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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, Burdenko's Journal of Neurosurgery 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 treatment of patients with cerebral aneurysms in the acute stage of rupture: dynamics of results during 2006—2018


FSAI «N.N. Burdenko National Medical Research Center of Neurosurgery» of the Ministry of Health of the Russia, Moscow, Russia

ABSTRACT
Treatment of cerebral aneurysms in the acute stage of subarachnoid hemorrhage (SRH) especially on the background of cerebral vasospasm continues to be a difficult task.

Objective — assessment of dynamics of the surgical treatment results of patients with cerebral aneurysms in acute period of SRH.

Material and methods. A comparative analysis of the results of patients' surgical treatment in NMRCN Burdenko about aneurysm in 1—21 days after hemorrhage was made. The following periods were selected: 2006—2014 г (343 patients) and 2015—2018 г (356 patients). Most patients had microsurgical operations in both periods. The tactics of choosing the surgery time was the main difference between the periods: particularly in 2015—2018 period the surgery was not postponed at patients with severe.

Results. Analysing the post surgical mortality, it was found that since 2006 there is a consistent trend towards a decrease in the number of patients who died after surgery. When calculating the average post surgical mortality for the studied periods this trend is confirmed — number of lethal cases in 2015—2018 reliably decreased when comparing with 2006—2014 г. — from 6.8 till 3.2%; p=0.03. At the same time, the number of patients with outcome of vegetative status (from 0.3 till 5%).

Conclusion. The tactics of surgical treatment of patients with cerebral aneurysms in the acute period of SRH regardless of severity of patient’s condition and time of hemorrhage did not lead to worse treatment. In contrast, post surgical mortality rates show a consistent decline. We associate this fact with a number of changes that have occurred in the management and treatment of patients. In particular, we have high hopes for developing new approaches to the treatment of vasospasm, which remains the leading cause of lethal cases. More definite conclusions will be made at the end of the treatment analysis of the respective patient groups.

Keywords: cerebral aneurysms, acute period of SRH, cerebral vasospasm, mortality at SRH.

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Abbreviations
SAH — subarachnoid hemorrhage
VS — vasospasm
GOS — Glasgow outcome scale

Treatment of cerebral aneurysms in acute stage of subarachnoid hemorrhage (SAH) is still a challenge for neurosurgeons, neurologists, neuro-resuscitators and other specialists. It is especially true for patients with SAH-associated complications. Changes in this area are reported in various recommendation protocols [1—4].

The first operations for cerebral aneurysms at the Burdenko National Research Center of Neurosurgery were performed in the early 60s of the last century. To date, there are about 11,000 patients with this disease who were operated in our center [5].

The first interventions for aneurysms in acute period of SAH also date the 60s [5—7]. Surgical
interventions in about 60 patients with aneurysms in acute stage of SAH are reported in the monograph of A. N. Konovalov (1973). A special analysis of this group was not carried out. However, unfavorable outcome was noted in the majority of critically ill patients [6]. Considering frequent adverse outcomes of these operations, surgical treatment of aneurysms in delayed period after SAG was preferred.

Scheduled surgical treatment of patients with cerebral aneurysms in acute stage of rupture has been started since the mid-90s of the last century at the Burdenko National Research Center of Neurosurgery. There were 506 patients for the period from 1995 to 2005 (hereinafter — period I) including 454 patients who were operated within 30 days after SAH. Postoperative mortality rate was 11% (50 patients). It was observed that surgery within 1—14 days after SAH was associated with the greatest risk of unfavorable outcome in critically ill patients (Hunt—Hess grade IV—V) [8]. The result of this research was the principle of differentiated preoperative selection of patients with possible postponing of surgery in severe patients. The same principle was mainly applied for the period from 2006 to 2014 (hereinafter — period II) although earlier surgical strategy became more common in severe patients.

Some principles of management and treatment of patients in acute stage after SAH have been significantly changed by 2015 at the Burdenko National Research Center of Neurosurgery. First, these changes were applied for pre- and postoperative control and intensive care [5]. Invasive treatment of vasospasm (VS) was also used including intraarterial and, a few years later, intrathecal administration of calcium channel blockers (verapamil) [9, 10]. These and some other changes influenced the outcomes of treatment of patients in acute stage after SAH.

The purpose of the study was to assess the dynamics of the results of surgical treatment of patients with cerebral aneurysms in acute period of SAH.

Material and methods

A comparative analysis included patients with cerebral aneurysms who were hospitalized to the Burdenko National Research Center of Neurosurgery in acute period of SAH. All patients were operated on within 1—21 days after hemorrhage. The following periods were distinguished for analysis: period II (2006—2014) with 343 patients and period III (2015—2018) with 356 patients. Preoperative Hunt—Hess grade, severity of hemorrhage (Fisher scale), the day of surgery after SAH, localization of aneurysm, GOS category of treatment at discharge from the Burdenko National Research Center of Neurosurgery were analyzed.

Results

Duration of follow-up periods was different (9 and 4 years). However, the number of patients in both groups was approximately the same (343 and 356 patients). This is due to increased number of operations in recent years.

The majority of patients have undergone microsurgical operations in all periods since 1995. Endovascular occlusion of the aneurysm was performed in 25, 42 and 13 patients in periods I, II and III, respectively. In general, there were 7.8% of endovascular procedures in acute period of SAH for the period 2006—2018. At the same time, endovascular operations were more common in patients with Hunt—Hess grade V at admission compared with open surgery (23.1 and 6.1%, respectively).

Condition of patients at admission in accordance with Hunt—Hess and Fisher scales was similar in periods II and III (no significant differences were found) (Fig. 1, 2). Dates of surgery after aneurysm rupture were also comparable. There was a slightly increased number of patients operated within 4—14 days after SAH (from 49.4 to 61.4%). Maximum VS was observed in this period (Fig. 3).

It was unsurprisingly that aneurysms of anterior cerebral and anterior communicating arteries prevailed in both periods (Fig. 4). Significant changes was observed in the incidence of decompressive craniotomy for intracranial hypertension and brain dislocation. In the period III, this value was decreased by about 2 times compared to the period II (68 vs. 34 cases, p=0.01). These changes were caused by the development of clearer indication for this operation [11]. It should be noted that the number of severe patients was the same in both periods (Fig. 5).

Certain variability of postoperative mortality within 16.7 — 0% was observed in different years. However, postoperative mortality is being steadily decreased since 2006 (Fig. 6). Analysis of mean postoperative mortality for both periods confirmed this finding. Significantly less number of deaths in
the period III was found compared to the period II (6.8 vs. 3.2%, \(p=0.03\)). At the same time, vegetative state became more common (0.3 vs. 5%). The same tendency was noted for the incidence of severe disability as GOS category III (17.8 vs. 26.3%) (Fig. 7).

Reduced mortality with simultaneous augmentation of the incidence of vegetative state (GOS category 2) or severe disability (GOS category 3) is also observed in the analysis of surgical outcomes depending on dates of surgery. At the same time, the most severe outcomes were observed after surgery within 3 days after SAH (Fig. 8, 9).

The outcome of treatment significantly depended on severity of condition at admission. Postoperative mortality depending on preoperative Hunt—Hess grade is shown in Fig. 10.

Discussion

Development of primary and regional vascular centers in the Russian Federation significantly improved the primary diagnosis and organization of medical care for patients in acute period of SAH [12]. The number of patients with aneurysms undergoing surgery in acute period of hemorrhage is being steadily increased in different regions of Russia. Analysis of the experience of various clinics showed significant differences in the results of surgical treatment [7]. In this regard, an experience of the Burdenko National Research Center of Neurosurgery may be useful for various hospitals, as operations in acute period of aneurysmal SAH have been carried out for about 25 years in this institution and the number of patients is close to 1200.

Analysis of the outcomes throughout the entire period showed steadily decrease of postoperative mortality in acute period of SAH. Thus, this value was 15.9% in 1995—1999 and 7.5% over the next 5 years (2000—2005, 11% for the entire period I). Analysis of data over these years has revealed some significant predictors of the outcomes. The most important factors were massive hemorrhage, intracerebral hematoma, intraventricular hemorrhage, brain edema, date of surgery, pre- and postoperative severity of VS and localization of the aneurysm. The most optimal dates of intervention were analyzed. Thus, there was a group of patients with postponed surgery due to either severe or rapidly aggravating VS (83 cases) or severe brain damage due to VS, intracerebral hematoma after intraventricular hemorrhage (39 cases). Many of these patients were subsequently operated on. However, 5 (6%) of patients of the first group and 10 (25%) patients of the second group died before surgery. Nevertheless, analysis of outcomes showed that postponement of surgery due to VS in patients with Hunt—Hess grade III reduces postoperative mortality and is not accompanied by increased overall mortality compared to the whole group. Delayed surgery in more severe patients (grade IV—V) resulted 3 times higher mortality compared with the whole group [2, 13]. These data together with improvement of
intensive care contributed to gradual expansion of indications for earlier surgery in severe patients that actually minimized mortality without surgery.

We found some features characterizing quality of work of the Burdenko National Research Center of Neurosurgery regarding treatment of patients in acute period of SAH over the past 13 years. First of all, postoperative mortality is still being decreased for the estimated period. Mean mortality rate is 3.2% in recent years. At the same time, the number of patients discharged in a vegetative state and with severe neurological defects is increased. As in the first period, there is a relatively high postoperative mortality in patients undergoing surgery within 3 days after SAH although this value is also significantly decreased especially in the third period (20, 17 and 6.8%, respectively).

Further comprehensive analysis and comparison of various groups of patients are required to identify the causes of reduced postoperative mortality and structure of neurological deficit followed by disability. However, some of these factors are clear now. Thus, intraoperative methods include complete rejection of controlled arterial hypotension, the use of fractional temporary preventive clipping of supplying arteries, routine intraoperative control of arterial blood flow (contact Doppler ultrasound, flowmetry, intraoperative fluorescence angiography). All these methods deserve a special analysis. Rejection of lumbar drainage to reduce intraoperative brain tension and more common use of intraoperative and postoperative external ventricular drainage should be also emphasized. We have specified the indications for decompressive craniotomy for the last few years. On the one hand, this reduced the number of these procedures. On the other hand, we obtained...

Significant changes have occurred in intensive care of patients after neurosurgery. Multimodal monitoring includes intracranial pressure control in almost all severe patients. Infusion of nimotop was replaced by administration of tablets considering possible hypotension. We completely abandoned 3-H therapy in favor of the concept of adequate brain perfusion control. This approach is currently recognized as the main tactic for the treatment of the consequences of VS [8—10]. Treatment of VS is also characterized by certain changes including the use of intraarterial and intracisternal infusion of verapamil. According to preliminary data, these methods can significantly reduce the consequences of this serious complication in case of correct indications, dates and monitoring methods [4, 10].

Changes in infectious safety protocols for intensive care units significantly reduced the

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"Fig. 6. Number of operated patients and postoperative mortality in 2006—2018."
incidence of serious infectious complications including meningitis and meningoventriculitis as the most common previous causes of postoperative mortality. The number of ventilator-associated infectious complications was also decreased.

One of the unresolved problems is a rare use of endovascular treatment in acute stage of SAH. The number of these procedures is less than 8% at the Burdenko National Research Center of Neurosurgery although this approach is more common in foreign and national practice [14—19]. The reasons of rare application of endovascular procedures in our clinic should be discussed considering available algorithms for choosing the treatment strategy [20] and significant experience of endovascular occlusion of aneurysms in our center [21].

An extremely important problem is increased incidence of vegetative state as the outcome of treatment. It should be noted that we analyzed only in-hospital results in this report. Final conclusion about the outcomes in these patients may only be made after analysis of long-term results, which are significantly better than the early ones as a rule.

Conclusion

Surgical treatment of patients with cerebral aneurysms in acute period of subarachnoid hemorrhage did not aggravate the outcomes regardless severity of condition and dates of hemorrhage. In contrast, postoperative mortality rates are steady declined. We associate this fact with certain changes in the management of these patients. In particular, we hope for new approaches to the treatment of vasospasm as a leading cause of adverse outcomes. However, more definite conclusions will be made after analysis of the respective groups of patients.

Authors’ participation:
Concept and design of the study — Sh. Sh.
Statistical analysis — D.N.
Writing the text — Sh.Sh., O.B., Yu.V., D.N.
Editing — Sh.Sh., O.B.

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Commentary

The article is devoted to the treatment of intracranial aneurysms (IA) as an urgent medical problem. Currently, methods of clipping and endovascular coiling of aneurysms are well known and widely described. One of the common issues is surgical strategy in patients with ruptured IA in acute period of subarachnoid hemorrhage (SAH) because surgery early after SAH may be accompanied by high mortality and disability rates. Vasospasm (VS) is one of the serious complication in acute period of SAH. Interventions in patients with significant VS are associated with advanced risk of cerebral ischemia and neurological deficit, low postoperative rehabilitation potential. However, follow-up of critically ill patients is inevitably associated with the risk of recurrent ruptures and high mortality in these patients. The authors rightly emphasize that evolution of the treatment of these patients has gone through several historical stages. Development of open and endovascular interventions and undifferentiated approach to indications for surgery were followed by rethinking the adverse outcomes in critically ill patients (Hunt — Hess grade III— V) with VS, delayed interventions, improving the quality of preoperative examination, neuromonitoring and perioperative management. Essential stages were development of various approaches for VS and cerebral ischemia and early rehabilitation of patients. The final stage is early surgical strategy again regardless VS and cerebral ischemia.

Evaluation of the outcomes is also a controversial issue for national neurosurgeons, since there are various definitions of duration of acute period of SAH. Thus, acute period of SAH is usually determined as 21 days in federal institutions. These centers performed these interventions in elective and delayed manner for the first time. In regional and emergency hospitals, acute period is recognized as 14 days after SAH. Various interpretations are probably due to different logistics and dates of hospitalization of these patients. Of course, patients with SAH are primarily hospitalized to municipal hospitals (including therapeutic institutions). In recent years, a significant increase of the number of surgical occlusions of IA has been noted in the Russian Federation (9384 operations in 2018, V.V. Krylov). Development of new federal neurosurgical centers and regional vascular centers became essential to ensure specialized surgical care in patients with SAH in the regions without risks associated with transportation. Time period until surgical intervention was also reduced. However, regular monitoring and comparison of the outcomes in various hospitals are necessary in order to ensure quality of treatment. Therefore, this research is undoubtedly necessary and timely.

The authors evaluate treatment outcomes in acute period of SAH for various periods at the Burdenko National Research Center of Neurosurgery and note significant decrease of postoperative mortality. The outcomes of treatment are analyzed depending on dates of SAH, severity of hemorrhage, Hunt — Hess grade. These data are very interesting. Nevertheless, it is noteworthy that patients with SAH undergoing surgery within 3 days after hemorrhage account only 1/5 of all patients admitted to the Burdenko National Research Center of Neurosurgery. Mortality rate is still the highest in these patients. The authors emphasize the changes in the treatment and prefer early occlusion of the aneurysm even in critically ill patients.

In my opinion, more comprehensive description of in-hospital logistics in acute period of SAH, risk factors of adverse outcomes, incidence of VS and management of this complication would be desirable in further reports. In general, the article makes a favorable impression. Undoubtedly, the authors raised an actual and interesting question — treatment of patients in acute period of IA rupture. An experience of the Burdenko National Research Center of Neurosurgery as one of the oldest neurosurgical institutions of the country is extremely important for motivation to improve own results and compare the results in various neurosurgical departments.

V.A. Lukyanchikov (Moscow, Russia)
Visual field disorder after surgery of temporal lobe epilepsy associated to hippocampus sclerosis

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ABSTRACT

Objective — assessment of frequency and severity of visual field disorders after neurosurgical operations at patients with pharmacoresistant form of epilepsy in hippocampus sclerosis.

Material and methods. The study included 48 patients having surgical operations for a pharmacoresistant form of temporal lobe epilepsy due to hippocampus sclerosis. Anterior lobectomy with amygdalohippocampectomy (LE + AHE) was performed in 25 patients; Selective amygdalohippocampectomy (SAHE) was performed in 23 patients. We evaluated both the frequency of cases of homonymous visual field disorders and their severity.

Results. After surgery the normal visual field was preserved at 7 (14.6%) patients. The appearance of visual field disorder by the type of homonymous hemianopsia was observed at 41 (85.4%) patients. When assessing the severity of visual field disorder, the smallest disorder was at patients who underwent sub-temporal access of SAHE: a statistically significant difference in the frequency of severe visual field disorder was revealed when comparing this group with patients having LE + AHE (p<0.02), as well as with patients having SAHE with access through sylvian gap (p<0.02).

Conclusion. SAHE with sub-temporal access allows maintaining or minimally injuring the central optic neuron fibers, including the Meyer loop at patients operated for symptomatic temporal lobe epilepsy.

Keywords: hippocampus sclerosis, visual field.

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Abbreviations
LE + AGE — lobectomy with amygdalohippocampectomy
SAGE — selective amygdalohippocampectomy

It is known that 30—40% of patients with symptomatic temporal lobe epilepsy are unresponsive to drug therapy and require surgical treatment with resection of the source of seizures [1]. However, postoperative visual field impairment (homonymous hemianopsia) is common due to injury of the visual pathway, primarily Meyer’s loop (Fig. 1).

According to the literature, incidence of visual field impairment varies from 15 to 100% [2—8]. One of the problems for neurosurgeon is choice of surgical approach followed by minimal injury of the visual pathways in the temporal lobe. Assessment of incidence and severity of visual field impairment by ophthalmologist after temporal epilepsy surgery is essential to select the optimal neurosurgical strategy and improve quality of life.

The purpose of the study was analysis of the incidence and severity of visual field impairment after neurosurgical operations in patients with a pharmacoresistant epilepsy and hippocampal sclerosis.

Material and methods

The study involved 48 patients who underwent surgery for symptomatic pharmacoresistant temporal lobe epilepsy due to hippocampal sclerosis. Patients with normal preoperative visual field were included only.

Lobectomy with amygdalohippocampectomy (LE + AGE) implied resection of medial temporal complex and anterior part of the temporal lobe up to 4 cm from temporal pole. This procedure was performed in 25 patients through conventional pterional approach (Fig. 2).

Selective amygdalohippocampectomy (SAGE) was performed in 23 patients. Two approaches were applied
in these cases: sub-temporal (14 operations) and transsylvian approach (9 operations). Minimally invasive approach through a 14 mm burr hole prevailed in patients who underwent sub-temporal surgery.

All patients underwent neurological examination and magnetic resonance imaging of the brain. Pre- and postoperative ophthalmological examination included analysis of visual acuity and visual fields, ophthalmoscopy, tonometry, biomicroscopy. Visual field was studied by automatic static perimetry using Humphrey II-730 analyzer (Humphrey Instruments Inc., USA) and Threshold test Central-30-2 program. Moreover, manual kinetic perimetry using Forster perimeter with a white 5 mm object was also applied.

Patients were divided into 3 groups depending on severity of visual field impairment and the type of homonymous hemianopsia. Severity was graded in the following fashion: grade I — incomplete upper quadrant homonymous hemianopsia (at least 20° from fixation point are preserved); grade II — upper quadrant homonymous hemianopsia (less than 20° from fixation point are preserved or complete loss of the upper quadrants); grade III — loss of the upper homonymous quadrants and narrowing of the lower quadrants (Fig. 3).

Results

Intact visual field after surgery was noted in 7 (14.6%) patients. Visual field impairment occurred in 41 (85.4%) patients including grade I in 28 (58.3%) cases, grade II in 10 (20.8%) cases, grade III in 3 (6.3%) cases (Fig. 3).

No significant correlation between the incidence of visual field impairment and type of surgical intervention or surgical approach was found (p>0.05). Negative changes of visual fields were observed in the majority of patients (22 out of 25) who underwent LE + AGE. Visual aggravation also occurred in 10 out of 14 patients who underwent SAGE through sub-temporal approach and in 9 patients after SAGE through transsylvian approach.

We analyzed severity of visual field impairment depending on the features of surgical intervention. In 16 (64%) out of 25 patients, LE + AGE was followed by the absence (3) or mild (grade I) visual field impairment (13). Severe visual field disturbances were detected in 9 (36%) patients of this group (grade II — 7 cases, grade III — 2 patients).

Visual field impairment grade I occurred in 5 (55%) out of 9 patients who underwent SAGE through transsylvian approach. Severe visual field disturbances were revealed in 4 patients (grade II — 3 patients, grade III — 1 patient).

Incidence of severe visual field impairment was similar after LE + AGE and SAGE through the Sylvian fissure (p>0.05).

Mild disorders were observed after SAGE through sub-temporal approach. There were no visual field defects in 4 out of 14 patients, visual impairment grade I was noted in 10 cases. There were significant differences in the incidence of visual field impairment after SAGE and LE + AGE (p<0.02). Similar data were obtained in comparison with SAGE through the Sylvian fissure (p<0.02).

Data on severity of visual field impairment after various operations are shown in the table.
Discussion

Optic radiation is a part of central neuron of optic pathway connecting lateral geniculate nucleus and primary visual cortex of the occipital lobe. Optic radiation in each hemisphere is a representation of the same (right or left) halves of the retina of both eyes. Lesion of this area results visual field loss (homonymous hemianopsia from the opposite side).

In 1907, A. Meyer [9] showed that visual radiation is divided into 3 beams: upper (or posterior), lower (or anterior) and central (Fig. 1).

In accordance with anatomical studies [10] and tractography [11], upper and central bundles pass backward through the temporal and parietal lobes and reach occipital lobe. Lower bundle (so-called Meyer’s loop) first passes forward and upward, circumflexes temporal horn of the lateral ventricle, turns outward and backward, merges with upper and central bundles and reaches primary visual cortex.

Central beam carries information from the central retina. Upper bundle of optic radiation of each hemisphere is a representation of the upper retinal unilateral quadrants in both eyes. Accordingly, these beams transmit information from the lower contralateral retinal quadrants. Lower bundle of optic radiation (Meyer’s loop) of each hemisphere is a representation of the unilateral lower retinal quadrant. Injury of the Meyer’s loop causes upper quadrant homonymous hemianopsia on the contralateral side. Meyer’s loop topography was studied in detail by U. Ebeling and H.J. Reulen [10]. The distance from the temporal lobe pole to the Meyer’s loop varies from 22 to 37 mm (mean 27 mm). Meyer’s loop may be located up to 10 mm anterior and 5 mm posterior to the temporal horn of the lateral ventricle. Topographic variability of the Meyer’s loop complicates surgical planning in patients with symptomatic temporal lobe epilepsy and increases the risk of visual pathway injury.

According to the literature, incidence of visual field impairment after surgery for symptomatic temporal lobe epilepsy varies from 15 to 100% [2—8, 12]. In our study, visual field impairment was observed in 86% of patients.

It is noteworthy that various methods are used for analysis of visual fields including kinetic perimetry on the Goldmann perimeter [2, 12, 13], automatic static perimetry [14—19]. Comparison of the results obtained by various methods is not entirely correct. For example, H. Manji and G.T. Plant [13] analyzed patients after surgery for symptomatic temporal lobe epilepsy. Kinetic perimetry on the Goldmann perimeter revealed upper quadrant homonymous hemianopsia in 13 out of 24 patients, binocular Esterman visual field test on the
Humphrey analyzer — in 11 out of 24 patients. A.T. Steensberg et al. [18] compared the Damato Multifixation Campimetry Online (DMCO campimetry) with automatic static perimetry on the Humphrey analyzer (program 30-2, SITA). The authors unambiguously preferred the last one as the “gold standard” of perimetry. H. Rick et al. [14] suggested quantitative assessment of visual field impairment after anterior temporal lobectomy using automatic static perimetry.

We examined visual fields by automatic static perimetry using Humphrey II-730 analyzer (Humphrey Instruments Inc., USA) and Threshold test Central-30-2 software program and manual kinetic perimetry using Forster’s perimeter. Automatic static perimetry with Threshold test Central-30-2 program is valuable to analyze visual field defects of various depths and examine in detail central visual field within 30°. Manual kinetic perimetry is used to determine the maximum visual field from the temporal side (up to 90°) in horizontal meridian.

There are 2 surgical procedures for temporal lobe epilepsy: anterior temporal lobectomy (with modifications) and SAGE through various surgical approaches.

Literature data on the incidence of homonymous visual field impairment depending on certain type of surgery for symptomatic temporal lobe epilepsy are contradictory. Anterior temporal lobectomy resulted visual field defects in 50—90% of cases [12, 13, 15—17, 19, 20]. In case of SAGE, this value ranges from 25 to 78% [12, 21—23]. Some authors prefer SAGE over anterior lobectomy regarding the incidence of postoperative visual field impairment [12, 15, 23], while others do not find significant differences [5, 24].

D. Delev et al. [21] analyzed incidence of visual field impairment after SAGE through various approaches. It was found that temporal-basal approach is followed by normal visual fields in 46% of patients, SAGE through transsylvian approach — in 13% of patients.

We did not find significant differences in the incidence of visual field impairment after LE + AGE, SAGE through transsylvian approach and SAGE through sub-temporal access.

However, SAGE through sub-temporal approach resulted the absence or mild (grade I) visual field impairment (homonymous hemianopsia). Severe visual disorders (grade II and III) were significantly more common after LE + AGE and SAGE through transsylvian approach. These data indicate the importance of assessing not only the incidence of visual field defects, but also their severity.

Available driver’s license is reported to be the criterion of the quality of life after surgery for symptomatic temporal lobe epilepsy in various publications [9, 12, 14, 17, 21]. European requirements in visual field for driving license are as follows: “horizontal visual field should be at least 120°, the extension should be at least 50° left and right and 20° up and down, no defects should be present within a radius of the central 20 degrees” [25].

In the Russian Federation, Decree of the Government of the Russian Federation dated December 29, 2014 No. 1604 “On lists of medical contraindications, indications and restrictions for driving” entered into force on January 6, 2015. According to this decree, driving is not allowed in case of narrowing of the visual field by more than 20° for any meridian [26].

Our gradation of visual field impairment is valuable to assess visual disorders for driving license acknowledgement. So, visual field impairment grade I

---

**Fig. 3. Evaluation criteria for homonymous visual field impairment (automatic static perimetry).**

- a — grade I: incomplete upper quadrant homonymous hemianopsia (field within at least 20° from fixation point is intact);
- b — grade II: upper quadrant homonymous hemianopsia (less than 20° from fixation point are preserved or complete loss of the upper quadrants);
- c — grade III: loss of the upper homonymous quadrants and narrowing of the lower quadrants.
Surgical procedure and postoperative visual field impairment in patients with symptomatic temporal lobe epilepsy

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Norm</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>In all</th>
</tr>
</thead>
<tbody>
<tr>
<td>LE+AGE</td>
<td>3</td>
<td>13</td>
<td>7</td>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>SAGE through subtemporal approach</td>
<td>4</td>
<td>10</td>
<td>—</td>
<td>—</td>
<td>14</td>
</tr>
<tr>
<td>SAGE through transsylvian approach</td>
<td>—</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>In all</td>
<td>7</td>
<td>28</td>
<td>10</td>
<td>3</td>
<td>48</td>
</tr>
</tbody>
</table>

Note. LE + AGE — lobectomy with amygdalohippocampectomy; SAGE — selective amygdalohippocampectomy.

does not affect quality of life and patients have no restrictions for driving license acknowledgement. Visual field impairment grade II and III aggravates quality of life and driving is prohibited in these patients.

B. Schmeiser et al. found that driving is not allowed in 48% of patients after surgery for temporal lobe epilepsy due to visual field impairment. According to the authors, this value is 58% after standard anterior lobectomy, 43% after anterior temporal or keyhole resection, 48% after amygdalohippocampectomy through transsylvian approach and 21% after amygdalohippocampectomy through sub-temporal approach [12].

According to Delev D. et al., driving was not contraindicated in 67% of patients after SAGE through temporobasal approach and in 33% of patients after SAGE through the Sylvian fissure [21].

In our study, 70% of patients could drive a car after surgery for temporal lobe epilepsy in accordance with Russian and European requirements. No patient had restrictions for driving in visual field criteria after SAGE through sub-temporal approach. At the same time, 36% of patients after LE + AGE and 44% of patients after SAGE through transsylvian approach did not receive driving license.

**Conclusion**

Diagnosis and analysis of causes of visual field impairment after surgery for symptomatic temporal lobe epilepsy is essential to choose optimal surgical strategy. Selective amygdalohippocampectomy through subtemporal approach is associated with minimal trauma of visual pathway including Meyer’s loop. This minimizes postoperative visual field impairment and results higher quality of life.

**Authors’ participation:**

Concept and design of the study — N.M.
Collection and analysis of data — N.M., D.I., E. S.
Statistical analysis — N.M.
Writing the text — N.M., D.I.
Figures — D.I.
Editing — D.I., N.K.

The authors declare no conflict of interest.

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6. https://doi.org/10.1093/brain/awb449
10. https://doi.org/10.1212/WNL.53.1.167


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Surgical treatment of pharmacoresistant temporal lobe epilepsy due to hippocampal sclerosis has been successfully developed for the recent years. At the same time, resection of epileptic focus should not impair quality of life of patients. Postoperative visual field impairment including homonymous hemianopsia forces us to look for surgical approaches without injury of central visual pathway, especially the Meyer’s loop. The authors of this article analyzed incidence and severity of visual field defects after surgery for hippocampal sclerosis depending on the type of surgical intervention: lobectomy with amygdalohippocampectomy, selective amygdalohippocampectomy through sub-temporal approach and transsylvian approach. It was shown that selective amygdalohippocampectomy through sub-temporal approach is associated with the absence or minimal injury of the Meyer’s loop. In my opinion, this report is a good example of collaboration of neurosurgeons and ophthalmologists for development of optimal treatment strategy. This article will be very interesting for readers of our journal.

V.A. Lazarev (Moscow, Russia)
Modern aspects of surgical treatment of nasal liquorrhea with localization of defect in frontal sinus

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ABSTRACT
Defects localized in the frontal sinus are difficult for surgical treatment, since there is a large number of anatomical variations in the structure of the naso-frontal canal and the sinus itself. With the development of endoscopic technology and paying attention to the modern tendency of minimal invasive surgery, new invasive approaches to reach frontal sinus, such as endoscopic approach according to Draf I—III and combined approaches were developed and put into practice.

Objective — to summarize and to analyze the results of treatment of nasal liquorrhea with localization of the defect in the frontal sinus using endoscopic endonasal and combined intra-extranasal approaches.

Material and methods. A retrospective analysis of a series of 43 cases of nasal liquorrhea with a frontal sinus defect being treated at the NMRCN Burdenko during the period from 2001 to 2017. To select access, a classification of frontal sinus defects according to their localization was developed. The analysis of demographic and clinical data of patients, as well as intraoperative and post-operative data analysis were done.

Results. In the series of 43 patients, endoscopic endonasal approach was performed in 28 (65%) cases. Combined approach was performed at 15 (35%) patients. The success rate of plastic surgery with endoscopic endonasal approach was 86% (24 of 28), with combined approach — 93% (14 of 15).

Conclusions. Endoscopic endonasal and combined approaches are the methods of choice for plastic surgery of defects of the skull base in the frontal sinus as they are effective and safe. The choice of approach depends on anatomical features of the frontal sinus and on the localization of defect.

Keywords: nasal liquorrhea, naso-frontal pocket, frontal sinus, skull base surgery, endoscopic endonasal surgery.

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Abbreviations
NL — nasal liquorrhea
CT — computed tomography
CTCG – computed cisternography
MRI — magnetic resonance imaging

Nasal liquorrhea (NL) is a cerebrospinal fluid leakage to nasal cavity or paranasal sinuses associated with congenital or acquired skull base and meninges defects. Causes of these defects may be different. Frontal sinus is the rarest localization of skull base defects (10—15%) accompanied by nasal liquorrhea. For example, cerebrospinal fistulas in cribriform plate are found in 35—39% of cases, roof of ethmoidal labyrinth — in 29—39%, in sphenoid sinus — 15—26% of cases [1, 2]. Traumatic (including iatrogenic) defect of frontal sinus followed by NL is observed in 30—75% of cases, spontaneous defect — 25—35% [3].

Frontal sinus defects are a difficult problem for surgeons, since there are a large number of anatomical variations in the structure of nasofrontal duct and sinus per se [4]. Historically, neurosurgeons closed these defects using trans-frontal-sinus approach with bicoronal incision [5].

Considering development of endoscopic technology and modern surgical tendency to minimal invasiveness, new approaches to frontal sinus were
developed such as Draf I—III endoscopic approach and combined approaches [6]. Combined approach implies endoscopic approach through the nasofrontal sinus and external frontotomy through anterior wall of the frontal sinus. According to recent reports, combined and endoscopic endonasal approaches result successful repair in 95—97% of cases with minimum complication rate and faster postoperative recovery [7]. Sample size was 5—46 in above-mentioned articles. However, clear practical recommendations for the treatment of these patients are still absent [8, 9].

Currently, the choice of surgical approach and postoperative outcomes are based on surgeon’s experience, equipment, anatomical features and localization of cerebrospinal fluid fistula. This is due to the absence of clear recommendations and standards [10].

The purpose of the study was to summarize and analyze the results of the treatment of frontal sinus defect followed by NL using endoscopic endonasal and combined intra- and extranasal approaches.

Material and methods

There were 430 NL patients who were operated at the Otorhinolaryngology Department of the Burdenko National Medical Research Center of Neurosurgery for the period from 2008 to 2018. Frontal sinus defect was observed in 43 (10%) patients.

A retrospective analysis was based on medical records data of these patients. Demographic characteristics (gender, age), clinical data (etiology of NL, symptoms, X-ray features, complications of NL), localization of the defect (nasofrontal duct, medial, median, lateral) and its dimensions (≥ 5 mm; <5 mm), features of treatment (surgical approach, plastic materials, lumbar drainage, navigation) were analyzed. The outcomes were assessed considering recurrence and complication rate. Follow-up period ranged from 1 month to 10 years (median 4.5 years). Literature data were reviewed for comparison with our results.

In our work, we used KARL STORZ endoscopic system (Germany). This system includes a monitor, HD video camera and halogen light source. A 4 mm rigid endoscopes with various angles (0°, 30°, 45°), mono- and bipolar cautery and a drill were also intraoperatively used. We used Medtronic Fusion navigation system (Medtronic Navigation, Ireland). Standard and angled endoscopic instruments were applied for manipulations inside the frontal sinus.

We used 2 approaches for skull base defect localized in frontal sinus: endoscopic endonasal (28 cases) and combined accesses (endoscopic endonasal combined with supraorbital transfrontal approach through an external skin incision within the eyebrow and anterior wall of frontal sinus, n=15).

Localization and dimensions of the defect, pneumatization of frontal sinus were considered to determine the type of surgical approach. Preoperative analysis of nasofrontal recess using high resolution computed tomography (CT) data was mandatory considering possible presence of different cells (agger nasi, frontal bulla, suproorbital and suprabullar cells) and 4 types of their localization [11, 12].

We classified frontal sinus defects depending on their localization in order to choose optimal approach (Fig. 1). Three groups of defects were distinguished. Group I — medial defects (fistulas in nasofrontal recess and injury of posterior wall of the frontal sinus up to the line drawn through lamina papyracea); group II — intermediate defects (defects of posterior wall of the frontal sinus between the lines drawn through lamina papyracea and middle of the orbit); group III — lateral defects (all injuries of posterior wall of the frontal sinus located lateral to the line drawn through middle of the orbit).

Surgical approach was selected in accordance with this classification.

Draf IIA endoscopic endonasal approach was used for medial defects. In case of this access, uncinated process was identified using endoscope 0°. Resection of this process within its attachment was followed by excision of mucous membrane remnant using a shaver. Ethmoid bulla and ethmoid labyrinth were dissected. These measures resulted favorable visualization and free manipulation within frontal recess and anterior parts of ethmoid labyrinth roof. Opening of frontal sinus was found using endoscope 30° and angled probe 90°. Anterior bone structures of the frontal recess were excised using a burr or Kerrison nippers to improve visualization. Complete dissection of bone cells around frontal sinus opening was followed by visualization of posterior wall of the frontal sinus as a rule. Ethmoid cells (agger nasi) protruding into the frontal sinus were also excised.

Endoscopic endonasal approach (Draf IIB) was used for intermediate defects. Resection of the frontal sinus from lamina papyracea to middle nasal concha resulted maximum exposure of the frontal sinus from one side. Combined approaches were less
common, for example in patients with hyperpneumatization of the frontal sinus (high localization) and/or large defect.

We did not use frontal sinusotomy type III (Draf III) due to unreasonably traumatism of this access and no bilateral defects in our sample.

Combined approach (endoscopic endonasal and supraorbital access through an external skin incision within the eyebrow) was always used for lateral defects because endoscopic endonasal approach could not provide adequate visualization and repair.

Above-described endoscopic approach was first performed for adequate postoperative drainage of the sinus. Next, we cut through skin and soft tissues along the superciliary arch. An incision was parallel to hair growth direction considering localization of local neurovascular bundles (supratrochlear, supraorbital). Soft tissue dissection was followed by drilling anterior wall of the frontal sinus above the defect. Localization of the defect was controlled by navigation system. Then, sinus examination and repair of cerebrospinal fluid fistula were performed under direct control.

Multilayer repair was used in all cases. The first graft was placed intracranially beyond the edges of the defect. The second graft was placed over the fistula with its significant overlap. Reinforcement of repair was achieved using fibrin-thrombin glue. Autografts were adipose tissue, fascia lata, bone and cartilage of nasal septum. Active postoperative care included thorough anemization of mucous membrane and endoscopy-assisted nasal sanation in order to prevent inflammatory complications and cicatrical stenosis of frontal sinus opening.

Results

A sample of 43 patients with frontal sinus defects included 17 (40%) men and 26 (60%) women aged 46 years (range 5—73 years). Spontaneous defects were observed in 19 (44%) cases, iatrogenic defects — in 13 (30%) patients, traumatic defects — in 11 (26%) cases. There were 4 patients with multiple defects (frontal sinus defects combined with defects of cribriform plate and roof of ethmoid labyrinth). NL was predominant symptom in 95% of patients. Previous meningitis was observed in 9 (21%) patients, pneumocephalus — in 8 (19%) patients.

Localization and dimension of the defect were determined using x-ray examination studies. CTCG was performed in 17 (40%) patients. A defect and signs of cerebrospinal fluid leakage into the frontal sinus were revealed (Fig. 2—4). In 6 (14%) cases, meningoencephalocele was confirmed by CT scan, CTCG scan, magnetic resonance imaging.

Demographic and clinical data of patients are shown in Table 1.

All 43 patients underwent multilayer skull base repair. Reconstruction was performed using fascia lata in 23 (53%) patients and combination of various materials (fascia, fatty tissue) — in 20 (47%) patients. Intraoperative lumbar drainage was applied in 20 (47%) patients. We used lumbar drainage in all patients at the stage of development of NL. Currently, indication for lumbar drainage is benign intracranial hypertension. Intraoperative navigation (Medtronic Fusion navigation system) was used in 22 (51%) patients. All cases, intraoperative navigation was valuable to quickly determine localization of the ostium and sinus defect (Table 2).

In our sample, endoscopic endonasal approach was performed in 28 (65%) cases, combined access — in 15 (35%) cases (Table 3).

Medial defects were found in 16 (37%) patients. Endoscopic endonasal approach was applied in all
these patients. Intermediate defects were detected in 15 (35%) patients. Isolated endoscopic endonasal approach was used in 12 cases, combined access—in 3 cases. Lateral defects were observed in 12 (28%) patients. Combined access was performed in all cases.

Endoscopic procedure was followed by recurrence in 4 cases (success rate 86%). Redo endoscopic endonasal repair was performed in 3 cases, transcranial repair—in 1 case. Transcranial approach was preferred due to tension pneumocephalus and the need for simultaneous removal of previously deployed ventriculo-peritoneal shunt. There were no recurrences after redo surgery. Thus, success rate of endoscopic endonasal repair considering redo procedures was 100%. A complication (mucocele of the frontal sinus) arose in one patient in 3 years after surgery due to cicatricial closure of the opening.

Combined approach was followed by 1 recurrence (success rate 93%) and redo surgery through transcranial access. Transcranial approach was preferred due to continued growth of intracranial osteoma in this patient. Therefore, transcranial approach was justified by simultaneous resection of the tumor and closure of the defect. Postoperative meningitis occurred in 3 (20%) patients. Antibacterial therapy was effective. We associate this complication with impaired somatic state of patients due to previous neurosurgical operations. There were no other complications and cosmetic defects. Rehabilitation was fast.

**Discussion**

There were 430 patients with NL for the period 2008—2018. Frontal sinus defect was observed in 10% of cases. This value is similar to that reported in the world literature, and this localization is the rarest [13, 14]. Repair of cerebrospinal fluid fistula in this area is difficult for several reasons: various anatomical variants of nasofrontal recess and sinus, restriction in the use of nasoseptal flap (due to insufficient length), high risk of stenosis of nasofrontal recess, absence of necessary equipment.

Plastic closure of a defect under "indirect" visibility is a very difficult task. First of all, it is necessary to find this defect. Mucous membrane is excised in the proposed area. Intraoperative navigation greatly facilitates searching process. As soon as defect is clearly visualized, it is necessary to clear bone edges for intracranial insertion of plastic material. Suitable equipment with certain angulation is required for these manipulations. Moreover, a set of different curettes, raspatories, probes and curved suckers is also necessary [15].

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Fig. 2. Computed cisternography.  
a — frontal plane; b — sagittal plane. A defect of posterior wall of the frontal sinus (arrow) is localized medial to the line drawn through cribriform plate.
Currently, 3 approaches for frontal sinus defect followed by NL are reported in the literature. These are transcranial, endoscopic endonasal and combined approaches [16—18].

Transcranial approach is valuable for repair of the defect under direct good visualization. However, this method is traumatic and associated with prolonged hospital-stay and postoperative rehabilitation [19]. This approach may be followed by various complications including intracerebral...

**Fig. 3. Computed cisternography.**

a — frontal plane, b — sagittal plane. A defect of posterior wall of the frontal sinus (arrow) is localized between the lines drawn through cribiform plate and the middle of the orbit.

**Fig. 4. Computed cisternography.**

a — frontal plane; b — sagittal plane; c — axial plane. A defect of posterior wall of the frontal sinus is localized lateral to the line drawn through the middle of the orbit (arrow).
hemorrhage, anosmia, neurological and mental deficiency, keloid scars, facial numbness and mucocele. Therefore, this method is currently recommended for large or multiple defects with recurrence after endoscopic repair [20].

Endoscopic endonasal skull base repair is effective for NL and characterized by lower risk of complications [21]. V. Jones et al. reported effective closure of the defect in 91.9% of cases after initial surgery and in 97.3% of cases after redo procedure [22]. In our research, we used endoscopic endonasal approach in 28 patients. Primary surgery was successful in 86% of patients. There were no recurrences after redo surgery (success rate 100%). According to the literature, this approach may be complicated by injury of anterior and posterior ethmoid arteries with subsequent intraorbital hematoma. We did not observe this complication in our sample. Postoperative stenosis of nasofrontal duct followed by mucocele of the frontal sinus is a common complication. This event was observed in 1 (4%) patient of our sample. It is necessary to ensure patency of frontal sinus ostium and adequate pneumatization of the sinus to prevent this complication. Creation of wide ostium considering anatomical features of certain patient, careful insertion of plastic material and adequate postoperative care for prevention of adhesions are obligatory [9].

Combined intra- and extranasal approach combines advantages of endoscopic and transcranial accesses as it is less traumatic and provides manipulations under direct visualization [23]. However, this approach is recommended for only high lateral defect of the frontal sinus inaccessible for endoscopic closure [24]. Y. Qintai et al. reported closure of the frontal sinus defect through combined approach in 15 patients. There were no recurrences or severe complications in their sample [25].

In our study, success rate of repair via combined approach was 93%. Complications (meningitis in 3 patients) were associated with severe concomitant diseases (diabetes mellitus, cardiovascular disorders) or long ICU-stay after previous advanced neurosurgery. We believe that overall safety of this approach is comparable to endoscopic procedure.

Thus, endoscopic and combined approaches are optimal for repair of complex defects of the frontal sinus. Choice of certain approach should be based on anatomical principle.

V. Patron et al. proposed a classification of frontal sinus defects. The authors identified three types of fistulas depending on their localization: type A (defects of nasofrontal recess), type B (low and medial defects of posterior wall of the frontal sinus), type C (high and lateral defects of posterior wall of the frontal sinus). The authors proposed endoscopic approach (Draf I—II) for defects type A, Draf II—III approach for defects type B and combined or transcranial approach for fistula type C [26].

M. Ankit et al. divide defects of posterior wall of the frontal sinus into two types regarding the plane of cribriform plate. They recommend endoscopic approach (Draf II) for defects located medial to this plate and combined access for more lateral defects [27].

We improved this classification and expanded indications for endoscopic approach. Draf IIA approach to frontal sinus is used for defects of nasofrontal recess and those placed medial to cribriform plate. If the defect is located between the lines drawn through cribriform plate and middle of the orbit, Draf IIB endoscopic endonasal approach is applied. Combined access is advisable for lateral

Table 1. Demographic and clinical characteristics of patients

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>n (% )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), years</td>
<td>46 (5—73)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17 (40)</td>
</tr>
<tr>
<td>Female</td>
<td>26 (60)</td>
</tr>
<tr>
<td>Clinical data, n (%)</td>
<td></td>
</tr>
<tr>
<td>Nasal liquorhea</td>
<td>41 (95)</td>
</tr>
<tr>
<td>Previous meningitis</td>
<td>9 (21)</td>
</tr>
<tr>
<td>Pneumocephalus</td>
<td>8 (19)</td>
</tr>
<tr>
<td>Etiology, n (%)</td>
<td></td>
</tr>
<tr>
<td>Traumatic (including iatrogenic)</td>
<td>24 (56)</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>19 (44)</td>
</tr>
<tr>
<td>CT, CTCG, MRI data</td>
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<tr>
<td>Meningoencephalocele</td>
<td>6 (14)</td>
</tr>
<tr>
<td>CSF leakage into frontal sinus</td>
<td>17 (40)</td>
</tr>
</tbody>
</table>

Note: CT — computed tomography; CTCG – computed cisternography; MRI — magnetic resonance imaging.

Table 2. Features of surgical treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plastic materials</td>
<td></td>
</tr>
<tr>
<td>Fascia lata</td>
<td>23 (53)</td>
</tr>
<tr>
<td>Combination of material</td>
<td>20 (47)</td>
</tr>
<tr>
<td>Additional techniques</td>
<td></td>
</tr>
<tr>
<td>Lumbar drainage</td>
<td>20 (47)</td>
</tr>
<tr>
<td>Intraoperative navigation</td>
<td>22 (51)</td>
</tr>
</tbody>
</table>
defect of the frontal sinus (lateral to the line drawn through the middle of the orbit) [27].

Several case reports and trials involving small samples have been recently published [15, 21, 22, 27, 28—33]. Data of these reports are summarized in Table 4. G. Gerbino et al. described the largest sample (46 cases) in 2000. All patients underwent transcranial surgery. However, high incidence of complications was observed [28].

Various authors report high success rate of repair and fewer complications after endoscopic procedures [15, 21, 22, 25, 29—31]. Combined approach is characterized by safety, high efficiency and low complication rate [22, 29, 30, 33].

Considering small sample size in all reports listed in Table 4, there are currently no clear recommendations for the treatment of frontal sinus defect followed by NL. Therefore, further researches with larger samples and higher evidence base are required.

**Conclusion**

1. Endoscopic endonasal and combined approaches are preferred for repair of skull base defects localized in frontal sinus, since they are effective (success rate 86% and 93%) and safe (complication rate 4—20%).

2. The choice of approach depends on anatomical features of frontal sinus and localization of the defect. Draf IIA approach to frontal sinus is used for defects of nasofrontal recess and those placed medial to cribriform plate. If the defect is located between the lines drawn through cribriform plate and middle of the orbit, Draf IIB endoscopic endonasal approach is applied. Combined access is advisable for lateral defect of the frontal sinus (lateral to the line drawn through the middle of the orbit).

**Authors’ participation:**

Concept and design of the study — E.V., N.A., D.N.
Collection and analysis of data — E.V., N.A.
Statistical analysis — E.V., N.A.
Writing the text — E.V., N.A.
Editing — D.N., D.N., A.D., V.A.

The authors declare no conflict of interest.

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**Table 3. Surgical approaches for frontal sinus defect repair**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Endoscopic</th>
<th>Combined</th>
</tr>
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<tbody>
<tr>
<td>Patients, n (%)</td>
<td>28 (65)</td>
<td>15 (35)</td>
</tr>
<tr>
<td>Type and localization of defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial defects, n (%)</td>
<td>16 (37)</td>
<td>—</td>
</tr>
<tr>
<td>Intermediate defects, n (%)</td>
<td>12 (28)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Lateral defects, n (%)</td>
<td>—</td>
<td>12 (28)</td>
</tr>
<tr>
<td>Recurrence, n (%)</td>
<td>4 (14)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Postoperative meningitis, n (%)</td>
<td>0 (0)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Mucocele of frontal sinus, n (%)</td>
<td>1 (4)</td>
<td>0 (0)</td>
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</table>
### Table 4. World literature data on repair of skull base defect localized in frontal sinus

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Number of patients</th>
<th>Approach</th>
<th>Lumbar drainage, n (%)</th>
<th>Design of the study</th>
<th>Success rate, n (%)</th>
<th>Recurrence, n (%)</th>
<th>Complication, n</th>
<th>Mucocele (1)</th>
<th>Meningitis (1)</th>
<th>Meningitis (3); Mucocele (1)</th>
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<td>G. Gerbin, 2000 [28]</td>
<td>46</td>
<td>Transcranial</td>
<td>No data</td>
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<td>46 (100)</td>
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<td>M. Purkey, 2009 [29]</td>
<td>8</td>
<td>Endoscopic</td>
<td>8 (100)</td>
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<td>8 (100)</td>
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<td>J. Shi, 2010 [30]</td>
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<td>Endoscopic Draf II—III</td>
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<td>12 (92.3)</td>
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<td>C. Roehm, 2011 [31]</td>
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<td>Endoscopic Draf II—III; Combined</td>
<td>—</td>
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<td>4 (17)</td>
<td>4 (17)</td>
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<td>M. Chaaban, 2014 [33]</td>
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<td>—</td>
<td>Prospective</td>
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<td>R. Raj Kumar, 2014</td>
<td>5</td>
<td>Combined; Endoscopic</td>
<td>—</td>
<td>Retrospective</td>
<td>5 (100)</td>
<td>—</td>
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<td>Qintai Yang, 2017 [25]</td>
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<td>Combined; Endoscopic</td>
<td>—</td>
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<td>20 (100)</td>
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<td>J. Javaneh, 2017 [21]</td>
<td>24</td>
<td>Endoscopic (Draf IIb, Draf III, Draf Ia)</td>
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<td>Retrospective</td>
<td>23 (95.83)</td>
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<td>Burdenko Neurosurgery Centre</td>
<td>43</td>
<td>Endoscopic (28), combined (15)</td>
<td>—</td>
<td>Retrospective</td>
<td>23 (95.83)</td>
<td>—</td>
<td>—</td>
<td>—</td>
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</tr>
</tbody>
</table>
REFERENCES

18. Burdenko JT. Journal of Neurosurgery 5, 2019
Surgical treatment of frontal sinus defect followed by nasal liquorhea is analyzed in the article. Undoubtedly, this problem is of practical and scientific interest for otorhinolaryngologists and neurosurgeons. The authors describe not only modern surgical strategy for frontal sinus defect, but also comprehensively reviewed the literature devoted to this issue. This research is absolutely actual and consistent with the current trend of expanding indications for endoscopic minimally invasive interventions.

Original classification of frontal sinus defects based on their localization and applied surgical approach is of greatest interest in this study. This classification is simple, understandable and has a real practical significance for improving the quality of treatment of this disease. Extensive authors’ experience and significant sample size (n=43) were essential to create this classification. As the authors note, significant advantage of these approaches is visualization of median and lateral parts of frontal sinus. However, first of all, characteristics of the defect and anatomical features of the frontal sinus should be considered.


A.Kh. Bekyashev (Moscow, Russia)
Results of surgical treatment of skull-base primary malignant tumors with intracranial invasion

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FSAI «N.N. Burdenko National Medical Research Center of Neurosurgery» of the Ministry of Health of the Russia, Moscow, Russia

ABSTRACT

Objective — of research: analysis of factors affecting life expectancy at patients with primary malignant tumors of anterior and middle parts of the skull base with intracranial invasion.

Material and methods. 139 patients (47 women and 92 men) with primary malignant tumors of the anterior and middle parts of the skull base with intracranial invasion (stage T4 according to TNM classification or stage C according to Kadish classification for estesioneuroblast) were treated at the NMRCN Burdenko for the period from 2004 till 2018. The study was conducted by the method of total sampling. The observations are divided into 2 groups: primarily operated (group I) and repeatedly operated (group II).

Results. The average age in both groups was 50 years. In most (64.7%) cases, the tumor affected the medial sections of the base of anterior and middle cranial fossae, and in 35.3% of cases it was localized laterally. All tumors were classified to T4 stage according to TNM classification or (9 olfactory neuroblastomas) to stage C according to Kadish classification.

Discussion. The impact on life expectancy was largely provided by postoperative radiation therapy, the repeated nature of operation, and the presence of brain infiltration. In the total cohort of patients 5-year OS, 5-year RVS, 5-year-old IDF and 5-year LC were 50.7, 35, 54.2 and 36.4%, respectively. In group I, the medians OS and IDF were equal and amounted to 138.3 months. The median RVS was 43.8 months. 5-year OS equal to 63.6%, 5-year RVS — 40.8%, 5-year-IDF — 64.8%, 5-year LC was up to 65.7%. The survival rate in the analyzed cohort for 1, 2, 3 years was 81.4, 71.8 and 67.8%, respectively. In group II, the treatment results for the group of repeatedly treated patients were significantly worse. There were no cases of 5-year survival. The 1-, 2-, and 3-year survival rates were 59.3, 50.8 and 31.8%, respectively. The median OS was 27.1 months, IDF was 27.1 months, RVS was 18.2 months, and LC was 9.1 months.

Conclusion. The results and analysis of literature justify the feasibility of surgical treatment of patients with malignant tumors of craniofacial localization at T4 stage. The purpose of surgical intervention should be: elimination of the immediate threat to the patient’s life due to edema and dislocation of the brain; the maximum possible removal of tumor tissue (cytoreduction); if possible, the elimination of the most significant symptoms for the patient (pain, nasal breathing disorders, cosmetic defect). If there are special reserves, it is obligatory to include radiation and chemotherapy in the treatment process.

Keywords: skull-base surgery, oncology, skull-base malignant tumors, life expectancy.

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TO CITE THIS ARTICLE:

Abbreviations
OS — overall survival
RFS — recurrence-free survival
DRS – disease-related survival
LC — local control

Patients with malignant craniofacial tumors followed by intracranial spread including invasion of cavernous sinus, internal carotid artery, cranial nerves, dura mater and brain matter were considered inoperable until recently. Theoretical justification for this approach was TNM classification and statement about unadvisable resection of T4 stage tumor. Accordingly, only palliative treatment is often rescribed in these patients after histological verification of the process [1—3].
TNM classification was created when effective adjuvant methods were absent and only radical surgical intervention could significantly affect life expectancy [4]. Current capabilities of chemo- and radiotherapy are comparable or even exceed those of surgical approach [5—7]. Thus, TNM stage of a tumor cannot longer be considered as a factor determining the expediency or inappropriateness of surgical intervention.

Further, a feature of skull base malignancies is intracranial hypertension and brain dislocation due to large intracranial nodes and peritumorous edema in case of intradural spread of the neoplasm. Edema and brain dislocation usually have the greatest impact on life expectancy. Moreover, peritumorous swelling of the brain can result convulsive seizures including status epilepticus that is difficulty controlled by anticonvulsant therapy. Finally, profuse nosebleeds observed in some of these patients may also be life-threatening [8–11]. In these situations, even non-radical surgical intervention may be effective for these severe complications and further adjuvant treatment gives the chance for life expectancy prolongation [12]. It should be borne in mind that median life expectancy of patients with skull base malignancies is significantly higher than in those with high-grade gliomas [13, 14].

Primary skull base malignancies often arise from the mucous membrane of paranasal sinuses. Incidence of lymph nodes metastases of these tumors ranges from 7% for sinonasal carcinoma to 23% for adenocarcinoma (mean 11%). Distant metastases occurred in no more than 19% of cases. The second common tumor is olfactory neuroblastoma (esthesioneuroblastoma). This tumor arises from olfactory epithelial cells and is often characterized by intradural spread, intracranial hypertension and brain dislocation [15, 16]. Incidence of metastases of esthesioneuroblastoma varies from 5 to 45% [17]. Mesenchymal tumors including chondrosarcoma, rhabdomyosarcoma and others are less common [9, 18, 19].

Currently, Burdenko Research Center of Neurosurgery has gained a unique experience in surgical treatment of primary skull base malignancies with intracranial spread.

The purpose of this study was to analyze the factors affecting life expectancy and recurrence-free period after primary and redo surgical interventions in patients with primary malignant tumors of anterior and middle skull base with intracranial spread.

**Material and methods**

There were 139 patients (47 women and 92 men) with primary malignancies of anterior and middle skull base with intracranial spread (stage T4 or Kadish stage C for esthesioneuroblastoma) for the period from 2004 to 2018. All patients were treated at the Burdenko Research Center of Neurosurgery [20]. The study was conducted by the method of total sampling. Inclusion criterion was histological verification of the diagnosis in morphological laboratory of the Burdenko Research Center of Neurosurgery. We analyzed both archival (86) and current (53 cases since 2014) observations. Formalized information including demographic data, complaints, anamnesis morbi, concomitant diseases, clinical picture, magnetic resonance imaging, computed tomography and direct cerebral angiography data and information about treatment was introduced into computer database. Karnofsky index was used to assess social and labor adaptation at various stages of treatment.

We guided by the principle of maximum resection of tumor up to intact tissues considering the statement of “physiological permissibility” (N.N. Burdenko). Major vessels germinated by the tumor were not excised. Brain parenchyma was dissected up to the borders with normal tissue in functionally less significant areas.

Patients were divided into 2 groups in order to identify the most important prognostic predictors for primary and redo procedures and determine optimal treatment strategy in these situations. These were groups of primary (group 1) and redo surgery (group 2).

The following factors were analyzed: gender, age, previous treatment, dura mater invasion, brain matter invasion, involvement of medial parts of anterior and middle cranial fossae, cavernous sinus, internal carotid artery, postoperative complications (including infectious), localization, type of resection and histological characteristics of the tumor, features of adjuvant treatment.

Endpoints of our study were 5-year overall survival (OS), 5-year recurrence-free survival (RFS), 5-year disease-related survival (DRS) and 5-year local tumor control (LC). OS was determined from the date of surgery to death or the last examination, RFS — from the date of surgery to the moment of recurrence and/or distant metastasis or death. LC was evaluated as the period from the date of surgery until recurrence or continued tumor growth.
within the surgical area. DRS was accepted as the period from the date of surgery until death associated with cancer. Mortality from other causes were not considered in this value.

Statistical analysis was performed using R programming language (version 3.4.4) in the IDE RStudio integrated software environment (version 1.1.442). OS and RFS were analyzed using Kaplan—Meyer method. Quantitative variables are shown as mean and standard deviation. Categorical variables are presented in percent. Non-parametric Mann—Whitney test was used to analyze differences of quantitative variables in independent samples. Correlation of categorical variables was evaluated using Chi-square test (χ2) and Fisher's exact test. Between-group differences of OS and RFS were analyzed using the log-rank test. Differences were significant at p-value<0.05.

Results

Characteristics of patients are shown in Table 1. Persons of employment age prevailed. Mean age was 50 years (Fig. 1). In most (64.7%) cases, tumor was localized in medial parts anterior and middle cranial fossae. More lateral placement was found in 35.3% of cases (orbit, middle cranial and/or infratemporal fossae).

Diagnosis was determined and histologically verified within 3 months after initial symptoms in 25 (18%) patients. In other 114 (82%) patients, diagnosis was confirmed later. Histological diagnosis was verified prior to admission in 63 (45.3%) patients. In 29 (20.9%) cases, biopsy was performed in a hospital. Surgery was previously performed in 50 out of 139 patients, radiotherapy — in 11 (7.9%) cases, chemotherapy — in 9 (6.5%) cases, chemo- and radiotherapy — in 19 (13.7%) patients.

Tumors stage T4a were observed in 9 (6.5%) patients, stage T4b — in 121 (87%) patients. Esthesioneuroblastoma stage C according to the Kadish classification was diagnosed in 9 (6.5%) patients. Regional and distant metastases were absent in most cases (58.3 and 59.7%, respectively). Dura mater invasion was found in 99 (75.6%) cases, brain infiltration — in 48 (35.8%) cases (Table 2).

Histological characteristics of tumors are shown in Table 3. Different types of cancer prevailed (squamous cell carcinoma as a rule).

Clinical characteristics of patients are shown in Table 4. The most common symptoms were pain, oculomotor disorders, exophthalmos and olfactory disturbances.

The following surgical approaches were used depending on topographic and anatomical localization of tumor: transnasal — 49 (35.3%) cases, frontobasal — 33 (23.7%) cases, orbitozygomatic — 19 (13.7%) patients, frontotemporal — 14 (10.1%) cases, temporal — 4 (2.9%) patients. Lateral orbitotomy was made in 3 (2.2%) cases, supraorbital approach — in 2 (1.4%) patients, transorbital approach — in 1 (0.7%) case. Combined transbasal + endoscopic transnasal approach was used in 11 (7.9%) patients, frontotemporal + endoscopic transnasal approach — in 1 (0.7%) cases, orbitozygomatic + endoscopic transnasal approach — in 1 (0.7%) patient. En-bloc resection was performed in 1 (0.7%) case. Two-stage resection was applied in 11 (7.9%) patients.

There were no R0-resections in our sample, i.e. macroscopically complete resection of tumor within the intact tissues was impossible in all cases. Combined (transcranial and endoscopic transnasal) approach improved quality of resection. The worst quality of resection was noted for endoscopic procedures (Fig. 2). Between-group differences between significant (p<0.0001).

Survival analysis in the study groups

Overall cohort of patients

Median postoperative OS was 138 months (95% CI 39.7 — 66.2) (Fig. 3).

According to univariate and multivariate analysis, postoperative radiotherapy, redo surgery and brain infiltration were the most significant predictors of survival (Fig. 4, 5). In overall cohort of patients, 5-year OS, RFS, DRS and LC were 50.7, 35.0, 54.2 and 36.4%, respectively.

Group 1

Median OS and DRS were similar (138.3 months). Median RFS was 43.8 months. Overall 5-year survival was 63.6%, 5-year RFS — 40.8%, 5-year DRS — 64.8%, 5-year LC — 65.7%. Postoperative 1-, 2- and 3-year survival rates were 81.4, 71.8 and 67.8%, respectively. There was no significant impact of brain infiltration on survival in these patients (Fig. 6, 7).
### Table 1. Baseline characteristics of patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n=89)</th>
<th>Group 2 (n=50)</th>
<th>Overall cohort of patients (n=139)</th>
<th>p*</th>
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<tbody>
<tr>
<td>Mean age, years</td>
<td>48.55±16</td>
<td>51.30±17.51</td>
<td>49.5±16.55</td>
<td>0.349</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>63 (70.8)</td>
<td>29 (58)</td>
<td>92 (66.2)</td>
<td>0.179</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>26 (29.2)</td>
<td>21 (42)</td>
<td>47 (33.8)</td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3, n (%), months</td>
<td>69 (77.5)</td>
<td>45 (90)</td>
<td>114 (82)</td>
<td>0.108</td>
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<tr>
<td>&lt;3, n (%), months</td>
<td>20 (22.5)</td>
<td>5 (10)</td>
<td>25 (18)</td>
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<tr>
<td>Mean preoperative hospital-stay, days</td>
<td>4.44</td>
<td>5.26</td>
<td>4.73</td>
<td>0.221</td>
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<td>Verification of diagnosis prior to admission:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>20 (22.5)</td>
<td>43 (86)</td>
<td>63 (45.3)</td>
<td>&lt;0.001</td>
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<td>No, n (%)</td>
<td>69 (77)</td>
<td>7 (14)</td>
<td>76 (54.7)</td>
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<tr>
<td>Affected side</td>
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<td></td>
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<tr>
<td>Left, n (%)</td>
<td>13 (14.6)</td>
<td>17 (34)</td>
<td>30 (21.6)</td>
<td>0.028</td>
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<td>Right, n (%)</td>
<td>13 (14.6)</td>
<td>6 (12)</td>
<td>19 (13.7)</td>
<td></td>
</tr>
<tr>
<td>Medial (bilateral) localization, n (%)</td>
<td>63 (70.8)</td>
<td>27 (54)</td>
<td>90 (64.7)</td>
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<tr>
<td>Previous treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No, n (%)</td>
<td>77 (86.5)</td>
<td>21 (42)</td>
<td>98 (70.5)</td>
<td>&lt;0.001</td>
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<tr>
<td>Chemotherapy, n (%)</td>
<td>4 (4.5)</td>
<td>5 (10)</td>
<td>9 (6.5)</td>
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<tr>
<td>Radiotherapy, n (%)</td>
<td>3 (3.4)</td>
<td>8 (16)</td>
<td>11 (7.9)</td>
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<tr>
<td>Chemo- and radiotherapy, n (%)</td>
<td>4 (4.5)</td>
<td>15 (30)</td>
<td>19 (13.7)</td>
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</tr>
<tr>
<td>No data, n (%)</td>
<td>1 (1.1)</td>
<td>1 (2)</td>
<td>2 (1.4)</td>
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</table>

Note. * — significant between-group differences.

**Group 2**

Outcomes were significantly worse in this group. A 5-year survival was absent. Annual, 2- and 3-year survival rates were 59.3, 50.8 and 31.8%, respectively. Median OS was 27.1 months, DRS — 27.1 months, RFS — 18.2 months, LC — 9.1 months. Brain infiltration was unfavorable prognostic factor in this group (Fig. 8, 9).

**Discussion**

Obviously, R0-resection is preferable for malignant tumor. According to our and foreign experience, prognosis is significantly worse in patients with local recurrence after previous surgery [21]. Craniofacial en-bloc resection is optimal, but these procedures are impossible a priori in patients with tumor stage T4. The only en-bloc resection in our sample was not radical due to erroneous preoperative classification of the tumor as TNM stage 3b. En-bloc resection of craniofacial T4 tumor with invasion of cavernous sinus and internal carotid artery proposed by S. Kiyoshi increases the risk of severe hemodynamic complications, requires special surgical skills, and, most importantly, does not significantly improve survival [22, 23].

Palliative or symptomatic treatment is usually recommended in patients with craniofacial and other malignant T4 tumor due to impossible adequate resection. Overall 5-year survival after primary surgery was 63.6% in our sample. Moreover, even redo surgery was followed by median OS of 27.1 months that significantly exceeds the median OS for glioblastoma (19 months) [13, 14, 24, 25].

According to various authors, 5-year OS, RFS, DRS, LC ranges from 16 to 67%, from 55 to 69%, from 24 to 54% and from 41 to 65%, respectively [6, 7, 10—12, 26—34]. It should be noted that some frequently cited reports [6, 7, 17, 26, 27] compared patients with tumors of various TNM stages (T1—T4) within the same group. Therefore, comparison of the authors’ results with our data would be incorrect. To date, there are 3 trials with similar to our inclusion criteria (Table 5) [22, 23, 30].

It should also be borne in mind that brain compression and dislocation due to peritumorous edema in patients with intradural spread and brain invasion are the most important factors influencing survival and discouraging adjuvant treatment. Intradural spread and brain invasion were found in 75.6 and 35.8% of our patients, respectively. The only approach in this situation is surgical treatment...
for elimination of immediate threat to the patient’s life and subsequent radio- and chemotherapy.

Conclusions

1. According to our results and literature data, surgical treatment is advisable in patients with T4 craniofacial malignancies.

2. The objectives of surgery should be elimination of immediate threat to the patient’s life due to edema and dislocation of the brain; maximum possible resection of tumor (cytoreduction). Elimination of the most important symptoms (pain, nasal breathing impairment, cosmetic defect) is desirable if it is possible.

3. Adjuvant radio- and chemotherapy is mandatory if contraindications are absent.
Table 3. Histological types of tumors

<table>
<thead>
<tr>
<th>Histological types</th>
<th>Number of patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinomas of the nasal cavity, paranasal sinuses and skull base</td>
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<tr>
<td>Squamous cell carcinoma</td>
<td>34</td>
</tr>
<tr>
<td>Low-grade cancer</td>
<td>20</td>
</tr>
<tr>
<td>Adenocystic cancer</td>
<td>14</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>13</td>
</tr>
<tr>
<td>Sinonasal low-grade carcinoma</td>
<td>8</td>
</tr>
<tr>
<td>Neuroendocrine carcinoma</td>
<td>6</td>
</tr>
<tr>
<td>Lymphoepithelial carcinoma</td>
<td>2</td>
</tr>
<tr>
<td>Transitional cell carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Neuroendocrine tumors</td>
<td></td>
</tr>
<tr>
<td>Esthesioneuroblastoma</td>
<td>9</td>
</tr>
<tr>
<td>Soft tissue malignancies</td>
<td></td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>6</td>
</tr>
<tr>
<td>MPNST (malignant peripheral nerve sheath tumor)</td>
<td>3</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
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</tr>
<tr>
<td>Fibrosarcoma</td>
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<tr>
<td>Myxofibrosarcoma</td>
<td>1</td>
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<tr>
<td>Epithelioid sarcoma</td>
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<tr>
<td>Myxoid liposarcoma</td>
<td>1</td>
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<tr>
<td>Myoepithelial carcinoma</td>
<td>1</td>
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<tr>
<td>Tumors of hematopoietic tissues</td>
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<tr>
<td>B-cell lymphoma</td>
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<tr>
<td>Lymphoma</td>
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<td>Plasmacytoma</td>
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<tr>
<td>Sinonasal papillomas</td>
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<tr>
<td>Inverted papilloma (with malignant transformation)</td>
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<tr>
<td>Other tumors</td>
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</tr>
<tr>
<td>Osteogenic: osteosarcoma</td>
<td>4</td>
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<tr>
<td>Nasopharyngeal: nasopharyngeal carcinoma</td>
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</tr>
<tr>
<td>Salivary gland tumors: acinar cell carcinoma</td>
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</tr>
<tr>
<td>Pituitary tumors: pituitary carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Skin tumors: basal cell carcinoma</td>
<td>1</td>
</tr>
</tbody>
</table>

Authors’ participation:
Concept and design of the study — V.A.
Collection and analysis of data — I.A., N.V., D.S., V.V., L.V.

Statistical analysis — G.V.
Writing the text — I.A.
Editing — A.V., V.V.

The authors declare no conflict of interest.
Table 4. Clinical manifestations of the tumor

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Group 1 (n=89)</th>
<th>Group 2 (n=50)</th>
<th>Overall cohort of patients (n=139)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative Karnofsky score, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>1 (1.1)</td>
<td>0 (0)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>30</td>
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Note. * — significant between-group differences.

Fig. 2. Type of resection depending on surgical approach.
Distribution of patients (n) depending on surgical procedure is shown in the Table.
Fig. 3. Kaplan—Mayer overall survival curve.

Fig. 4. Kaplan—Mayer overall survival curves after primary and redo interventions.
Survival after primary surgery — blue curve, survival after redo surgery — red curve.

$p = 0.014$
Fig. 5. Kaplan—Mayer overall survival curves depending on brain infiltration.
Overall survival for patients without brain infiltration — blue curve, survival for patients with brain infiltration — red curve.

Fig. 6. Kaplan—Mayer overall survival curves in the group 1 depending on brain infiltration.
Overall survival of patients without brain infiltration — blue dotted curve, survival of patients with brain infiltration — red curve.
Fig. 7. Kaplan—Mayer overall survival curves in the group 1 depending on postoperative radiotherapy.
Overall survival without radiotherapy — red curve, overall survival with postoperative radiotherapy — blue curve.

Fig. 8. Kaplan—Mayer overall survival curves in the group 2 depending on brain infiltration.
Overall survival of patients with brain infiltration — blue curve, survival of patients without brain infiltration — red curve.
**Fig. 9.** Kaplan—Mayer overall survival curves in the group 2 depending on postoperative radiotherapy.

Overall survival of patients with postoperative radiotherapy — blue curve, overall survival without radiotherapy — red curve.

**Table 5.** Survival rates in similar trials

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<th>Authors</th>
<th>Number of patients, n</th>
<th>Overall survival, %</th>
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**REFERENCES**


Commentary

The report of V. A. Cherekaev et al. is devoted to important problem of treatment of patients with craniofacial malignancies. Unfortunately, en-bloc resection is not always possible due to anatomical and topographic features of this area. Therefore, these patients do not often receive medical care that could improve life expectancy and quality of life. The authors reported one of the largest materials in the world practice and demonstrated that life expectancy after primary non-radical surgery exceeds 5 years in most patients. Moreover, this value is 2.5 years even after redo interventions, i.e. patients live significantly longer than those with glioblastoma. Thus, it is obvious that surgical interventions for T4 craniofacial tumors are justified and should be recommended in specialized clinics.

A.M. Zaitsev (Moscow, Russia)
Primary pineal melanocytoma: clinical case and literature review

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FSAI «N.N. Burdenko National Medical Research Center of Neurosurgery» of the Ministry of Health of the Russia, Moscow, Russia

ABSTRACT

Primary pineal melanocytomas are extremely rare pathologies and predominantly are clinically manifested by nonspecific symptoms of a pineal affect, which could be characteristic for tumors of different histological nature located in the same region. Also these tumors differ from other melanocytic tumors by their slow growth and relatively favorable clinical prognosis.

Keywords: melanocytoma, surgery, pineal, primary melanocytoma, pineal region.

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Abbreviations
CNS — central nervous system
MI — marker index
CT — computed tomography
MRI — magnetic resonance imaging

Primary melanocytic tumors of central nervous system (CNS) involve several rare tumors including both benign and malignant neoplastic processes. According to the WHO classification 2016, this group of tumors includes meningeal melanocytosis, melanocytoma, melanoma and melanomatosis. These tumors may be characterized by focal or diffuse growth with spread through the meninges [1].

C. Limas and F. O. Tio first described primary melanocytoma of CNS in 1972 [2]. Meningeal melanocytoma accounts only 0.06—0.1% of all primary brain tumors. The annual incidence is 1 case per 10 million [1]. The absence of clear clinical criteria and inaccuracy of terminology cause the absence of statistically significant information in the world literature regarding the incidence of melanocytomas [1]. To date, only 13—30 cases of these tumors are reported in the world literature [1, 3, 4]. The majority of these neoplasms are localized in thoracic or cervical spine [1].

Primary pineal melanocytoma is an even rarer neoplasm, and, according to the literature, only two cases have been registered [5, 6].

Clinical case

A 67-year-old patient M. was hospitalized to the Burdenko National Research Center of Neurosurgery with complaints of decreased strength in the legs, memory and vision impairment, weakness in the left hand and tremor during squeezing the hand. Initial symptoms (weakness in the left hand) occurred in 2014. The patient turned to neurologist at the place of residence. Neurologist recommended magnetic resonance imaging (MRI) of the brain. Pineal tumor 2.5×1.9×2.0 cm with intensive homogeneous accumulation of contrast agent and no signs of occlusive hydrocephalus were diagnosed. Neurosurgeon recommended follow-up and MRI every 6 months. Until August 2017, the patient felt satisfactory and no MRI signs of tumor progression were observed. Significant clinical deterioration with unsteadiness of gait, impaired vision and periodic urinary incontinence occurred in September 2017. Pineal tumor with occlusive hydrocephalus were diagnosed after control examination (MRI). The patient was referred to the Burdenko National Research Center of Neurosurgery.

At admission, patient’s condition is serious but stable. Neurological examination revealed no signs of intracranial...
hypertension, moderate memory disorders, periodic urinary incontinence, static and gait disorders. There were no clear oculomotor disorders. However, mild symptoms at the level of medial longitudinal fasciculus were not excluded considering patient’s complaints.

MRI data are shown in Fig. 1. Pineal tumor with clear contours and dorsolateral spread to the left was found in axial, sagittal and frontal MR-scans of the brain. Coronal images confirmed close adherence of the tumor to the edge of tentorium on the left (Fig. 1a–c). The tumor severely deformed the midbrain. However, the boundary between the tumor and brain stem was clearly visible (Fig. 1d). Mild peritumorous and periventricular edema was visualized (Fig. 1e). Maximum dimensions of the tumor were 20×26×21 mm.

Excision of tumor of tentorial incisure and upper parts of cerebellar vermis on the left was performed on 19.09.2017 for pineal tumor followed by occlusive hydrocephalus. Surgery was made under endotracheal anesthesia in patient’s sitting position. A linear incision of soft tissues was made in cervical-occipital area along the middle line. Edges of the wound were divorced. Osteoplastic craniotomy over cerebellar hemispheres results exposure of lower edges of the transverse sinuses. Dura mater was moderately tensioned. The sheath was dissected by a semi-oval incision with the base turned to the sinuses. An approach to the pineal area above the right cerebellar hemisphere near tentorial incisure was made. Tentorium was dissected due to the need for access to the tumor. A tumor was found at the proximal parts of rectus sinus. Superficial parts of the tumor were pushed apart by the forceps. This measure was followed by drainage of xanthochromic content from the opened cyst.

black heterogeneous tumor tissue was found at a depth of several millimeters. Peripheral parts of the tumor were represented by melanin accumulations of soft consistency. Wire cutters and ultrasonic sucker were effective for removal of these tissues. Tumor fragments with very dense stroma were found deeper so that microsurgical scissors were required to dissect this tissue. Papillomatous black tissue was also found in tumor stroma. Dissection of tumor in caudal areas and on the left side was the most difficult since neoplasm was practically inaccessible for direct vision. Very intense bleeding occurred at the final stage of dissection. Large arterial vessels were found on posterior pole of the tumor. These arteries were coagulated and intersected. Moreover, there was small well-supplied tumor node on the right side. This fragment was removed only at the end of surgery. Most likely, it was a site of original growth of the tumor (edge of tentorium). This fragment of tumor was carefully coagulated that resulted almost complete hemostasis. Hemostasis was followed by closure of dura mater. Closure of craniotomy and soft tissue suturing in layer-by-layer fashion were performed. The result of urgent biopsy was benign melanomatous tumor (possibly meningioma).

Conclusion of final histological examination: tumor tissue consisting of elongated cells with a tendency to form “nest” structures and focal pigment deposits (Fig. 2a, b). Immunohistochemical examination revealed positive expression of MelanA++ (Fig. 2c, d), S100 ±, HMB 45+ (Fig. 2e), marker index (M1) Ki67 up to 6—7%. Conclusion of intravital histological examination: morphological picture and immune phenotype of the tumor correspond to melanocytoma with increased proliferative activity.

Postoperative period was difficult with neurological deficiency. There were impaired consciousness (sopor), tetraparesis with reduced muscle tone on the left, increased tendon reflexes on the right, severe oculomotor disorders: gaze rotation upwards, divergent strabismus, Magendie’s symptom.

MRI of the brain in T1 mode performed on 21.09.2017 did not reveal residual tumor (Fig. 3a, b). Small ischemic focus in the left upper cerebellar peduncle was visualized in DWI mode (Fig. 3c).

Patient was at the hospital for a long time. Complex therapy was followed by clinical improvement. The patient began to move within the ward and follow the instructions. Vertical gaze rotation and left-sided hemiparesis up to 4 scores were persistent. The patient was transferred to rehabilitation center for further treatment.

**Discussion**

Melanocytoma is a slow-growing benign neoplasm. Maximum incidence is observed in people aged 40—50 years. Melanocytoma is usually localized in cervical and thoracic spine, posterior cranial fossa and Meckel’s cavity. Probably, this is due to higher density of melanocytes in normal meninges in these areas. Histologically, melanocytoma consists of well-differentiated melanocytes with various grade of pigmentation, moderate cellular and nuclear atypia and low proliferative activity (up to one mitosis per 10 visual fields under 400-fold magnification) [6]. Genetically, this type of tumor is characterized by point mutations in GNAQ or GNA11 genes with frequent involvement of codon 209. The same mutations are observed in uveal melanoma cells and blue nevus followed by metastases to central nervous system. The most common cytogenetic rearrangements are deletions of chromosome 3 and long arm of chromosome 6. Markers Melan-A and melanosomal HMB-45 are used for immunohistochemical verification of melanocytoma. The same markers are expressed in CNS melanomas.

Like other melanocytic tumors, primary melanocytic tumors of CNS develop from melanocytes originating from neural crest cells [7]. Melanocyte precursors, so-called melanoblasts, migrate mainly through the dorsolateral pathway during embryonic development and move into skin during the first trimester of pregnancy [8]. Fewer melanoblasts penetrate the mucous membranes of respiratory, digestive and urogenital tracts, inner ear, vascular membrane of the eye and leptomeningeal structures. The highest concentration of melanocytes in leptomeningeal complex is usually observed on
ventrolateral surfaces of the medulla oblongata and around upper spinal cord [9]. Function of melanocytes in these structures is still unclear. The most recognized assumption is that leptomeningeal melanocytes capture toxic cations and free radicals from the bloodstream for their subsequent detoxification [10].

Differential diagnosis of primary melanocytoma includes melanoma of CNS and metastatic melanocytic tumors.

Melanoma is a primary malignancy of central nervous system with the properties of aggressive tumor growth arising from leptomeningeal melanocytes. Primary melanoma of CNS is histologically similar to melanomas of any other localization. Anaplastic spindle-shaped or epithelioid cells forming the structure of loose nests, bundles or having a continuous growth pattern are characterized by variable cytoplasmic expression of melanin. Some melanomas contain large cells with bizarre nuclei, numerous typical and atypical mitotic figures with significant pleomorphism and large nucleoli. At the same time, other melanomas are densely cellular and less pleomorphic, usually consist of tightly packed spindle-shaped cells with a high nuclear-cytoplasmic ratio. Melanomas are more pleomorphic, anaplastic, mitotically active and have a higher cellular density compared with melanocytomas. Moreover, these tumors are often characterized by advanced tissue invasion and coagulative necrosis.

Primary melanomas of CNS also contain GNAQ or GNA11 gene mutations. However, these mutations are less common than in melanocytomas. Tumors with these mutations appear to progress to melanoma similar to uveal melanoma. This tumor is characterized by GNAQ or GNA11 gene mutations as early events of carcinogenesis.
Fig. 2. Histological and immunohistochemical examination of specimen.

a — hematoxylin and eosin staining, magnification × 100. Melanin deposits in melanosomes of tumor cells are shown by the arrows; b — hematoxylin and eosin staining, magnification × 200. Melanosomes with typical ovoid or sometimes polygonal shape (arrows); c — immunohistochemical staining using antibodies to Melan-A antigen labeled with horseradish peroxidase, magnification × 100. Cells with a clear peroxidase marker (arrows); d — immunohistochemical staining using antibodies to Melan-A antigen labeled with horseradish peroxidase, magnification × 400. Significant cytoplasmic accumulation of Melan-A in tumor cells; e — immunohistochemical staining using antibodies to HMB-45 antigen labeled with horseradish peroxidase, magnification × 100. Peroxidase labels on antibodies to this marker, which is expressed on the membrane of melanosomes (arrows).
accompanied by BAP1 inactivation, as well as SF3B1 or EIF1AX mutation as they turn into malignant tumors. Mutations in TERT gene promoter, NRAS, BRAF and KIT genes are common in cutaneous melanomas and metastatic melanomatous foci in CNS. However, these mutations are rare in primary melanocytic neoplasms of CNS in adults. These rearrangements in genome is a sign of metastatic lesion [11].

Genetic characteristics and differences of primary tumors (melanocytomas, melanoma of CNS and metastatic melanocytic tumors) were comprehensively analyzed in a large recent study [12]. It was found that NRAS or BRAF mutations were common in cutaneous melanoma while NF1, RAC1, PIK3CA and ARID1A gene mutation were rarer. Uveal melanomas followed by metastases in CNS were characterized by mutations in GNAQ, GNA11 and BAP1 genes. In contrast, primary melanocytic tumors of CNS almost exclusively showed mutations in GNAQ (71%) or GNA11 (12%) genes. Interestingly, all tumors with GNA11 gene mutation and diagnosis of primary melanocytoma of CNS recurred. Inactivating BAP1 mutation and deletion of chromosome 3 were also shown in one recurrent case. At the same time, deletion of chromosome 3 and BAP1 gene mutation are typical for uveal melanoma as proven markers of poor prognosis in these patients [12].
MRI and CT are used to confirm localization of tumor despite the absence of specific signs for diagnosis of pineal melanocytoma. Melanocytic neoplasms are usually characterized by isodense or hypodense signal, homogeneous contrast accumulation with or without CT-signs of calcification. Preoperative MRI is valuable for diagnosis, assessment of lesion grade and dividing intracranial melanomas into melatonic and amelatonic. Over 10% of cells of melatonic tumors contain melatonin. Paramagnetic properties of melatonin result shortened T1 relaxation period. Therefore, these cells are hyperintensive in T1-weighted images and hypointensive in T2-weighted images. Amelatonic tumors consist of less than 10% of melatonin-containing cells. These cells are hypointensive in T1 mode and hyperintensive in T2 mode [13, 14].

**Conclusion**

Primary pineal melanocytomas are an extremely rare tumors. These neoplasms are predominantly followed by nonspecific symptoms of lesion of this zone. These symptoms are also characteristic for tumors of other histological structure located in this area. These tumors differ from other melanocytic tumors by slow growth and relatively favorable clinical prognosis.

**Authors’ participation:**
Concept and design of the study — A.K., D.P.
Collection and analysis of data — N.G., A.B.
Statistical analysis — A.B., N.G., P.N.
Writing the text — A.B., N.G., P.N.
Editing — A.K., D.P.

**The authors declare no conflict of interest.**
REFERENCES


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Commentary

This report is interesting as a rare case of primary pineal melanocytoma. Melanocytoma is classified as highly differentiated tumor of low malignancy grade and arises from leptomeningeal melanocytes of neuroaxis. Typically, these tumors have spinal localization. However, intracranial (often infratentorial) localization may be observed. A rare case of pineal melanocytoma in a 67-year-old patient is reported in the article. Patient’s complaints, neurological examination, preoperative and postoperative neuroimaging data are described in detail. The authors comprehensively described neurosurgical stages. The site of initial tumor growth (tentorial edge) was revealed. Histological structure of tumor confirmed by immunohistochemical analysis is reported. Positive expression of Mela-A, S100 and HMB-45 biomarkers is pathognomonic for melanocytoma. Complicated postoperative period is explained by localization of tumor, need for coagulation of large arterial vessels in order to stop intense bleeding. Postoperative MRI did not reveal residual tumor. The authors briefly discussed the problem of primary melanocytes and showed the difficulties in their diagnosis before surgery, and more precisely, before histological examination. This report is very informative and interesting for neurosurgeons because it stimulates to search for new optimal ways to improve diagnosis and radical surgical treatment of these rare tumors.

O.N. Dreval (Moscow, Russia)
Hypoglossal schwannoma: literature review and case report

© V.N. SHIMANSKY, K.V. SHEVCHENKO, V.K. POSHATAEV, S.V. TANYASHIN, F.D. ABDURAKHIMOV

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ABSTRACT

Hypoglossal schwannoma is a rare tumor this frequency approximately less than 5% all non-vestibular schwannomas. Also, it may be sign of neurofibromatosis type 2. Usually, the tong deviation in side of the tumor is the first symptom of the disease. When the tumor size is increased, bulbar disorders and cervico-occipital pain are develop. MRI is the main method of diagnostic. Until the 1970s, mortality after surgical removal reached 50% and was due to bulbar and respiratory dysfunctions. Nowadays, the cause of death remains the same. After introduction stereotactic radiotherapy into clinical practice total removal is not necessary. The purpose of surgery stay is removal of intracranial part of the tumor and decompression of the brainstem (subtotal removal). Radiotherapy or radiosurgery is performed on the intracanal fragment of the tumor. The case of successful surgical treatment of a patient with hypoglossal schwannoma is presented in this article. Subtotal removal was performed via median suboccipital approach. Radiosurgery is planned for residual part of the tumor, located in the hypoglossal nerve channel.

Keywords: schwannoma, neuroma, hypoglossal channel, hypoglossal nerve, hypoglossal schwannoma.

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Abbreviations
MRI — magnetic resonance imaging (MRI)
CT — spiral computed tomography

Neurinoma is a benign tumor originating from Schwann’s sheath of cranial and peripheral nerves. Neurinoma (schwannoma) of hypoglossal nerve is a rather rare pathology accounting about 5% of all non-vestibular intracranial neuromas [1–5]. Neurinoma of hypoglossal nerve was first described by De Martel in 1933 [6]. A hypothesis was also put forward in that time that this tumor initially growths from intracanal segment of hypoglossal nerve. This mechanism is similar to that in vestibular neuromas (growth from internal auditory canal is the most common). S.M. Weindling et al. reported 40 patients with lesion of this area. Neurinoma of hypoglossal nerve was observed only in 16 patients, juxta-articular cysts — in 15 cases, osseous cysts of hypoglossal channel — in 9 cases [7]. Tumors may be sporadic (usually) or associated with neurofibromatosis type 2 [5, 7]. The disease is diagnosed at the age of 11—78.5 years (37—56 years as a rule). Neurinoma is slightly more common in women [6, 7].

Typical manifestation of tumor includes deviation and hypotrophy of the tongue. Spread of tumor to the brainstem and upper cervical segments of spinal cord results pain in cervical spine. Destruction of hypoglossal nerve canal, jugular orifice and compression of bulbar nerves are followed by disorders of swallowing and phonation. Compression of brainstem and cerebellum may be accompanied by disturbances of statics and gait, pyramidal insufficiency [1, 3, 5].

Magnetic resonance imaging (MRI) of the brain is the leading diagnostic method. MRI pattern of this tumor is similar to neurinoma of any other localization. MRI clearly visualized several parts of hypoglossal schwannoma at the stage of clinical manifestations. Intracranial part of the tumor is usually located at the level of craniovertebral junction and causes compression of medulla oblongata. Intracranial fragment of tumor is located within the enlarged hypoglossal channel. Extracranial segment leaves the enlarged hypoglossal channel and results compression of internal carotid artery, internal jugular vein, fibers of the first spinal nerves and caudal nerve roots. Spiral computed
tomography (CT) of the brain is useful to evaluate bone anatomy, severity of hypoglossal channel destruction, its relationship with jugular orifice [7]. There are several types of tumor in accordance with classification of hypoglossal schwannoma proposed by A. Kaye (1984):

type A — intradural tumor;
type B — dumbbell-shaped tumor;
type C — extracranial tumor.
Type D is additionally distinguished recently (peripheral hypoglossal schwannoma) [2, 3, 5].

Management is similar to that for schwannoma of other localizations and includes follow-up, surgery and radiotherapy. Follow-up is applied if patient refuses any treatment or in those with small tumor de novo [1, 3, 5].

Retrosigmoid suboccipital, median suboccipital, transcondylar and far-lateral approaches are used in surgical treatment [4, 5]. Until the 70s of the last century, postoperative mortality reached 50% and was caused by aggravation of bulbar symptoms and respiratory failure as a rule. At that time, preoperative tracheostomy was even recommended for these patients [4, 5]. Currently, surgical treatment includes mandatory neurophysiological monitoring of the caudal nerves (IX—XII cranial nerves).

Complete removal of tumor is associated with high risk of adverse outcome even in case of neurophysiological monitoring. Total excision is possible only in case of traumatic transcondylar approach. However, this technique is also not a guarantee of total removal while the likelihood of complications is quite high [3, 5, 6]. Postoperative bulbar disorders occur in 100% of cases. Their severity determines the outcome. These disorders may be transient (dysphonia) and permanent up to the absence of any swallowing and respiratory movements that requires probe nutrition and mechanical ventilation. Subtotal removal of tumor, decompression of brainstem and cranial nerves followed by stereotactic radiotherapy are the most preferable for these tumors [3, 5].

**Case report**

A 43-year-old patient V. was hospitalized to the Burdenko National Medical Research Center of Neurosurgery with complaints of cervical-occipital pain. Pain was predominantly right-sided and occurred 4 months ago.

Clinical examination revealed right-sided deviation of the tongue, mild dysfunction of bulbar nerves without disorders of swallowing, cervical-occipital pain with predominant right-sided localization and irradiation to the right shoulder.

Contrast-enhanced MRI of the brain revealed right-sided tumor near the brainstem originating from the enlarged hypoglossal channel and compressing medulla oblongata. Smaller component of the tumor was located inside the channel and spread extracranially (Fig. 1).

CT in bone mode found enlarged hypoglossal channel with destruction of its walls. Posterolateral wall was practically absent. As a result, there was a communication between the canal and jugular orifice (Fig. 2).

Caudal nerves and corticospinal tract were reconstructed using diffusion-tensor tractography. Compression of corticospinal tract was followed by its left-sided dislocation. Roots of the upper cervical segments of the spinal cord and hypoglossal nerve were placed at the lower pole of the tumor. Deformed glossopharyngeal and vagus nerves were located on the upper pole of the tumor (Fig. 3).

Surgical treatment was preferred. In patient’s prone position, median suboccipital approach with resection of C1 posterior arch and squamous part of occipital bone followed by right-sided lateralization of craniotomy was performed. Dura mater was dissected in an arcuate manner over the right cerebellar hemisphere and brain stem up to CII and fixed on the ligatures. Dissection of arachnoid membrane of the large occipital cistern and cerebellar hemisphere retraction were followed by visualization of encapsulated light yellow tumor with few superficial vessels. Tumor originated from the lateral part of large occipital foramen. Localization of the roots of abducens nerve and CI root was determined after neurophysiological monitoring of cranial nerves on the lower and anterior surfaces.

Separate roots of abducens nerve, glossopharyngeal and vagus nerves were also located on the oral pole. Dissection of tumor capsule was followed by excision of the neoplasm. Tumor looked like a typical neurinoma with dense bleeding stroma. Dissection of the lower part of tumor became possible as soon as tumor dimension was reduced. Vertebral artery and posterior lower cerebellar artery were found under the caudal pole of the tumor. These vessels and nerves were separated from the tumor and this part of the neurinoma was removed. At the next stage, upper part of the tumor was dissected with separation of IX—XI nerve roots. Further, clear dissection plane was found between...
the brain stem and the tumor. Neoplasm was dissected along this plane and removed up to the edge of the large occipital foramen. It was found that bulbar nerves passed into the intact jugular orifice and the tumor spread into enlarged and destructed hypoglossal channel. Searching stimulation was failed to verify the structure of hypoglossal nerve. There were only few positive responses from tumor surface. Most likely, tumor originated from an intracanal portion of hypoglossal nerve.

Multiple roots were visualized under the arachnoid membrane on the anterior surface of the tumor. We obtained responses from the IX—XI cranial nerves and unclear response from the XII nerve. Dissection of intracanal part of the tumor within jugular orifice was accompanied by venous bleeding. Tumor was dense inside the canal and its dissection and aspiration with a vacuum aspirator were not possible. Excision of this part of tumor was refused considering complete resection of intracranial part of the tumor with brain stem decompression. Moreover, intraosseous part of the tumor had no clinical significance while its dissection was associated with advanced risk of complications. Thus, subtotal removal of tumor was performed. Adequate hemostasis was followed by dura mater suturing and closure of craniotomy using bone flap. The wound was sewn in layer-by-layer fashion. Surgical stages are shown in Fig. 4.

MRI of the brain after 3 days revealed residual tumor inside the hypoglossal channel (Fig. 5).

Postoperative neurological examination revealed local pain syndrome, aggravation of bulbar disorders without indications for insertion of nasogastric probe or tracheostomy, mild static and gait disorders.

Histological examination — typical neurinoma. Next, radiotherapy is scheduled for residual intracanal tumor.

**Conclusion**

Hypoglossal neurinoma is a rather rare and poorly studied pathology accounting less than 5% of all non-vestibular neurinomas. Clinical manifestation usually occur in patients with large tumor causing compression of the brain stem and caudal nerve roots. In this regard, surgery is the main method of treatment. Total resection of tumor is difficult and possible only through traumatic transcondylar or far-lateral approaches. Moreover, this procedures are...
accompanied by severe postoperative neurological complications associated with injury of bulbar nerves predominantly. Subsequently, many patients die from brain stem circulatory disorders or concomitant infectious complications.

Effectiveness of stereotactic radiotherapy is slightly inferior to surgical treatment regarding tumor growth control. Need for radical surgery disappeared as soon as stereotactic radiotherapy was introduced into clinical practice. It is especially important if resection is associated with advanced risk of complications and mortality. In our case, we were also guided by this approach to the treatment of the patient. Less traumatic median suboccipital approach with slight lateralization towards the pathological focus was preferred. Subtotal removal of tumor resulted brain stem decompression. Intracranial part of the tumor was completely removed due to well-defined dissection plane between tumor surface and neurovascular structures. Intraosseous residual tumor will be subjected to radiotherapy. This approach is associated with reduced risk of persistent bulbar disorders, better social and labor rehabilitation and postoperative quality of life.

Authors’ participation:
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Statistical analysis — K. Sh., V. P.
Writing the text — K. Sh., V. P.
Editing — V. Sh., S. T.

The authors declare no conflict of interest.
Fig. 4. Surgical intervention in patient V.

a — dura mater dissection over cerebellar hemisphere and brain stem; b, c — neurophysiological monitoring of IX, X, XI cranial nerves; d — hypoglossal neurinoma, one of the roots of XI nerve is on the posterior surface of the tumor (arrow); e — dissection of tumor capsule and reduction of tumor volume; f — dissection and excision of the upper pole of the tumor; g — dissection of the upper medial part of the tumor, IX nerve root is on this segment of tumor (arrow); h — dissection of the lower pole of the tumor (XI nerve and CI roots are on this surface of tumor (arrow)); i, j — dissection of the lower and lower medial part of the tumor (vertebral artery and ostium of posterior lower cerebellar artery — arrows); k — IX, X, XI, XII nerve roots are visualized through the arachnoid membrane after removal of anterior part of the tumor (arrows); l — caudal roots stimulation (response is received from all nerves).
Fig. 5. MRI of the brain in 3 days after surgery.
Contrast-enhanced MRI determines residual tumor inside the hypoglossal canal on the right (arrow).

REFERENCES


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Commentary

Hypoglossal schwannoma with predominant intracranial spread is reported in the article. Hypoglossal neurinomas may be localized near the brain stem and in upper cervical area. In some cases, these tumors may take a dumbbell-like shape. To date, less than 30 case reports of hypoglossal neurinomas have been published that highlights the rarity of this pathology. Specific neurological manifestations are slowly progressive hemiatrophy and deviation of the tongue with fasciculations. Further growth of the tumor results brain stem compression and damage to the nearby cranial nerves. Extracranial hypoglossal tumor is also accompanied by disorders of swallowing and local swelling in upper cervical area. Characteristic diagnostic sign of hypoglossal neurinoma emanating from the intracanal segment of the nerve is enlargement of hypoglossal canal that was demonstrated in the article. In patients with hypoglossal neurinoma followed by compression of the medulla oblongata and bulbar syndrome, the main purpose of surgery is brain stem decompression that was successfully carried out by the authors. In case of intracranial tumor, some authors use an extreme lateral, transcondylar approach facilitating total removal of tumor. The authors’ choice of the median approach with lateralization towards the tumor seems justified, as it provides less traumatic approach along the nuchal line. Moreover, staged intracapsular resection of neurinoma allows timely revealing dissection plane with brain stem, vertebral artery and its branches and cranial nerves. Intracanal tumor may be subsequently subjected to radiotherapy without need for advanced resection because dissection is often accompanied by venous bleeding from the tumor’s vessels and sometimes jugular vein bulb. This case report with brief literature review shows the success of chosen surgical strategy, serves as example of successful solution of difficult clinical problem and emphasizes authors’ professionalism.

Yu.A. Grigoryan (Moscow, Russia)
Transsphenoidal extirpation of pituitary adenomas in patients with McCune—Albright syndrome (two cases from practice and literature review)


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ABSTRACT

Introduction. McCune—Albright Syndrome is a rare genetic disease characterized by the formation of fibrous osteodysplasia foci of various localization, including the bones of skull base. Having a gross lesion of the main bone body and the simultaneous formation of the pituitary adenoma, its transnasal removal becomes very difficult.

Material and methods. Two clinical observations are presented where at patients with the classic manifestation of McCune—Albright syndrome we were able to successfully remove somatotropinomas with endoextrasellar growth. In both cases the presence of visual disorder was the indication for surgery.

Results. Despite pronounced deviations in the anatomy of the skull base bones in both cases we managed to access the Turkish saddle. Removal of the pituitary tumor did not differ from standard surgery. Improved vision after surgery was observed in two patients. Tumors were removed subtotally and clinical and biochemical remission of acromegaly was not achieved. In both cases, the tumors had morphological signs of atypia. Patients continued to receive therapy with somatostatin analogues and radiation.

Discussion. The possibility of performing transnasal surgery in this category of patients using specific instruments and intraoperative navigation is shown.

Keywords: pituitary adenoma, McCune—Albright syndrome, osteofibroma.

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Abbreviations
IGF-1 — insulin-like growth factor 1
MRI — magnetic resonance imaging
SCT — spiral computed tomography
HGH — human growth hormone
DM — dura mater

McCune—Albright syndrome is a hereditary disease characterized by a triad of clinical manifestations: 1) endocrine disorders with premature puberty as the most common symptom; 2) typical skin pigmentation (café au lait); 3) fibrous osteodysplasia.

For the first time, V.R. Braytsev described this syndrome in 1922 in national literature and defined this lesion as "fibrotic tumors". After 16 years, endocrinologist F. Albright formulated signs of disease as "disseminated fibrous osteitis, pigmentation fields and endocrine disorders with premature puberty in girls".

The cause of disease is a somatic mutation of a gene encoding the α-subunit of the G-protein followed by intracellular activation of cyclic adenosine monophosphate (c-AMP). Clinical manifestations depend on the quantity and quality...
of cells mutated at the embryonic stage. Two signs from above-mentioned clinical triad are sufficient for diagnosis [1, 2]. In some cases, patients with McCune—Albright syndrome have various endocrine diseases, in particular, pituitary adenomas. Pituitary tumors are usually HGH-producing adenomas (less common corticotropinoma) with or without concomitant hypersecretion of prolactin. Acromegaly in these patients is usually accompanied by significant HGH hypersecretion [3].

Changes of skeleton bones are often multiple, asymmetric or unilateral in some cases [4]. Fibrous osteodysplasia is often asymptomatic with slow clinical progression. Cranial vault lesion is manifested by severe deformation, orbital lesion—exophthalmos, skull base—symptoms of compression of cranial nerve (including optic nerve), inner ear structures [3]. Lesion of skeleton is often accompanied by pathological fractures. Osteosarcoma in the foci of osteodysplasia develops in less than 1% of cases [1, 5].

Patients with McCune—Albright syndrome are admitted to a neurosurgical clinic mainly with HGH-releasing pituitary adenoma or with mixed type of adenoma producing HGH and prolactin [2]. Drug therapy with somatostatin analogues and/or dopamine agonists is often considered the only treatment option because safe surgery is impeded and even impossible due to common significant lesion of the skull base. Effectiveness and safety of radiotherapy have not been unambiguously determined due to small number of observations and potential risk of irradiation-induced sarcomatous transformation of the affected bones [6, 7]. Symptoms of chiasmal compression (impairment of vision first of all) determines the indications for neurosurgical treatment. Transsphenoidal approach to sella turcica is technically difficult due to severe deformation of sphenoid bone followed by complete absence of anatomical landmarks, impaired orientation, advanced risk of injury of internal carotid artery in case of deviation from the axis of approach [8]. Intraoperative neuronavigation is obligatory for these procedures [9].

Currently, transnasal endoscopic surgery is applied for more than 90% of pituitary adenomas at the Burdenko National Medical Research Center of Neurosurgery. We routinely perform the most difficult transnasal endoscopic procedures thanks to continuous improvement of endoscopic techniques, accumulation of surgical experience and development of modern methods of skull base repair [10—13].

We report the results of transnasal endoscopic surgery for two HGH-releasing adenomas in patients with McCune—Albright syndrome. The main clinical information about the patients is shown in Tables 1—4.

Case report 1

The patient is a 14-year-old adolescent. He was ahead of his peers in growth from an early age. Growth was especially accelerated for the last 3 years. Symptoms of diabetes insipidus (thirst and polyuria) occurred. Recurrent fractures of the left ulna were observed in 2007 and 2008 on the background of diagnosed fibrous dysplasia of the left radius and humerus. In November 2015, surgery was performed for juvenile epiphysiolysis of the head of the left femur. Impaired vision required magnetic resonance imaging (MRI) of the brain in 2015. As a result, HGH-releasing pituitary adenoma was found (Tables 2, 3, Fig. 1).

Examination at the Burdenko National Medical Research Center of Neurosurgery confirmed the following diagnosis: acromegaly, active phase; pituitary adenoma; panhypopituitarism (secondary hypothyroidism, hypocorticism, hypogonadism); diabetes insipidus; McCune—Albright syndrome; fibrous dysplasia; chiasmal syndrome (Tables 2, 3).

We performed endoscopic endonasal transsphenoidal removal of a large endo-supra-latero(S)sellar pituitary adenoma. Bilateral approach to sphenoid sinus was performed. The left half of the sinus was filled with a large ossified calculus spreading to the floor of sella turcica (Fig. 2). Floor of sella turcica was drilled using a boron. Dura mater dissection was followed by exposure of heterogeneous tissue of pituitary adenoma with putty-like consistency. Larger suckers were required to remove this tissue. Gradual dissection of the tumor by curettes resulted almost complete removal of the tumor including from the lateral parts of left cavernous sinus. However, thin dense layers of the tumor remained in several sites of DM. Dissection was failed in these areas. Tumor was removed from both large nodes (right anterior and left posterior). Cerebrospinal fluid drainage was followed by straightening of tumor capsule. There was no liquorhrea. Closure of the capsule of removed tumor was refused considering occurrence of a huge cavity with bleeding walls at the end of surgery and the absence of liquorhrea confirmed by stress tests.
Histological examination confirmed HGH-releasing adenoma with a high marker of proliferative activity of tumor cells (Ki-67 6—7%) (Table 4).

Postoperative period was uneventful. Prophylactic lumbar drainage was carried out for three days. There was no nasal liquorhea. No neurological aggravation was observed. Increase of visual acuity of the left eye was noted after surgery (Table 3).

Control SCT confirmed almost complete removal of tumor (Fig. 1). However, clinical and biochemical remission of acromegaly was absent (Table 2). Combined therapy with prolonged analogues of somatostatin and cabergoline was accompanied by high levels of IGF-1 and HGH. Stereotactic radiotherapy was administered considering invasive nature of the tumor and the absence of remission.

### Case report 2

A 28-year-old man has noted enlargement of nose, hands, feet, lips, tongue for 10 years. Impaired vision for the last 2 years required magnetic resonance imaging (MRI). Active phase of acromegaly was diagnosed (Tables 1, 2). The patient was previously treated with somatostatin analogues without clear effect.

Examination at the Burdenko National Medical Research Center of Neurosurgery confirmed pituitary adenoma; active phase of acromegaly;
chiasmal syndrome; McCune—Albright syndrome; fibrotic dysplasia with lesion of cranial vault and skull base; skin pigmentation (café au lait). Endocrine-inactive neoplasms of both adrenal glands were also identified.

Asymmetric lesion of sphenoid bone involved thickening of the wings and anterior clinoid process on the right, right half of ethmoid bone, clivus up to the rostrum. Cavity of sphenoid sinus was absent. We performed endoscopic endonasal transsphenoid removal of endosuprasellar pituitary tumor. Tunnel-like trepanation of thickened bone altered due to dysplasia was performed along the midline using navigation (BrainLab, Germany) and various burs. We initially found basilar artery bifurcation due to significant vertical navigation error. Horizontal DM above the location of basilar artery appeared to be the floor of sella turcica. However, we found the tissue looked like a brain matter after DM dissection. At the same time, a small dark tissue node was found to the right of the midline. This tissue covered by DM looked like venous sinus. Tissue similar to pituitary tumor was found after DM dissection. However, searching for sella turcica was continued considering small volume and osseous walls of the node. Intraoperative biopsy confirmed that both tissue samples were the fragments of pituitary adenoma. According to SCT data, trepanation was performed strictly along the midline immediately below the floor of sella turcica. Therefore, trepanation was expanded upward. Anterior wall of sella turcica was found. Soft bluish-colored pituitary adenoma was excised from the cavity of sella turcica. The tumor spread to the cavity of right cavernous sinus. Posterior knee of carotid artery was found in this sinus after aspiration. A hematostatic gauze was placed into cavernous sinus, Tachocomb (Linz, Austria) hematostatic sponge — into sella turcica and on the walls of residual cavity. DM defect in the area of basilar artery was covered by autofascial flap, adipose tissue, another fascial flap, bone plate from the nasal septum, another adipose tissue fragment covered by mucoperiosteal flap. Layers of repair were sealed with fibrin-thrombin glue.

Histological examination confirmed HGH-releasing adenoma with high Ki-67 value (5—6%) (Table 4). Postoperative period was uneventful. An improvement of visual function was noted (Table 3). Nasal liquorrhea was absent.

Control MRI in 3 months after surgery revealed “empty sella turcica”. Plastic material was retained in infrasellar defect. Small residual tumors were found in both cavernous sinuses that explained the absence of clinical and biochemical remission of disease (Table 2, Fig. 3). Radiotherapy was recommended for residual tumors.

Discussion

Clinical manifestations of McCune — Albright syndrome were classic in our observations. Dimension and localization of pituitary adenomas determined the choice of transnasal approach to achieve the most complete and safe resection regardless condition of affected skull base. Severity of osteodysplastic disorders of sphenoid bone was various in both patients. Asymmetric lesion of skull base was observed in both cases. In the first case, sphenoid sinus and anatomical landmarks on the contralateral affected bones were preserved that allowed resection of affected bone up to sella turcica. In the second case, no anatomical landmarks were preserved. As a result, resection was possible only under navigational control. The absence of horizontal error prevented the loss of the landmark of midline. Vertical error resulted bone resection up to clivus under sella turcica at the first stage. Adequate navigation and approach to the tumor

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Fig. 1. Clinical case 1.
a, b – preoperative MRI; c, d – preoperative SCT; e, f – postoperative SCT; g, h – postoperative MRI.
T – tumor; D – focal fibrous osteodysplasia; Ch — chiasm.
without intraoperative complications were achieved thanks to only computed tomography. Unconventional for transnasal surgery device (pneumatic drill with burs of increased diameter (5—6 mm)) was required for fast and safe resection of thickened bone in the second case.

Surgical technique was almost similar to standard transnasal surgery. The purpose of excision of endocrine-active pituitary macroadenoma is ensuring chiasmal decompression and hormonal remission of disease. Normalization of HGH and IGF-1 levels is achieved in 80% of cases after excision of HGH-releasing tumors [14]. We did not get the desired result in our observations. For example, X-ray signs of almost complete removal of the tumor were not accompanied by normalization of HGH and IGF-1 levels. In the first case, this is due to significant infiltration of DM by a dense tumor, in the second case — spread of the tumor into cavernous sinuses.

The use of non-standard techniques at the final surgical stage resulted uncomplicated postoperative period. In the first case, open large cavity of tumor capsule ensured favorable conditions for fast and effective decompression of the optic nerves. The absence of hemostatic agents and plastic materials in this cavity was valuable to confirm radical excision early after surgery and schedule radiotherapy.

In the second case, complex skull base repair prevented postoperative liquorrhea and resulted early activation of the patient.

Drug therapy with somatostatin analogues is usually ineffective in patients with McCune—Albright syndrome. Therefore, stereotactic radiotherapy is recommended considering invasive tumor growth, high index of proliferative activity and no remission of acromegaly. Irradiation is applied for reduction of growth hormone hypersecretion and prevention of tumor growth despite the possible risk of malignant transformation of fibrous dysplasia tissue.

Fig. 2. Clinical case 1. Intraoperative images.
a — bone affected by fibrous osteodysplasia (fd) in front of sella turcica (m — mucous membrane of nasal cavity); b — right half of sella turcica (s) found after partial resection of affected bone (fd); c — both halves of sella turcica (s) after complete resection of affected bone (fd).
Fig. 3. Clinical case 2.

a, b – preoperative MRI; c, d – preoperative SCT; e – intraoperative CT: before (upper image) and after (lower image) additional bone resection near anterior wall of sella turcica; f – postoperative SCT; g, h – postoperative MRI. T or 1 — tumor; D — focal fibrous osteodysplasia; Ch — chiasm; 2 — zone of resected bone altered by dysplasia; 3 — pituitary stalk.
Conclusion

Skull base deformation may be extremely significant in patients with McCune—Albright syndrome. Nevertheless, transnasal surgery for pituitary adenoma is possible in these patients. This is very difficult technical procedure. These interventions may be performed only by highly qualified neurosurgeons using modern navigation technology and non-standard surgical methods.

Authors’ participation:
Concept and design of the study — M.A., P.L., L.I., N.A.
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REFERENCES


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Commentary

BTtwo rare cases of endoscopic transnasal surgery for HGH-releasing pituitary adenoma in patients with McCune–Albright syndrome are reported in the article. Both cases are interesting by deformations and fibrous growths of skull base structures, difficult surgical interventions and their non-standard completion. The content of the work is fully consistent with the subject of the journal. Undoubtedly, scientific novelty and practical importance of this report are significant because surgical treatment of these patients was previously extremely traumatic or impossible. Endoscopic technologies, navigation equipment and neurosurgeons experienced in the treatment of this pathology made it possible to successfully conduct these interventions. The design of the article includes description of clinical cases with consistent presentation of surgical protocol, results and postoperative outcomes followed by solution of questions about further treatment strategy. References are presented quite fully. The abstract briefly describes the report and contains all necessary headings and keywords. The work made a very favorable impression on me. Laconic presentation, informative figures and well-ordered clinical data in tables make the perception of the material easy. The work will be interesting for neurosurgeons and other specialists.

A.Yu. Grigoryev (Moscow, Russia)
Successful combination treatment of giant bicameral fusiform partially thrombosed vertebral artery aneurysm at 12-year-old patient (practical case and literature review)

© YU.V. PILIPENKO, AN.N. KONOVALOV, SH.SH. ELIAVA, A.V. BOCHAROV, D.N. OKISHEV

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ABSTRACT

Giant cerebral aneurysms are diagnosed more often in children than in adults. Treatment of giant aneurysms is carried out both by endovascular and microsurgical methods. Literature information on combination of microsurgical and endovascular operations of cerebral aneurysms at children is little.

A clinical case of the combined treatment of a giant bicameral fusiform partially thrombosed aneurysm of the right vertebral artery at a 12-year-old patient and a literature review on this topic are presented.

The patient underwent several complex neurosurgical interventions during two operations: 1) microsurgery including revascularization of the right posterior lower cerebellar artery, thrombectomy and trapping of the larger chamber of fusiform aneurysm of the right vertebral artery, and 2) endovascular, which consists in the installation of redirecting stent from the left vertebral artery to main artery.

The uniqueness of the case which we presented lies in the fact that the tactics of stage combined treatment for a complex aneurysm at child was originally planned and successfully implemented.

The treatment allowed to ensure a complete shutdown of aneurysm and to exclude postoperative cerebral complications.

Keywords: aneurysm at children, giant aneurysm, fusiform aneurysm, EC-IC bypass, anastomosis, combined treatment, stenting, thrombectomy, clipping.

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in posterior lower cerebellar artery (PLCA). This may be achieved by VA occlusion distal to PLCA ostium.

Occlusion of the aneurysm-related VA is permissible only in case of adequate collateral blood supply of basilar artery (similar diameter of contralateral VA and (or) effective blood flow through the posterior communicating arteries from the internal carotid arteries).

PLCA revascularization before aneurysm-related artery occlusion is advisable if large trunk of PLCA origins from the aneurysm [18, 20—22].

A successful combined treatment of a giant bicameral fusiform partially thrombosed aneurysm of the right VA in a 12-year-old patient is reported in this article. There were 2 neurosurgical interventions: 1) microsurgical revascularization of the right PLCA, thrombectomy and trapping of the largest chamber of fusiform aneurysm of the right VA; 2) stenting with blood flow redirection from the left VA to the basilar artery that excluded retrograde filling of minor chamber of fusiform aneurysm of the VA.

Case report

A 12-year-old patient V. was born from the first pregnancy, grew and developed in accordance with sex and age. Parents denied chronic diseases in the child. Hereditary history is not burdened.

Anamnesis morbi. Periodic dizziness and nausea have occurred since May 2017. These symptoms did not significantly impair quality of life. The patient and parents associated these signs with overwork. The reason for examination was an episode of severe dizziness on October 20, 2017. Magnetic resonance imaging (MRI) on October 21, 2017 and computed tomographic angiography (CTA) on October 25, 2017 revealed a giant bicameral fusiform aneurysm of the right VA (Fig. 1a, b) followed by compression and upper medial displacement of the brain stem. The maximum diameter of the proximal aneurysm chamber was 4 cm, distal chamber — 2.5 cm. There was a small isthmus between the chambers seemed like an intact artery. A large trunk of the right PLCA emerged from the proximal aneurysm chamber (Fig. 1c, d). Aneurysm spread from the proximal segments of V4 segment of the right VA to confluence with the left VA and proximal basilar artery. Left VA was visually intact.

The patient was consulted in various clinics. Deployment of flow-redirecting stent at the level of aneurysm or proximal deconstruction of the right VA were discussed. In both cases, specialists considered the risk of occlusion of the right PLCA originating from the aneurysm with subsequent ischemic disorders and significant brain stem compression. The last complication could be aggravated in case of thrombosis of aneurysm after endovascular surgery.

Clinical deterioration was noted on 12.11.2017 with severe headache, hypertension up to 210 mm Hg and aggravation of ataxia. The ambulance team delivered the patient to the hospital. CT revealed the signs of proximal aneurysm chamber thrombosis (Fig. 2).

Cerebral angiography was performed on November 13, 2017. It was found that partial thrombosis resulted decrease of the volume of patent proximal aneurysm chamber by approximately 70% in comparison with CTA data from October 25, 2017 (Fig. 3a). Contrast enhancement of distal aneurysm chamber from the right VA was trivial. Retrograde filling of the distal chamber from the left VA was well (Fig. 3b).

Considering acute thrombosis of the aneurysm followed by cerebellar and brain stem compression symptoms (instable blood pressure, coordination disorders, severe asthenia), endovascular treatment alone was refused. Symptomatic therapy was administered.

Parents of the child requested a consultation at the Burdenko Research Center for Neurosurgery. As a result, decision about hospitalization was accepted. The patient was admitted to the intensive care unit on November 17, 2017 in supine position on the gurney.

Physical examination: general condition was fair. Constitutional type was asthenic. Blood pressure was increased up to 150 mm Hg that required hypotensive therapy. There was sinus rhythm with heart rate 80—100 beats per min. Breathing rate did not exceed 18—20 per minute. Neurological status: consciousness was clear. Orientation in time and place was normal. There were moderate vertical gaze palsy, mild dysphonia and dysphagia, moderate intentional tremor and impaired coordination tests (more significant on the right). Meningeal symptoms were absent. No motor and sensory disturbances were noted.

Two-stage combined surgical treatment was preferred after a council of vascular neurosurgeons of microsurgical and endovascular departments.

Microsurgical operation was scheduled at the first stage. The main objective was revascularization of the right PLCA. The following measures for
aneurysm occlusion were considered: proximal (in relation to the aneurysm) clipping of the right VA, trapping of the largest aneurysm chamber, complete trapping of bicameral aneurysm along with the V4 segment of the right VA. Thrombectomy was essential to reduce aneurysm-associated brain stem compression. At the same time, impossible thrombectomy in proximal clipping due to bleeding from the aneurysm cavity was taken into account if trapping would be failed.

The second (endovascular) stage was considered if microsurgical operation would have ended only by proximal occlusion or trapping of the largest aneurysm chamber. In this case, there would be a high probability of retrograde filling of the aneurysm through contralateral VA and basilar artery.

Stenting for blood flow redirection from the left VA into the main artery would solve this problem.

**Treatment**

*Microsurgical operation* was performed on 20.11.2017. In prone position, right-sided "hockey-stick" skin incision was followed by suboccipital craniotomy with right lateralization. Dura mater was dissected in semi-oval fashion and retracted to the right. Dissection of a large occipital cistern resulted drainage of significant amount of cerebrospinal fluid. A large partially thrombosed chamber of a giant
bicameral fusiform aneurysm of the right VA was found. Right PLCA emerged from the aneurysm (Fig. 4a). Aneurysm had dense walls and deformed medulla oblongata. In the intradural space, right VA was visually intact for approximately 1 cm and then entered a fusiform aneurysm. Proximal segments of the right PLCA were somewhat dilated in comparison with distal parts. In addition, small arteries branched off to the medulla oblongata within 1 cm from the PLCA ostium.

Right occipital artery was dissected from soft tissues. A segment of PLCA was chosen in 2 cm from the ostium which was visually normal. Temporary cross-clamping of the right PLCA in this segment (lateral medullary) was followed by creation of anastomosis in "end-to-side" fashion using interrupted sutures 10/0 between right PLCA and right occipital artery (Fig. 4b). Blood flow was restored after 40 minutes. Flowmetry and fluorescence video-angiography confirmed satisfactory function of the graft (22 ml/min) (Fig. 4c). PLCA was clamped using titanium mini-clip near the aneurysm. Thus, there was antegrade blood flow from the occipital artery through the anastomosis towards cerebellar hemispheres and partial retrograde blood flow towards perforating arteries originating from the proximal right PLCA. A standard titanium clip was used to clamp proximal parts of the intracranial segment of the right VA (Fig. 4d). Large chamber relaxed somewhat. These measures were valuable for subsequent safe separation of the aneurysm and medulla oblongata without advanced traction of the brain. Exposure of distal (smaller) aneurysm chamber was followed by identification of a narrow segment connecting both chambers. This segment was characterized by whitish and rigid walls. Their density was similar to that of the aneurysm and differed from a normal vessel. A small vessel emerged from this isthmus between both chambers towards ventral medulla oblongata. Temporary clip was deployed proximal to this perforating artery.

Dissection of a large chamber with thrombectomy were performed (Fig. 4e). Satisfactory brain stem decompression was achieved. Temporary clip on the isthmus between both chambers was replaced by permanent titanium mini-clip that resulted trapping of the large aneurysm chamber (Fig. 4f). Patent perforating artery emerging from the isthmus was confirmed by fluorescence video angiography. Dura mater was sutured with continuous suture and fixed along the perimeter to the bone. The area of occipital artery passing through the dura mater was sealed by a muscle. Bone flap was fixed by craniofixes. Soft tissues were sutured in layer-by-layer fashion.

Thus, surgery resulted occlusion and significant reduction of the large aneurysm chamber (4 cm) of the right VA. A smaller but also large (about 2.5 cm) chamber remained patent. It was a fusiform
enlargement of distal parts of the right VA spreading up to confluence with contralateral VA and proximal parts of basilar artery. Dissection towards confluence of VAs for trapping of the entire aneurysm was refused for two reasons. These are advanced trauma due to the need for significant medial traction of medulla oblongata and risk of acute ischemia in the basin of perforating artery emerging from the isthmus between both chambers of the aneurysm.

Postoperative period. Aggravation of bulbar disorders (impairment of swallowing and dysphonia) was observed in postoperative period. Over the next week, these disorders significantly regressed. CT of the head (22.11.2017, 2 days after surgery) did not reveal signs of ischemic and hemorrhagic complications. Thrombosis of patent aneurysm chamber was also absent. Brain stem compression was eliminated (Fig. 5). The patient was verticalized in 5 days after surgery and began to walk with support.

Cerebral angiography was performed in 8 days after surgery (28.11.2017). Right VA was contrasted up to intracranial part (Fig. 6a). Right PLCA was filled from the basin of the right external carotid artery through the anastomosis with right occipital artery (Fig. 6b). Residual patent distal chamber of fusiform aneurysm of the right VA was visualized (Fig. 6c). Contrast enhanced segment was the same (maximum diameter 2.5 cm).

Sutures were removed in 8 days after surgery. Primary tension healing of the wound was noted. The patient was discharged in 9 days after surgery.
surgery (29.11.2017). In the future, patient’s condition remained satisfactory.

The patient was hospitalized after 2 months (29.01.2018) for the second stage of the treatment.

Endovascular procedure was performed 30.01.2018. Preoperative angiography showed the same signs compared with previous examination (distal chamber 2.5 cm with contrast enhancement from the left VA). Stenting with blood flow redirection from the left VA to proximal parts of basilar artery was performed. There was no aggravation of neurological disorders after endovascular surgery. CTA was carried out on February, 2, 2018 (in 3 days after endovascular surgery). Significant reduction of blood flow in the aneurysm followed by its thrombosis by more than 90% was observed (Fig. 7). Age- and weight-appropriate antiplatelet therapy was prescribed for the next three months.

The patient was discharged in 5 days after endovascular surgery (04.02.2018).

CTA in 3 months after discharge confirmed complete occlusion of the aneurysm and no compression of the brain stem (Fig. 8).

Quality of life of the patient was completely restored.

Discussion

Aneurysms in children may be caused by connective tissue disorders (Ehlers—Danlos syndrome type IV, Marfan syndrome, autosomal dominant polycystic kidney disease, etc.), head injury, inflammatory vasculopathy and combination of these factors [2, 3, 6, 8, 9, 23—25]. Vascular wall dissection may be also the mechanism of aneurysm development in children. At the same time, diagnosis of predisposing pathology is difficult in most cases.

Development and enlargement of aneurysms in children may be quite fast and take months, weeks and even days [3, 5, 25]. One of the possible explanations of higher incidence of giant aneurysms in children is the absence of atherosclerotic plaques and elasticity of vascular wall. These features facilitate more significant aneurysm dilatation before the rupture. At the same time, aneurysms of posterior parts of the circle of Willis are more common in children and characterized by higher risk of rupture and unfavorable outcome [2, 3, 5, 6, 8—10]. It has also been noted that fusiform aneurysms are more common in children and there is a predisposition of these aneurysms to intraluminal thrombosis [1—3, 6, 26].

Complete spontaneous thrombosis of aneurysms is more common in children than in adults [27—29]. Aneurysms are thrombosed together with aneurysm-related artery sometimes that results ischemic cerebral disorders and unfavorable outcome [3, 27].

In this case report, clinical manifestation caused by cerebellar and brain stem compression was rapid, especially after aneurysm thrombosis onset. Considering these disorders, acceleration of hospitalization and surgical treatment was required.

Two giant aneurysms of the right VA could be supposed after analysis of preoperative angiographic images, as it seemed that there was a segment of intact vessel between these aneurysms. However, intraoperative examination did not confirm these assumptions because this vascular segment had dense whitish walls and probably intraluminal thrombi. In fact, this segment was similar to the aneurysm. Therefore, we used the term "bicameral aneurysm" in the title of this article. We also suppose that thrombosis of the proximal aneurysm chamber and progressive compression of the brain stem were due
to the presence of narrowed segment between both chambers and impaired blood flow in this segment.

Combined treatment implies the use of several techniques for occlusion of aneurysm in one patient. Staged microsurgical and endovascular procedures are applied for multiple aneurysms as a rule, because the last ones cannot be simultaneously occluded within one intervention due to clinical and anatomical features [8, 30, 31]. Hemorrhage-related aneurysm or aneurysm with the highest risk of rupture are repaired at the first stage. In our case, primary intervention was aimed at the large chamber of a giant aneurysm associated with brain compression.

Anastomosis between occipital artery and PLCA was introduced into clinical practice long ago [11].

---

**Fig. 6.** Angiography after microsurgical operation in a 12-year-old patient V.

a — right-sided vertebral angiography; b — right angiography of external carotid artery: the arrow indicates the anastomosis between posterior lower cerebellar artery and occipital artery on the right; c — left-sided vertebral angiography.

**Fig. 7.** Subtotal thrombosis of distal chamber of giant bicameral fusiform aneurysm of the right vertebral artery after stenting in a 12-year-old patient V.

a — CT of the brain without contrast enhancement; b — CTA of the brain. Yellow arrow indicates the stent, red arrow — residual patent part of the aneurysm.
However, anastomoses "in situ" are preferred for vertebrobasilar revascularization in recent years [18, 20, 21].

The main disadvantages of occipital artery as a donor vessel are multiple branches and small diameter of the distal parts. Dissection of this artery is quite difficult and may be accompanied by its injury due to significant tortuosity of occipital artery.

In our case, anastomosis with right occipital artery for PLCA revascularization was used because other methods of blood flow replacement in this area were considered as ineffective. Anastomosis "in situ" with left PLCA was refused due to small diameter of this artery while right PLCA reimplantation to the proximal parts of right VA was rejected due to impossible transposition of right PLCA stump at this distance. In addition, diameter of right occipital artery within its considerable length was comparable with that of right PLCA and thin subcutaneous adipose tissue made dissection of right occipital artery relatively simple.

Trapping and occlusion of proximal aneurysm chamber made distal chamber similar to saccular aneurysm. The neck of this aneurysm was transition of left VA to basilar artery.

We refused early postoperative stenting in order to restore satisfactory condition of the patient, because distal chamber was not followed by significant brain stem compression and high risk of rupture due to dense walls, wide neck and the absence of diverticula. Moreover, endovascular procedure required administration of antiplatelet agents. In our opinion, these medicines could increase the risk of bleeding in early postoperative period after microsurgical intervention.

Endovascular deployment of flow-directing stent resulted blood flow redirection from left VA to basilar artery and significantly decrease of blood supply to the aneurysm chamber. Only perforating artery between the aneurysm chambers could require retrograde blood supply through the stent cells. However, gradual thrombosis of distal aneurysm chamber probably ensured restructuring of blood flow with blood supply of this area from collateral arteries and prevented acute ischemia of medulla oblongata.

There are literature data on successful microsurgical or endovascular treatment of patients with giant vertebrobasilar aneurysms (including children) [2, 10, 11, 22, 32]. There is also case report

*Fig. 8. Complete occlusion of the right vertebral artery aneurysm after combined microsurgical and endovascular treatment in a 12-year-old patient V.*

a — CT of the brain without contrast enhancement; b — CTA of the brain.
of successful combined treatment of a giant fusiform aneurysm of posterior cerebral artery in adolescent. In this case, anastomosis with superficial temporal artery was followed by endovascular occlusion of posterior cerebral artery by spirals proximal to the aneurysm [33].

Successful combined treatment of a giant partially thrombosed aneurysm of the distal V4 segment of right VA spreading to basilar artery is reported in national literature [34].

A uniqueness of our case is in initially scheduled staged combined treatment of one giant bicameral partially thrombosed aneurysm of VA. Complex surgical interventions were successfully implemented in the child: microsurgical revascularization of PLCA, trapping clipping, thrombectomy and flow-redirecting stenting. This strategy ensured complete occlusion of the aneurysm and excluded postoperative cerebral complications.

**Conclusion**

Successful surgical treatment of complex (giant, fusiform and partially thrombosed) vertebral artery aneurysms is possible in combined staged application of microsurgical and endovascular techniques. Favorable reparative capabilities in children allow increasing surgical invasiveness for radical repair.

The authors declare no conflict of interest.
REFERENCES


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Thought-out, carefully scheduled and successful surgical treatment of extremely difficult and rare disease is reported in the article. The authors reported a child with giant partially thrombosed bicameral aneurysm of the intracranial segment of the vertebral artery involving posterior lower cerebellar artery. A feature of the course of disease was spontaneous thrombosis of proximal (larger) chamber of the aneurysm followed by aggravation of brain stem compression. The authors gave all necessary information about development of disease, neurological status, survey data, strategy and stages of surgical treatment. Microsurgical and endovascular interventions are described in detail and illustrated by intraoperative images and results of postoperative neuroimaging. Patient's condition in early postoperative period is reported.

Discussion of this report contains analysis of available literature data on surgical treatment of these aneurysms. The authors reported their own conclusions regarding treatment strategy in a particular patient.

In general, this report is undoubtedly of great scientific and practical interest due to possible analysis of difficult problem of the treatment of giant vertebral artery aneurysms. The authors did not focus on only one surgical approach and competently used the advantages of microsurgical and endovascular procedures. The article will be useful for specialists in vascular neurosurgery.

A.V. Dubovoy (Novosibirsk, Russia)
Mononeuropathy of dorsal interosseous nerve: compression by return radial arteries

© D.S. DRUZHININ¹, M.L. NOVIKOV¹, A.V. FEDOROV¹, E.S. DRUZHININA², S.S. NIKITIN²

¹Medical Center «Motus», Yaroslavl, Russia; ²Medical Center «Practical neurology», Moscow, Russia; ³FSBEI of HE «Russian National Research Medical University named after N.I. Pirogov» of Ministry of Health, Moscow, Russia

ABSTRACT
Among many causes of compression neuropathies involving the radial nerve, compression of the posterior interosseous nerve (PIN) by the returning radial arteries is rare.

Objective — to describe the clinical instrumental characteristics of cases of mononeuropathy caused by compression of the return radial arteries.

Material and methods. Two observations with neuropathy of the deep branch of the radial nerve, manifested by weakness in the corresponding muscles, inconsistent pain syndrome with previous stereotypic (recurring) physical activity are presented.

Results. According to the results of ultrasound examination of posterior interosseous nerve, a local hypoechogenic increase in the cross-sectional area of nerve of different lengths was revealed. During surgical decompression of the nerve, in the first case, a tight arterial loop was found around the nerve, in the second case, expanded arterial trunks, one of which, of small diameter, covered the nerve in the «loop», and the other, larger, pierced the nerve. After the operation, regression of motor deficiency and relief of pain were noted.

Keywords: peripheral nerve ultrasound, posterior interosseous nerve, recurrent radial arteries, compression neuropathy.

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Common radial nerve forms superficial and deep branches 2—3 cm proximal to the elbow joint. Deep branch passes between superficial and deep muscular bundles of supinator muscle. Fibrous edge of this muscle is called the arcade of Frohze [1]. Distal deep branch is located on dorsal surface of the forearm under short and long radial extensors of the wrist. A continuation of the deep branch is posterior interosseous nerve (PIN) of the forearm passing between long and short extensors of the thumb up to the wrist joint [2, 3].

Compression-induced neuropathy of median and ulnar nerves is more common in routine practice while tunnel neuropathy of radial nerve branches is quite rare [2]. Lesion of the deep branch and PIN is confirmed by characteristic clinical signs of involvement of dorsal forearm muscles [1—6]: dysfunction of extensor digitorum muscle, long and short pollicis extensor muscles, abductor pollicis longus muscle, extensor indicis muscle and extensor digiti minimi muscle with normal function of brachioradial muscle, supinator muscle and extensors of the wrist.

Various causes of PIN lesion are described in the literature: compression at the level of the arcade of Frohze [3], deep branch compression by recurrent radial arteries [4, 5], lipoma-associated compression in supinator tunnel [6], focal nerve constriction in hourglass fashion [7—9]. Characteristic signs of certain types of lesion cannot be determined using clinical and anamnestic data. Therefore, neuroimaging (MRI, US) is essential in diagnosis of the causes of PIN lesion. Possibilities of MRI of this area are limited due to “oblique” course of the nerve.
[4, 5, 10—12]. Ultrasound makes it possible to identify a nerve on the dorsal surface of the forearm from different accesses [13, 14]. Early diagnosis of the causes of nerve lesion is valuable for further effective surgical treatment.

The purpose of the study was to present clinical and instrumental characteristics of mononeuropathy caused by compression by recurrent radial arteries.

**Material and methods**

There were 2 patients with acute manifestation of mononeuropathy of the right PIN. These were a 64-year-old woman and a 48-year-old man. Motor deficiency was clinically evaluated using the MRS sum score (Medical Research Council Scale for Muscle Strength) in 3 (male) and 6 months (female) after paresis. MRS sum score is a five-point scale for strength assessment (0 scores – paralysis; 5 scores – intact function). Electromyography (EMG) of the key muscles with a needle electrode on a Neuro MVP-4 scanner (Neurosoft LLC, Russia) and ultrasound on a Sonoscape 20 Pro scanner (Sonoscape, China) with a linear transducer 13—15 MHz were performed.

Radial nerve was visualized from the level of the lower third of the shoulder up to bifurcation into superficial and deep branches. In the area of supinator muscle, deep branch was visualized up to the middle third of the forearm. Vascularization of the nerves was evaluated using Doppler ultrasound. Examination was performed on the contralateral side too.

Both patients underwent surgical treatment considering the causes of PIN lesion.

**Results**

Both patients had motor deficiency in the muscles innervated by PIN within previous 3—6 months. Pain syndrome was unstable, mild and was not typical for neuropathic nature. No sensitive disorders were found.

Intense stereotypical physical activity preceded manifestation of PIN neuropathy. It was flexion and extension of the arm in the elbow and wrist joints combined with its pronation and supination.

Ultrasound revealed hypoechoic enlargement of PIN in both cases (Figure). Attention was drawn to different extent of the altered nerve segment. In the first case, there was a 7-mm lesion with distal narrowing of the nerve at the level of 1 cm distal to elbow joint space. Doppler ultrasound revealed an arterial trunk distal to the enlarged nerve segment as a possible cause of PIN compression. In the second observation, there was a 15-mm altered nerve length with unclear external contour. Doppler ultrasound revealed multiple dilated arterial trunks along the lower edge of the nerve.

In both cases, needle EMG found signs of denervation including fibrillation potentials and positive sharp waves in extensor digitorum muscle and long pollicis extensor muscle. Isolated lesion of PIN with intact trunk of common radial nerve was confirmed by the absence of neurophysiological disorders in radial extensor of the wrist.

Both patients underwent surgery. The procedures were performed via standard approach and consisted of dissection and decompression of the nerve. In the first case, tight arterial loop around posterior interosseous nerve resulted its compression. In the second observation, dilated arterial trunks passed close to the lower edge of the nerve. One of these nerves with a small diameter comprised the nerve into a loop. Another larger artery penetrated the nerve (Figure). Cautery and intersection of recurrent radial arteries resulted release of the nerve. Postoperative period was uneventful with first intention wound healing. Physical exercises were recommended with an emphasis on extensor muscles. Moreover, restriction of excessive physical activity with wrist joint extension was also prescribed.

Control examination in a month after surgery revealed reduced motor deficiency and pain syndrome regression in both patients. Improvement of motor function was more significant in extensor digitorum muscle and less significant in extensor digiti minimi muscle (Table).

**Discussion**

Radial recurrent arteries are the branches of radial artery. The last one passes between PIN trunk and anastomosing with distal segment of deep brachial artery [15]. Various neurovascular compression syndromes of hands with different treatment strategy are described in the literature. These are compression of anterior interosseous nerve by the branch of anterior interosseous artery [16], ulnar nerve compression in Guyon’s canal due to thrombosis [17] or aneurysm of the ulnar artery [18], PIN compression by recurrent radial arteries [19], brachial plexus compression by posterior scapular artery [20].

**Table**

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Extensor digitorum</th>
<th>Extensor digiti minimi</th>
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<td>Reduced</td>
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<td>Pain syndrome</td>
<td>Regressed</td>
<td>Regressed</td>
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<tr>
<td>Sensitivity disorders</td>
<td>Absent</td>
<td>Absent</td>
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Comparative characteristics of a 64-year-old patient (left) and a 48-year-old patient (right).

a — ultrasound image; b — intraoperative view of deep radial branch compression by radial recurrent arteries; c — 3D reconstruction.
Ultrasound signs of neuropathy due to compression by radial recurrent arteries were described in only one case in 2013. C. Rolla Bigliani et al. reported deformation of the nerve with subsequent intraoperative confirmation of the diagnosis [19].

**Conclusion**

Neuropathy of posterior interosseous nerve associated with compression by radial recurrent arteries is reported in this article. We demonstrated the role of preoperative ultrasound examination for analysis of further treatment strategy in these patients. Ultrasound examination data were completely confirmed by intraoperative picture. Surgical treatment of these patients is effective for regression of pain syndrome and motor deficiency.

<table>
<thead>
<tr>
<th>Case (visit)</th>
<th>Triceps</th>
<th>BR</th>
<th>Sup</th>
<th>ECR</th>
<th>EDC</th>
<th>EI</th>
<th>EPL</th>
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<td>5</td>
<td>5</td>
<td>0</td>
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<tr>
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<td>5</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Case 2 (1)</td>
<td>5</td>
<td>5</td>
<td>5</td>
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<td>1</td>
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<tr>
<td>Case 2 (2)</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>2.5</td>
</tr>
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</table>

*Note. Data are shown before (1) and after (2) surgical decompression of the nerve. BR — brachioradialis muscle; Sup — supinator muscle; ECR — radial wrist extensor muscle; EDC — extensor digitorum muscle; EI — extensor digiti minimi muscle; EPL — long pollicis extensor muscle.*

Authors’ participation:
Concept and design of the study — D.S.
Collection and analysis of data — D.S., M.L.
Statistical analysis — A.V.
Writing the text — D.S., M.L., A.V.
Editing — E.S., S.S.

The authors declare no conflict of interest.
REFERENCES


Commentary

This report is devoted to the actual issue of compression-induced neuropathies of upper limb and importance of ultrasound in diagnosis of compression. Considering similar clinical symptoms of compression-induced neuropathies of the radial nerve, diagnosis of compression level is the first important issue in planning and selection of surgical strategy. Ultrasound used by the authors is valuable to identify rare variants of this lesion. Small number of Russian-language reports devoted to rare neuropathies makes this publication relevant including in the “Questions of neurosurgery” journal. It is also important that the authors pay attention to such clinical situations and describe rare cases in Russian-language literature. The authors comprehensively reviewed the literature prior to publication of this report. References involve relevant articles reflecting development and current state of this problem. Design of the work meets the requirements. Conclusions are justified and reflect the content of the work. Practical significance of report is obvious because the authors pay attention of specialists to the need for use of ultrasound in diagnostic algorithm of peripheral nervous system pathology.

A.V. Shtok (Moscow, Russia)
Current trends in the development of neuroanesthesiology

© A.YU. LUBNIN

Federal State Independent Institution N. Burdenko National Medical Research Center for Neurosurgery of the RF Health Ministry Burdenko Neurosurgical Center, Moscow, Russia

ABSTRACT

The paper presents the author’s analysis of the main trends in the development of modern neuroanesthesiology over the past five to ten years. These, in the author’s opinion, include the introduction and elaboration of blood-sparing techniques, monitoring the depth of anesthesia, fast track concept, applying regional (conduction) anesthesia techniques, xenon anesthesia, development of effective and safe protocols for DVT and PTE prophylaxis for neurosurgical patients, study of the hemostatic system using bedside methods for assessing hemostasis (thromboelastogram) and correcting hypocoagulation by activated recombinant VII factor.

Keywords: neuroanesthesiology — development trends.

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Neuroanesthesiology is a part of general anesthesiology ensuring anesthetic management of neurosurgical interventions on the brain and spinal cord. Neuroanesthesiology has its own history and iconic people. This topic deserves a separate consideration. Today we turn to the main trends of its development [1—4]. I work in this area for over 36 years and is informed about the most interesting and significant, in my opinion, trends in modern neuroanesthesiology. Let’s get to know them in more detail.

1. Introduction and development of modern blood-sparing technologies. Brain is not characterized by the most active blood-supply in human body. It accounts for less than 15—20% of cardiac output. However, blood loss during neurosurgical interventions may be up to several tens of liters and results adverse outcomes. Compensation of intraoperative blood loss with transfusions is not advisable for many reasons. Currently, there are 2 confirmed facts for patients with cerebral damage: 1) anemia worsens the outcomes in these patients; 2) donor blood transfusion also worsens treatment results [5]. Modern blood-sparing technologies is a reasonable alternative to transfusion. Back in 2003, we published a conceptual work on this issue in the “Anesthesiology and Intensive Care” journal. The relevance of this report has not declined too much over the past years [6].

The first stage is prediction of the problem. Preoperative predictors of massive intraoperative blood loss are shown in Table 1. The key aspect is direct or indirect assessment of blood flow in the tumor and adjacent brain structures. A particular problem is hemostatic disorders. However, this is a complex and global aspect requiring a special consideration [7—12].

The next stage is the choice of one or combination of various blood-sparing technologies ensuring the greatest clinical effect in particular patient. We have used this approach for a long time. Australians called this approach as “Patient blood management” [13]. The main blood-sparing methods with confirmed clinical effectiveness are shown in Table 2. We’ll review in more detail some the most effective and studied techniques in neurosurgical patients.

Preoperative blood donation. This is a well-known and effective blood-sparing technology in elective surgery [13, 14]. Unfortunately, this approach including its economic effect is unjustifiably questioned from time to time. However, the problem of application of this method is another in neurosurgical patients. According to all current statements of transfusion, organic lesion of central nervous system is a contraindication for blood donation due to the risk of various complications. The most unpleasant of these events is generalized convulsive seizures. It would seem, what further to talk about? However, this conclusion seemed to us insufficiently reasoned at one time. Therefore, we conducted a small clinical trial in patients with brain tumors including those with previous epileptic
seizures [15]. Blood donation was performed under continuous registration of electroencephalogram throughout the entire procedure in neurosurgical patients. As we expected, blood donation was not followed by EEG-signs of increased epileptic activity if adequate anticonvulsant therapy was previously selected.

Preoperative embolization of tumor vessels. This blood-sparing technique is characterized by fantastic effectiveness. Unfortunately, this approach is not as simple as it seems at first glance. Well-experienced endovascular surgeons are required for these procedures. In this regard, we were lucky, because the world endovascular neurosurgery was born in our clinic and began with the work of its founder academician F.A. Serbinenko. As early as 2002, we published a review on this issue in “Neurosurgery issues” journal and comprehensively analyzed this technique [16]. We can say that preoperative embolization of tumor vessels is extremely effective and safe procedure. A classic example is effective preoperative embolization of juvenile nasopharyngeal and skull base angiofibromas. Effective devascularization of this tumor is shown in Fig. 1. This procedure may be followed by reduced intraoperative blood loss up to 200—300 ml.

Acute isovolemic hemodilution. This technique was extremely common 10—15 years ago. However, this approach is currently undergoing a period of undeserved oblivion. In fact, this simple inexpensive and effective blood-sparing technology is valuable to abandon blood transfusion even in cases of blood loss up to 40—50% of total blood volume. The technology was well described in the literature several times [13, 14, 17]. According to one of the meta-analyses published in 2004 [18], two aspects are essential for effective dilution: 1) blood exfusion should be sufficiently large; 2) blood loss should be massive.

Washed red blood cells reinfusion. We wrote a lot about this technique and even published a book [19]. An interested reader can turn directly to these sources. I only note that this is a special blood-sparing technique. Mechanism of this method differs from the other ones. Washed red blood cells reinfusion may be effectively combined with other blood-sparing techniques (controlled arterial hypotension, isovolemic hemodilution, preoperative autologous blood donation). This is the only blood-sparing technology with gradual augmentation of efficiency along with increase of intraoperative blood loss. Various manufacturers currently produce commercially available devices (sell-savers) to implement this methodology [20]. Certain problems of this technique should be emphasized. For example, this is the risk of contamination of reinfused red blood cells by tumor cells and subsequent dissemination in cancer surgery. At least two methods are used for this problem: 1) x-ray irradiation of washed red

### Table 1. Predictors of massive intraoperative blood loss in neurosurgical patients (A.Yu. Lubnin, V.V. Gromova, 2003 [6])

<table>
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<tr>
<th>№</th>
<th>Risk factor</th>
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<tr>
<td>1</td>
<td>Large tumor adjacent to major cranial and cerebral arteries and veins</td>
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<tr>
<td>2</td>
<td>CT- and MR-signs of active contrast accumulation by the tumor</td>
</tr>
<tr>
<td>3</td>
<td>Significant proper vascular network of the tumor confirmed by cerebral angiography</td>
</tr>
<tr>
<td>4</td>
<td>Previous neurosurgical interventions complicated by severe intraoperative blood loss</td>
</tr>
<tr>
<td>5</td>
<td>Congenital and acquired hemostatic disorders (anticoagulants and antiplatelet drugs intake)</td>
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### Table 2. Major modern blood-sparing technologies (A.Yu. Lubnin, V.V. Gromova, 2003 [6])

<table>
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<tr>
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<tbody>
<tr>
<td>1</td>
<td>Preoperative blood donation</td>
</tr>
<tr>
<td>2</td>
<td>Local anesthesia of incision with or without addition of vasoconstrictors</td>
</tr>
<tr>
<td>3</td>
<td>Pre- and intraoperative embolization of tumor vessels and stroma</td>
</tr>
<tr>
<td>4</td>
<td>Controlled arterial hypotension</td>
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<td>5</td>
<td>Acute isovolemic hemodilution</td>
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<td>6</td>
<td>Re-infusion of autologous blood (washed red blood cells infusion)</td>
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<tr>
<td>7</td>
<td>Systemic administration of fibrinolysis inhibitors</td>
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</table>
blood cells using special devices; 2) leukocyte filters. Both methods are well studied and their effectiveness is confirmed [19, 20]. Bacterial contamination of infusate primarily due to air microflora of operating theatre is a common problem. However, there are no catastrophic consequences of this process for a patient for some unclear reasons [21—24]. Moreover, significantly reduced risk of postoperative infectious complications after red blood cells reinfusion compared to transfusion was confirmed. Perhaps, this is due to the known immunosuppressive effect of donor blood transfusions [25].

2. Monitoring the depth of anesthesia. Technologies for monitoring the depth of anesthesia (MDA) is one of the indisputable achievements of modern anesthesiology. This question has two important aspects. Undoubtedly, the phenomenon of spontaneous intraoperative recovery of consciousness is extremely undesirable. Indeed, this event may be followed by serious consequences for a patient including the so-called “post-traumatic stress disorders” and even suicidal attempts. However, in my opinion, risk of negative effect of excessively deep anesthesia on the brain outweighs all other risks especially in certain categories of patients (children and elderly patients). The consequences of excessively deep anesthesia are postoperative cognitive impairment and delirium [26]. Currently, we can quantitatively measure the hypnotic component of anesthesia using some modern technologies [27]. However, there is a well-grounded question regarding neurosurgical patients, especially those with intracranial pathology. Are these methods effective for quantitative measurement of anything in the organ undergoing surgical intervention? We began analysis of this problem some time ago. We have chosen BiS technology (“bioinformatics and synergetics”) as the most convenient and informative method among various modern and affordable commercial technologies for monitoring of the depth of anesthesia. Further experience of monitoring in neurosurgical patients using BiS technology has shown the absolute reality of this approach [28].

In addition to standard clinical situations, MDA using BiS technology was especially useful in special situations:

1) awake craniotomy, when control of the depth of anesthesia is crucial for adequate and fast awakening of the patient during surgery for intraoperative neuropsychological testing;

2) hemodynamic instability due to massive intraoperative blood loss or severe initial cardiac diseases with low cardiac output. In both of these situations, the anesthesiologist instinctively reduces the flow of anesthetic agent, since almost all anesthetics inhibit systemic hemodynamics. Therefore, spontaneous recovery of consciousness is possible;

3) it is quite difficult to choose the optimal rate of propofol infusion in patients with initially impaired consciousness without MDA;

4) anesthesia in pregnant women with neurosurgical pathology. It is clear that these patients require minimally sufficient anesthesia for minimization of the pharmacological load on both participants of the process.

3. Regional methods of anesthesia. At first glance, formulation of this question seems absurd per se. Neurosurgery (especially intracranial) and regional methods of anesthesia are incompatible! However, this is only at first glance. There is always a place for regional methods of anesthesia in modern anesthesiology. Neurosurgery is not an exception. We are talking about regional scalp block (RSB) during intracranial interventions and epidural anesthesia for spinal neurosurgical interventions. We have previously published many reports devoted to this issue and an interested reader can turn to these articles [29]. It is important to understand that we are talking not only about the special situation of awake craniotomy. This is also true for all intracranial operations when RSB may be successfully used as analgesic component of anesthetic management! This approach is associated with extremely high hemodynamic and endocrine-metabolic stability, minimal pharmacological load, rapid postoperative recovery of consciousness and effective postoperative analgesia within a day after surgery [30].

4. Fast track concept in modern neuroanesthesiology. In 2016, we published a conceptual work devoted to this issue in “Anesthesiology and Intensive Care” journal [31]. I have visited various national and foreign neurosurgical clinics over 36 years of my work as neuroanesthesiologist and came across with the point of view that deep sedation is advisable after intracranial intervention in order to ensure metabolic rest for the brain. This rather disputable thesis has not been convincingly supported by any data. Moreover, this approach is associated with serious problems including dynamic neurological monitoring in early postoperative period to diagnose acute postoperative hematoma as the most formidable complication. There are other serious arguments in favor of the
fast track concept for neurosurgical patients. These aspects are considered in detail in the above-mentioned report.

5. Xenon anesthesia in neurosurgery. Xenon is called anesthetic of the 21st century. Apparently, this is true. This unreactive gas does not undergo any chemical reactions in human body. Fast saturation and elimination, the fastest awakening after anesthesia among all available modern anesthetics are the features of xenon. The absence of hemodynamic impairment makes xenon the only one of all modern anesthetics not associated with decrease of blood pressure. Moreover, slight increase of blood pressure is observed. In addition, there are experimental data on anti-ischemic protective effect of xenon. Indeed, everything looks quite positive, and we wrote some reports on this issue [32–36]. There are some technical drawbacks: high cost (25 dollars per 1 liter while anesthetic consumption ranges from 8 to 15 liters for 4—5-hour procedure depending on anesthesia device) and need for special anesthetic and respiratory equipment. Currently, we use two devices for xenon anesthesia in our department: Taema Felix (France) and Axeoma (Finland). The first device requires minimal corrections by anesthesiologist but is associated with increased consumption of the gas. The second device requires constant manual correction of ventilation and gas flow parameters. However, this system is extremely economical and reliable. Financial problems are surmountable over time while positive aspects remain. So, we believe in a bright future for xenon anesthesia in neurosurgery.

6. Consciousness as a modality of neuromonitoring in neurosurgery. It is clear that general anesthesia and consciousness are difficult to compatible things and the presence of one of them means the absence of the other as a rule. This statement was true for some time in neuroanesthesiology. However, situation has changed radically. Some neurosurgical interventions require intraoperative recovery of consciousness up to relatively high level (talking with a psychologist and testing). Moreover, certain interventions are generally not feasible in unconscious patient. Thus, we can talk about changed paradigm in anesthesiology.

Let’s consider why intraoperative recovery of consciousness is so important in some cases.

1. Awake craniotomy. This is a special type of neurosurgical intervention performed in patients with lesion (tumors, AVMs) of functionally important areas (speech production centers first of all) of cerebral hemispheres. This approach is used for maximum preservation of these centers and prevention of subsequent persistent neurological deficit. We have already written about this anesthetic technique [37].

2. Carotid artery repair. Preserved consciousness and dynamic neurological control at the stage of ICA cross-clamping are valuable to diagnose reversible cerebral ischemia and prevent irreversible ischemic injury.

3. Installation of stimulating electrodes into subcortical structures. This neurosurgical procedure is increasingly used for various subcortical hyperkinesis and dystonia. Insertion of electrodes is fundamentally impossible if intraoperative verbal contact with a patient is absent.

4. Endovascular neurosurgical interventions. There is an ambiguous attitude to this issue. However, all authors acknowledge that dynamic neurological control, for example during endovascular vascular occlusion of hemispheric AVM, can prevent persistent postoperative neurological deficit. The role of intraoperative dynamic neurological monitoring in an awake patient for prevention of adverse postoperative outcomes was is considered in one of the recently published reports [38].

7. Acute postoperative pain in neurosurgical patients. For a long time, it was believed that craniotomy is not followed by severe pain syndrome in early postoperative period. This assumption was made considering the absence of movements within the wound after craniotomy (unlike thoracic or abdominal surgery) and advanced tissue tension as predictors of intense pain. The fallacy of this opinion was convincingly proved in some studies of the second half of the 1990s [39–44]. It turned out that up to 84% of neurosurgical patients experienced moderate-to-severe pain within a day after craniotomy! Thus, the relevance of acute postoperative pain in neurosurgery was finally recognized.

Persistent acute postoperative pain is an undesirable phenomenon after any surgical intervention considering various pain-related complications including arterial hypertension, tachycardia, myocardial ischemia, systemic metabolic disorders, organ failure, impaired immunity, cognitive and emotional disorders [45]. In neurosurgical patients, pain syndrome may be associated with certain specific complications.

1. Arterial hypertension is the second most important causative factor (after hypocoagulation) of so formidable complication as acute postoperative
hematoma, especially in immediate postoperative period [46, 47].

2. Hyperglycemia associated with the effect of contra-insular hormones on the background of persistent pain exacerbates the course of cerebral ischemia [48].

3. Reorganization of renal blood flow (juxtamedullary bypass) occurring for the same reasons results fluid retention and aggravates postoperative cerebral edema [49].

These are not all the negative aspects of persistent postoperative pain.

Numerous therapeutic approaches have been proposed for effective treatment and prevention of acute postoperative pain. Effectiveness of these methods is not the same. However, comprehensive description of these approaches is not justified in this report, since these methods were considered in detail in recent our and foreign reports [50-52]. Summarizing these work, we can conclude that on-demand intravenous infusion of morphine is currently recognized as the “gold standard” in the treatment of acute postoperative pain in neurosurgery. This particular method is considered as the basic to assess the effectiveness of all other techniques. Unfortunately, this method is not widespread in our country. However, organizational and technical problems prompted us to use transdermal therapeutic systems with fentanyl (Durogesic matrix or national analogues). We have compared various analgesic modes including regional scalp block with naropin, Lornoxicam according to the scheme and in on-demand mode and Durogesic matrix. It was found that transdermal fentanyl resulted the lowest VAS scores of postoperative pain within 72 hours after craniotomy [53].

In spinal neurosurgery, situation seems even simpler considering possible administration of prolonged epidural anesthesia with local anesthetics (programmed infusion through infusion pumps and elastomeric pumps) if dura mater is intact [54, 55]. Obviously, adequate prevention and treatment of acute postoperative pain in neurosurgical patients imply a reasonable combination of various techniques [56].

8. Hemostatic system in neurosurgical patients and its bedside control. Probably, monitoring and correction of hemostatic disorders in neurosurgery (and, perhaps, in ophthalmic surgery) have the most important significance compared with other surgical fields. This is confirmed by recent large reviews and even manuals devoted to this issue [7, 9—12]. Intracranial and spinal neurosurgery may be followed by such a serious problem as acute postoperative hematoma that aggravates postoperative mortality and disability [57—59]. It would seem that current progress of laboratory diagnosis should eliminate any similar problems. Unfortunately, this is not true. Preoperative screening of hemostatic system turned to be too serious problem. On the one hand, there are various hemostatic characteristics. Analysis of each parameter require time, money and equipment. On the other hand, an attempt of total preoperative laboratory screening of hemostatic system was ineffective in neurosurgical patients [60]. It may seem strange, but comprehensive analysis of previous hemorrhagic and embolic events and development of special questionnaires are effective to identify high risk patients prior to surgery [61]. Drug-induced hemostatic disorders is not significant problem if a patient himself and his relatives did not hide the fact of intake of anticoagulants and antiplatelet agents. However, I would like to emphasize the appearance of relatively new bedside methods for hemostasis system examination over the past decade. These are thromboelastography (TEG), thromboelastometry (Rotem), Sonoclot coagulation analysis and others. TEG technique was developed in Germany in 1943. Currently, this method has become computerized, simper and completely bedside. Thus, anesthesiologist can sample patient’s blood in case of suspected hemostatic abnormalities and receive information about certain hemostatic disorders within 30—40 minutes. Various authors emphasize the expert value of TEG. There is a wonderful national atlas on TEG [62]. An excellent review on the application of techniques in neurosurgery [63—65] and our original article [66] were published. Thus, there are modern methods for fast and objective analysis of hemostasis system in a particular patient and need for correction of these disorders may be determined using these data. This approach is useful to reduce consumption of fresh frozen plasma by at least 4 times for correction of hypocoagulation in neurosurgical patients! [67]

There is another aspect of hemostatic system in neurosurgical patients which may be attributed to breakthrough technologies. This is administration of activated factor VII for hemostasis in case of massive blood loss and associated severe hemostatic disorders. It is important to emphasize this moment. Gerlach et al. [68] reported severe intraoperative hemorrhage in a patient with basal hemangiosarcoma after previous radio- and chemotherapy. A huge
volume of transfusion (30 doses of packed red blood cells) including fibrinogen, cryoprecipitate and factor concentrates were required. However, these measures were ineffective. Favorable effect was achieved only after a double (with an interval of 2 hours) intravenous administration of activated factor VII (NovoSeven, Novo-Nordisk, Denmark) in an adequate dose. Currently, there are many similar cases described in the literature and in our practice. Moreover, national drug Coagil VII (Generium, Russia) has been successfully developed. I would not like to review in detail this large and complex problem and a reader can turn to the recent publication devoted to this issue [69].

9. Deep vein thrombosis (DVT) and pulmonary embolism in neurosurgical patients. Undoubtedly, the problem of perioperative DVT and pulmonary embolism (PE) in neurosurgical patients is less actual than in those with traumatic injuries (incidence of DVT is up to 80%). However, neurosurgical interventions are also followed by DVT and PE in 25% and 3% of patients, respectively [70–72]. Moreover, these complications often occur immediately prior to discharge from the hospital. The problem of effective prevention of DVT and PE is currently resolved in all surgical fields including patients undergoing neurosurgical procedures. However, another picture was observed 10 years ago. Attempts to adapt anticoagulant preventive schemes used after other surgical procedures (oncology, traumatology, abdominal surgery, etc.) with administration of low molecular weight heparins (LMWH) or unfractionated heparin (UFH) in prophylactic doses were failed in neurosurgery due to unacceptable augmentation of intracranial hemorrhagic complications [7]. We determined the safer approach in neurosurgery with mechanical methods of DVT prevention (intermittent pneumatic compression or electrical stimulation of the lower leg muscles) during surgery and within 2 days after intervention. This period is characterized by the highest risk of hemorrhagic complications. Pharmacological methods of prevention were applied later [73]. We were the first to use this approach. Currently, this method is accepted in the world and in our country. Moreover, mechanical methods are recommended as preferable prevention of thromboembolic events in the guidelines of Russian Society of Phlebologists: “intermittent pneumatic compression of the lower extremities is recommended after major neurosurgical procedures considering the high risk of postoperative intracranial hemorrhage. LMWH or UFH may be prescribed in several days after surgery in patients with high risk of venous thromboembolic complications” [74]. Undoubtedly, it’s nice to realize that the innovation that you invented and implemented becomes a part of international protocols.

Conclusion

Of course, this review of the development of modern neuroanesthesiology is not exhaustive. Moreover, this is only the author’s point of view, which may be disputable. At the same time, the main changes of traditional approaches in neuroanesthesiology are reported. These innovations positively change our usual practice.

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Minimally invasive spinal surgery: stages of development

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ABSTRACT

In recent decades, spinal surgery has changed significantly. The active use of modern knowledge of anatomy, various diagnostic modules, specialized surgical equipment and high-tech tools has made it possible to transform classical surgical techniques into a new area of spinal neurosurgery — minimally invasive spine surgery (MISS). Its main goals are to reduce damage to the skin and adjacent tissues, significantly reduce the level of pain, reduce the duration of inpatient treatment and fully restore functional status in the shortest possible time. This article reflects the main criteria for MISS compliance and types of surgical interventions, provides information on the advantages of minimally invasive surgical technologies and their possible disadvantages. Currently, the use of MISS is observed in all areas of vertebrology — for degenerative diseases, tumors, inflammatory and traumatic lesions of the spine. At the same time, minimizing surgical aggression while maximizing the achievement of goal becomes the main rule of modern spinal surgery.

Keywords: minimally invasive surgery, spine, decompression, stabilization, puncture surgical technology, microsurgery, endoscopy.

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Abbreviations
FJ — facet joint
IVD — intervertebral disc
SMS — spinal motion segment
EBM — evidence-based medicine
MISS — minimally invasive spine surgery

The life expectancy of population is being gradually increased in most countries. Therefore, high functional level of patients after spine surgery is especially important problem [1, 2]. At the same time, active industrialization and low socio-economic level in some countries contribute to increased incidence of degenerative, traumatic and metastatic spinal lesions [3—5].

Knowledge is an important component affecting adaptation of society to changes in life conditions. The main aspect of spinal surgery is information about clinical manifestations and instrumental diagnosis of spinal diseases, techniques and technologies of surgical interventions, anatomical and physiological characteristics of certain spinal segment [6, 7].

Previous goals of surgical treatment of the majority of spinal diseases included only pain relief and elimination of neurological symptoms. Currently, these purposes are replaced by more ambitious ones [8]. These are improvement of the quality of life via reduced injury of osseous and ligamentous structures and paravertebral muscles and maintaining the functional state of certain spinal motion segment (SMS) [9, 10]. The following approaches have been developed to achieve these goals: minimally invasive (percutaneous) surgery, interventions through minimally invasive approaches and surgeries aimed at preserving natural biomechanics in certain spinal segment [11—13]. These methods embody a completely new philosophy and modern thinking regarding surgical technologies.
which are combined under the term “minimally invasive spine surgery” [14, 15].

Any surgical procedure consists of two constituent elements. These are surgical approach and specialized manipulations. It is believed that minimal possible incision with the depth exceeding its length may be determined as minimally invasive access [16]. In this case, intermuscular and avascular trajectory with preservation of ligamentous structures is taken into account [11, 17]. Microsurgical, minimally open, endoscopic and percutaneous approaches are actively used for these goals [13, 15].

It is believed that MISS is not intended to completely replace “major” surgery with “minor” one. It is absolutely new direction in spinal surgery associated with favorable functional activity and high quality of life of patients [18]. MISS involves all fields of vertebral surgery although this approach has been recently developed.

The main goals of MISS are less injury of the skin and adjacent tissues, significant reduction of pain syndrome and hospital-stay and complete functional recovery in the shortest possible time [9, 11, 19].

Currently, there are over 700 publications in the PubMed database for the request of “minimal invasive spine surgery”. However, uniform definition and criteria of MISS are still absent.

It was found that minimally invasive techniques have advantages over conventional open procedures [19—21]. At the same time, significant difficulties were noted in adapting surgeons to MISS techniques. These problems are associated with a long learning curve, need for complex technical equipment and specialized tools [22, 23]. In this regard, mastering of new technologies may be accompanied by higher incidence of complications and prolongation of interventions [24, 25].

**MISS criteria**

We reviewed professional literature and identified 4 components characterizing surgical intervention as MISS:

**Anatomical aspect.** Significant modern informational progress stimulates the development of spinal surgical technologies. Fundamental data characterizing the function of various spinal structures are disclosed. Various researchers specified surgical and radiological anatomy of the spine [26, 27]. Another important aspect in adapting surgical technology is active introduction of modern diagnostic techniques. Thus, layer-by-layer tissue analysis followed by virtual images of the area of interest is essential for diagnosis and perioperative neuronavigation [28]. The last method is extremely useful for accurate localization of pathological substrate, determination of the optimal trajectory of approach and reduction of iatrogenic injury of the tissues [29]. Combination of clinical data and specialized neuroimaging modules facilitate functional diagnosis and prediction of surgical outcomes [30].

**Technical aspect.** Modern spine surgery is directly related to the development of medical technical equipment. Modern devices include X-ray tables for optimal on-line intraoperative imaging of surgical area. An equipment also includes electron-optical image intensifier, magnetic resonance scanner, computed tomography scanner, neuronavigation devices, lighting and magnification systems (microscopes, endoscopes, individual head magnifiers), equipment for bone decompression and exposure of the neural structures, as well as retractors and specialized tools for manipulations at any depth of various anatomical corridors [15, 23, 31].

Moreover, widespread introduction of high-quality intraoperative neuronavigation contributed to the active use of robotic devices for manipulations in narrowed spaces [32, 33].

**Personnel aspect.** The generally accepted approaches to learning of spinal neurosurgical interventions have undergone significant changes. So, conventional teaching model consisted of predominant theoretical self-education [15]. Later, an important role of cadaveric and laboratory training was emphasized to improve skills, since the learning curve is directly proportional to learning time [22]. From the modern positions, MISS requires multivalent skills of neurosurgeon, traumatologist, orthopedist, abdominal surgeon, thoracic surgeon, vascular surgeon and radiologist [34].

A particular modern challenge for spinal surgeons is choosing the optimal surgical technology and type of construction. This problem is actual due to wide information availability and controversial data in the specialized literature on the results of deployment of various implants [35].

**Instrumental aspect.** Currently, new surgical techniques and implants are being actively introduced into clinical practice. However, long-term effects of their osseous integration and general effect on the human body are still unclear despite the obvious advantages of their physical and mechanical characteristics over those of bone autografts. In many
respects, the dominant positions for new technical devices are determined by the goals of manufacturing companies which make profit [36]. Increased costs in spinal surgery are actively blocked by government programs and insurance companies because their objective is effective elimination of problem from the standpoint of evidence-based medicine with the best economic result [37].

We have summarized the optimal requirements for implants and tools for MISS using a comprehensive literature data analysis and our own experience (over 6,500 implantations of various devices since 2008). These are safe and quick explantation; minimal bone resection; optimal configuration for implantation under optical magnification; available 3D maneuver with reduction and compression of deformation; reliable fixation with the implant; antireflective coating; simple and fast setting-up of the system; convenient manipulations within deep and narrow wound channel; high learning ability to work with the system; various sizes; various methods of sterilization.

**Justification for MISS introduction**

The use of certain surgical technology is often based on surgeon’s experience. In rare cases, this choice is determined by treatment and diagnostic protocols. However, the majority of these protocols are only advisory in nature.

The principles of evidence-based medicine (EBM) are actively being introduced to objectify the correct decision-making in spine surgery [38]. The main characteristic of this approach is combination of scientifically confirmed facts and personal experience of specialists for diagnosis and treatment of various diseases [39].

The main disadvantages of EBM are impossible application of double blind protocols and significant impact of manufacturers on the results of trials [40]. Studies with small sample size and low methodological quality have a negative role because these researches do not correspond to the number of operations in the world [41].

At the same time, it is impossible to rely solely on statistical characteristics of surgical outcomes. First of all, it is important to skeptically analyze own surgical results and estimate each clinical and instrumental outcome. It is especially true in the case of complications or unsatisfactory results that is necessary to determine the best treatment strategy [11, 42].

**Types and methods of MISS technologies**

Minimally invasive interventions in patients with degenerative spine diseases are the most popular. Decompression and stabilization procedures are used in this patients [11, 13].

**Decompression techniques**

*Puncture surgical techniques.* These methods were originally developed in 1984 by P.W. Ascher and F. Heppner as minimally invasive interventions for the treatment of degenerative lumbar spine diseases [43]. Currently, these methods are used for repair of intervertebral disc (IVD) and facet joints (FJ). Laser denervation and radiofrequency thermocoagulation are destructive methods followed by changes of intradiscal pressure and transformation of pulposus nucleus in the first case [44] and destruction of the lateral branch of spinal roots of facet joints in the second case [45]. Effectiveness of these techniques depends on severity of degenerative changes in spinal structures and correctness of surgical intervention.

*Spinal microsurgery.* Currently, a modification of posterior cervical discectomy proposed by W.B. Scoville and D.D. Whitcomb in 1966 is widely used [46]. Tubular retractors and micro-instruments resulted spinal root decompression with minimal postoperative pain and no injury of paravertebral muscles during endoscopic micro-discectomy [47].

The same technology for lumbar spine was developed by R. Williams at the end of the 20th century [48]. Currently, this approach is considered as the “gold standard” for surgical treatment of most degenerative spinal diseases and results optimal visualization of certain spinal segment without advanced resection of posterior spinal structures [49, 50]. The first report about microsurgical techniques and specialized equipment for minimally invasive lumbar discectomy was published by C. Faubert and W. Caspar in 1991 [51]. To date, microsurgical instruments and modern retractors reduced the risk of neural structure injury, incidence of infectious complications and postoperative pain syndrome severity [52].

*Endoscopic spinal surgery.* In 1962, H.S.Y. Fang and G.B. Ong reported endoscopy-assisted transoral surgery of cervical spine using a non-specialized device [53]. This equipment provided adequate visualization in a narrow space of the oral cavity [54]. H.C. Jacobeus applied endoscopy in thoracic surgery for diagnosis and treatment of pulmonary tuberculosis in 1910 [55]. Development of specialized instruments and improvement of surgical techniques
have contributed to the active use of thoracoscopic interventions since 1990 for IVD hernias, sympathectomies, traumatic injuries, correction of deformity, paravertebral abscesses and in oncological surgery [56—58]. In 1994, H.D. Jho successfully introduced posterolateral endoscopic interventions for degenerative diseases of thoracic spine [59]. These operations are useful for spinal canal reconstruction [60] or excision of intradural extramedullary tumor [61] with minimal trauma to soft tissues and no pleural drainage.

Percutaneous lumbar nucleotomy was first performed by S. Hijikata et al. using an arthroscope under local anesthesia in 1975 [62]. R. Forst and B. Hausmann are founders of classical lumbar endoscopic spine surgery. They examined the interdisc space using the modified endoscopic camera through the cannula in 1983 [63]. Later, P. Kambin and L. Zhou first described lumbar arthroscopic discectomy in 1988 [64]. In 1993, P.J. Mayer and M. Brock used specialized tools [65].

Active introduction of endoscopic techniques was associated with development of tubular systems in the mid-90s of the XX century. H. Mathews [66] and D. Ditsworth [67] described posterolateral and transforaminal (foraminoscopic) percutaneous approaches and changed the concept of spine surgery from indirect central nucleotomy to direct excision of degenerated intervertebral disc from the inside of the spinal canal. In 1999, K. Foley et al. first used microendoscopic discectomy through a tubular retractor for lateral hernia as an alternative to open approach [68]. Currently, this procedure is successfully used for sequestered and lateroforaminal hernias of IVD [69, 70].

Modern possibilities of posterolateral, transforaminal and interlaminar approaches allow effective decompression for any IVD prolapse [71, 72].

**Intermuscular approach.** It was found that subperiosteal approach and advanced dissection of paravertebral muscles result their atrophy and necrosis. L.L. Wiltse and C.W. Spencer developed a paraspinal approach at the end of the 80s of the last century. This technique significantly reduced iatrogenic injury of soft tissues [73]. However, the absence of a special retractor makes impossible minimally invasive manipulations in this anatomical corridor [74].

**Foramininal approach** was described by P. Kambin and M.D. Brager. This inside-out technique implies an approach to neural structures through a 8—9 cm skin incision from the midline under 35° and working area between afferent and efferent spinal nerves [75]. Percutaneous disc decompression through this approach is highly effective for moderate degenerative changes of IVD [76, 77].

Posterolateral approach is also widely used in surgery of thoracic spine tumors and infectious diseases [78, 79].

**Stabilization techniques**

These methods are effectively used for traumatic, malignant and degenerative diseases of cervical, thoracic and lumbar spine and may be performed through anterior, lateral and posterior approaches.

Analysis of specialized literature sources [10, 11, 13, 18, 80] revealed the MISS capabilities, which made it possible to actively use spinal stabilization methods. These are:

- high incidence of interbody fusion cage deployment for spinal diseases without advanced surgical aggression against surrounding tissues;
- active application of intraoperative visualization as a valuable technology for safe internal spine fusion surgery;
- development of osteoblastic materials to improve bone block formation after rigid spine fusion procedure;
- evolution of instruments and implants which are convenient to be used in a narrow anatomical space;
- introduction of new anatomical corridors to the spinal column.

**Puncture stabilization techniques.** Vertebroplasty has been used since 1984, when P. Galibert and H. Deramond injected polymethylmethacrylate bone cement into the vertebral body via transpedicular approach [81]. The first report on an alternative method of vertebral segment reinforcement (kyphoplasty) was made by S.R. Garfin in the 90s of the XX century [82]. Currently, these techniques are used for various processes associated with vertebral destruction including hemangioma, vertebral tumors, traumatic fractures and osteoporosis [83, 84]. Above-mentioned methods imply direct percutaneous transpedicular injection of bone cement (vertebroplasty) or injection into a special reservoir (kyphoplasty, stentoplasty) [85]. These methods are effective for local pain syndrome relief due to exothermic effect and restoration of vertebral support within the shortest possible time.
Percutaneous transpedicular fixation. Initially, percutaneous delivery of transpedicular screw was described by F.P. Magerl in 1984 [86]. Later, this method was combined with tubular retractors and Wilte approach. This fixation involves the consistent use of a Jamshidi needle and a guide needle. A screw is inserted through this needle under fluoroscopic or navigation control [9]. Sextant system (Medtronic, USA) was the first system which completely satisfied the MISS criteria. This system was effective for implantation of a rod pre-modeled for physiological lordosis and assembling a short-segment rigid transpedicular fusion system [87].

Alternative posterior fusion techniques. There are various modifications of these methods. In some cases, these techniques result less damage to soft tissues with effective stabilization of certain spinal segments. These methods include cortical screws, percutaneous iliac structures, facet stabilizing devices, front and side plates, interspinous implants [88–90]. Each of the above-mentions technologies has its own history of development and improvement. This information is beyond the scope of this publication.

Posterior fusion techniques (posterior lumbar interbody fusion, PLIF; transforaminal lumbar interbody fusion, TLIF). In 2002, L.T. Khoo et al. first reported the results of MI-PLIF carried out using tubular retractors and microsurgical technique [91]. This intervention required bilateral approach with facet joint resection and discectomy despite the low invasiveness. Considering these drawbacks, L.T. Holly et al. described unilateral MI-TLIF in 2006 [92]. In case of sufficient surgical experience, this technique is characterized by better technical characteristics of intervention (blood loss, duration of surgery), minimal pain syndrome, fast social and labor rehabilitation, low risk of adverse effects [93, 94]. Combination of MI-TLIF and spinal endoscopic techniques resulted availability of outpatient decompression and fusion surgery through the Kambin’s triangle under local anesthesia [95].

Anterior fusion techniques (anterior lumbar interbody fusion, ALIF). MISS technologies for ALIF are directly related to the beginning of the use of laparoscopic technologies in 1991 [96]. These methods completely replaced transperitoneal anterior interbody fusion proposed by F.H. Albee (1911) [97] and retroperitoneal approach developed by T. Iwahara (1944) [98]. In 1997, H.M. Mayer introduced minimally invasive open anterior approach to lumbar spine using a specialized retractor system and instruments [99]. It was found that this minimally invasive intervention effectively reduces surgical aggression, incidence of perioperative complications and severity of postoperative pain syndrome [100].

Lateral fusion techniques (lateral lumbar interbody fusion, LLIF). LLIF technique was proposed by L. Pimenta and T.L. Schaffa in 2001 [101] and modified by B.M. Ozgur et al. in 2006 [102]. This method is a type of retroperitoneal approach to the lumbar spine and characterized by possible polysegmental manipulations on thoracic spine and significant coronal and segmental correction [100]. The absence of channel manipulations, indirect decompression and the possibility of advanced resection of IVD are the advantages of LLIF [103]. However, the widespread use of this technique is limited by the high risk of lumbar plexus injury and dependence on the individual anatomy of the patient (chest, iliac crest) [104]. One of the modifications of lateral approach to the spine is oblique lateral interbody fusion (OLIF) proposed by C. Silvestre et al. in 2012 [105]. This technique is characterized by lower risk of lumbar plexus injury and high possibilities for correction of sagittal balance [106].

Axial lumbar interbody fusion (AxiaLIF). The technique was proposed by N. Marotta in 2006 as an alternative to anterior and posterior decompression-fusion interventions. The method is valuable to avoid injury of great vessels and paravertebral muscles [107]. AxiaLIF technique via percutaneous presacral approach makes it possible to carry out minimally invasive lower lumbar spine fusion through the sacrum using specialized retractor and micro-instruments [108].

Conclusion

Significant progress has been noted in spinal surgery that is characterized by the development and implementation of new technologies in the diagnosis and treatment of various spinal diseases. Minimally invasive spine surgery is an independent area of modern vertebrology. Individual standards and practical recommendations aimed at reducing the economic costs of rehabilitation and functional improvement in long-term postoperative period are required for development of this direction.
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Repetitive resection and intrasurgery radiation therapy of brain malignant gliomas: history of question and modern state of problem

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ABSTRACT
Numerous studies have shown that the degree of primary resection of malignant gliomas of the brain (MG) directly correlates with rates of relapse-free and overall patient survival. Currently, there is no unequivocal opinion regarding the indications and effectiveness of repeated resection in relapse of MG after combined treatment. Surgical intervention, taking into account the pathomorphological features of these tumors, is not healing and should be supplemented with certain methods of adjuvant treatment. The article reviews and analyzes publications devoted to repeated resection and various methods of intraoperative radiation therapy in the treatment of MG.

Based on the analysis, the authors of the article came to the conclusion that it is advisable to start their own research on the use of intraoperative balloon brachytherapy in the treatment of recurrent MG based on modern technological solutions.

Keywords: glioblastoma, anaplastic astrocytoma, anaplastic oligodendroglioma, radiation therapy, brachytherapy, intraoperative radiation therapy.

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Abbreviations
3MG — malignant gliomas
GB — glioblastoma
AA — anaplastic astrocytoma
AO — anaplastic oligodendroglioma
FEBRT — fractionated external-beam radiotherapy
TFD — total focal dose
OS — overall survival
IRT — intraoperative radiotherapy
IBEB — intraoperative balloon electronic brachytherapy

Malignant brain gliomas are a group of intracerebral tumors with rapid progression and infiltrative growth that determines their unfavorable prognosis in most cases. Glioblastoma (GB) is the most common, anaplastic astrocytoma (AA) and anaplastic oligodendroglioma (AO) are less common[1]. Annual incidence of MG is 4—6 cases per 100,000 that accounts about 40% of all primary brain tumors. Incidence of MG is less only that of brain metastases of tumors growing outside central nervous system [2]. MG resection is not curative, although numerous studies have shown that surgical intervention is necessary and type of resection directly affects recurrence-free and overall survival [3—7]. According to the majority of recommendations, patient should continue treatment within 4—6 weeks after surgery in accordance with one or another adjuvant treatment protocol depending on histological and molecular genetic profile of the tumor [8, 9]. This management is based
on detrimental effect irradiation and chemotherapy on residual macro- and microscopic elements of the neoplasm in peritumorous tissue of the brain. Fractionated external-beam radiotherapy is included into the majority of protocols. Irradiation should be implemented on modern equipment with available 3D modeling of irradiation zone. However, the majority of MG recur within 6—7 months after adjuvant therapy in resection edge and within 2—3 cm from this edge [10—13]. In case of recurrent MG, redo surgery can imply biopsy for morphological verification of recurrent tumor or resection of the maximum safe volume of the neoplasm. Candidates for redo resection are 20—30% of patients with recurrent MG [14]. There is currently no unequivocal opinion regarding the indications and effectiveness of repeated resection for recurrent MG. Postoperative median survival in patients with recurrent GB is 8—12 months as a rule [15, 16], in patients with AA — 12—18 months [17—19]. There is currently no convincing evidence that these results are better than would be expected after radio- and/ or chemotherapy alone. However, redo surgery may be beneficial for some patients (for example, in those with symptomatic mass- effect). The most significant clinical predictor of better survival after redo surgery is high Karnofsky score [14, 16—18, 20]. Other favorable prognostic factors are young age, longer interval after the first operation and redo resection grade [21—23].

One study showed that ependymal spread of the tumor is the most important negative prognostic factor in patients undergoing redo surgery for glioblastoma [24]. Particular caution is required in patients with preoperative intake of bevacizumab due to the risk of impaired wound healing.

Optimal methods and modes of adjuvant treatment after surgery for recurrent MG are still unclear [16].

Fractionated external-beam radiotherapy is recognized as an effective treatment for newly diagnosed MG. According to the literature, effective total focal dose of FEBRT in this case is 60—84 Gy. FEBRT after MG resection significantly improved overall survival. Repeated FEBRT for recurrent tumors is undesirable since local recurrence occurs within 6—7 months after surgery as a rule and repeated irradiation is associated with advanced risk of severe post-irradiation reaction. Radiosurgery is advisable only in some cases of recurrent MG due to infiltrative growth, dimensions and severity of lesion.

Intraoperative radiotherapy may be effective for local tumor control in patients with recurrent MG. IRT implies irradiation of tumor bed and residual macro- and microscopic tumor elements. Early postoperative irradiation can stop and disrupt proliferation of residual tumor cells. Moreover, effective dose exposure around post-resection cavity is achieved. At the same time, surrounding brain tissue is not exposed under advanced irradiation that significantly reduce irradiation-induced necrosis. In addition, high single doses can cause local and systemic immune responses followed by activation of cytotoxic function [25, 26].

Japanese researchers M. Abe et al. were ones of the first who reported the use of IRT in neuro-oncological practice in 1971. They described 2 cases of recurrent malignant intracerebral tumors [27]. Irradiation was carried out using cobalt-60 (60Co) facility and betatron with various electron energies. In the first case, resection of fibrosarcoma of occipital lobe was performed in a 57-year-old woman (single irradiation course with a dose of 3500 P, irradiation field collimator of 8 cm and electron beam energy of 18 MeV). Postoperative period was uneventful. Satisfactory clinical outcome was stable within 5 months after surgery. In the second case, resection of recurrent GB of the right frontal lobe in a 37-year-old woman was followed by single course of radiotherapy (dose of 4000 R, irradiation field collimator of 4 cm, electron beam energy of 12 MeV). Clinical deterioration after 2 months required redo craniotomy. Irradiation-induced necrosis without signs of local recurrence was observed. The patient died in 87 days after surgery on the background of permanent fever. Autopsy was not performed.

N. Sakai et al. reported encouraging results of surgical treatment of MG with IRT in 1991 [28]. IRT was used in 32 out of 73 patients with histologically confirmed AA and GB. In all cases, maximum safe resection and FEBRT (TFD 30 Gy for 25 fractions or 61 Gy for 10 fractions) were followed by chemotherapy with nimustine (ACNU). Repeated craniotomy and IRT with doses of 10—50 Gy (mean 26.7 Gy) per one course were performed in 1 week after surgery using a microtron (MM-22, ScanditronixAB, Sweden). In patients after IRT, 24- and 36-month survival was 57.1 and 33.5%, respectively (mean 26.2 months). In other patients, these values were significantly lower (23.6 and 13.1%, respectively, p<0.01) (mean 20.7 months).
M. Matsutani et al. have applied IRT in 170 patients (85 gliomas, 81 cerebral metastases, 4 other neoplasms) using Shimadzu-20 MeV betatron (Shimadzu, Japan) with electron beam energy of 8—20 MeV for the period 1977—1990. Spatial shape of electron beam was changed by various conical applicators. Resection of intracerebral tumor was followed by filling of post-resection cavity by moistened sterile swabs. Intraoperative irradiation (15—30 Gy for 5—10 min) involved brain tissue at a depth of 1—2 cm from resection edge. There are interesting results in a subgroup of 30 patients with newly diagnosed and recurrent GB who underwent IRT (mean dose 18.3 Gy) combined with FEBRT (mean dose 58.5 Gy, range 30—80 Gy). Median recurrence-free and overall survival was 73 and 119 weeks, respectively. Annual, 2- and 3-year survival was 97, 61 and 33%, respectively [29].

A. Fujiwara et al. used FEBRT combined with IRT in 20 out of 36 patients with MG [30]. A balloon was placed inside post-resection cavity immediately after resection of tumor. This balloon resulted a regular rounded shape of the cavity. IRT (20—25 Gy) was performed using a linear accelerator (Toshiba, Japan) with 80% of isodose within 1.8—3.3 cm from the edge of residual cavity under ultrasonic control. All patients received TFD of 40—50 Gy for 20—25 courses in 2 weeks after surgery. Radiotherapy was followed by chemotherapy with ACNU, cisplatin and carboplatin. Better median survival after IRT compared with the control group was reported (14 and 10 months, respectively). Some trials did not demonstrate significant efficacy of IRT. In 2002, K. Nemoto et al. reported the results of treatment of 21 patients with GB and 11 patients with AA [31]. Excision was followed by IRT of the tumor bed using a linear accelerator (mean dose of 14.9 Gy, range 12—15 Gy). FEBRT with TFD of 60 Gy was performed in 2 weeks after surgery. In patients with AA, annual, 2- and 5-year survival rates were 81, 43, and 21%, respectively. In patients with GB, these values were 70, 18, and 6%, respectively. There were no significant between-group differences.

Spanish researchers reported the results of combined treatment of 17 patients with MG (7 GB, 4 AA, 6 AO) using IRT. Irradiation was carried out immediately after resection of the neoplasm on a linear electron accelerator with a beam energy of 12—18 MeV. A radiation energy beam was formed by conical applicators. ILT with single fraction of 10—15 Gy was used in patients with recurrent tumors and previous external radiotherapy. A dose of 15—20 Gy was used in primary patients. Total resection of macroscopic tumor volume was achieved in 14 patients. In other cases, there was tumor biopsy only. IRT of tumor bed involved surrounding brain tissue within 1—2 cm from the edge of resection cavity. Postoperative combined treatment of newly diagnosed MG and IRT implied fractional irradiation of the whole brain with a TFD of 45—50 Gy and intraoperative irradiation of postoperative cavity and 2—3 cm of surrounding tissue with a dose of 15 Gy.

Patients with recurrent MG had previous external fractional irradiation with a TFD of 50—60 Gy by the moment of IRT. A 18-month survival was 56% in patients with MH who received the combined treatment for the first time and 47% in those with recurrent MG [32].

In 2005, P. Schueller et al. reported the results of IRT in 71 patients with MG [33]. The study included 26 patients with various anaplastic gliomas (AA, AO) and 45 patients with GB. The maximum safe microsurgical resection of supratentorial malignancies was performed under computed navigation. IRT (dose of 20 Gy) was performed in 52 patients with a newly diagnosed tumor using an original neuronavigation device to guide the irradiating beam. Subsequently, FEBRT with TFD of 60 Gy was administered. The study also enrolled 19 patients with recurrent MG who underwent IRT with irradiation dose of 20—25 Gy. Mean survival in patients with AA was 14.9 months, in patients with GB — 14.2 months. A 2-year survival rates were 26.9 and 6.8%, respectively (p=0.0296). Thus, there were no advantages of IRT over FEBRT for OS in this trial. K. Takakura and O. Kubo irradiated 55 MG patients using spherical applicators. A 2-year survival was 89% in patients with AA and 42% in patients with GB. These data exceeded the control values from the Japanese registry of tumors (77 and 21%) [34].

In 2012, I. Zamzuri et al. reported a case report of a 42-year-old patient with GB who underwent resection of about 80% of tumor in accordance with intraoperative assessment [35]. Redo craniotomy and IRT with a dose of 10 Gy were performed in 2 weeks after initial operation. They used an equipment of the Zeiss company (Germany) with a spherical applicator. FEBRT of the whole brain with a TFD of 40 Gy was combined with chemotherapy (temozolomide). There were no clinical and tomographic signs of recurrence within 2-year follow-up period.
There were 24 patients with recurrent GB who were treated at the Johns Hopkins Hospital (USA) for the period 2000–2004. GliaSite radiation therapy system (RTS) was applied [36]. GliaSite balloon was placed inside the post-resection cavity immediately after removal of tumor. Injection port connected to the balloon was taken out subcutaneously in the scalp. Then, the balloon was filled with an isotonic sodium chloride solution through this port so that the surfaces of balloon and post-resection cavity fit snugly over each other over the entire area. Surgeries were completed in standard fashion. Adequacy of balloon localization and isodose curves were assessed using postoperative CT data. Drainage of isotonic sodium chloride solution from the balloon was followed by its filling with radioactive drug Iotrex (iodine-125; ^{125}I). Balloon brachytherapy has been carried out for several days in accordance with specialized algorithms for dose calculation. Mean dose was 53.1 Gy (standard deviation 9.2 Gy, range 29.9–80 Gy). Symmetrical dose distribution was achieved in all 24 patients that emphasizes the advantage of balloons over flat and spherical applicators. Moreover, balloons are more suitable for cavities with complex spatial configuration as the most common result of resection. Median OS was 23.3 months compared to 18 months after redo FEBRT of GB (according to the literature) [37]. A serious drawback of this method is the need for redo surgery to remove GliaSite balloon. In addition, the patient should be isolated from others for radiation safety. Considering these disadvantages, manufacturing of GliaSite was discontinued in 2008.

In 2018, F.A. Giordano et al. reported phase I—II results of the INTRAGO trial. This study was started in 2014 and devoted to analysis of the efficacy of IRT with INTRABEAM system (Zeiss, Germany) in patients with newly diagnosed GB. Literature review preceded the study. There was an important conclusion in this review that the majority of studies performed before 2014 had single-center design and small sample size. FEBRT was carried out using various models of linear accelerators as a rule. The researchers faced with low accuracy in FEBRT planning, difficult choice of adequate collimators, etc. These features significantly reduced the effectiveness of the treatment [38]. F.A. Giordano et al. performed IRT using INTRABEAM system (Zeiss, Germany) with solid-state spherical applicators, which were inserted into the post-resection cavity at the final stage of surgery. IRT with a single dose of 20 Gy on the applicator surface was made in 3 patients. Subsequently, the dose was increased up to 30 Gy and 40 Gy in other patients. Dose escalation was carried out in the absence of so-called dose-limiting toxicity. The authors determined this parameter as the absence of impaired wound healing and need for surgical debridement, IRT-associated hemorrhage and ischemia, symptomatic irradiation-induced necrosis as indication for surgery, need to interrupt external irradiation. Further adjuvant chemoradiotherapy with temozolomide was carried out in accordance with the protocol generally accepted in neurooncology. This protocol was proposed by R. Stupp et al. in 2005 [39]. The objective of the study was analysis of effective and safe dose for IRT. The trial enrolled 15 patients older than 45 years (median 62 (46—72) years) by the moment of publication. According to postoperative MRI data, total resection (over 98% of the tumor) was achieved in only 2 patients. There was no methylation of MGMT gene promoter in 10 patients. Median of local progression free survival was 17.8 months (95% CI 9.7—25.9) in 12 patients who underwent treatment with full observance of the research protocol. Median of recurrence-free period in the entire group was 11.3 months (95% CI 5.4—17). It was associated with distant local progression outside the primary tumor. The authors concluded that IRT is predominantly advisable for local GB. Dose-limiting toxicity was not observed. Therefore, the authors concluded that selected dose range was relatively safe [40].

In 2009, S. Bensaleh et al. published a review devoted to the use of balloon brachytherapy (MammoSite system) for early breast cancer [41]. This device is a balloon connected to a double-lumen catheter. The balloon is placed inside the post-resection cavity in the mammary gland immediately after removal of tumor. Filling of the balloon by a fluid through the catheter resulted inflation of the balloon and its close contact with the walls of post-resection cavity. Irradiation plan was made using CT data. Irradiation involved tissues within 1 cm from the balloon surface. The balloon was filled by radioactive iridium-192 (^{192}Ir) through a separate port for these purposes. TFD of 34 Gy was achieved for 10 fractions (twice a day) with subsequent elimination of the balloon. S. Bensaleh et al. analyzed 11 trials and found that MammoSite system and methods of external accelerated partial irradiation result similar 3- and 5-year disease-free survival in patients with early breast cancer. A significant drawback of this method is the need for the
MammoSite system to remain in the body for at least 2 days. Some authors reported the risk of infectious complications 16%.

In 2011, D.J. Scanderberg et al. reported a 47-year-old man with recurrent AO of the right frontal lobe. Contura device (SenoRx, USA) originally developed for IRT of local breast cancer was applied in this patient [42]. This device consists of balloon-applicator connected to a multi-lumen catheter for introduction of radiation sources. The equipment is applied for high-dose radiotherapy (HDR). Balloon-applicator was placed in post-resection cavity at the final stage of surgery. Computed tomography of the brain, planning and implementation of balloon brachytherapy with a single focal dose of 20 Gy at a distance of 1 cm from the balloon surface were performed in 24 hours after surgery. The balloon was eliminated immediately after brachytherapy. Follow-up period was 6 months. The authors reported no signs of recurrence and any postoperative complications.

There has been a significant improvement of IRT in the treatment of MG over the past few decades. This is facilitated by the introduction of innovative equipment for radiotherapy, rapid development of pre- and intraoperative neuroimaging technologies, as well as software for conformal planning of radiotherapy.

One of the latest achievements in oncological radiology is equipment for intraoperative balloon electronic brachytherapy (IBEB) Xoft ElectronicBrachytherapy System, Axxent (Xoft Inc., USA). This system is equipped by own miniature x-ray source that allows direct irradiation of the tumor bed. Unlike conventional high-dose brachytherapy methods, the Axxent device does not require the use of radioactive isotopes, heavy shields or capital equipment. A miniature x-ray tube with a voltage of 50 kV placed at the end of the source delivers radiation through the applicator during brachytherapy procedure. The source is designed for maximum irradiation of tissue around the applicator. Balloon spherical applicator consists of an inflatable balloon made of silicone elastomer with a contrast agent in the wall of the balloon and multi-lumen catheter with three ports. The balloon is filled only with sterile isotonic solution. The middle port is connected to the central cavity and designed for introduction of x-ray source during radiotherapy. Inflated balloon results a boundary with surgical cavity and provides a clear shape of this cavity for delivering the prescribed irradiation dose during radiotherapy. Radiotherapist and medical physicist jointly draw up a treatment plan to deliver the prescribed dose to the target tissue volume [43].

There are data on improved outcomes of the treatment of various oncological diseases using IBEB implemented on the equipment of the Xoft company [44–48].

Undoubtedly, the problem of MG management is still far from being solved, since the most difficult mechanisms of neuro-oncogenesis are still unclear. Moreover, there are no effective methods from the category of chemotherapy, targeted molecules, etc. Many tumors are initially unresectable and/or characterized by primarily multiple growth.

Developing technologies for surgical and radiological control of local MG recurrence should be investigated regarding their safety and efficacy. Even total resection of these tumors does not result complete recovery and should be supplemented by adjuvant treatment considering the features of these neoplasms. Numerous studies have shown that quality of primary resection directly correlates with overall and recurrence-free survival. Radiotherapy also improves survival rates.

Type of resection of recurrent MG is still debatable. Chemotherapeutic agents, target molecules, immunotherapy methods and tumor treating fields (TTFs) are characterized by moderate efficacy. Repeated external irradiation is not always applicable because of early recurrence and high risk of severe irradiation-induced necrosis.

**Conclusion**

The authors of this article believe that radical resection with intraoperative balloon electronic brachytherapy may be effective and safe in patients with local recurrence of malignant glioma. We started the use of intraoperative balloon electronic brachytherapy for recurrent MG using an Axxent device (Xoft Inc., USA) in order to analyze this approach (registration certificate of the Russian Federation for medical device dated 04.17.2015 No. RZN 2015/2593). This study will include adults with recurrent malignant glioma after combined treatment. All patients will undergo maximum and safe neoplasm resection followed by immediate intraoperative balloon electronic brachytherapy (Xoft equipment) with a prescribed single dose of 20 Gy on the surface of the applicator balloon. Recurrence-free and overall survival, as well as side effects will be analyzed. We will use clinical and tomographic
control with contrast-enhanced and perfusion magnetic resonance imaging of the brain within 24 hours after surgery and then contrast-enhanced and perfusion magnetic resonance imaging of the brain and, according to indications, positron emission tomography of the brain with 18-FDOPA every 3 months until tumor recurrence (in accordance with Response Assessment in Neuro-Oncology criteria). Monthly assessment of Karnofsky score, general and neurological status are scheduled.

Future study is intended to analyze the effectiveness and safety of intraoperative radiotherapy in the treatment of malignant gliomas of the brain.

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Use of navigation in skull base surgery

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ABSTRACT
The review briefly presents the history of development of navigation systems in neurosurgery. The idea of the existing principles underlying the navigation systems used in neurosurgery is given. Currently, the basic principles of navigation are optical and electromagnetic. Studies are presented comparing the accuracy of various navigation systems. Optical navigation demonstrates greater accuracy compared to electromagnetic, but both methods demonstrate a submillimeter error in the experiment. The history of use of navigation in the surgery of the skull base is analyzed in detail, the most relevant areas of use of navigation within the surgery of the skull base are considered: craniofacial reconstruction, endoscopic endonasal surgery, surgery of common tumors of the skull base affecting the infratemporal, pterygopalatine fossa, temporomandibular joint. Indications for the use of navigation, limitations of the methodology are explained.

Keywords: optical navigation, electromagnetic navigation, skull base tumors, craniofacial reconstruction, cranoorbito trauma, augmented reality.

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Abbreviations
MRI — magnetic resonance imaging
CT — computed tomography
PRE — point registration error

One of the main objectives of surgery has always been achievement of a certain anatomical structure through the safest and least traumatic trajectory. This desire facilitated development of intraoperative navigation systems. The first attempts to use navigation in surgery date back to the 19th century when drawn images of deep anatomical structures were “tied” to external anatomical landmarks.

Instruments desired for minimal surgical trauma are especially required in neurosurgery compared to other specialties. Brain and surrounding structures consist of closely located vital and functionally significant formations and even minimal inaccuracy can lead to a fatal result.

In our opinion, navigation in neurosurgery is based on comparison of preoperative neuroimaging data and intraoperative visualization of anatomical structures.

Stereotactic systems was the first stage of the development of navigation. Initial procedures were performed by using of anatomical drawings. Considering these figures, surgeons orientated in accordance with the marks on the frame mounted on the patient’s head. Radiography was followed by development of stereotactic frame system proposed by E.A. Spiegel and H.T. Wycis in the 50s of the 20th century. However, craniograms and ventriculograms did not provide complete information about cerebral structures and extracranial tissues. Development of computed tomography (CT) in the 70s brought stereotactic surgery to a new level of accuracy and safety. However, the need to fix the frame limited the use of stereotactic approach for standard neurosurgical operations, until David Roberts proposed the concept of frameless stereotaxis in 1986 [1].

This event paved the way for development of real-time systems for instrument position control in relation to anatomical structures [2]. The history of the development of intraoperative navigation systems in skull base surgery is primarily associated with professor Georg Schondorff. He was a chief of the Department of Otorhinolaryngology in Aachen and created a prototype of navigation station in close cooperation with physicists and engineers. The first navigation-assisted skull base surgery was performed...
Otorhinolaryngologists integrated navigation systems into endoscopic surgery of paranasal sinuses after development of frameless navigation systems for neurosurgery. The first system was proposed in 1980 by Dr. L. Klimek from Aachen [4]. Navigation techniques based on stationary robotic tools were used prior to improvement of optical navigation systems. These systems may be arbitrarily called mechanical navigation. Navigation device was placed near the operating table on a flexible stand consisting of several movable segments. Inclination angles of these segments were assessed by the built-in microcomputer for analysis of spatial position of the instrument. These navigation systems were inconvenient. However, there was a possibility for more confident manipulations in the conditions of abnormal anatomy.

In 1995, M. Roth et al. proposed a convenient scheme of navigation in surgery of paranasal sinuses. This method was based on optical principle [5]. Modern optical navigation systems include a pair of infrared camera located on a tripod and control unit with a monitor. Surgeon applies the tools with 3—4 reflecting spheres for positioning. These instruments should always be under direct visualization of the camera.

The third current type of frameless navigation is systems based on electromagnetic principle. The concept of electromagnetic navigation was proposed by A. Kato in 1991 [6]. Soon, electromagnetic navigation began to be used in endonasal endoscopic surgery [7]. Unlike optical systems, electromagnetic navigation implies positioning of the instruments in a permanent magnetic field. Magnetic field is created by a generator located near the surgical field. Registration procedure is performed in order to compare CT and MRI images with the patient’s body. There are 2 registration methods regardless of navigation technology (optical or electromagnetic). The first method is matching of several points on CT or MR-scans and anatomical landmarks. Instead of anatomical landmarks, you can apply special stickers which are pre-fixed to the body prior to CT or MRI. The second method is a surface registration. In this case, the recorder moves along the body surface. Then, control unit matches the patient’s virtual model and CT or MRI-scans.

Thus, there are 3 methods in modern navigation depending on the principle of registration.

1. Mechanical navigation. Registration is performed by linking the robotic instrument to the patient’s anatomical landmarks. Positioning of the instrument at each time point is based on calculation of segmental angles of the robotic instrument.

2. Optical navigation. Registration is based on the position of reflecting spheres (emitting diodes) mounted on the patient and the instruments located in the field of view of the paired infrared camera. Position of the instruments and anatomical structures is made through spatial triangulation of the spheres.

3. Electromagnetic navigation. Registration is based on analysis of the position of magnetic marks located on the patient’s body and instruments in magnetic field. Magnetic field is created by the generator.

Such terms as “ultrasound” and “fluorescence” navigation are used in medical literature and everyday clinical practice. In our opinion, this results in terminological confusion, since these methods are not based on matching of preoperative visualization data and patient’s body. Instead, these procedures are applied for real-time examination of the tissues. In our opinion, the terms “ultrasound (fluorescence) intraoperative diagnosis” will be more successful for these methods.

The use of navigation in surgery for intracerebral tumors, craniofacial reconstruction and endoscopic endonasal surgery is described in modern literature. This review is devoted to navigation technology as a separate direction in the context of the use in skull base surgery. Particular attention is paid to national achievements in this field which are highlighted in the reviews and clinical series of national authors from the Burdenko Russian Research Center for Neurosurgery [8, 9]. Various reports are devoted to development of navigation systems, principles of their work and analysis of their accuracy. There is an experience of electromagnetic navigation in 98 patients with neurosurgical pathology including 36 patients who underwent endoscopic interventions. Certain factors affecting the accuracy of navigation and requiring additional control by the surgeon were identified.

Navigation in craniofacial reconstruction

Craniofacial injury results severe cosmetic defects. Abnormal orbital anatomy may be followed by displacement of the eyeball, cosmetic and functional disorders. Navigation systems are actively applied in surgical treatment of comminuted orbital injuries for orientation under complex anatomy [10,
11]. Considering unsatisfactory results of reconstructions, surgeons used new technologies to improve functional and cosmetic results. This is a combination of preoperative computer planning, stereolithographic modeling and intraoperative navigation [12—14]. A “reflection” of the orbital structures from the intact side is superimposed on the affected side using computer modeling for symmetrical reconstruction of the orbital walls. Control points were outlined in accordance with this reflection for intraoperative control of reconstruction. The authors report that the first stage was preoperative planning using 3D-reconstruction of CT images of the skull bones. They used computer reflection of the intact orbital walls for modeling of the proper position of affected orbital walls. Control points were outlined for intraoperative control. The second stage was stereolithographic modeling of individual titanium implants. Intraoperative control of correct position of the implants was performed by matching of the implant with control points using navigation [15]. The navigable (equipped with a navigation sensor) holders of individual implants were developed to increase accuracy of manipulations [16]. There are publications demonstrating the advantages of navigation during craniofacial reconstruction. Effectiveness of navigation was confirmed in experimental trials on cadavers with comprehensive analysis of the measurements [17, 18]. Navigation is also used for endoscopic repair of the orbital walls [19, 20]. Navigation-assisted correction of exophthalmos in patients with endocrine ophthalmopathy is described in national literature [21, 22]. The use of navigation in reconstruction of orbitozygomatic complex is also reported in national literature. Navigation is successfully applied in manufacturing of anatomically correct implants for closure of defects after removal of craniofacial tumors [23] and resection of bone fragments after craniofacial trauma [24—26].

**Navigation in endoscopic endonasal surgery**

Optical and electromagnetic navigation systems are routinely used in modern endoscopic endonasal surgery as in transcranial surgery. Standard system includes a computational unit, software, monitor, infrared camera (or magnetic field generator in case of electromagnetic navigation), navigable tools (Fig. 1).

However, there are features of navigation in endoscopic approaches. Usually, patient’s head does not require rigid fixation. Therefore, infrared or electromagnetic markers should be fixed directly to patient’s head rather head fixation system. In this regard, electromagnetic marking seems more convenient. This system has much smaller dimensions in comparison with massive reference with reflective spheres and may be fixed non-invasively on an adhesive basis (Fig. 2).

Another advantage of electromagnetic navigation in endonasal surgery is miniature dimensions of the navigable instruments and available navigation of conventional instruments (aspirators, cauters, endoscopes) by attaching navigational magnetic marks. The use of massive navigation devices with reflective spheres on endoscopic instruments is difficult due to the peculiarities of endoscopic manipulations (long instruments located close to each other during surgery).

Like any other technology, navigation should be used in strict accordance with indications because expensive equipment is used. Moreover, surgery time is also increased. American Academy of Otolaryngology Head and Neck Surgery developed indications for navigation-assisted endoscopic endonasal procedures in 2002 [27]:

1) redo endoscopic endonasal interventions;
2) abnormal anatomy of the paranasal sinuses due to congenital disorders, trauma or previous surgery;
3) advanced sinonasal polyposis;
4) processes involving frontal, sphenoid sinuses and posterior parts of ethmoid labyrinths;
5) diseases involving skull base, orbit, optic nerve and carotid artery;
6) nasal liquorrhea or skull base defect;
7) benign and malignant sinonasal tumors.

Navigation reasonably increases surgeon’s confidence intraoperatively. However, need to avoid unjustified application of navigation is obvious. This is due to not only high cost. Insufficient knowledge of anatomy may be followed by increased risk of injury of critical structures.

According to the literature, surgeons positively assess intraoperative navigation. However, there are few significant data on reduced incidence of postoperative complications after navigation-assisted surgery. For example, A. Tabae et al. reported significantly less number of redo surgeries in the group of electromagnetic navigation (16.5%) within 2.5 years after surgery compared to procedures without intraoperative navigation (43.2%) [28]. G.K. Krings et al. compared surgery with electromagnetic navigation (97 patients) and surgical
procedures without navigation (63 patients). They found significantly less number of postoperative complications in the first group (1% vs. 11%) [29].

The results of navigation-assisted endoscopic endonasal surgery are also reported in national literature [30]. The authors were among the first in national literature who described the use of navigation for endoscopic removal of tumors and foreign bodies of nasal cavity, paranasal sinuses and anterior skull base.

The results of navigation-assisted endoscopic endonasal skull base surgery are described too [31, 32]. The authors emphasized less time of operations and incidence of postoperative complications, as well as increased surgeon’s confidence during manipulations on skull base structures. Russian neurosurgeons also reported the use of navigation in endoscopic endonasal skull base surgery [33]. The first reports in national literature devoted to navigation-assisted endoscopic endonasal surgery have been found since 2000 [34]. In our country, intraoperative navigation is successfully used in outpatient [35] and in-hospital otorhinolaryngology [36]. There is interesting national experience of navigation-assisted endoscopic endonasal surgery in pediatric practice [37]. National researchers emphasize justified routine application of navigation in endoscopic endonasal interventions in children due to narrowness of nasal passages and anatomical variability of nasal cavity and paranasal sinuses in these patients. Recent studies are devoted to the use of navigation for manufacturing of individual implants for complex skull base defects closure after extended endoscopic endonasal transsphenoidal procedures [38]. Visualization technologies for navigation-assisted surgery are also improved. For example, B.J. Dixon et al. reported the use of augmented reality technology for 3D visualization and warning of the surgeon about the proximity of critical skull base structures [39]. Augmented reality technology implies superimposing of additional images (projections of hidden anatomical structures, for example, carotid artery) on a real image (for example, endoscopic picture). Navigation in endoscopic endonasal surgery is valuable to enlarge accessible for manipulation areas. Undoubtedly, the possibilities of endoscopic endonasal approach to the orbit [40, 41], pterygopalatine and infratemporal fossae [42] may be expanded using navigation.

Navigation accuracy, comparison of methods

Accuracy is the most important characteristic of certain method of navigation. The so-called point registration error is used to quantify the accuracy of navigation. This is the distance from the position of navigated instrument to the real position of the point of interest on the object in millimeters. This value is useful to objectively assess the error of navigation system. Higher PRE is associated with greater error and lower accuracy of navigation system. Similar measurements were carried out by F. Kral et al. [43] for anterior skull base. The researchers used anatomical specimens and navigation system. The study was unique because electromagnetic and optical modules were combined in navigation system. This feature significantly increased the representativeness of data. Accuracy of optical navigation significantly exceeded accuracy of electromagnetic one. However, both systems were characterized by less than 1 mm errors. Mean PRE of optical navigation was 0.12 mm, electromagnetic navigation — 0.37 mm. The same research group
analyzed structures of the middle cranial fossa and temporal pyramid and found similar results (0.22 vs. 0.99 mm) [44]. N. Komune et al. [45] analyzed the accuracy of electromagnetic navigation in experimental cadaveric study of middle cranial fossa and temporal pyramid. According to their data, mean PRE was 0.49 mm. K. Matsushima et al. analyzed the accuracy of electromagnetic navigation in retrosigmoid and endoscopic approaches to the structures of posterior cranial fossa and temporal pyramid. According to their data, mean PRE did not exceed 0.5 mm for all control anatomical points. Thus, both navigation methods demonstrate less than 1 mm errors despite lower accuracy of electromagnetic navigation compared to optical one. This is optimal for skull base surgery [45].

**Navigation in transcranial skull base surgery**

The first reports devoted to navigation in skull base surgery appear in the second half of the 90s of the twentieth century. Historically, mechanical navigation was the first navigation technique. In 1995, R.L. Carrau et al. reported the first experience of mechanical navigation during craniofacial resection [46]. An article devoted to the use of navigation in surgery for intracranial meningiomas including skull base tumors was published in the same year [47]. The same group of researchers reported a sample of 20 patients who underwent navigation-assisted skull base surgery in 1996 [48]. A report devoted to the use of mechanical navigation system (ISG viewing wand) in skull base surgery was published too [49]. This initial experience showed the importance of intraoperative navigation to differentiate critical structures, boundaries of sinusoidal craniotomy. A report of navigation-assisted surgery for middle cranial fossa diseases was published in the same year [50]. S. Hassfeld et al. reported a large sample of patients and compared optical and mechanical navigation in skull base surgery in 1998 [51]. At that time, the accuracy of both methods did not exceed 2.7 mm. The first reports devoted to the use of prototypes of electromagnetic navigation systems in skull base surgery have been published in 1999 [52]. The reports devoted to application of the first industrial electromagnetic navigation system InstaTrak 2000 in skull base surgery were published in 2001 [53]. At that time, system accuracy was estimated within PRE range of 1.2—2.8 mm. Optical navigation has been applied in skull base surgery since 2002 [54]. Navigation is valuable in anterior skull base surgery to determine resection margins in patients with advanced malignancies [55]. An important role of navigation in open skull base surgery for the tumors of middle cranial fossa and lower parts of external skull base should be emphasized. Large muscle mass within infratemporal and pterygopalatine fossae and the proximity of critical structures (internal carotid and maxillary arteries, auditory tube, facial nerve, structures of temporal pyramid, temporomandibular joint) complicate orientation and increase the risk of perioperative complications. Navigation is useful to identify various anatomical structures and avoid injury of vital structures in this area by implementing augmented reality technologies [56, 57].

Augmented reality technologies imply superimposing of projections of anatomical structures (for example, carotid artery) and functional maps (tracts, cortical centers) on the intraoperative images. Intraoperative navigation is valuable in patients with tumors affecting temporomandibular joint, because this method allows to determine resection margins and control the adequacy of skull base and mandible reconstruction [58]. Navigation eliminates the use of fluoroscopic control and reduces radiation load on the patient and staff during percutaneous manipulations (for example, percutaneous biopsy of tumor within foramen ovale) on the structures of skull base [59, 60]. It is necessary to mention a large sample of S.C. Bir et al. The authors applied intraoperative navigation in surgery for intracranial meningiomas. The study enrolled 188 patients with skull base meningioma who underwent navigation-assisted surgery and 153 interventions without navigation. It was found that intraoperative navigation is associated with better recurrence-free survival, less blood loss, shorter hospital-stay and lower complication rate [61].

There was a comparison of different methods of reference registration and fixation depending on the part of skull base. T.D. Grauvogel et al. found the greatest accuracy for invasive references (titanium screws, Fig. 3), that is optimal for complex open procedures on the midline skull base. Adhesive facial reference results less than 1 mm accuracy in craniofacial surgery. Hybrid registration (non-invasive fixation combined with surface registration) can improve navigation accuracy in non-invasive fixation of reference [62].

Navigation is also successfully used during frontotemporal craniotomy to determine the boundaries of frontal sinuses and avoid their unjustified dissection [63]. Navigation seems to be
advisable for advanced tumors of anterior skull base [64] and resection of craniofacial fibrous dysplasia. Preoperative 3D modeling is used for symmetric reconstruction with projection of intact skull base contour on the affected side. Intraoperative navigation is valuable to accurately determine the type of resection and restore symmetry [65].

Navigation in training of neurosurgeon

Navigation is used to train specialists in skull base surgery. 3D skull base models are reconstructed using neuroimaging data with their subsequent 3D-printing. These models are used to study normal and pathological anatomy of skull base under navigational control [66].

Conclusion

Navigation is essential in skull base surgery. Feasibility for application of this method is associated with several factors. It is known that individual anatomical variability of skull base structures often complicates intraoperative orientation. Navigation is very useful in cases of narrowed visible surgical field (for example, nasal cavity in a child) or impaired visibility due to large amount of soft tissues (infratemporal fossa).

Tumor process also impairs normal anatomy of organs and tissues besides anatomical variability per se. Compilation of neuroimaging data and a real object is useful to determine the changed position of anatomical objects. This is especially important for identifying critical structures of skull base and preventing their injury. In our opinion, navigation of carotid artery is of the greatest clinical significance in patients with large and advanced skull base tumors. The use of navigation allows you to quickly reduce tumor volume away from the carotid artery and then safely manipulate near the vessel under navigational control. It is known that the use of navigation in surgery of intracerebral tumors is complicated by brain-shift effect. In this case, brain displacement after excision of tumor eliminates the value of navigational control of resection quality and prevention of injury of significant functional structures. On the contrary, rigid bone structures of skull base increases the value of intraoperative navigation in skull base surgery. Navigation is actual for percutaneous biopsy of deep tumors of skull base because this approach makes it possible to abandon the use of fluoroscopic control for these minimally invasive procedures. Navigation accuracy is still insufficient to completely replace stereotactic biopsy of intracerebral tumors because exact coordinates of the target is essential in these patients. However, less than 1 mm navigation accuracy is quite enough for a biopsy of skull base tumors.

Undoubtedly, navigation is extremely important for craniofacial reconstruction and resection of fibrotic dysplasia.

Keyhole surgery is an important field of modern neurosurgery. Minimally invasive approaches and endoscopic assistance are significantly associated with reduced surgical trauma, postoperative hospital-stay, risk of wound complications, improved cosmetic outcomes, etc. At the same time, this approach is obligatory associated with routine use of navigation for preoperative planning, adequate positioning of a patient on the operating table and manipulations under narrowed visibility compared to standard procedures.

Development of navigation systems is associated with progress in the use of augmented reality technologies, virtual modeling of pathological processes and compilation of these data with 3D-models of a patient (Fig. 4).

The study of navigation principles is organically included into educational programs for neurosurgeons. Training programs are also realized through creation of hybrid simulators for skull base surgery. At the same time, it is necessary to remember that navigation is an expensive method associated with increased duration of surgery. Moreover, this
technology does not replace skills and knowledge of surgeon. So, the use of navigation is justified only after comprehensive study of anatomy and surgical technique. Navigation is used in almost all areas of skull base surgery, that emphasizes obvious relevance of this technology to increase efficiency and safety of manipulations in this complex anatomical area.

The authors declare no conflicts of interest.


REFERENCES


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