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In accordance with the resolution of the Higher Attestation Commission of the Ministry of Education and Science of the Russian Federation, the N.N. Burdenko 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.
Surgery of Skull Base Tumors Extending to the Orbit, Paranasal Sinuses, Nasal Cavity, Pterygopalatine and Infratemporal Fossae: the History and Current State of Diagnosis and Approaches to Surgical Treatment

V.A. CHEREKAEV¹, A.B. KADASHEVA¹, D.A. GOLBIN¹, A.I. BELOV¹, A.V. KOZLOV¹, I.V. RESHETO¹, N.V. LASUNIN¹, D.S. SPIRIN¹

¹N.N. Burdenko Neurosurgical Institute, Russian Academy of Medical Sciences, Moscow; ²P.A. Herzen Moscow Research Oncological Institute, Ministry of Health of the Russian Federation, Moscow, Russia

When ophthalmic surgeons (representing one of the oldest branches of surgery) and neurosurgeons (representing the relatively young branch) have met at the border of the cranial cavity and the orbit, many doubts emerged about the possibility to cross this barrier from either side, American surgeon H. Cushing, the founder of modern neurosurgery, wrote in 1938 [22].

Globally, large experience in treatment of craniofacial tumors – a complex pathology, involving the skull base, orbit, paranasal sinuses, infratemporal fossa – has been accumulated to the present moment. It is mainly presented by publications from the U.S. and Europe (Table 1).

A significant contribution to the development of diagnosis and treatment methods for these neoplasms made by N.N. Burdenko Neurosurgical Institute possessing the world’s largest clinical material, has been widely recognized. This is confirmed by the priority articles that have been published by the members of the Institute both in the Soviet period (since 1986) and in the

Table 1. Comparison of the main published surgical series of craniofacial tumors

<table>
<thead>
<tr>
<th>Series</th>
<th>Year</th>
<th>Country</th>
<th>Number of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningiomas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N.N. Burdenko Neurosurgical Institute</td>
<td>2007–2011</td>
<td>Russia</td>
<td>205</td>
</tr>
<tr>
<td>L. Yong et al. [42]</td>
<td>2009</td>
<td>China</td>
<td>37</td>
</tr>
<tr>
<td>J. Bonnal et al. [18]</td>
<td>1980</td>
<td>Belgium</td>
<td>34</td>
</tr>
<tr>
<td>S. Honeybul et al. [26]</td>
<td>2001</td>
<td>Great Britain</td>
<td>15</td>
</tr>
<tr>
<td>M. Ammirati et al. [14]</td>
<td>1990</td>
<td>Germany</td>
<td>4</td>
</tr>
<tr>
<td>Juvenile craniofacial angiofibromas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N.N. Burdenko Neurosurgical Institute</td>
<td>2007–2011</td>
<td>Russia</td>
<td>47</td>
</tr>
<tr>
<td>G. Roger et al. [38]</td>
<td>2002</td>
<td>France</td>
<td>9</td>
</tr>
<tr>
<td>C. Bales et al. [15]</td>
<td>2002</td>
<td>USA</td>
<td>5</td>
</tr>
<tr>
<td>E. Mair et al. [31]</td>
<td>2003</td>
<td>USA</td>
<td>5</td>
</tr>
<tr>
<td>P. Nicolai et al. [36]</td>
<td>2003</td>
<td>Italy</td>
<td>4</td>
</tr>
<tr>
<td>Craniofacial neurinomas and neurofibromas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N.N. Burdenko Neurosurgical Institute</td>
<td>2007–2011</td>
<td>Russia</td>
<td>24</td>
</tr>
<tr>
<td>K. Yoshida et al. [43]</td>
<td>1999</td>
<td>Japan</td>
<td>6</td>
</tr>
<tr>
<td>G. Rallis et al. [37]</td>
<td>2011</td>
<td>Greece</td>
<td>1</td>
</tr>
<tr>
<td>F. Servadei et al. [40]</td>
<td>2012</td>
<td>Italy</td>
<td>1</td>
</tr>
<tr>
<td>P. McCormick et al. [32]</td>
<td>1988</td>
<td>USA</td>
<td>1</td>
</tr>
<tr>
<td>Tumors of a chondroid series</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N.N. Burdenko Neurosurgical Institute</td>
<td>2007–2011</td>
<td>Russia</td>
<td>10</td>
</tr>
<tr>
<td>Different authors</td>
<td></td>
<td></td>
<td>Single cases</td>
</tr>
</tbody>
</table>

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present in top American and European journals: Journal of Neurosurgery, Neurosurgery, Journal of Craniofacial Surgery, Surgical Neurology, Journal of Neurooncology [17, 19, 20, 25, 29, 30, 33, 41]. In this review, we have attempted to present the history and current state of the craniofacial oncology problem.

Despite the relative rarity (about 5% of all tumors operated on at the N.N. Burdenko Neurosurgical Institute), the problem of skull base tumors extending to the orbit, paranasal sinuses, nasal cavity, pterygopalatine and infratemporal fossa, which are also known as "craniofacial ones", is among the most topical and complex in basal neurosurgery. This is due to such factors as simultaneous extra- and intracranial spread, the need for interdisciplinary collaboration in determining treatment tactics, the choice of an optimal surgical approach, complexity of plasty of a skull base defect, etc.

It should be noted that there is no anatomical concept of the "craniofacial region". The term "craniofacial tumor" is conditional. It means a neoplasm of the skull base extending both intracranially and to extracranial structures of the facial skeleton [7, 10]. Upon that, the source of growth may be located either inside the skull cavity or on the external base of the skull.

As a whole, craniofacial tumors present a very heterogeneous group of diseases, which includes benign, malignant, and pseudotumor neoplasms, with being beyond the classification of CNS tumors by the World Health Organization, because a considerable number of tumors also belong to soft tissue and bone neoplasms [16]. All these types of pathology are combined only on topographic principle. Below, a summary histological classification is presented, based on our data for 2007–2011 (Table 2).

**Emerging craniofacial oncology as a new direction of basal surgery**

The problem of surgical treatment for craniofacial tumors has been developing at the N.N. Burdenko Neurosurgical Institute since the middle of the XXth century. In the USSR, the first dissertation on an approach to craniofacial tumors was defended by A.G. Zhagrin under the guidance of Academician of the USSR Academy of Medical Sciences, Prof. B.G. Egorov in 1954 [4]. The Honored Scientist of the RSFSR Prof. G.A. Gabibov was the founder and inspirer of the development of craniofacial surgery in our country. Since craniofacial surgery, which is a part of basal surgery, requires a multidisciplinary approach, the leading experts of allied disciplines: oncology (Prof. V.O. Olshtansky), neuro-ophthalmology (Prof. O.N. Sokolova), ontonurology (Prof. N.S. Blagoveschenskaya), plastic and reconstructive surgery (Prof. A.I. Nerobeev), had participated in establishing this direction at the Institute. Currently, operative interventions using craniofacial approaches are performed by professionals of the 6th neurosurgical department. This is the first neurosurgical department in the former USSR which specialized in this field that was set up in 1999, while a new building of the Neurosurgical Institute was opened simultaneously. Over 1,500 patients with tumors with craniofacial spread have been operated on at the department since its establishment.

Surgery of craniofacial tumors is a new trend in oncology. It is believed that the founder of modern craniofacial surgery was the H. Cushing’s student, Hugh Cairns, who along with ophthalmologists and plastic surgeons was developing for the first time a technique for plasty of skull base defects in the 1940s. It should be noted that in our country and abroad, fundamentally different approaches to treatment of this pathology have been adopted. While the feature of a domestic practice is concentrating these patients mainly at large neurological and oncological centers, in western countries, treatment of craniofacial tumors is performed by teams of surgeons of different specialties (consisting usually of a neurosurgeon, an ENT surgeon, an ophthalmic surgeon, a maxillofacial surgeon, if necessary, and other specialists), with each of them performing a definite function confined to practical opportunities of a particular discipline. The absence of a universal standard is apparently related to the fact that craniofacial tumors do not actually belong to any specialty and are the border issue. However, their forced inclusion into the group of neurosurgical diseases or tumors of the head and neck is reasonable, and has a certain sense in very specific conditions of the medical care organization in our country, where patients with complex pathology are concentrated mainly at large tertiary centers, rather than at general hospitals, as is customary for example, in Europe or the USA. Nevertheless, given the current state of the health care system in Russia and abroad, it is impossible to call any of the approaches either right or wrong. Just one fact is unambiguous that in the health care systems abroad, the attitude to the specialist’s invasion of a "foreign" specialty territory is traditionally negative. It should be noted that at the N.N. Burdenko Neurosurgical Institute, the multidisciplinary approach in the full sense of the word has remained to date only in the diagnosis, which is absolutely valid in terms of quality.

The evolution of the surgical technique conformed to the trends of the basal surgery development in general. A period of large traumatic approaches was very popular in skull base surgery in the 1980s–1990s. The preference was given to cranio-orbital zygomatic trepanation, transfacial approaches, and later to the transbasal approach by Derome [21, 24]. Striving for performing a larger approach inevitably affected the cosmetic results of surgeries: face incisions were usually practiced; moreover, the rate of postoperative complications was quite high – up to 30% [23].

Basic research of anatomy and microsurgical techniques of craniofacial approaches was conducted at the N.N. Burdenko Neurosurgical Institute. In particular, for the first time in the world, the transcranial approach...
to the intraorbital portion of the optic nerve had been developed in detail [17], which had been used successfully in clinical practice for many years. This approach provided the opportunity to reach the optic nerve in three different ways: 1) through the space between the upper oblique muscle laterally and the muscle lifting the upper eyelid, and the upper rectus muscle medially; 2) between the muscle lifting the upper eyelid, and upper rectus muscle; 3) through the gap confined medially by the muscle lifting the upper eyelid, and the upper rectus

<table>
<thead>
<tr>
<th>Craniofacial tumors</th>
<th>Quantity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningiomas</td>
<td>63,4</td>
</tr>
<tr>
<td>Non-meningeal mesenchymal tumors:</td>
<td>12,1</td>
</tr>
<tr>
<td>juvenile angiofibroma</td>
<td></td>
</tr>
<tr>
<td>cavernous hemangioma</td>
<td></td>
</tr>
<tr>
<td>hemangioma</td>
<td></td>
</tr>
<tr>
<td>hemangiopericytoma</td>
<td></td>
</tr>
<tr>
<td>melanoma</td>
<td></td>
</tr>
<tr>
<td>leiomyosarcoma</td>
<td></td>
</tr>
<tr>
<td>solitary fibrous tumor</td>
<td></td>
</tr>
<tr>
<td>cementing fibroma</td>
<td></td>
</tr>
<tr>
<td>ossifying fibroma</td>
<td></td>
</tr>
<tr>
<td>fibrosarcoma</td>
<td></td>
</tr>
<tr>
<td>neurofibrosarcoma</td>
<td></td>
</tr>
<tr>
<td>myofibrosarcoma</td>
<td></td>
</tr>
<tr>
<td>Epithelial tumors:</td>
<td>7,9</td>
</tr>
<tr>
<td>cancer</td>
<td></td>
</tr>
<tr>
<td>cancer metastasis</td>
<td></td>
</tr>
<tr>
<td>Tumors from peripheral nerves:</td>
<td>4,0</td>
</tr>
<tr>
<td>neurofibroma</td>
<td></td>
</tr>
<tr>
<td>neurinoma</td>
<td></td>
</tr>
<tr>
<td>ganglioneuroma</td>
<td></td>
</tr>
<tr>
<td>MPNST**</td>
<td></td>
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<tr>
<td>Osteogenic tumors:</td>
<td>2,3</td>
</tr>
<tr>
<td>osteoma</td>
<td></td>
</tr>
<tr>
<td>chondrosarcoma</td>
<td></td>
</tr>
<tr>
<td>chordoma</td>
<td></td>
</tr>
<tr>
<td>chondroid chordoma</td>
<td></td>
</tr>
<tr>
<td>chondroma</td>
<td></td>
</tr>
<tr>
<td>osteoidosteoma</td>
<td></td>
</tr>
<tr>
<td>Undifferentiated neoplastic diseases of bone:</td>
<td>1,9</td>
</tr>
<tr>
<td>fibrous dysplasia</td>
<td></td>
</tr>
<tr>
<td>bone cyst</td>
<td></td>
</tr>
<tr>
<td>aneurysmal bone cyst</td>
<td></td>
</tr>
<tr>
<td>Inflammatory and infectious diseases with pseudotumor state of the disease:</td>
<td>1,9</td>
</tr>
<tr>
<td>processes with known etiology and pathogenesis</td>
<td></td>
</tr>
<tr>
<td>polyp</td>
<td></td>
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<tr>
<td>eosinophilic granuloma</td>
<td></td>
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<tr>
<td>foreign body granuloma</td>
<td></td>
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<tr>
<td>Wegener's granulomatosis</td>
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<tr>
<td>idiopathic processes</td>
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<tr>
<td>pseudotumor</td>
<td></td>
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<tr>
<td>Lymphoproliferative processes:</td>
<td>1,1</td>
</tr>
<tr>
<td>lymphoma</td>
<td></td>
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<tr>
<td>plasmacytoma</td>
<td></td>
</tr>
<tr>
<td>histiocytosis X</td>
<td></td>
</tr>
<tr>
<td>Cyst and tumor-like lesions:</td>
<td>0,9</td>
</tr>
<tr>
<td>epidermoid cyst</td>
<td></td>
</tr>
<tr>
<td>dermoid cyst</td>
<td></td>
</tr>
<tr>
<td>xanthogranuloma</td>
<td></td>
</tr>
<tr>
<td>Neuronal tumors:</td>
<td>0,8</td>
</tr>
<tr>
<td>olfactory neuroblastoma</td>
<td></td>
</tr>
<tr>
<td>Unspecified</td>
<td>1,9</td>
</tr>
</tbody>
</table>

Footnote: * – 647 patient with craniofacial neoplasms had been operated over 2007–2011 years. ** – Malignant peripheral nerve sheath tumor.
muscle and the anterior rectus muscle laterally. The last of the three ways turned out to be the most convenient and safe. Despite the fact that the transcranial approach to the orbit is primarily of historical interest, this study is very relevant today, since the principles of orbital microsurgery have not changed significantly and have regularly been used in the modern cranio-orbital approaches: supraorbital, orbitozygomatic, lateral orbitotomy (see below). An important contribution to the development of craniofacial surgery was made by the study of microanatomy of the superior orbital fissure — one of the most complex and key structures of the skull base, located on the border of the cranial cavity and the orbit [7, 33]. This pioneering study was published in the Journal of Neurosurgery; the article by Natori and Rhoton appeared in print only in 1995.

Further improvement of the surgical technique was aimed at increasing cosmesis of skin incisions and reducing osteotomy side effects, ousting wide craniotomies with the economical extradural approaches, introducing functional endoscopic sinus surgery (FESS) techniques as well as endoscopic assistance and other technologies.

Modern philosophy of basal surgery was formulated by outstanding neurosurgeons (M. Yaşargil, M. Samii, O. Al-Mefty, et al.). Not only was there a desire for maximal completeness of tumor removal and minimal postoperative mortality, but also recovery and preservation of the high quality of life for patients come to recover from. This imposes certain restrictions on aggressive surgical procedures and sets more stringent requirements for the professionalism of surgeons [39]. These same principles are applicable in full to craniofacial oncology. An optimal surgical approach has to be minimally traumatic, maximally comfortable for visualization and manipulations as well as to facilitate the achievement of a high degree of completeness, a control for a tumor growth (if possible), good functional outcomes and cosmetic results.

It is necessary to lay special emphasis on the most important current tendency in skull base tumor surgery — the refusal of undue completeness at a high risk of complications in favor of either non-radical surgery with follow-up or adjuvant therapy (if the tumor is sensitive to radiation therapy and/or chemotherapy). New strategies in treatment of craniofacial tumors have allowed to reach the worldwide average outcomes of treatment (currently surgical complication rate does not exceed 7–8%).

**Current state of diagnosis and treatment of craniofacial tumors at the N.N. Burdenko Neurosurgical Institute**

**Diagnosis.** We have developed an algorithm for diagnosing tumors with craniofacial spread, with an objective examination being an integral part of it. For a comprehensive examination of symptoms in the patient with a craniofacial tumor, the participation of a neurologist, a neuro-ophtalmologist, and an otoneurologist is required since the main feature of the craniofacial tumor manifestation is the presence of not so much neurological as neuro-ophtalmological and nasal symptoms [5].

**Nasal symptoms:** dysosmia (hypo-, anosmia), difficulty in nasal breathing, nasal discharge, nasal bleeding (profuse, moderate), nasal liquorhea (profuse, moderate, hidden), obturation of the nasal cavity by a neoplasm (polyp, tumor, meningoecele).

**Neuro-ophtalmological symptoms:** visual disturbances (reduction of vision up to amaurosis), visual field defects (scotomas, hemianopia of different types), changes in the cornea and conjunctiva, ptosis or semi-ptosis of the upper eyelid, swelling of the eyelids, lagophthalmos, eyeball dystopia (axial, vertical, horizontal), asymmetry of the pupil diameter, the impaired pupil reaction to light and convergences, oculomotor disturbances, changes in the optic nerve disc (edema, atrophy), syndromic disorders (orbital apex, superior orbital fissure, chiasmatic, Foster Kennedy syndromes).

**Other symptoms:** impaired sensitivity of facial skin and mucous membranes, facial pain, swelling and deformation of the face, malnutrition and impaired function of the muscles innervated by the nerve V (temporal, pterygoid, chewing), limitation of mouth opening due to blockage of the temporomandibular joint, dysfunction of the facial nerve, changes in the outer ear canal skin, otoliquorrhea, eardrum changes (e.g., retraction of the tympanic membrane is characteristic of a block of the eustachian tube upon the propagation of the tumor in the infratemporal fossa), hearing impairment, nystagmus, ataxia, balance and gait disorders, a deformity of the palate, a dysfunction of the palate, pharynx, larynx, and tongue muscles, and taste disturbances.

Besides these local symptoms, associated first with lesions of the external base of the skull, other known cerebral and focal neurological symptoms attributable to the tumor’s impact on the base of the anterior and middle cranial fossae can be observed. These include: cephalalgia, emotional, personality and amnestic disorders, symptomatic epilepsy, incoordination, and in rare circumstances, speech and movement disorders including extrapyramidal symptoms.

Instrumental diagnosis of tumors of craniofacial spread is primarily based on the use of radiological methods of visualization (spiral computed tomography (SCT), MRI). According to the plan for examination of patients with craniofacial tumors used at the Institute, an evaluation of the following parameters is required:

1. Spread of a tumor (damage to certain structures of the internal and external base of the skull).
2. The type of the osseous tissue changes (hyperostosis, destruction, deformity, compression atrophy, trabecularism).
3. The growth type: circumscribed, infiltrative.
5. The presence of the secondary changes (necrosis, cyst, peritumoral swelling of the brain substance, hemor-
rhage, mass effect, petrifications, congestive changes in the paranasal sinuses, etc.).

6. The presence of pathological blood vessels.

7. Features of tumor perfusion according to a SCT perfusion study (hypoperfusion, hyperperfusion, heterogeneous perfusion, hyperperfusion of matrix, stroma or the paracortical area of a tumor; indices CBV the mean blood volume and CBF — the mean blood flow velocity).

8. The signal from a tumor according to the diffusion-weighted MRI data (hyperintense, isointense, hypointense, a diffusion coefficient value).


In certain cases, direct or noninvasive angiography (SCT angiography) is performed for: 1) determining the nature of relationships of the tumor to major vessels primarily to the internal carotid artery and its branches (stenosis, obturation); 2) identifying the sources of blood supply to the tumor with a purpose of their possible subsequent embolization (see below).

Thus, the current approach to radiological examination of patients with craniofacial tumors involves the use of spiral CT, before and after administration of a contrast substance, in three projections, in bone and brain modes, if necessary – with three-dimensional reconstruction as well as SCT-angiography and SCT-perfusion (Fig. 1) [13]. MRI examinations are performed using standard sequences — T2WI, FLAIR, T1WI before and after administration of a contrast substance, with STIR or FAT SAT (sequences with fat suppression, which is especially important in the evaluation of patients with orbital lesions), in addition, the diffusion-weighted imaging (DWI).

In the presence of liquorrhea, standard SCT and/or MRI as well as SCT and/or MR cisternography are used.

One of the main goals of a preoperative examination is establishing a preliminary diagnosis, which is crucial for determining treatment tactics. For example, in cases of a suspected common malignant process or disease, requiring conservative treatment, tumor biopsy is first indicated. Endonasal endoscopic biopsy is the "golden standard" of craniofacial tumor verification; however, if the tumor is unattainable for this approach, then open biopsy can be performed. In craniofacial surgery, needle biopsy of tumors is used infrequently because it is uninformative, especially in situations that require an immunohistochemical study of the material.

Ultrasonic methods of examination are seldom used. One of the main indications is determining the degree of the eyeball involvement in the neoplastic process.

Surgery. We have developed the following principles of surgical treatment of patients with craniofacial tumors:

1. Preoperative embolization of feeding vessels.
2. A low-traumatic extradural approach to the neoplasm with minimal brain tissue traction.
3. Tumor removal with resection of affected parts of the skull base.
4. Tumor removal in the "blind zones", which are not accessible to the direct survey, using the endoscopic technique.
5. Preservation of the neurovascular structures.
6. Tight closure of skull base defects.

Endovascular embolization of tumor afferents is used as the first stage of surgical treatment of tumors with rich

![Fig. 1. A giant craniofacial angiofibroma.](image)
Left — Contrast-enhanced SCT; right — SCT perfusion imaging. Red regions indicate very high blood flow parameters in the tumor.

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blood supply (juvenile angiofibroma, meningioma) in the presence of feeding vessels available for switching off (Fig. 2). Usually, these afferents belong to the system of the external carotid artery (most often — the maxillary artery and its branches, the superficial temporal artery, the ascending pharyngeal artery). The afferents of the internal carotid artery system are usually not available for endovascular occlusion. Embolization is often performed simultaneously with direct diagnostic angiography; it exists in two versions, depending on an artery catheterization technique: selective and super selective. Different materials, PVA, ONYX, etc, are used to switch off the afferents. The time interval between the embolization of feeding vessels and the tumor removal should not exceed 72 hours because of starting revascularization.

Craniofacial approaches to the skull base with minimal brain traction have certain features, on which the indications for their use are based, depending on the spread of the tumor (Table 3; Figs. 3—8). In special cases, for example, other approaches are used: orbitozygomatic + infratemporal, orbitozygomatic + endonasal endoscopic, through the frontal sinus + endonasal endoscopic, subfrontal + endoscopic endonasal, orbitozygomatic + transbasal, orbitozygomatic + through the frontal sinus.

Various methods of an intraoperative control are used for optimal intraoperative visualization, increasing completeness of tumor removal, and improving functional results of operations.

1. Endoscopic techniques. It is necessary to distinguish between endoscopic control (exploration of the surgical...
wound using an endoscope) and endoscopic assistance (performing certain stages of operation under endoscopic control). The application of endoscopes with an angular view allows visualizing "blind zones" without further expanding the approach, which is often associated with the intersection of the neurovascular structures, and more complete tumor removal [3].

2. Electrophysiological methods. A technique, proposed for the first time in the world, of intraoperative identification of the nerves III, IV, and VI upon removing cranio-orbital tumors, especially meningiomas, involving the cavernous sinus and superior orbital fissure, has been used well in our practice. The essence of the method is finding these nerves in a tumor conglomerate using electrostimulation and registration of the M-response from electrodes placed on the muscle lifting the upper eyelid (nerve III), and the superior oblique (nerve IV) and lateral rectus (nerve VI) muscles (Fig. 9). This results in more complete tumor removal with good postoperative functional outcome [12].

3. Neuronavigation. Bony structures of the skull base are the perfect reference, when using navigation systems, because of the absolute lack of dislocation during the operation. Performing SCT with increments of 1—2 mm is preferable. An indication for intraoperative neuronavigation is the proximity of the tumor to the critical structures (optic nerves, internal carotid arteries, etc.)
<table>
<thead>
<tr>
<th>Approach</th>
<th>Indications</th>
<th>Technique</th>
<th>Possibility of plasty with local tissues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbitozygomatic (Fig. 3)</td>
<td>Tumors of anterior sections of the middle cranial fossa with extracranial extending mainly to the infratemporal and pterygopalatine fossae</td>
<td>Unilateral coronal incision of soft tissues. Dissection of the temporalis muscle. Skeletization of the supraorbital rim and partially orbitozygomatic rim. Osteotomy for making a bone flap including the zygomatic process of the frontal bone, frontal process, 1/3 or 1/2 of body and the temporal process of the zygomatic bone, zygomatic process of the temporal bone. Resection of the external parts of the wings of the sphenoid bone, opening the superior and inferior orbital fissures, optic canal, round and oval holes (if necessary). Approach can be supplemented by endoscopic assistance.</td>
<td>++ + +</td>
</tr>
<tr>
<td>Pterional + orbitozygomatic (Fig. 4)</td>
<td>A large lump in the middle cranial fossa and extracranial extending mainly to the infratemporal and pterygopalatine fossa.</td>
<td>Unilateral coronal incision of soft tissues. Dissection of the temporalis muscle. Osteotomy for making an orbitozygomatic bone flap (see above). Pterional craniotomy. Resection of the external parts of the wings of the sphenoid bone, opening the superior and inferior orbital fissures, optic canal, round and oval holes (if necessary). Approach can be supplemented by endoscopic assistance.</td>
<td>++ +</td>
</tr>
<tr>
<td>Through the frontal sinus (Fig. 5)</td>
<td>Tumors of the medial part of the anterior cranial fossa with extra- and intracranial spread (condition: the well-developed frontal sinus).</td>
<td>Bicoronal incision of soft tissues. Delimitation of the frontal sinus using diaphanoscopy. Osteoplastic trepanation of the anterior wall of the frontal sinus with the transition to the upper walls of the orbit and the noseband. Resection of the posterior wall of the frontal sinus. Ethmoidectomy, frontal sphenoidectomy. &quot;Economical option&quot;: resection of the inferomedial portions of the frontal sinus and lattice cells from the orbital cavity side. Approach can be supplemented by endoscopic assistance.</td>
<td>+</td>
</tr>
<tr>
<td>Lateral orbitotomy (Fig. 6)</td>
<td>For small tumors in the lateral and apical parts of the orbit.</td>
<td>Unilateral coronal incision of soft tissues. Dissection of the temporalis muscle. Osteotomy for the formation of the lateral orbital flap including the zygomatic process of the frontal bone, frontal process of the zygomatic bone, and partially, the lateral wall of the orbit. Resection of the external parts of the wings of the sphenoid bone, opening the superior orbital fissure, optic canal (if necessary).</td>
<td>++</td>
</tr>
<tr>
<td>Supraorbital (Fig. 7)</td>
<td>Orbital apex tumors of the &quot;hourglass&quot; type with extra- and intracranial spread, involving the optic canal.</td>
<td>Unilateral coronal incision of soft tissues. Dissection of the temporalis muscle. Osteotomy for the formation of the supraorbital flap including the lateral portions of the squama, supraorbital rim and zygomatic process of the frontal bone, the frontal process of the zygomatic bone, the roof of the orbit, and the external parts of the greater wings of the sphenoid bone. Resection of the lateral sphenoid wing parts, opening the superior orbital fissure and optic canal.</td>
<td>+ + +</td>
</tr>
<tr>
<td>Endonasal endoscopic (Fig. 8)</td>
<td>Tumors of the medial portions of the anterior, middle, and/or posterior cranial fossa with intra- and extracranial spread</td>
<td>Depending on the location and spread of the tumor: the frontal and/or posterior ethmoidectomy, frontotomy by Draf III, sphenoidectomy, medial maxillotomy. Options: an approach through the cribriform plates, plate of the sphenoid bone, extended transsphenoidal approaches, the transpterygoid approach.</td>
<td>+</td>
</tr>
</tbody>
</table>

Footnote: CP – the calvarial peristeum, TMF – the temporalis muscle and/or fascia, BFP – the buccal fat pad.
as well as repeated interventions, when orientation in the wound is extremely difficult due to the lack of anatomy distortion.

Plasty of skull base defects is one of the most difficult problems in performing surgery of skull base tumors, extending to the orbit, paranasal sinuses, and nasal cavity, pterygopalatine and infratemporal fossae. Persistent defects of the skull base creates an extremely high risk for serious complications; primarily liquorhea and infectious (meningitis, meningoencephalitis) as well as disturbances of cerebrospinal fluid dynamics, tension pneumocephalus, meningo- and encephalocele, etc. [2]. Often the extent of the operation is determined not so much by technical difficulties in tumor removal, as by the capabilities of defect hermetic closure plasty.

Skull base defects can be congenital (e.g., developmental abnormalities and dysembiogenetic tumors) and acquired (posttraumatic, resulting from a tumor process, iatrogenic, combined). By localization, skull base defects are divided into medial and lateral. These include defects of the paranasal sinuses, nasopharynx as well as petrous cavities and structures of the ear, including the auditory tube. Defects can be isolated or combined.

The aim of the defect reconstruction is sealing the subdural space and its complete isolation from the sinononal tract to prevent postoperative liquorhea associated with a high risk of suppurative complications and preservation of the neurovascular structures and the visual functions. A graft should be performed for the "supporting" function to prevent the formation of meningoencephalocele in the area of a skull base defect.

Among the flaps available for the plasty of skull base defects, the advanced pedicled local tissues are preferable to use. The advanced pedicled flap adapts better to the complex surface of a defect and is more mobile. Its use significantly reduces the incidence of postoperative liquorhea even in patients treated with radio- and/or chemotherapy [35].

Withdrawal of the calvarial periosteum is performed from a bicoronal incision of soft tissues. Subgaleal and subperiosteal layers of loose connective tissue allow its peeling off from the fascia and the skull bones. The posterior pole of the periosteum flap is formed the most posterior to the coronal suture, in the occipital region. Laterally the flap is confined by the superior temporal lines. The flap’s base is located in the frontal region, where it receives its blood supply from the supraorbital and supratrochlear arteries. The flap can be used for

![Fig. 7. Supraorbital approach.](image)

Green – osteoplastic trepanation; purple – the resection region of the wing of the sphenoid bone.

![Fig. 8. Endonasal endoscopic approach.](image)

Blue arrows – anterior and posterior transteethmoidal approaches; red – the transsphenoidal approach; green – the lateral extension of the transnasal approach.
plasty of base defects of both the front (Fig. 10) and the middle cranial fossa — in 1, 2 or even 3 layers, but it is not rigid enough.

The temporal muscle can be used completely or in the cleaved form (the inner layer). It receives its blood supply from the front and deep temporal arteries (branches of the maxillary artery), which go to the muscle from the infratemporal fossa. Form and features of blood supply allow the use of the temporal muscle as a rotated flap.

(Fig. 11). The temporal fascia can also be used together with the muscle.

The buccal fat pad is the only fat plastic material of the head having a vascular pedicle. Located deep in the

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Fig. 9. An example of intraoperative identification of the nerves in the superior orbital fissure upon removing cranio-orbital meningioma.
A - electrodes are mounted on the muscle that raises the upper eyelid (nerve III), on the superior oblique muscle (nerve IV) and lateral rectus muscle (nerve VI);
B – the M-response from the electrode from the muscle that raises the upper eyelid; C – the M-response from the electrode from the lateral rectus muscle.

Fig. 10. A scheme of plasty for a defect of the base of the anterior cranial fossa with the pedicled calvarial periosteum flap (arrow).

Fig. 11. Plasty of a defect of the greater wing of the sphenoid bone and sphenoid sinus right with the temporalis muscle flap (arrows). Postoperative MRI.
Soft tissues of the face, it receives its blood supply from branches of the pterygopalatine segment of the maxillary artery as well as branches of the facial artery. The flap of the sucking pad is formed by its extraction from the bed preserving the pedicle, which contains branches of the maxillary artery. This flap, well known in maxillofacial surgery, was first proposed by us for plasty of middle cranial fossa defects of various localizations (Fig. 12) [9, 19].

Orbital tissues, due to abundance of the fatty tissue, can also be used for plasty of small defects of, mainly, the middle localization. Moreover, we put forth the idea of making "a bridge" out of tissues of medial parts of both eye sockets. The bridge can serve as an additional support to maintain the plastic material in median defects of the skull base (Fig. 13).

Principles of closing defects are largely common, regardless of their origin [2]. The literature provides the whole spectrum of existing methods — from simple sealing of the defect with fibrin-thrombin glue to autografting with the musculocutaneous flaps and omentum. The emergence of the autografting microsurgical technique allowed doctors to freely transfer many axial flaps, which earlier had been moved within the radius of the pedicle, to distant defects by connecting, through the microsurgical vascular suture, the flap’s pedicle to the blood supply source within the defect area. Participation of plastic surgeons is necessary in cases of extensive defects after removing benign tumors and upon en-bloc resection of the skull base in patients with malignant tumors.

**Conclusion**

Despite the fact that surgery of craniofacial tumors is a relatively new direction of basal surgery, there are currently clear trends towards radical changes. In place of traumatic basal approaches, which require complex methods for plasty of the skull base, less invasive ones, supplemented by endoscopic-assistance, have come. The endonasal endoscopic approach has increasingly been implemented in practice, with its potential increasing due to improvements in instrumentation, hemostasis facilities, and surgical techniques. The modern practice of craniofacial oncology requires more accurate diagnosis...
for the spread of tumors, a study of microsurgical and endoscopic anatomy, an introduction of new methods of the skull base reconstruction.

The issues of treatment for certain types of craniofacial neoplasms will be addressed in detail in the next article.

REFERENCES

Arteriovenous malformations (AVM) of the brain are congenital malformations of cerebral vessels developed during the fetal period. Current standards of the AVM treatment include the endovascular technique, microneurosurgical removal, and stereotactic irradiation.

**Materials and Methods.** Within the period from 2005 through 2011, 139 patients with arteriovenous malformations of the brain were treated using a Gamma Knife device (Elekta, model C, Sweden). Eighty-nine out of 139 (64%) patients had past history of bleeding. Paroxysmal symptoms of varying severity dominated in the clinical picture of 35 patients (27%). Previous microsurgical resection was performed in 10 patients (intracranial hematoma — resection, in 9 patients; stereotactic hematoma evacuation, in one patient). Twenty-eight patients experienced partial embolization of vascular malformations before radiosurgery. stereotactic hematoma evacuation, in one patient). Twenty-eight patients experienced partial embolization of vascular malformations before radiosurgery. The boundary radiation dose ranged from 18 to 28 Gy (mean dose of 20 Gy); the day dose ranged from 40 to 80% (average 50% isodose). The maximum dose ranged between 18 and 60 Gy (mean dose of 38 Gy).

**Results.** Control angiography or helical CT screening angiography was performed in all 85 patients who were treated, with the follow-up data for more than two years. It showed that total obliteration occurred in 75% of cases. Frequency of symptomatic radiation reactions was less than 5%. Two years or more after treatment, complete obliteration was observed in 74% of patients.

**Conclusions.** Higher frequency of AVM obliteration was observed with up to 2 cm³ and the irradiation dose of at least 24 Gy.

**Keywords:** arteriovenous malformations, radiosurgery, obliteration, radiation reaction.
Elekt (Sweden) Gamma Knife, model C. A Gamma Knife is a device that contains 201 sources of radioactive cobalt (60Co) fixed along a hemisphere in a tube shield. The beams of ionizing irradiation produced by a source are highly and accurately focused on the center of the device, forming a near-spherical dose distribution with radii of 4, 8, 14, or 18 mm on 50% isodose [4]. In all cases, the treatment was performed according to the previously described technique [4, 34]. Fixation of a Leksell stereotactic frame was performed under regional anesthesia. MRI and digital angiography (AG) were mandatory examinations for all patients with AVM after the fixation of a stereotactic frame using special localizers. Irradiation was planned on a working station with HP-UX 11i operating system with the Leksell Gamma Plan Wizard 5.34 (LGP) planning system. The LGP planning system allows a specialist to obtain shaped dose distributions corresponding to the three-dimensional configuration of a target; a target configuration is set by its own digital MRI and AG images, and distribution is achieved by fitting of the localization of the isocenters and their weights (relative irradiation time for each isocenter). With the use of a special Amfora program, the MRI images were mapped onto the AG data. The LGP allows one to display any isodose curve over tomography images both in the two- and three-dimension forms, as well as to construct dose-volume histograms both for the target and adjacent critical structures, which are set and contoured by a doctor; these factors are taken into account in the selection of an optimal plan of irradiation. The planning uses such parameters of irradiation as the prescribed dose and the prescribed isodose. A prescribed dose is a dose of ionizing irradiation set along the edge of the target. The term means the percentage of a prescribed dose to the maximal dose in a target. A plan that covers, with high conformity and selectivity, a target of virtually any geometry while minimally irradiating the adjacent healthy brain tissue may be produced by picking the diameters of collimators and number of isocenters, and varying the head slope angle and time of each center’s irradiation. In such a case, a stroma of the malformation serves as a target. In the cases which required a lowering of the AVM irradiation volume, arteriovenous nidus was the target.

The irradiation by itself takes from 15 min to 1–2 hours. The automatic positioning system Gamma Knife allows one to perform rapid, high-accurate (about 0.1 mm) moving between the isocenters. All the patients together obtained professional advice of vascular surgeons; decisions on the treatment strategy were made together as well. AVM persisting in patients for 3–12 months after subarachnoid hemorrhage (SAH) was an indication for treatment. These were either patients with contraindications to surgical and/or endovascular treatment or patients with residual functioning AVM fragments after surgical or endovascular treatment.

Our series included 67 males and 72 females aged 7–69 years (mean age, 35 years). Eighty-nine out of 139 patients (64%) had past history of hemorrhage; thirty-five persons (27%) had predominating paroxysmal symptoms of various intensity; ten patients had previous microsurgical resections: removal of intracranial hematoma in nine cases and stereotactic hematoma evacuation in one case. In twenty-eight patients, radiosurgery was preceded by partial embolization of vessels of malformation stroma; in three of them endovascular treatment was performed twice. In one patient, irradiation was preceded by combined treatment (hematoma removal + embolization).

Distribution of AVMs according to their localization is presented in Table 1. According to the Spetzler–Martin grading system, all patients with AVM (n=139) were classified as follows:

- I degree — 18 (12%);
- II degree — 65 (47%);
- III degree — 41 (30%);
- IV degree — 15 (11%);
- V degree — 0.

Diameter of an arteriovenous ganglion was 3.3–44.5 cm (median = 2.2 cm). The volume of an irradiated AV ganglion varied from 0.021 to 18.8 cm³ (median = 3.9 cm³). In all cases, the treatment was planned according to the results of cerebral AG and T1- and T2-weighted contrast-enhanced MRI of the brain.

Identification of the entire AVM volume that can be obtained from cerebral AG performed from all systems is one of the key factors of irradiation planning (Fig. 1).

Selecting a target on an AG image is a principal factor for planning. Sections of the initial phases of angiographic examination, when stroma of the malformation with a feeding artery can be best observed, while the draining vein cannot be observed or is under formation, are commonly used planning. The draining vein may dim the malformation, leading to incorrect interpretation of malformation dimensions and volumes for irradiation.

A planning volume was drafted along the AVM contours provided by MRI combined with the AG data (Fig. 2); requirements on MRI are as follows: with and without contrast enhancement in T1- and T2-weighted modes with the increments of 1 mm.

Table 1: Occurrence of AVM according to the localization of the pathological process

<table>
<thead>
<tr>
<th>AVM localization</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parietal lobe</td>
<td>41</td>
</tr>
<tr>
<td>Occipital lobe</td>
<td>27</td>
</tr>
<tr>
<td>Temporal lobe</td>
<td>22</td>
</tr>
<tr>
<td>Frontal lobe</td>
<td>15</td>
</tr>
<tr>
<td>Thalamic region</td>
<td>11</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>7</td>
</tr>
<tr>
<td>Corpus callosum</td>
<td>5</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>5</td>
</tr>
<tr>
<td>Brain stem</td>
<td>3</td>
</tr>
<tr>
<td>Intraventricular localization</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>139</td>
</tr>
</tbody>
</table>
It is difficult to use this combination, since the AG data give two-dimensional ellipsoid images, while the volume is presented by projections. The actual volume can be obtained only from the MRI data (Fig. 3).

The boundary dose lied within the range of 18–28 Gy (average dose = 20 Gy); the isodose ranged from 40 to 80% (the mean isodose = 50%); the maximal dose varied from 18 to 60 Gy (mean dose = 38 Gy). The number of isocenters used to cover all the formation varied from 1 to 18 (5 in average).

In the post-irradiation period, all the patients underwent MRI examination in the standard mode: in the early period and if worsening was observed — every six months; and annually — later on.

When AVM obliteration was revealed from the MRI-AG data, digital cerebral AG was performed; CT-AG was used in some cases. One of these examinations was required to determine obliteration intensity after the irradiation in our patients.

**Results**

Intensity of post-irradiation obliteration can be reliably determined by cerebral AG (Fig. 4).
Obliteration of AVM stroma after its irradiation takes 2–3 years; therefore, objective assessment of its results earlier than this date makes no sense. We have assessed the obliteration results in 106 patients who were treated since 2005 through 2009 and managed to collect the follow-up data for the 2–6-year period from 85 (80%) of them.

Obliteration of AVM

Control angiographic examination or HCT-AG was performed in all 85 patients who had follow-up data and had been treated more than two years ago. Complete obliteration was registered in 75% cases (64 out of 85 patients) (Fig. 5). MR-evaluation of the results was performed annually; AG evaluation was performed later than two years after irradiation.

In 9 patients (10%), control examination revealed a decrease in dimensions of the functional part of AVM and reduction in bloodstream (decrease in draining vein dimensions), while in 12 others (15%), dimensions and occurrence of AVM had no dynamics as compared with their pretreatment dimensions and volume (Fig. 6).

Hemorrhages after radiosurgery

Pre-treatment hemorrhages were registered in 89 (64%) patients out of 139; 23 of them had two or more hemorrhages before treatment. After radiosurgery, repeated hemorrhage occurred only in three patients (2.2%) within six and twelve months after irradiation (Figs. 6 and 7).

The aggravation of focal neurological symptoms in the form of pyramidal symptoms was observed in these patients. Their condition stabilized when the treatment was started; however, none of three patients had complete regression of neurological symptoms. One patient died from the repeated hemorrhage.

Dynamics of the neurological status in patients with AVM after radiosurgery

A total of 139 patients had the following pre-treatment symptoms: neurological symptoms in 95 patients (68%); hemorrhages in 89 (64%); focal/non-focal neurological symptoms in 95 (68%), and episindrome in 35 (27%) patients.

In 43 patients (48%), the neurological symptoms regressed partially or completely within 6–42 months after irradiation. In 13 patients (9.3%), perifocal edema aggravated during 1–12 months, 2–36 months (median, 12 months) after the treatment. This generally manifested as aggravation of non-focal symptoms. In five out of thirteen patients, the symptoms gradually regressed due to nonsurgical treatment. In eight patients, development of the edema was accompanied with persistent aggravation of focal symptoms requiring longer administration of steroid therapy.

Assessment of the patient’s condition according to the Karnofsky score: pre-irradiation score of 100 — 41 patients, score of 90 — 37, score of 80 — 31, score of 70 — 22, and score of 60 — 8 patients. In twelve patients, the Karnofsky score decreased after the surgery. In one patient, this event was related to hemorrhage. In 25 patients (18%), the Karnofsky score increased after the treatment.

Thirty-five patients (25%) experienced epileptic seizures before the irradiation. The seizures manifested in various ways: from small focal limb jerking or facial
Fig. 5. Plan of irradiation with a Gamma Knife device (a) and carotid cerebral AG (b, c: frontal and lateral views): AVM in the right part of the basal ganglia region; d, e — control carotid AG: complete AVM obliteration after the radiosurgical irradiation with a Gamma Knife device within two years after the irradiation.
spasms to grand mal seizures with loss of consciousness and development of clonic-tonic seizures. Changes in epileptic episodes (decrease in their frequency) were registered in 14 (41%) out of 35 patients within 1–60 months after irradiation. In three patients, on the contrary, seizure frequency increased a year after irradiation. In twelve patients, the seizures were completely arrested after irradiation. Antiseizure therapy was selected for all patients with episynдрome.

A much better recovery of neurological symptoms was observed in patients under 25 years of age and in patients with past history of hemorrhage.

Development of perifocal edema after radiosurgery was observed in patients older than 50 years without preceding surgery or embolization and with 5–10 cm³ AV ganglion volume, and in patients who received the dose of at least 23 Gy dose per an AVM edge.

Results of statistical processing of the data

The following factors that could influence the results of treatment were used to evaluate the treatment results: patient’s gender and age, surgery, embolization, past history of SAH, volume and localization of AVM, classification of AVM according to the Spetzler grading system, and the maximal and boundary irradiation doses. Statistical data were obtained using the Kaplan-Meier method.

Statistical analysis demonstrated that gender does not affect success of obliteration. In young patients, obliteration tended to occur somewhat more frequently. It was demonstrated that factors of prescribed dose (PD), dimensions (AXIAL_D, AX_NORM_DIAMETER, Z_THICK), and volume are statistically different in two groups (p<0.05); their effects on processes of post-irradiation obliteration were revealed (Figs. 8, 9).

No significant effects of other factors on obliteration processes were found. Effects of such factors as previous SAH, embolization, surgery, and preceding radiation therapy were not significantly different in both groups. Statistical processing of the treatment outcomes demonstrated that the significantly higher obliteration (p<0.05) was observed in patients with AVM volume less than 1.0 cm³, maximal linear dimension not more than 15 mm, and a prescribed dose more than 24 Gy.

Discussion

Immediate effect of AVM treatment can be ensured only by radical resection or embolization. Unfortunately,
according to several authors [3, 16, 34, 53], embolization leads to complete obliteration in less than 40% of cases, while frequency of post-embolization permanent complications and mortality reaches 11% [71]. Taking this fact into consideration, the endovascular treatment is not always a method of choice but is used as adjuvant therapy preceding microsurgical and radiosurgical interventions [4, 5, 23, 24, 37, 74].

Open resection of AVM ensures radical treatment by radical removal of the lesion; a rather low frequency of adverse effects and mortality is attained at many neurosurgical centers [6, 38, 48, 51, 61, 72]. However, when an AVM localizes in deep structures of the brain, microsurgical resection can cause development of permanent neurological complications and high mortality [46]. Radical resection cannot be achieved when an AVM localizes in functionally important regions or is widely extended [15, 40]. Resection of an AVM in deep structures of the brain can result in considerable worsening of quality of life [60], especially in patients without past history of hemorrhage [40]. Mortality after the open surgery can be affected by the risk caused by the following circumstance: the surgery is performed for acute hematoma as a life-saving measure, while patient’s condition is aggravating. Radiosurgery is a planned treatment, patient’s condition is stabilized and, in case of a past history of hemorrhage, the hematomas had been resolved already. A considerable number of patients referred for radiosurgery treatment are considered as inoperable due to the high risk of complications. Radiosurgical treatment of AVM is usually recommended in cases when a safe and radical open surgery or valid endovascular intervention are impossible.

The main limitation of radiosurgery is the limitation of irradiation volume making the treatment safe and efficient, since an increase in the mean dose >20 Gy increases the risk of adverse effects >10% per matrix volume of 20 cm³ [18–20, 32, 33]. For large and extended AVMs, staged radiosurgery is suggested (that is, treatment of only a part of the lesion at each stage, with general intervals of 3–6 months); this method was first applied in Pittsburgh in the second half of 2000 for AVMs of larger volumes. The staged radiosurgery is a rather efficient and promising treatment method [17, 56]. It was shown that in some hard cases a lesion can be successfully cured with multimodal treatment approach (radiosurgery, microsurgery, and embolization) [14, 39, 60, 66]. Radiosurgery irradiation triggers the mechanism of AVM vessels obliteration that generally begins within 2–3 years.

Fig. 7. The brain MRI: signs of past hemorrhage in the right frontal lobe (a); cerebral AG before treatment: Small AVM in the view of the right thalamic region (b); brain MRI: intracerebral hematoma in the view of the right thalamic region one year after the radiosurgical irradiation (c).
Five years after a single radiosurgery procedure, probability of obliteration varies from 50 to 95% [4, 5, 7—10, 17, 21, 22, 33—35, 38—43, 47, 48, 51, 52, 56, 57, 61—63, 66, 71, 74, 76, 77].

An analysis of the outcomes of treating AVM with the Gamma Knife device in more than 1,000 Pittsburgh patients showed the following percentage of complete obliteration: 73% — according to the data of control angiogram 2.5–3 years after irradiation; and 86% according to the MRI-AG data [17]. The accuracy of MRI evaluation of AVM obliteration is 96%; that of AG evaluation is 75% [65].

The presence of functioning residues and absence of blood stream reduction (demonstrated by the control AG-examination 2.5–3 years after the radiosurgery) indicates to advisability of repeated radiosurgery. It must be performed according to the same criteria of the dose, volume and isodose, as the first treatment. Notably, neurological adverse effects following the repeated treatment are rather more common than those after the primary one [45]. Some authors [45] have reported 15–20% frequency of symptomatic adverse effects after the secondary radiosurgery.

In 2007, R. Liscák et al. presented the results collected from 330 AVM patients that were examined and treated using the Gamma Knife device during the eight year-period. The collection includes 76 cases, in which the secondary radiosurgery was performed when complete obliteration failed within the three year-post-treatment period. In 222 patients (74%), complete obliteration was reached after the first radiosurgery run, while in 47 (69%) — after the repeated run. The control angiographic examination, which showed the complete obliteration of

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**Fig. 8.** Factors affecting the process of AVM obliteration after the radiosurgical irradiation ($p<0.05$). (1 and 2 — the patient groups under comparison. 1 — the patient group with the most common obliterations, 2 — the patient group with lack of registered obliteration).

- a — prescribed dose (PD): 1 — obliteration at PD >24 Gy; 2 — lack of obliteration or incomplete obliteration at PD <24 Gy;
- b — axial diameter: 1 — obliteration at AVM not more than 15 mm; 2 — lack of obliteration or incomplete obliteration when the AVM is more than 15 mm in size;
- c — volume: 1 — obliteration when the AVM volume is <1 cm³; 2 — lack of obliteration or incomplete obliteration when the AVM volume is 1 cm³.
Fig. 9. Obliteration occurrence in patients with brain AVM after the surgical irradiation with a Gamma Knife device (follow-up performed for over 24 months) is 75%.

the stroma vessels, was performed 12–96 months after the primary run of radiosurgery [42].

The previous results of the Gamma Knife radiosurgery are presented in Table 2.

In our series of observations, a surgery or embolization preceded radiosurgery in thirty patients. The surgical treatment (partial resection) had no effect on the results of obliteration after radiosurgical irradiation [32, 42, 43, 52, 71].

B. Karlsson and C. Lindquist [32, 33] believe that embolization is not recommended as the first method of AVM treatment, when radiosurgery or microsurgery are be enough. In addition, the same authors mention worsening of the radiosurgery outcomes, when it is performed after the endovascular treatment. This could result from the delayed recanalization.

In the recent reports, the embolization was often followed by adverse effects: frequency of permanent adverse effects and mortality after embolization reached 11% [32, 42, 43, 52, 71].

Hemorrhage symptoms are the most common manifestations of cerebral AVM [9, 10, 49]. The risk of adverse effects and mortality caused by hemorrhages are the main reasons for active treatment of AVM patients [60].

Males have higher incidence of obliteration. At that, AVM volumes were similar in males (median 3.65 cm$^3$) and in females (median 3.75 cm$^3$); the median value of the limit dose was 21 Gy for both genders. This might be caused by higher vessel sensitivity in males, although this observation must be confirmed by further clinical studies.

As for the dynamics of neurological symptoms after radiosurgery, a number of scientists [6, 38, 48, 51, 61, 72] believe that improvement of the neurological status occurs through non-focal brain symptoms or regression of paroxysmal symptoms, which are registered in 35–60% of cases. In our series, the neurological status was improved in 45% of patients and was higher in younger patients with past history of bleeding.

### Table 2. Results of radiosurgical irradiation of patients with cerebral AVM using the Gamma Knife device according to the data of various authors

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Number of patients</th>
<th>Obliteration, %</th>
<th>Complications, %</th>
<th>Mortality, %</th>
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<td>M. Bollet et al.</td>
<td>2004</td>
<td>112</td>
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<td>144</td>
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<td>434</td>
<td>67</td>
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<td>H. Inoue, C. Ohye</td>
<td>2002</td>
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<td>D. Kondziolka et al.</td>
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<td>1129</td>
<td>74</td>
<td>4.4</td>
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<td>R. Liscák et al.</td>
<td>2007</td>
<td>222</td>
<td>74</td>
<td>2.9</td>
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Taking into account that the annual risk of mortality caused by untreated AVMs is 1% [3], while the risk of adverse effects after radiosurgery is minimal (according to R. Liscák et al. [42]), radiosurgical interventions using the Gamma Knife device are justified in patients of any age.

In our series of observations, there is a trend toward decreased frequency of recurrent hemorrhages in radiosurgically irradiated patients.

The same trend was observed in a number of series [3, 11, 33, 42, 51, 62]. In our series of observations, only three patients experienced recurrent hemorrhages within 6–18 months after the radiosurgery; AVM obliteration was detected in one of them a year after the repeated hemorrhage.

Both our team and a number of other authors have noted a decrease in incidence of recurrent hemorrhages. We have noted bleedings following radiosurgery; however, they are unlikely to be adverse effects of treatment but are rather caused by treatment failure or natural course of the disease. Similar events were also described in patients who received endovascular or microsurgical treatment.

The percentage of patients with recurrent bleedings after radiosurgery is 3.4–10 [11–13, 25–30, 54, 55, 60, 63, 73, 77]. In the absence of treatment, the annual risk of recurrent hemorrhages is 2–4%; the risk of mortality is 1%; and the total risk of severe adverse effects and death is 2.7% [9, 18–20, 49, 50, 67, 70]. According to R. Liscák et al. [42], the annual risk of bleeding is 2.5% before treatment and less than 1% after the radiosurgery. The incidence of fatal bleedings is 0–3.5% [13, 21, 30, 36, 44, 53, 54, 60, 63]. In our series of observations, recurrent bleeding occurred in one patient (1%).

The main reasons behind the treatment failure upon radiosurgical interventions are the relatively large volumes of AVM, low doses of irradiation, and high Spetzler-Martin score [44, 70]. The Spetzler-Martin AVM score, which accounts for the diameter of an AVM focus, its localization in the region of the adjacent structures, and type of venous drainage, can be used to evaluate prognosis and outcome of radiosurgical interventions. B. Pollock [52] proposed a classification for analyzing radiosurgical outcomes; this classification allows one to determine probability of positive treatment outcomes, taking volume and localization of the AVM, and the patient’s age as the most significant variables. J. Flickinger used the following equation to calculate the classification score of an AVM change: score = 0.1 (volume in cm³) + 0.02 (age in years) x 0.5 (localization: basal ganglia, thalamus, brain stem = 1; the others = 0). A focus volume is more significant than its maximal diameter. The lower diameter allows a surgeon to use safely a higher dose of ionizing irradiation, which is another considerable factor of AVM obliteration after a radiosurgical intervention [68, 69, 75]. In addition, our results showed that a higher incidence of obliteration was reached at lower AVM volume and at higher minimal and maximal doses of applied ionizing energy.

Adverse radiation effects

Adverse radiation effects include the acute, subacute and delayed ones. The acute adverse effects are related to conditions that worsen due to cerebral AG and immediate (within 24 h) reaction to the irradiation. These effects, in the form of headache, development of focal neurological symptoms and epileptic seizures, especially with paroxysmal symptoms history, occur in 3–8% of cases, and can usually be arrested within several hours [13, 21, 31, 55, 58, 59, 69]. Development of serious or permanent adverse effects related to the treatment procedure by itself was observed in one child from our series who did not receive irradiation. The vasospasm occurred during AG run.

Subacute adverse effects typically occur within 6–12 months. According to the foreign authors [13, 21, 30, 53, 54, 60, 63], these effects can be described as edemas and X-ray lesions, the so-called X-ray necroses. Not all edemas (increase in the region of a signal change in T1-weighted mode) are accompanied by development of neurological symptoms. As a rule, the neurological symptoms occur when an AVM is located in a functional region. According to several authors [13, 21, 30, 53, 54, 60, 63], these reactions can be observed in 12–15% of cases. As mentioned above, in 13 (9.3%) out of 139 patients in our series within 1–12 months, a peripheral edema developed during 2–36 months (median, 12 months) after the procedure. It generally manifested as development of non-focal brain symptoms in the form of headache. Non-surgical therapy caused gradual regression of these symptoms in 5 out of 13 patients.

Delayed adverse effects can occur within a year after the treatment and later.

X-ray necrosis is morphological damage to the medullary substance, which can manifest as permanent neurological deficits, when necrosis foci are located in functionally important regions. The mechanism of X-ray damage has not been determined. Development of X-ray reactions is often related to a considerable volume of irradiation; therefore, radiosurgical treatment is used in cases when the target volume is less than 20 cm³. The reactions may be underlain by an autoimmune reaction. The irradiation is believed to cause formation of free radicals that trigger lipid peroxidation in neuron membranes and in myelin [64, 67, 75]. A histological examination reveals demyelination of nerve fibers, hyalinosis of small arterioles, ischemic infarction and necrosis of brain tissue. In our series, X-ray necroses were registered in 4 (2.8%) patients. In all cases, X-ray reactions were noted at AVM dimensions >2 cm³ and at prescribed doses >24 Gy [64]. In patients with resected AVMs, X-ray reactions after irradiation of AVM residues are uncommon [53].

Edema after radiosurgical interventions is caused by the toxic effect on the adjacent tissues or AVM rather than by hemodynamic changes following obliteration. The latter may require participation of endothelial vessel growth factor, whose presence in vessel malformations
has been proved [16, 31, 34, 53, 55, 58, 59, 69]. Excretion of this factor into the adjacent brain tissues after radiation damage can induce edema.

Cyst formation is one of the late adverse effects. This phenomenon was found in 1.6–3.4% of patients and can manifest itself within 3–15 years after the treatment. This may be caused by changes in capillary permeability after irradiation. These cysts need surgical intervention quite rarely: according to some authors [4, 26, 34, 42, 43], surgical treatment for cysts is required in less than 1% of cases.

There is a small probability of that AVM may manifest after complete obliteration; this may be caused by radiosurgical treatment [2, 34]. D. Kondziolka et al. [34] described one case of hemorrhage occurrence after the AVM was confirmed by angiography examination data. No adverse effects of such sort were observed in our series.

This paper presents the analysis of the irradiation results in patients with brain AVMs treated with a Gamma Knife device. The Department of Radiology has accumulated the data on irradiation of patients with brain AVMs treated using Novalis and CyberKnife linear accelerators. Accumulation and analysis of the delayed results of AVMs irradiation performed using other devices will be continued, and the results of treatment with various devices will be analyzed and compared.

Conclusions

Gamma Knife radiosurgery of patients with brain AVMs of various localization is an efficient and minimally invasive method resulting in high frequent obliterations of malformation stroma and a relatively small number of adverse effects. The frequency of symptomatic X-ray reactions is less than 5%. In 74 patients, complete obliteration was observed within two years after the surgery or later. The higher probability of obliteration development was observed when an AVM was less than 2 cm³ in volume and a prescribed irradiation dose was 24 Gy or higher.

Recurrent hemorrhages tend to decrease (1%) even when obliteration did not occur, including earlier than within three years after the treatment.

REFERENCES

ORIGINAL ARTICLES


Modern vascular neurosurgery refers to arteriovenous malformations (AVM) of the brain as hard for radical treatment. The purpose of treatment of an AVM patient is to eliminate the AVM from the bloodstream with the minimal threat for patient’s health and quality of life. The current standards of treatment of AVM patients include the use of endovascular, microsurgical, and radiosurgical methods according to individual indications. The use of a specific method or, sometimes, their combinations depends on AVM dimensions and blood supply; their localization and relation to functionally important brain regions; patient’s age and history of hemorrhage. The patients of such kind should undoubtedly be treated at specialized centers having these facilities.

Microsurgery is the most radical treatment method; however, it is limited with AVM accessibility with respect to the functional brain regions. Their Spetzler-Martin score is typically degree I-II. The endovascular method can be used when AVM afferents are well-developed, and is efficient in 40—45% of cases only, despite high technologies in development of glue compositions (ONIX, etc.). Stereotactic radiosurgery is usually recommended for AVM patients in cases where safe and radical microsurgery is unavailable.

The authors present their own experience in stereotactic radiosurgery of 139 patients with brain AVMs. The patients were treated with a Gamma Knife device (Electa, Sweden) at the Center of Stereotactic Radiosurgery at the Burdenko Neurosurgical Institute in 2005—2011. Results of treatment of 106 patients were evaluated. The 2—6-year follow-up data of 85 (80%) patients were collected; these results are interesting and long-awaited by neurosurgeons. Minimal invasiveness and high efficiency of the method, high incidence of oblations of AVM stroma (up to 74%), and a relatively small number of adverse effects were confirmed and described in details. A higher probability of AVM obliteration development was registered for small (less than 2 cm³) AVMs and higher prescribed dose of irradiation (>24 Gy). The main factors of radiosurgical treatment failure include an increase in AVM volume, a decrease in irradiation dose, and an increase in AVM grade according to the Spetzler-Martin grading system.

The article is undoubtedly of significant interest for neurosurgeons, X-ray surgeons, and specialists in X-ray diagnostics and treatment. Its publication in both neurosurgical and other relevant journals is reasonable.

V.A. Lazarev (Moscow)
Functional MRI Studies of the Hemisphere Dominant for Speech in Patients with Brain Tumors

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Objective. To study the hemisphere dominant for speech, according to functional magnetic resonance imaging (fMRI) data for patients with brain tumors as compared to the histology of tumors, as well as to the profile of functional asymmetry.

Methods. fMRI was performed in 21 patients. The tumors localized in the left and right hemispheres in 15 and 6 cases, respectively. Tumors of frontal, frontotemporal, and temporal localization dominated. In most patients, the tumors were large; at least one of the dimensions was greater than 5 cm (not counting the perifocal edema). According to the histology data, the tumors were of grade IV and grade I–III malignancy in 8 and 13 patients, respectively. fMRI study was performed on a Signa Excite MRI scanner with magnetic field strength of 1.5 T. Reciting the months of the year in a reverse order was used as a speech test. fMRI data were compared with the profile of functional asymmetry, according to the results of the Annette questionnaire and the dichotic listening test. Statistical data processing was carried out.

Results. Broca’s area in the left hemisphere was found in 7 patients, 6 patients had a benign tumor. One patient with glioblastoma had a tumor of the right hemisphere. The right-sided Broca’s area was detected in 3 patients (2 cases with left-sided tumors and one patient with right-sided tumor). Mild motor aphasia was observed in one patient with left-sided tumor. Symmetrical brain activation in both hemispheres was observed in 6 patients who had only grade II–III tumors (mostly large ones) of the left hemisphere. Signs of left-handedness were detected in those patients in only half of the cases. No Broca’s area was found in 4 patients. All of them had very large malignant tumors. One more patient was unable to learn the program of the research. It should be emphasized that the data obtained during the dichotic listening test, questionnaire, and fMRI were often inconsistent.

Conclusion. The authors attribute the difficulties of identifying speech zones in patients with large, especially malignant tumors by fMRI, to the impaired vascular autoregulation in the hemisphere affected by a tumor, to swelling, and features of neoangiogenesis, which reduce the activity of BOLD-signal. Bilateral activation in speech loads could be a reflection of brain plasticity in long-growing tumors. The full range of clinical data should be taken into account when solving the problem of the hemisphere dominant for speech.

Keywords: fMRI, hemisphere dominant for speech, brain tumors.

The list of indications for removing brain tumors (including the ones that used to be previously considered inoperable) has recently been broadened due to mastering of surgical techniques. Microscopic surgeries are conducted in the vicinity of the speech and motor areas without destroying them. However, it is especially important to clearly define the hemisphere dominant for speech and the borders of speech areas.

A large number of studies have been devoted to analyzing the possibility of determining the hemisphere dominant for speech using functional magnetic resonance imaging (fMRI) under various speech loads. It is noteworthy that the resulting data are rather inconsistent. On one hand, high compliance between the fMRI data and the Wada test, mainly in patients with epilepsy [3, 7, 9, 20, 22], has been reported. On the other hand, the problems associated with interpretation of the results and inconsistency of the fMRI data and invasive methods for determining the hemisphere dominant for speech (the Wada test and intraoperative electrostimulation after waking up) in patients with brain tumors were reported [13, 18, 19, 25]. When comparing the fMRI data and the results of intraoperative electrostimulation of the speech areas when a patient awakes up, it has been demonstrated that, as opposed to the classical concept, the localization of speech fields is characterized by wide diversity between individuals. For example, the speech system can be represented partially or completely in the other hemisphere and can have a lot of additional speech areas that cannot be removed [5, 8, 23]. The result of determining the hemisphere dominant for speech can also depend on the localization of the pathological focus with respect to the expected speech areas, as well as tests offered to patients [13, 22]. Particular difficulties arise from examination of patients with large tumors of the brain.

This work was aimed at studying the hemisphere dominant for speech according to the fMRI data in patients with brain tumors in comparison to histology of tumors, as well as the profile of functional asymmetry.
Material and Methods

Before brain tumors were removed, 21 patients (15 females and 6 males) aged 19 to 68 years (with the mean age of 38.9 years) had been studied using fMRI. Two patients had insignificant paresis and hemihypesthesia of the limbs (contralateral with respect to the tumor) in their neurologic status. Two patients (with frontal tumors) had elements of efferent motor aphasia; one more patient (with temporal tumor) had the elements of acoustic-mnestic aphasia. No focal neurological symptoms were observed in other patients.

In 15 people, the tumor localized in the left hemisphere (in frontal and frontotemporal regions, temporal and tempoparietal areas, and in parietal, frontoparietal and parieto-occipital regions in 10, 2 and 3 patients, respectively). A tumor of the right hemisphere was revealed in 6 patients (tumors localized in the temporal dole – 3 patients; frontal and frontotemporal region – 2 patients; and parietal lobe – one patient). The tumors of frontal, temporal, and frontotemporal localization were the predominant ones; they potentially occupied the speech areas or directly approached them.

In most patients, the tumors were large, with at least one of the dimensions being greater than 5 cm (without counting the perifocal edema). According to the histology data, tumors were of grade IV malignancy in 8 cases (7 glioblastomas and one case of metastasis of lung cancer). Benign tumors were found in 13 patients: one case of grade I dysembryoplastic neuroepithelial tumor and 12 cases of grade II–III tumors (7 different astrocytomas, 2 meningiomas, one oligodendroglioma, and one oligoastrocytoma).

The fMRI data were compared with the profile of functional asymmetry that had been identified using a questionnaire proposed by M. Annette (1970) and the dichotic listening test (modified by B.S. Kotik, 1974). Statistical processing of the results obtained for the profile of the functional asymmetry was performed using SPSS Statistics 17.0 software. Since all the data had nominal values, the $\chi^2$ test (Pearson’s test) was employed (analysis of contingency tables).

Among the patients there were 13 right-handers; 6 patients considered themselves to be right-handers but had two or more signs of left-handedness (e.g. they constantly applied a handset to the left ear and mostly used a left hand to perform any action when doing housework). Two patients were the retrained left-handers.

Results of fMRI, dichotic listening test, and questionnaire for determining left-handedness were compared with pre- and postoperative examination aimed at detecting speech disorders.

To qualify the detected impairments in higher mental functions, syndromic patients underwent neuropsychological analysis performed by A.R. Luria [1]. It was mandatory for this study that a patient was active, followed the task, and switched on time in accordance with the instructions; thus, the patients were selected for fMRI relying on the neuropsychological examination data.

fMRI study was performed using a Signa Excite MRI scanner (General Electric) with a field strength of 1.5 T. Patient’s head in nonmagnetic headphones was carefully immobilized. Recording was carried out by the so-called block paradigm consisting of alternating periods of rest and response to the applied loads with the duration of 30 s. The data were processed using SPM5 and MIRcro software. Real-time statistical maps of significant ($p<0.05$) changes in the level of blood oxygenation under functional loads were built. The resulting activation maps were overlaid onto the T1-weighted images and projected onto a three-dimensional model of the brain, where color intensity was consistent with the level of activation of the active zones. The location of the identified areas of activation with respect to gyri and sulci was analyzed; SPM5 software was used to determine the volume of activation zones (in voxel).

In accordance with the fact that the Broca’s motor speech area is responsible for switching from one sound to another [1], patients were offered a speech load: to recite months of the year in the reverse order (the so-called de-automated series). The patient was lying motionless and with his eyes closed, and was reciting the months silently. This was done to avoid stimulating the additional activation foci in the brain, which correspond to the area of innervation of the oral musculature. In some cases, the patient was offered the second test: to silently recite nouns starting with the high-frequency letter “K”.

Results

The Broca’s area was found in 7 patients (tumors of the left and the right hemispheres in 4 and 3 patients, respectively) in the form of activation of the posterior parts of the inferior frontal gyrus (or interface with the middle frontal gyrus) in the left hemisphere (Fig. 1). Noteworthy, 6 of the patients had benign tumors (3 astrocytomas; one of the following tumors: dysembryoplastic neuroepithelial tumor, meningioma and oligoastrocytoma). The only patient with glioblastoma from this group had a tumor of the right hemisphere.

Three patients who had Broca’s area on the left side (detected according to the fMRI data) had signs of left-handedness according to the Annette’s questionnaire but considered themselves right-handers. It is particularly remarkable that the coefficient of right ear (CRE) in the dichotic listening test was negative in two patients: one patient with reoperation for glioblastoma of the right frontal lobe, and one patient with a giant right-side meningioma of the sphenoid bone wings. This could be indicative of dominance of the right hemisphere for speech, as opposed to fMRI, where the speech load activated the Broca’s area on the left. A divergence in determination of speech laterализation was determined for the data obtained by two noninvasive methods (fMRI and dichotic listening test).
No speech disorders were revealed after surgery in these patients with tumors and Broca’s area, both located in the left hemisphere (the fMRI data on localization of the Broca’s area were used).

**Right-side Broca’s area** was detected in 3 patients with left-sided and right-sided tumors in two and one cases, respectively. All three patients had signs of left-handedness according to the questionnaire; however, all of them showed a positive CRE in the dichotic listening test. This was not consistent with fMRI data again. It should be emphasized that mild efferent motor aphasia was detected in one of these patients with the presence of a very large malignant tumor in the left frontotemporal region. This fact points to the presence of the Broca’s area in the left hemisphere; however, fMRI allowed one to find it only on the right hemisphere. Neither emergence nor aggravation of speech disorders was observed in patients after surgery. However, only a biopsy was performed in the female patient with aphasia elements caused by left-sided tumor of the frontotemporal region; in 2 patients, the tumor localized outside the speech areas.

Symmetrical **Broca’s areas in both hemispheres** were detected in 6 patients, all of whom had only **grade II—III** tumors (astrocytoma, oligodendroglioma, oligoastrocytoma, and meningioma; the tumors were large in most cases) of the **left hemisphere**. This group of patients was not homogeneous in terms of left-handedness. Three out of 6 patients were right-handers, had relatives with right-handedness and showed a positive CRE in the dichotic

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**Fig. 1.** Astrocytoma of the left frontotemporal region.

T2-weighted (a) and T2–FLAIR (b) MRI detects a diffusely growing tumor with an elevated MRI signal. fMRI combined with the stress load test to identify the Broca’s areas (c) demonstrates the localization of the Broca’s area (1). The activation zone in the lower parts of the precentral gyrus (2) corresponds to the speech motor center (the patient was trying to pronounce the generated words).
and metastasis of lung cancer) with large perifocal edema. Of them had very large malignant tumors (glioblastomas; these patients showed a negative CRE in the dichotic listening test. Among them, one patient had acoustic-mnestic aphasia; which confirmed the presence of speech areas (not found by fMRI) in the affected left hemisphere. The fourth patient was a retrained left-hander and had a tumor of the right hemisphere; her CRE was –44% (which was indicative of dominance of the right hemisphere for speech), while the Broca’s area was found in the right hemisphere upon intraoperative electrostimulation.

One more patient with a very large malignant tumor of the right frontotemporal region was unable to maintain the tasks well, which made the results unreliable.

**Discussion**

Our results showed that the detection of the Broca’s area in patients with large tumors of hemispheres can be a rather challenging task. The Broca’s area on the left side of the brain was found only in 7 right-handed patients; the brain activation was bilateral in 6 patients. The speech area on the right side of the brain was found in 3 patients, while it was not detected in 4 cases at all.

Two questions arise: 1) why the Broca’s area was not identified in some patients, and 2) what the bilateral brain activation in the zones corresponding to the Broca’s area and the Broca’s homologous region in the right hemisphere means.

According to many authors [13, 18, 22], the detection, lateralization of the speech area, and the degree of reliability depend on the use of certain voice stress tests and features of programs for statistical processing of the fMRI data. It has been shown that speech areas may be identified in different hemispheres when different speech tests are used; even frontal and temporal speech fields may have different lateralization in the same patient [10]. Thus, the use of a panel of tests is recommended [18], and that is what we plan to do in future. However, regardless of the tests, the uniformity of tumors in terms of their malignancy in patients allocated to groups catches one’s attention: the Broca’s area was not identified only in patients with large malignant tumors and perioperative edema, while bilateral representation was observed in patients with long-growing benign tumors. It is reasonable to assume that the results of research are primarily influenced by the factor of tumor existence (especially its histology and biology, which contribute to the growth rate), the presence of edema, features of neoangiogenesis and tumor metabolism.

Similar difficulties in identifying the speech zones in the presence of gliomas were also described by other authors. F. Roux et al. [18] compared the data of fMRI, intraoperative electrical stimulation with the pre- and postoperative speech status to reveal consistency between all these methods only in 3 out of 8 patients with gliomas.
The authors draw a conclusion that fMRI in patients with tumors should always be supplemented with intraoperative electrical stimulation. J. Ulner et al. [25] examined 50 patients (31 of whom had gliomas) using fMRI to find a discrepancy between the fMRI data regarding the speech lateralization and the results of invasive methods in 7 patients. In 27% of patients they observed “lesion-induced pseudo-dominance” with detecting the activity and in the opposite hemisphere.

fMRI is based on the ability of BOLD (blood oxygen level dependent) signal to identify active areas of the brain under corresponding loads. According to the literature [19, 21, 25], the failure to reveal speech activity areas in patients with gliomas can be associated with a decrease in BOLD activity in the tumor-affected hemisphere as compared to the healthy one. In the hemispheres on the tumor side, the difference in blood flow in the active and impaired brain areas under loads was either poorly detected or undetected by proper statistical analysis both in the tumor area and distantly. In turn, the reduced BOLD activity depends on disturbance of vascular autoregulation in tumors, in particular in the newly developed vessels with pathological structure [15, 16]. J. Pillai and D. Zaca [16] have shown that gliomas with high malignancy (grade IV) are have a relatively high blood as compared to gliomas of lower malignancy because of neoangiogenesis; however, declined vascular reactivity was found not only in the tumor, but in the hemisphere on the tumor’s side as well. The authors mentioned the “lesion-induced neurovascular uncoupling”, which causes false fMRI results.

Fig. 2. Astrocytoma of the left frontotemporal region.
T2-weighted (a) and T2-FLAIR (b) MRI detects the diffusely growing tumor with an elevated MRI signal. fMRI with the stress load test to identify the Broca's area (c) demonstrates bilateral localization of the Broca's area (1). Bilateral activation zones in the frontal lobes (2) correspond to the auxiliary areas involved in implementing this task.
The mass effect of a tumor (especially malignant one with an extensive perifocal edema) also plays a role. Not only do the tumor mass and edema hamper the arterial perfusion, but they also lead to compression of the veins. Hence, the oxygenated blood under functional loads is drained faster from the activated field, reducing the intensity of the BOLD signal [18]. All these circumstances may cause difficulties in identifying speech zones in patients with relatively fast-growing malignant tumors. It should be emphasized that aphasias elements were detected before surgery in 2 patients with malignant tumors in the speech areas of the left hemisphere, indicating that the speech areas localize on the left side of the brain. However, no Broca’s area was detected by fMRI in one patient at all, while it was found on the right side in another patient (no speech zone on the left side of the brain was identified as well).

The second question that needs to be discussed is as follows: what is a reason behind the emerging of bilateral lesions in brain activity under speech loads in right-handed patients? Bilateral foci of activity were detected in our study only in patients with relatively benign (i.e., slowly growing) tumors. It would be reasonable to assume that the bilateral foci of brain activation reflect the compensation of functions in the impaired regions of the brain.

The questions regarding functional background of compensation for the impaired functions are currently being actively discussed in the literature. The emergence of activation foci in the non-dominant hemisphere is associated with good and long-term compensation for speech functions in patients with stroke [24]. Symmetrical speech zones are frequently found in both hemispheres in patients with epilepsy, especially with the left-sided epileptic focus and early onset of seizures [17], as well as in the presence of arteriovenous malformation (AVM) in the left hemisphere [11, 26]. An isolated transfer of representation of expressive speech into the opposite hemisphere revealed by the combined use of fMRI and impressive inrasurgery electrical stimulation in patients with epilepsy [2] (and impressive speech, in patients with glioma of the left islet and tempoparietal region [10, 14]) has been reported. Displacement of the speech zones within the left hemisphere accompanying its pathology has been shown as well. Hence, atypical localization of the Wernicke’s area was revealed under electrical stimulation in the anterior temporal cortex or inferior temporal gyrus of the left hemisphere in patients with temporal lobe epilepsy and low IQ [6].

However, despite the generally agreed point of view regarding the transition of the speech areas to the opposite hemisphere in patients with early (more often, prenatal or perinatal) injury of the left hemisphere, F. Liegois et al. [12] reported their paradoxical data, which were obtained by examining children and adolescents with AVM. It has been shown using fMRI that 5 children with AVM localized near or within the speech areas of the left hemisphere, and 5 children with AVM of the left hemisphere but localized away from the speech areas, have 4 cases of dominance of the left hemisphere for speech and 4 cases of dominance of the right hemisphere, respectively. This effect, however, can be associated with features of the blood supply to AVM in each individual.

There is another point of view regarding the emergence of the bilateral activity foci. J. Ulner et al. [25] assume that the increase in activity in the areas homologous to speech zones in the right hemisphere can only represent the features of statistical processing of the fMRI data, when the BOLD effect of the tumor-affected hemisphere is reduced to a certain extent, while the activity in the other hemisphere increases to a certain extent.

A. Thiel et al. [24] examined 61 right-handed patients with hemispheric tumors and 12 healthy volunteers using positron emission tomography (PET). The authors demonstrated that the areas of the frontal lobe adjacent to the speech zone are often additionally activated in the patients. However, bilateral brain activation was observed in 63% of patients with frontal or posterior temporal foci only, while an activity reversion to the right hemisphere under a speech load was observed in 18% of cases. Accordingly, there are two types of functional compensation: 1) interhemispheric type with the emergence of the activation zones in the areas homologous to the speech zones in the opposite hemisphere; 2) intrahemispheric type, when the zones adjacent to the speech zones are activated.

Despite the small number of observations, it seems to us that bilateral activation under voice load still attests to manifestation of brain plasticity and some functional compensation, since it was detected either in the presence of relatively benign, more slowly growing tumors (according to our data) or if the tumors directly localize inside the voice zones or in their close vicinity [24]. In connection with the discussion of brain plasticity when the speech areas are damaged, the study by S. Bonelli et al. [4] is of great interest to us. These authors have studied the activation of speech zones before and after anterior temporo-lateral lesionectomy in 44 patients with drug-resistant epilepsy. Prior to surgery, activation of the left-sided Broca’s area was observed in right-handed patients. However, bilateral activation of the Broca’s area and the homologous region of the right frontal lobe was detected using fMRI within 4 months after surgery in some patients (after temporal lobectomy). It should be mentioned that speech disorders (functional disorders of naming by the temporal type) were less pronounced in this very group of patients. However, since the right hemisphere plays a special role in speech production, complete compensation for speech functions could not be provided by this hemisphere only; therefore, bilateral activation could cause aphasia. However, this issue requires further study, and a comprehensive examination of patients with different aphasia and without them, as well as with different tumor localization, is the way towards this goal.

In our study, we found no significant correlation between the functional asymmetry profile and fMRI results;
this again puts the tumor at the forefront in interpreting the fMRI data. However, frequent detection (mostly in patients with tumors of the left hemisphere) of the negative CRE during the dichotic listening test has caught our attention. There was a statistically significant ($p<0.05$) absence of correlation between the self-esteem (patients considered themselves to be right-handed) and the dichotic listening data (negative CRE, according to the conventional views, indicates dominance of the right hemisphere for speech). A similar result has also forced us to think that the tumor factor significantly affects the result obtained upon the dichotic listening test, especially in patients with left-sided foci. Frequent detection of the negative CRE in right-handed patients with hemispheric tumors requires further research, in particular as compared to the data of clinical observation, fMRI, and intraoperative electrical stimulation.

**Conclusion**

The presence of a hemispheric tumor (in particular, large and malignant ones) may significantly affect detection of the speech zones using fMRI. One should take into account the entire range of clinical data to ensure safe resection of the tumor from the supposed speech zones.

**REFERENCES**

stand the features of localization of such an important for an individual function as speech to develop basic understanding of the functional activity of the brain and for other purpose in mind. The obtained knowledge is refracted in terms of the impact of the neoplastic process on preservation of this function, including allowance for the effect of translocation. The authors are extremely interested in the application aspect of the problem: what amount of surgical intervention, approaches, etc., are required and sufficient in terms of neurosurgery, since the main task is to minimize the consequences of surgery. The maximally person-centered approach — the goal of the modern high-tech medicine — is another very important feature of this study. Of course, there have been some similar studies published; however, they are rare in Russia and frequently employ methodologically incorrect approaches. The authors have managed to combine the modern and elegant (in terms of its design) study with the approach-correct and high-quality research. When reading this paper, we had thoughts that corresponded to the main conclusions drawn by the authors. The results are consistent with our data on localization and translocation of the speech areas.

T. N. Trofimova (Moscow)
Degenerative diseases of the lumbosacral spine still remain an important problem of modern neurosurgery. Degenerative stenosis of the spinal canal clearly illustrates this fact. With allowance for the increasing life span in developed countries, the number of patients with this disease increases. Thus, about 400,000 of the US residents seek for medical advice each year; examination reveals degenerative stenosis of the lumbosacral spinal canal subject to medical assistance. Current diagnostic techniques, such as MRI and HCT, virtually eliminate the problems associated with visualization of this disease [1]. However, patients seek for primary medical advice at medical care units, where there are no appropriate visualization techniques. This fact often complicates the process of stenosis diagnosis. One of the ways to solve this problem involves advanced computer technologies [2–4]. Development of computer technologies considerably broadens the possibilities of clinical medicine presenting all premises for using the Internet technologies to solve special neurosurgical problems. This approach (the use of Internet technologies to solve medical problems) was implemented in the Medicine 2.0 concept. The main advantages of information computer technologies are as follows: wide accessibility for a large number of users, and the platform and tools that allow one to process large amounts of data. These data can always be used for decision making concerning the diagnosis, selection of a treatment strategy with allowance for patient’s individual parameters, assessment of potential efficiency of the treatment method in a certain patient, etc. Noteworthy, current evidence-based practice is also being regarded as a set of measures purposed to search for information and analysis it with the aim of decision making for clinical medicine [5, 6]. This information should be based on systematic and scrupulous clinical research purposed to search for reliable scientifically-based facts [7, 8]. The use of this information to develop on-line computerized diagnosis systems is a fresh idea, topical due to wide audience of potential users. Problem-oriented registries should be mentioned as one of the sources of information required for creating such systems.

The purpose of the study was to develop a virtual system supporting clinical diagnosis of the degenerative lumbosacral spinal stenosis based on the Spine Registry data.

Materials and Methods. The criteria for diagnosis system were selected by analyzing the symptoms present in 298 patients with lumbar spinal stenosis. Sensitivity and specificity of the system under development was assessed by analyzing the group of patients with disc herniation.

Results and Discussion. The presented clinical diagnosis supporting system allows one to identify patients with degenerative lumbar spinal stenosis at the stage of primary visit. The sensitivity and specificity of the system are 90 and 71%, respectively. The on-line mode of the diagnosis system in the structure of the Spine Registry ensures maximal accessibility for specialists, regardless of their current location. Development of the Medicine 2.0 software is a topical direction of the further research, which can be facilitated by using specialized registries for consolidated data acquisition.

Keywords: degenerative lumbosacral spinal stenosis, Spine Registry, virtual diagnostics system, Medicine 2.0.
The patients operated on for degenerative stenosis of the lumbosacral spine comprise the most representative group. We have formed a special module uniting all the symptoms and signs typical of patients with this disease to analyze their clinical parameters, to assess the outcomes and to perform dynamic follow-up. The data concerning patients of the retrospective group were input using a script. The parameters input into the module should meet the following requirements:

1. They are to be meaningful parameters of a patient with degenerative stenosis of the lumbosacral spine.
2. They are to be meaningful parameters of degenerative stenosis of the lumbosacral spine.
3. They are to be recognizable at the stage of patient’s primary visit.
4. They should comprehensively characterize the treatment result – outcome.
5. The reasonability of their registration should be verified.

The signs typical of these patients were used to develop the system supporting clinical diagnosis of degenerative lumbosacral spinal stenosis.

We have examined all signs of degenerative stenosis available from the literature and analyzed the schemes of differentiation between degenerative stenosis and other diseases, both degenerative (disc herniation) and non-degenerative (atherosclerosis of the lower limbs).

In the present study, we have examined the clinical parameters of 298 patients with degenerative stenosis of the spinal canal (group 1) and 320 patients with disc herniation in the lumbosacral spine (group 2).

All patients were diagnosed based on the results of neurological examination and the golden standard of diagnosis, MRI and CT. The outcomes of surgical treatment were assessed using the modified criteria proposed by Kawabata et al.

All signs to be input into the diagnosis system were selected according to the analysis of the symptoms of degenerative stenosis patients, their past history data, and the results of neurological examination. Parameters used to differentiate degenerative stenosis from diseases that typically manifest as weakness and leg pain when walking, diabetes mellitus and atherosclerosis of the lower limbs, were also input into the system. The main parameters of the differential diagnosis were borrowed from the Clinical Guidelines on the Diagnosis and Treatment of Degenerative Lumbar Spinal Stenosis of the North American Spine Society issued in 2013 (NASS, 2013). It is worth mentioning that the patients of the disc herniation group were tested in order to assess sensitivity and specificity of the system.

The demographic parameters of the groups under study are presented in Table 1.

Table 2 lists the main symptoms and parameters of patients from groups 1 and 2.

The analysis of signs allowed us to select questions for the system and to input the following requested signs:

1. Age.
2. Progression of symptoms at walking and regression at rest.
3. The Charcot syndrome (periodic paresthesia and pains in calf muscles forcing a patient to stop walking.
4. Regression of symptoms when leaning forward.
5. Positive Lasègue’s sign.
6. Change in Achilles tendon reflex.
7. Diabetes mellitus.
8. Atherosclerosis of the lower limbs.

The selected signs were enciphered; the code was based on an extent to which a sign was significant for diagnosis of lumbosacral spine degenerative stenosis.

**Results**

The clinical diagnosis supporting system was constructed around the clinical signs (sequence of the questions) and their values (Table 3).

The result is obtained by summing up the score (values). Therefore, the total score ranges from −5 to +10.

Table 4 shows the data on total score obtained using the system in Group 1 and 2 patients (618 patients).

---

**Table 1. Demographic characteristics of patients in groups 1 and 2**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Degenerative spinal stenosis (group 1)</th>
<th>Disc hernia (group 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, abs. (%)</td>
<td>154 (52)</td>
<td>170 (53)</td>
</tr>
<tr>
<td>Females, abs. (%)</td>
<td>144 (48)</td>
<td>150 (47)</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>67</td>
<td>41</td>
</tr>
<tr>
<td>Duration of disease, months</td>
<td>23</td>
<td>5</td>
</tr>
</tbody>
</table>

**Table 2. Demographic characteristics of patients in groups 1 and 2 (%)**

<table>
<thead>
<tr>
<th>Sign (clinical symptom)</th>
<th>Degenerative spinal stenosis (group 1)</th>
<th>Disc hernia (group 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 50 years</td>
<td>95</td>
<td>20</td>
</tr>
<tr>
<td>&gt; 60 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain syndrome or leg hypesthesia</td>
<td>95</td>
<td>85</td>
</tr>
<tr>
<td>Pain syndrome in the lumbar spine</td>
<td>94</td>
<td>70</td>
</tr>
<tr>
<td>Symptoms progress at walking and regress at rest</td>
<td>95</td>
<td>18</td>
</tr>
<tr>
<td>Regression of symptoms when leaning forward</td>
<td>73</td>
<td>8</td>
</tr>
<tr>
<td>Progress of symptoms in the upright position</td>
<td>85</td>
<td>25</td>
</tr>
<tr>
<td>Hypesthesia in both legs</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>Leg weakness</td>
<td>34</td>
<td>39</td>
</tr>
<tr>
<td>Pelvic organs dysfunction</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Lasègue’s sign:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>unilateral</td>
<td>15</td>
<td>37</td>
</tr>
<tr>
<td>crossed</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Impaired sensitivity in lower limbs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>70</td>
<td>85</td>
</tr>
<tr>
<td>hypesthesia</td>
<td>28</td>
<td>14</td>
</tr>
<tr>
<td>anesthesia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Patellar tendon reflex:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>standard</td>
<td>65</td>
<td>70</td>
</tr>
<tr>
<td>asymmetry</td>
<td>33</td>
<td>29</td>
</tr>
<tr>
<td>absent</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Achilles tendon reflex:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>standard</td>
<td>45</td>
<td>52</td>
</tr>
<tr>
<td>asymmetry</td>
<td>50</td>
<td>46</td>
</tr>
<tr>
<td>absent</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Extension of degenerations according to MRI examination:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st level</td>
<td>179</td>
<td>320</td>
</tr>
<tr>
<td>2nd level</td>
<td>84</td>
<td>0</td>
</tr>
<tr>
<td>3rd level</td>
<td>35</td>
<td>0</td>
</tr>
</tbody>
</table>
Our analysis demonstrated that the total score of 7 or higher totals points to the presence of clinical signs typical of degenerative lumbosacral spinal stenosis. It is necessary to remind that development of a diagnostic test requires special statistical studies, which reveal its main parameters: sensitivity and specificity.

Sensitivity and specificity of the test at its threshold total score, equal to 7, are as follows: sensitivity is 0.899 (95% CI 0.865—0.933) and specificity is 0.709 (95% CI 0.660—0.759).

Hence, sensitivity of the diagnosis system is 90%, while its specificity is 71%.

During the analysis, we calculated parameters affecting the features of the test software and comprehensively characterizing its properties (Table 5).

Table 5 shows that positive likelihood relation (the total score higher than 6) was 3.094, that is, patients with degenerative lumbosacral spinal stenosis can obtain this result threefold more likely than patients with lumbosacral disc herniation. The system supporting clinical diagnosis of degenerative lumbosacral spinal stenosis is presented in the structure of the Spine Registry and available at www.spineregistry.ru/calculators/DSCalc.html.

Discussion

The use of computer- and Internet-based information technologies to solve medicine problems is losing its novelty but still remains a topical and promising trend closely related to the Medicine 2.0 concept. This study presents the system supporting clinical diagnosis of degenerative lumbosacral spinal stenosis included in the structure of the on-line Spine Registry. The concept of such structures is closely related to their ability to process large data arrays (in our case, these data are easily available through the Spine Registry). We consider the development of such systems for various nosological forms and an on-line patient-consulting system a promising direction and continue our work on these problems. The use of the potential of the Internet

### Table 3. System of clinical diagnostics supporting at degenerative lumbosacral spinal stenosis

<table>
<thead>
<tr>
<th>Requested sign</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td></td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>1</td>
</tr>
<tr>
<td>&gt;70 years</td>
<td>2</td>
</tr>
<tr>
<td>Progression of symptoms at walking and regression at rest</td>
<td></td>
</tr>
<tr>
<td>Charcot syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Regression of symptoms when leaning forward</td>
<td>3</td>
</tr>
<tr>
<td>Positive Lasegue’s sign</td>
<td>3</td>
</tr>
<tr>
<td>Change in the Achilles tendon reflex</td>
<td>−1</td>
</tr>
<tr>
<td>Diabetes mellitus and/or atherosclerosis of the lower limb vessels</td>
<td>−5</td>
</tr>
</tbody>
</table>

### Table 4. Distribution of the total score in patients with degenerative lumbar spinal stenosis (group 1) and disc hernia (group 2)

<table>
<thead>
<tr>
<th>Total score</th>
<th>Number of patients with degenerative lumbar spinal stenosis</th>
<th>Number of patients with disc hernia</th>
</tr>
</thead>
<tbody>
<tr>
<td>−5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>−4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>−3</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>−2</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>−1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>94</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>48</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>124</td>
<td>76</td>
</tr>
<tr>
<td>8</td>
<td>139</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>298</td>
<td>320</td>
</tr>
</tbody>
</table>
and the specialized registries uniting a great number of specialists makes it possible to develop novel solutions for various clinical problems.

Conclusions

1. The created clinical diagnosis supporting system allows a specialist to identify patients with degenerative stenosis of the lumbosacral spinal canal at the stage of the patient’s first visit.

2. Sensitivity and specificity of the created diagnosis supporting system are 90 and 71%, respectively.

3. The on-line version of the diagnosis supporting system in the structure of the Spine Registry (www.spineregistry.ru/calculators/DSCalc.html) makes it available for specialists, regardless of their current location.

4. Development of the Medicine 2.0 concept is a topical direction of further research, which can be facilitated by centralized data collection using the specialized registries.

REFERENCES


Table 5. Statistical parameters of clinical diagnosis supporting system in patients with degenerative lumbosacral spinal stenosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive prognostic value (PPV)</td>
<td>0.742</td>
</tr>
<tr>
<td>Negative prognostic value (NPV)</td>
<td>0.883</td>
</tr>
<tr>
<td>Positive likelihood ratio (LR+)</td>
<td>3.094</td>
</tr>
<tr>
<td>Negative likelihood ratio (LR–)</td>
<td>0.142</td>
</tr>
</tbody>
</table>

Commentary

The article focuses on the new and topical subject: application of computer information technologies for decision making on special clinical problems. The authors’ original approach to the development of the system and Internet presentation is worth readers’ attention. It can be considered as the development of a new direction: Medicine 2.0 or, more appropriate, Vertebrology 2.0. The system was based on the Spine Registry, which once again proves that the Registry is needed and discloses its additional features. The authors have processed a large amount of data and performed statistical processing, which is thoroughly described in the Discussion section.

Thus, the article is timely and relevant for neurosurgeons, trauma and orthopedic surgeons, as well as for general surgery. It bears undoubted signs of both academic novelty and practical effect; therefore, it is recommended for publishing.

A.A. Kuleshov (Moscow)
Flexible Endoscopy in Surgical Treatment of Spinal Adhesive Arachnoiditis and Arachnoid Cysts

A.A. KASHCHEEV, S.O. ARESTOV, A.O. GUSHCHA

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Thecaloscopy is less-invasive exploration of spinal subarachnoid space with an ultra-thin flexible endoscope and endoscopic fenestration of scars and adhesions. Thecaloscopy was used in Russian neurosurgery for the first time. Since 2009, 32 patients with following diagnosis have been operated on: 17 – spinal adhesive arachnoiditis (8 – local forms, 9 – diffuse forms), 12 – spinal arachnoid cysts (7 – post-traumatic cysts, 5 – idiopathic cysts), 3 – extramedullary tumors (thecaloscopic videoassistance and biopsy). In all cases, the subarachnoid space was explored and pathologic lesions were treated by endoscopic perforation of cyst or dissection of adhesions using special instrumentation. The mean follow-up period in our group was 11.4 months. Neurological improvement (estimated as 1.4 by modified Frankel scale, 1.8 by Ashworth spasticity scale) was seen in 87% of patients operated on for spinal arachnopathies. Transient neurological deterioration (mild disturbances of deep sensitivity) was found in 9% of patients and was managed successfully with conservative treatment. One (3.1%) patient was operated on three times because of recurrence of adhesions. There were no serious intraoperative complications (e.g., severe bleeding, dura mater perforation, etc.). Postoperative complications included one case of wound leakage and one case of postoperative intercostal neuralgic pain. The mean hospitalization time was 7.6 days. According to our data, thecaloscopy is an efficient and safe method, and could be widely used for treatment of spinal arachnopathies, adhesive arachnoiditis, and arachnoid cysts. Taking into account that adhesive spinal arachnoiditis is a systemic process and spinal arachnoid cysts can be extended as well, thecaloscopy can be regarded as the most radical and less-invasive way of surgical treatment existing in neurosurgery.

Keywords: thecaloscopy, epiduroscopy, spinal arachnoiditis, arachnoid cysts, subarachnoid space, flexible endoscopy, neuroendoscopy, syringomyelia.
to the prevalent symptoms: 1) conductive; 2) radicular; 3) mixed; and 4) dorsal columnar [1].

Spinal arachnoiditis can be characterized by acute, sub-acute, or chronic disease progression. Acute spinal arachnoiditis is mostly found in patients with severe systemic infections, such as sepsis and bacterial meningitis. It is often accompanied with hyperthermia, fever, acute phase symptoms. In the most severe cases it is complicated by hemorheological disorders, multiorgan failure, etc. Neurologic symptoms develop quickly over only a few days or even hours; in particular, acute progression of severe conductive symptoms emerges. Sub-acute spinal arachnoiditis also accompanies infections, but in a more latent form, developing over months; it is characterized by normal or subfebrile temperature. In the neurologic status, radicular symptoms come to forefront, while conductive symptoms emerge later. In patients with chronic spinal arachnoiditis, it is often impossible to determine an exact infectious agent; disease progresses very slowly; spastic and afferent paresis, as well as pelvic disorders, is prevalent [3].

It should be mentioned that arachnoid spinal cysts often clinically resemble an extramedullary tumor; this fact used to cause diagnostic errors before neuroimaging started to be widely used. An arachnoid cyst causes slow-progressing conductive disorders, cerebrospinal fluid circulation disorders, rarely — radicular symptoms localizing at one of the adhesions on the cyst wall. Numerous studies have been devoted to experimental methods for modeling arachnoid cysts and their role in syringomyelia development. Thus, the presence of compression of the subarachnoid space has been proved to cause widening of the central canal and formation of a syringomyelitic cyst [7].

Planning of pre-operative examination

As mentioned above, the clinical picture of cysto-adhesive spinal arachnoiditis may be different; patient’s condition may vary from subclinical health complaints to severe disability. In a few cases, especially after bacterial meningitis, spinal symptoms can be overlaid with the clinical presentation of intracranial pathology. Moreover, many arachnoid cysts (especially the idiopathic ones) are asymptomatic; they may be detected incidentally during MRI examination.

Therefore, the main objective of pre-operative examination is to determine whether the neurologic symptoms are caused by spinal arachnoiditis or arachnoid cyst and to eliminate the possibility of intercurrent pathology. A precise algorithm of the examination may differ depending on a certain patient; but the mandatory plan of pre-operative examination includes the following items:

— neurological examination (both by a neurosurgeon and a neurologist);
— MRI of all possibly involved sections of the spine and spinal cord (magnetic field intensity more than 1.5 T) with MR myelography and quantitative dynamics of the cerebrospinal fluid if necessary;
— routine laboratory studies (measuring the level of C-reactive protein in blood) and analyses for highly infectious diseases.

If necessary, the following methods are also can be used:

— neurophysiological methods (electroneuromyography, somatosensory-evoked potentials, transcranial magnetic stimulation);
— lumbar puncture (to measure pressure in the cerebrospinal fluid; total, biochemical and microbiological analyses of CSF);
— MRI of the adjacent spine sections;
— CT scanning of the spine;
— Consulting neurologists specializing in neurodegenerative and demyelinating diseases.

Description of the procedure

Technical equipment for the method

The use of a flexible endoscope (fiberscope) manufactured by Karl Storz (Germany) is described in this study (Fig. 1). The endoscope can be either 40 or 70 cm long. The latter version is sufficient for complete revision of the entire subarachnoid space from the cauda equina roots to the cranovertebral transition in an adult patient. The fiberscope is compatible with a standard endoscope stand.

A manipulator on the base of the fiberscope allows bending of its distal part up to 270° in two directions (Fig. 2). This function allows one to perform complete visualization and revision of the ventral and dorsal subarachnoid spaces.

The working surface is 2.8 mm in diameter; has a light source, camera, and working channel 1.2 mm in diameter (Fig. 3, 4). This channel can be used for irrigation during the surgery and to insert manipulators for biopsy and adhesion detachment under visual control.

The recent technology has allowed placing the camera at the distal part of the endoscope; this technology was registered by Karl Storz under the “chip-on-tip” trade name. Optical resolution of the “chip-on-tip” devices is superior to standard fibrescopes with the same diameter of the working surface. The preliminary results of clinical use of digital endoscopes show that they can be useful for interventions in the brain, as well as in the spinal cord: for perforation of the floor of III cerebral sinus, biopsy of tumors of the cerebral sinus system, endoscopic drainage and fibrinolysis of hypertensive intracerebral hemorrhages. Visualization of intracranial structures is of high quality when this technology is used.

Surgery technique

The intervention is performed on patients in the prone position. Both endotracheal and local infiltration with anesthesia ensured through the puncture approach is possible due to the low invasiveness of the method. In surgeries on the superior cervical spine, patient’s head is

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rigidly fixed with a Mayfield head holder. The endoscopic stand is placed facing the working surgeon. Intraoperative radiography is used.

According to the principles of the minimally invasive surgery, the approach should be as small as possible, but it should entirely conform to intervention objectives. Therefore, it is possible to choose different approach localizations.

The approach is performed strictly above the compression site in the cases of local spinal cysts or single adhesions (Fig. 5), making it possible to conduct microsurgical dissection of the adhesions (Fig. 6).
In the cases of extended arachnoid cysts, it is reasonable to use the approach in the middle of the cyst (Fig. 7). This allows one to perform convenient manipulations with the endoscope both in the cranial and caudal directions.

In the cases of severe adhesions, extended adhesive arachnoiditis, and presence of a wide range of symptoms caused by damage to various sections of the spinal cord and its roots (Fig. 8) and when adhesions are localized in a dangerous area (conus, epi-conus), it is the safest to use the approach caudally from the conus. This makes it possible to perform manipulations under conditions of larger vertical dimensions of the subarachnoid space and reduces the risk of aggravation of the neurologic symptoms.

When using an open approach, skin and soft tissues are incised in the projection of the target spine section under the control of the intraoperative radiography according to the tactics selected. Spinous processes and vertebral arches are skeletonized at the target level. Then, laminectomy is performed, typically at the arch of a single vertebra (corresponding to the 5–7 cm long skin incision). The length of the dura mater incision is usually less than 2 cm. Effective hemostasis (using modern hemostatic materials) is of high importance, since even the minimal bleeding hinders endoscopic imaging.

The main stage (thecaloscopy) begins after the microsurgical dissection of visible adhesions and cyst walls. The fiberscope is inserted into the dorsal subarachnoid space and, if necessary, into the ventral space by bending the distal end of the instrument with the manipulator.
Fig. 8. Extensive post-infectious arachnoiditis of the middle thoracic spine.

Fig. 9. Thecaloscopy of the ventral subarachnoid space. An arrow shows the distal end of thecaloscope.

(Fig. 9). If necessary, endoscope position is controlled using an electro-optical converter.

This method allows precise visualization of adhesions and cyst walls (Fig. 10), as well as different anatomic (Fig. 11) or pathologic (Fig. 12) formations.

Adhesion separation and cyst fenestration manipulations can be performed either using the working area or using manipulators (Fig. 13). All thecaloscopic manipulations should be smooth, without applying the force, in order to prevent traction of the spinal cord and aggravation of the neurologic symptoms. It is to be noted that the technical features of the method require a surgeon to have certain experience in image interpretation; in particular, it is important to get used to its “mesh-like” appearance, which is typical of all ultrathin flexible endoscopes; to the better image quality when the fiberscope moves backwards, and to the need for proper orientation in the two-dimensional space.

Thecaloscopy can be used to separate intramedullary adhesions in surgeries for severe syringomyelia with myelotomy (Fig. 14).

Prolonged irrigation with physiological saline is used to stop bleeding from arachnoid envelope vessels (Fig. 15), which are often pathologically changed. No hemorrhage of significant volume and duration has been observed in our practice. Semiconductor diode laser also can be used for vessel coagulation.

Much attention is paid for prevention of wound liquorhea, which is relatively probable in patients with arachnoiditis due to morphological changes in the dura mater. Hermetic suturing is insufficient in some cases and plastic repair of the dura mater is required.

Postoperative management of the patients

Patients were typically activated as early as possible, preferably the next day after the surgery. Early beginning of rehabilitation under the control of neurorehabilitation specialists is very important. Antibiotic prophylaxis, glucocorticosteroid therapy, and symptomatic treatment are employed. Lumbar puncture is performed the next day after surgery with estimation of the pressure in CSF and washing with doxycycline solution to sanitize the subarachnoid space. The mean hospital stay in the case of microsurgical approach is 7–10 days. It should be noted that puncture thecaloscopy can be performed at one-day inpatient hospital stay.
Evaluation of surgery results

It is reasonable to evaluate the treatment results on the day when a patient was activated, at hospital discharge, 6 months after the surgery, and then annually. The following methods are typically used for evaluation:

- neurological examination in the dynamics;
- modified Frankel scale;
- neuroimaging results (MRI including MR myelography);
- record of complications.

Fig. 10. Arachnoid adhesions (a, b) and arachnoid cyst wall (c), thecaloscopic view.

Fig. 11. View of the cauda equina roots in the spinal cord for ventral (a) and dorsal (b) endoscope insertion. The site where the spinal cord roots originates from the cauda equina (c).

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Complications and unsatisfactory results

Our data suggest that thecaloscopy rarely causes complications; their frequency is no higher than in other spinal neurosurgeries. No serious intraoperative complications were observed. Besides general surgical and anesthetic complications, development of liquorrhea or a liquor cyst of soft tissues, as well as reactive aseptic meningitis, is possible.

A possible unsatisfactory result of the surgery can be recurrent adhesion, which can develop over different periods and cause aggravation of neurologic symptoms (3.1% patients in our group). These cases are rare according to our data [5]; predictors of such results are likely to be as follows: prevalence of arachnopathies, general inflammation processes, immunoreactive disorders, and proneness to develop adhesions (Fig. 16). A patient should be warned about the possibility of such result.

Results of using thecaloscopy

We used this method for the first time in November 2009. Since 2009, 32 patients have been operated on: 17 – for spinal adhesive arachnoiditis (8 – local forms, 9 – diffuse forms), 12 – spinal arachnoid cysts (7 – post-traumatic cysts, 5 – idiopathic cysts), 3 – extramedullary tumors (thecaloscopic video assistance, and biopsy). In all cases, the subarachnoid space was examined in both the dorsal and ventral sections. Surgery for cysts and adhesions included thecaloscopic separation of adhesions and exploration of the subarachnoid space caudally and cranially from the surgical approach site. The modified Frankel scale, the Ashworth scale, and the MRI data were used to evaluate the results.

The mean follow-up period in our group was 11.4 months. Neurological improvement (estimated as 1.4 according to the modified Frankel scale, 1.8 according to the Ashworth scale) was observed in 87% of patients operated on for spinal arachnopathies (Fig. 17).

Transient neurological deterioration (mild disturbances of deep sensitivity) was found in 9% of patients and were managed successfully with conservative treatment. One (3.1%) patient with severe widespread adhesive arachnoiditis was operated on 3 times with 6- or 8-month intervals due to recurrent adhesions detected by MRI. After each thecaloscopy, patient’s condition improved; however, it deteriorated back to the initial level after the mentioned intervals. No serious intraoperative
complications (e.g., severe bleeding, dura mater perforation etc.) were observed. Postoperative complications included one case of wound leakage and one case of postoperative intercostal neuralgia pain. The mean hospital stay was 7.6 days. According to the MRI data acquired after the surgery, recurrent adhesions were found in one (3.1%) patient; thus, reoperation was performed 7 months after the primary intervention.

Clinical case

A 29-year-old female patient S. belonging to the disability group I. At the moment of hospitalization to the Neurosurgical Department of the Research Center of Neurology, she had complaints for movement problems, spastic feeling in legs, reduced sensitivity in limbs, and episodic involuntary urination and defecation. She could walk for short distances with assistance. At the age of 17 years, the patient acquired complicated traumas in a criminal accident: closed cerebrocranial injury, brain concussion, injury of the spine and spinal cord at the cervical thoracic transition. The patient had multiple knife wounds of the neck, abdominal, thoracic cavities, pneumothorax on the left side, and spleen rupture. Immediately after the wounding, movements in limbs were completely absent, as well as sensitivity and self-contained urination and defecation. A significant improvement was achieved after the long-term rehabilitation: the patient began walking; pelvic organ functions partially restored. Approximately 1.5 years prior to the hospitalization she noticed slow aggravation of neurologic symptoms, difficulty in limb movements, and aggravation of numbness. Conservative therapy and rehabilitation were ineffective; a neurosurgeon recommended surgical treatment.

Diagnosis: post-traumatic arachnopathy at the C7–T1 level. Myelopathy at the C7–T1 level.

Neurological status: spastic tetraparesis up to 3 points in legs, up to 4 points in arms; reduced surface sensitivity starting from the T2 level; severe disturbances of deep sensitivity in legs; dysfunction pelvic organs (neurogenic urocyst). MRI revealed myelopathy at the C7–T1 level together with arachnopathy, disorders in CSF dynamics (in the MR myelography mode) (Fig. 18).
Laminectomy was performed at the T1 level along with adhesiolysis and thecaloscopic separation of adhesions. A rigid adhesion fixing the spinal cord at the C7–T1 level was detected intrasurgically; the adhesion was dissected. Thecaloscopy in caudal direction from the approach site (T4–T5) detected a rigid ventral and dorsal adhesion fixing the spinal cord and belonging to the arachnoid cyst wall (Fig. 11). They were endoscopically dissected, which resulted in the normalization of spinal cord pulsation and CSF passage (Fig. 15).

The patient was activated the next day after the surgery. Neurological improvement was seen as reduced spasticity (score 1 according to the Ashworth scale); no pelvic disorders were observed; surface and deep sensitivities improved. The wound was healed by primary intention. The patient was discharged on the 6th day after the surgery. Control examination after 6 months detected stabilization in the neurological status with no signs of relapse. The patient was able to walk and continued her high education.

Thus, the aggravation of the symptoms 11 years after the injury was most likely caused by decompensation of spinal blood circulation and progression of the adhesive process in the damaged area, compression of the spinal cord and disorders in CSF dynamics. Some authors [6] believe that autoimmune reactions cause there delayed adhesions (similar to the delayed period of severe cerebrocranial injury). Thecaloscopy made it possible to perform fenestration of adhesions and decompression of the spinal cord, including more caudally from the approach site where the adhesions were not verified by preoperative MRI. This method allowed one to achieve stable improvement in neurologic symptoms, significant improvement of patient’s quality of life, and promoted early medical and social rehabilitation.

**Conclusions**

Thecaloscopy was used in Russian neurosurgery for the first time. According to our data, thecaloscopy is an efficient and safe method; it can be widely used for spinal arachnopathies, adhesive arachnoiditis, and arachnoid cysts. Preliminary results of our study reveal the advantages of this method over open microsurgical interven-
tion; better clinical results were achieved with shorter length of stay and faster rehabilitation of the patient. In addition, thecaloscopy can be used for biopsy of extramedullary formations, and for video assistance in patients with the tethered spinal cord syndrome. Further studies will allow us to assess the long-term treatment results; they give grounds for broadening the range of indications for thecaloscopy.

REFERENCES


Commentary

The study is devoted to flexible endoscopy, a novel technology in spine surgery, which was used in Russia for the first time only several years ago. The authors of the article are the leading team of surgeons who use the flexible endoscope in surgical treatment of spinal adhesive arachnoiditis and arachnoid cysts. Thecaloscopy is a less-invasive surgical technique performed via insertion of the flexible endoscope into the dural sac with diagnosis or treatment purposes. Over the long-term period of studies, the authors have accumulated a large body of observations on using this technique. A total of 32 patients have been operated on: 17 — for spinal adhesive arachnoiditis (8 – local forms, 9 – diffuse forms), 12 — spinal arachnoid cysts (7 — posttraumatic cysts, 5 — idiopathic cysts), 3 — extramedullary tumors (thecaloscopic video assistance and biopsy). Surgery for cysts and adhesions included thecaloscopic separation of adhesions and exploration of the subarachnoid space caudally and cranially from the approach site. It should be mentioned that the authors managed to define indications for surgery. These are: true and pseudo-arachnoid cysts of the spinal cord of different length and genesis (including post-traumatic); adhesive spinal arachnoiditis, causing conductive or radicular symptoms, influencing life quality of the patient and resistant for rehabilitation treatment and conservative therapy; syringomyelia, connected with adhesion processes in subarachnoid space of spinal cord; extramedullary tumors (thecaloscopic video assistance and biopsy); and the tethered spinal cord syndrome. The authors have drawn a conclusion that thecaloscopy is an efficient and safe method and can be widely used for spinal arachnopathies, adhesive arachnoiditis and arachnoid cysts. Thecaloscopy can also be used for biopsy of extramedullary formations and for video assistance in patients with the tethered spinal cord syndrome.

However, the amount of manipulations that can be performed in the dural space is limited because of the use of single instrument and low image quality caused by small endoscope diameter. But technologies are being constantly mastered. Small-diameter endoscopes have recently started to be used in neurosurgery. They are equipped with a camera at the distal end, producing high-quality image, while the endoscope diameter is minimal. Advances in instrumentation and combining the instruments with manipulators will make it possible to perform more sophisticated surgeries with the minimal damage to the adjacent tissues. These facts argue in favor of the potential of using and improving this technique in the near future.

This article presents valuable scientific information; it is well-illustrated and provides a complete insight into using the technology.

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Patients with infiltrative sphenopetroclival meningiomas, which propagate in orbit and infratemporal fossa, constitute a special group. Only a few such cases are described in the literature [5, 9, 19, 30, 38, 55]. Such tumors differ from “classical” sphenopetroclival meningiomas by their clinical-topographic features. For example, oculomotor disorders can be a symptom of lesions in the posterior cranial fossa, the cavernous sinus, or orbit. The surgical approach regarding tumors that spread into the orbit and infratemporal fossa also has its own characteristics. These result from the need to expand access in removing the tumor from the adjacent structures of the outer skull base. Therefore, we propose a grouping of such observations in a special category, and, relying on target diagnosis and treatment, call these tumors, which spread into the orbit, the middle cranial fossa, infratemporal fossa, and the region of the petroclival junction, orbitosphenopetroclival meningiomas (OSPCM). The term could not be found in the literature, but a characterization and analysis of our own data, cited below, justify, in our opinion, the allocation of a classification unit in this case. The widely distributed craniofacial and cranio-orbital meningiomas, meningiomas of the middle cranial fossa (meningiomas of the cavernous sinus and the wings of the sphenoid bone), and sphenopetroclival meningiomas are close to OSPCM in their topographical anatomical and clinical characteristics.

The term “orbitosphenopetroclival meningiomas” is used here for the first time. This explains the absence of publications in the literature on the topic. As this takes place, the number of papers devoted to topographically similar tumors is a reflection of the huge interest in the problem of treatment of common tumors of the skull base: first and foremost, cranio-orbital and sphenopetroclival meningiomas.

A. Cranio-orbital meningiomas

1. Original growth, histology, and epidemiology

Cranio-orbital meningiomas usually occur in the dura mater of the wing of the sphenoid bone. They grow intraosseously and cause significant hyperostosis of the rear and side walls, as well as the roof of the orbit, and the floor of the middle cranial fossa. This results in tumor invasion of the orbit region [56, 71]. There can also be optic nerve sheath meningiomas that spread into the cranial cavity, and meningiomas originating from orbital peristeum. Cranio-orbital meningiomas are subdivided into three groups: the lateral (46%), medial (44.4%), and common ones (9.6%) [3, 4]. Lateral hyperostotic meningiomas involve the superior and inferior orbital fissures, the base of the middle cranial fossa, as well as the infratemporal and pterygopalatine fossa. Medial hyperostotic cranio-orbital meningiomas affect the anterior clinoid process, the optic canal, the superior orbital fissure, and the ethmoid sinus. This type of tumor is characterized by visual disorders of varying severity. Common hyperostotic cranio-orbital meningiomas include the features of the lateral and medial ones.

Meningiomas of this localization constitute 9–16% of all intracranial meningiomas [44, 71]. Cranio-orbital meningiomas occur more frequently (up to 17 times more) in women [12, 58, 59, 63, 64]. The clinical manifestation of the disease occurs mainly at 40–50 years of age [65].

Histologically, most cranio-orbital meningiomas are of the first degree of malignancy according to the WHO classification [63]. Significant tumor infiltration of the dura mater, muscles of the infratemporal fossa, and mucosal tissues of the orbit have been histologically confirmed in all specimens of invasive meningiomas. In all cases, hyperostosis is tumor invasion: failure to remove the tumor is directly related to the risk of recurrence [1].

2. Clinical manifestations

Exophthalmos is the leading symptom in the majority of patients (55–93%) with cranio-orbital meningiomas; its appearance results from hyperostosis and tumor infiltration of the contents of the orbit and the cavernous sinus [11]. Besides, visual acuity is reduced in 45–77% of patients. This is frequently accompanied by the emergence of a defect in sight field. Fundoscopy has revealed atrophy of the optic nerve in 16–32% of patients and
swelling in 6–31%. Deformation of the temporomalar region (44%), retrobulbar headache (17–29%), oculomotor disturbances (6–11%), and ptosis (0–6%) are other common symptoms [59, 63–65]. Tearing, which is associated with outflow obstruction at the nasolacrimal canal of irritation or ciliary ganglion, chemosis, and trophic disorders appear with an increase in the size of the intraorbital tumor.

The analysis of the symptoms that accompany the tumors affecting the bone base of the middle cranial fossa shows that the most pronounced clinical symptoms of tumor penetration into the narrow bony space, optic canal, the superior and inferior orbital fissures, the round or oval foramina, etc. manifest as a visual impairment, ocular motor disorders, and dysfunctions of the trigeminal nerve. The symptoms appear very early and more significantly if the tumor has failed to destroy the bone skull base, and, especially, if it has not produced in them any hyperostotic changes around the respective orifices and channels, which are most characteristic of meningiomas [2]. One can select the groups of clinical symptoms which are characteristic of lesions in the corresponding anatomical regions. Hence, propagation of the tumor in the ethmoid sinus or frontal sinus, except for anosmia, may result in difficulty in nasal breathing, emergence of discharge from the nose, and nose deformity. With propagation of the tumors in the rear cells of the ethmoid sinus (the bones of which are involved in the formation of the channel walls of the optic nerves), reduced vision is possible. Under propagation of the tumor in the nasopharynx, a changed in voice and nasal tone or twang ensue, and difficulties in swallowing and pain can be observed. In the case of propagation of meningioma into the nasal cavity, otolaryngologists can observe it as a pale-pink semicircular bulging of thick consistency in the upper parts of the nose, covered with normal mucosa.

With propagation of the tumor into the orbit through its medial wall (which is formed by the frontal process of the maxilla, the lacrimal bone, orbital plate of the ethmoid bone, and the body of the sphenoid bone), the disease manifests itself in exophthalmos, impaired eye movement, reduced vision, and various pain syndromes. The neoplasm of the medial regions of the middle cranial fossa, grown into the orbit, can exhibit almost identical clinical manifestations. The topography of the process is determined by computed tomography. The most probable area of original growth of the tumor can be determined relying on the dynamics of the appearing symptoms. Hence, intraorbital tumors usually debut sufficiently rapidly (even if the volume of the neoplasms is small) with clinical features of surrounding lesions of the orbit, while in case of intracranially distributed tumors, lesions of the cavernous sinus and middle medial fossa appear. In tumors emanating from inside the cavernous sinus, exophthalmos may appear later than other symptoms, following the appearance of intraorbital invasion. In middle-cranial fossa meningioma affecting the round orifice, the maxillary nerve (the second branch of the trigeminal nerve) is affected. In the propagation of the tumor into the region of the foramen oval, the mandibular nerve (the third branch of the trigeminal nerve) is affected; this manifests in impaired sensation in the lower jaw and hypotrophy of the chewing muscles. The clinical presentation of lesions in the infratemporal fossa at advanced stages of the disease manifests itself in face deformation, jaw joint blockade of various severity, and impaired sensation in the area of the second and third branches of the trigeminal nerve. These can come together with conductive hearing loss, which occurs due to the compression of the cartilaginous portion of the Eustachian tube in the infratemporal fossa, and a disruption of taste on the anterior two-thirds of the tongue due to the impact on the tympani, extending to the infratemporal fossa.

3. Surgical treatment

The aim of surgical treatment is to perform the maximum tumor resection with decompression of the optic nerve and tumor resection of the tumor-affected bone (hyperostosis or thinning due to destruction). According to P. Saeed et al. [58], the goal is to restore visual acuity and reduce exophthalmos, but not perform radical resection of the tumor. As a rule, removal of cranio-orbital meningiomas is performed through the frontotemporal, simple pterional, or orbitozygomatic approaches [18–20]. V. Lund et al. [37] have reported on the effective application of endonasal decompression of the medial wall of the orbit in 12 patients and decompression in 8 patients with opticopathy and reduced visual acuity due to cranio-orbital meningioma.

4. Results of surgical treatment

Resection of cranio-orbital meningioma reduces exophthalmos in the early postoperative period in 77–96% of patients [56, 58, 64, 65, 71]. However, other experts, relying on MRI data, have shown that significant exophthalmos remains after surgery in 53% of patients [64]. Prolonged dysfunction of the venous outflow and fibrosis, leading to lesser mobility of the orbit contents, could be the culprit here [58]. Visual acuity can be improved after surgery in 30–80% of patients; however, up to 9% of patients exhibit a permanent postoperative decrease in visual acuity. A study by P. Saeed et al. [58] showed stabilization of or improvement in visual acuity for 2 or fewer lines in the Snellen chart in 40 (61%) patients; 15 of them had a visual acuity of 0.8 or higher and 3 patients suffered preoperative amaurosis on the affected side. Visual acuity improved in 20 (30%) patients; for more than 4 lines and more than 2 lines in the Snellen chart in 8 and 12 of the patients, respectively. However, in 6 (9%) cases, visual acuity dropped. In 16 (84%) out of 19 patients who voiced preoperative complaints regarding the retrobulbar pain, the pain disappeared after surgery. U. Schick [65] reported postoperative improvement in 12 (30.8%) out of 39
patients with poor visual acuity and improvement, according to the perimetry data, in 10 (35.7%) out of 28 patients with the visual field defect. However, in 2 (2.6%) patients, a decrease in visual acuity was observed in the postoperative period, including blindness in 1 patient with originally low acuity.

5. Complications

At the moment, mortality under surgical treatment of cranio-orbital meningiomas is close to zero. However, postoperative complications, such as blurred vision and transient (6–49%) or resistant dysfunction of cranial nerves (7–18%), are still common [12, 26, 52, 56, 58, 66]. U. Schick (2009) published the results of surgical treatment of 77 patients with cranio-orbital meningiomas. Mild and severe postoperative complications emerged in 14.3% and 4% of the patients, respectively. One patient developed a brain abscess, 8 (10.4%) had postoperative liquorrhrea, which healed after lumbar drainage. In 3 (3.9%) patients, epileptic seizures were observed during the first weeks after surgery. In 4 (5.2%) patients, after separating the upper rectus muscle and the muscle lifting the eyelid, transient diplopia was discovered. Among the neurological complications, there was a single (1.3%) case of oculomotor paresis, a case of abducens nerve palsy, one case of trigeminal neuralgia in the innervation area of the second branch, and 3 (3.9%) cases of hypoesthesia in the innervation area of the third branch of the trigeminal nerve. Two (2.6%) patients showed severe postoperative complications in the form of aphasia and hemiparesis [65]. A similar frequency of onset of complications was observed in the study by P. Saeed et al. [58]. Accumulation of cerebrospinal fluid under the aponeurosis was observed in 5 (7.6%) out of 66 patients who had undergone resection of cranio-orbital meningiomas; in one case a revision and lumbo-peritoneal shunt placement were required. Transient ophthalmoparesis was observed in 2 patients who had undergone resection of the lateral orbital wall. Postoperative diplopia occurred in 40 patients; it was either transient or permanent in 32 (48.5%) and 8 (12.1%) cases, respectively. Stable dysfunction of cranial nerves in the form of oculomotor nerve palsy was observed in 6 (9%) patients. Two patients exhibited palsy of the sixth and fourth cranial nerves; palsy of the trigeminal and facial nerves were observed in 6 (9%) and 3 (4.5%) cases, respectively. S. Oya et al. [52] mentioned in their study such complications as hypoesthesia (resulting from the dysfunction of the trigeminal nerve) in 9 (23%) patients; oculomotor nerve palsy and seizures, in 3 (7.7%) and 2 (5.1%) cases, respectively.

6. Radicality of resection, frequency of relapses

The radicality and clinical effect of surgery are the main criteria in assessing the effectiveness of a surgical treatment of skull base tumors. The radicality of the removal of infiltrative meningiomas of the skull base is evaluated by the criteria established in basal surgery [64]. Total resection means the complete removal of the tumor; only infiltration of the cavernous sinus and the inclined process remain. Postoperative remnants of the tumor can be detected by neither CT scanning nor MRI. Under subtotal resection, small fragments of the tumor that infiltrate the main vessels, cavernous sinus, the optic nerve sheath in the channels and the orbit, and oculomotor nerves are detected. These remnants of the tumor are observed in control radiological studies. Macroscopic tumor fragments in partial tumor resection can be visualized using X-ray contrast methods in the postoperative period.

The relapse frequency of cranio-orbital meningiomas after surgical treatment is 14–39% [52, 56, 58, 65], or 8–25%, according to other sources [19, 20]. The reason behind such a high frequency is the fact that total resection of the tumor in the area of the functioning anatomical structures of the orbit, in the cavernous sinus, and near the cranial nerves and blood vessels appears impossible. The infiltration by the tumor of the superior orbital fissure also often makes it impossible to perform a total resection of oculomotor nerves leaving their functioning intact [71]. Thus, a residual tumor in many patients remains after surgery to remedy cranio-orbital meningioma. According to P. Saeed et al. [59], total resection has been possible only in five (7.6%) out of 66 patients. Fifteen out of 61 patients with residual tumor underwent radiotherapy after surgery. A relapse was observed in 11 (17%) patients. The median time between the surgery and the recurrence was 46 months (10–108 months). The relapse in 4 patients was accompanied by a decrease in visual acuity and an increase in exophthalmos, while just a slight (<3 mm) rise in exophthalmos was observed in the other four patients. S. Oya et al. [52] reported on total tumor resection, near-total resection, and subtotal resection in 15, 20 (51.3%), and 4 (10.3%) out of 39 patients, respectively. A relapse was observed in 7 (17.9%) patients within 40.7 months (on average) after the surgery. Total resection of the tumor was performed by S. Honig et al. [26] in 10 out of 30 cases. Eight patients underwent a course of adjuvant radiotherapy. Another eight (26.7%) patients relapsed. In the study by U. Schick et al. [65], total resection of the tumor was performed in 42 (54.5%) patients. The remaining 35 (45.5%) patients underwent subtotal resection; tumor fragments were left in the orbit and the cavernous sinus in 8 and 12 cases, respectively. Infiltration of the superior orbital fissure and extensive infiltration of the skull base were observed in 12 and 3 patients, respectively. Nine patients underwent a course of adjuvant stereotactic conformal radiotherapy. Ten (13%) patients had a tumor relapse. P. Scarone et al. [64] performed total tumor resection (Simpson grade II) in 27 (90%) out of 30 cases. The remaining 3 patients underwent subtotal resection. The radicality of the resection was limited by the fact that the tumor had invaded the dura mater at the level of the superior orbital fissure, infiltrated the orbital tissues, and invaded the cavernous...
are of malignancy degree I according to the WHO classification, yet, data from the literature lead us to conclude that the majority of petroclival meningiomas (Grade I) [6]. Yet, data from the literature [13, 75] lead us to believe that the appropriateness of surgical intervention should be determined by the clinical manifestations of the disease in the patient, and it should be primarily directed towards optic nerve decompression (in the case of reduced vision) and the elimination of exophthalmos.

B. Sphenopetroclival Meningiomas

1. Sources of growth, histology, epidemiology

Sphenopetroclival meningiomas are meningiomas which locate in the area of the petroclival junction and exhibit parasellar and endosellar propagation [82]. Due to its rarity, this type of meningiomas is usually not classified separately but lumped with petroclival meningiomas.

Petroclival meningiomas, similar to the meningiomas of other areas, are observed in women and men at a ratio of 3:1 [32]. The average age of manifestation is the middle of the fourth decade [75]. The study by T. Kawase et al. [29] describes the results of treatment of 10 patients with sphenopetroclival meningiomas; the average age of the patients was 55 years; the male to female ratio was 1:4.

The published articles focused on surgical treatment of petroclival meningiomas usually indicate only the degree of malignancy of meningiomas according to the WHO classification, and rarely do they provide information on the prevalence of various histotypes. In the study by S. Nishimura et al. [50], meningotheliomatous meningioma was the most common histological type of meningioma in the clivus and top of the pyramid (16 cases). Fibroblastic, angiomatous (one with signs of atypia), and mixed types were also observed in 3, 2, and 3 cases, respectively. A. Spallone et al. [72] described fibroblastic, endotheliomatous, and transitional meningiomas in 12, 13, and 6 cases, respectively. According to the dissertation by V.N. Szymansky titled “Meningiomas of posterior skull base fossa: clinical presentation, diagnosis and surgical treatment,” all petroclival meningiomas (130 observations) belong to the group of benign meningiomas (Grade I) [6]. Yet, data from the literature [13, 75] lead us to conclude that the majority of petroclival meningiomas are of malignancy degree I according to the WHO classification, while anaplastic and atypical meningiomas occur in rare cases.

2. Clinical manifestations

These tumors are characterized by slow growth and may remain undetected for a long time. Sphenopetroclival meningioma in most patients manifests in headache, cerebellar disorders (69–87%), and dysfunction of cranial nerves (90–95%). Among other cranial nerves, the trigeminal nerve is the most commonly affected (43–68%); its damage manifests in facial hypoesthesia and weakness of the chewing muscles or trigeminal neuralgia, which in some cases occurs on the contralateral side. Vestibular-cochlear (31–75%) and the facial (11–67%) cranial nerves are also frequently affected. Bulbar symptoms appear under caudal growth or large tumor size. Bulbar disorders are observed in 7–38% of cases: they are less frequent in patients with dysfunction of oculomotor nerves (VI – in 11–77%; IV – in 14–26%; and III – in 11–38% of cases), despite the proximity and mandatory inclusion of these nerves in the tumor. Symptoms of cerebellar lesions caused by its compression are observed in 69–87% of cases. Most patients exhibit cerebellar dysfunction in the form of disturbance of statics and coordination and symptoms of increased intracranial pressure. Brain stem compression manifests itself in signs of impaired corticospinal tracts in the form of spastic paresis in 8–38% of patients (ipsilateral paresis results from the dislocation and compression of the opposite pedicle of the brain stem with the free edge of the tentorium or foramen magnum, or with contralateral paresis) and somatosensory disorders in 3–31% of patients. The impaired vision caused by lesions in the optic nerve is also observed (2–33%). Edema of the optic nerve disc (usually mild) is observed in most cases (77%). Nausea, vomiting, mental disorders caused by intracranial hypertension (which can result from the mass effect of the tumor), and obstructive hydrocephalus also appear in patients [13, 27, 36, 46, 67, 72]. Occlusive hydrocephalus, oral-brainstem symptoms, ipsilateral lesions of the cranial nerves develop early at the rostral location of the tumor, while cerebellar symptoms emerge later.

3. Surgical treatment

The aim of surgical intervention is to reduce the tumor size and eliminate the compression on the brain stem. Sphenopetroclival meningiomas are located deep in a field with a complex anatomy, surrounded by multiple important neural and vascular structures, and they have an infra- and supratentorial localization. These anatomical features make surgical treatment of these tumors very challenging. The orbitozygomatic approach can be used to remove sphenopetroclival meningiomas [61]. T. Kawase et al. [29] have proposed using the anterior transpetrosal-transtentorial approach, which consists in standard access to the middle cranial fossa in combination with resection of the anterior part of the pyramid.
The removal of sphenopetrosclival meningioma can also be performed in two steps using different combinations of the infra- and supratentorial approaches [60, 67]. Subocipital retrosigmoid and transpetrosal accesses are among the most widely employed ones in surgical access to these tumors [13, 21, 36, 46, 56, 62]; each one has its own advantages and disadvantages.

4. Results of surgical treatment

Complications

Despite the progress achieved in surgical techniques, the frequency of postoperative complications in the surgical treatment of petroclival meningiomas remains relatively high. First, there is the dysfunction of cranial nerves, which is transient in 41% of cases and resistant in 20–32% of cases. Second, dysfunction of cranial nerves of the oculomotor group was observed in 9–17% of patients [36, 45, 46, 67]. T. Kawase et al. [29] published the results of the surgical treatment of 10 patients with sphenopetrosclival meningiomas. The postoperative period was satisfactory in 8 patients; however, there was a case of liquorrhea requiring plastic surgery, and pneumocephalus. Five patients developed paresis, while dysfunction of the nerves of the oculomotor group, paresis of the facial nerve, and a new persistent neurological deficit emerged in 5, 1, and 8 cases, respectively.

The study by J. Yang et al. [81] provides data on the results of surgical treatment of 25 patients with large and giant petroclival meningiomas. Seventeen of them were characterized by parasellar spread. The postoperative complications included a new rise in neurological deficit (that existed before the surgery) in 16 (64%) patients; in particular, palsy of the oculomotor nerve; dysfunction of the trigeminal nerve, abducens paresis, bulbar paresis, transient aphasia, and hemiplegia in 11 (44%), 10 (40%), 8 (32%), 2 (8%), 5 (20%) and 5 (20%) patients, respectively. The hemiplegia was transient in 3 cases. Six (24%) patients exhibited the formation of subgaleal hematoma and intracranial hypertension resulting from excessive traction of the temporal lobe. Meningitis and transient liquorrhea developed in 3 (12%) and 1 patients, respectively.

In the surgical treatment of large petroclival meningiomas (> 3 cm in diameter), Yamakami I. et al. [80] observed the emergence of a new resistant dysfunction of cranial nerves in 7 (35%) out of 20 patients: the oculomotor, trochlear, abducens, and facial nerves in 2 (10%), 5 (25%), 2 (10%), and 3 (15%) patients, respectively. Other persistent neurological deficits occurred in 5 (25%) patients: the locked-in syndrome, cerebellar ataxia, and hemiparesis in 1, 1 and 3 patients, respectively. There was also a case of transient aphasia resulting from the venous infarction of the left temporal lobe, a case of liquorrhea requiring plastic surgery, and pneumonia in 1 patient.

V.N. Shymansky [6] notes that the Karnofsky index (KI) always drops after surgery in patients with PCM regardless of the radicality of tumor resection. An uncomplicated postoperative course was observed in 68 (52.3%) patients; there was no rise in the new neurological deficit before surgery. A complicated postoperative course was observed in 37 (28.5%) patients. The course of postoperative period was aggravated in 25 (19.2%) patients. The mortality of tumor removal amounted to 7 (5.39%) out of 130 cases. Relying on the group of complications, the development of hemiparesis in the early and late postoperative periods was observed in 6 (6.9%) and 2 (2.3%), cerebellar disorders in 0 and 1 (1.1%), bulbar disorders in 7 (7.9%) and 6 (6.7%), hearing loss in 14 (15.7%) and 13 (14.6%), paresis of the facial nerve in 30 (33.7%) and 12 (13.5%), destruction of the trigeminal nerve in 9 (10.1%) and 20 (22.5%), and oculomotor disorders in 15 (16.9%) and 3 (3.4%) cases, respectively.

H. Jung et al. [28] concluded that remnants of petroclival meningiomas grow slower than the original petroclival meningioma; 5-year absence of tumor progression was recorded in 60% of cases. Therefore, subtotal/partial resection is a more favorable strategy in the modern surgical approach to the treatment of petroclival meningiomas in elderly patients or in patients with tumoral infiltration of the cranial nerves, arteries, brain stem, and sphenoidal sinus.

5. Radical surgery/frequency of relapses

Relying on the experience of the Burdenko Neurosurgical Institute, V.N. Shymansky [6] noted that the onset of recurrence in a group with PCM after incomplete removal of the tumor occurs within 5 years on average. In 89 patients with petroclival meningiomas, total and subtotal/partial removal were possible in 6 (6.7%) and 16 (17.9%), respectively. The mortality of tumor resection was 7 (5.39%) out of 130 cases.

T. Kawase et al. [29] were able to perform radical resection of tumors in 7 out of 10 patients; such aggressive resection led to the emergence of a persistent neurological deficit in 80% of the patients. The tumor recurred after subtotal resection in one of 3 patients.

In the study by J. Yang et al [81], resection was also performed in 17 (68%) of 25 patients, and the frequency of neurological complications was likewise high (64%).

At the moment, the approach to the surgical treatment of sphenopetrosclival meningiomas has changed. There is a tendency towards an intentional reduction of the radicality of the resection in order to reduce the risk of neurological complications. Thus, I. Yamaki et al. [80] performed total resection in only 8 (40%) out of 20 patients with large petroclival meningiomas. MRI data showed continued tumor growth in just 3 (15%) patients; the interval between the resection and the tumor recurrence was 37–74 months. Subtotal/partial resection is more favorable in elderly patients or in patients with tumor infiltration of the cranial nerves, arteries, brain stem, and sphenoidal sinus.
C. Methods of adjuvant treatment of common meningoïmas of the skull base

1. Radiation therapy

Radiotherapy is the most important treatment option in patients with common meningoïmas of the skull base, including patients with OSPCM. Radiosurgery is employed when tumors are smaller than 30 mm in diameter. It remains an open question as to whether all patients with a residual tumor should undergo radiotherapy immediately after surgery, or only patients with an identified further growth should do so. Based on the results of long-term studies, it appears that irradiation allows to successfully manage the growth of subtotally removed meningoïmas [8, 22, 43, 76, 78]. Success in long-term (10–20 years) control over benign meningoïmas and atypical forms is 70–90% and 50–70%, respectively. The goal of radiation therapy is to prevent further growth of meningoïmas. As a rule, tumor shrinkage, a clinically stable disease, and improvement are observed after radiotherapy in 15–40%, 50–80%, and in about 30–40% of cases, respectively.

During irradiation of meningoïmas of the skull base, it is especially important to keep safe the anatomical structures that are sensitive to radiation (visual pathways, brain stem, eyeballs, lacrimal gland, and the pituitary gland), which may localize next to the tumor or inside of it. Due to high precision in the delivery of the radiation dose, conformity (compliance of the form of dose distribution to the shape of the tumor), the high dose gradient and the option of fractionation, modern methods of radiotherapy allow one to avoid damaging functionally important structures. With larger tumors and when functionally important organs are located inside the tumor, dividing the radiation treatment into steps can significantly reduce potential risks.

According to many experts [16, 31, 33, 42, 49, 54, 68], radiosurgery is the optimal method for the treatment of small meningoïmas. The doses can range from 12–16 Gy; the most often employed dose is 14 Gy [34, 47]. Radiosurgery [using a Gamma Knife unit or other devices based on the LINAC (linear accelerator LINear ALCerator)] has been proposed to treat tumors located farther than 1–2 mm away from the optic nerve and/or optic chiasm, with a volume of less than 14 cm³ (about 3 cm in diameter) [31, 42, 54, 83]. It has been reported that the probability of a 5- to 10-year control over the tumor growth rate using stereotactic radiosurgery is 90–95% [16, 42, 43, 49, 68]. Late complications, namely, neuropathy of the cranial nerves, are observed in 1–10% of patients. The rare late complications include pituitary insufficiency, radiation injury, and ischemic complications [16, 42, 43, 49, 68].

The use of fractionated irradiation is considered optimal in treating large meningoïmas and when functionally important organs are located inside the tumor [39, 70]. The irradiation mode of classical fractionation is commonly used. This means providing a fraction per day 5 days a week, with a fraction value of 1.6–2.5 Gy to achieve an effective dose of 50–54 Gy. The irradiation mode of hypofractionation is less frequently employed: the dose per fraction is increased up to 3–8 Gy, and the total number of fractions is usually 2–7. The mode is best used between the standard fractionation and radiosurgery. Unfortunately, only a few published works have been devoted to the latter procedure, and there is a lack of studies on the irradiation of OSPCM. For this reason, data on irradiation in the classical mode of fractionation will be provided further.

Irradiation of meningoïma in the conventional mode of fractionation allows one to exert control over tumor growth in 92–100% of the cases [15, 17, 35, 40, 68]. As this takes place, a decrease in tumor size is observed in 14–53% of cases [15, 25, 53, 68]. The wide scattering of the frequency of tumor reduction is associated with the difference in the criteria for determining the tumor response. Although the main goal of the treatment is to exert control over the growth of the tumor, irradiation allows one to achieve clinical improvement in 20–71% of cases [15, 17, 35, 40, 68]. As this takes place, irradiation using the mode of standard fractionation is associated with a small frequency (0–17%) of persistent complications [15, 17, 35, 40, 68]. These include neuropathies of cranial nerves, swelling of the brain matter and radiation necrosis, hypothalamic-pituitary disorders, ischemic complications resulting from the damage done to the internal carotid artery and its branches, as well as minimal likelihood of developing secondary tumors.

A fractionated dose of irradiation can be delivered to a target using the stereotactic method, which allows more precise immobilization and a three-dimensional coordinate system for better limitation of the tumor and reduction of preset errors. There exist many commercial systems that enable delivery of a fractionated stereotactic radiation dose with a 2- to 5-mm expansion of GTV (gross tumor volume) with relation to the PTV (planning tumor volume). Several studies have demonstrated an excellent local control rate of growth (90–100%) with a minimal risk of late complications [7, 10, 15, 41]. Although the risk of neurocognitive decline caused by the standard procedure of irradiation is considered low, the use of the stereotactic method can further reduce this risk [7, 10, 15, 41]. The data presented above refer to the more common photon irradiation. Irradiation with a flux of particles is also used for meningoïmas, and it has its own advantages. Because of the ability of the particle flux to release the bulk of its energy into a strictly defined area (Bragg peak), the load on normal tissues is significantly reduced as compared with photon irradiation [14, 69]. The biological effect of the use of protons and neutrons may be greater than that from the use of photon irra-
diation. Proton therapy has been used very success-
fully in skull base meningiomas, with satisfactory con-
trol over growth and minimum toxicity to the body
being its hallmarks [24, 51, 77, 79]. Difficulty consists
in the fact that the equipment for producing the proton
beam requires considerable space. The cost of irradiation
therewith becomes almost prohibitive. Radiotherapy
and radiosurgery, along with microsurgical removal,
are an important step in the treatment of skull base
meningiomas and allow one to exert control over tumor
growth in 92–100 and 91–100% of cases. This is done
with a low rate of complications in 0–17 and 0–10.5%
of cases, respectively [15, 17, 34, 35, 40, 48, 54, 68,
73]. Irradiation also leads to clinical improvement in
20–71% of patients with radiosurgery and 25–66% of
cases after radiosurgery.

2. Drug therapy

OSPCM are prone to continued growth, primarily
due to the infiltrative nature of their growth. We have
studied numerous publications focused on attempts to
treat common, medically recurrent meningiomas of
varying degrees of malignancy. Unfortunately, from the
standpoint of evidence-based medicine, there have been
no results allowing the effective use of one or another
drug in clinical practice. There have been attempts to
use cytostatics, inhibitors of sex hormones, blockers of
the receptors of somatotropin and insulin-like growth
factor 1, hydroxyurea, calcium channel blockers, inter-
feron-alpha, erlotinib and gefitinib, imatinib, Avastin
(bevacizumab), and inhibitors of cyclooxygenase-2
(celecoxib). The photodynamic therapy appears to show
promise, with the use of 5-minolevulinic acid, but the
problem has yet to be studied.

Conclusion

Thus, the progress achieved through neurosurgical
techniques, the use of modern approaches in conjunc-
tion with endoscopy and neuronavigation, the achieve-
ments of neuroanesthesiology and resuscitation, and
the widespread use of adjuvant therapies (stereotactic
radiosurgery and radiotherapy), certainly have recently
significantly improved results in the treatment of
patients with advanced craniofacial meningiomas and
led to an increase in the average survival rate. Develop-
ning an optimum treatment requires a careful analysis
of the results of the treatment, which would include the
assessment of the overall and disease-free survival
rate for the whole group and for different histological
types of tumors, and assessment of the neurological,
psychological status of patients in the delayed period.
A proper assessment of tumor spreading patterns is
highly important for the determination of a treatment
strategy.

Because of the increase in the follow-up period, the
evaluation of the quality of life and social adaptation of
patients becomes an important task. However, there are
obvious difficulties associated with treating this group
of patients. Thus, the desire to maximize radical re-
moval of the tumor is accompanied by a high risk of
postoperative complications in the form of a persistent
neurological deficit and disability, or even death of the
patient. Performing subtotal resection allows one to re-
duce the risk of complications, but it increases the re-
lapse frequency.

Radiosurgery or radiotherapy of residual tumors
exhibit a high degree of control over tumor growth,
accompanied by a risk of post-radiation reactions with
damage to critical parts of the brain. A study of the
potential of chemotherapy, growth inhibitors, and hor-
monal agents regarding benign meningiomas is under-
way, but in reviewing evidence-based medicine, en-
couraging results have yet to appear. Many studies have
evaluated the outcome of therapy for patients with
meningioma of varying degrees of malignancy who
underwent different treatments. However, while the
criterion for potential efficacy of a drug for benign
meningiomas can be an improvement in progression-
free survival for 6 months for more than 50% of cases,
the criterion for the more malignant meningiomas
remains uncertain [23]. The use of effective methods
of chemotherapy or a combination of chemotherapy/
radiation is complicated due to lack of understanding
of the signaling pathways affecting the growth of me-
nangioma, the apoptosis of tumor cells, and intraos-
seous invasion. Thus, the problem of common crani-
ofacial infiltrative meningiomas is usually associated
with studying molecular oncobiology in comparison
with pathomorphological and clinical data, and elab-
orating additional methods for treating meningiomas,
which are not amenable to surgical treatment and radi-
otherapy.

On this basis, treatment of a group of patients with
tumors of predominantly orbitosphenopetrocelival
localization that had formed for decades and who were
initially treated with non-radical surgery methods is a
challenge, even for the most advanced neurosurgical
centers. Rather high rates of postoperative mortality and
complications still remain. In such a context, in patients
with a long history and significant tumor spread it
would be reasonable to use a combination of all avail-
able methods, as well as palliative surgery to preserve
vital functions (saving vision, providing the nasal
breathing, mouth opening, preventing intracranial hy-
pertension, and pain relief). The rational and consistent
use of all possible methods and a “sensible” approach
to the patient could allow one to preserve and extend
his life, with better social adaptation and higher quali-
ty of life. A careful analysis of retrospective and pro-
spective groups of patients with OSPCM may allow one
to determine the clues for each method of treatment at
a certain stage of the disease and, therefore, makes such
a study as ours relevant.
Surgery of tumors of the skull base propagating to the orbit


Posterior fossa

Roberti F., Sekhar L.N., Kalavakonda C., Wright D.C.


Long-term results with ex-

Scarone P., Léclerq D., Heran F., Robert G.
orbital meningiomas: interdisciplinary surgical approach, resectability and

Experience with 36 sugical cases of petroclival

Samii М., Tatagiba M.

Neurosurg Rev 2011; 34: 171—179.


Intensity modulated radiosurgery (IMRT) for recurrent, residual, or untreated skullbase meningiomas: pre-


Pomerantz S., Umanovsky F., Elidan J., Ashkenazi E., Valarezo A., Shalit M.


Saeed P., van Furth W.R., Tanck M., Kooremans F., Freling N., van der Sprenkel J.W., Stal


Wara W.M., Shenile G.E., Newman H. et al. Radiation therapy of meningi-

Weber D.C., Lomas A.J., Rutz H.P. et al. Spot-scanning proton radiation therapy for recurrent, residual or untreated intracranial meningiomas. Ra-

Yamakami I., Higuchi Y., Horiguchi K., Saeki N.


Von H.R., Raggam P., Dornhoffer M., Sahlit M.


Zachenhofer I., Wolfsberger S., Aichholzer M. et al.


Shrieve D.C., Hazzard L., Boucher K., Jensen R.L. Dose fractionation in ste- reotactic radiotherapy for parasellar meningiomas: radiobiological consider-


Spallone A., Makhmudov U.B., Makhamedjanov D.J., Tcherekajev V.A. Petro-


Stafford S.L., Pollock B.E., Leoritt J.A. et al. A study on the radiation toler-


Taylor B.W.J., Marcus R.B.J., Friedman W.A. et al. The meningioma contro-


Pomerantz S., Umanovsky F., Elidan J., Ashkenazi E., Valarezo A., Shalit M.


Resection of large petroclival menin-

Surgical treatment of sphenoorbital menin-


Saeed P., van Furth W.R., Tancz M., Kooremans F., Freing N., Streek-

stra G.I., Regensburg N.I., van der Sprenkel J.W.B., Peerdeman S.M., van Overbeeke J.J., Mourits M.P. Natural history of sphen-o orbital meningi-

Samii M., Gerganov V., Giordano M., Samii A. Two step approach for surgical 


Samii M., Tatagiba M., Carvalho G.A. Resection of large petroclival menin-

Sandalciovlu I.E., Gasser T., Mohr C., Stolke D., Wiedenhammer H. Spheno-

Scaroni P., LeClerq D., Heran F., Robert G. Long-term results with ex-

ophthalmos in a surgical series of 30 sphenoorbital meningiomas. J Neuro-
surg 2009; 111: 1069—1077.

Schick U. Sphenoorbitale Meningeome. Ergebnisse der Langzeitbehand-
lung. HNO 2010; 58: 37—43.
Topics to be covered in our next issue:

- Radiosurgery of metastatic renal cell cancer to the brain
- Injury of the internal carotid artery caused by endoscopic resection of pituitary adenomas
- Anesthesiological management in transnasal surgery