Transsphenoidal Surgery of Craniopharyngiomas: from Palliative Surgeries to Radical Removal

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The fundamental principles of transsphenoidal surgery of craniopharyngiomas are presented. The stages of development of the methodology of these surgeries at the Burdenko Neurosurgical Institute, from palliative surgeries to the modern high technology radical removal through the anterior extended approach have been described. Additional stereotactic irradiation ensures secure control of the disease during a long time. The paper basically provides the description of the surgical procedure and the preliminary analysis of the findings, which demonstrate efficacy and safeness of the endoscopic removal of craniopharyngiomas.

Keywords: *craniopharyngioma, endoscopy, transsphenoidal surgery, anterior extended approach, stereotactic radiotherapy.*

The Burdenko Neurosurgical Institute is the center where a large number of patients with hard-to-reach tumors (including craniopharyngiomas) have been admitted to since the Soviet period.

The first surgeries (cyst punctures, complete or partial tumor resection) were performed by A. A. Arendt and his colleagues before and during the era of microsurgery [1]. The microsurgical removal of craniopharyngiomas was launched to practice at the Institute in 1971.

Craniopharyngiomas are benign epithelial tumors that develop from remnants of cells in Rathke's pouch connecting the primary oral cavity to the pituitary gland in the embryonic period. It has also been suggested that craniopharyngiomas may develop as a result of metaplasia of epithelial cells in the chiasma–sellar area. Tumors can be formed anywhere in the projection of remnants of the craniopharyngeal duct. Tumors most commonly develop along the infundibular stalk from sella turcica to the hypothalamus, but may also localize in the nasopharynx, sphenoid, or intraventricularly [7, 10, 12–15].

Craniopharyngiomas most frequently manifest in two age groups: in children 5–14 years old (5.6–13% of intracranial tumors) and in adults aged 50–74 years (2–5%) [8, 16, 17].

By their nature, craniopharyngiomas are histologically benign epithelial tumors; however, they recur in 30% of cases within 10 years after total resection [11].

Adamantinomatous (adamantinomas) and papillary craniopharyngiomas are the two main histological types of craniopharyngiomas. In essence, these tumor types differ both histologically and by radiological presentation.

Only 10% of craniopharyngiomas have a completely solid structure, while remaining 90% of this kind of tumors produce cysts of various sizes. Cyst formation is the dominating property in 60% of craniopharyngiomas [6].

Classification

There are different classifications of craniopharyngiomas which are based on the relationships between tumor and the chiasm/sella turcica.

The specialists of the Burdenko Neurosurgical Institute employ their own classification, originally proposed by V.V. Grekhov [2] and then developed by J. Steno [18]. This classification has experienced some changes. In accordance with this, craniopharyngiomas may be classified under three topographical variants:

1) endo- and endosuprasellar craniopharyngiomas originating from the sella turcica;

2) stalk craniopharyngiomas developing at the level of the pituitary stalk and growing suprasellarly in different directions;

3) intra-extraventricular (relative to the third ventricle) tumors developing at the level of the pituitary gland infundibulum and extending into the third ventricular cavity, as well as growing extraventricularly into the chiasmatic and interpeduncular cisterns.

In addition, we identify a group of craniopharyngiomas that develop extra-axially without a clear link with the pituitary stalk. These tumors occur primarily in young children and often form giant cysts. They localize in the chiasmal region and in the middle cranial fossa, are often distributed in the posterior cranial fossa, and can penetrate into the lateral and third brain ventricles by displacing the brain structures.

Surgical management is the main treatment for craniopharyngiomas, and it is desirable to seek a radical re-

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moval of the tumor. Various methods of palliative treatment (evacuation of cysts, partial removal, bypass surgeries) in most situations provide only temporary improvement of the patient's condition.

Intracranial surgery via different (both transsphenoidal and transcranial) surgical approaches remains the main treatment procedure for suprasellar craniopharyngiomas. According to our experience, we believe that the combination of the transcranial approach with one of the transsphenoidal ones (pterional or subfrontal) is the most reasonable method for managing craniopharyngiomas spreading into the third ventricle.

Since 1987, craniopharyngiomas located in the sella turcica and partly outside it have been removed microsurgically through the transsphenoidal approach. Since 2005, these tumors have been resected endoscopically. However, over the past few years the active development of transnasal endoscopic surgery has been observed. Application of extended endoscopic approaches made it possible to completely remove both endosellar craniopharyngiomas and the tumors that initially grow suprasellarly (including craniopharyngiomas spreading into the third ventricle). This allows one to minimize the traction on the optic nerves and the hypothalamic structures.

Doses and regimens of stereotactic irradiation, which is increasingly used in craniopharyngioma treatment, still require clarification.

Materials and Methods

Over the past decade, 100–120 patients with craniopharyngiomas seeking for surgical treatment are annually admitted to the Burdenko Neurosurgical Institute.

The total number of surgeries (including reoperations) exceeds 2,500; about 1,500 surgeries have been performed by A.N. Konovalov. A partial analysis of the clinical experience of the Institute in treatment of craniopharyngiomas was carried out by Zh.B. Semenova in 2000 [5].

Since 2006, all transnasal surgeries in our hospital have been performed only using an endoscope. From that time until the end of 2012, transnasal operations were performed in 240 (32.9%) of 730 patients surgically treated for craniopharyngioma. The tumor resection the extended anterior approach was performed in 61 cases (25.4%). As the methodology is mastered and the analysis of the first findings has confirmed its effectiveness, transsphenoidal endoscopic removal of craniopharyngiomas was employed more often **(Fig. 1)**.

Development stages of transnasal removal of craniopharyngiomas

For a long time we used the transsphenoidal approach for **intracapsular removal only of the tumors** with the initial intracellar growth. In doing so, the endoscopic method was employed for partial removal of the tumor and draining of cysts in craniopharyngiomas with the initial intrasellar growth (endosellar and endosuprasellar craniopharyngiomas according to the classification developed at the Burdenko Neurosurgical Institute). The pituitary gland and pituitary stalk during intrasellar tumor formation move backwards and upwards. The cyst capsule lines up the walls of the enlarged sella turcica, and, under conditions of suprasellar spreading, displaces the sellar diaphragm upwards and merges with it **(Fig. 2)**.

Two methods of surgical removal of this anatomical variant of craniopharyngiomas are possible:

1. A complete removal of tumor and cyst drainage. The partial removal of the tumor cyst wall (subdiaphragmally) is also possible.

2. The radical removal of tumor along with the cyst wall (including its top merged with the sellar diaphragm).

The first option of endoscopic removal of endosellar and endosuprasellar craniopharyngiomas has been used by us over many years.

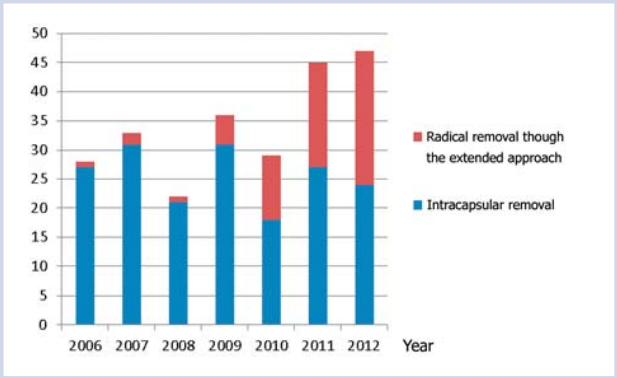


***Fig. 1*. The dynamics of application of the transnasal approach.**

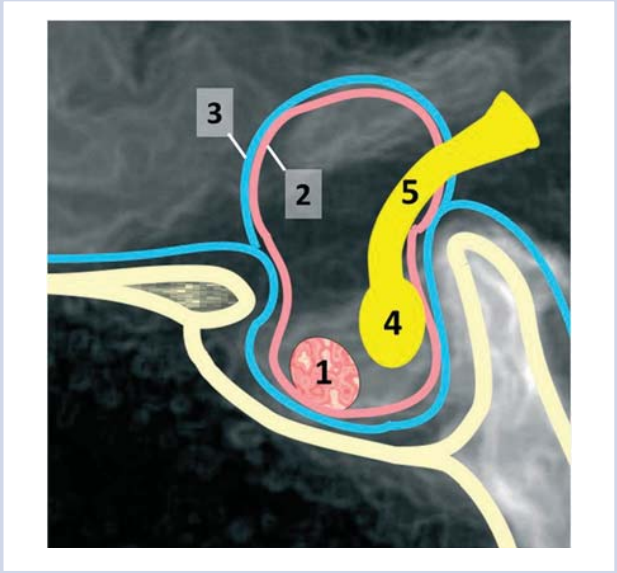
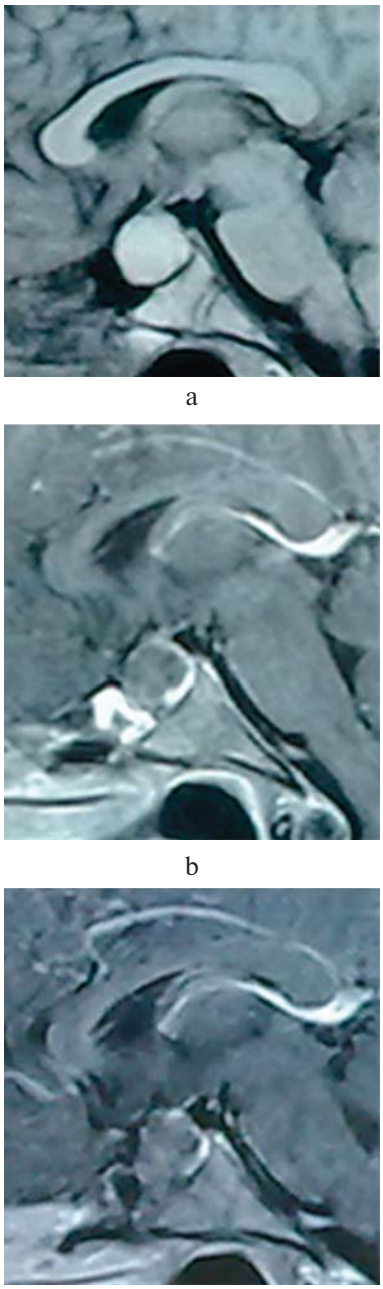


***Fig. 2*. The scheme of anatomical relationships between endosuprasellar craniopharyngioma, sella turcica, pituitary gland, and pituary stalk.**

1 – solid part of craniopharyngioma; 2 – craniopharyngioma cyst capsule; 3 – the raised sellar diaphragm; 4 – the pituitary gland; 5 – pituitary stalk.



a

b

c

***Fig. 3*. Example of stable craniopharyngioma after transnasal evacuation.**

a — MRI performed before transnasal surgery; b — MRI performed within 1.5 years after the transnasal surgery. The cyst size does not exceed the preoperative values; c — MRI performed within 2.5 years after transnasal surgery. Cyst dimensions in the dynamics have not changed.

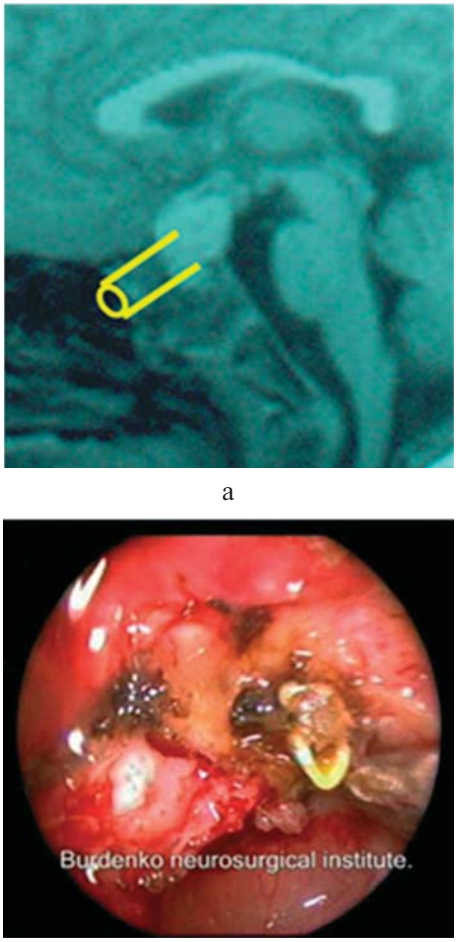


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***Fig. 4*. Transnasal drainage of cystic craniopharyngioma.**

a – a scheme of setting the drainage tube in craniopharyngioma cysts; b – intraoperative image: the scar tissue in the lumen of the drainage tube.

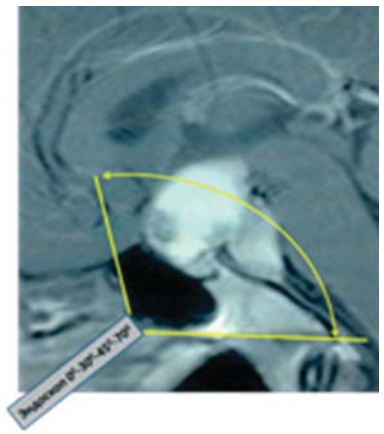
In the case of the absence of intraoperative liquorrhea, we left the tumor cyst bottom open in the surgery end to allow its contents to flow away into the sphenoidal sinus. Unfortunately, these surgeries provided only a short-tem effect, since the cyst walls fixed with different speeds the artificial defect provided by a surgeon. **Fig. 3** shows the rare observation: no reaccumulation was observed during 2.5 years after the transnasal opening of the craniopharyngioma walls.

The reaccumulation (closure) of tumor cavities is the most often observed outcome.

The attempts **to install drains in the cyst cavity** during transnasal surgeries were ineffective. After some time, the drain tube was completely incorporated into the dense scar tissue **(Fig. 4)**.

The radical surgery, in which the tumor capsule is completely removed, remains the only effective treatment method.

The radical removal of craniopharyngioma through **transnasal endoscopic** surgeries has become possible due to the improved visualization of the operating field and panoramic view allowing the complete inspection of all tumor parts **(Fig. 5)**. If the tumor capsule could be segregated from the dura mater of the sellar walls and diaphragm, the removal of **endosellar** craniopharyngiomas is not difficult. Every so often, the pituitary stalk and pi-



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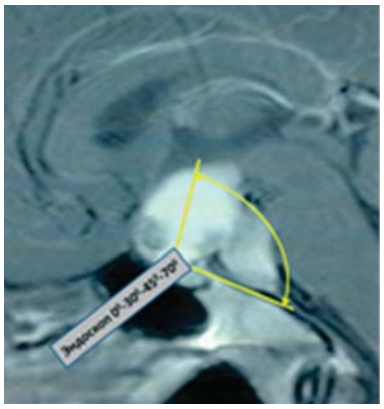

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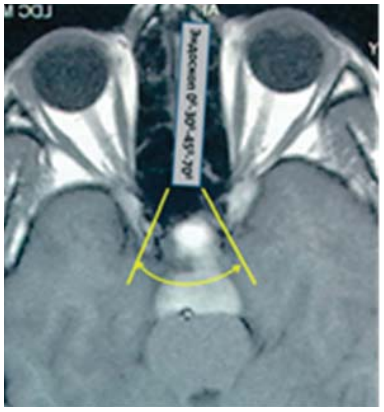

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***Fig. 5*. Accessibility zones of craniopharyngioma for endoscopic transnasal removal.**

a – the accessibility of the tumor in the sagittal plane via the extended approach; b – the example of possible removal of the tumor located on clivus without resection of dorsum sellae and clivus; c – the accessibility of tumor in the axial plane.

tuitary gland itself remain intact and are not functionally affected during such surgeries. A defect in the remnants of the sellar diaphragm is typically formed in patients who had undergone this surgery; however, it is usually small and can be easily fixed using plasty.

Owing to the introduction of extended approaches to the practice (in particular, the anterior one), the radical removal of **suprasellar** craniopharyngiomas localized on the pituitary stalk and infundibulum (intra-extraventricular craniopharyngiomas) has become completely possible [3]. Resection of the anterior wall of the sella turcica and the posterior regions of planum sphenoidale may provide a good panoramic view of the chiasmal region. Tumors available for the removal in this case are the ones localized from the middle of planum sphenoidale to the C1 vertebra, between the two carotid arteries, and spreading into the third ventricular cavity until the foramina of Monro. The launch of using the extended approaches showed that multiple small arterial vessels supplying the basal parts of the chiasm and diencephalic region, can be saved in most cases.

Most retrochiasmal craniopharyngiomas are available for transnasal removal. Due to this fact, the technique has recently become the "method of choice." Besides, it has become clear that in most cases, these tumors are formed from both the pituitary stalk (often its upper third) and the infundibular area **(Fig. 6)**. Pituitary stalk or its remnants had to be completely cut to ensure tumor mobilization and completely remove it in almost all of these observations.

Both conventional and modified tools from the endoscopy kit were employed to remove craniopharyngiomas.

The tumor capsule was separated from the basal parts of the chiasm and the third ventricle floor using suction devices, microdissectors, wire cutters with significant bending angles and a significant length of the working parts, as well as microscissors of different shape.

Two surgeons should very often work together: one pulls the tumor capsule with forceps, while the other one gradually separates the capsule from brain structures and blood vessels using various dissectors and curette. Destruction of the petrifaction products with various density and removal of solid tumor fragments in most cases are not possible without using an ultrasonic destructor. We use the device equipped with a long thin tip and supplied with a set of protective tips (manufactured by Soring).

Postoperative intellectual and endocrine disorders are rare and appear to be less pronounced in patients subjected to careful separation of the tumor from the remnants of the third ventricle floor. Thirty of 56 patients of the series had no pituitary failure prior to the radical tumor removal through the extended endoscopic approach. After the tumor resection, this disorder appeared in 19 of 30 patients (63.3%). Korsakoff syndrome signs, initially found in 7 patients (12.5%), regressed in 6 (85.7%) of them. The high-detail surgical field provided by endoscopy allows one to clearly see the "glial" capsule of craniopharyngioma (the area where the tumor capsule passes into the medullary substance without visible boundaries) and to separate the capsule from the medullary substance **(Fig. 7)**. Moreover, in most cases it is possible to save most of the thinnest blood vessels that provide blood flow to the

basal surface of the optic chiasm, the third ventricle floor, infundibulum, and pituitary stalk. In most cases it is possible to separate the blood vessels from the tumor without the use of coagulation **(Fig. 8)**. The optic nerves and chiasm in such surgeries do not experience serious traction, and visual impairment is transitory in most cases. The vision loss was observed only in 6 of 56 patients (12.8%). 47 patients (83.9%) had visual impairment; the improvement occurred in 27 of them (57.5%).

The craniopharyngioma capsule could be totally resected not in all cases. In our series the radical removal of the tumor was achieved in 39 patients (69.6%), while the remaining 17 patients (30.4%) underwent subtotal removal.

Thinning of the capsule to the state of a thin arachnoid-like film in a number of cases makes its separation from the chiasmal area structures impossible. This creates preconditions for tumor recurrence and determines the indications for stereotactic irradiation **(Figs. 9, 10)**.

The need to remove tumors of different shape, size and density of petrificates is another individual problem of craniopharyngioma resection. Small and large "loose" petrificates could be usually removed completely; an ultrasonic destructor is often used for this purpose. However, because of the propagation features of sound waves, the ultrasonic destructor with curved working part is still not available. It makes the removal of dense tumor fragments located outside the direct field of view extremely difficult. In two cases, we managed to remove the large staghorn-like ossification by neither defragmentation nor ultrasonic degradation because they tightly merged with the chiasmal region.

The increased requirements for hemostasis during the surgery are associated with the removal of the tumor

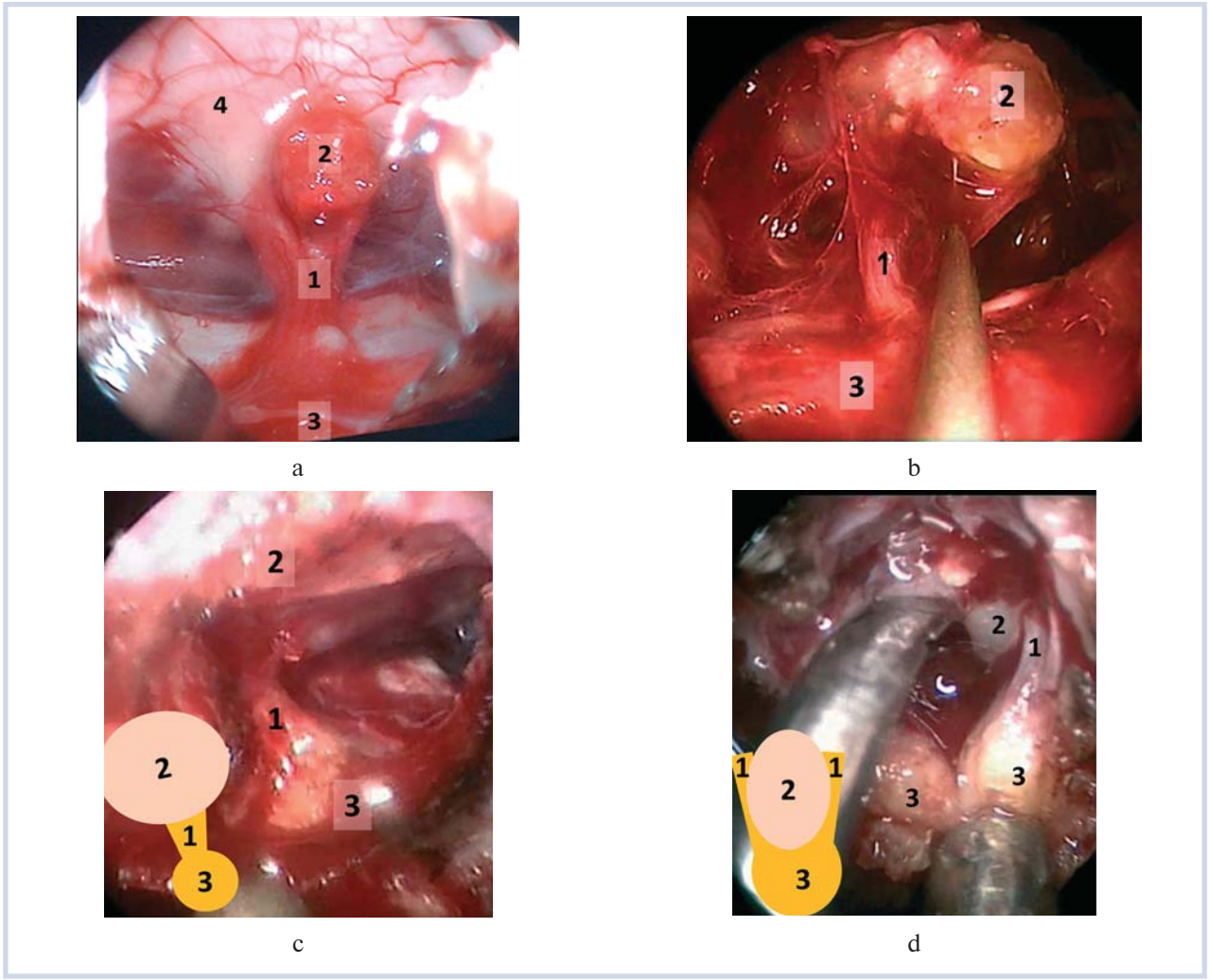


***Fig. 6*. Various possible ratios of pituitary stalk and tumor.**

a – Case 1. Craniopharyngioma (2) adjacent to the pituitary stalk (1) and not destroying it. The pituitary gland (3) is intact; b – Case 2. Craniopharyngioma (2) was formed in the hypothalamus infundibulum. The pituitary stalk (1) is shortened, but retained. The pituitary gland (3) is intact; c – Case 3. Craniopharyngioma (2) was formed in the hypothalamus infundibulum and the proximal parts of the pituitary stalk (1), which is visualized, but sharply reduced. The pituitary gland (3) is intact; d – Case 4. Craniopharyngioma was formed in the pituitary stalk. Tumor (2) localized directly above the pituitary gland (3) and was surrounded by a thin layer of the pituitary stalk tissue (1).

from the suprasellar space and from the ventricular system. SurgiFlow drug was used to stop and prevent bleeding from small capillaries. The hemostatic gauze pads Surgicel and Sergicel fibrilar were used to stop bleeding from a small-caliber arteries and veins. TachoComb drug was actively applied to fix the defects of large vessels and strengthen their walls.

Unfortunately, no "convenient" (simultaneously delicate and strong) bipolar coagulation instruments are available at the moment. We need to use both kinds (straight and curved in different directions) of monopolar coagulation suctions.

Reliable plasty of the major defects of the skull base during the radical transnasal surgery is of particular importance for preventing postoperative nasal liquorrhea. We used various adhesives and hemostatic materials, lumbar drainage, autotissues (in particular, autotissues with preserved blood supply) for the same purpose [4]. Currently, we believe that the use of different combinations of these materials for formation of the so-called "sandwich" is the best version of "multilayer" plastic surgery.

The walls of drained cyst or unremoved tumor fragments were exposed to stereotactic irradiation. Depending on tumor size and localization, three irradiation modes were used:

— stereotactic radiosurgery at 10—15 Gy (a total focal dose, TFD);

— stereotactic radiotherapy in hypofractionation mode at 5 Gy (a single focal dose, SFD) to 25 Gy (TFD);

— stereotactic radiotherapy in the standard fractionation mode at 1.8—2 Gy (SFD) and 50—54 Gy (TFD).

Stereotactic irradiation was very effective in craniopharyngioma treatment. 120 patients have undergone stereotactic irradiation at the Burdenko Neurosurgical Institute since 2005. The catamnestic data are currently known for 80 of them (66.7). A significant reduction of tumor size was detected in 22 (27.5%) patients. The tumor remained stable in 42 (52.5%) patients. Only 18 (22.5%) patients had tumor progression.

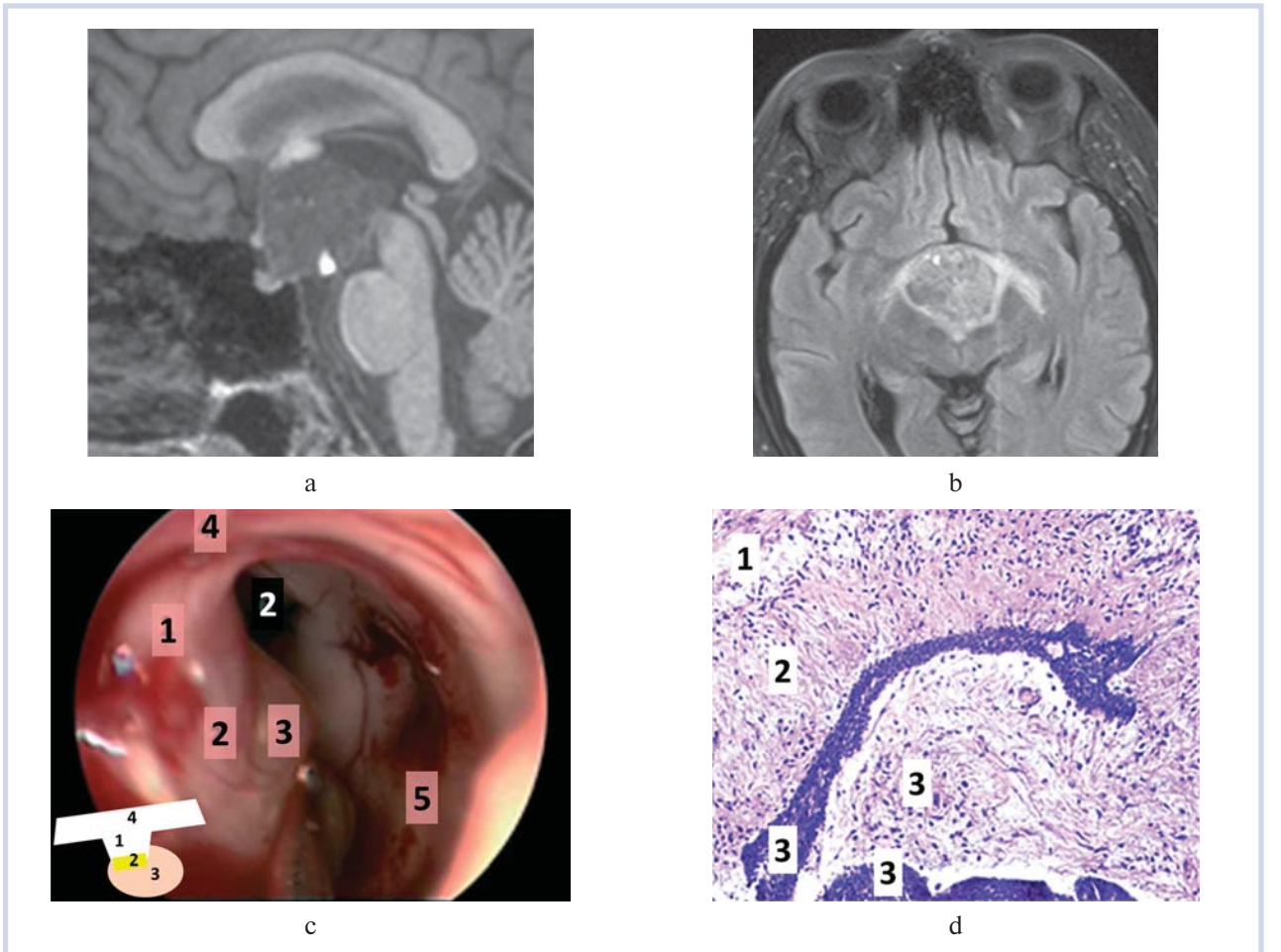


***Fig. 7*. Identification of infiltration of diencephalic structures.**

a, b – MRI performed before surgery; c – intraoperative photos: 1 – medulla of basal surface of the optic chiasm, 2 – "glial" capsule, 3 – tumor capsule, 4 — the anterior edge of the optic chiasm, 5 – a side wall of the third ventricle with single petechial hemorrhages after the tumor capsule had been separated; d – a histological specimen of "glial" capsule (zone 2 in Fig. 7c): 1 – medulla, 2 – "glial" capsule, 3 – tumor tissue.

Discussion

Improvement of endoscopic techniques in recent years has allowed one to significantly change the surgical outcomes. Craniopharyngiomas spread beyond the sella turcica became available for transnasal removal. The resection procedure employs the same general principles of transcranial microsurgery: dissection of the tumor and brain structures, micropreparation of the vessels surrounding the tumor, and resection using an ultrasonic disintegrator. An almost complete lack of rough traction of visual pathways and structures in the diencephalic area is a distinctive feature of the described surgery, which significantly improves the functional out-

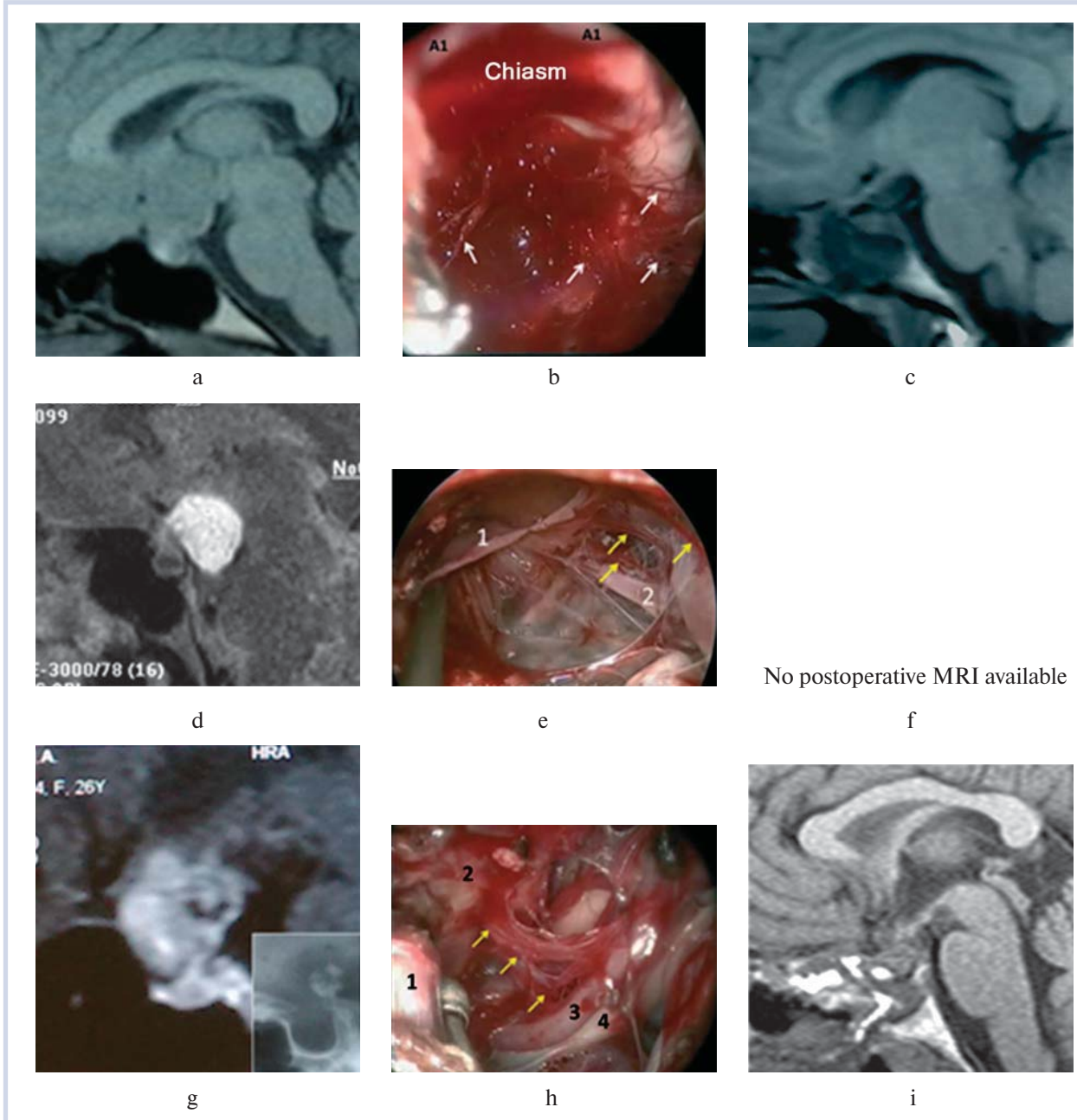


***Fig. 8*. Possibility to maintain blood supply in the diencephalic region at transsphenoidal endoscopic removal of craniopharyngioma.**

a–b – Case 1: a – MRI performed before surgery; b – intraoperative image. Arrows indicate the numerous saved arterial vessels supplying the basal surface of the optic chiasm and diencephalic region; c – MRI (control) performed within 4 months after the tumor removal. d–f – case 2: d – MRI performed before surgery; e – intraoperative image. The saved arterial vessels in the arachnoid membrane supplying the basal surface of the optic chiasm and the diencephalic region are indicated with arrows. 1 – tool-detachable tumor capsule; 2 – posterior communicating artery; f – no MRI obtained after surgery. g—i – case 3: g — MRI performed before surgery. The heterogeneity area in the tumor's posterior region is a petrifaction site; h – intraoperative image. The saved arterial vessels supplying the diencephalic region are indicated with arrows (2). 1 – tumor; 3 – the left posterior communicating artery; 4 – the left oculomotor nerve; i — MRI (control) performed within 4 months after the tumor had been removed.

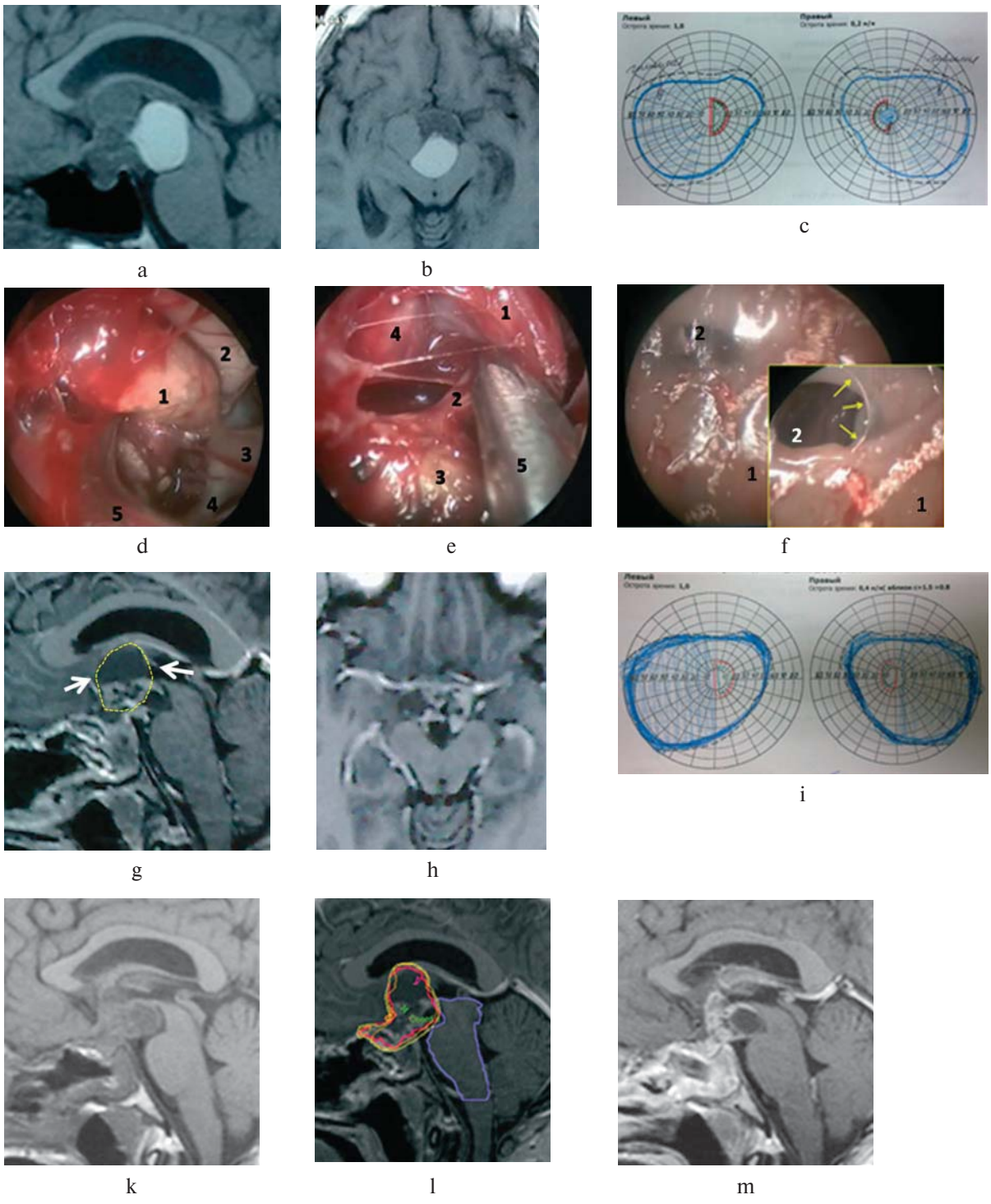
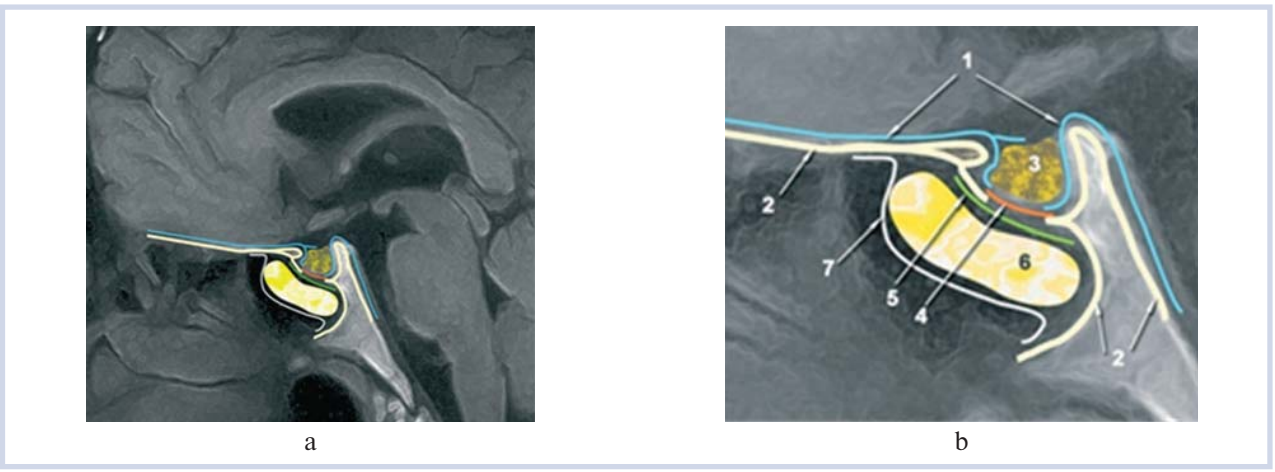


***Fig. 9*. An example of subtotal removal of craniopharyngioma followed by radiation therapy in the area of the remaining cyst capsule.**

a, b – MRI performed before surgery. Craniopharyngioma is a heterogeneous structure with combination of solid and cystic components; c – scheme of visual fields before surgery. The chiasmatic syndrome is presented with bitemporal hemianopsia and the central scotoma on the left; d — intraoperative image. The step of separating the solid portion of the tumor (1) from the basal surface of the left optic nerve (2), the left posterior communicating artery (3), and the left oculomotor nerve (4). Traction was performed with a curved suction (5); e — intraoperative image. The step of separating the solid portion of the tumor (1) from the basal surface of the optic chiasm (4) using the tool (5). The pituitary stalk (2) reaching the upper pole of the pituitary gland (3) was detected during the tumor traction; f — intraoperative image. Posterior portions of the tumor were presented with the cyst (1), its wall resembles a thin translucent film and could not be separated. The large image – the cyst capsule before opening. The small image – the cyst capsule is opened (the capsule edge is indicated with arrows), this allows one to see the third ventricular cavity (2); g, h — MRI (control) performed within 3 months after surgery. The remnants of the tumor and its capsule are shown with arrows and yellow dotted contour; i — the scheme of visiual fields after the tumor removal. Bitemporal hemianopsia still persists. Central scotoma OS regressed; k — MRI performed before irradiation; l — the scheme of distribution of dose curves after irradiation with the Novalis machine; m — MRI (control) performed within 3 months after irradiation. The cyst size decreased slightly, its capsule is clearly thickened.



a b

***Fig. 10*. Scheme of multilayer "sandwich" plasty (see explanation in the text).**

1 – dura; 2 — skull bone base; 3 – fibrin sponge TachoComb; 4 – fascia fragment, 5 – bone fragment; 6 – autologous adipose tissue; 7 – adhesive composition.

come of the surgery and reduces the risk of severe diencephalic lesions.

As mentioned earlier, the craniopharyngioma capsule removal fails in some cases, thus creating preconditions for a relapse. The clinical data obtained at the Burdenko Neurosurgical Institute was analyzed by Zh.B. Semenova in 2000. A high degree of recurrence of craniopharyngiomas, primarily adamantinomas, as well as its dependence on the radicality of tumor removal and biological activity of the tumor, was revealed. On the average, the tumor relapsed in 21.5% of patients after subtotal and total removal, and in 53.2% of patients after partial resection. The relapse rate of papillomatous craniopharyngiomas was 7.8% [5]. Similar data were obtained in many series of observations and primarily in the generalized experience of French neurosurgeons M. Choux and G. Lena [9].

Infiltrative tumor growth and its spread are the main reasons for non-radical removal. Biological activity of the tumor is an important factor in tumor recurrence.

The significance of various markers of tumor growth (Tenascin, KI-S1, PCNALI, Ki-67, CerebB2, p53, EGFR) was investigated in a large series of observations conducted at the institute. The level of Ki-67 in the tumor was the only factor significant for craniopharyngioma recurrence.

Conclusion

What can be expected in the development of this problem in the future? First of all, it is further improvement of the transsphenoidal approach and its wider application for craniopharyngiomas of different localization. Obviously, the refinement and optimization of the irradiation modes will allow one to reduce the recurrence rate of these tumors at their non-radical removal. Generalization of the existing fragmentary data on craniopharyngioma morphology by studying the large groups of patients, potentially in multicenter studies, will allow one to identify new, more significant, criteria of tumor aggressiveness.

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Commentary

This study prepared by a large group of authors is devoted to describing the basic principles of transsphenoidal surgery of craniopharyngiomas. The article shows the stages in a long path made by the researchers of the Burdenko Neurosurgical Institute. Over the past 8 years, there has been a drastic change in the approach to surgical treatment of endosellar and endosuprasellar craniopharyngiomas, namely, microscopically controlled intracapsular removal of tumors was replaced by endoscopically controlled radical removal of the tumor and its capsule. The authors demonstrated the potentiality of remoing tumors spreading to the foramen of Monro, which previously had been unavailable for transnasal removal. The paper describes the general principles of the technique as well as the first data confirming, at least, its safety. The amount of clinical material obtained by the authors already exceeds the data collected by most of the world centers. Further improvement of the surgical technique and a detailed analysis of the results, including errors and complications, should certainly be reflected in subsequent publications.

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