of words (evaluates audio-verbal memory) [55, 60, 83], an encryption test (allows assessment of the information processing rate) [93], and a fine motor skill test [53] can be used. Depending on the lesion location, an examination can be supplemented by the Wechsler intelligence test (WAIS-IV), which provides an overall evaluation of verbal and nonverbal intelligence [93]. The Rey complex figure test evaluates the visual-constructive functions. Also, tests for non-verbalisable figure memory (Rey Visual Design Learning Test, Rey Complex Figure Test) [65, 89], tests of verbal and non-verbal working memory (Digit Span Forward, Digit Span Backward, Spatial Span Forward, Spatial Span Backward) [65, 89], and tests for speech examination [22] are also used.

A small set of relatively simple tests that can be performed during intraoperative awakening is used for intraoperative mapping. Each test should include a sufficient number of trials that enable continuous testing of a function during brain stimulation. As an example, let us mention several tests used for intraoperative localization of the speech and motor zones, which are most often identified during these operations. A fist clenching and opening test is used to localize the hand motor area; a knee flexion and extension test is used to localize the leg motor area. A picture naming test is used to assess the speech functions. In this case, verb naming is more sensitive for localization of the Broca’s area than noun naming. Forward and backward sequential counting allows assessment of speech fluidity and switching.

Therefore, neuropsychological testing of the cognitive functions is an important component of a comprehensive examination of patients with brain tumors in the preoperative and postoperative period, which determines both a surgical approach and subsequent rehabilitation measures.

5. Conclusion

The first surgeries with intraoperative awakening of patients were performed by W. Penfield and H. Ojemann at the Montreal Neurological Institute in the 1930—40s. Their research provided more detailed information on the localization of various cortical functions of the human brain. Despite the fact that most of the long association pathways of the human brain were described in the XIXth century, intraoperative examinations of the white matter tracts of the human brain were not widely used until recently.

Implementation of DT MRI allowed identification of functionally important pathways of the cerebral white matter and their topographic and anatomic relationship both in health and in disease [18, 33]. Since that moment, MRI tractography
has extensively been used worldwide for preoperative and intraoperative imaging of the pathways. However, for many years, the primary focus was on the pyramidal and, to a lesser degree, optic tracts of the brain. The remaining pathways were much less studied [20]. DT MRI allowed planning of a surgical approach and an extent of surgical resection of intracranial tumors with allowance for the location of pathways and their involvement in the pathological process (displacement, deformity, invasion, damage) to achieve the most radical tumor resection with minimum postoperative damages [80]. A detailed description of the microsurgical anatomy of the cerebral white matter is provided in publications by M.V. Putsillo et al. [9] and J. Fernandez-Miranda et al. [45].

An important role of the long association pathways for different functions of the human brain was demonstrated in subsequent studies of Prof. H. Duffau et al. [40, 42]. The modern neuroanatomical concept of language brain function includes the posterior pathway (acoustic-phonological-motor system) involving the Broca’s, Wernicke’s and Geshvild areas and the uncinate tract [56]; and the occipital fascicle and possibly the inferior longitudinal fascicle [5]. Therefore, identification of both the cortical speech zones and their connecting pathways is required upon resection of intracerebral tumors located in the fronto-occipital fascicle and possibly the inferior longitudinal fascicle and the uncinate tract [56]. Therefore, identification of both the cortical speech zones and their connecting pathways is required upon resection of intracerebral tumors located in the fronto-parieto-temporal region of the speech dominant hemisphere.

Investigation of preoperative anatomy of the long association pathways and intraoperative neurophysiology using modern testing methods allows planning of an optimal approach to removal of intracerebral tumors as well as determines the prognosis of surgery radicalness. For example, the inferior fronto-occipital fascicle condition can be a predictor of total resection of the tumor located near this tract, while infiltration of the tumor into the tract fibers in the external capsule area is considered to be the critical point in this case [24].

A new concept of surgery for intracranial tumors was developed that was termed “preventive surgical neurooncology”, which term has widely been used in the literature. Survival and improvement of the life quality of patients is currently the priority area in surgery of gliomas [39]. In these circumstances, this review is aimed at revising technical aspects of glioma surgery development with allowance for the latest advances in neuroscience with regard to the role and functions of the long association pathways. In other words, during surgery, the neurosurgeon should first of all see the brain with its three-dimensional anatomical and functional organization [39].

Dissection of the cerebral pathways provides the opportunity to study their anatomical and topographical features and facilitates improvement of the neurosurgical planning strategy during resection of intracerebral tumors, arteriovenous malformations, and other focal brain lesions. It is advisable to use the Klinger fiber dissection method for training of neurosurgeons [70].

Investigation of preoperative anatomy of cortical representations and pathways of the brain using intraoperative neurophysiology and modern testing methods allows planning of an optimal approach and tactics of neurosurgical interventions in patients with various brain pathologies.

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REFERENCES
DISCUSSION


Modern neurosurgery attributes the key role to the cortical functionally important areas, while much less attention is paid to studying the anatomical and physiological features of the white matter pathways. Resection of pathological brain lesions may result in damage not only to the functionally important cortical areas but also to the pathways, which may also lead to an increase in neurological deficit during the postoperative period. In this regard, the perfect knowledge of the anatomical and functional characteristics of various white matter tracts is very important for the neurosurgeon.

This review provides key information on some long association pathways in the cerebral white matter (superior and inferior longitudinal fascicles, inferior fronto-occipital fascicle, arcuate fascicle, and uncinate tract). Information on their structure, functions, and methods of preoperative and intraoperative identification is provided in the historical context. It would be appropriate to provide morphometric data for each tract.

The article is illustrated with pictures from international articles, whose authors are the world’s leading experts in the field of the human brain tracts (Catani, Duffau, etc.), which allows the reader to imagine the location of some long association pathways in the human brain white matter in anatomic preparations and MRI tractography images.

Unfortunately, the issues of the structure and functions of some of these pathways are not fully studied by now. Therefore, further detailed studies of anatomical specimens both without CNS pathology and with various brain lesions (particularly hemispheric gliomas) are required. A comparative and contrastive analysis of the obtained data with the MRI tractography data is also required. The article lacks a detailed description of the method used for fixation and anatomical preparation of the described brain tracts.

This work is highly relevant and it will be not only interesting but also useful for practicing neurosurgeons.

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