Endoscope in cranial neurosurgery



Dr. Jean-Yves Fournier Department of Neurosurgery Cantonal Hospital St Gall, Switzerland

Endoscope in cranial neurosurgery

1.	Introduction	4		
2.	History of neuroendoscopy and training simulation in neurosurgery	5		
Firs	t endoscopes in the history of medicine	5		
Tra	nssphenoidal endoscopic surgery	6		
1	From Sir Victor Horsley to Norman Dott.	6		
2	Reintroduction of the transsphenoidal approach initiated by Gérard Guiot	7		
3	Refinement of the method			
Cer	ebral endoscopy	9		
History of training simulation in neurosurgery and its place today				
Р	hysical simulators			
V	írtual reality simulators			
Ν	leurosurgical training simulation in 2017	19		
3.	Transsphenoidal surgery	21		
Pitu	itary surgery	21		
Iı	ntroduction	21		
S	urgical approach to pituitary adenomas			
A	dvantages and limitations of the endoscopic technique	23		
Iı	ntroduction of the endoscopic technique	25		
S	urgical techniques	25		
0	wn experience			
Other "non-pituitary" lesions of the anterior skull base				
Iı	ntroduction	40		
M	leningiomas of the anterior skull base	41		
0	lwn experience	44		
Rep	Repair of CSF leak and anterior skull base reconstruction			
С	onfirmation and localization of the CSF leak	54		
G	rafting materials	55		
Ε	ndoscopic reconstruction techniques	60		
Oth	er complications	64		
Ε	xtracranial or otorhinolaryngological complications	64		
Iı	ntracranial or neurosurgical complications	64		
Con	clusions and observations regarding training issues	67		
4.	Cerebral endoscopy	69		
Obs	tructive hydrocephalus and endoscopic third ventriculostomy	69		
Ν	leuroendoscopes and instruments	69		
0	wn experience	79		
Oth	er indications associated with hydrocephalus or cystic formations	86		
С	omplex hydrocephalus	86		
Ε	ndoscopic shunt placement	87		
A	rachnoid cysts	88		
Intr	aventricular tumors			
С	olloid cysts	92		
0	wn experience	95		
Ρ	ara- and intraventricular tumors, intraventricular cysts			
Trai	ining issues			

5.	Difficulties in the introduction of spinal endoscopy as a solitary starter witho	out		
bacl	kup	110		
0wr	n experience: Evaluation of the absence of a backup on the learning curve for fully			
endoscopic interlaminar discectomy				
Μ	laterials and Methods	111		
R	esults	113		
D	liscussion	117		
С	onclusion	118		
6.	Teaching / Trainings problems	119		
Changes in surgical training concepts				
Training transsphenoidal endoscopy				
0wr	n experience: development of a training model for transsphenoidal endoscopy			
Futu	ure developments and diffusion of the model			
Con	clusions			
7.	Future technical developments, perspectives	134		
End	Endoscope improvements			
Rep	Repair material and techniques			
Neu	Neuronavigation and intraoperative imaging			
Inst	rumentation improvements			
8.	Conclusions	138		
9.	References	139		

1. Introduction

The concept of using optical instruments in order to see into body cavities is by no means a new one, but until the end of the 20th century the endoscope did not belong to the usual instruments of a standard neurosurgical theatre as it was the case in other surgical specialties such as orthopedic surgery, urology or head and neck surgery. It had been used by some pioneers such as Walter Dandy at the beginning of the 20th century but was soon abandoned because of insufficient illumination and difficulties in controlling the operating field as compared to opened techniques. Thanks to its application in the treatment of obstructive hydrocephalus it made its re-entry in our discipline in the late 80s and became a routine instrument for the neurosurgeons dealing with this pathology in greater centers, especially in children hospitals. In the last two decades the endoscope has been increasingly applied in the treatment of pathologies of the anterior skull base. Its applications here have been diverse, either as an adjunct during classical microscopic procedures or as the sole visualization tool. The localization of the pathologies that can be reached through an endoscopic approach range from the frontal sinus to the odontoid process. The progressive developments have been made either by teams of neurosurgeons (Cappabianca, Cavallo in Naples) or by hybrid teams of neurosurgeons associated with endoscopic rhinologists (as in the following institutions, visited by the author: Kassam-Snyderman, Jho-Carrau in Pittsburgh, Bojanowski-Lavigne in Montréal, Bresson-Herman in Lariboisière, Paris). In the Department of Neurosurgery at the Cantonal Hospital in St Gall the endoscope was first introduced for the treatment of obstructive hydrocephalus in 1998 and as the sole visualization instrument for transsphenoidal operations in 2004 in collaboration with the ENT Department.

This work presents the cranial endoscope applications that have become routine for most neurosurgical centers in the last decades and have been introduced in the Department of Neurosurgery of the Cantonal Hospital in St Gall since 1998 by the author; it analyzes the results of these first series as compared with those of the literature. Finally it exposes the challenges that neurosurgeons have to face when learning to work with the endoscope and presents some possible solutions to improve teaching for young neurosurgeons who, in contrast to their ENT colleagues, have very few opportunities at an early stage of their training to use the endoscope or to see endoscopic procedures regularly.

2. History of neuroendoscopy and training simulation in neurosurgery

As mentioned in the introduction the routine use of the endoscope in neurosurgery was made possible by two essential applications: the treatment of obstructive hydrocephalus on one side and the resection of tumors of the anterior skull base, essentially pituitary adenomas, on the other side. These two applications have a different development history: the modern treatment of obstructive hydrocephalus began in the late 80s and was made purely by neurosurgeons including pediatric neurosurgeons, whereas the endoscopic resection of tumors of the anterior skull base was often developed in centers where neurosurgeons and rhinologists cooperated and did the whole procedure together, thus producing an invaluable "cross-fertilization" as quoted by Snyderman[344]. It also really started only 20 years ago. Another difference is that these two applications differ completely in the way and in the milieu they are performed: cerebral endoscopy is done "under water" with tiny instruments through one and recently two narrow, coaxial working channels, whereas transsphenoidal endoscopic surgery is performed through the paranasal air sinuses using one or two instruments besides the endoscope itself. Both techniques aim at treating intracranial lesions by using the endoscope as the sole vision tool; however, they developed sequentially in time, so their respective histories have to and will be treated separately hereafter.

First endoscopes in the history of medicine

The first model of a tube associated with a light source to look into body cavities was developed in 1806 by a German doctor, Philipp Bozzini, who named his instrument the "Lichtleiter" [18]. Although his instrument was tried to look through several body cavities it never reached wide use. In 1853 a urologist, Antonin Jean Desormeaux combined a 45 degree mirror with a kerosene lamp that burned alcohol to look into the bladder. His system would know much more success and he is recognized as "the father of cystoscopy" [398]. In 1879 Maximilian Carl-Fredrich Nitze made the next improvement when he created an endoscope where several lenses were placed in series to which he associated a platinum filament lamp at the end of the instrument. He is quoted as saying that "in order to light up a room one must carry the lamp inside" [338]. In the following years a variety of light system were developed in order to reduce the problems associated with their use, especially the heat at the tip of the instruments with the risk of causing burns. This led to experiments not only with diverse sources of light but also to develop cooling systems. In 1883 David Newman used an Edison light bulb which did not need any cooling system[171]. Due to these improvements the endoscope had by the end of the 19th century become a routine instrument to perform examinations such as bronchoscopy, gastroscopy or cystoscopy[338]. In 1889 Boisseau

du Rocher introduced another improvement which would become very important for intraventricular endoscopy: he developed the first endoscope with an outer sheath and a working channel, allowing safe use of different instruments during cystoscopy[1].

Transsphenoidal endoscopic surgery

The history of transsphenoidal endoscopy has to be replaced in the larger context of the history of pituitary surgery as a whole. Surgery for pituitary tumors occupy a small chapter in general neurosurgery as they constitute 5% of intracranial tumors. Nevertheless, due to the wide spectrum of clinical manifestations they have aroused much interest from the beginning of neurosurgery at the end of the XIX.th century. The history of pituitary surgery itself has been subdivided in 3 periods by Landolt: the early period from Sir Victor Horsley to Norman Dott; the period of the reintroduction of the transsphenoidal approach initiated by Gérard Guiot to the introduction of bromocriptine, the first effective antisecretory drug; and the period of refinement of the individual treatment methods lasting until today[217].

1 From Sir Victor Horsley to Norman Dott.

Sir Victor Horsley in London is recognized as a pioneer in intracranial surgery for cerebral tumors and is credited for being the first who addressed successfully a tumor of the pituitary region in 1896. Before him Caton and Paul had tried, without success, to extirpate a pituitary tumor through a subtemporal approach[44]. Horsley published a first series of 10 cases operated successfully through an intracranial subfrontal approach[169].

In 1904 Fedor Krause in Berlin used a transfrontal exposure to the pituitary with an extradural subfrontal approach and published in 1912 the first description of the transfrontal exposure of the pituitary [212]. He later preferred the transsphenoidal procedure because he estimated that the transcranial exposure was "dangerous and serious and should only be used for large tumors" [217]. In the beginning of the XX.th century other pioneers contributed with their modifications to technical improvements of the procedure: McArthur, a general surgeon in Chicago, included the orbital ridge in his frontal flap, thus improving the access to the sellar region and minimizing trauma to vital structures[243]. Charles Frazier also used a right frontal craniotomy with resection of the supraorbital ridge if necessary; he performed an extradural approach with dural opening in the area of the planum sphenoidale but later moved on to an intradural approach[104]. He also used the transsphenoidal method and stated that surgeons dealing with pituitary lesions should be familiar with both methods [105]. Finally he is also credited for a visionary statement, considering the development of medical treatment of prolactinomas when he wrote that "the mere acquisition of fat with sexual impotency is a phrase which of itself scarcely justifies resort to surgical therapy, at least until the influence of glandular feeding has been given a Thorough trial" [104]; Heuer developed in May 1914 an approach to the chiasm which differed from the transfrontal exposures used so far. Called to the front in 1917, his method was described by

Walter Dandy in 1918[159] and consisted in a fronto-lateral craniotomy with exposure of the pituitary along the sphenoid ridge.

Harvey Cushing tried the subtemporal approach to the pituitary in 6 patients, moved on to the transsphenoidal technique and finally made his mind for what he called a "unilateral osteoplastic transfrontal method" [60]. He had operated on 231 patients transsphenoidally with a mortality rate of only 5.6%, a very good figure for that time. Among the arguments which motivated him to abandon the transsphenoidal approach he mentioned the improvements of visual disturbances which were more often observed after the transfrontal approach as compared to the transsphenoidal (21% vs 9% respectively) and the fact that many patients had already been operated on their noses thus adding difficulties for the approach. Because of his dominance in the field, his negative statements prompted many neurosurgeons to abandon the transsphenoidal approach. One of his pupils, Norman Dott from Edinburgh, did not follow his advice. However, the transcranial surgery for pituitary tumors was still associated with high mortality and morbidity rates, from 30 to 70%, and these facts motivated other pioneers to search for a less traumatizing and less dangerous approach.

2 Reintroduction of the transsphenoidal approach initiated by Gérard Guiot

In 1897, Giordano in Italy, was the first to describe an experimental technique on cadavers for a transglabellar supranasal approach[120]. Hermann Schloffer, Professor of Surgery at the University of Innsbruck, wrote an article in 1906 in which he debated about the feasibility of pituitary surgery[324]. One year later in 1907 he was the first to perform the approach described by Giordano successfully on a patient[325]. The approach consisted of a lateral rhinotomy with complete rotation of the nose to the right side followed by removal of the septum, all turbinates and the medial wall of the orbit and of the maxillary sinus; the ethmoidal and the sphenoid sinus were exenterated. The patient died however 2 and a half months later[326] and the autopsy showed a large tumor rest blocking the foramen of Monroe[325]. Schloffer deplored the fact that preoperative evaluation consisting only of neurological examination and skull radiographs did not suggest such a large tumor and whished a technique which would allow for better selection of the cases for surgery. His wish could not be fulfilled until Dandy introduced the pneumoencephalography years later. In 1909 Theodor Kocher in Bern added the submucosal resection of the septum[203].

In 1904 Hajek, a rhinologist from Vienna, described a method to drain the sphenoid sinus for the treatment of empyema[139]. The access to the sphenoid sinus was achieved with removal of the middle turbinate and resection of the posterior ethmoid cells with specially designed punches bearing his name until today. Oskar Hirsch from Vienna used Hajek's approach and was the first to introduce in 1910 an exposure of the sella entirely through the nasal cavity[162]. He performed this procedure for the first time on August 4th 1914, on the very same day where Cushing performed an identical procedure in Baltimore. Hirsch changed later to the transseptal exposure, the technique associated with his name. He changed to this transseptal technique in order to work in clean areas as postoperative meningitis was at that time the most feared complication of

transnasal pituitary surgery as most of the patients would die of it. The created interseptal space of the transseptal technique has with the exception of the incision in the antrum no communication with the nasal cavity[163]. Nearly simultaneously to Hirsch's work Halstead pioneered the sublabial approach[142].

As mentioned above one of Cushing's pupils, Norman Dott in Edinburgh, continued to perform the operation he had learned in Baltimore. He operated 120 adenomas without mortality. As he mentioned in a letter he wrote to and published by Alex Landolt from Zurich[217], Gérard Guiot suspected that Norman Dott did not publish his series out of respect for his mentor Harvey Cushing who had condemned so strongly this approach. Nevertheless Gérard Guiot could learn the technique in Edinburgh and introduced some modifications, as for example the semi-sitting position, thus operating in front of the patient, whereas Norman Dott was operating with the patient recumbent, himself sitting during the procedure with the head of the patient between the legs. Gérard Guiot is also credited for introducing the image intensification, thus gaining an intraoperative information of the position of his instruments in the sagittal plane (trouver la référence). He was also the first to explore the sellar region with an endoscope [136]. Together with Derome they operated more than 5000 cases of pituitary adenomas, thus gaining a worldwide reputation and they also developed an enlarged transsphenoidal approach as well as well as a trans-frontal and transsphenoidal combined approach for invading large skull base tumors[73].

3 Refinement of the method

In fact it was accidentally that Jules Hardy came to pituitary surgery. He had the opportunity to become a fellow of the McLaughlin foundation in Toronto and was sent to Paris in 1961 to improve his knowledge in stereotactic surgery for involuntary movements, a technique developed also by Gérard Guiot. During his stay at the hospital Foch he was also introduced to the transsphenoidal procedures and brought both techniques back to Montréal in 1962[146]. After exploring the sellar region with the pediatric cystoscope in order to look for tumor rests he found the microscope more easy and useful and introduced the use of the microscope combined with radiofluoroscopy which became the gold standard[148]. The introduction of the microscope allowed him to differentiate between adenoma and normal gland tissue, something judged impossible so far and leading to panhypopituitarism after resection of pituitary tumors. This capacity to distinguish these different tissues under magnification allowed him then to treat hormone active microadenomas efficiently[145, 147] thus introducing the concept of selective adenomectomy of microadenomas under preservation of the normal pituitary gland.

At the end of the XX.th century many technological innovations have been applied to the field of transsphenoidal pituitary surgery in order to decrease morbidity, such as neuronavigation[85], Doppler ultrasonography[11] and intraoperative magnetic resonance imaging[351]. Even if Bushe and Halves reported in 1978 the first application of the endoscope for pituitary surgery[34] the method did not get its popularity until the mid 1990s, when open techniques were superseded by endoscopic sinus surgery with its excellent visualization and good surgical results, thus motivating neurosurgeons to

evaluate its use in transsphenoidal surgery. There are several ways in which the endoscope has been initially used for transsphenoidal pituitary surgery. One of the possibilities is to use the endoscope for the nasal approach, then switch to conventional microscopic technique for the adenoma resection and finally returning to the endoscope for final inspection looking for tumor rests, as described by Yaniv and Rappaport[393]. This combined technique allows for decreased morbidity for the nasal phase while taking advantage of the 3 dimensional vision of the microscope for the tumor resection, and finally using angled endoscopes to look for regions normally outside of the microscope view.

Jho and Carrau reported the same year their early experiences[185] and some months later the first large series of transsphenoidal operations for pituitary adenomas performed exclusively with the endoscope[184]. The technique presented consisted of an approach done with the endoscope hold in the non-dominant hand and with one instrument in the other during the approach until the anterior sphenoidotomy was performed followed by a phase of tumor resection during which the endoscope would be fixed to a holder allowing the surgeon to operate with both hands. The authors claimed that one of the main advantages of the endoscope was the excellent panoramic visualization of the sellar and suprasellar regions as well as the better anatomy[185]. Anatomical studies performed on cadavers confirmed that the volume of exposure provided by the endoscope was significantly larger than by the microscope[348]. The authors also reported on shorter hospitalization and faster postoperative recovery but this was challenged at that time[218, 219].

One of the regularly claimed drawbacks of the endoscope is the lost of the third dimension and thus of the depth evaluation. However, studies have demonstrated that the dimensional image do not lead to a reduction of the performance. In an experimental study, Tasman even demonstrated that manipulations were performed faster under the endoscope and more faults in point sequences were done under the microscope than with the endoscope[357, 358]. He argued that various monocular phenomena obviously allow sufficient spatial orientation so that monocular vision under the endoscope does not appear to be a real disadvantage.

Cerebral endoscopy

An understanding of the pathophysiology of the cerebro-spinal fluid (CSF) was only possible after elementary works about this topic were done by Key and Retzius in 1875[197], which opened the door to the development of causal therapy. Later on, in 1913, Dandy and Blackfan were able in their work to calculate the daily production of CSF which they evaluated between 160 and 400 ml and postulated its production in the plexus choroideus and its resorption in the arachnoid granulations of Pacchioni[65]. A first attempt to treat hydrocephalus endoscopically was made by a urologist from Chicago, Lespinasse, in 1910 but his contribution to early neuroendoscopy was only published in 1936 by Davis in his textbook Neurological Surgery[66]. The idea of the treatment was to introduce a cystoscope and fulgurate the choroid plexus on both sides in order to reduce CSF production and thus perform what Lespinasse called "an intern's shunt"[127].

The concept of re-establishing a communication between the internal and external subarachnoid spaces in patients with obstructive hydrocephalus has been established by the neurosurgeon who is actually considered as the father of neuroendoscopy, Walter Dandy. He coined the terms ventriculostomy and ventriculoscope and also described the perforation of the lamina terminalis via a subfrontal craniotomy in order to achieve communication between the third ventricle and the basal cisterns. After having published his paper on ventriculography at the end of his residency in 1918[63] he described in 1922 a technique for third ventriculostomy using a primitive endoscope for the treatment of hydrocephalus[64]. He performed actually choroid plexus resections with a cystoscope in two infants but had to admit after some years of enthusiasm that the vision provided by the endoscope could not be compared with the images given by the pneumencephalogram[124, 159]. In 1923 a urologist, Wiliam Mixter, reported the first endoscopic third ventriculostomy performed using a urethroscope for the treatment of obstructive hydrocephalus in a 9-month-old girl[248]. The perforation was enlarged to 4 mm; the membrane around the perforation was floating with the pulse and the bulging of the fontanels decreased rapidly, thus proving the patency of the opening which was double checked by the injection of dye found in the CSF at a lumbar puncture half a minute later. The bulging of the fontanels decreased also rapidly. Edwin Payr, a professor of surgery at the university of Leipzig presented in 1919 the preliminary tests and feasibility of "Enzephaloskopie" and was considered in Germany as the pioneer in neuroendoscopy[70], although he is better known for his works using vein grafts to drain CSF from the ventricles into the sagittal sinus and jugular vein[274]. Another German professor of surgery, John Volkmann from the university of Halle, developed a special "Enzephaloskop" which he tried first on frozen and fresh cadavers before his first inspection of the choroid plexus of a 3 years old child with hydrocephalus[374]. The "Enzephaloskop" presented an outside diameter of 6mm and 2 irrigation channels, it was 22cm long[375]. The same year Fay and Grant from Philadelphia took an picture of the dilated ventricle of a child, using a camera fixed on a cystoscope[95]. Tracy J. Putnam in 1934 made modifications on Mixter's urethroscope for better intraventricular use and cauterization of the choroid plexus[289]. Various efforts were made in vain in order to reduce morbidity and high mortality rates, which were reported to be as high as 30%, often caused by intracranial hemorrhage[378]. Scarff, head of the department of Neurological Surgery at Columbia University in New York, published in 1951 a series of 19 patients treated with a new device he called ventriculoscope. In order to avoid the ventricular collapse observed by Dandy the system was connected to an irrigation to maintain the intraventricular pressure. A moveable probe was used to perforate the floor of the third ventricle under clear vision. Of the 19 patients 15 improved with permanent reduction of their intraventricular pressure, 3 did not improve and 1 died[319]. In Paris, Feld improved Scarff's ventriculoscope by introducing 2 new elements: one was a fixation device connected to the operation table

and allowing to fix the endoscope and the other was the development of a working channel for the introduction of an instrument, as for example a biopsy forceps[96]. In 1961 Dereymacker reported on 15 patients who received a ventriculostomy using a pleuroscope; the perforation was done with the blunt tip of the pleuroscope and was successful only in 2 of the 15 cases [72]. Gérard Guiot from Paris is considered as one of the pioneer in the revival of modern neuroendoscopy. In his publication on intracranial endoscopic explorations [136] he presented not only the intraventricular application but also presented the endoscope as an instrument for the exploration of other intracranial cavities and pathological cavities as well as for the sellar region. He presented a newly designed instrument, the so-called universal endoscope, that was to be applied to these different pathological conditions. These new applications were allowed in particular by the technical improvements with a much more intense illumination than in previous ventriculoscope models ("several hundred times more"). Moreover he mentioned in this article that the technical improvements of surgical instruments made of the endoscope not only a diagnostic but also a therapeutic tool. In this paper he mentions in particular his conviction that the development of the endoscopic applications observed in other medical specialties can also be applied to neurosurgery.

In spite of all these innovations, neuroendoscopy was still considered too risky by most surgeons and fell out of favor, in particular as new valve-regulated shunt systems seemed at first to offer greater safety with less complications[1].

however, with a persistent high rate of shunt malfunction associated with regular operative revisions and the rapid development of endoscopic technologies, the motivation for developing a more physiological and anatomical diversion for CSF has gained once again more attention, so that finally in the late 1970s and 1980s neuroendoscopy would know its renaissance, mainly due technical advancements and a wide use for minimal invasive inspections of different body cavities[378]. In 1959 Harold H. Hopkins a British optical scientist filed a patent application for the invention of *air-in glass* rod lens systems allowing an eighty times greater eighty times improved light and image transmission[167, 378], allowing improved visual control over anatomical structures. The application of this decisive technical improvement was first done for neurosurgery by Griffith form Bristol who developed the first neuroendoscope based on Hopkins optic systems and applied it to the treatment of hydrocephalus by children [130, 131]. Furthermore technological integration of fibrebundle-endoscopy in neurosurgery led to the development of the "Ventriculofiberscope" by Takanori Fukushima from Tokyo in 1973[108, 262]. These two major improvements can still be found in rigid and flexible endoscopes today.

Optimization of orientation and trajectory planning in ventricular endoscope applications was achieved with the introduction of the neuronavigation based on preoperatively acquired patient specific magnetic resonance imaging (MRI)[123]. Of course can a simple endoscopic third ventriculostomy (ETV) for the treatment of hydrocephalus due to aqueductal stenosis safely be conducted by the experienced neurosurgeon without neuronavigation[297]. The use of neuronavigation for ETV is more likely beneficial in combined surgical treatment of obstructive hydrocephalus caused by a tumor, causing elevated intracranial pressure (ICP) due to obstruction of cerebrospinal fluid (CSF) outflow pathways. In these cases the double burr whole technique is often applied, using one burr hole for ETV, and a more anterior burr hole permitting better access to structures lying further posterior. The discussion whether ETV should be performed before or after the tumor resection or biopsy is still ongoing since major bleeding from tumor resection can obscure vision permanently and make a safe perforation of the floor of the third ventricle impossible. Some surgeons favor ETV before treating the tumor, while others do see some benefit in raised ICP due to hydrocephalus in controlling bleeding from tumor biopsies or resection, resulting in the ETV being conducted at the end of combined operations. The author in his personal experience preferred to perform the ETV at the beginning of the procedure as intraventricular pressure can be adequately controlled with modern irrigation devices and there is no need to take the risk not to be able to perform the ETV at the end of the procedure because the vision is obscured by tumor bleeding.

Nowadays ETV has become a well-established procedure and is the treatment of first choice for of obstructive hydrocephalus due to aqueductal stenosis or intraventricular, tectal, pineal, or posterior fossa tumors[6, 113, 134, 156, 179, 254].

Though there have been many technological developments in order to make ETV a safe and simple procedure a well-known risk for perioperative complications remains[28, 166, 251]. These very same developments came along with a responsibility for the neuroendoscopic trainee on one hand to familiarize himself with the complex instruments and their combined use, and on the other hand, a responsibility for the teaching senior neurosurgeon to supervise the mastery during operations performed by trainees.

History of training simulation in neurosurgery and its place today

Training in medical education can be traced back as far as to the first efforts made in the 6th century BC by Alcmaeon of Croton and later by Galenus who gave first dissection descriptions[276]. The first extensive publication on human anatomy based on cadaver dissection was published by Andreas Vesalius during the 16th century under the famous title "De humani corporis fabrica"[376] (Online interactive French version by Jaqueline Vons and Stéphane Velut from the University of Tours: http://www3.biusante.parisdescartes.fr/vesale/debut.htm).

However, several aspects of cadaveric model training have limited and still limit until today their application such as financial aspects, legal and religious obstacles, unregular availability so that the development of physical models for medical education has been encouraged[303]. Moreover, in recent years, the introduction and application of working hours regulations in the US[250, 288] and in Europe[220, 361, 402] has led to a dramatic reduction of the surgical exposition of trainees in all specialties, sometimes

with debated or even negative effects on patient's outcome[164]. For this reason it became progressively clear in the last 2 decades that the traditional education system had to evolve from the usual "see one, do one" to a more elaborated "see one, simulate one, and do one under supervision", as stated by Whitfield and colleagues[400]. But the reduction of duty hours for residents is by far not the only factor that motivated the development of simulation for surgical training in recent years. At least 3 other factors have motivated the development of training opportunities out of the theatre in recent decades: improvement in educational methods, economical pressure to optimize operating room and safety issues.

Advances in educational theory have demonstrated that the traditional way of surgical teaching based on observation, sheer volume exposure and graded responsibility is not the most efficient. This German-style residency training system was introduced at Johns Hopkins Hospital by Sir William Halsted in 1889[41] and remained until recently the cornerstone of surgical training. Theories of the ways in which motor skills are transmitted and acquired have been developed. One of those widely accepted concepts is the three-stage theory of motor skill acquisition (Table 1.1) developed by Fitts and Posner[98].

Fitts-Posner 3 stage theory of motor skill acquisition						
Stage	Goal	Activity	Performance			
Cognition	Understand the task	Explanation,	Erratic, distinct			
		demonstration	steps			
Integration	Comprehend and perform	Deliberate practice,	More fluid, fewer			
	mechanics	feedback	interruptions			
Automation	Perform task with speed,	Automated	Continuous, fluid,			
	efficiency and precision	performance, focus	adaptive			
		on refining				

Table 1.1: adapted from Fitts and Posner[98]

One of the consequences of the application of this model for surgical practice has been the move of the earlier stages outside of the operating room. The practice with repetition and acquisition of automatisms will allow the trainee to master basic skills so that when moving into the theatre he will be able to focus on more complex issues, technical or nontechnical[301]. The mastering of technical skills outside of the operation room will avoid a possible cognitive overload with too high demand on working memory with diminished performance of other processes which can lead to errors or simply to unnecessary prolonged operation times in novices[21, 387].

Among this learning process, deliberate practice seems to play a key role. Deliberate practice implies repeated practice focused on a defined task with coaching and

immediate feedbacks. It has been extensively described and contains 9 decisive elements[98]:

- 1. Motivated learners
- 2. Defined objectives
- 3. Appropriate level
- 4. Focused and repetitive practice
- 5. Reliable measurements
- 6. Informative feedbacks from supervisors
- 7. Promotes learning and corrects errors
- 8. Evaluates performance against the final standard and also to ensure completion of minimal outcomes for all trainees
- 9. Progression in training

Some authors such as Ericsson even argue that the number of hours spent in deliberate practice might be a more important determinant of the level of expertise than just the hours spent in surgery[86]. Thus, since the early 2000s great support has been given to this deliberate practice with formative debrief and feedbacks and several instances have supported this type of training before supervised practicing on patients be allowed.

Another stimulating factor which has led to the reduction of exposition of trainees is the economic pressure that has led hospitals to optimize the occupation of the operating theatres thus limiting again the opportunities for trainees to practice.

Moreover, increasing complexity and the greater emphasis put on medical errors have also limited the supervisor's possibilities to train their residents. This phenomena is particularly important in neurosurgery where errors can lead to devastating consequences. Not surprisingly, neurosurgery ranks as the most liable of all medical specialties to malpractice suits; in the US for example, 19.1% of neurosurgeons are facing at least a claim a year[75].

Finally a boost has been given to the development of these training simulators by technological developments in 2 main domains: computerized virtual reality (VR) and 3D printing technologies. These 2 types of technologies can also serve as the main criteria for classifying neurosurgical training simulators into physical and VR simulators[208].

Most if not all the above mentioned factors and technical developments have in fact taken place in the last decade, a fact which is reflected by the increase of the publications on the subject of training simulation in neurosurgery since the 2000s. in a PubMed search, Konakondla and Schirmer found 124 publications, the vast majority of them being published after 2000 or even after 2005[208]. Exploring associations among sets of terms they found a high level concurrency between the concepts of "neurosurgery", "medical simulation" and "virtual reality".

Physical simulators

These include cadaver models, live animal models, animal tissues and synthetic models. *Cadaveric models*

If cadaveric dissections have been historically the gold standard they can no longer be considered as real training units with its one-time use limitation in the light of modern educational concepts. Nevertheless they undoubtedly provide a unique opportunity to verify anatomic knowledge and to apply the skills acquired elsewhere with deliberate practice, thus diminishing the waste of precious anatomic dedicated material by insufficiently prepared trainees.

Animal models and animal tissues

Living rats (in vivo rodents) are classically used in microsurgical training programs in neurosurgery, typically in vascular training for anastomosis[172, 277]. Alternatively, prepared animal parts such as chicken wing arteries[172], porcine arteries[327] or turkey necks[55] have also been used.

Physical 3D printed simulators

The regular improvements in 3D printing processes has allowed for a great deal of possibilities in neurosurgery to create reproductible models that can be manipulated. One of the advantages of these physical models is that they allow real tools and instruments to be used by the trainee thus gaining an appreciation for their physical properties and proprioception. Amongst the other advantages of the physical 3D models one can mention the reduced costs as compared to expensive software and hardware simulators, they are often easily portable and reusable and carry minimal risks. The production of patient specific models is also possible, thus going from basic skill learnings to specific procedures simulation or rehearsal. These improvements in the 3D printing could also in the future reduce one of the recognized disadvantage of these models which is the low fidelity towards reality. Several examples demonstrate that modern 3D printing possibilities with continuous improvement of materials tend more and more to approach reality. This is for example the case for the training of endoscopic third ventriculostomy[30, 97, 388]. Some of these devices are so affordable that they allowed the development of full education programs as for example in Africa[280]. Another organ which allows for realistic training is the spine. One example has been established as a spine course by the Simulation Committee of the Congress of Neurological Surgeons in 2012 already. The simulator for anterior cervical discectomy and fusion provides physical models that mimic the soft tissue and the bony elements and allows the trainees to use real-world surgical instruments such as Kerrison rongeurs or drills[293]. Other models have been developed to focus on complication avoidance in spinal surgery[384]. Even the training of the management of specific events that should be avoided during spinal surgery can be trained such as the management of cerebrospinal fluid leaks[119].

The author had himself regular experiences with modern spinal training models in the setting of instruction courses for the training of the implantation of the annular closure device "Barricaid" (Fig. 1.1).



Figure 1.1: illustration showing the principle of the Barricaid annular closure device

He organized three internal training sessions for the residents and registrars of the neurosurgical department of the Cantonal Hospital of St Gall in 2016 and two international symposium in 2017, one for German speaking colleagues and one for English speaking colleagues coming from abroad. The training sessions were organized with the use of the physical model "Realspine" for the training of microscopic lumbar disc herniation operations developed by Realists[®] in Leipzig, Germany.



Figure 1.2: Realspine model for training of lumbar discectomy with fluoroscopic simulation using navigation data.

The model (Fig. 1.2) offers an extremely realistic environment to train interlaminar fenestration and discectomy with everyday instruments and microscope. It allows also

the implantation of the annular closure device "Barricaid" which is made normally under lateral fluoroscopy. In order to allow for a similar guidance possibility and to avoid irradiation during simulation training a combination with a navigation system has been developed which delivers similar imaging information.



Fig.1.3: intraoperative view of the Realspine model with bleeding simulation.

The model allows also for realistic stearable bleeding simulation (Fig. 1.3) and even for dural tear with cerebro-spinal fluid leak in case of durotomy.

Virtual reality simulators

Virtual reality simulators present several advantages as compared to physical models: first they do not suffer from the issue of repetition with material consummation. As a result their cost can be possibly reduced substantially over time. Due to programming possibilities and the absence of graphical limitations they can not only simulate normal anatomy but also variations and pathological states. One drawback remains that they often do not allow the use of real tools and instruments in order to acquire their proprioception. However, this is an evolving situation as recent models not only offer improved haptic feedbacks but also tend to integrate standard instruments whenever possible.

Historically one can distinguish three types of VR simulators:

The <u>simplified VR systems</u> such as the Dextroscope (Braco, Princeton, NJ, USA) creates a 3D patient-specific holographic image to create a virtual anatomy of a specific patient[205]. Other examples of these types include the "Virtual Dissector" developed by Bernardo et al and focused on skull base approaches[22].

The <u>augmented VR systems</u> enable some computer-user interaction through an interface as in the "Robo-Sim-Endoscopic neurosurgical simulator" developed for ventriculostomy simulation[291].

Finally the <u>immersive VR systems</u> are the most recent and elaborated types. They provide a physical perception in a virtual world including haptic and kinesthetic modalities.

One of the first and best documented immersive VR systems is the NeuroTouch[71]. It was developed in 2008 by the National Research Council in Canada. It incorporates bimanual tools with haptic feedback and a real-time computer-generated virtual tissue that reacts to manipulation. The binocular vision of the operating field is provided by a stereoscope. Instruments that can be used include an ultrasonic aspirator, suction, bipolar cautery and microscissors that closely approximate real tools. The instruments can interact with the real-time virtual tissue in such a manner that the user is able for example to differentiate between normal and tumorous tissue which will be oozing blood when resected. The tissue pulsate at a rate of 60 beats per minute. Although this system represents a clear step forward several authors argue that it still is not identical with real tissue and sensations[21, 208]. Initially focused on oncology, the system meanwhile includes several modules allowing for the training of cranial, endoscopic[307] and spinal procedures.

Another system, the ImmersiveTouch, was introduced in 2005 by the University of Illinois in Chicago for performing ventriculostomy and meanwhile provides diverse simulation for neurosurgical trainees[9]. With its high-resolution screen and 3D glasses it provides a realistic interactive stereoscopic environment with haptic feedback tools. It offers several training modules developed from real MR data for normal anatomy and diseases. There 3 different packages that can be purchased: base, pro and premium, offering increasing complexity. Modules have been developed for cerebral aneurysm clipping, spine surgery, hemostasis, percutaneous spinal fixation, percutaneous trigeminal rhizotomy, anterior clinoidectomy and ventriculostomy[4].

Finally the "Temposurg" was developed at the University of Hamburg, Germany, and is dedicated to temporal bone surgery[204]; Like the Voxelman[©] [371]developed for the ENT trainees it provides a 3D virtual surgical field of the temporal bone with haptic feedback and offers a realistic training tool to acquire surgical skills for temporal bone surgery.

Another advantage of the VR systems is that with the definition of standardized metrics they will provide immediate feedbacks with scores. This possibility will probably allow in a near future the deliberate training with electronic feedback, thus increasing the opportunities for deliberate training independently from the availability of mentors, which will in turn reduce one part of the costs and organization limitations.

The question of the financial aspects of these training simulation programs remains quite obscure. There is some intuition that the investment should finally benefit patients, however little research has been made regarding the financial feasibility of these training programs. To date, only the simulation curriculum offered at the University of Texas, Galveston, has been studied precisely regarding its costs. The program offers 68 exercises per year and per resident, including cadaveric simulations, physical simulator products and haptic feedback simulators. The yearly costs for one resident reached 341,978 \$ to start and 27,876.36 \$ the following years to continue[117]. Even if these figures are hardly transposable to other institution they might serve as a framework for future evaluations.

A dark side of the financial aspects, besides technical and equipment costs, which is also difficult to evaluate is the cost of providing training simulation: the time allocated by the trainees and by the trainers has a price and besides the training sessions trainers also have to be instructed to some degree[400].

One recent study comparing VR and 3D printed models for training of endoscopic 3rd ventriculostomy found that, in their present state, 3D printed training models seem superior for familiarizing trainees with the endoscope, the instruments used and the techniques, while VR simulators were superior to improve three-dimensional anatomical knowledges[31]. One of the relevant differences was the fact that physical training models provided superior instrument handling, allowed the trainees to use usual instruments, try and compare different ones and even have the opportunity to try new instruments. This also seems to meet the preference of trainees who, in an evaluation of laparoscopic training, preferred to use "box trainer" with normal instruments as compared with VR simulators, with a majority of 80%[235].

Neurosurgical training simulation in 2017

In spite of numerous contributions, the field of training simulation with modern VR simulators or physic 3D printed models remains relatively new in neurosurgery as demonstrated by Konakondla and Schirmer[208]. Moreover several reviewers in recent publications still consider that the current models are less than ideal for real-life translation, but recognize that significant strides with haptic feedback have been encouraging[21, 200, 208]. In 2014, in the first systematic review of the literature about the use of simulation in neurosurgical education and training, Krikman and colleagues found 28 articles describing a simulation-based intervention used in an educational context and presented outcome data. Overall they found a poor quality of the studies with significant shortfalls in methodology and design of most of the works and stated that future studies should improve study design and provide long-term follow-up data on simulated and/or patient outcomes [200]. In particular, if some studies, especially the more recent ones[16, 264]s, did use the 3 classical dimensions of training model validity (face, content and construct), several studies did not provide systematic evaluation of their model regarding these dimensions. Face and content are subjective measurements, the former deals with the quality of the replication of working conditions, level of difficulty as compared with the reality and possibility of being successful in completing the training task whereas the latter, content validity, concerns the potential of the model to improve the ability of the trainees or in other words, if the model is able to teach the trainees the skills targeted.

Construct validity regards the ability of the model to distinguish between the beginner and the experienced participants.

As stated above, the whole field of training simulation is still young in neurosurgery, as compared with other surgical specialties such as general surgery, ENT or urology and has not yet taken hold[208]. There is a clear trend to establish it in neurosurgical curricula[5, 140, 150, 241, 321, 335] but its place still has to be clearly defined. Another critical point regarding training simulation remains the fact that so far no study has been able to demonstrate the translation of simulation training to real surgery. So future studies, ideally large, randomized, prospective and controlled, should aim at demonstrating the degree of translation from simulation to the patient by measuring its impact on outcome[200, 208], which will facilitate its optimal integration into residency programs[200].

In spite of all these limitations, there is no doubt that the traditional model of surgical education with endless hours of passive observation of a mentor into the operating room has definitely come to an end. Advances in imaging, computing power, interface technology as well as 3D-printing processes and materials will contaminate the field of neurosurgical training simulation which will become readily available, affordable and more effective.

3. Transsphenoidal surgery

Pituitary surgery

Introduction

Pituitary adenomas account for 10-15% of all intracranial tumors and present an overall prevalence of 16.7%[92]. Pituitary tumors can become symptomatic through their mass effect or via their hormone disturbances. If producing one type of hormone so-called secretory adenomas will become relatively rapidly symptomatic because of a hypersecretory syndrome, non-secretory adenomas on the other hand will not come to clinical attention until they cause a mass effect. Mass effect itself will be acting either on the normal pituitary gland itself, which will present a reduced function, or on surrounding structures, the most classically involved in this case being the chiasm with a superior quadrantanopsia progressing to a classical bitemporal hemianopsia. The most frequent type of functioning pituitary adenoma is the prolactinoma (Table 3.1) accounting for approximately 40% of all pituitary tumors[369]. Their clinical presentation will vary with the gender of the patient. Women will present with the classical association of amenorrhea and galactorrhea, men will usually harbor a history of impotence and decreased libido, very seldom galactorrhea though this has been observed in males too. Prolactinoma remains the only subtype of pituitary adenoma where medical therapy is the first-line therapy. Surgery will be performed in cases with apoplexy or with difficulty in the medical treatment, be it intolerance or resistance with either persistent high levels of prolactin or persistent mass effect. Another particular situation is the development of a CSF fistula in the first weeks of the treatment of a voluminous prolactinoma[32, 271].

The second most frequent subtype of pituitary adenoma which accounts for 30% of all pituitary tumors are the so-called nonfunctioning adenomas. Even if they are characterized by the absence of relevant hormone production the majority of them will be positive for some kind of pituitary hormone as can be demonstrated in immunohistochemical examinations. Most frequently they will be positive for gonadotrophins in as many as 80% of the cases and only 6% will be true "null-cell" tumors[315]. Nevertheless, as they do not produce a clinical relevant amount of hormone they will be revealed by symptoms mostly due to their mass effect. These can include headache and visual fields defects. The compression of normal pituitary tissue will result in partial or complete anterior pituitary insufficiency and in cases with extension into the cavernous sinus cranial nerve palsies can be observed. These tumors can also be associated with an elevation of the prolactin level due to compression of the pituitary stalk (so-called stalk effect).

The second most frequent subtype of hormone-secreting pituitary adenoma and the third most frequent type of pituitary adenoma is the growth hormone (GH)-secreting

adenoma, accounting for 20% of all pituitary tumors. They are more frequent in males and present with acromegaly in adults and gigantism in children. The patient with a classical acromegaly presents an enlargement of the hands, feet, and bones of the face. Other features include development of carpal tunnel syndrome, arthritis and arthralgias, hypertension, diabetes mellitus, and hyperhidrosis[370]. The morbidity and mortality of the disease is increased in these patients because of the development of associated pathologies such as diabetes, hypertension and organomegaly. In spite of recent reports favoring medical therapy, the first choice therapy remains surgery in these patients[245].

Adrenocorticotropic hormone (ACTH)-secreting adenomas represent the last frequent group and account for 10-12% of the adenomas. It remains the most common source of endogenous overproduction of cortisol, responsible for 60-80% of the cases and is then called Cushing's disease. They present with the classical features combining weight gain with hyperglicemia, hypertension and purple striae. They are prone to osteoporosis. Cognitive and psychiatric disorders are also observed as well as amenorrhea and thin skin. Surgery is indicated and reaches remission rates of 75%[342].

% (ca)	1st line Therapy
ł0	Medical
80	Surgery
20	Surgery
0	Surgery
	% (ca) 20 20 20 20 20

Table 3.1 : frequency of the different subtypesand 1st line therapy.

Surgical approach to pituitary adenomas

The removal of a tumor located in such a central region as the sella and moreover surrounded by vital structures such as the carotid arteries, optic nerves, hypothalamus, cavernous sinus with cranial nerves and finally the normal pituitary gland itself represents a significant challenge as this has to be done through a deep and narrow space using relatively long instruments. The transsphenoidal route remains the safest and most efficacious to reach pathologies in the sellar region and independently of the adopted technique, if microscopic or endoscopic, the procedure consists in 3 main steps:

- 1° the approach and exposure of the lesion
- 2° the removal of the pathology
- 3° the reconstruction phase.

Although there still are indications for craniotomies, predictors of successful resection have been identified, such as the size of the tumor, the degree of extension and the experience of the surgeon[12]. In order to identify the limitations of the transsphenoidal approach, Zada and colleagues have reviewed the cases where both approaches, transsphenoidal and open craniotomy, had been taken into consideration and have identified 8 factors that limited the extension of resection, limited the risks of the operation and contributed to perioperative complications[397].

These factors included :

- _ significant suprasellar extension
- _lateral extension
- _ retrosellar extension
- _ brain invasion with edema
- _ firm tumor consistency
- _ involvement or vasospasm of the arteries of the circle of Willis
- _encasement of the optic apparatus
- _invasion of the optic foramina.

There are 3 main goals of pituitary surgery : normalization of secretion of excess hormones, suppression of the mass effect and preservation of normal pituitary function. The suppression of the mass effect is demonstrated by the improvement in the visual symptoms which can be reached in 70-80% of cases with preoperative compression of the optic chiasm.[396] Preservation of pituitary function depends of course on the extent of the initial tumor and is usually possible with up to 65% of cases that may even recover lost function[94].

Advantages and limitations of the endoscopic technique

Endoscopic neurosurgery has been gaining popularity in the last two decades as the first choice technique for transsphenoidal resection of sellar lesions[180, 211, 238, 246, 259, 309, 320, 354]. From a technical point of view, endoscopic (E) resections are expected to be better than microscopic (M) resections due to improved visibility[354]. One of the most important advantages of endoscopy is by no doubt the panoramic picture provided, allowing for a rapid and safe orientation into the sphenoid sinus with identification of classical landmarks such as the opticocarotid protuberances or the opticocarotid recess which are rarely visualized in the limited field of view provided by the microscope[180]. The identification of these landmarks might not be important or even necessary when resecting small adenomas but will be of critical importance when addressing larger and more invasive tumors. Another advantage of the endoscope relies in the capacity to change the line of sight. The microscope provides a clear three dimensional view of the sella but once set in place does not allow many further movements whereas the endoscope remains mobile and allows one to see « around the corner ». This can be a clear advantage when removing tumors reaching the region of the optic chiasm, invading the cavernous sinus or in close inspection of the interface between the tumor and the normal pituitary tissue. If necessary, vision around the corner can be improved with angled optics, such as 30 or 45° optics. It is also expected that the endoscopic approach obviates the need for sublabial or trans-septal approach, thus avoiding the associated complications. Still so-called extra-cranial complications of the endoscopic approach do exist[341] but they can be minimized by techniques such as septal pushover and direct sphenoidotomy[181].

Another difference between microscope and endoscope is the type of illumination: whereas the microscope delivers a cone of light which tapers from the source until it reaches the target, the endoscope delivers light and magnification via an inverted cone of light and the light source itself can be brought in the immediate vicinity of the target.

Among the limitations of the endoscopic technique the loss of the third dimension is regularly mentioned. Although this might be a problem at the beginning of a learning curve it has been demonstrated that there were no majors differences between the skills under a microscope (binocular vision) and an endoscope (monocular vision) for simple tasks[357, 358]. Another element to which neurosurgeons have to get used to is that the endoscopic image presents a kind of deformation increasing with the distance from the central point. For example, looking at a plane surface such as a printed page, the microscope shows a perfect representation all the letters with absolute conservation of the parallelism (Fig 3.1 left), whereas the endoscope will present some distortion with an increasing loss of the parallelism as one leaves the central point (Fig. 3.1 right).



Fig 3.1: Microscopic image (left), endoscopic image (right) of a plane surface.

Looking into a cavity, one of the advantages of the endoscope with its more important field depth becomes obvious and this despite the above mentioned deformation (Fig 3.2)



Fig 3.2: Microscopic (left) and endoscopic (right) images of a cavity.

Despite the fact of this clear advantage of the endoscopic image when looking into cavities the beginner neurosurgeon will need some time to get used to this kind of representation.

Introduction of the endoscopic technique

There are several ways to use the endoscope for transsphenoidal pituitary surgery. These range from endoscopic-assisted microscopic surgery using a speculum, singlesurgeon single-nostril endoscopy with limited sellar opening, single-surgeon dual nostril endoscopy with extended exposure and finally to dual surgeon dual nostril endoscopy with expanded exposure (so-called expanded endonasal endoscopic approach, EEEA) [392]. The endoscope can also be used to perform the anterior sphenoidotomy prior to inserting the speculum and then performing the rest of the procedure under microscope. In our institution we adopted the EEEA in 2004 without a period of transition. A period of transition is certainly mandatory in institutions where a singlesurgeon technique is adopted or when the surgeons have no experience with the endoscope. In our situation we could directly switch to the EEEA because of previous experience with other endoscopic operations. As stated by several authors, these factors are decisive to reach a less steep learning curve [176, 347].

Introducing the endoscopic technique in a neurosurgical unit can be done mainly in two ways. One possibility is to use the endoscope at the end of or during a classical microscopic procedure; although this will not add supplementary risks for the patient, this can be quite cumbersome, the endoscope representing a certain nuisance during the standard microscopic procedure[176].

The second way is to work in team with an experienced endoscopic rhinologist. This solution has the advantage of accelerating some of the operative steps as the rhinologist performs the transnasal approach rapidly, and gives the team security in the manipulation of the endoscope itself during resection of the tumour[176]. In our institution two neurosurgeons perform transsphenoidal surgery. The younger was encouraged by the experienced to develop the endoscopic technique and introduced it in cooperation with an endoscopic rhinologist. We have collected our observations over the last 8 years, in order to have a quality control and to make sure the introduction of the new technique had not been associated with more risks for the patients.

Surgical techniques

In our institution the patients operated microscopically were operated with a classical microscopic technique[79] beginning with a submucosal transseptal approach and placement of a nasal speculum. This approach is done by an otorhinolaryngologist who leaves the theatre during the so-called neurosurgical resection phase. Fluoroscopic imaging is used to improve accuracy, giving sagittal information about the localization of the speculum in relation to the sellar floor. The resection is conducted bimanually. The

otorhinolaryngologist returns at the end of the procedure for the septal reconstruction and closure.

The patients operated endoscopically were operated by a team during the whole operation, which is composed of one experienced endoscopic rhinologist and a neurosurgeon (the author) with some microscopic experience in pituitary surgery and more than 5 years of experience in cerebral endoscopy at the beginning of the series but no previous experience in transsphenoidal endoscopy.

Material and Instrumentation

For standard endoscopic procedures through the nose the same endoscope models as those used by ENT colleagues can be used. The system consists of rigid endoscopes 18 cm in length including 0°, 30° and 45° (Karl Storz ® & Co, Tuttlingen, Germany) connected to a HD flat screen via a full HD camera using a 3CCD Xenon light source. Storz ® produces also an irrigation system (Clear Vision) that can be activated with a foot pedal, but depending on the technique some operators will prefer to irrigate directly using syringes, especially if performing a 4 hand technique as is the case in our team. A holder can also be used but one has to be aware of the loss of the depth impression given by a dynamic use of the endoscope.

Even if it uses the same corridor as the microsurgical procedure the endoscopic procedure requires dedicated instruments that are straight, non bayonet and whose articulation is kept in the rear of the instrument with a straight and thin element going through the nasal cavity, be it a scissor, a rongeur or a forceps as for example the Cappabianca bipolar forceps (Fig. 3.3: left). These so-called single shaft coaxial instruments (Fig. 3.3: right) allow for maximizing angle of rotations and minimizing at the same time the obstruction in small working corridors, which is definitely more limited with standard 2-shafted microsurgical instruments[349]. Ideally the head of the instrument should also be rotatable so as to allow the hand to take a natural position and there is no need for the hand to take a twisted position to modify the position of the tip. The development of single-shaft low profile instruments is not an phenomenon limited to endoscopic neurosurgery: also in microsurgery the development of new approaches with very limited or no brain retraction has motivated the development of such instruments[231].



Fig. 3.3: Above left: example of single-shaft bipolar forceps with pistol grip designed for endoscopic surgery. Above right: example of coaxial scissors with rotatable blades and coaxial biopsy forceps. Bottom left: bipolar forceps allowing simultaneous aspiration at the upper tip of the forceps. Bottom right: same as above left but with curved tips, allowing for para-axial coagulation.

Patient positioning and preparation

The patient under general anesthesia is placed in a recumbent position with a minimal elevation of the head. The right shoulder is positioned at the right upper corner of the operating table. Some authors will turn the head 10° towards the operating side, we prefer to keep it straight. During the preparation phase the head is fixed in a Mayfield clamp as the navigation is used in most of the procedures. If a limited procedure is planned and no navigation is needed the head can be supported on a horseshoe, which avoids the pain of the fixation pins of the Mayfield and allows for some lateral movements of the head during the procedure which can in some instances increase visualization. The nasal mucosa is decongested with cotton pledgets soaked in adrenaline 1:5000 (1ml of adrenaline 1mg/ml diluted in 4 ml saline) placed in the middle meatus. In addition, the mucoperiosteum of the lateral nasal wall and the mucoperiosteum and mucoperichondrium of the septum are infiltrated with a Lidocaine / Adrenaline solution (1% lidocaine and 1/200.000 adrenaline). The endotracheal tube is fixed on the left side in order not to disturb the operators who will stay on the right side. At this moment an oro-gastric tube is placed in order to allow suction and evacuation of the blood that can flow down during the procedure. The oral cavity is also

packed with gauze around the oro-tracheal tube to further prevent blood from reaching the stomach. This is important as blood into the stomach will act as a potent emetic and will thus be responsible for postoperative vomiting that can lead to unnecessary measures, even emergency CTs because of undue suspected acute intracranial complication.

Lumbar drains are not routinely placed but are reserved for special situations such as revision surgery or in the presence of an expected large basal defect with planned extensive reconstruction of the skull base including a naso-septal vascularized pediculated flap, as for example in the case of a giant adenoma. More detailed description regarding the different reconstruction options and their indication are not the subject of this chapter and will be discussed in the chapter dealing with the so-called non-pituitary pathologies of the anterior skull base.

During the induction phase a bolus of Solu-Cortef 100mg is given according to the standard stress-prophylaxis schema established by the colleagues of the endocrinology department. The patient also receives a bolus of A single dose of cefamandole (2nd generation cephalosporine) is given prior to starting the procedure.

The nose and region of the upper lip are prepped with Betadine[®]. The entry of the nasal cavities is also prepped with cotton woods soaked in Betadine[®]. The draping is made with a U-shaped drape folded around the crest of the nose and with a straight drape taped at the upper lip. Depending on the planned reconstruction the periumbilical region and the right lateral thigh are prepped and draped for fat or fascia lata harvesting.

Nasal phase

The procedure usually starts with a 0° Storz endoscope. The approach is performed under induced hypotension (< 110 mmHg syst.) and begins with an inspection of the nasal cavities to recognize the anatomic landmarks. The arch of the choane, the lower and medial turbinates and the nasal septum are identified (Fig. 3.4) as well as irregularities such as septal deviation. Moving more posteriorly under the inferior turbinate the medial border of the choane can be seen, consisting of the vomer which constitutes a medial landmark. Once the orientation is made the procedure begins with a gentle lateralization without resection of the medial turbinate on both sides with care not to disrupt the mucosa. Gentle handling of the mucosa will avoid bleeding with repeated blurred vision from permanent oozing blood. We do not perform a systematic complete right middle turbinectomy as usually recommended [194] or even a resection of the inferior half of the middle turbinate as proposed as a limited alternative[341] because we usually had sufficient working space with the bilateral lateralization of the middle turbinate in most of the cases of pituitary tumors. Only in particular situations with septal deviation or particularly narrow anatomy we have found it necessary to resect the middle turbinate. Nonetheless it is important not to apply excessive force during the mobilization of the middle turbinate as this could lead to breaking its insertion and in extreme cases to a fracture of the anterior skull base with risks of CSF leak.

If a large arachnoid defect is expected the sphenopalatine artery is identified and a nasoseptal flap prepared for watertight closure[137].

At this stage of the operation the sphenoid ostiae should be visualized, they can be found 1.5cm above the upper limit of the choane. Sometimes the ostiae are covered with mucosa and in this case they will be identified with a blunt instrument such as a freer.



Fig.3.4a: Right nostril with middle turbinate (MT) and nasal septum (NS). Fig. 3.4b: same nasal cavity after lateralization of the MT and identification of the ostium sphenoidale (blue arrow).

Sphenoid phase

After identification of the sphenoid ostiae the sphenoethmoidal recesses and the region around the ostiae are coagulated in order to minimize bleeding from septal branches of the sphenopalatine artery. Both ostiae are widened using Cloward punches. We have found it practical to use 2 or 3 mm punches with turnable head for this phase. After widening of the ostium sphenoidale on both sides an anterior sphenoidotomy with posterior septectomy is performed. This can also be performed with Cloward or Hajek punches or with a high speed drill. For the resection of the posterior part of the nasal septum the back-biting punch developed by professor Stammberger from the ENT department of the University of Graz in Austria is a very convenient instrument. Another possibility is of course to use a soft-tissue shaver. Some authors have recommended to perform a superior window in the septum rather than a complete posterior septotomy as a more limited approach[341].

The anterior sphenoidotomy has to be large enough as this will be the most narrow part of the long working corridor to the sphenoid sinus and the opening should provide enough space for the endoscope itself and for at least two instrument and is needed if a two nostril four hand technique is to be used[43]. It should also allow for the use of long instruments that may be angled which have to be used with larger tumors[232] and it has to allow inferiorly for the placement of the suction under the sella and superiorly for visualization up to the planum sphenoidale. However care must be taken as not to extend the anterior sphenoidotomy too far infero-laterally in order not to injure the sphenopalatine artery. The resection of the posterior part of the nasal septum is important not only to provide space but also because it will avoid that the instruments introduced on one side push the mucosa of the septum to the contralateral side against the tip of the endoscope thus causing repetitive blurring of the vision. At the beginning of our series as we did rather limited opening we regularly encountered this problem that was rapidly solved by adopting a more radical resection of the posterior part of the nasal septum. At the same time care must be taken not to extend the septotomy too far anteriorly; the anterior margin of the middle turbinate is recommended as the anterior limit of the septotomy[232].

Once the access to the sphenoid sinus is achieved the anatomical orientation can be done (Fig 3.5). In order to see the bony landmarks clearly and to avoid oozing blood during later phases the mucosa of the sphenoid sinus is stripped off with a rongeur. Usually we resect the whole mucosa of the sphenoid sinus but again some authors do only resect the mucosa in the immediate perisellar region and resect beyond these margins only if the parasellar anatomy is not obvious on primary inspection[341].



Fig. 3.5: panoramic view of the sella after resection of the mucosa with identification of the sella (S), clivus (C), internal carotid artery (ICA) under the carotid protuberances on both sides, planum sphenoidale (PS).

The bony septum of the sphenoid sinus, the so-called intersphenoid sinus, is also resected. Here care must be taken as to its orientation because not rarely they are asymmetrical or even lead laterally to one of the carotid protuberances. This will best be evaluated preoperatively on the bone window of a CT scan as other anatomical particularities such as presellar conchal sphenoid sinus or Onodi cells which will be recognized on coronal CT images as a horizontal septum in the upper part of the sphenoid sinus. The midline will be appreciated by looking at the mid-point between the carotid protuberances or opticocarotid recesses. Once the sella is opened the mid-point between the medial walls of the cavernous sinuses can also be used to localize the midline.

Sellar phase:

If the approach up to the sellar floor is done by the ENT member of our team, at this point the real team work starts with the 3 hand technique. The opening of the sella is

done either with 2 and 3mm Cloward punches or with a diamond burr. When opening with punches the initial perforation can be done with a small bone chisel allowing then to introduce the small Cloward punch. In the presence of a macroadenoma the sellar floor can be so eroded that a blunt opening with a dissector is also possible. Seldom in the presence of an acromegaly, the bone can be so thickened that it has to be opened with the diamond burr. If possible a square piece of bone should be saved as this can eventually be used at the end of the procedure for the sellar reconstruction, either by using it simply as an element for the reconstruction of the sellar floor[80] or as a "buttress" in the gasket-seal closure as described by Schwartz et al [222]. The opening of the sella is extended inferiorly to the sellar floor and laterally up to the proximal margin of the ICAs as identified anatomically, with the neuronavigation (Curve, BrainLab, Germany) and with intraoperative micro-Doppler[82]. The identification of skull base structures during endoscopic sinus and anterior skull base surgery has been demonstrated in a study on mental workload and ergonometric to be one of the phases of these procedures that benefit the most from the navigation (Stelter and colleagues[352]: oral presentation at the 21. Jahrestagung der Gesellschaft für Schädelbasischirurgie, Tübingen, 11-13th October 2013. Mentale Arbeitsbelastung und Ergonometrie bei endoskopischen Nasennebenhöhlen- und Schädelbasiseingriffen). Superiorly the bluish color of the dura will eventually allow for identification of the superior intercavernous or circular sinus[47] and the resection is done so as to offer enough working space for the instruments without going too close to the tuberculum sellae in order to avoid a dural tear and CSF leak at this place. As the suprasellar arachnoid is close to the superior intercavernous sinus one will avoid coagulating too aggressively in its proximity, again in order to avoid a CSF leak. Instead passive hemostats can be used to control this venous bleeding, such as oxygenated cellulose (Tabotamp ®) or collagen (Helitene ®). In some instances a small dural vessel can be identified which provides reliable localization of the midline[232].

Opening of the dura

The dura is opened sharply, using either N° 11 or 15 blades or dedicated micro blades or scissors. Some recommend to introduce these sharp instruments through a nasal speculum so as not to avoid unnecessary injuries to the nasal mucosa[232]. The incision should cut only the dura and keep the underlying tissue, in particular pituitary capsule and the tumorous pseudocapsule, intact. Different types of incisions have been described, for example H- or reverted U-shaped. Here also care has to be taken in order not to go too far superiorly and incise the arachnoid fold. If a wide exposure is necessary the corners of the dural window can be incised diagonally. Cauterization will result in shrinkage of remaining dural folds or corners.

Tumor resection

The resection of the adenoma is performed with two hands using suction and dissectors, rarely curettes. No endoscope holder was used in order to keep the pseudo-depth perception given by the dynamic movements of the endoscope[357, 358] and apply thus the three-hand technique recommended by Kassam[194]. In most of the procedures the neuronavigation was used. During the last 2 years of the series a micro-Doppler[82] was

systematically used to confirm the information of the navigation regarding of the internal carotid artery (ICA).

It is accepted that a so-called pseudocapsule can be found at the interface between the normal pituitary gland and the tumorous tissue, an observation already made at the beginning of last century[56]. Lee et al could identify a clear pseudocapsule in more than 55% out of 616 cases of pituitary adenomas [221]. They also observed that a pseudocapsule was more often present in prolactinomas (70%) than in GH- (55%) or ACTH-secreting adenomas (40%). As it has been observed that tumor cells are present in the pseudocapsule and even into the adjacent pituitary gland it is recommended to use this plan to perform a so-called extra-capsular dissection [195]. This dissection is best performed using a traction-countertraction technique with either 2 instruments or with microcttonoids and will start logically inferiorly then proceeding laterally and finally cranially. The control for tumor remnants can be done using 30 or 45° endoscopes as these will allow to look around the corner and inspect for example upwards in the direction of the optic chiasm or laterally towards the medial wall of the cavernous sinus. The medial wall of the cavernous sinus is a structure that can be readily seen at the end of the resection using an angled endoscope. Controversy remains as the exact composition of this medial wall [76, 394] and some author think that most large adenomas do not invade the cavernous sinus but merely compress its medial wall (Kassam, notes at the course on "Minimally Invasive Endoscopic Surgery of the Cranial Base and Pituitary Fossa", Pittsburgh, 23. – 25. September 2007). Further the inspection can be optimized by performing it underwater while infusing saline under light pressure into the sella and tumor cavity. This will optimize the vision, facilitating the identification of the tumor-gland interface and eventually also mobilize tumor remnants. Once the margins of the tumor are clearly defined it can be mobilized en-bloc or in the case of a macroadenoma it will be entered sharply and debulked before fragments are mobilized. In many cases the relative fluid consistence of the macroadenoma will facilitate the descent of the cranial elements and the arachnoid will soon appear into the field of view but sometimes the tumor is so rigid that no spontaneous descent happens. In these cases the operator can ask the anesthesiologist to perform a Valsalva maneuver in order to increase lightly the intracranial pressure which will force the most cranial remnants to descend.

Hemostasis and closure

Once the resection is completed the resection cavity is rinsed abundantly with saline. In general satisfactory hemostasis can be achieved without the application of any further material, especially if the tumor resection is complete. In cases where bleeding sources remain active the hemostasis will be reached with the application of topic hemostats such as Tabotamp or Helitene as most of the remaining bleeding sources are venous. Another hemostatic mean recommended by Kassam and Carrau (personal notes during course on endoscopic skull base surgery, Pittsburgh 2008) is the use of warm Ringer solution. Seldom have we found it necessary to use more elaborated materials such as FloSeal or Surgiflo which combine gelatin with human thrombin and are more expansive. They can however be very helpful in the presence of diffuse oozing without

clearly identified sources. Even if bleeding remains minor in most of the cases it remains of concern as it will obscure the field and thus diminish precision and security. In order to better control this permanent "oozing" of blood with its consecutive blurred vision, Locatelli and colleagues[228], from the Universitiy of Pavia in collaboration with the group of Paolo Castelnuovo from the Department of Otorhinolaryngology of the University of Insubria, in Varese, Italy, have developed a special technique which they called "diving technique". They have applied it in more than 350 surgeries and claim that by performing part of the procedure under water or performing an intrasellar hydroscopy, they get better control of the small bleedings otherwise regularly disturbing pituitary surgery, especially from the cavernous sinus. They also report to find more easily a plane of dissection between normal pituitary gland or cavernous sinus and tumor tissue by using continuous flushing as water dissection. So the technique offers an optimization of the visualization through better bleeding control and is an adjunct for careful dissection.

Once a satisfactory hemostasis has been achieved the reconstruction is done using a variety of materials. For smaller lesions and without the observation of intraoperative CSF we have proceeded initially to fairly simple closure using mainly gelatin and fibrin glue. If CSF was observed intraoperatively and the leak was not identified or very small we have generally found it useful to use small autologous free mucosal graft taken either at the septum or at one of the middle turbinates. In the presence of a large arachnoid defect we have harvested fascia lata and fat from the lateral right thigh. In the presence of very large tumors where the risk of intraoperative CSF leak was primarily judged to be high the pediculated vascularized flap after Hadad-Bassagasteguy[137] was prepared at the beginning of the procedure as well as a piece of fascia lata and the patients received a lumbar drain for 4 days preoperatively. A recent study demonstrated with the systematic use of intraoperative fluorescein that the occurrence of an intraoperative CSF leak during classical pituitary surgery was much more frequent than expected[178], reaching 44% in tumors <2cm and 72% in tumors >2cm. They concluded that tumor diameter and volume were the best predictors of intraoperative CSF leak, becoming significantly more frequent at a diameter of 2cm and above a volume of 1.5cm³ and recommended the use of a decision algorithm including the systematic use of lumbar drain and HBF for lesions >2,5cm. This recommendation is in accordance with the attitude we adopted from the beginning. The only element that was modified during the second half of the series is the introduction of a solid element in the reconstruction of the sella even in the absence of intraoperative visible CSF leaks because we have observed cases of delayed leaks after high pressure maneuver as for example sneezing causing a tear in the arachnoid. In order to avoid these very frustrating occurrences we have adopted a more systematic reconstruction of the solid part of the sella, as recommended for example by Dufour et al[80].

Own experience

Material and methods

Data were collected retrospectively of all the patients operated primarily for a sellar lesion microscopically or endoscopically in our institution between November 2004 and August 2012. Patients operated on transcranially for a sellar pathology were not included. Data collected included demographics, diagnosis, characteristics of the lesion, perioperative and postoperative course including complications, evaluation of the pituitary function and resection rate. Clinical data collected included age, sex, weight, height, time of onset of the first symptoms, time of diagnosis, neurological signs, time of first imaging and the presence of relevant associated diseases. All the images were reviewed to collect the data about the lesion itself which included dimensions of the lesion, the presence of bleeding, compression of the chiasm, deviation of the pituitary stalk, cavernous sinus invasion and surrounding of the internal carotid artery; the lesions were classified on preoperative MR-images according to the Knosp-Steiner classification[202]. Procedure characteristics such as duration of the procedure, blood loss and intraoperative as well as postoperative complications including cerebrospinal fluid leaks and persistent fistula and the way they were managed, bleeding, diabetes insipidus, pituitary insufficiency, infection and presence of a tumor rest were collected; evaluation of the resection and tumor rest was done in 3 months postoperative MRimages. The tumor rests were measured and classified in small and large rests depending if the volume of the rest measured more or less than one ml. Statistics were conducted by Fisher's exact and student's t-tests.

Results, comparison with the literature

In total 116 patients have been operated on transsphenoidally between November 2004 and August 2012; 52 were operated endoscopically and 64 microscopically. (E: n=52, M: n=64; +/- 10-19 cases/yr.). There was no randomization of the patients between the two techniques; they were operated on according to the availability of the surgeons and, at the beginning, according to the feasibility of the procedure by the endoscopic team. Age and gender distribution did not differ between the two groups (mean=54yrs, 67% male). Mean follow up was 35 months (range 01.4-95).

During the first 3 years of the observation period the colleagues of the Department of Endocrinology have compared the results obtained endoscopically and microscopically in order to have a first evaluation of the new technique and also in order not to miss any unfavorable development. The charts of patients who were referred for transsphenoidal pituitary surgery during this period were reviewed. Descriptive and nonparametric (Mann-Whithney-U-test) statistics were used for analysis of these data. During these first 3 years of observation 31 and 26 patients were operated microscopically (M) and endoscopically (E) respectively. Pituitary lesions consisted of endocrine inactive tumors and cysts (17M/18E), GH-producing tumors (11M/3E), ACTH-producing adenomas (3M/2E) and prolactinomas (0M/3E). Percent tumor volume reduction (82 vs. 93%, M vs. E) and the percentage of patients with small (<1ml) residual tumors (88 vs. 79%) were comparable (Fig. 3.6) as were the effects on pituitary function (Fig. 3.7) (unchanged 21M vs. 18E, improved 7M vs. 5E, deteriorated 3M vs. 3E). Resolution of hormone excess was achieved in 36% (M) and 38% (E) of the patients.

Fig. 3.6: Tumor resection; small is < 1ml.

Fig. 3.7: Pituitary function in postoperative course.

During this initial observation period of 3 years, observed complications can be summarized as follows: transient postoperative diabetes insipidus occurred more frequently in the endoscopic group (33% vs. 7%), whereas no difference was observed for other perioperative complications (SIADH 3 vs. 7%, cerebral salt wasting 0 vs. 4%, postoperative liquorrhea 13 vs. 15%, postoperative infections 3 vs. 11%, revision surgery 13 vs. 12%, M vs. E) (Fig. 3.8). Our colleagues from the endocrinology department thus concluded that during this initial transition period a similar extent of tumor resection and cure from hormone excess in endocrine active tumors could be achieved. Besides the transient postoperative diabetes insipidus that was higher in the endoscopic group, no other complication was increased in the endoscopic group as compared to the microscopic group.



Figure 3.8: Postoperative complications.

After these first observations the technique was further implemented and during the rest of the observation period the proportion of endoscopic procedures steadily increased (Figure 3.9). Neuronavigation was used in 80% of E-cases, but never in M-cases where fluoroscopic imaging was used systematically.



Figure 3.9: increasing proportion of endoscopic procedures during the observation period.

The most frequent pathology was hormone inactive adenoma (60% E, 51% M, see Table 3.2). The endoscopic group (E-group) consisted of larger and more invasive lesions, although not significant (Table 3.3).
Pathology	Microscopic	Endoscopic
Hormone	33	31
inactive		
PRL*	1	9
ACTH**	5	4
GH***	14	3
Rathke's cyst	5	3
Others	6	2
Total	64	52

Table 3.2: Distribution of the pathologies in the 2 groups.*Prolactinoma **Cushing *** Growth hormone secreting adenoma

	Micro	Endo
Giant : >40mm	8%	19%
Knosp Grade IV	8%	20%
Bilateral cav. sin. invasion	16.1%	31.4%

Table 3.3: Incidence of giant, Knosp Grade IV and bilateral cavernous sinus invasion.

The duration of the procedures (Figure 3.10) was stable in the experienced M-group (+/- 94 min). The E-group showed a clear learning curve in mean operation-time (2004-2007: 154 min, 2008-2012: 93 min).



Figure 3.10: learning curve.

Intraoperative CSF leaks were seen in 31% (E) vs. 42% (M) of cases (Table 3.4). More Ecases were re-operated, however more M-cases received a lumbar drainage (5 vs. 1, 8 vs. 19 patients respectively). In both groups 2 patients had to be re-operated because of a large residual tumor. The ICA was damaged in 1 E-case where a large calcified macroprolactinoma invaded the wall of the ICA. After rapid tamponnade the vessel lesion has been treated endovascularly with success and the patient showed very mild residual symptoms after 1 year follow-up. Transient postoperative diabetes insipidus (DI) occurred significantly more often after an endoscopic operation (17 vs. 5%, p=0.03), however, there was no significant difference in long term with persistent DI in 2 endoscopic cases and 3 microscopic cases. Postoperative anterior pituitary dysfunction rate in formerly intact patients was higher in the micro group (25% vs. 19%). Improved visual outcome was similar in both groups with 46%, although patients in the E-group had longer preoperative visual deficits and more chiasm compression (mild or severe chiasm compression in 72.55% (E) and 51.57% (M)). Total resection was better in microscopic patients (48% vs. 42%) by trend, whereas after endoscopic operations a small residuum (<1ml) was seen more often (38% vs. 29%). A large residuum (>1ml) was seen in 20% (E) vs. 23% (M) of patients.

Complication	Microscopic	Endoscopic
CSF intraop.	27 (42.2%)	16 (30.8%)
CSF leak postop,	2 (3.1%)	5 (9.6%)
Infection	1 (1.6%)	1 (1.9%)
DI ¹ perioperative	2 (3.1%)*	9 (17.3%)*
DI ¹ permanent	3 (4.7%)	2 (3.8%)
SIADH ²	7 (10.9%)	2 (3.8%)
ICA ³ injury	1 (1.6%)	1 (1.9%)

Table 3.4: Complications.

1DI: diabetes insipidus. 2 SIADH: syndrome of inappropriate diuretic hormone. 3 ICA: internal carotid artery. *Statistically significant: P<0.05

Discussion

Our retrospective study shows that the introduction of the endoscopic technique was not associated with a relevant higher incidence of complications. It presents several limitations as it is a retrospective study comparing two surgical teams in a low volume center.

Although long-term results from the literature comparing outcomes with microscopic and endoscopic techniques are still missing, a systematic review of the reported literature on endoscopic pituitary surgery analyzing 9 studies and pooled data from >800 patients suggests that endoscopic transsphenoidal surgery is similar in effectiveness and risks as compared to traditional approaches[354]. Evidence is lacking of proof of the supposed superiority of endoscopic transsphenoidal surgery. Another systematic review of the literature comparing microscopic versus endoscopic surgery in the treatment of pituitary adenomas[309] showed that major outcome measures (extent of tumor resection, changes in hormone levels) did not differ between the two approaches. Other factors like complications, time in the operating room, length of hospital stay and patient discomfort were significantly less in the endoscopic approach. However 10 of the 11 studies compared groups <30 subjects. Regarding the improvement in functioning pituitary adenomas one study showed that the endoscopic technique was superior in non-invasive macroadenomas but did not differ in microadenomas or invasive macroadenomas[61].

Some of the marginal differences in the rate of resection observed between the two groups can be at least partially explained by the slight differences in the two groups, with a tendency for larger and more invasive tumors associated with longer duration of visual deficits as well as more preoperative hormonal deficits in the E group. Regarding the CSF fistulas, although the E series had less intraoperative leaks there were more postoperative revisions. The incidences of revision and lumbar drainage reflect the different approaches regarding their management. The experienced M surgeon preferred to try to get patients dry with the application of a lumbar drain in the postoperative period if CSF leak would persist or appear. The E team tried to avoid the patient the discomfort associated with lumbar drainage for several days and if the reconstruction technique was not optimal from the beginning it improved with experience: 4 of our 5 postoperative CSF fistulas concerned the group of the first 26 patients, in the second half of the series only one case presented a postoperative fistula. This reflects the improved reconstructive technique of the sellar defect adopted, an observation also reported by other authors[83]. The pediculated vascularized septal flap after Hadad was performed in patients with very large lesions where the probability of CSF fistula was assessed as high and seemed to have a protective effect, as only 1 out of 6 cases with large lesions and Hadad flap had to be revised. With an incidence of postoperative CSF fistulas of 9.6% our endoscopic series is comparable with data of the literature, as shown by the systematic review by Rotenberg which showed a mean incidence of 14.3%[309] or by the meta-analysis of Ammirati (Ammirati 2012) where it was evaluated to be 7.00% (4.84% to 9.52%).

In contradiction with other observers[339] we observed a higher incidence in transient postoperative DI in the E group, but the incidence of persistent DI was consistent with observations of the Ammirati analysis[7] where an incidence of 2.31% (1.41% to 3.41%) was reported.

There are several ways to use the endoscope for transsphenoidal pituitary surgery. These range from endoscopic-assisted microscopic surgery using a speculum, singlesurgeon single-nostril endoscopy with limited sellar opening, single-surgeon dual nostril endoscopy with extended exposure and finally to dual surgeon dual nostril endoscopy with expanded exposure (so-called expanded endonasal endoscopic approach, EEEA) [392]. In our institution we adopted the EEEA in 2004 without a period of transition. A period of transition is certainly mandatory in institutions where a single-surgeon technique is adopted or when both surgeons don't have any experience with the endoscope. In our situation we could directly switch to the EEEA because of previous experience with other endoscopic operations. As stated by several authors, these factors are decisive to reach a less steep learning curve[176, 347].

Even if reduction of postoperative discomfort is not the most important issue, it is a point that has also to be taken into consideration. In our series, 3 of the endoscopic operated patients had been operated on microscopically years before and their reactions to the new procedure was unanimous: one of the patients, when visited on the intensive care unit on the afternoon of the procedure, asked when he would be at least operated on and could not believe he was already operated. The 2 others also reported that there was no comparison regarding the pain and breathing discomfort. As for today, even if the endoscopic technique has become the standard technique in most larger neurosurgical clinics, the results of published studies were able to demonstrate its safety stated that the results were comparable with the traditional microscopic technique but with the exception of the noninvasive functioning macroadenomas a clear superiority in functional outcome has not been demonstrated. A recently published large series from Pittsburgh with retrospective analysis of 555 patients operated endoscopically concluded that the remission and complication rates were comparable to those of previous microscopic and endoscopic series and that an ideal comparison between the two techniques would only be provided by a randomized controlled trial, something they judged as very unlikely to ever happen[269].

Conclusion

Between 2004 and 2012 endoscopic technique was not better, yet not worse in its introduction phase. Considering the small sample size and the comparison of a learning endoscopic team with a very experienced microscopic neurosurgeon better results are to be expected in the future with increasing experience and the refinements of operative techniques.

Other "non-pituitary" lesions of the anterior skull base

Introduction

In the past years endoscopic neurosurgery has gained much popularity in transnasal and other minimal invasive approaches to intracranial lesion. In anterior skull base surgery the use of the endoscope transnasally represents an attractive alternative to classical bifrontal craniotomies for evident reasons of avoiding large incisions, craniotomy and brain retraction. On the contrary, opponents of endoscopic neurosurgery have pointed out correctly that the implementation of this technique has not led to a decrease of complications such as CSF leaks and infections[206]. However, Kassam et al. showed in 800 patients that endoscopic transnasal neurosurgery is equivalent to transcranial approaches concerning CSF leaks and infections, although there seemed to be a learning curve as was also shown in transcranial approaches in the past[192].

Skull base lesions that have been operated endoscopically through the nose, either transsphenoidally or trans-ethmoidally, include in first line meningiomas of the anterior skull base; these meningiomas arise either from the tuberculum sellae region or from the olfactory groove/ethmoidal region. In the same region rarer tumors such as esthesioneuroblastomas can also be reached. Clivus chordomas also represent a lesion that can be reached directly through the transsphenoidal approach. Remaining on the midline the cranio-cervical junction can be reached and represents the inferior limit of the accessible area via the endoscopic transsphenoidal route. This approach represents an alternative to the gold standard transoral approach for lesions of the rostral craniocervical junction and it avoids the disadvantages of the transoral route[58]. It will allow the resection for example of the odontoid process as it can be indicated in rheumatoid arthritis with craniocervical settling or in the presence of an expanding pannus or the resection of extradural or intradural tumors involving the rostral craniocervical junction [193, 328, 390]. It can also be indicated in the case of malformations of the craniocervical junction such as basilar invagination[122, 272] or Chiari [144] or in the setting of post-traumatic lesions as with nonunion or odontoid fractures[91].

Meningiomas of the anterior skull base

The anterior skull base is made of 3 bones: the ethmoid bone with its lamina cribrosa, the frontal bone with the posterior wall of the frontal sinus limiting anteriorly the anterior skull base and the sphenoid bone with its lesser wing being the posterior margin of the anterior skull base[298].

The medial wall of the orbit representing the lateral limits for an endoscopic transnasal resection, meningiomas of the anterior skull base amenable to endoscopic pituitary surgery will be located in the vicinity of the midline (Fig 3.11). These so-called "anterior midline skull base (MASB) meningiomas" constitute 12-20% of all intracranial meningiomas[290] and comprise, from posteriorly to anteriorly, tuberculum sellae meningiomas, meningiomas of the planum sphenoidale and olfactory groove meningiomas. Already in 1938 in one of the first large publications on meningiomas Cushing and Eisenhardt noticed the differences between olfactory groove and tuberculum sellae meningiomas, separated in space by 2 cm and harboring very different clinical presentations, the tuberculum sellae meningiomas presenting classically quite early with visual symptoms whereas olfactory groove meningiomas were more insidious and could reach a much larger size before causing headache or mental changes.



Fig. 3.11: region of interest for "midline anterior skull base meningiomas".

Because tuberculum sellae and planum sphenoidale meningiomas are operated via the same transsphenoidal approach and present similar complications they will be regrouped in the group of the so-called "parasellar" meningiomas (Fig.12). Olfactory groove meningiomas are operated via a transethmoidal (or transcribriform) route and present different specific difficulties and complications.



Fig. 3.12: Transsphenoidal (blue) and transethmoidal (red) routes for respective parasellar and olfactory groove meningiomas.

Approaches for midline anterior skull base meningiomas

Traditionally meningiomas of the anterior skull base have been approach via different types of craniotomies including a classical pterional or a subfrontal (unilateral, supraorbital, and oblique approach), bifrontal, lateral supraorbital, and lateral suboccipital craniotomy. An anterior interhemispheric approach has also been used and still has its advocates today who claim a decreased risk for the olfactory nerves because of the absence of retraction of the subfrontal brain surface from the orbital roof as well as a decreased surgical risk to the microvascualture[59]. Finally with the development of endoscopic pituitary surgery these lesions have also been resected via either a transsphenoidal or transethmoidal route, depending on their location in the anterior skull base. The raising interest for the endoscopic technique was greatly motivated by

the obvious avoidance of brain retraction. However, since the publications of endoscopic series or reports at international meetings on skull base surgery for meningiomas who made it clear that the main problem of the endoscopic technique remained the water-tight reconstruction, other minimal invasive techniques have regained in interest. For example the fronto-temporal craniotomy combined with an orbital osteotomy (removal of the supraorbital bar) and optic canal unroofing (bilaterally, if needed) or a small frontolateral craniotomy, or a craniotomy performed through an eyebrow or an eyelid incision represent modern alternatives[334, 360].

Parasellar meningiomas

Tuberculum sellae meningiomas and planum sphenoidale meningiomas represent ideal targets for endoscopic transsphenoidal surgery both from an anatomic point of view and also as a didactic new target for surgeons who have mastered the endoscopic pituitary technique: they are located just above or in front of the pituitary gland, the most frequent target for the technique otherwise. As mentioned by Kulwin et al the transsphenoidal route represents an attractive alternative to the transcranial route because it is "a subchiasmatic approach for a subchiasmatic lesion" [214]. As these tumors tend to develop in the immediate vicinity of the optic nerves and chiasm, one of the decisive outcome factors will be the vision. One of the recognized difficulties in treating these lesions is the fact that some patient will still present some deterioration of their vision postoperatively. Because the transsphenoidal approach needs less or no manipulation of the optic structures it is expected to be more efficient regarding visual recuperation. It has already been demonstrated that visual decline after endoscopic surgery was lower than after open surgery [26, 77] but these results have been criticized because it was thought that meningiomas considered for endoscopic surgery were smaller than for open surgery thus minimizing the risks of postoperative visual decline[214]. The approach to parasellar meningiomas does not differ from the classical approach for pituitary tumors and thus will not be described here again. Regarding the closure, of course this step will have to be managed with great care as it will be systematically a grade 3 CSF leak (intradural nerves and vessels visible).

Olfactory groove meningiomas

Olfactory groove meningiomas are by definition based on the olfactory cribriform dura and can be accessed via a so-called transcribriform route. This approach involves a different sinonasal approach than perisellar meningiomas and their approach as well as their resection and the final reconstruction represent a kind of culmination in the spectrum of the pathologies addressed by the endoscopic interdisciplinary team. Gardner et al recommend that they be addressed by an experienced team, late in the learning curve[115]. The specific challenges of this lesion are due to its more anterior localization with specific approach and closure difficulties requiring anatomic knowledge and the necessary intradural microdissection with possible involvement of the anterior cerebral complex.

The goal of the sinonasal approach will be to create a working channel to the lamina cribrosa. This will require bilateral uncinectomies and ethmoidectomies associated to

bilateral sphenoidotomies joined by the resection of the rostrum and the intersphenoidal septum.

Own experience

Material and methods

Due to reports such as that from Cappabianca, Kassam or Neubauer the endoscope is becoming a valuable established tool that should be part of basic neurosurgical training in order to use the best approach possible in each case[37, 45, 192, 256]. In accordance with these innovations in the neurosurgical field, endoscopic transnasal resection of intracranial lesions was implemented in 2004. At first only pituitary tumors were operated with this technique as described in the previous chapter. After building up experience with pituitary lesions other pathologies of the anterior fossa were approached this way. We have reviewed our first 21 patients for complications as to whether endoscopic transnasal techniques are feasible at a small volume neurosurgical department.

A special permission of the BAG (Federal Office of Public Health) was obtained due to the retrospective nature of this study, as well as regular approval of the ethics committee of St. Gall.

Data were collected retrospectively of all the patients operated endoscopically for a lesion anterior of the sella in our institution between November 2005 and August 2012. Patients operated on transcranially were not included. Data collected included demographics, diagnosis, characteristics of the lesion, perioperative and postoperative course including complications, evaluation of the pituitary function and resection rate. Clinical data collected included age, sex, time of onset of the first symptoms, time of diagnosis, neurological signs, time of first imaging and the presence of relevant associated diseases. Preoperative images were reviewed to describe dimensions and invasiveness of the lesion, compression of the chiasm/optic nerves, deviation of the pituitary stalk, infiltration of the cavernous sinus invasion and encasement of the internal carotid artery. Intraoperative and postoperative data were collected: duration, blood loss, intraoperative as well as postoperative complications (< 30 days), bleeding, pituitary insufficiency, infection and resection grade. Final evaluation of the resection rate was conducted in 3 months postoperative MR-images. Residual tumor was measured and classified in small (<1 ml) and large (>1 ml) depending if the volume of the rest measured more or less than one ml. Statistics were conducted by Fisher's exact and student's t-tests.

Surgical technique

All procedures were performed by a team of one neurosurgeon (the author) and one endoscopic rhinologist (PD Dr. Jan A. Tasman). The author had 5 years of experience with cerebral endoscopy and microscopic pituitary surgery at the beginning of the series and 2 years of experience with endoscopic pituitary surgery. Dr. Tasman is an experienced endoscopic rhinologist. The procedure is conducted under induced hypotension (< 110 mmHg systolic blood pressure). The skull is fixed in a Mayfield clamp and the nasal mucosa is decongested with cotton pledgets soaked in adrenaline

1:5000 (1ml of adrenaline 1mg/ml diluted in 4 ml saline) placed in the middle meatus. In addition, the mucoperiosteum of the lateral nasal wall and the mucoperiosteum and mucoperichondrium of the septum are infiltrated with a lidocaine / Adrenaline solution (1% lidocaine and 1/200.000 adrenaline). The procedure always starts with a 0° Storz endoscope; depending on the situation a 45° endoscope is sometimes used. The first step consist in the lateralization of the middle turbinate on both sides; only in a few cases the size of the lesion or the local anatomical situation made the resection of one middle turbinate necessary. If a large arachnoid defect is expected the sphenopalatine artery is identified on one side and an HBF prepared for watertight closure[137]. After identification of the ostium sphenoidale on both sides an anterior sphenoidotomy with posterior septectomy is conducted. Then the neurosurgeon takes over and after identifying the surface of insertion of the lesion with the neuronavigation a diamond burr as well as 2 and 3mm Cloward punches are used to open the skull base. The resection of the pathology is performed with two hands using suction combined with dissectors or scissors and, depending on the consistency of the tumor the ultrasound aspirator can be used in some cases. No endoscope holder was used in order to keep the pseudo-depth perception given by the dynamic movements of the endoscope[357] and thus apply the three-hand technique recommended by Kassam[194]. In most of the procedures neuronavigation was used. During the last 2 years of the series a micro-Doppler was systematically used to confirm the information of the navigation regarding the position of the internal carotid arteries (ICA).

Results

In total 18 patients were operated endoscopically transnasally for lesions of the anterior skull base, excluding pituitary lesions. Seven patients were male. In 11 patients a resection was conducted and in 8 patients only a biopsy. One patient received first a biopsy and after diagnosis confirmation a resection was conducted a few weeks later. Mean age was 56 years for biopsy patients and 53 years for resection patients. Perioperative details of biopsy cases are summarized in Table 3.5, resection cases in Table 3.6. The most often resected pathology was meningioma (n=9) as shown in Figure 3.13. Size of the operated lesions have been calculated in ml and are shown in figure 3.14. As usually olfactory groove meningiomas reach a much larger size before they become symptomatic as compared with Tuberculum sellae meningiomas, which are diagnosed when they are small as they will rapidly cause some chiasmatic compression with visual disturbances.

Mean duration of surgery was 228 min (range 45 to 480 min). Nine of 11 resections had a Level IV complexity[192]. Eight tumors could be resected radically or only a small residue was left behind.

Pathology	Size	SBI	Approach	Complications	Clinical
					presentation
JOF	Spread through whole rhinobase	+	Trans nasal	No	Headache
Petrous schwannoma, type Antoni A	42*22*22	+	Trans nasal	No	Diplopia, blurred vision
Uterine leimomyosarcoma metastasis	22*22*7	+	Trans nasal	No	VI palsy
Squamous cell carcinoma metastasis	31*10*26	+	Trans maxillar, via F. rotundum	First biopsy non diagnostic, second biopsy	Trigeminal hypesthesia, VI palsy
Neuroblastoma metastasis	52*23*20	+	Trans nasal	No	Visual loss
Tuberculosis right orbit	31*20*11	-	Transorbital	No	Exophthalmos
Dural enhancement of unknown origin	Dural thickening	-	Transplanum	No	Diplopia, facial pain
Bronchus carcinoma metastasis	30*20*24	-	Trans nasal	No	Diplopia, facial pain

Table 3.5: Biopsy cases.

SBI: skull base infiltration. JOF: juvenile ossifying fibroma.

Pathology	Size	Level	Approach	Resection rate	Further treatment
Clivus chordoma	25*30*15	III	Transclival / transsellar	large residue	Proton beam
Schwannoma	42*22*22	III	Transclival / transsellar	large residue	Gamma-Knife
JOF	49*39*30	III	transorbital	radical	
TSM	9*9*4	IV	transtuberculum	small residue	
OGM	14*22*20	IV	transcribriform	large residue	Gamma-Knife
PSM	13*10*6	IV	planum sphenoidale	radical	
OGM	40*44*24	IV	transcribriform	large residue	Stereotactic radiosurgery
OGM	40*40*30	IV	transcribriform	radical	
TSM	13*12*12	IV	transtuberculum	radical	
OGM	33*33*28	IV	transcribriform	radical	
TSM	10*9*6	IV	transtuberculum	radical	
OGM	20*34*40	IV	transcribriform	small residue	

 Table 3.6: Resection cases.

JOF: juvenile ossifying fibroma. TSM: Tuberculum sellae meningioma. OGM: olfactory groove meningioma. PSM: Planum sphenoidale meningioma



Fig. 3.13: List of the 19 pathologies: 9 meningiomas, 1 schwannoma (biopsied and then operated), 2 JOF, 1 clivus chordoma, 4 metastasis, 1 tuberculosis, 1 dural enhancement of unknown origin.

Complications, use of lumbar drainage (LD) and re-operations indications for the resection operations are listed in Table 3.7.

Pathology	Complication	LD	HBF	Re-operation	Indication
clivus chordoma	-	-	-	-	
Petrous schwannoma	-	-	-	-	
JOF	-	-	-	-	
TSM	-	+	-	-	
OGM	-	+	+	-	
PSM	-	+	+	-	
OGM	-	-	+	-	
OGM	CSF leak, transient hydrocephalus	-	+	+	CSF leak: transnasal
TSM	-	+	-	-	
OGM	postop hematoma, pneumocephalus	+	+	+	hemorrhage: transnasal
TSM	CSF leak	+	+	+	CSF leak: transnasal
OGM	pers CSF leak, persistent hydrocephalus	-	+	+	1: CSF leak: transnasal, 2:CSF leak, pneumocephalus: craniotomy

Table 3.7: Complications of resection cases.

JOF: juvenile ossifying fibroma. TSM: Tuberculum sellae meningioma. OGM: olfactory groove meningioma. PSM: Planum sphenoidale meningioma. HBF: pediculated vascularized flap after Hadad-Bassagasteguy.



Fig. 3.14: Size of the operated lesions (in ml). Note the clear difference in size between TSM and OGM.

TSM: Tuberculum sellae meningiomas. OGM: olfactory groove meningiomas. PSM: Planum sphenoidale meningioma. JOF: juvenile ossifying firbroma.

Three postoperative CSF leaks, 2 pneumocephalus and 2 hemorrhages occurred in 4 patients. Preventive measure by lumbar drainage of CSF was conducted in 6 patients, of which 2 developed a persistent CSF leak. Two patients received an external ventricular drainage (EVD), one after intraoperative subarachnoid hemorrhage and consecutive hydrocephalus, another one because of extensive swelling of the frontal lobes. The first one eventually needed a ventriculo-peritoneal shunt. In spite of the other preventive measure by HBF, applied in 7 patients, 4 patients suffered from postoperative CSF leakage and/or pneumocephalus. These four patients all had to be reoperated at least once, as shown in Table 3. Two patients had to be reoperated a second time transcranially. In total 2 postoperative infections occurred, one due to a CSF leak, the other one probably EVD-associated. One patient was treated prophylactically with antibiotics after implantation of an LD. There were no procedure-associated vascular or nerve injuries. Anosmia was already present preoperatively in the 3 patients with large olfactory meningiomas; none of the other patients developed anosmia postoperatively. Mean follow up after resection was 30 months. Only a subjective outcome could be extracted from the charts. Good outcome was seen in 8 patients. Two patients presented neuropsychological deficits after they had developed a fistula with tension pneumocephalus, one of them also had suffered meningitis. One patient reported unspecific twitches without evident epilepsy.

Illustrative cases

Case 1

Case history

A 43 years old lady presented with a 3 months history of progressive diplopia to the left and a diminished sensitivity of the left ear. The neurological examination revealed left abducens palsy and a diminished sensation of the left pinna.

Imaging study

The MRI of the head revealed a 5 cm lesion of the petro-clival region with homogenous contrast enhancement (Fig. 3.15).



Fig. 3.15: Axial T1 weighted contrast-enhanced MRI (a) showing homogenous enhancement of the petro-clival lesion on the left-hand side (navigation images: "left is left") and vicinity of the ICA. Axial (b), and sagittal (c) CT demonstrating extensive erosion/destruction of the left petrous bone and clivus.

Approach

An endoscopic transsphenoidal biopsy was performed and the histological examination found a schwannoma Antoni Type A. An endoscopic transsphenoidal resection was performed and in order to reach the most postero-lateral parts of the schwannoma a suction tube was curved and integrated into the navigation system (Fig. 3.16).



Fig. 3.16: Suction tube with curved tip and navigation tracking device (Left). Intraoperative navigation screenshots shoeing position of the suctions 'tip (Right).

With this navigated suction tube and the 45° optic the most lateral part of the lesion could be reached and thanks to the rather smooth consistency of the lesion a nearly total resection could be achieved with tumor rests limited to capsular elements adherent to the left ICA (Fig. 3.17).



Fig. 3.17: Postoperative axial contrast enhanced MRI images demonstrating resection cavity and minimal tumor rest along the horizontal segment of the left ICA (red arrow).

The postoperative course was uneventful and radiological follow-up showed a small recurrence in the vicinity of the hypoglossal foramen 2 years after the operation. This recurrence could be controlled with gamma-knife radiosurgery which caused intermittent slight tongue palsy for less than 6 months. The follow-up over the next 4 years showed thus far no further evolution.

Discussion

Our data show that implementation of endoscopic transnasal resection of anterior skull base lesions is feasible in a low volume center with similar complication rates as compared to large volume centers in their beginning phase; however, as mentioned by experienced authors, special attention to training and cooperation with ENT must be paid[176]. Biopsies of lesions of the anterior skull base can be performed without problems in cooperation with an ENT surgeon.

Patients benefit increasingly of the minimal invasiveness offered by endoscopic approaches. Training programs should be adapted accordingly so that young neurosurgeons will be trained early in using an endoscope alike young neurosurgeons in the 60s and 70s after the implementation of the microscope. Kassam and colleagues showed that in a large volume center there was no difference between transcranial and endoscopic transnasal techniques as far as complications are concerned[192]. The central problem in transnasal anterior skull base surgery remains the incidence of postoperative fistula. This complication plays an even larger role in the resection of more anteriorly situated lesions[209]. In our study postoperative fistula of CSF and/or air occurred in 4 of 11 patients. In all of these patients a meningioma was removed, of which 3 were olfactory groove meningiomas with a diameter > 3 cm (58%,[209]). Nonetheless, others have reported lower CSF leakage rates of 20-33 % before implementation of the HBF[78, 102, 209]. After consistent HBF application a reduction of 30% could be accomplished [191, 209]. In our experience, HBF was introduced after the team visited a course on "minimally invasive endoscopic surgery of the cranial base and pituitary fossa" in Pittsburgh in September 2007. Between the years 2004 and 2012 in total 13 HBF were applied in primary transnasal skull base procedures, including pituitary pathologies. As confirmed during the revision operation, the fistulas all had developed at the anterior border of the reconstruction, where the flap was possibly too short. This is an identified drawback of the HBF for lesion reaching the posterior wall of the frontal sinus[244].

Two of our patients with postoperative fistula suffered a tension pneumocephalus, which was presumably also due to malfunctioning of the HBF causing a kind of valve mechanism. This complication is considered as rare after transsphenoidal pituitary surgery[316] and is possibly underreported in cases of anterior skull base surgery. It can lead to visual disturbances [36, 174, 395] or compression of the frontal lobes with decreased consciousness[312, 317]. For these reasons it has to be recognized as a potentially dangerous complication and therefore patients should be monitored closely. Next to HBFs, a preventive measure of postoperative CSF fistula is the LD placed directly postoperatively. Five of our patients received a lumbar drain, of which only 1 patient developed a postoperative CSF leak. None of the four patients with a postoperative CSF leak received a lumbar drain as treatment, but were reoperated instead, because the surgical team aimed at minimizing the daily discomfort caused by an LD. Kassam showed that in 23.6% of patients with a postoperative fistula, treatment with lumbar drain only was an alternative, but 76.4% of patients were operated anyway[209]. As this small series shows an advantage of perioperative lumbar drains, the surgical team has changed their protocol accordingly.

Persistent postoperative fistula are the most important risk factor for infections[209]. In our series 2 postoperative infections were diagnosed, both in patients with postoperative fistula, although one patient probably developed an EVD-associated meningitis. This stresses furthermore the importance of not only precise (intradural) resection but also precise closure, which is an easier task in transcranial approaches than transnasal. Therefore teamwork with an experienced endoscopic ENT surgeon is a decisive adjunct for small volume centers, especially during the implementation phase[176].

Regarding the resection of meningiomas of the anterior skull base, the most important complications happened with the largest lesions, with the exception of one case with postoperative CSF fistula after resection of a 1cm Tuberculum sellae meningioma that could be controlled with lumbar drainage for 4 days. Even if no strict limit in size can be given, the experience of the author and some data of the literature seem to plead for caution with the indication for transsphenoidal resection of lesions where the diameter of the skull base defect will be over 2.5 or 3 cm. this limit of 3 cm had already been mentioned in 2007 by Tabae and colleagues[355]. Some recognized skull base surgeons with large endoscopic experience have even mentioned that they have completely stopped with endoscopic resection of intradural lesions of the anterior skull base,

typically meningiomas. This is the case for example of Prof. André Grotenhuis from Nijmegen, Holland, who told the author during the 14th International Workshop on Endoscopic Neurosurgery held in Gent in December 2008 that he had experienced so often postoperative fistulas despite the application of multilayer technique that he thought of abandoning this approach for these pathologies. Another endoscopic neurosurgeon performing endoscopic pituitary surgery 4 days a week, Prof. Henry Dufour from Hospital La Timone in Marseille, said during his presentation on endoscopic pituitary surgery at the meeting of the "Société de Neurochirurgie de Langue Française" in November 2013 in Versailles that he abandoned this technique for meningiomas of the anterior skull base because he experienced too many fistulas. In their meta-analysis of 60 studies regrouping 1426 patients reported after operations for anterior skull base meningiomas and comparing endoscopic endonasal versus open transcranial resections, Komotar and colleagues concluded that the transcranial resection resulted in higher rates of total resections with lower postoperative CSF leak rates[207]. They also mentioned that if the endoscopic transnasal approach might be safe and effective in certain skull base meningiomas, careful patient selection and the use of multilayer closure techniques were essential. This survey showed that during the analyzed period the use of multilayer techniques and of pediculated vascularized mucosal flaps was not yet systematic and it can be anticipated that more recent series with a more systematic application of these reconstruction techniques will show different results.

Besides the size, the expected consistency and the clear encasement of neurovascular structures should also motivate the preoperative reflection. In the light of these experiences and of the latest data of the literature, the author's endoscopic team has decided to restrain endoscopic transnasal resection of anterior skull base meningiomas for lesions where the expected defect at the end of the resection will clearly remain below 3 cm of diameter. Because of the different clinical presentations of the 2 groups, one can reasonably expect that the number of transnasal endoscopic operations for olfactory groove meningiomas will rather decline in the next years whereas those for Tuberculum sellae meningiomas will remain stable, as they have greater chances of being diagnosed at a reasonable size where operators will find themselves confident regarding the water-tight closure. Moreover, as mentioned below in the detailed description of the pediculated vascularized flap after Hadad-Bassagasteguy, one of the limitations of this excellent reconstruction technique resides in its sometimes limited anterior extension which can become critic in olfactory groove meningiomas extending far anteriorly. This could be a second argument against this procedure and another cause of further decline of the endoscopic application for these lesions.

Another recognized risk factor for infection is the duration of surgery in which the cutoff of 4 hours has been proven to be important by the National nosocomial infections surveillance system in 2004[336]. This is in accordance with the observation that procedures with a higher level of complexity (IV and V;[192, 345]) have a higher risk for postoperative infections[209]. Our mean operation time of 3h48 hours was not optimal. Operating time of the patients that developed meningitis was indeed > 4 hours (480 and 240 min). Meaning that these patients had 2 risk factors for developing an infection: fistula and OR time > 4 hours. However, the mean operating time was significantly increased by one case with coagulation disorders not detected by routine preoperative testing. This led to permanent oozing during the nasal phase at the beginning and end of the procedure, whereas the meningioma resection itself was less of a problem. By further training duration of surgery should decline, as shown previously in a group of 54 endoscopically operated pituitary patients[100].

Vascular injuries, especially of the ICA, during microscopic pituitary surgery are reported in about 1% of the cases[52, 294] but have a higher incidence in anterior skull base surgery with more extended approaches where it can reach up to 5- 9%[57, 103, 114]. There were no vascular injuries in the series. Two patients showed abnormal high blood loss.

As mentioned above, one patient presented an undetected coagulopathy and another one bled uncommonly from the mucosa.

Cranial nerve injuries can occur in up to 1.8% of cases during endoscopic anterior skull bases surgery[192] but none were observed in our series.

Our study is limited by the small sample size and retrospective design, which made statistical comparisons of our data with previously published series impossible. It was decisive for the author and is certainly wise to have performed a fair amount of endoscopic "standard" procedures such as pituitary adenomas. The author suggests more than 30 procedures, in order to acquire routine in team work with ENT and in endoscopic handling for the neurosurgeon before proceeding to the next step. Future research should focus on broad exposure and training of endoscopic techniques, especially for neurosurgical residents who have few opportunities to familiarize themselves with the endoscopic environment. This problem has already been recognized, as shown by the efforts made to offer other training options including simulation models[19, 106, 161, 256].

Conclusion

Our series shows that endoscopic transnasal resection of anterior skull base tumors such as meningiomas can be implemented in a low volume center after acquiring routine with endoscopic pituitary adenoma surgery. It can be safely conducted for lesions < 3 cm and represents an elegant and safe alternative to transcranial approaches. Complications are more frequent in lesions > 3 cm, and/or located maximally anteriorly so that for these situations alternative techniques have to be taken into account, be it another reconstruction flap based more anteriorly or a transcranial approach. Early lumbar drainage seems to protect against fistula more than HBFs in the learning-phase. In order to reduce the learning-phase in patients, simulation training will play an increasing role in the future.

Repair of CSF leak and anterior skull base reconstruction

CSF leak can be spontaneous or traumatic, the latter being further divided into accidental or iatrogenic. Finally iatrogenic fistulas, which are more common than accidental fistulas, can be either involuntary as a complication of a surgical procedure or they can also belong to the surgical approach, as is the case in anterior skull base tumor surgery.

The importance of a perfect reconstruction has become the major subject of concern, as postoperative fistula represents one of the most frequent relevant complications of endoscopic approaches to the anterior skull base and remains the main drawback when compared to open techniques. Recognition and management of a fistula is of utmost importance because of the potentially devastating complications associated with meningitis and pneumocephalus. Regarding unintentional CSF fistulas it can be observed after endoscopic sinus surgery, neurosurgical procedures and during endoscopic anterior skull base surgery.

Endoscopic sinus surgery belongs to one of the most frequent procedures performed by rhinologists and an incidence of 0.5% postoperative CSF leaks has been observed in a large series[350]. The most prone areas for this complication are the cribriform plate, the posterior fovea ethmoidalis, the recessus frontalis and the upper part of the sphenoid sinus. Besides transsphenoidal procedures for sellar region pathologies neurosurgery presents several other procedures which can be associated with this complication. Besides the procedures addressing directly skull base pathologies, basically all fronto-basal craniotomies with opening of a frontal sinus are also potentially at risk and Deschler et al found a CSF leak rate of 13% after major open anterior skull base surgery[74].

In the past most neurosurgeons would have repaired these defects via a craniotomy, but in the last decades endoscopic rhinologists have been increasingly involved in the management of these skull base defects since the first description of endoscopic CSF leak repair by Wigand in 1981. These revision procedures were probably among the first opportunities for interdisciplinary collaboration in the field and have demonstrated neurosurgeons the benefits of the endoscopic approach as compared to the open craniotomies with avoidance of large scalp incisions and avoidance of brain retraction, thus reducing the risks of postoperative anosmia, seizures and various neurological deficits.

Regarding endoscopic skull base surgery, as mentioned above the incidence of postoperative CSF fistulas has stimulated the development of new closure techniques that have reduced the incidence of this complication. Many authors consider especially the contribution of the vascularized pedicled nasoseptal flap as decisive[129].

Confirmation and localization of the CSF leak

In many instances of CSF leaks, the cause and the suspected location of the leak are obvious, as for example after surgery for anterior skull base lesions and no extensive investigations are needed. However, in certain circumstances the diagnosis of CSF leak has to be confirmed and sometimes the localization of the defect is not obvious. To confirm the diagnosis a sample of the leaking material is collected and sent for analysis in order to identify CSF-specific proteins in nasal secretions. Although simple, cheap and convenient, the diagnostic sensitivity and specificity of Glucose oxidase are considered unsatisfactory: bacterial contamination may cause false negative results and the test is frequently false positive in diabetic patients. Specific CSF biomarkers such as beta-2-transferrin (beta-2-trf) or beta trace protein (beta TP) are needed for reliable diagnosis[239]. If spontaneous leak occurs as soon as the patient leans forward there will be no difficulty in gathering enough fluid for chemical analysis. In some instances with intermittent or very scarce leak it can be more difficult to get a usable sample. In these instances a pledget can be placed endoscopically in the immediate vicinity of the previous operating site and left in place for one night.

Regarding localization of the leak different radiological investigations have been used, including CT, MRI cisternography and MRI cisternography in combination with single photon emission tomography or radioisotopic imaging. Another helpful localization tool is represented by fluorescein (Akorn Inc., Buffalo Groove, IL) administered intrathecally prior to the revision. Prior to intubation, the anesthesiologist performs a lumbar puncture, takes 10 ml of CSF in which he dilutes 0.25ml of a 10% fluorescein solution. The solution is then re-injected slowly intrathecally in 10-15 minutes in order to avoid adverse reactions[281] such as seizures or neurotoxic effects as described with higher concentration. The site of the leak will be readily identifiable as an intense green fluid under microscopic or endoscopic vision without additional filter (Fig. 3.18).



Fig. 3.18: intraoperative view of a patient presenting bilateral CSF fistula 8 years after completion of radiotherapy for recurring non-functioning pituitary adenoma.

Grafting materials

A large variety of materials has been used to repair defects or the seal the reconstruction. Reconstruction materials include autologous material and collagen matrix, acellular human dermis have also been used in the past but have become less popular because of the very theoretical risk of infectious disease transmission that has not been observed in more than 2 million applications[386].

Autologous material

Repair of anterior skull base defects have been performed using fat, fascia lata, mucosal graft, either free or as a pedicled flap. Rigid materials such as bone or cartilage have also been applied, generally in combination with the abovementioned materials. Autologous tissues remain popular because of their safe biocompatibility, availability and low costs. The drawbacks are represented by some donor site morbidity with the need for a separate incision and the time needed to harvest them. Sometimes concerns are also made regarding the limited tissue supply.

Fat

Fat tissue is generally used to fill some empty space or to obliterate the sphenoid sinus and is thus considered as an adjuvant material. In this setting it is generally used in a socalled "plug" fashion. Harvesting the abdominal fat is done via a small incision; in our department we perform a small incision of maximal 2 cm in the umbilicus region in order to minimize pain and cosmetic issues. One option that can facilitate the manipulation of the fat plug and stabilize its position is to place it in square piece of oxidized cellulose gauze (Tabotamp®, Johnson & Johnson, Spreitenbach, Switzerland) closed over the plug with a suture[173].

Interestingly fat pad has also been used to perform a so-called hypophysopexy in order to allow better delimitation of the normal pituitary tissue from remaining tumoral tissue in the cavernous sinus prior to radiotherapy[359].

Fascia

For the repair of larger defects fascia lata is the traditional material. An alternative is represented by the fascia temporalis. Multilayer application of fascia has been shown to be an efficient option in the management of high-flow fistulas for example with opened cisterns[233]. The first layer was traditionally placed as a so-called inlay (or underlay) intra-cranially, between the dura and the bone of the skull base. After application of some kind of sealant, generally fibrin glue, a second layer was placed as an overlay extra-cranially[287]. With the advent or more elaborated multilayer reconstruction procedures, especially with the introduction of pedicled vascularized flaps that would be placed as the last layer, the disposition of the different layers has been modified and will be described in the section dedicated to endoscopic reconstruction.

Mucosa

Free mucosal flaps can often be harvested during the approach, from the septum, one of the turbinates or the nasal floor. If the resection of the middle turbinate belongs to the planned approach, harvesting its mucosa will not add morbidity to the procedure. Some care must be taken when harvesting mucosa from the middle turbinate in order not to cause a CSF leak at the superior part of the turbinate, where it is attached to the skull base. One also has to be aware that removing the septal mucosa will expose cartilage that may take long to heal and also it can compromise later use of a nasoseptal flap[353]. The harvested piece should be larger than the defect as there is some contraction of the graft and it should ideally cover the borders of the defect by some

millimeters. For very small defects or intraoperative limited CSF leaks free mucosa is an ideal material with limited harvest time and simple harvesting technique as well as the possibility of customizing the size, up to a certain degree. In such situations mucosal free flap covered with fibrin glue was the only material used by the author's team and some others do also manage these defect with this simple limited method[364]. For larger defects some rigid support might be required and here a piece of septal cartilage or bone placed intracranially will do.

In order to assure a successful reconstruction a meticulous placement of the mucosal graft remains essential and some details have to be kept in mind: the glandular mucussecreting surface of the graft has to be placed on the external or sinusal side, directed towards the nasal cavity, as incorrect placement can result in the development of an intracranial mucocele[379]. If a multilayer technique is applied, as the mucosal graft should never be placed intracranially another material such as fascia or collagen fleece, has to be used as underlay graft.

Bone and cartilage

These autologous materials are not applied for sealing per se but rather in order to give the reconstruction more rigidity; as such they are usually used in combination with other soft materials. They are discussed with non-autologous rigid materials in the section dealing with the controversial issue of rigid support.

Collagen-based products

Innovation has been made in the preparation and the combination of collagen in order to provide ideal dural substitution material. They present the advantages of avoiding donor site morbidity and do not necessitate any complex preparation as they are "ready to use". These materials are provided in different forms such as fleeces or sponges and consist of engineered collagen of animal origin, either bovine or equine. The preparation consists in removing the cells and the antigens from the animal's tissue, usually Achilles tendons. A chemical treatment will then stimulate the creation of cross-links among the fibers, thus creating a porous structure that will enhance in-growth of fibroblasts and angiogenesis[39]. Meanwhile there are nearly 20 types of such products and only 2 of them, tried by the author's endoscopic team, will be presented here.

The first type, DuraGen® (Integra Neurosciences, Plainsboro, NJ, USA), is a matrix of bovine collagen type I that can be handled directly and has been used by various authors as one layer in multilayer reconstruction, in combination with a sealant.

The second type, Tachosil® (Takeda, Pfäffikon, SZ, Switzerland) is a product that was actually initially developed for hemostasis in the setting of liver and general surgery. Because of its adhesive properties and despite the fact that it was not authorized for this indication, neither FDA nor CE approved, neurosurgeons rapidly adopted it as an adjunct for dural closure. It consists of a glue-coated sponge of horse tendon collagen type I. the originality of the product consists in the combination of the collagen fleece with, on one side, a layer of human fibrinogen and thrombin and bovine aprotinin as plasmin inhibitor. Once humid, either with Ringer solution or with the blook oozing out of the operation field, the clotting factors are activated: fibrinogen (factor I) and

thrombin (factor IIa) react together, thus proceeding to the last step of the coagulation cascade on the adhesive side applied to the dural defect or to seal a approximating dural suture[242]. Although the author has made very positive experience with the application of this product in open cranial neurosurgery, its application in endoscopic pituitary surgery was rather disappointing due to the fact that the least contact of the fleece with the humid nasal mucosa would initiate the coagulation cascade on the adhesive side and cause the fleece to retract, preventing adequate application. Nevertheless there are authors that still apply it, especially in microscopic pituitary surgery where the presence of the speculum avoids contact between the fleece and the mucosa until it is adapted at the skull base.

Sealants

As the described repair techniques do not offer immediate watertight closure most of them are associated with adjunct measures, including the use of sealants. Until the advent of vascularized mucosal flaps it was claimed that these sealants would increase graft adherence. Basically 2 types of sealants can be used: biological and artificial. The most widely used biological sealant, Tisseal® (Baxter, Deerfield, Ill, USA), consists of 2 components, human fibrinogen (or so-called sealer protein) and thrombin, made from pooled human plasma. When mixing the sealer protein and the thrombin, soluble fibrinogen is transformed in fibrin, forming a rubber-like mass that adheres to the wound surfaces. Interestingly this is also a product developed for hemostasis and used as a sealant for colonic anastomoses. Its use as a sealant for dural waterproofness is theoretically off label[287].

The most commonly artificial sealant used in neurosurgery is represented by DuraSeal® (Covidien, Mansfield, Mass, USA) and consists of a hydrogel based on polyethyleneglycol and trilydin amine. In contrast to Tisseal it has been approved by the FDA as dural sealant, but only for spine surgery, although it is also noted to be neurotoxic by the manufacturer! It has been used in pituitary surgery in many procedures without adverse reaction[215]. It can either be applied directly with the provided syringe or with the use of a special air-pump system which will allow applying the small amount on a much larger surface, a relevant improvement in face of the quite elevated price of the product. In order to facilitate transnasal application of both products, a double lumen needle is provided by both manufacturers. However, despite their biocompatibility and the absence of relevant inflammatory reaction or of foreign body reaction, these 2 liquid sealants still present some limitations in their application: because of the short optimal polymerization period and the suboptimal application angle in transsphenoidal endoscopic surgery their application "under" the skull base can at times be somewhat cumbersome. In open cranial surgery it is used to seal leaky sutures, in endoscopic skull base reconstruction it is used at the borders of the different types of grafts applied.

Rigid support

Rigid reconstruction belongs to supportive measures and its indication remains a subject of controversy[287]: if some authors, such as Dufour[80], feel that all types of skull base repair for fistula should have a rigid component, others claim that the use of

vascularized flaps does not need to be associated with complementary rigid reconstruction and, moreover, it will prevent the formation of sequestra sometimes observed with large rigid grafts[89]. Some authors, such as Tabae et al[355] indicate a rigid reconstruction depending on which layer of the skull base have been removed, while others will make their indication depending on the size of the defect, although no strict criteria regarding the size of defect requiring rigid support could ever been defined. The incidence of CSF fistula does not help to solve the controversy, on the contrary: large series of first-attempt CSF leak closure rates were as high as those found in series where no routine rigid reconstruction was used.

Both, autologous and synthetic materials are available. Bone and cartilage can often be harvested during the approach procedure thus preventing additional donor site morbidity as with calvarial grafts, iliac crest or ribs that all have been described. Cartilage can be harvested during the approach for example from the septum, whereas bone can be taken from the septum or sometimes from the sphenoid anterior wall or from a well-developed intersphenoidal septum.

Synthetic material are divided into so-called "bone substitute" and plates. Bone substitute are represented by PMMA (polymehtylmethacrylate) or hydroxyapatite. PMMA is probably more convenient because of its shorter duration to become hard as compared with hydroxyapatite as well as its ability to harden under water. Titanium mesh is the most commonly employed plate type followed by expanded PTFE (polytetrafluoroethylene). The obvious advantages of availability without necessary harvesting site there is some concern regarding infection and artefacts on imaging. The author's team has practically only experience with autologous rigid material, especially in the setting of the so-called "gasket seal" technique described further in the endoscopic reconstruction techniques section.

Lumbar CSF drainage

The placement of a CSF drainage also belongs to supportive measures and its indication remains very variable. If CSF diversion during the postoperative period can maintain a lower intracranial pressure and thus theoretically reduce the incidence of postoperative CSF fistulas, its systematic use does not seem to be reasonable in the light of the imposed discomfort for the patient as well as what regards possible associated complications, including infection, over-drainage, retained tip of the catheter or bed-rest associated thrombosis or embolism. Some authors use it as a first line therapy in patients developing postoperative CSF leaks and claim a high success rate and avoid thus a revision operation in most of the cases. This was the case for example in the larges series by Tabae et al where out of 127 patients 11 developed a postoperative CSF leak which responded in 10 cases to lumbar drainage for 3-5 days[355]. Others are more aggressive and in the presence of a postoperative CSF leak will take the patient back to the operating room for a direct revision and decide in favour of a lumbar drainage only in cases where a high flow leak is observed during the revision[399]. In such cases they would also place the drainage for 3 to 5 days, with maximum 10ml/h. As described above in the section describing the experience with endoscopic pituitary surgery in St

Gall, the author's endoscopic team adopted this attitude in order to avoid the risks and discomfort of lumbar drainage.

Endoscopic reconstruction techniques

Choice of material and technique

Given the spectrum of the defect types and size a wide variety of reconstructions have been developed and their application has to be tailored to the situation encountered. This has led to the development of different algorithms. In summary simple defects are dealt with simple techniques and complex defects involving several structures of the skull base and dural layers will need more elaborated reconstructions. One of these algorithms was proposed in 2007 by Tabae et al[355] and distinguished 5 types of defects with adapted closure techniques which are summarized hereafter:

Type of defect	Definition	Reconstruction
Ι	Small CSF leak or bony defect	single layer, fat ("bath plug")or fascia
IIA	Sella, no CSF	Gelfoam, bone, sealant
IIB	Sella with CSF	Fat in tumor cavity, bone, sealant
IIIA	Suprasellar, anterior fossa	Fat, fascia inlay, bone overlay, sealant
IIIB	Ventricular space open	Fascia inlay, bone overlay, sealant

Another type of CSF leak classification with tailored reconstructions has been presented by Esposito et al[89]. It distinguishes 3 types of intraoperative CSF leaks with corresponding increasing reconstruction complexity, summarized in the following table:

Grade	Definition	Reconstruction
0	No CSF, confirmed by Valsalva	Collagen sponge only
1	Small "weeping" leak	Single layer collagen sponge
	Small diaphragmatic defect	Titanium mesh buttress wedged intrasellar
		Second layer collagen sponge
2	Moderate CSF leak	Collagen sponge over fat
	Obvious diaphragmatic defect	Intrasellar titanium mesh buttress
		Fat in sphenoid sinus
3	Large CSF leak	Same as 2 + CSF drainage

These 2 algorithms present tailored reconstruction procedures, depending on the degree of the intraoperative observed CSF leak. In many situations this degree can be preoperatively anticipated, allowing better preparation of the surgical team. Some risks factors for CSF leak have been clearly identified and for example Tabae et al mentioned complex procedures with longer operating time as well as anticipated defects >3 cm, conversely the absence of intraoperative CSF identification was identified as a strong predictor for the absence of a postoperative fistula[355]. Zanation et al identified 6 factors for increased risk of intraoperative CSF leak:

- 1. patients with a high body mass index as it is associated with higher intracranial pressure
- 2. pathology : lesions involving the arachnoid cisterns, craniopharyngiomas
- 3. intraoperative penetration of ventricles or cisterns
- 4. size and site of the defect. procedures involving the anterior cranial base are much more likely to leak
- 5. poor tissue healing, especially in extensive ACTH-producing adenomas
- 6. tissue availability reduced for reconstruction, such as after prior surgery or radiotherapy

As far as factor 1 is concerned, high body mass index, this can be in fact extended to any situation with increased intracranial pressure, especially hydrocephalus, as this condition is encountered not so rarely, either with the initial pathology or in the setting of revisions. It represents an obvious factor for repair failure and must therefore sometimes be treated with derivation or ventriculostomy.

Regarding factor 6, radiotherapy should not only be considered if the patient has already been irradiated but if radiotherapy is anticipated one can also expect poor tissue healing.

The preoperative recognition of all these factors is of utmost importance, as it can determine strategic decisions regarding repair technique, and some of them have to be taken prior to starting the procedure: after a classical approach with coagulation branches of the sphenopalatine artery the option of a nasoseptal flap will be lost.

Free graft reconstructions

In reconstructions with free graft material the first fascia lata layer is usually placed as a subdural inlay (between brain and dura) that should extend beyond the dural margins by 5 to 10 mm in all directions; the second fascia layer is then placed as the first overlay in the epidural space (between dura and skull base). Finally the pedicled flap will build the overlay. Only if bony edges are insufficient to hold the second fascia layer adequately in place it will be placed as an overlay extra-cranially, on the nasal side of the defect [399]. After each layer application a biological or a synthetic type of glue is applied on the margins. If some author recommend the application of absorbable gelatin sponge layers in order to hold the grafts in place, we did not find it necessary and usually fixed the graft materials with a standard nasal tamponade such as Rhinotamp® (Vostra, GmbH, Aachen, Germany), made of thermally stable foam endowed with an adhesion resistance coating. The features of the coating prevent adhesion to the nasal mucosa and will ensure easy atraumatic removal.

Pedicled vascularized flap reconstructions

The remaining high incidence of postoperative CSF fistula after endoscopic endonasal surgery, especially in the presence of high flow intraoperative CSF leaks and despite multilayer reconstruction and the application of adjunctive measures such as nasal packing or balloon catheter for external support and perioperative lumbar drainage to lower CSF pressure have stimulated the development of alternative reconstruction techniques. The introduction of the vascularized naso-septal flap after Hadad-Bassagasteguy (HBF) has allowed for a significant reduction in postoperative fistulas from an incidence of nearly 30% for anterior cranial fossa meningiomas to less than 5%[137].

The HBF is reserved for situations where a large skull base defect is planned or a high flow CSF fistula is anticipated. In contrast to the other reconstruction techniques, the decision has however to be taken prior to starting the procedure as in case of a standard approach the posterior septal artery might be coagulated and thus prevent the preparation of a vascularized flap. Basically, its mobility allows it to be used for skull base defects that extend from the frontal sinus to the clivus. However, our experience with anterior skull base meningiomas has demonstrated that it can be sometimes rather just to reach adequately the anterior part of the ethmoid plate.

A previous history of septal or sinus surgery or pituitary surgery is not an a priori contraindication to the use of the HBF. In the presence of a large sphenoidotomy the preservation of the vascularization of the septal mucosa can be assessed with a Doppler probe at the beginning of the surgery. Either side can be chosen depending on different factors such as the presence of a septal deviation, side of the anticipated dural defect or preference of the surgeon. It can be prepared only on one side in order not to completely devascularize the septal cartilage.

Preparation of the flap

After "push over" of the turbinates the sphenoethmoidal recess is exposed and the bridge of mucosa containing the vessel and located between the ostium sphenoidale and the choane is identified. An angled monopolar needle is used to perform the incisions. The inferior incision is made at the bottom of the septal mucosa, just above the junction between the septum and the nasal floor, starting from the margin of the posterior choane and reaching anteriorly the anterior margin of the septal mucosa as it ends behind the vestibular skin. The superior incision is performed parallel to the nasal roof but has to be kept at least 1 cm below the top in order not to cause lesion of the olfactory mucosa. Finally the superior and inferior incisions are connected anteriorly, behind the muco-cutaneous junction. At this point the septal mucosa can be elevated in a subperichondral and subperiostal fashion starting anteriorly and going back to reach the anterior wall of the sphenoid sinus. After prolonging the inferior incision to the lateral nasal wall, the pedicle of the flap can be carefully elevated from the underlying bone at the base of the pterygoids up to the vidian canal laterally. The mucosal flap is then placed into the nasopharynx or antrum during the rest of the procedure. As it is recognized that free cartilage can need time to heal or patients can complain of "feeling cold air", my rhinologist colleague, Dr. Jan A. Tasman, has developed a technique

to cover the defect by flapping anteriorly and suturing the contralateral posterior septal mucosa to the anterior margin of the remaining mucosa on the flap side after the posterior septectomy has been completed.

Reconstruction

At the end of the tumor resection phase, the flap is mobilized out of the choane. Care has to be taken in order to prepare the pedicle without avulsions; the flap can in the meantime have become so adherent to the surrounding structures, especially if the resection phase has taken a long time, as to necessitate a new dissection! In order to facilitate the placement of the flap at the base of the skull, we have found it helpful to perform a resection of the sphenoid floor on the side of the flap during the approach phase after the mobilization of the anterior wall and rostrum of the sphenoid sinus, as this floor could otherwise be an obstacle to posterior mobilization of the useful surface of the flap.

On the other hand, in case of reconstruction of the ethmoid region, the flap can be sometimes rather short, as already mentioned above. One possibility to compensate for this shortness is to fill the sphenoid sinus with large autologous fat plugs in order to provide a more direct trajectory and avoiding the flap to follow the contours of the sphenoid sinus.

Any torsion of the pedicle region of the flap has to be avoided and the periosteal surface must be placed in contact with the dura and bone of the skull base, the mucous-secreting surface remaining towards the sinusal cavity. In a course on Minimally Invasive Endoscopic Surgery of the Cranial Base and Pituitary Fossa visited by our endoscopic team at the UPMC (University of Pittsburgh Medical Center) in September 2007, Amin Kassam and Ricardo Carrau insisted on the fact that no synthetic material be placed between the mucosal flap and the skull base, a precaution also considered as imperative by Prevedello[286]. Some authors still prefer to perform a two layer reconstruction and use synthetic dural substitute. We have maintained the principle of no synthetic material and perform a 3 layers reconstruction with application of a fascia inlay between the brain and the dura, a fascia overlay if possible between bone and dura and extracranially in the presence of insufficient bone margins. The margins of all these layers are covered with fibrin glue. Once correctly in place, the flap can be covered with Tabotamp® and Spongostan® can be applied in order to maintain the achieved conformation at the base of the skull. Finally, in order to counter-balance the pressure exerted by CSF some kind of external support has to be applied. The Pittsburgh team applies an inflated Foley balloon catheter, under endoscopic vision in order to avoid any exaggerated pressure intracranially. We have had positive experience with the standard tamponade introduced only on one side so as to avoid the discomfort associated with full nasal obstruction. Occasionally 2 tamponades where needed to maintain the flap in place, bilateral tamponades have only been placed in case of bleeding nasal mucosa on both sides. The tamponade is removed on the 4-5th postoperative day.

Other complications

If CSF fistula remains the major concern in anterior skull base endoscopy other complications have to be avoided. Some of them remain minor but still have a relevant impact on the patient's quality of life and others can be devastating and life-threatening.

Extracranial or otorhinolaryngological complications

If major complications are not encountered during the endonasal approach phase, some postoperative complications will be disturbing or painful for the patient, thus spoiling the success of the rest of the procedure.

The occurrence of postoperative synechiae will impair normal air circulation through the sinusal cavities and can be avoided with respectful handling of the mucosa during the preparation and, depending on the anatomical situation, with application of an adhesion resistant coated tamponade.

Following cranial nerves can be at stake during preparation:

_ branches of the trigeminal nerve with consecutive local anesthesia or hyperesthesia (midfacial and palatal numbness).

_ Filae olfactoriae with potential anosmia

Their lesion can be avoided with careful preparation, but sometimes the sacrifice of a neural structure belongs to the approach, as for example the filae olfactoriae when approaching an olfactory meningioma via a transethmoidal/transcribriform route or the vidian nerve in a transpterygoid approach. In case of sacrifice of the vidian nerve, an ipsilateral loss of emotional tear is observed but a dry eye is seldom of concern, excepted in elderly patients and patients with concomitant loss of the function of the ophthalmic branch of the trigeminal nerve.

Epistaxis due to a lesion of a branch of the external carotid artery can be readily managed intraoperatively, but can be more dangerous when happening postoperatively. The author's endoscopic team have observed only one such case in the last 10 years with an epistaxis occurring more than 2 weeks after the operation, due to the reopening of a coagulated branch of the sphenopalatine artery that had to be managed emergently in another hospital.

Intracranial or neurosurgical complications

Besides the major issue of CSF leak addressed in the previous section neurosurgical complications are mainly represented by lesions of neuro-vascular structures.

Neurological complications

During procedures in the sellar region the cranial nerves contained into the cavernous sinus can be damaged, with sensory deficits in the corresponding trigeminal territory and the 3 cranial nerves for eye motion with consecutive diplopia associated with ptosis and mydriasis if the oculomotor nerve is concerned. Because of its more medial course into the cavernous sinus the abducens nerve is most frequently concerned and has been shown to occur in 1 of 400 cases of pituitary surgery[292]. In case of large suprasellar extension of expansive mass the compressed optic nerves can become so thinned that great care must be taken and any manipulation avoided as this would result in a dramatic visual loss. If these nerves are anatomically preserved the slight intraoperative

manipulation can be enough to cause a postoperative disturbance that should recover with time.

In case of procedures for intradural processes the inferior cortical surface of the brain will have to be exposed and eventually dissected from the tumor. Here the analysis of preoperative MRI images will offer indications on the potentially difficulty of the dissection, depending on vessels encasement or if a thin remaining CSF layer can be observed or not.

Vascular complications

During pituitary surgery for large adenomas bleeding from the cavernous sinus can be controlled with local application of hemostatic materials such as oxidized cellulose as for example Tabotamp® or a gelatin sponge like Spongostan® (both products manufactured by Ehticon, Somerville, NJ, USA). If the venous bleeding is abundant the application of hemostatic matrix composed of animal-derived gelatin and human thrombin such as Floseal® (Baxter, Deerfield, Ill, USA) or Surgiflo® (Ethicon, Somerville, NJ, USA) can be ineffective because of washing effect. In such respect these "foam" preparations can reveal themselves disappointing for transsphenoidal application as the surgeon will not be able to apply immediate compression of the material over the bleeding as is the case in open surgery where the efficacy of these products can be remarkable. Another simple mean to control venous bleeding and often forgotten by neurosurgeons by readily used by rhinologists is gentle rinsing with warm water (40°).

Finally the last but not least structure at risk is the cavernous internal carotid artery (ICA). The lesion of this structure remains one of the most feared and stressful complications of transsphenoidal pituitary surgery. Clearly pre-defined decision trees have been developed in order to manage this life-threatening complication, such as the Sofferman protocol[249]. Its incidence in transsphenoidal pituitary surgery has been reported by Raymond and colleagues to be 1.1%[294] and can reach 5 to 9% in extended endoscopic anterior skull base surgery for parasellar lesions as demonstrated by Coudwell and colleagues[57]. Several risk factors for ICA injury have been identified, including anatomical variations, prior surgery or radiotherapy, prior therapy with bromocriptine, acromegaly and tumor encasement [346, 368]. As the occurrence of this type of lesion remains fortunately low, the efficacy of the different hemostatic techniques are difficult to assess and in order to gain more information an animal model has been developed where 5 different techniques have been tried[367]. Muscle patch and the use of U-clip anastomotic device have been shown to be able to achieve hemostasis while preserving vessel patency, whereas Floseal®, oxidized cellulose and Chitosan, a gel combining chitosan and dextran used in sinus surgery [366], were not effective. This model has also been used for training of endoscopic teams. The author's endoscopic team had one such complication that was managed with nasal packing, transfer to the angiography suite and embolization of the internal carotid artery. The 67 years old patient suffered from a 4 cm calcified prolactin-producing macroadenoma diagnosed 2 years earlier during investigations for painful gynecomastia with a prolactin level over 1700 micro g/L. Already at the time of diagnosis the tumor

presented a relevant compression of the optic chiasm with beginning visual disturbances. Because of unsatisfactory response to medical treatment with bromocriptine and progressive visual loss, the case was presented at the local monthly interdisciplinary pituitary board and intervention was decided. The MRI images demonstrated a large suprasellar extension with encasement of both ICAs (Fig. 3.19).



Fig. 3.19: preoperative MRI, contrast enhanced coronal (a) and sagittal (b) T1 images, axial T2 images (c) showing ICA encasement and axial CT (d) demonstrating multiple calcifications.

Because of the calcified nature of the lesion as well as the presence of evident risks factors (ICA encasement, bromocriptine therapy) a preoperative CT including navigations sequences to be fused with MRI images and a CT angiogram was performed, the latter to formally rule out a suprasellar calcified aneurysm. As this could be ruled out, the operation was performed in the usual manner. Because of the extremely calcified nature the ultrasonic aspirator (Söring GmbH, Quickborn, Germany) was used in combination with smooth aspiration cannulas. During the resection of the peripheral upper left part of the tumor, the mobilization of a calcified element with the smooth cannula triggered a massive intraoperative arterial bleeding causing the so-called "japan flag" on the video screen. After rapid nasal packing with Rhinotamp, the patient was brought to the angiographic suite where the perforation of the ICA could be localized

(Fig. 3.20a). As expected efficient nasal packing does not resolve the bleeding but achieves local control and thus offers the time window necessary to perform the angiography. As preservation of the local circulation, in particular of the ophthalmic artery, with application of a covered stent in the cavernous ICA remains technically difficult[346], permanent occlusion of the ICA with coils is the most frequent chosen option, as was in our case.



Fig. 3.20: Initial angiogram (a) of the left ICA demonstrating the site of the ICA lesion, right ICA angiogram with compression of the left carotid (b) with demonstration of good anterior communication, post-interventional angiogram (c) with obliteration of the left ICA and slight contrast enhancement of the retina (ii).

In spite of occlusion of the ophthalmic artery there was no blindness because of sufficient collateralization through branches of the external carotid artery, as can be seen on Fig 3.15c on the post-interventional angiography with visible contrast enhancement of the retina.

Conclusions and observations regarding training issues

Transsphenoidal endoscopy has been established as the standard procedure for pituitary adenomas in our low-case center thanks to its interdisciplinary implementation.

Its application to other pathologies such as midline anterior skull base meningiomas still necessitates a thorough preoperative analysis of the pros and contras as compared with either traditional open craniotomies or minimally invasive approaches to the anterior skull base. As demonstrated by our meta-analysis of the literature over the years 2011 to 2013 as compared to the meta-analysis of Komotar et al, the technique reaches a similar safety regarding the main complication of postoperative CSF fistula and there is a certain trend to apply more often minimally invasive techniques; a consequence on the selection of the meningioma types, especially as to the size, could not yet be clearly identified.

Finally, direct endoscopic transsphenoidal biopsy represents a very simple and efficient tool to rapidly obtain diagnosis and can even be performed in an ambulatory setting. In

several instances, the diagnostic information was extremely useful in order to determine therapeutic strategies and we seldom regretted to have performed it.

Still, the acquisition of the endoscopic skills for a "microsopic" neurosurgeon, even experienced, remains a challenge for several reasons: he will have to get used to the distorted 2-dimensional image, the indirect view, the work in a narrow space and the use of specialized single-shaft instruments. Especially the combination of indirect view and confined working space has been identified as a potential for technical errors[307]. Moreover he will have to learn to work in team, be it with another neurosurgeon or, as we did it at our institution, with an endoscopic rhinologist. All these difficulties cannot be mastered at once and altogether. As a consequence there is clearly here an indication for a "decomposition" of the skills that have to be mastered. One part of it, the basic haptic skills, should be acquired out of the operating room because it has been demonstrated that this can be done in a reliable fashion[301].

Several training models for endoscopic sinus surgery have been developed already decades ago by endoscopic rhinologists[46] who have early identified the potential of these training models. The need for "out of the theatre" training options has been recognized also in the last decades because of the increasing pressure on the clinical environment, on one side because of the reduction of teaching opportunities in the operating room due to shorter workweek and the growing importance of limiting medical errors[301]. Some institutions have already included endoscopic endonasal approach to the sella as one of their modules into their neurosurgical residency training curriculum[226, 307].

4. Cerebral endoscopy

Obstructive hydrocephalus and endoscopic third ventriculostomy

Obstructive hydrocephalus is the most frequent indication for cerebral endoscopy and thus endoscopic third ventriculostomy (ETV) the most frequently used endoscopic procedure[156]. As mentioned in the historical chapter, neuroendoscopy really started with obstructive hydrocephalus at the beginning of the 20th century and, after a period of regression, technical improvements have allowed its renaissance in the 1980^s and early 1990^s.

Neuroendoscopes and instruments

Classical neuroendoscopic systems

Classical endoscopes for cerebral endoscopy have followed several improvements since their "re-introduction" 30 years ago. If initial versions presented relative narrow working channels and had a reduced image quality as compared to so-called "inspection optics", modern versions have excellent image quality despite 2 working channels. In order to illustrate this development the 2 systems used in the neurosurgical department of the Kantonsspital St Gallen will be presented. Both are produced by the firm Storz (Tuttlingen, Germany).

The first system which meanwhile belongs to the oldest generation was introduced in 1999 as the first ventriculostomies were performed.

The Gaab system (Fig 4.1) comprises a working sheath with an external diameter of 6.5mm, an inspection optic with an outer diameter of 4mm and a 6° working optic with only one 3mm working channel. The main disadvantage of this system was that the working optic was grieved with a certain loss of image quality due to the room taken by the working channel and to the fact that the working optic hat to replace the inspection optic after anatomic orientation. All those manipulations are time consuming and associated with some risks.



Fig. 4.1: Gaab 6° working optic with its single 3mm working channel.

The more recently acquired Lotta system (Fig. 4.2) presents several advantages: besides the fact that the working optic has an excellent image quality, even slightly better than the inspection optic of the Gaab system, it allows for performing the puncture of the ventricle under direct vision, without the need for a supplementary sheath for performing the puncture, and it has 2 working channels. This last characteristic is expected to facilitate all procedures where manipulations are performed such as in biopsies or tumor removal. When working with only one channel the tumor has always some tendency to be pushed by the instrument, be it scissors, a biopsy forceps or an ultrasonic aspirator. With 2 channels the surgeon can work in a more "microsurgical" fashion, grasping the tumor on one side and cutting or puncturing on the other side.



Fig. 4.2: Lotta system with 2 working channels and one third for rinsing. The endoscope is directly mounted with the reflecting balls for the navigation tracking system.

Other neuroendoscopic systems

Even if most of the procedures will be done with classical rigid endoscopes with one or more recently 2 working channels the diverse applications of the endoscopic technique in cerebral endoscopy allows the use of different types of endoscopes. In the so-called endoscope assisted procedure where microsurgical instruments are used next to the endoscope special versions of rigid endoscopes have been developed. As the problem in these procedures is that the endoscope uses part of the instrument's working space they have been developed so as to offer the best image quality with the narrowest diameter. Of course they don't have any working channel as surgical instruments will be used besides the endoscope.

Instrumentation

The number of instrument utilized in neuroendoscopy remains limited but is under constant evolution and improvement. For the most frequent and basic procedure, the ventriculostomy, a balloon catheter is indispensable. There are several models on the market, some with only one balloon and others with a double balloon. The difficulty of dilating a perforation at the base of the 3rd ventricle with only one balloon comes from the fact that in the presence of a relative stiff floor the balloon will slip forward or backward without causing any dilation of the perforation. The advantage of the double balloon is that it will be blocked at the level of the perforation and thus be in a stable position to perform the dilatation (Fig. 4.3).



Fig. 4.3: double (left) and simple (right) balloons for endoscopic ventriculostomy.

Regarding cutting instruments various types of microscissors are available. Models with one blunt side are regularly preferred as they can be used as blunt instruments and are less dangerous when kept closed.

Biopsy forceps of various diameters will be used to perform tumor biopsies or resections of smaller lesions (Fig. 4.4)



Fig. 4.4: Example of forceps for endoscopic biopsy.

One of the problems of endoscopic tumor resection is that the working channel being of a maximal diameter of 3mm a piecemeal resection will become very time consuming as soon as the tumor diameter reaches 2cm. in these situation 2 possibilities can be tried in order to accelerate the resection: one is the grasping of larger pieces and taking the whole endoscope with the large piece, leaving the working sheath in place. The other possibility is to use a specially designed ultrasonic aspirator that fits into the narrow working channel. One of the drawbacks of these very thin ultrasonic aspirators can be that they get quite rapidly stuck with tumor material.

Finally a coagulation probe is of course mandatory. Even if the use of a coagulation probe will be avoided as long as possible, especially when working in regions with sensible surrounding structures, it belongs to the armamentarium of endoscopic surgery. During the firs decade monopolar probes have been used but rapidly bipolar probes have been developed. As no forceps can be used through the narrow working channels blunt single shafts probes with an extremity made of 2 half spheres were designed, some of them even rotatable, as the one used in our department (Fig. 4.5). The probe was initially purchased for endoscopic lumbar discectomy procedures but revealed itself much more user-friendly than the straight probe initially used: in order to reach bleeding spots at the periphery of the field of vision, the endoscope doesn't have to be displaced, an always uncomfortable measure, but just has to be bent and orientated in the desired direction, a much more stable was to reach the bleeding spot.



Fig. 4.5: Trigger Flex bipolar probe with curved tip (left), monopolar rigid probes (right).

Anatomical considerations

Even if performing a ventriculostomy can be seen as a fairly simple procedure consisting after all only in "making a hole", the very location of the structure to be perforated makes it a non trivial procedure and a clear knowledge of the local anatomy is absolutely mandatory before starting and corresponding references works are recommended[299]. Classical landmarks must be identified as soon as the tip of the endoscope enters the lateral ventricle: the interventricular septum or septum pellucidum attached at the corpus callosum, the choroid plexus with its typical appearance will readily be recognized. When coming through a classical frontal burr hole for a ventriculostomy the operator will see 2 compartments of the lateral ventricle: the frontal horn and the body or atrium of the lateral ventricle separated by the foramen interventricualre[333]. The frontal horn is limited by 5 walls: the inferior, anterior and superior are made by the rostrum, genu and body of the corpus callosum respectively. The head of the nucleus caudatus builds the lateral wall and the septum pellucidum the medial wall. The atrium is limited by 4 walls: the body of the corpus callosum builds the superior wall, the septum is medially, the body of the nucleus caudatus laterally and the
thalamus forms the floor of the atrium. It is important to note that the frontal horn is devoid of choroid plexus, whereas it is present in the atrium, a distinction which can be helpful for the orientation in difficult situation as for example with blurred vision due to bleeding.

If arteries are used for orientation in open microscopic surgery, in the ventricles the veins will be more reliable anatomical landmarks in spite of their variability. Arteries will readily not be visible at endoscopy as for example the anterior choroidal artery which runs through the choroidal fissure, the cleft between the fornix and thalamus. Thus in the lateral ventricle the subependymal veins will be used[300]: the thalamostriate vein running postero-anteriorly and the anterior septal vein converge towards the posterior border of the foramen of Monroe (53% of cases) where they will end into the internal cerebral vein can be used as landmarks. Operators not only have to know the topographical ventricular anatomy, they will have to be aware of the functional regions they are passing by: as the goal of the procedure is the perforation of the 3rd ventricle the endoscope will have to be passed through the foramen of Monroe, the anterior limit of which is formed by the fornix. Lesions of this structure can be associated with dramatic short-term memory deficits and thus it has to be spared from any exaggerated pressure, especially during the period of the ventriculostomy where the shaft of the endoscope remains into the foramen of Monroe. This can be easily forgotten as this structure will lie behind the tip of the endoscope and will not be visible anymore and this precisely during the time where the operator will be fully absorbed by doing the perforation of the floor. For the same reason undue movements of the tip of the endoscope into the 3rd ventricle are not allowed as they could cause tears of the fornix. The roof of the 3rd ventricle is formed by different structures including the fornix, the hippocampal commissures and the tela choroidea; hanging at the roof are the medial posterior choroidal arteries, the internal cerebral veins and the plexus. The posterior wall is very narrow and formed, from top to bottom, by the suprapineal recess, the habenular commissure, the pineal recess, the posterior commissure and the opening of the aqueduct. The lateral walls are formed by diencephalic tissue, the larger part being the thalamus and the inferior part the hypothalamus. The anterior wall is formed by the anterior commissure and the lamina terminalis above the optic chiasm. The anatomy of the floor of the 3rd ventricle does not present any difficulty and the two decisive structures, the infundibular recess with its funnel shape, corresponding to the implantation of the pituitary stalk and the mammillary bodies, are readily identified[332]. However, the aspect of the floor can be very different from one patient to the other, in some instances being so transparent that the basilar artery will be seen at first glance, in other instances being so opaque that the recognition of even the

mammillary bodies can become difficult. Moreover longstanding hydrocephalus with chronically elevated intracranial pressure can lead to relevant anatomical changes of the floor with loss of usual anatomical landmarks, as for example in association with an empty sella [253]. Finally the membrane described in 1956[224] by Liliequist has to be identified as its persistence could lead to failure of the procedure. This membrane extends from the upper border of the dorsum sellae and presents posteriorly two

leaflets, one mesencephalic reaching the mammillary bodies and a diencephalic leaflet reaching the tip of the basilar artery[107]. Its identification at the end of the procedure is of utmost importance as its persistence could lead to failure of the procedure[35].

Etiologies

Obstructive hydrocephalus can be caused by a variety of pathologies and the success rate of the procedure is related to the underlying cause as well as to the age of the patient, increasing age at onset or age at the intervention both being positive factors for success. Among classical causes of obstructive hydrocephalus acquired acqueductal stenosis has the best success rate, in particular higher than congenital acqueductal stenosis[186]. Regarding other causes some are recognized to be associated with a higher failure rate, especially postinfectious and posthemorrhagic obstructive hydrocephalus[93, 385]. Finally ETV can be applied in the setting of tumors involving the posterior fossa, the 3rd ventricle or the midbrain. Some controversy remains as to the timing and indication for tumors of the posterior fossa as the operation of the tumor itself can resolve the obstruction, nevertheless it provides a rapid and safe solution[15]. Care must be given to the preoperative study of the anatomy, especially regarding the position of the basilar artery and the configuration of the prepontine space[372]. In the presence of tumors of the pineal region, third ventricle and midbrain the ETV can be associated to a biopsy and will thus allow for the diagnosis. Depending on the location of the tumor a second burr hole will have to be planned.

Although some authors have tried to use it in normal pressure hydrocephalus (NPH)[111] it remained a controversy because NPH is a communicating form of hydrocephalus and ETV should not help in this situation, at least as far as common understanding of CSF pathophysiology can explain it. A recent study has also showed that the results of the ventriculo-peritoneal derivation are clearly better than the ETV in these patients[279] thus sustaining the intuition that it shouldn't be effective in this setting. Nevertheless the diagnosis of long standing overt ventriculomegaly of adulthood (LOVA) should not be missed as these patients who present with a triventricular hydrocephalus due to an aqueductal stenosis and sometimes have an associated macrocephaly will clearly benefit from ETV[261].

Preoperative planning

Ideally all patients should have an MRI of the head prior to surgery as it is the ideal tool for planning, diagnosis and it will also be used for follow-up. If particular anatomy or narrow foraminae of Monroe are present a navigation sequence will also be performed. Attention will first be focused on the possible etiologies of the obstruction of course and cardiac-gated cine sequences are helpful to make a correct diagnosis of obstructive hydrocephalus[236]. Once the etiology is identified and there is an indication for the ETV the attention will be focused on the particular anatomical characteristics of the patient, looking for the size of the interventricular foraminae, the position of the basilar artery as related to the floor of the 3rd ventricle, the mammillary bodies and the infundibular recess; the width of the space between the dorsum sellae and the pons will also be evaluated. Even if the distance between the infundibular recess and the tip of the

basilar artery remains fairly comparable between normal subjects (10.5+/-2.3mm) and patients with hydrocephalus (12+/-3.7mm) as measured by Hayashi[151], there are relevant anatomical variations whose preoperative recognition is decisive to increase the safety of the procedure. Here midsagittal sequences will allow to study neurovascular structures beneath the floor.

In the presence of a tumor or a cyst as a cause of obstruction any asymmetry will be checked in order to choose the most appropriate side to perform the ventriculostomy or the side which will allow to perform a biopsy through the same trajectory, if possible.

Surgical technique

Preparation

The procedure is done under general anesthesia. The patient is placed in a recumbent position with the head elevated 15° and fixed in a 3 pin holder even in the cases done without neuronavigation. The region of the incision is minimally shaved; the scalp prepped with a propanol solution and the patient is aseptically draped. A single dose of cefamandole (2nd generation cephalosporine) is given prior to starting the procedure.

Trajectory and image guidance

A standard midpupillary coronal burr hole can be used but optimization of the trajectory can be achieved with preoperative planning on the neuronavigation system (Vector-Vision, Brainlab AG, Feldkirchen, Germany). Pioneers of neuroendoscopy have used stereotactic guidance in order either to plan the trajectories or to plan a biopsy of an intraventricular tumor to be performed during the same session[154]. By analyzing the data of 17 patients treated with stereotactic-guided ETV, Kanner found that the ideal localization for the burr hole was 28mm from the midline and 8mm anterior to the coronal suture, thus not corresponding exactly to Kocher's point[190]. Nevertheless they stated that the trajectory be oriented to the individual anatomical relationship and nowadays this is best done using neuronavigation.

At the neurosurgical department of the Kantonsspital St Gallen neuronavigation has been introduced in 1999 and rapidly replaced stereotactic surgery for brain biopsies because of practical aspects: thanks to the separation of the imaging planning process and the biopsy procedure the reservation of the operation theatre for a brain biopsy was reduced by a factor 4 with the navigation. Still, in small and deep seated lesions stereotactic biopsy remains the technique of choice.

The neuronavigation will allow the surgeon to place the burr hole on the line defined by the spot of the ventriculostomy and the center of the non-dominant foramen of Monroe (Fig. 4.6). This optimal positioning of the burr hole is essential in all cases where the anatomy is irregular with atypical or enlarged ventricles, when the foraminae of Monroe are narrow and when the CSF is expected to be bloody or blurry[69]. Use of neuronavigation in those situations will help reduce inadvertent or unnecessary traction to vital structures[165, 297].



Fig 4.6: Planning of the burr hole (green) and trajectory.

The graduated operating sheath (outer diameter 6.5mm) with its obturator or trocar is used to directly puncture the lateral ventricle. This sheath can be integrated into the navigation system to be introduced free hand but under navigation guidance along the planned trajectory until the perforation of the ventricle wall is felt (Fig. 4.7) and further guidance with direct endoscopic vision can be done.



Fig. 4.7: working sheath for the Gaab system mounted with reflecting balls for the tracking system of the neuronavigation.

Even if most of ETV can be easily done without navigation because the structures are so dilated that the ventricles won't be missed we have found it useful to combine it because of training issues for the surgeon and the operating personal. The combination of the navigation introduces another complex element into the operative field and by using it only in the situation where they are needed because of difficult orientation it will eventually not be a help but an added problem in an already complex case. Moreover, in case of even slight intraoperative bleeding the CSF becomes blurred and orientation can be lost. In these situations the surgeon will have to stop movements and he will be happy of the supplementary orientation information offered by the navigation system, as the position of the endoscope's tip will be precisely known (Fig. 4.8).



Fig. 4.8: The integration of the endoscope into the navigation system offers information on the position of the endoscope during the whole procedure, a technical adjunct storzespecially appreciated during phases with blurring of the CSF.

Once into the ventricle the sheath is fixed to a holder and the trocar is removed. The endoscope and camera still have to be hold by either operator or assistant but just to be stabilized. The assistant will appreciate the relief offered by the holder, especially if the procedure should last longer than planned. If needed CSF is obtained for desired studies, intracranial pressure is not routinely measured. A 0° diagnostic optic with an outer diameter of 4.0 mm (Karl Storz GmbH & Co., Tuttlingen, Germany) is introduced for orientation. After identification of the usual landmarks the optic is advanced through the foramen of Monroe into the third ventricle and the operating sheath is fixed with an articulated holding arm. The 0° optic is changed for the wide angle working endoscope with its 3mm working channel (Gaab Neuro-Endoscope 6°, Karl Storz GmbH & Co., Tuttlingen, Germany). The slight 6° angled channel allows for the instrument to be visible into the center of the image.

Perforation of the floor of the 3rd ventricle

The most dangerous part of the procedure remains the perforation of the floor of the 3rd ventricle because of the vicinity of the basilar artery. The procedure is not seldom also

complicated by the fact that the floor is resistant and opaque after longstanding hydrocephalus[302].

During the development phase of neuroendoscopy, a great variety of instruments have been used to do the perforation. Guiot used a leucotome to puncture the floor under television control[135], a technique also used by Pierre-Khan[278]. Sayers[318] or Vries[377] have used a puncturing needle, with stereotactic guidance and with a flexible endoscope, respectively. Others have used directly the endoscope as a blunt instrument to do the perforation[175]. Laser have also been used[54] as well as an ultrasonic cutting probe[267] or electrocoagulation and cutting probes[157]. Grotenhuis developed a device, the non-through perforator and dilator, which combines the use of a suction probe fixing the floor of the 3rd ventricle to a perforator and dilator thus allowing for maximal security[133].

With time a tendency to abandon sharp instruments as well as monopolar coagulation probes can be noted and nowadays most operators will perform a blunt perforation using a closed forceps or the bipolar probe sometimes preceded by a small coagulation spot with a bipolar probe[372].

In our series too a blunt perforation was performed, using the double balloon version of a 3 French Fogarty-type catheter (Integra Neurosciences, Plainsboro, NJ, USA) or later on the steerable bipolar probe in order to better control the exact site of perforation. With other non-steerable instruments we sometimes experienced situations where a small perforation was initially made paramedially and it was then impossible to get one in the midline as the Fogarty catheter would fall back into the first perforation. The paramedian location of the perforation is not acceptable as it could favor a compression lesion of the oculomotor nerve during the inflation of the balloon.

Then the perforation is dilated to reach an estimated diameter of 4-5 mm. Small venous bleeding from the margins of the perforation is controlled either with gentle tepid irrigation or the inflated balloon for 1 to 2 minutes. Only in rare cases the bipolar coagulation directional probe had to be used. In one case the bipolar probe was used without current to do the perforation, using its greater rigidity as compared to the balloon catheter which was bending itself over a very stiff floor. Once the perforation is done the tip of the endoscope is pushed forward to see the basilar artery and make sure that no relevant trabeculations remain.

The endoscope is then retired, an external ventricular drain is not routinely inserted but only in cases where there has been bleeding and removed after 24-48 hours. A systematic postoperative MRI is done on day one to verify the patency of the ventriculostomy.

During the whole procedure the drainage channel has to remain opened; an inadvertent closure of this channel with a persistent irrigation would lead to a rapid elevation of the intracranial pressure with initially tachycardia and hypertension followed by bradycardia and hypotension as noted by Van Aken in 6 patients out of the analyze of the charts of 67 patients who had undergone ETV for obstructive hydrocephalus[2]. These observed changes were clearly the result of an increased in intracranial pressure, a manifestation of the so-called Cushing reflex which Harvey Cushing investigated in

during his time as a visiting physician working at the Physiology Institute of the University of Berne where he worked under the mentorship of Kronecker and Kocher[160].

Management of intraoperative bleeding

As CSF is rapidly obscured by blood, hemostasis is of paramount importance during endoscopic intraventricular surgery and everything has to be done to avoid any bleeding. Already with a concentration of 1ml blood per liter of CSF the vision will be blurred. One acute problem will be impossible orientation and thus any excessive movements must be avoided. It is recommended to approach the tip of the endoscope from the bleeding source in order to identify precisely the spot of origin of the bleeding. In most of the cases bleeding during an ETV will be coming from a lesion of the septal, thalamostriate or ependymal veins or from small vessels at the floor of the 3rd ventricle. As soon as the source of the bleeding is identified, coagulation with the bipolar probe is attempted in order to keep the vision clear. If it is not successful or the source has not been identified abundant rinsing with tepid Ringer lactate solution (37-38°) is attempted and in many cases this measure can also be sufficient. If not, it will at least restore vision in order to localize the bleeding source. Bleeding from small vessels at the base of the 3rd ventricle can be controlled without bipolar coagulation using the inflated balloon in the ventriculostomy for 1-2 minutes. Another possibility for uncontrolled situation is the so-called dry field technique can be applied: the CSF is sucked out of the ventricles and thus the coagulation enhanced[372]. This measure has been employed successfully in some cases as explained in the illustrative case of cystic craniopharyngiomas presented below in the section on intraventricular tmors.

Own experience

Material and methods

Data were collected retrospectively of all patients operated endoscopically in our institution between January 1999 and December 2012 for the treatment of obstructive hydrocephalus. A special permission of the BAG (Federal Office of Public Health) was obtained due to the retrospective nature of this study, as well as regular approval of the local ethics committee.

Only those interventions were included that had been performed by the author, who at the end of his residency introduced and established neuroendoscopic surgery in the Department. Clinical data collected include age, sex, height, weight, time of onset and type of first symptoms, time of diagnosis, diagnosis (Table 4.2), co-morbidities, as well as pre- and postoperative neurological status. Pre- and postoperative MRI-images and/or CT scans were reviewed by JYF and HAL.

Indications for ETV	Number of cases
Aqueduct stenosis	28
Tumor	16
Arachnoid cysts	3
Colloid cysts	3
Posttraumatic hemorrhage	2
Subarachnoid / intraventricular	1
hemorrhage	
Total	53

Table 4.2: Treated pathologies as a cause of obstructive hydrocephalus.

Indication, diagnosis, duration of operation and hospitalization and intraoperative, early postoperative (<30d) and late postoperative (>30d) complications were analyzed. Outcome was categorized in four groups: unchanged, better, worse, worse due to other cause (i.e. primary tumor progress), screening records for follow-up interviews, patients' statements, work abilities, neuropsychological and physical examination results.

The possible significance of the learning curve on those factors was evaluated. Statistical analyses were conducted by Fisher's exact and student's t-tests.

Results

In total 55 interventions were performed in 53 patients. Male/female ratio was 1.65:1. Age ranged from 1 to 87 years (mean age 49.5 years), including three children. Sixty-two percent of operations were elective. The operation indications / diagnoses are shown in Table 1. In all patients a systematic postoperative MRI performed within 24 hours of the procedure demonstrated a patent ventriculostomy with flow void artefact (Fig. 4.9).



Fig. 4.9: Left: pre-operative sagittal MRI demonstrating classical features of obstructive hydrocephalus, due in this case to aqueduct stenosis and including dilatation of 3rd ventricle with downwards bulging of its floor, dilatation of the supra-pinealis recess and fenestrated interventricular septum. Right: post-operative MRI within 24 hours demonstrating the flow artifact through the hole at the floor of the 3rd ventricle which has also ascended in its original position.

Forty operations were straightforward ETVs, 8 were associated with placement of an EVD in case of preoperative or possible postoperative hydrocephalus treatment and 5 ETVs were performed prior to tumor resection or biopsy. During 29 interventions navigation was applied.

Operating time (OT) for all interventions was 40 minutes with a mean of 59 minutes during the first half of the inclusion period and 30 minutes during the second half. For non-navigated procedures the learning curve analysis of operating time shows a steep curve with a mean OT of 62 minutes. With neuronavigation the learning curve starting in 2005 was even steeper (mean OT 49 min). The shortest OT (17min) was measured during the second half of the observation period for a straightforward non-navigated ETV (Fig. 4.10). During the so-called transition time, implementation of neuronavigation was at first associated with longer OT (Fig 4.11).



Figure 4.10: Showing mean OT over years of gaining clinical expertise. At the beginning of the observation period the learning curve for simple ETVs is steeper for non-navigated procedures with a relatively long OT (approx.: 62min.) in the beginning in contrast to shorter OT (approx.: 49min) when beginning to associate neuronavigation. The shortest OT (17min.) was measured while performing a simple non-navigated ETV.



Figure 4.11: During transition time (green line) when neuronavigation was added to the E3V procedure the learning curve was inverted at first.

In total 11 perioperative complications occurred (Table 4.3) without severe adverse events. Mortality rate was 0%. Four times the procedure was aborted intra-operatively due to blurred vision and consequently the placement of a ventriculoperitoneal shunt was necessary.

Age(y) / gender	Underlying	Type of	Type of		
	disease	complication	intervention		
Intraoperative complications					
72y, female	aqueductal stenosis	bleeding due to	ETV		
		injury of thalamus			
26y, male	colloid cyst	damage to fornix	combined approach		
		with transient short	for colloid cyst		
		term memory	resection with ETV		
		impairment			
Early complications	(<30 days postoperat	ively)			
57y, male	aqueductal stenosis	damage to	navigated ETV		
		oculomotor nerve			
		resulting in self-			
		limited third nerve			
		palsy			
59y, female	aqueductal stenosis	IVH three days	nETV, VA-shunt		
		postoperatively	removal , VP-		
			shunting		
59y, male	colloid cyst	acute SDH first day	nETV, EVD		

		postoperatively			
		after second			
		surgical			
		intervention for			
		treatment of acute			
		НС			
Late postoperative complications (> 30 days postoperatively)					
79y, male	colloid cyst	bilateral hygroma	ETV, removal of		
		33 days	blood clots from		
		postoperatively	foramen of Monroe		
		after second			
		intervention for			
		treatment of acute			
		НС			
Stoma closures					
57y, male	aqueduct stenosis	stoma closure after	navigated ETV		
-			0		
		6 weeks	0		
62y, male	glioma of the pineal	6 weeks stoma closure 10	ETV, tumor		
62y, male	glioma of the pineal gland WHO III	6 weeks stoma closure 10 days	ETV, tumor resection was four		
62y, male	glioma of the pineal gland WHO III	6 weeks stoma closure 10 days postoperatively	ETV, tumor resection was four days prior to ETV		
62y, male 73y, male	glioma of the pineal gland WHO III aqueduct stenosis	6 weeks stoma closure 10 days postoperatively stoma closure days	ETV, tumor resection was four days prior to ETV ETV		
62y, male 73y, male	glioma of the pineal gland WHO III aqueduct stenosis	6 weeks stoma closure 10 days postoperatively stoma closure days after procedure	ETV, tumor resection was four days prior to ETV ETV		
62y, male 73y, male 57y, female	glioma of the pineal gland WHO III aqueduct stenosis aqueduct stenosis	6 weeks stoma closure 10 days postoperatively stoma closure days after procedure partial closure of	ETV, tumor resection was four days prior to ETV ETV navigated ETV		
62y, male 73y, male 57y, female	glioma of the pineal gland WHO III aqueduct stenosis aqueduct stenosis	6 weeks stoma closure 10 days postoperatively stoma closure days after procedure partial closure of stoma 4 days	ETV, tumor resection was four days prior to ETV ETV navigated ETV		
62y, male 73y, male 57y, female	glioma of the pineal gland WHO III aqueduct stenosis aqueduct stenosis	6 weeks stoma closure 10 days postoperatively stoma closure days after procedure partial closure of stoma 4 days postoperatively	ETV, tumor resection was four days prior to ETV ETV navigated ETV		
62y, male 73y, male 57y, female 80y, female	glioma of the pineal gland WHO III aqueduct stenosis aqueduct stenosis aqueduct stenosis	6 weeks stoma closure 10 days postoperatively stoma closure days after procedure partial closure of stoma 4 days postoperatively Stoma closure 33	ETV, tumor resection was four days prior to ETV ETV navigated ETV ETV		
62y, male 73y, male 57y, female 80y, female	glioma of the pineal gland WHO III aqueduct stenosis aqueduct stenosis aqueduct stenosis	6 weeks stoma closure 10 days postoperatively stoma closure days after procedure partial closure of stoma 4 days postoperatively Stoma closure 33 days	ETV, tumor resection was four days prior to ETV ETV navigated ETV ETV		
62y, male 73y, male 57y, female 80y, female	glioma of the pineal gland WHO III aqueduct stenosis aqueduct stenosis aqueduct stenosis	6 weeks stoma closure 10 days postoperatively stoma closure days after procedure partial closure of stoma 4 days postoperatively Stoma closure 33 days postoperatively	ETV, tumor resection was four days prior to ETV ETV navigated ETV ETV		

Table 4.3: Complications: categorized in intraoperative, early (<30 days postoperatively), and late (>30 days postoperatively) postoperative complications. Stoma closures occurred as procedure independent complications, since patent stomas with actual flow – void signals were seen in all individuals on early (within 24h) postoperative MRI.

Early postoperative complications (<30 day) included one case of temporary third nerve palsy (< 1 month), one acute subdural hematoma after a navigated double burr-whole-access combined ETV and tumor resection and one intraventricular hemorrhage after combined ETV and lesion biopsy via double burr-whole access. Ventriculitis occurred in 2 patients who were in the ICU with an EVD for a prolonged period of time due to acute illness prior to final diagnosis and ETV (2 patients with traumatic brain injury and 1 patient with brainstem glioma).

Late postoperative complications (>30d postoperatively) consisted of one case of persisting symptoms despite patent stoma and one chronic subdural hematoma requiring surgical evacuation. One patient had a lesion of the fornix resulting in a six months period of impaired short-term memory. There was no significant difference in perioperative complications and outcome when comparing navigated and non-navigated procedures.

Overall stoma closure rate was 10.9% (n=6). Four patients presented an early closure (<30 days) of the stoma, 2 patients with persisting symptoms could be re-operated with Redo ETV and 2 patients obtained a VP-shunt. Late symptomatic stoma closure (>30d) occurred in 2 patients after 46 and 82 days and was treated by VP-shunt. Though in one patient Re-Do ETV was technically successful as postoperative flow-void MRI images confirmed, symptoms did not resolve clinically.

Follow-up period of 52 (98%) patients ranged from 1.5 to 90 months (mean follow-up 20.5 months). One Patient was lost to follow-up. One to six months postoperatively 35 patients (85%) had clinically improved, four remained unchanged (10%), one worsened due to primary disease progression and one patient temporarily worsened (2.5%) (Fornix lesion). Postoperative outcome more than half a year later was still improved in 27 cases (80%), 5 cases (15%) were worse due to underlying pathology, worsened in one case (2.5%) and unchanged in another case (2.5%).

Discussion

Our results show a reduction of operation time, especially for non-navigated ETV as a result of acquired experience. The combination with neuronavigation was associated with a temporary slowing down of the learning curve and no significant better outcome. Our operation time in the first half of the series was longer than in the literature[187], whereas it was comparable to the literature at the end of the second half of our observation period (in general 30 min).

Limitations

The limitations of our observation are its retrospective character and the limited number of cases. Remaining a rare procedure, comparison of ETV results with the literature is limited as well.

Complications

During the first half of the period 3 procedures were aborted due to bad visibility, and resulted in shunt placement. With the introduction of a new rinsing system (ClearVision, Karl Storz GmbH & Co., Tuttlingen, Germany) and the experience gained these visibility problems could be reduced to one single abortion during the second half. The overall incidence of neurologic complications for the series reached 3.6%, which is in the lower range when compared to Bouras et al (2.9% to 16.1%)[28]. The only 2 cases of temporary neurologic deficits due to a lesion of the third nerve and of the fornix occurred in the first half of the observation period. Such complications were not observed during the second half of the series due to training effects and implementation of neuronavigation in trajectory planning.

There were 2 cases of EVD associated cases of ventriculitis in patients with prolonged ICU stay, which had one or more EVDs for longer periods before ETV was considered. Both of these complications occurred in cases with complex circumstances where the ETV-procedure itself was not responsible. These complications were not observed in patients with ETV for aqueductal stenosis. Postoperative bleedings did not occur in straightforward ETV, but only in procedures including biopsy or resection.

Outcome

Our overall stoma closure rate of 10.9% (n=6) is similar to rates reported in the literature (8 - 22%)[149, 155, 237]. Surgeon independent late stoma closure with necessity for shunting occurred twice whilst early closure occurred during the first half of the period following incomplete inspection of the interpeduncular cistern due to inexperience. Though technically successful in all 4 redo ETVs as shown in the postoperative flow-void sequenced MRI studies, only one patient benefited clinically from the procedure.

Clinical status improved in 86% of cases, which is comparable to the reported success rates in the literature where more than 80% improvement is expected[51, 182]. However, we performed and included only pathologies, proven to benefit from an ETV[6, 112, 134, 156, 179]. Therefore ETV was not performed in patients with normal pressure hydrocephalus (NPH)[279]. Therefore the main indication for ETV remains obstructive hydrocephalus, which is the least frequent subtype of hydrocephalus in adults[113, 166, 187, 213, 304].

Neuronavigation

Regarding the combination with neuronavigation Rhode and colleagues analyzed 126 endoscopic procedures and found that if ETV could be performed without navigation it should be routinely integrated for more complex procedures such as tumor resections or cyst fenestrations[297]. Our series shows that the combination of both techniques slows down the procedure at first. This implies that training the combination of neuronavigation with endoscopy during straight-forward cases will facilitate its application in more complex cases.

Conclusion

Our series illustrates the learning curve for ETV. The combination with neuronavigation was associated at first with slowing down of the procedure, and did not lead to a better outcome. However, routine with this co-application should be acquired during straightforward ETV to avoid slowing down the less frequent, complex, ETV procedures.

Other indications associated with hydrocephalus or cystic formations

Complex hydrocephalus

The management of complex hydrocephalus with multiloculated isolated compartments remains a challenge despite technological advances in imaging and operative procedures. The main cause remains infection and intraventricular hemorrhage. No ideal procedure will be able to solve all types of pathologies encountered but the therapeutic strategy will have to be tailored to each situation. Among the possible procedures that can be used, endoscopy offers the opportunity to reach one of the main goals of the management: to make the different compartments communicate in order to limit the number of necessary ventricular catheter for the ventriculo-peritoneal derivation system in cases where shunt-independency cannot be achieve. Another

important objective of the treatment can be, in a minority of patients harboring multiloculated hydrocephalus, shunt independency.

In order to achieve these goals a variety of procedures can be offered, including endoscopic septum pellucidum fenestration (septum pellucidotomy), endoscopic third ventriculostomy (ETV), choroid plexectomy-fulguration and aqueductal plasty. Sometimes these procedures will have to be combined or to be planned in several stages.

Applying the above-mentioned principles, Teo and colleagues[362] made following observations in their retrospective study of 114 patients with 143 endoscopic procedures harboring different types of complex hydrocephalus, including isolated 4th ventricle, arachnoid cysts and multiloculated hydrocephalus:

- Therapy could be reduced to one single shunt in 82 (72%) of the cases
- Shunt independency was achieved in 32 (28%).

Another advantage of the use of the endoscope is that it will finally reduce the number of necessary procedures. In their retrospective analysis of 93 patients with only multiloculated hydrocephalus, Zuccaro and colleagues[401] looked at the number of procedures and could achieve treatment in 55 patients with only one procedure, in 30 patients with 2 procedures and in 8 with 3 or more.

One technical difficulty during endoscopy in this setting is the lack of classical anatomical landmarks with rapid loss of orientation, especially in very large cavities. In order to palliate this difficulty different types of adjuncts can be used. The combination of neuronavigaton with endoscopy has allowed for better preoperative planning of entry sites and trajectories as well as improved intraoperative orientation [165, 330]. As navigation images might not reflect the reality any more as soon as the ventricular system is opened and CSF is aspirated or flees out with consecutive brain shift, some authors have combined endoscopy with intraoperative imaging in order to actualize navigation imaging. If ultrasound remains the less expensive method for intraoperative imaging it is more often used by pediatric neurosurgeons and has some limitations regarding image quality. Another imaging modality represented by CT is more expensive but still more affordable than the intraoperative MRI. Its disadvantage lies in the associated irradiation, ruling it out for pediatric applications, one of the main populations concerned with multiloculated hydrocephalus. Finally, intraoperative MRI offers the best image quality bur also the highest costs. One of the other drawbacks of this modality is prolonged operating time, which is not negligible. In their feasibility study on combination of intraoperative magnetic resonance imaging with navigated endoscopy, Paraskevopoulos and colleagues[270] estimated the average added time for setup to be 40 minutes. Moreover, besides the acquisition cost there are also some limitations or at least some supplementary costs regarding dedicated MR imagingcompatible instruments. As a whole the method remains extremely expensive and there is little doubt that it will be compensated by the money saved because of some shorter hospital's stays or a couple of avoided shunt revisions.

Endoscopic shunt placement

The introduction of the ventricular catheter in patients with hydrocephalus can benefit from technical assistance as neuronavigation or XperCT-guided methods[118]. The benefits of inserting ventricular catheters under endoscopic vision have been challenged in an international multicenter study that demonstrated lack of benefit[196].

Arachnoid cysts

Arachnoid cysts are defined as benign cystic lesions filled with CSF and that do not communicate with the ventricular system[158]. The most common localizations are in the middle fossa near the temporal pole (50-60%) and in the posterior fossa with the most frequent being the cerebello-pontine angle (10%)[265]. It is best identified on MR images where they appear as sharply delineated round or ovoid extra-axial cysts with CSF attenuation that displace brain structures.

Modern therapeutic options include microsurgical approaches, endoscopic approaches and cystoperitoneal shunting. In their evaluation of these different options Wang and colleagues[380] found the endoscopic approach highly effective for most of the cases of the suprasellar and quadrigeminal regions. Microsurgical approach was rather recommended for cortical arachnoid cysts or for cysts with possible cystic tumor or cyst-related epilepsy. Finally cystoperitoneal shunting was found to be effective for very large cysts.

Regarding temporal arachnoid cysts, as the treatment consists in the marsupialization of the cyst into the basal cistern and will imply a fine dissection of often thickened and/or opaque arachnoid membranes at the medio-basal part of the cyst, the author found it safer to perform under microscopic 3-dimensional vision with standard microinstruments. The mobilization and incision of adherent arachnoid membranes in the vicinity of the internal carotid artery, the optic or oculomotor nerves can become quite challenging under 2-dimensional vision and with an instrumentation that cannot match the standards of the microsurgical ones. For this reason it is doubtful if the patient really has much to gain from a small burr hole endoscopic approach with suboptimal precarious dissection of neurovascular structures at the skull base as compared to a minimal craniotomy with safe microscopic dissection. The incision and mini-craniotomy needed for the microscopic procedure will be minimally larger than that of the endoscopic approach and there won't be any brain retraction, so that it also remains minimal invasive and remains the preferred approach of the author. The situation is different for suprasellar or quadrigeminal arachnoid cysts, where the lesion is deeply located and necessitates a long approach in microscopic surgery whereas it will be easily accessed endoscopically.

Intraventricular tumors

Intraventricular tumors or cysts are ideal candidates for neuroendoscopic surgery: they are located in the cavity of the ventricle filled with CSF; the often associated dilatation of the ventricular system will also allow for the needed working space. In cases where dilatation is not present frameless stereotactic guidance will help in reaching the target so that ventricular dilatation is not considered an indispensable condition any more[38]. The endoscope can be used to perform principally 3 types of applications: it can be used to perform a biopsy, to treat the hydrocephalus by either performing an ETV or a cystostomy and finally in selected cases it can allow for tumor resection. Even if technical improvements such as the development of endoscopes with 2 effective working channels or the endoscopic ultrasonic tumor aspirator have increased the

possibilities of tumor resections through the endoscope the ideal candidates should meet some of the following criteria: the tumor should present a moderate vascularity; it should have a rather soft consistency so as to be removable with aspiration; the greater diameter should not exceed 2 or maximally 3 cm[109]; location into the ventricle itself, ideally with associated hydrocephalus, rather low histological grade[363]. From these conditions results that the list of tumors that are good candidates for a purely endoscopic complete resection remains short: colloid cysts, intraventricular cystic craniopharyngiomas and some other rarer entities such as intraventricular central neurocytomas or small plexus papillomas are recognized candidates for endoscopic transventricular resection.

Illustrative case

Cystic craniopharyngioma

An 8 years old boy presented at the local children's hospital with acute headache and vomiting. He rapidly deteriorated after admission and the emergency head CT showed a 4 cm sellar and suprasellar cystic formation filling the 3rd ventricle with some basal calcifications and massive obstructive hydrocephalus with bilateral obliteration of the foramen of Monroe (Fig. 4.12).



Fig. 4.12: Non-enhanced emergency CT. Axial (a) images demonstrate massive hydrocephalus with tranependymal CSF resorption. Coronal (b) and sagittal (C) images demonstrating filling of the 3rd ventricle, bilateral Monroe blockade and some basal calcifications.

After emergency placement of an external ventricular drainage an MRI was performed and confirmed the cystic nature of the lesion with a very thin enhancement of the capsule (Fig. 4.13).



Fig. 4.13: T2 weighted sagittal (a), T1 contrast enhanced sagittal (b) and coronal (c) images demonstrating 4 cm cyst in the 3rd ventricle with obstructive hydrocephalus and minimal enhancement of the thin capsule.

The endocrinological examination could rule out hormonal disturbances and an endoscopic fenestration through a classical approach was planned on the neuronavigation system. A 5 mm burr hole was performed in the left frontal region under navigation guidance, thus exploiting the remaining dilatation of the lateral ventricle on that side. On entering the ventricle the aspect of the cyst capsule showed typical aspects of a craniopharyngioma, in particular with its multiple small calcifications (Fig. 4.14).



Fig. 4.14: Endoscopic view of the left foramen of Monroe obstructed by the cystic craniopharyngioma (a). Sagittal (b), and (c) coronal navigation images showing endoscope position.

After coagulation and opening of the cyst, an oil-like liquid could be aspirated and a partial resection of the upper half of the capsule as well as opening of the base of the cyst with endoscopic 3rd ventriculostomy was performed. Because of strong adhesion and failing to find a dissection plan between the lateral walls and the hypothalamus, resection of the lateral walls had to remain partial. During the resection with the endoscopic ultrasonic aspirator, vision was regularly blurred due to very minimal bleedings. In order to be able to work under clear vision, the ventricular system was completely cleared of its CSF and further resection was performed under "dry" circumstances (Fig. 4.15).



Fig. 4.15: Beginning of resection of the base of the tumor above the 3rd ventricular floor (a). Failure to performing blunt ventriculostomy with the tip of the balloon catheter because of too fibrous arachnoid membrane (b); note the slight fog over the optic and causing slight blurred image, due to the warm air into ventricle and basal cistern after aspirating the CSF in order to operate in so-called dry technique. Sharp opening of arachnoid membranes right of basilar artery (c). Final situation with small aperture of basal cisterns. Note the entry of the right abducens into Dorello's canal (arrow) and visible perforating arteries through the fenestration, in front of the pons.

B: basilar artery. DS: Dorsum sellae. P1: 1st segment of the posterior cerebral artery. Perf: perforating arteries arising from the basilar artery in front of the pons. SCA: superior cerebellar artery.

The patient's postoperative neurological examination showed no alteration, in particular no diplopia and the postoperative MRI (Fig. 4.16) showed the collapse of the cyst with opened foraminae of Monroe and free opening of the aqueduct. For safety reasons a second external ventricular drainage was placed into the 3rd ventricle but remained closed on purpose, in order to constrain the CSF to use the new way through the ventriculostomy.



Fig. 4.16: Postoperative MRI on day 1. T2 weighted sagittal (a) and axial (b) images demonstrating flow void in the aqueduct and reduction of ventriculomegaly with persisting air into frontal horns. Coronal T1 weighted contrast images (c) showed as expected remaining lateral cyst walls and opened foraminae of Monroe.

Colloid cysts

Introduction

Colloid cyst endoscopic resection was first described in 1983[285] and since then they remained the intraventricular lesions that has been the most often resected endoscopically. They are histologically benign lesions that represent 0.5-to 2% of all intracranial neoplasms[67] and they develop in the anterior part of the roof of the third ventricle where they are attached to, sometimes more posteriorly but rarely at other locations. Among the other reported rare locations these include the septum pellucidum, the lateral ventricles, the fourth ventricle and the preportine region [143]. They can be responsible for intermittent blockade of the foramen of Monroe. Because of this occlusive potential they can cause acute deterioration and have been associated with sudden death due to acute raise of intracranial pressure [313, 343, 365]. Classically patients operated on are symptomatic, presenting neurological and/or neuropsychological deficits but without acutely increased intracranial pressure[227]. The treatment from asymptomatic colloid cysts remains controversial [283]. The gold standard treatment remains one of the microsurgical approaches, either the transcortical-transventricular approach or the transcallosal approach. With improvement of the endoscopic material and the trend of minimal invasive procedures endoscopic resection of colloid cysts has become a true alternative to microsurgery. The advantages of the endoscopic over the endoscopic approach have been documented and are a lower morbidity, a shorter operation time and a shorter hospital stay [223, 363]. Colloid cysts become symptomatic as the cyst enlarges and cause a variety of presentations that can be classified in 3 groups: chronic headaches as the leading symptom, fluctuating dementia with or without raised intracranial pressure and intermittent paroxysmal attacks separated by symptom-free intervals. Other symptoms include nausea, short-term memory deficits (related to fornix compression) and the classical Hakim triad seen otherwise in NPH. A consensus does exist as to the treatment

of symptomatic cysts and growing cysts on radiological follow-ups. Rapidly progressive headache should be seen as an emergency.

Preoperative work-up include MRI of the head and ideally in a non emergency situation a neuropsychological examination should be obtained. The classical location and appearance of the cyst will confirm the diagnosis and a navigation sequence is obtained for trajectory planning.

Surgical technique

Material requirements

A rigid endoscope with a working channel of 2-3mm is necessary. Ideally two working channels are much better as they will allow for a two hand surgical technique, avoiding the lesion to tend to go away from any instrument used to resect it, be it suction, a scissors or an ultrasonic aspirator. Because of these difficulties encountered with the first purchased one channel working endoscope (Gaab endoscope, Storz, Tuttlingen, Germany) the neurosurgical clinic of the Kantonsspital St Gallen has recently adopted a two working channel system (Lotta endoscope, Storz, Tuttlingen, Germany) (Fig 4.17)



Fig. 4.17: Biportal endoscope (Lotta) with tracking balls for integration into the neuronavigation system.

Usual grasping tools and biopsy forceps as well as a bipolar probe are needed and microscissors with only one mobile branch are preferred as they are easier to control in endoscopy. A suction tube is also needed to aspirate the viscous content of the cyst. A surgical ultrasonic aspirator compatible with the endoscopic working channel can also be of help but is not mandatory. The use of a holding arm is generally recommended as the procedure will last more than one hour in most cases. Finally an irrigation system is also important as with time the CSF will be obscured by blood and tumor debris.

One important adjunct to the endoscope system is the combination with the neuronavigation system. This will allow for trajectory planning and for intraoperative control of the endoscope shaft in periods with blurred vision. To be able to navigate the endoscope, the shaft is equipped with tracking balls allowing the axis of the endoscope with its length and width to be calibrated (Fig 4.2).

Everybody will agree that a ventricle system, especially in the presence of massive hydrocephalus, can be punctured without neuronavigation using classical external landmarks. However the use of the image-guidance allows for optimal placement of the burr hole as well as optimal angulation of the sheath[149]. Intraoperative differences of some millimeters or a suboptimal angulation can create additional difficulties and should be absolutely avoided.

Preparation

The procedure is done under general anesthesia with the patient in recumbent position. The head is slightly elevated with a flexion of approximately 20° and as neuronavigation is used a three-pin head holder is used. Prophylactic antibiotic is given during preparation. the shaving and prep is done after determination of the exact entry point which is determined with the navigation after registration. If navigation for any reason is not used the entry point will be placed more anteriorly as for an ETV because the region of interest where the surgical work will be done is not the floor of the 3rd ventricle but the foramen of Monroe and the anterior part of the roof of the 3rd ventricle where the cyst is attached. So in the absence of navigation the burr hole and hence the incision would be planned 4 cm lateral to the midline and 4 cm in front of the coronal suture[67]. Some authors recommend a less anterior burr hole, only 1cm anterior to the coronal suture but even more laterally, 5 to 7 cm lateral from the midline[84]. The non-dominant side is chosen, unless special considerations such as cyst extension or ventricular size impose the other side. The region is shaved and prepped with propanol solution and the patient is aseptically draped.

Procedure

After performing the burr hole the dura is coagulated and incised and a small coagulation and incision of the cortical surface is performed prior to the insertion of the working sheath with its trocar. Once the ventricular wall has been pierced the trocar is retired and the 0° endoscope is introduced for orientation: the cyst will be identified without difficulties, occluding the foramen of Monroe. At this point the working sheath is fixed to the holder as the optic will remain into the lateral ventricle during the whole procedure. The 0° optic is changed for the working endoscope. With the bipolar probe the visible part of the cyst capsule is coagulated and then opened with scissors. The liquid can be aspirated though it can be quite viscous and sometimes larger cannulas have to be used. Once the semi-liquid material has been aspirated and the capsule is practically empty it can be tried to pull gently on it. In some instances the capsule can be mobilized that way allowing thus a total resection. In cases where the capsule is firmly attached it is recommended not to tear as this will cause bleeding. The region of insertion has then to be coagulated and cut, leaving a small piece of capsule at its

insertion which will be coagulated. Longatti et al insisted on the fact that particularly the productive inner layer of the capsule should be coagulated[230]. After multiple perforations of the capsule they inserted a Fogarty catheter into the cyst and inflated the balloon to squeeze the residual material that would stick to the balloon and be removed with it before ending their procedure with a coagulation of the cyst.

If needed other procedures can be performed during the same session as needed, mainly a fenestration of the septum pellucidum and an ETV. The working endoscope is changed for the inspection 0° endoscope for a last inspection and finally the endoscope is retired with the working sheath. External ventricle drainage is left in place in cases where relevant bleeding was observed. A systematic postoperative MRI is obtained to evaluate the rate of resection, the ventricular size as well as the patency of the eventually performed ETV or septostomy.

Postoperative complications and long term results

In a retrospective series of 90 cases operated on in Paris and Nijmegen during 11 years and presented at the "Société de Neurochirurgie de Langue Française" in 2007 following complications were observed: 1 death of unknown causes and one case of persistent short-term memory deficits as permanent morbidity and transient complications included one case of septic meningitis, 10 cases of aseptic meningitis, 9 transient memory deficits, 2 psycho-organic syndromes, 1 wound infection, 1 CSF leak, 1 hemiparesis and 2 visual deficits. With a mean follow-up of 50 months (range: 70 days-11 years) recurrences occurred in 6 patients who were reoperated endoscopically. Another series by Longatti et al including 61 patients of the Cooperative study by the Italian neuroendoscopy group on the treatment of colloid cysts[229] with a mean follow-up of 32 months (range 1-132 months) found 1 septic meningitis, 1 temporary hemiparesis, 3 early intraventricular hemorrhages and 1 trajectory hematoma.

Own experience

Material and methods

A retrospective chart review of all patients who underwent endoscopic resection of a third ventricular colloid cyst (TVCC) in the Department of Neurosurgery of the Cantonal Hospital of St. Gall between August 2006 and October 2012 was conducted. Pre- and postoperative clinical courses, details of the surgical procedure as well as radiological data were evaluated. Diagnosis of colloid cysts was based on magnetic resonance imaging (MRI) and postoperative histological examination. The extent of resection has been assessed on the basis of the initial postoperative MRI, performed within 6 months after surgery. The last follow-up MRI of each patient was used to evaluate recurrences. Clinical outcome was evaluated directly after the operative procedure and during outpatient follow-ups. Standard neuropsychological testing was performed, whenever the patient assessment or family interview raised suspicion of memory impairment.

Results

During the time of interest, 9 patients (1 female and 8 male) have undergone endoscopic resection of a TVCC at our institution. The mean age of patients was 53 (range 25-79).

Presenting symptoms included primarily headache (44%), memory deficit (33%), nausea and vomiting (22%), as well as gait disturbance (22%). Singultus, balance disturbance and normal pressure hydrocephalus symptomatology were all observed in one patient (11%). The time from symptom onset to treatment ranged from 2 weeks to 4 years (median 2 months). One patient was asymptomatic, and the colloid cyst was an incidental finding.

All cysts were associated with biventricular hydrocephalus. The diameter of the cysts ranged from 7 to 27 mm (mean 16 mm).

The Approach was performed from the right side in 6, and from the left side in 3 patients. Operating time ranged from 100 to 170min (mean= 132min). Clamped external ventricular drainage was kept systematically for a few days after surgery. In 4 patients occlusive hydrocephalus due to obstruction of the mesencephalic aqueduct entry by blood clots (2/4) or cyst fragments (2/4) occurred. As EVD weaning was unsuccessful in these patients, endoscopic third ventriculostomy (ETV) was performed in a second procedure. One of these repeat endoscopic procedures was complicated by an acute subdural hematoma requiring craniotomy. The patient recovered completely from a mild hemiparesis and aphasia within weeks. However, he suffers from residual postoperative short-term memory deficits. Transient postoperative memory deficits were observed in one patient. The oldest patient developed symptomatic bilateral hygromas requiring burr-hole drainage four weeks after the endoscopic intervention. No patient required a ventriculoperitonal shunt. The interventions did not cause symptomatic epilepsy in any case and no postoperative infection occurred. Data regarding patient characteristics and results are summarized in Table 4.5. The preoperative clinical manifestation improved in all patients.

Patient	Age, sex	Symptoms	Cyst size (mm)	Extend of resection	Complications	Recurrence	Follow-up (mth)
1	59, M	incidential finding	18	subtotal	occlusive hydrocephalus, acute subdural hematoma (after ETV) with transient hemiparesis and aphasia , persist. short-term memory deficits	no	37
2	69, M	gait disturbances, memory deficit	15	total	no	no	3
3	47, M	singultus	20	subtotal	no	yes	47
4	25, M	headache, nausea and vomiting, memory deficit	15	total	occlusive hydrocephalus, transient short-term memory deficits	no	67
5	37, M	headache	8	total	occlusive hydrocephalus	no	38
6	79, M	normopressure hydrocephalus symptomatology	27	subtotal	occlusive hydrocephalus, delayed bilateral hygromas	no	3
7	53, M	headache	15	total	no	no	9
8	31, F	headache, nausea and vomiting, memory deficit	7	total	no	no	38
9	73, M	gait and balance disturbances	20	total	no	no	35

Table 4.5: Clinical summary of the patients who underwent endoscopic resection of a third ventricular colloid cyst.

Post-discharge follow-up ranged from 9 to 67 months (mean= 34 months). Complete cyst removal was achieved in five patients, while in the remaining four patients remnants of the cyst wall were visible on postoperative MRI. The annual radiological follow-up scans showed evidence of cyst re-growth (8mm) in one patient, which was asymptomatic one year after the initially radiologically complete resection. Only

subtotal cyst-removal was achieved by an endoscopic re-operation. Since then (3 years), the 5mm measuring remnant has again expanded to 8mm without causing any symptoms.

All patients were operated on using the Gaab endoscope system described in the chapter on ETV in 6 cases the approach was made on the right side, in 3 on the left. Neuronavigation was used to plan the entry point and a rotatable bipolar probe was used to coagulate the capsular rests. MRI follow-ups showed a complete removal in 5 patients (55%), a small residual cyst in 3 (33%) and a large rest in one patient (11%). Neurological outcome was worsened in one patient with persistent memory deficits and improved in the 8 other patients (88%).

During the time of interest, 9 patients (1 female and 8 male) have undergone endoscopic resection of a TVCC at our institution.

Surgery was performed through a right side approach in 6, and from the left side in 3 patients. Operating time ranged from 100 to 170min (mean, 132min). In 4 patients occlusive hydrocephalus due to obstruction of the mesencephalic aqueduct entry by blood clots (2/4) or cyst-wall fragments (2/4) occurred after removal of the external ventricular drainage in the days after surgery. In these patients endoscopic third ventriculostomy (ETV) was performed in a second procedure. One of these repeat endoscopic procedures was complicated by an acute subdural hematoma requiring craniotomy. The patient recovered completely from mild hemiparesis and aphasia within weeks. However, he suffers until today from postoperative short-term memory deficits. Transient postoperative memory deficits were observed in one patient. The oldest patient developed symptomatic bilateral hygromas requiring burr-hole drainage four weeks after the endoscopic intervention. The preoperative clinical manifestation improved in all patients. External ventricular drainage was kept systematically for 1 to 3 days after surgery.

No patient needed a ventriculoperitonal derivation. The interventions didn't cause symptomatic epilepsy in any case and no postoperative infection occurred. Post-discharge follow-up ranged from 3 to 67 month (mean, 31month). Complete cyst removal (Fig. 4.18) was achieved in five patients (56%), while in the remaining four patients remnants of the cyst wall were visible on postoperative MRI (44%). The annual radiological follow-up controls showed no evidence of cyst-regrowth in all but one patient. In the latter case, asymptomatic cyst recurrence one year after the initial radiologically complete resection (0 mm -> 8mm) has led to an endoscopic re-do. This time, only subtotal cyst-removal was achieved. Since then (two years), the 5mm measuring remnant has again expanded to 8mm without causing any symptoms.



Fig. 4.18: Sagittal (a) and axial (b) MRI view of a third ventricular colloid cyst; sagittal (c) and axial (d) MRI after endoscopic resection demonstrating radical resection.

Discussion

The most frequent transient postoperative complication in our series that occurred in 4 patients (44%) was symptomatic occlusive hydrocephalus due to obstruction of the mesencephalic aqueduct entry, either by blood clots (2/4) or cyst-wall fragments (2/4). As a clamped EVD was routinely left in place, the drainage could be opened on the ward. In all four patients ETV was performed in a second procedure, as EVD weaning was unsuccessful. One of these repeat endoscopic procedures to perform an ETV in one of the cases of obstructive hydrocephalus was complicated by an acute subdural hematoma requiring craniotomy. The patient recovered completely from mild hemiparesis and aphasia within weeks. However, he suffers until today from postoperative short-term memory deficits. As macroscopical damage of the columna fornicis was not observed intraoperatively, it remains unknown if the forniceal damage resulted from the first or second endoscopic procedure. In order to reduce the risk for

invaliding memory deficits, the neuronavigation should be used to choose an optimal work-trajectory. A shallower trajectory with a more lateral starting point may help to avoid relevant traction on the columna fornicis[168].

The high incidence of postoperative occlusive hydrocephalus raises the question whether or not to perform ETV in a routine manner. While some groups perform ETV under specific circumstances such as non-resectable posterior remnants of the cyst[27, 84], others complete systematically the procedure with an ETV[216]. However, Kwiek et al. report two transient oculomotor nerve palsies from routinely performed ETV in 18 endoscopic removals of TVCC's[216]. Therefore, supplementary risk of ETV has to be weighted against the generally low risk of subsequent occlusive hydrocephalus. Moreover performing an ETV through the antero-laterally placed burr hole as recommended for the resection of TVCC will either place the fornix at stake for undue traction or necessitate a second burr hole to avoid this. For these reasons we would not recommend to perform systematically an ETV. None of our patients required a permanent ventriculoperitonal derivation.

One of the explanations for the duration of the procedure in our series is the use of the original Gaab endoscope system. This system has only one working channel, a certain disadvantage when performing more than a ventriculostomy and after this series the Lotta neuroendoscope was adopted. The difficulty with handling tumors with only one working channel is that the operator cannot fix the tumor when trying to apply instruments like scissors or aspiration because the tumor tissue will have a tendency to be pushed away by the instrument thus diminishing its efficacy. This will cause a loss of time trying to get the tumor into a position where the instrument can be applied efficiently.

The proportion of total resection will probably increase with experience and also with improved material. The introduction of a second working channel will definitively improve tumor control and hence the region of the insertion will become better accessible. Nevertheless, the diminished ability to perform a complete resection with the endoscopic technique as compared to open microscopic technique is one of the main arguments of its opponents. The question of the meaning of the residual cyst is also interesting: despite a great variety in the total resection rates reported in endoscopic series one observation is readily made: even in the presence of a relevant cyst rest the need for a reoperation remains very low. In the series by Horn et al, from 21 patients 9 had a rest but only 2 needed a reoperation [168]. In the series by Decq et al 12 out of 15 had some rest but none needed a reoperation[68]. In the series of Hellwig et al, most of the 20 patients had residual cysts but only one patient needed a reoperation after 1 year [153]. In the series by King et al a complete resection was achieved in 80% of the cases and after a follow-up of 2 years no patient developed a recurrence, independently of the resection rate [199]. In one study comparing 27 patients operated on through the transcallosal approach with 28 patients operated on endoscopically Horn observed that if more patients of the endoscopic group presented a residual cyst there were no recurrences in both groups with a follow-up of less than one year [168].

However most of these series have to be interpreted prudently as the follow-ups remain rather short.

Regarding the complication one has to remain aware of despite being minimally invasive the endoscopic resection of colloid cyst can be associated with neurological complications, some of which are severe, as hemiparesis or short-term memory deficits[153, 199, 223].

Particularly at stake during manipulation in the vicinity of the foramen of Monroe is the fornix, the lesion of which can produce the short-term memory deficits described, transient or permanent. In order to minimize manipulations in this region different trajectories haven been recommended. One proposed alternative is to place the burr hole more anteriorly in order to see more of the tumor and thus less mobilization of the tip of the endoscope will be needed; another advantage of more anterior burr holes is that the region of insertion of the cyst at the roof of the 3rd ventricle will be eventually seen thus facilitating the coagulation of the rest or the separation of the capsule from its attachment at the plexus or veins. Another variation is to place the entry point more laterally than for an ETV. This will bring the tip of the endoscope in front of the plan of the foramen of Monroe and the endoscope further inferior to the fornix; this positioning of the endoscope and instruments should also lead to reduced retraction of this structure[168].

Para- and intraventricular tumors, intraventricular cysts

Neoplastic lesions of the lateral or third ventricle

The applications of the endoscope in the setting of neuro-oncology include endoscopic tumor biopsies, endoscopic treatment of obstructive hydrocephalus and tumor resection. In some instances the endoscope can be a very elegant tool to perform a biopsy in the presence of hydrocephalus caused by intra-axial tumors located in the vicinity of the ventricular system and at the same time a ventriculostomy.

A lesion will be considered as suitable for an endoscopic resection if it bulges into the ventricle, can be reached with a straight trajectory, is not multifocal and does not exceeds 2 cm in diameter[38, 109]. In their series Gaab and Schroeder reported that 2 of their 30 patients operated endoscopically had to be re-operated subsequently because the tumor size was exceeding 2 cm[109]. A small implanted base would also be a very favorable condition. The endoscopic resection of larger tumors through the relative narrow working channels will be very time consuming and the benefits of the minimal invasive character of the procedure will be lost.

Depending on the location of the lesion a third ventriculostomy can be performed during the same procedure through the same hole or a second burr hole can be needed to reach the tumor for a biopsy. This can be best planned preoperatively on a navigation system (Fig 4.19).



Fig 4.19: Example of navigation planning in a 22 years old patient for an endoscopic third ventriculostomy (yellow arrow) followed by an endoscopic biopsy of a tumor obliterating the upper aqueduct of Sylvius (red arrow), both trajectories passing through the right foramen of Monroe (magenta circle). The histology revealed a low grade glioma (WHO gr I), the hydrocephalus resolved and the patient was controlled yearly with MRI of the head.

Besides colloid cysts, a list of rarely encountered intra- or para-ventricular lesions can be considered for an endoscopic procedure, be it a partial tumor resection, a biopsy or a marsupialization and include: para-ventricular low grade gliomas, choroid plexus tumors, central neurocytomas, subependymal giant cell astrocytomas, subependymomas or craniopharyngiomas with predominantly intraventricular development, intraventricular subependymal cysts.

As these pathologies are quite rare, the theoretically advantages of the endoscopic technique such as lower morbidity, shorter operation time and shorter hospitalization duration have not been demonstrated for these types of lesions[363] as it was the case with colloid cysts.

Endoscopic biopsy

The main advantage of this technique as compared to stereotactic biopsy is that it offers the operator a direct view of the lesion. This will secure a positive diagnosis, will allow to choosing the best visible place to take the probe and finally allow a controlled hemostasis in case of bleeding. In their series of endoscopic biopsies, Cappabianca et al reached a positive diagnosis in 90% of the cases. This high rate of positive diagnosis was also reported by other groups[109, 234, 257]. The diagnosis included gliomas, lymphomas, neurocytomas, germinomas, pinealomas, epidermoids, teratomas and craniopharyngiomas[38]; they had only one relevant postoperative bleeding in their 37 cases thus confirming the low incidence of hemorrhagic complications as observed by others[234], although the risk of a fatal complication is not zero[275]. In the presence of large ventricles with a clear bulge of the lesion the biopsy can be performed free-hand; in the presence of a small lesion, narrow ventricles or without any bulging the endoscope can be combined with the neuronavigation. In case of bleeding, usually a

small oozing at the spot of the biopsy, this can be controlled with passive measures such as irrigation or light compression with in inflated balloon. Only if these measures do not work, coagulation with the rotatable bipolar probe at a low intensity can be tried.

Tumor resection

The decision to perform an endoscopic tumor resection has to be carefully taken, as there are numerous vital structures at stake in or around the ventricles such as the deep cerebral veins or the basal ganglia, hypothalamus or fornix. The ideal trajectory to the tumor will best be simulated on the planning station of the neuronavigation system as in some instances it can be advantageous to go through the contralateral ventricle. The burr hole has to be large enough to allow some movements of the endoscope shaft. The resection itself will be done using instruments that allow removal of large fragments or the aspiration, depending on the tumor consistency.

If the tumor tissue doesn't present a high bleeding tendency after a biopsy has been taken and location as well as volume are reasonable a partial resection can be attempted using the dedicated ultrasonic tumor aspirator (CUSA ® or Söring ®) through the working channel (Fig 4.20). This will be often the case in low grade tumors as these are nearly avascular and a resection of a large portion will be done safely.



Fig. 4.20: Endoscopic ultrasonic aspirator system: working endoscope (A), transducer (B), mounted system (C).

Should a bleeding occur, the same methods as mentioned in the section about endoscopic biopsy will be applied. Cappabianca et al presented the possibility to insert a small cotton pad be introduced through the working channel after the endoscope has been retired so as to apply the pad on the bleeding region with slight pressure for a couple of minutes[38]. The attached string allow for removal of the pad. The presence of an intraventricular tumor without concomitant hydrocephalus represents a particular situation. Although it should be avoided because of obvious difficulties with puncturing the ventricle and then with intraventricular orientation, Cappabianca et al have exposed the technique making it possible to work in normal sized ventricles. The prerequisite with this kind of surgery is of course a great deal of experience of the operator with endoscopic and neuronavigation systems. In order to maintain a working space the procedure is done under continuous irrigation to inflate the ventricular system. In order to avoid any elevated pressure the operation has to be done with a constant open purge. This can be achieved either with un unused opened working channel or with an endoscope smaller than the sheath[38].

In our limited experience most of these intra-axial tumors being located in or very close to eloquent areas, the procedure will generally be limited to a biopsy priory associated to a third ventriculostomy in the presence of obstructive hydrocephalus. Controversy exists as to which procedure should be done first. One argument in favor of doing the biopsy at first is that the ventricular system could become narrow in the presence of an acute hydrocephalus, rendering the puncture of the ventriculostomy first is that the biopsy can cause some bleeding which would cause the vision to be blurred thus rendering the ventriculostomy difficult. We found this argument stronger and perform first the ventriculostomy, the filling of the ventricular system being assured with Ringer infused carefully.

Endoscopic marsupialization of intraventricular cysts

Besides colloid cysts other intraventricular cysts can become symptomatic and need a therapeutic intervention, as for example ependymal cysts, cysts of the velum interpositum, of cavum vergae or epidermoid cysts. Ependymal cysts are rare congenital lesions that can be observed in the third or lateral ventricles[121, 273], the most common site being the trigone of the lateral ventricle. It can be seen on MRI images as a non-enhancing thin-walled cyst with CSF intensity. They remain most of the time asymptomatic but can sometimes be the cause of headache, seizures or symptoms and signs of raised intracranial pressure. In such cases an endoscopic marsupialization can be performed. Here care must be taken not only to perforate the superior wall of the cyst, as the persistency of the basal part of the cyst could cause further obstruction of the Foramen of Monroe. For this reason it is recommended to try, as far as it is possible, to perforate also the basal part of the lesion.

Illustrative cases

Case 1

A 22 years old female patient was admitted for acute headache, vomiting and minimal facial palsy on one side. She also presented a history of previous fatigue and weight loss of 12 kg over one half year. The neurological examination revealed double vision on the left side and a bitemporal hemianopsia. On the emergency CT scan (Fig. 4.21) a 3cm round lesion with a density superior to that of the CSF was identified into the 3rd ventricle with consecutive obstructive hydrocephalus.



Fig. 4.21: Emergency non-enhanced axial (a), coronal (b) and sagittal (c) CT scan with large sellar and supra-sellar mass causing obstructive hydrocephalus.

After the placement of external ventricle drainage, the MRI scans (Fig. 4.22) demonstrated a 4.5 cm high cystic sellar and supra-sellar mass extending from the sellar floor to the elevated corpus callosum with bilateral Monroe blockade and with thin peripheral contrast enhancement.



Fig. 4.22: T2-weighted axial (a), T1 gadolinium enhanced coronal (b) and sagittal (c) MRA demonstrating the cystic nature of the lesion with capsular contrast enhancement and bilateral Monroe blockade.

The endocrinologic examinations (Tab. 4.6) revealed a panhypopituitarismus, a marginal hyperprolactinemia and no diabetes insipidus.

Hormone tested	Value	Normal values
PRL	38.0 μg/l	<20
T3 frei	3.53 pmol/l	3.2-6.0
T4 frei	5.6 pmol/l	6.8-18.0
TSH	1.19 mU/l	0.25-4.0
IGF-1	4.2 nmol/l	15.08-46.54
a-Fetoprotein	1.3 μg/l	<13
β-HCG	<0.5 U/l	

Tab. 4.6: Hormone values.

The ophthalmologic examination confirmed the severe bitemporal hemianopsia and found a papilloedema as well as a compressive neuropathy in the visual evoqued potentials (VEP).

A transventricular endoscopic fenestration was performed with consecutive rapid resolution of the obstructive hydrocephalus (Fig. 4.23) and progressive complete resolution of the visual disturbances. The panhypopituitarismus persisted.



Fig. 4.23: T2 weighted axial (a), T1 gadolinium contrast enhanced coronal (b) and sagittal MRI images demonstrating resolution of obstructive hydrocephalus and T2 weighted sagittal images showing opened aqueduct.

Case 2

This 28 years old female patient presented with progressive bilateral parieto-occipital headache and dizziness. The neurological examination was normal and the preoperative MRI images (Fig. 4.24) revealed a 6.5 cm intraventricular cystic formation with obstructive hydrocephalus.



Fig. 4.24: T1 weighted axial image demonstrating large intraventricular cyst of the velum interpositum.

A navigation sequence was performed and an endoscopic image-guided fenestration planned (Fig. 4.25).



Fig. 4.25: Planning for image-guided endoscopic fenestration of a 6.5 cm large intraventricular cyst of the velum interpositum.

The intervention allowed for performing a large fenestration with consecutive intraoperative collapse of the cyst (Fig. 4.26) thus alleviating the necessity of further antero-basal perforation as normally recommended.



Fig. 4.26: Intraoperative endoscopic view (upper left) of the fenestration with navigation images showing position of the endoscope (green line).

The headache resolved within the next 24 hours. Postoperative collapse persisted in the last 6 years as demonstrated on the last radiological examination (Fig. 4.27) performed 5 years after the procedure at the beginning of the patient's second pregnancy and the patient has remained asymptomatic thus far.



Fig. 4.27: T1 weighted axial (a), T2 weighted coronal (b) and sagittal (c) MRI images 5 years postoperatively demonstrating persisting cyst collapse and resolution of the obstructive hydrocephalus.

Training issues

From the literature it is often not clear how many procedures each surgeon performs per year and how many are needed to reach an 'experienced' level. In a systematic review of complications after ETV, even in large series the number of procedures per year per surgeon varied greatly (n=1.3 to 12) but remained generally below 12 procedures with a mean value of 5.6 which represents clearly less than one procedure per month (Table 4.4).

Author	Total operations (N°)	Time period reviewed (yrs.)	Operations per year	Surgeons/ Institution performing procedure	Cases/ year/ surgeon
Ersahin[88], 2008	155	7	24	NA	
Hader[138], 2008	131	8	16	NA	
Baykan[13], 2005	210	10	21	NA	
Sacko[314], 2010	368	8	46	NA	
Grunert [134], 2003	171	8	21	NA	
Jenkinson [18 2] , 2009	190	8	23	NA	
Kadrian[189], 2005	203	22	9	7	1.3
Van Beijnum[14], 2008	202	9	22	2	11
Schroeder [32 9] , 2002	193	8	24	NA	12
Naftel[255], 2011	151	14	11	7	1.5
Abhaya[213], 2009	618	17	36	12	3
Durnford[81], 2011	181	16	11	2	5.5
Rhode 2012	126	9	14	3	4.6

Table 4.4: Case load in large series. The mean number of yearly ETV per institution was 21.5 and where available, the number of ETV performed yearly by the involved surgeons was calculated. The mean number of ETVs per surgeon per year was 5.6.

A recent global survey of the usage of endoscopy in neurosurgery showed that an annual average of 27 intraventricular procedures are performed per surgeon per year, rarely exceeding 2 interventions per month[90]. This leads ultimately to the questions of
which centers should perform this procedure in regards to patient's safety and expertise. Only after answering this question the best training approaches can be developed. Due to these low numbers there is an even greater lack of exposure and opportunity to train for residents and young neurosurgeons. Training haptics and handling an endoscope, outside of patients, in training models, will therefore be a helpful aid in training [141, 225, 305].

As the consequences of the rare major complications can be devastating, further research in simulation training models is necessary[322]. In conformity with the debates about necessity of competence center formation, the need for standardized specialized neuroendoscopic training becomes evident.

Regarding the acquisition of the endoscopic skills, it was much slower than for the transsphenoidal endoscopy, mainly because the number of obstructive hydrocephalus cases remain a minority of overall hydrocephalus pathologies. On the other hand the elements that have to be acquired are not as complex as for the transsphenoidal applications:

The anatomy is well known and the instruments are moved within the working channel, thus keeping the azimuth angle (angle between the instrument and the optical axis) near to 0°[161]. Because of this low azimuth angle there are less refined psychomotor skills to be acquired as compared with transsphenoidal endoscopic applications. Nevertheless, these few basic haptic skills can be acquired out of the theatre and several types of models have been developed after our learning period[30, 97, 388], either using virtual simulation or 3D printed models. Because of the rarity of the procedure with less than 2 cases per months in most of the centers there is no question that these teaching models will clearly have their place in future skills laboratory curricula.

5. Difficulties in the introduction of spinal endoscopy as a solitary starter without backup

The introduction of a new procedure or technique in a surgical department represents a challenge whose difficulty is largely dependent on the degree of innovation. The acquisition of some new spinal procedures for a neurosurgeon that has performed more than 1000 spinal procedures including stabilization represents for example a limited challenge: the 3 dimensional anatomy is mastered and the orientation with fluoroscopy belongs to daily practice. In this setting the introduction for example of balloon kyphoplasty can be done after an efficient learning process as offered in short courses with theoretical introduction, hands-on cadaver course and seeing one procedure. A clinical visit with performance of one procedure under supervision would ideally complete such a course.

Introducing endoscopic surgery, be it transsphenoidal or intraventricular or even for interlaminar full endoscopic discectomy, represents a greater amount of innovation. It includes a different type of vision and new surgical instruments, and moreover the number of procedures performed for intraventricular pathologies and for anterior skull base processes does not reach the figures of spinal procedures. Finally the anatomical knowledge has to be optimized because of the extremely sensible neurovascular structures encountered. All these elements make out-of-theatre training an absolute pre-requisite.

As a solitary starter no one in the department masters the procedure or the technique and so the question rises regarding supervision or back-up. Regarding the transnasal endoscopic procedures, a large amount of difficulty can be reduced by the collaboration with a motivated endoscopic rhinologist. In their study, Stelter and colleagues have investigated the mental stress of rhinologists during endoscopic sinusal and skull base procedures[352]. The whole procedure was monitored using a bio-feedback instrumentation (NeXus 10, MindMedia) which registered the cardiac frequency during the different situations encountered. Not only could they demonstrate that the most mentally demanding phase was the orientation at the skull base with the 45° where navigation played a relieving role, but also that the presence of a neurosurgeon at the table was a clear relieving factor. This was thought to be due to workload shift associated with his presence for one part and to the shared responsibility on the other side. These results can reasonably be transposed to the reverse situation for the neurosurgeon performing an endoscopic pituitary adenoma resection.

As far as the intraventricular endoscopy is concerned, such a support will not be at disposal if introducing the technique from the very beginning.

The presence of a more experienced colleague at his side will have an important influence on the learning curve of any beginner for evident reasons of security. The stress experienced by an individual surgeon is not only connected to the difficulty grade of the procedure but also to his degree of responsibility within the team. The same devastating complication as intraoperative rupture of the intracavernous internal carotid artery during pituitary surgery will have a more intense stressing effect if being the sole operator in charge as if being called to help a colleague who is in principle in charge of the procedure.

Own experience: Evaluation of the absence of a backup on the learning curve for fully endoscopic interlaminar discectomy

Even if spinal endoscopy does not belong to the topic of this work, its application for the treatment of lumbar disc herniation offers a much more regular opportunity to use the endoscope and thus allowed to gather more information regarding learning curves associated with the introduction of the endoscope into the Department also from a starting point where nobody had any experience with it.

The influence of the presence or absence of a backup could be evaluated and demonstrated its decisive influence on the learning curve for fully endoscopic discectomy in the Department.

At our institution we perform 500 micro-discectomies (MD) for lumbar disc herniation per year. The author started with interlaminar full endoscopic discectomy (IL FED) in selected cases in 2007 and was followed one year later by a registrar. Both surgeons had participated in a training course for full endoscopic discectomy prior to clinical application. The author had to participate in a second course, because of the time elapsed between the first course and the moment where the spinal endoscope and instruments were actually delivered.

The goal of the study was to analyze the surgical results in view of the surgeon's individual learning curves. We tested the following two hypotheses:

- Surgeon #2 had a faster learning curve than Surgeon #1 as he was supervised by Surgeon #1 and benefitted from his experience.
- Significantly more recurrences and complications/conversions occurred before a steady state of the learning curve was reached.

The data about recurrences and pain are presented very briefly but are not discussed here as they are out of this work's topic.

Materials and Methods

Patient Population & Follow-up

All charts of patients (n=76) who were operated on by Surgeon #1 (n=53) and Surgeon #2 (n=23) using IL FED between April 2007 and April 2012 were reviewed with respect to operation time (primary endpoint), incidence of intraoperative complications and need for intraoperative conversion from IL FED to MD, postoperative infections, recurrent LDH and opioid use, leg- and lumbar back pain pre- and postoperatively measured with the visual analogue scale (VAS), length of postoperative hospitalization as well as need for stationary rehabilitation. Additionally to this retrospective data collection, all patients who underwent successful IL FED without conversion were prospectively asked to fill out a mailed questionnaire. The questionnaire assessed current leg- and lumbar back pain (using the VAS scale), need for opioid medication, ability to work, need for revision surgery (including date of relapse and date of revision

surgery) for recurrent LDH at the same level confirmed by MRI and any kind of postoperative complications, which may have been observed at other neurosurgical clinics). The functional status was assessed with the German version of the North American Spine Society (NASS) outcome assessment[62] which is partly based on the Oswestry Disability Index and uses 11 items to assess pain-related disability and 6 items to assess neurogenic symptoms – each item ranging from 1 (best) to 6 (worst). The short-form 12 (SF-12) questionnaire[252] was used to assess Health-related Quality of life (HrQoL). Patients were also asked, whether they would have the same operation performed again provided they had the same outcome.

All retrospective variables were compared between the patients who underwent surgery before (group A; n=43) and after (group B; n=25) a steady state of the surgeon's learning curve (determined by the operation time) was reached. The same analysis was performed for HrQoL and long-term pain intensity for those patients who returned the questionnaire. Patients scheduled for IL FED who were intraoperatively converted to MD were taken into consideration for the analysis of possible complications only, but excluded from analysis of secondary outcomes.

Ethical Considerations

Written informed consent was requested from all included patients. The study was approved by the cantonal ethics committee of St Gall.

Inclusion & Exclusion Criteria

All included patients had radicular leg pain irresponsive to conservative therapy with or without neurological deficit corresponding to a single-level mediolateral disc herniation of either the level L4-5 or L5-S1. Diagnosis was confirmed by magnetic resonance imaging (MRI) in all cases. Exclusion criteria were any kind of previous lumbar surgery (except diagnostic/therapeutic infiltrations), symptomatic LDH of any level other than L4-5 or L5-S1, multi-level LDH, foraminal or extraforaminal LDH, lumbar stenosis, lumbar instability and advanced degeneration of the involved segments.

Surgical Technique

Surgery was performed under general anesthesia in knee-chest position. A <10 mm long skin incision was made guided by anterior-posterior fluoroscopy approximately 1cm lateral to the midline. A Kirschner wire aiming at the inferior edge of the superior lamina was inserted to guide the introduction of the dilator. Once the dilator was placed at the superior border of the interlaminar window it was then replaced by an oblique cannula. A 30° working endoscope (Richard Wolf GmBH, Knittlingen, Germany) was inserted and the ligamentum flavum identified, irrigated and bluntly perforated. When necessary the perforation was enlarged with scissors. Under constant irrigation and protection of the nerve root with the bevelled cannula, the sequester was removed in one piece or in fragments. After thorough inspection for any remaining sequester or bleeding, the cannula was removed and the skin closed.

Results

Patient Characteristics

A total of 76 patients were identified who had received IL FED surgery at our institution. After exclusion of eight patients who were converted from IL FED to MD intraoperatively, a total of 68 patients were asked to participate in the study. Of those, 47 returned their mailed questionnaire for the long-term clinical outcome analysis. Time of follow-up ranged from one to six years (mean 3.37 years).

Baseline data of included patients such as sex, age, level and side of LDH were equally distributed between patients of group A and group B (patients who underwent surgery before and after the asymptote of the learning curve) while an overall preponderance of left-sided lumbosacral disc herniation in male patients was noted (Table 5.1).

		Group A n=43		Group B n=25		Σ n=68		p-value
Sex	Female	15	35%	10	40%	25	37%	0 705
	Male	28	65%	15	60%	43	63%	0.795
Age (years)	mean ± SD	38.5 ± 10.8 17.2 -62		40.7 ± 11.1		39.3 ± 10.9		0.571
	range			24.7 – 58.8		17.2 – 62		
Level	L4-5	3	7%	4	16%	7	10%	0.409
	L5-S1	40	93%	21	84%	61	90%	0.403
Side	Right	11	26%	12	48%	23	34%	0.069
	Left	32	74%	13	52%	45	66%	0.000
Pain duration	mean ± SD	98.5 ± 1	98.5 ± 108.4		135.6 ± 138.7 112.2		120.8	0.005
(days)	range	5 – 360		4 – 360		4 – 360		0.200
VAS leg pre-op	mean ± SD	4.5 ± 2.6		4.4 ± 2.6		4.5 ± 2.5		0.858
VAS lumbar pre-op	mean ± SD	2.1 ± 1.9		2.3 ± 2.6		2.2 ± 2.1*		0.875
Opioid use	pre-op	14	33%	13	52%	27	40%	0.131

Table 5.1: Patients characteristics

Analysis of the Primary Endpoint

Operation Time

The operative case numbers comprise all patients originally intended for IL FED (n=76). The analysis of the primary endpoint, operation time, however, is solely based on the patient cohort of 68 patients who received IL FED, thus excluding the patients who were converted to MD intraoperatively. Surgeon #1 reached an average operation time of 42.7 minutes after 40 operations (including 5 patients who were converted to MD intraoperatively). Surgeon #2 had a shorter learning curve, reaching an average of 47.3 minutes after 16 operations (including 2 patients who were converted to MD intraoperatively) (Figure 5.1).



Figure 5.1: Average operation time becomes an asymptote with 42.7 minutes after 40 operations (35 IL FED + 5 conversions to MD) for surgeon #1 and 47.3 minutes after 16 operations (14 IL FED + 2 conversions to MD) for surgeon #2. The unconnected dots represent converted patients, which count as operative case numbers but are omitted for the analysis of the operation time.

Operation time decreased significantly for both surgeons with 65.5 ± 26.5 minutes before and 47.2 ± 17.9 minutes after a steady state of the learning curve was reached (p=0.001; Table 5.2).

		Group A n=43	Group B n=25	Σ n=68	p-value	
Operation duration	mean ± SD	65.5 ± 26.5	47.2 ± 17.9	58.8 ± 25.2	0.001	
(minutes)	range	28 – 165	20 – 90	20 – 165	0.001	
Blood loss (ml)	mean ± SD	2.6 ± 2.6	1.8 ± 2.9	2.3 ± 2.7	0.075	
	range	0 – 10	0 – 10	0 – 10	0.075	

*missing data - only 47 out of 68 patients returned their follow-up questionnaire

Pos	Post-op hospi- mean ± SD		3 ± 1.3		2.8 ±	2.8 ± 1.2			0.712
talisation days range		2-7		2-6		2-7		0.712	
Recurrent disc herniation		14	33%	5	20%	19	28%	0.401	
	Early (< 4 w	eeks)	6		4	4		53%	0.202
	Late (> 4 we	eeks)	8		1	1		47%	0.303
Rev	ision operation		11	26%	5	20%	16	24%	0.768
	Early (< 4 w	eeks)	6		4		10	63%	0.000
	Late (> 4 we	eks)	5		1		6	37%	0.608
Out	come – Pain								
	1 st post-op day	mean ± SD	1.1 ± 1.3	3	2.0 ±	1.9	1.4 ± 1.	ô	0.048
0	2 nd post-op day	mean ± SD	1.3 ± 1.8	8	1.2 ±	1.4	1.2 ± 1.	7	0.916
NS le	follow-up*	mean ± SD	21+20		19+24		20+27		0.940
Sector State Sector State Sector State (mean 3.37 years)			2.1 ± 2.0		1.0 ±	1.5 ± 2.4		1	
	1 st post-op day	mean ± SD	0.7 ± 1.1		1.4 ±	1.5	1 ± 1.3		0.252
mbar	2 nd post-op day	mean ± SD	0.4 ± 0.7		0.7 ±	0.8	0.5 ± 0.7	7	0.397
vS lu	follow-up*	mean ± SD	25.2	0	10.	+20 23+26		2	0.605
✓ (mean 3.37 years)		2.5 ± 2.0		1.9±2.0		2.3 ± 2.0			
Opio	oid use	follow-up*	1	2%	0	0	1	1%	n/a
Outcome – Life Quality & Work Ability									
NASS mean ± SD		1.92 ± 1.03		2.03 ± 1.16		1.96 ± 1	.07	0.682	
Pain/Disability* range		1 – 5.18		1 – 5.36		1 – 5.36		0.002	
NASS mean ± SD		mean ± SD	2.36 ± 1.34		2.27 ± 1.08		2.33 ± 1.25		0.801
Neuro* range		range	1 – 5.17		1 – 4.16		1 – 5.17		0.001
SF-12 me		mean ± SD	55.66 ±	6.05	54.82 ± 8.7		55.38 ± 6.95		0.00
MCS* range		range	42.28 - 64.9		34.86 - 67.09		34.86 - 67.09		0.00
SF-	12	mean ± SD	47.46 ± 11.22		48.38 ± 7.75		47.77 ±	10.12	0.402
PCS	S*	range	19.93 –	58.38*	31.24	- 55.91	19.93 –	58.38	0.432
Reduced Work Capacity*		2	1	1		3	6%	n/a	

Table 5.2: Perioperative Parameters & Follow-up

Analysis of the Secondary Endpoints

Perioperative Parameters & In-patient Follow-up

Blood loss was similar between both groups and ranged between none and a maximum of 10 ml (Table 5.2). No patient required a blood transfusion or a drain. Six patients of surgeon #1 and two patients of surgeon #2 were intraoperatively converted from IL FED to MD due to technical difficulties (two), complications (three) or surgeon's uncertainty (three) (Table 3). Thus, conversion rate was 10.5%. Comparing the conversion rates before (group A) and after the steady state of the learning curve (group B) no statistically significant difference was shown (p=0.704). This was attributed by the larger patient cohort of group A. In addition to the complications that led to conversions, one small dural tear without consequences was documented in group B, adding the complications up to an absolute number of four (5%). Further difficulties encountered during IL FED leading to extended operation times are listed in table 3. Among these were reduced visibility, orientation loss, demanding anatomical obstacles (e.g. hypertrophied facet-joints) during the surgical approach and one technical problem with the endoscope. No infections were registered.

The post-operative hospitalization time was 3 ± 1.3 days on average without group differences (group A: 3 ± 1.3 and group B: 2.8 ± 1.2). Only one patient was discharged to a stationary rehabilitation due to pre- and postoperative leg paresis.

Recurrences

Nineteen patients (28%) experienced radiologically (MRI) confirmed recurrent LDH. Postoperative MRI was not routinely performed but always in cases of recurrent sciatica. Five out of these 19 recurrent LDH patients had more than one recurrent LDH. There was no statistically significant difference in the incidence of LDH recurrences before (14 patients in group A) and after (5 patients in group B) the asymptote of the learning curve was reached (p=0.401). The majority of recurrences (n=10) occurred within 4 weeks after first IL FED. Sixteen patients were re-operated either using IL FED (n=6) or MD (n=10). Three of these operations were performed at another neurosurgery clinic. Finally one patient required a spondylodesis after four years and lumbar disc prosthesis due to discopathy after 15 months. Of note, 50% of all recurrent LDH were treated surgically within four weeks after symptom onset - one patient was revised endoscopically on the first post-operative day.

This high rate of recurrences lead the authors first to interrupt the performance of IL FED and it is only after an analyze of the literature on the subject that it could be reintroduced. The literature about recurrence of lumbar disc herniation reports an overall rate of about 11% but as shown by Carragee[40] the risk of recurrence can be very different depending on several factors, the most important being the disc height and the size of the annular defect as measured intraoperatively. These findings have been recently confirmed by the study of Kim[198] which also demonstrated the importance of disc height and size of the annular defect on the incidence of postoperative herniation recurrences. In the series of Carragee the risk of recurrences in the so-called "fragmentdefect" group reached 27%.

As we intended to introduce the endoscopic technique we were very much aware of the technical difficulties of introducing this new technique and of the shallow learning curve mentioned in the literature as quoted above. Because of these well documented difficulties following measures have been undertaken: one visit of 2 days in the department of Dr. Sebastian Ruetten in Aerne, Germany, followed a couple of months later by a course with hands-on cadaver workshop at the Université René Descartes in Paris; as the delay between the last cadaver workshop and the arrival of the spinal endoscope was more than 6 months a second course with again practical anatomical training was visited in Cologne short before the first procedure. Finally, simple cases have been chosen and the vast majority of the selected cases were young patients with large sequesters, high discs and no degenerative changes in order to have a nice window for the endoscope. However, by choosing these cases we selected precisely the population with the highest recurrence risk. This is probably the decisive factor for the high incidence of recurrences we observed in our series.

Pain

The intensity of leg- and lumbar pain on postoperative day one and two as well as for follow-up (mean 3.37 years) was equal between both study groups as shown in table 2. While 40% of the patients were on opioid medication preoperatively, only 2% required them at the time of follow-up. It should be noted that one patient in group A completed his follow-up questionnaire while he suffered from severe pain (VAS 10) due to a LDH relapse. Notwithstanding, he was subsequently admitted for revision surgery and included in the statistics.

HrQoL & Working Capacity

The NASS pain/disability score (1.96 \pm 1.07) and NASS neuro score (2.33 \pm 1.25) showed no significant difference amongst patients in both groups (n=47) at the time of follow-up (Table 5.2). The same held true for the SF-12 mental component summary (MCS), (55.38 \pm 6.95), as well as for the SF-12 physical component summary (PCS) (47.77 \pm 10.12), (table 2).

Only three patients had a reduced working capacity at the time of follow-up. One further patient was on maternity leave and two patients were pensioners.

Discussion

Our study is an analysis of the introduction period of IL FED into a neurosurgical department with spinal focus. The learning curves demonstrate a total number of about 40 procedures needed for an experienced spinal surgeon (surgeon #1) to reach a steady state operation time without internal supervision. In addition to professional courses, internal supervision is by no doubt is helpful to shorten the learning period: surgeon #2, who was supervised by surgeon #1, reached similar operation times after only 16 procedures. Our data indicate that the total number of problems and complications is higher in the "learning phase" for both surgeons. However, the mid- to long-term clinical outcome of patients operated during that period was not negatively affected.

Learning curve

IL FED has previously been shown to be associated with a significant learning curve[42, 116, 170, 183, 258, 306, 311, 382, 391]. It is a well-known fact from minimally invasive surgery training, that the learning phase can be shortened and thus complications be reduced when surgeons are supervised by a more experienced colleague[258]. Longer operation times in our series were predominantly caused by difficulties in the anatomical orientation, which was found to be most challenging in the early stages of IL FED introduction. Apart from the new adoption of the two-dimensional endoscopic view, the correct and safe identification of the ligamentum flavum was one major hurdle at the beginning of the introductory phase of IL FED. It appears white under endoscopic view as opposed to yellow when using the microscope. Other authors have analyzed their learning progress in IL FED using the operation time as a primary endpoint. Ruetten et al[311] and Nowitzke et al[258] described an asymptote of the learning curve after approximately 30 cases. Rong et al[306] showed that operation time became steady after the 19th case. Because of this relatively long learning phase, IL FED is highly debated amongst specialists in spinal surgery and the assessments of learning curves

considered as critical[17]. Wang et al.[381] pointed out that the introduction of new techniques associated with shallow learning curves but without clear superiority over the 'gold standard' treatments should be questioned.

In our opinion it is mandatory to visit an endoscopic training course in order to maximize patient's safety at the beginning of the learning curve. Ideally, a spinal surgeon well-experienced with endoscopic lumbar discectomy assists a learner until the steady state of the learning curve is reached.

Conclusion

The analysis of the learning curves of the author and of his colleague showed that the presence of a backup has an influence on the learning curve in that the presence of a more experienced colleague will give confidence to the beginner and avoid him to fall on the same stumbling blocks. We recommend every spinal surgeon interested in learning IL FED to be aware of the shallow learning curve and be mentored by a spinal surgeon who is well experienced in IL FED. During the learning phase cases should be selected very carefully according to skill level.

6. Teaching / Trainings problems

Changes in surgical training concepts

If traditional surgical training relied mainly on hours spent as assistants into the operating room observing their mentors, several developments have made this type of training for residents of the 21st century completely obsolete [284], inclusive in neurosurgery[225].

Due to the combination of advances in educational theory and the increase from diverse pressures the reliability and opportunity of the method has been questioned. Due to regulations the workweeks of residents have become shorter[220] and this factor is considered as the main one[225]. Besides, the trend for an optimization of the operating room occupation have reduced the time for training into the theatre. Moreover the will to limit medical errors as well as the increasing complexity of cases also reduce the faculty's opportunities to assist their residents. As a consequence interest for training opportunities out of the operating room grew.

Parallel to these developments new theories on the way to teach surgical skills have been developed which no longer sustain a system relying only on sheer volume of exposure but rather on dedicated training activities. Fitts and Posner thus defined a three-stage theory of motor skill acquisition which is recognized by the motor skill literature as well as the surgical literature[99, 210].

Stag	Goal	Activity	Performance
Cognition	Understand task	Explanation,	Erratic, distinct
		demonstration	steps
Integration	Comprehend and	Deliberate practice,	More fluid, less
	perform mechanics	feedback	interruptions
Automation	Speed, efficiency,	Focus on refining	Continuous, fluid,
	precision	performance	adaptive

The Fitts-Posner	[.] Three Stage	Theory of Motor	Skill Acquisition
-------------------------	--------------------------	------------------------	--------------------------

Table 2.1 Fitts and Posner stages[98]

There seem to be a clear consensus that earlier stages of skill acquisition should take place outside the theatre[3, 48, 225, 301, 307] which, when mastered, will allow the trainee in the theatre to focus on more complex issues[301]. Thus the concept of deliberate practice was developed in which the trainee focuses on a defined task to improve a specific skill; this task, defined by a teacher, is repeated with coaching and immediate feedback. Experts such as Ericsson argue that deliberate practice rather than hours spent into the theatre are decisive for the improvement of performance[87]. This evolution in the understanding of skill acquisition has led to the elaboration of surgical skills laboratory and dissection curriculum for neurosurgical residency training[49, 201, 226, 268].

Training transsphenoidal endoscopy

Transsphenoidal endoscopic surgery has gained popularity in the last 2 decades and is becoming one of the standard techniques for resection of tumors of the anterior cranial base, the most frequent lesion here remaining pituitary adenomas. Professor Stammberger from Graz, a famous pioneer endoscopic rhinologist, even stated at the 21st meeting of the German Society for Skull Base Surgery on 11-12th October 2013 in Tübingen, that endoscopic pituitary surgery is the standard and stated that "the endoscopic approach is meanwhile so established that one should nearly be ashamed to say that he is able to do it endoscopically".

In contrast to their ENT colleagues, neurosurgical residents have practically no endoscopic experience when they reach the stadium of transsphenoidal procedures. ENT trainees will have the possibility to use the endoscope daily for routine controls and operations with limited risks within the nasal cavity. When they reach the stadium which allows them to operate on larger tumors under the skull base they have done a large number of procedures in pure endoscopic nasal surgery. When one observes the two types of work done by ENT surgeons and neurosurgeons, it is obvious that the type of fine motor skills remains slightly different: ENT surgeons have to work on mucosa, cartilage and bone, all structures with some degree of resistance where often some degree of pressure has to be applied with instrument such as dissectors or rasps. In contrast neurosurgeons move themselves in a terrain where these types of movements are forbidden, as the encountered structures would often not resist even a slight pressure.

On the other side, neurosurgery does not offer the possibility to their trainees to perform many endoscopic operations as most of the procedures done endoscopically in neurosurgery concern the central skull base with important neurovascular structures in the immediate vicinity of the pathology where a false manipulation can be potentially associated with devastating consequences for the patient. Even in large centers with ENT tutors motivated to train young neurosurgeons in combined routine operations such as pituitary adenomas, these tutors have complained how difficult and discouraging it can be to assist young neurosurgical trainees who have no experience at all with the endoscopic work (personal observation, Hôpital Notre Dame, CHUM, Montréal, QC, Canada, June-September 2013).

Another factor reducing the number of possibilities for neurosurgical trainees to acquire endoscopic skills is the fact that the number of procedures done transsphenoidally with the endoscope can vary greatly from one center to the other but remain quite low. In a global survey of 2012, Esposito et al found out that endoscopic neurosurgeons working endoscopically perform 27 per year per surgeon[90]. As a consequence it can be difficult in many centers to train young colleagues for procedures which are performed less than 2 or 3 times a month.

The emphasis on OR efficiency has also contributed to reduce the time available for surgical instruction[295].

The last factor with negative influence on training opportunities is the combination of high profile error cases with ongoing restrictions in residents duty (and training) hours

associated with work regulations as observed in general surgery[110]. As trainees are not allowed to work for 24 hours or 7 days without interruption any more the teams had to be increased in order to fill on call programs. This increase in the number of team members combined with the reduction of working hours has led to a dramatic reduction of surgical exposure for trainees. At the same time high profile error cases with lifethreatening complications in introducing minimal invasive surgery (MIN), especially in early stages of laparoscopic cholecystectomy, in the UK and the USA have led to consider other training paradigms.

As a consequence all these factors have stimulated the interest for simulation based medical education (SBME) in order to offer training possibilities outside the operating theatre and this at the earliest stage of education as it has been clearly demonstrated that fine motor skills are acquired more rapidly and more precisely at an early age[373].

Ideal training simulation remains the anatomic laboratory where the neurosurgeon can be directly confronted with the normal anatomy. However, cadaveric workshops remain expensive and cannot be repeated very frequently and thus cannot be used as training tool to acquire specific skills. In some instances cadaver cannot be used as they lack the necessary minimal ventriculomegaly and thus are clearly not an option[152]. However, anatomic labs still belong to medical education and are decisive instruments to consolidate anatomical knowledge.

Another modern possibility for surgical training is offered by computer technology. Simulation software allow the surgeon to simulate an endoscopic procedure on the screen and even to simulate patient-specific procedure and to be confronted with pathological anatomy. If first models using virtual reality lacked the tactile feedback needed in surgical skills training, the lately developed systems have tactile feedback[71, 305].

The National Research Council Canada has described a training program with standardized training modules for surgical skills acquisition in neurosurgical oncology using a system with virtual reality (VR), the NeuroTouch[50]. The five modules allow to train 5 different surgical skills or tasks including 1° ventriculostomy, 2° endoscopic nasal navigation, 3° tumor debulking, 4° hemostasis and 5° microdissection. It represents a fist attempt to develop a standardized program for the acquisition of fundamental skills in neurosurgery. First experiments have shown that neurosurgical trainees obtained better score than medical students but further work is needed to validate the use of the different modules in a training curriculum. Still these systems remain quite expensive, are not at disposal at once and will need regular software updates, which will also bring some supplementary costs. With their diffusion and wider use some cost reduction can be expected.

Some authors in other discipline have already addressed the question and developed models using quail eggs in order to train for example sinus surgery for ENT trainees[260]. A simpler training model for transsphenoidal neurosurgery using eggs

has been developed in Japan[263]. This model uses a commercially available skull model (3B Scientific, Niigata, Japan) with an approximated simulation of the nasal cavities harboring only the bony elements and lacking the mild parts of the face, thus not recreating a realistic length of the anatomical working channel through the nose to the skull base. Moreover they performed a quite wide opening of the egg shell and of the anterior egg white, thus not allowing the training "around the corner" which is one of the key advantages of the endoscope as compared to the microscope. Other authors have developed a "hybrid" model using cadaver heads and silicone material simulating a skull base tumor[125]. Even if this model is one of the most realistic it remains as expensive as other cadaveric workshops and does not allow repetition.

Own experience: development of a training model for transsphenoidal endoscopy In order to offer neurosurgical trainees a realistic alternative to these training options we developed a project with following objectives: to develop an affordable method for repetitive training of endoscopic skills in a narrow channel, allowing training of the movements needed for resection of pituitary adenoma.

In a first stage a very simple and schematic model of the nasal cavity using Styropore was designed in which a cavity was prepared to receive a boiled egg (Figure 6.1).



Figure 6.1: Styropore model.

In a second step and in collaboration with ENT surgeons and with engineer of the firm Inspire, a spin-off firm of the technical university of Zurich (Eidgenössische Technische Hochschule, ETH ZH) we developed a 3 dimensional model of the head with particular attention to the nasal cavities and with a fixation device designed to be able to receive the egg. The model (Figure 6.2) consists of 3 elements:

1° A hard 3D reconstruction of the head.

2° A softer removable part reproducing the region of the nose and sphenoid sinus.

3° A specially designed device to receive a boiled egg.



Fig. 6.2: Left: model's 3 elements: hard 3D reconstruction of the head (a), soft part for nose and sinuses (b), box for the egg (c). Right: mounted model with rigid endoscope interacting with soft nasal part.

The softer part has been developed in order to allow some mobility as it is the case in reality and also in order to avoid lesion of the endoscope in a rigid structure. As the model has been developed to train neurosurgeons, the nasal cavity has been reconstructed as it is at the end of the approach: 2 channels have been prepared through the nasal cavity up to the anterior wall of the sphenoid sinus, with enlarged sphenoid ostiae and resection of the posterior nasal septum.

Regarding the tactile feedback we have chosen boiled eggs which have the advantage of presenting a fragile shell and 2 structures of different consistencies allowing for training fine motor skills.

For the insertion of the boiled egg at the level of the sella a dedicated device had to be developed. This device consists of a solid box with a softer filling with a cavity for the egg to be worked on. We have developed 2 types of soft filling in order to have the possibility to insert either a small variant of commonly found chicken eggs (45 gram) or a quail egg (Fig 6.3).



Fig. 6.3: A: soft fillings for chicken (L) and quail (R) eggs. B: egg worked in position.

In order to get a stable fixation of the egg within the solid head model a device had to be constructed which could receive the soft fillings. This device consisted of one rigid frame to hold the 2 fillings halves (Fig. 6.4) and a box incorporated to the rear of the solid 3D reconstruction of the head with a locking system to fix the frame with the fillings and the egg in the box (Fig. 6.5).



Fig. 6.4: Above: rigid frame (grey) containing the egg and the 2 soft fillings (brown). Below: photographs of soft fillings and frame opened(left) and mounted (right).



Fig. 6.5: Fixation box opened (left), introduction of the frame with the fillings (right).



Fig. 6.6: Schematic representation of the fixation box closed and photograph of the rear side of the mounted model.

Finally studies were made in order to get the lower part of the egg at the level of the sellar floor in order to recreate the normal working distance (Fig. 6.7).



Fig. 6.7: Studies to place the "bottom" of the egg holding device at the level of the sellar floor.

The model allows for training under endoscopic (or microsopic) vision through a narrow approach at a depth of 12 cm; the boiled egg itself offers the possibility of training the careful opening of the fragile shell, either with a "Meissel" and a punch or with a diamond burr. In order to increase the difficulty a 10 mm square can be marked at the base of the shell and the exercise can consist in remaining within the marked square without touching of the line. To standardize this square marking a curved rubber stamp with the curvature of the inferior part of the chicken egg was also developed (Fig. 6.8).



Fig. 6.8: rubber stamp for egg marking.

Thanks to the different consistency between the egg white and the yolk, the next step of the exercise consists into resecting the yolk without any lesion of the posterior part of the white, the anterior part of the white having to be partially resected in order to access to the yolk.

With this combination of the model with the boiled egg a realistic simulation of the movements done under the endoscope through a narrow approach at a depth of 12 cm can be done and thus the fine motor skills needed for careful resection of sellar processes can be trained (Fig. 6.9).



Fig. 6.9: Training model with 0°endoscope on its fixation device, HD screen.

The production of the model remains affordable (3,500.00 CHF = 3,898.37 USD) especially as they have to be invested only once.

The model allows frequent repeated trainings for neurosurgical residents starting with endoscopy (post-graduate year 2-3).

The aspects or skills that can be trained include handling of the endoscope with indirect view onscreen, the work in a 12 cm narrow channel and the bimanual coordination. The aspects or skills that cannot be trained are the transnasal approach phase and as the egg yolk remains a schematic artificial structure the recognition of anatomic landmarks is not necessary and thus not trained.

Evaluation of the model

In order to evaluate the model a study involving neurosurgical trainees was designed in which a 2 phases task was defined. The first task consisted in opening of the egg shell

within the 10mm square marking. The second task consisted in the resection of the egg yolk with minimal or no lesion of the posterior half of the egg white. In order to evaluate the precision of the work a score was developed (Fig. 6.10), evaluating the precision of the opening of the sella, the completeness of the egg yolk resection and the resection precision with respect of the posterior white egg. The best score would be 0 and the worst 18 points.

0		
-	Left: experienced	Right: Beginner
ction, pro quadran	t (8 "egg yolk quadrants")	
0		
1/2		
8		
pro quadrant (4 p	osterior "egg white quadrants"))
0		
2		
8		
	18 "ba	nd points"
	2 ction, pro quadran 0 1/2 1 8 , pro quadrant (4 p 0 2 8	Left: experienced ction, pro quadrant (8 "egg yolk quadrants") 0 1/2 1 8 pro quadrant (4 posterior "egg white quadrants") 0 2 8 18 "ba

Fig. 6.10: Score for endoscopic transsphenoidal egg yolk resection.

Results:

In total, eight residents from St. Gall and nine from Basel completed both sessions of the test. Due to a change of residents more than the planned 15 could be included. An analysis between the St. Gall and Basel groups showed a significant difference in operation time, but not in the other metrics.

Consequently, the data shown below are medians of all participants. Two experienced pituitary surgeons, one using the endoscopic technique and the other the microscope technique, were used as references.

Opening

The opening of the eggshell within the margins did not show a significant learning effect. Resection

The resection of the egg yolk showed a decrease of 4 points between the first (median 13, range 1–16) and second test (median, 9, range 0–16) and a further statistically insignificant decrease of 1 point between the second and third (median 8, 0–16) test using the microscope (p=0.02 and p=0.2, respectively).

Overall the egg yolk resection score was on average 5 lower with endoscopy (median 7, range 0–16) than with microscopy (median 12, range 0–16; p<0.0001) (see Fig. 6.11 A). This suggests that using the known microscopic technique fewer learning effects were observed and that even using the new endoscopic technique the residents benefited from the larger angle of view.



Fig. 6.11: Comparison of scores within and between the microscopic (red) and endoscopic (blue) techniques. The expert value has been inserted as a line (microscopic red line, endoscopic blue line) in all graphs. A Resection of egg yolk (° = # are significant between the microscopic and endoscopic technique; * is significant within the microscopic technique). B Preservation of egg white (° is overall significant difference between the microscopic and endoscopic technique). C Operation time (no significant differences). D Total score of opening, resection and preservation (° is overall significant difference between the microscopic and endoscopic technique)

Preservation

The preservation of egg white, symbolizing preservation of normal surrounding tissue, did not show a statistically significant difference in microscopy among the first (median 2, range 0–6), second (median 2, range 0–8) and third test (median 2, range 0–6) (second test vs. first test: p=0.8; third test vs. second test: p=0.7). However, egg white preservation with endoscopy (median 3, range 0–8) was about 1 point higher on average than with microscopy (median 2, range 0–6, p=0.003) (see Fig. 6.11 B). This suggests that using the new endoscopic method interfered with available fine surgical motoric performance.

Operation time

Operation time showed a slight reduction using the microscope only between the first (median 45, range 29–45) and second test (median 42.5, range 22–45; p=0.08) and increased again slightly in the third test (median 45, range 18–45; p=0.7). With the endoscope, the new technique for all residents, time was slightly but not statistically significant longer by an average of 3 min (endoscope: median 42, range 22–45; microscope: median 42, range 18–45; p=0.02; see Fig. 6.11 C). This suggests that the cutoff of 45 min was not adequately chosen for this test.

Total score

The total score for opening, resecting the egg yolk and preserving the egg white showed a reduction in microscopy between the first (median 16, range 3–21) and second test (median 12, range 3–19; p=0.003) and a further statistically insignificant reduction by 0.5 between the second and third test (median 11.5, 2–20; p=0.09). The use of the endoscope (median 12, 2–21) was associated with a 2-point lower total score compared with the microscope (median 14, 4–21; p=0.0005; see Fig. 6.11 D). This suggests that the endoscopic technique has benefits due to the wider angle of view, even though this was the technique in which the participants had no previous experience.

Validation

All participants started with the microscopic technique, in which all had experience. This could be considered an impure method because the first microscopic is also a learning tool for the endoscopic test. However, as all participants performed the test the same way, this bias should have been minimized in the end. There was a standard explanation at the beginning of the test and a minimum of didactics during the test. For actual training of residents and not only validation of a model, the didactic component should play a major role.

Our validation results show that there is a difference between the familiar microscopic and the new endoscopic technique. A trend toward faster learning is shown by a steeper egg yolk in the endoscopic graph. However, the resection rate was immediately better with the endoscope. This was probably due to the better range of vision with an endoscope.

Preservation of the 'normal tissue' was worse in the endoscopic tests, showing that three repetitions is not enough to be as good at fine tasks as with a microscope. In our opinion, this underlines the necessity of repeated training.

The opening of the eggshell did not show a learning curve. Possible reasons for this are the technique of using a chisel, hammer and Cloward punches. Using the chisel and hammer was a technique most residents had never used before, but fine-tuning of the opening was done with Cloward punches, which are often used in spinal procedures. The egg shell breaks relatively easily into larger fragments compared to human bone, making the need for positioning of the Cloward punches much more important than in spinal cases. Training in opening with a diamond drill might be a better approach for future training modifications.

Operation time differed significantly between the two groups of residents. There is no clear explanation for this. All participants were told they had a maximum of 45 min for each egg. Possibly the motivation for prestige differed between both groups. Some residents outperformed the experts (shown in Fig. 6.11). This is best explained by evidence from laparoscopic studies. Ou et al.[266] showed that video game experience improves laparoscopic skills. This was especially true for games with high video spatial elements, which improve laparoscopic skills in terms of completion time, efficiency and fewer errors[323]. Some authors even found that past and present video game experience was a superior predictor of laparoscopic skills compared to the level of training[308]. As the trainees in our experiment belong to a younger generation, several of them might have regular experience in video games, which could at least partially explain their better performance.

Limitations

As the two groups were rated by two different raters, recording every test on video instead of taking photos of the egg cut in half at the end of the test would have enabled better inter-rater variability checks. In addition, learning from watching your own videos is advantageous.

From a statistical point of view, a power calculation was necessary. The design of the study was planned as closely as possible to known criteria for such validation studies[101, 296].

A true power calculation was not possible as new metrics were used, and a limited number of participants was available. As described earlier, the inability to detect and handle unexpected complications makes this model less close to reality.

Future developments and diffusion of the model

The relatively simple conception our training model does not prevent further developments: the egg fixation device could be filled with a "customized" product which could represent a real macro-adenoma. Such models have already been used[126] and could be applied or integrated into our model thus offering the possibility of training on a patient-specific model at an affordable cost as the volume of 3D printing remains limited to a small cube. Costs and time should not be a problem in the future as 3D printing technologies continue to improve, becoming faster, easier, cheaper and more accurate over time[10]. One of the challenges with 3D printing of cerebral models remains the quality of the material. If the rendering is very realistic for organs such as bone, the vasculature, or the heart, it remains difficult to reach for soft organs like the brain. But here too the technology advances and recent improvements have allowed to create 3D patient specific brain models which are graspable and present realistic anatomical features[282].

The model has been patented by the European Patent Office and in order to promote its use a joint venture is currently under finalization with the endoscope-producing firm Storz: the sales manager responsible for neuro-endoscopy want to take the so-called "the EGG" model on their portfolio (Fig. 6.12). Thanks to this collaboration with one of the leader on the endoscopic European market we hope that numerous young neurosurgeon will have the opportunity to acquire their basic endoscopic skills out of the theatre as it should be today. As quoted above, there is at this time no argument to spend more money or to wait for the development and the diffusion of complex high-fidelity models and waiting for prices to go down.

Regarding other training opportunities, the author intends to combine his experiences in endoscopic lumbar disc sequestrectomy[188] and in training workshops for the annular closure device "Barricaid" in order to evaluate the possibility of using the Realspine training model of Realists® to train endoscopic sequestrectomy. Precisely because of the learning difficulties of this method[310, 383, 389], the possibility of acquiring the necessary skills out of the theatre seems to represent an ideal field of application.

"The EGG" Trainingsmodell

für die endoskopische transphenoidale Hypophysenchirurgie



Das Modell besteht aus einer 3D-Rekonstruktion eines Kopfes aus hartem Kunststoff mit einem weicheren, abnehmbaren Bestandteil im Bereich der Nase und der Keilbeinhöhle. Durch das Einfügen eines gekochten Eis innerhalb zweier Halbschalen erlaubt das Modell die Nachstellung der Sellareröffnung (Resektion der Eierschale) mit nachfolgender Tumorresektion (Entnahme des Eigelbs). Hierbei ist die Zielsetzung das umgebende Gewebe (Eiweiß) weitgehend zu schonen und die Visuomotorik unter endoskopischer Sicht zu trainieren und optimieren.

Besondere Merkmale:

- Wiederverwendbares Modell zur Erlernung des endoskopischen Arbeitens (Hand-Augen-Koordination)
- Abnehmbarer Einsatz aus Kunststoff zur Rekonstruktion der Nase und Keilbeinhöhle mit vereinfachter Anatomie (ohne Nasenmuschel)
- Schwierigkeitsgrad kann durch Verwendung unterschiedlicher Eiergrößen variiert werden





3-17

Fig. 6.12: Storz' leaflet project.

Conclusions

The model developed allows for the training of basic endoscopic skills and is designated for experienced trainees or young registrar who are going to start with transsphenoidal endoscopy and truly are "juniors" in endoscopy at that stage of their training. As we developed the model in our low-volume center we had to favor the solution of an interdisciplinary team thus leaving the nasal phase of the procedure to our rhinologist colleague. For this reason there is no anatomic detail of the model regarding the nasal phase.

It allows for frequent repeated trainings of:

 Handling the endoscope with indirect view onscreen 	\checkmark
 Working in 12 cm narrow channel 	\checkmark
 Distinguishing between 2 different tissue consistence 	\checkmark
 Training of bimanual coordination 	\checkmark
 Working with an certain azimuth angle 	\checkmark
 Use of standard instruments 	\checkmark
It does not allow training of the following elements:	

- blood flow
- recognition of anatomic landmarks
- Weight of metric points chosen arbitrarily

One could argue that because of its non-anatomical character and the absence of bleeding it is suboptimal for training and lacks fidelity. However, high-fidelity models have a price and the question is, if the investment does make sense. Fidelity might not be as important as one could think: as demonstrated in other specialties, there is no need at a junior level to have a high level of fidelity to reach improvement in performance. For example in urology, the use of high-fidelity-video endoscopic urology systems did not provide more improvement in performance as compared with simple bench model[240]. The effectiveness of simulation training has been demonstrated primarily for trainees of the lower levels[8, 128, 132, 240, 337].

So despite its relatively simple conception our training model seems to meet exactly the needs of "juniors" neurosurgical endoscopic trainees.

7. Future technical developments, perspectives

The establishment of the endoscope in daily neurosurgical practice is an established fact. Technological improvements in the next decade will concern the endoscope itself as well as the arsenal of instruments that can be used either through the working channels

of neuroendoscopes or besides the endoscope in all transsphenoidal or endoscopeassisted procedures.

Endoscope improvements

One of the repeatedly mentioned drawbacks of endoscopes is the 2-dimensional vision with loss of the depth precision. Despite the fact that it has been demonstrated that this loss of the 3rd dimension is not as decisive an issue as initially thought efforts are constantly made in order to improve vision and especially depth perception. The first so-called 3D endoscopes have therefore been developed[33, 356]. First experiments have already been made[340] and have shown in a training model that it improved the performance and the depth perception of young trainees; experienced surgeons on the other hand did not like the initial learning curve but in the few cases of nasal and skull base operated on with the 3D endoscope it was felt to be very beneficial especially during vascular dissection. The fact that depth perception and task performances were improved in novices was expected to ultimately improve the learning curve.

Repair material and techniques

The ideal characteristics of material for repair of skull base defects can be deducted from the disadvantages presented by the different materials in use today: it should be widely available, user friendly, inexpensive, free of risks regarding toxicity and should cause no or only minimal regional inflammation or immunological response[23]. Finally it should be at the same time a dural substitute on the cerebral side and provide a matrix for remucosalization on the sinusal side.

As far as the reconstruction of anterior skull base defects is concerned, the major drawback of all the techniques applied today is that none of them provides immediate waterproofness and all of them also necessitate therefor some kind of supplementary adjunctive measure, such as lumbar CSF drainage, prolonged nasal packing and sealants. In transcranial procedures, immediate waterproofness is usually obtained by combination of a meticulous tissue apposition and (seldom) watertight suture of the dura with some adjunctive measure, be it fibrin glue or collagen fleeces. The environment encountered in transnasal endoscopic surgery remains presently unfavorable for suture techniques and it is improbable that things are going to change greatly in this field in the next years. An innovative technique that could provide immediate waterproofness is represented by laser tissue welding. In this technique laser energy is applied to a chromophore doped biologic solder at the wound edge. The issues regard the strength of the welding and the possible collateral damage, mainly thermal tissue injury. As this technique is applied successfully in vascular surgery to perform for example superficial temporal to middle cerebral artery [177] where the pressure values are higher, one would expect it to be applicable to mucosal suture where it should withstand the hydrostatic forces. Experimental studies have demonstrated that the technique is capable of achieving an immediate burst strength over four times that of normal human intracranial pressure or significantly higher than those of suture repair[24, 25]. These studies have also demonstrated the absence of thermal collateral

injury. A study to assess safety and feasibility in human limited to sinus surgery for repair of mucosal injuries has already been performed successfully. In the light of these results laser tissue welding represents a promising future development for anterior skull base repair.

Neuronavigation and intraoperative imaging

The co-application of endoscopy and neuronavigation for intraventricular pathologies and skull base procedures has been recently reviewed and showed a wide range of indications for the use of the co-application, varying from always to never[90]. Besides the debate on when and how this combined application should be done, both techniques continue to be improved separately. One of the most recent improvements in navigation systems is the possibility of using electromagnetic tracking systems. On the contrary to optic tracking systems, electromagnetic tracking systems eliminate all the issues of line of sight or pin fixation of the head, which are of particular concern in endoscopic procedures and is one of the reason why some surgeons are reluctant to use navigation more systematically during endoscopic procedures. Probably the more systematic use of this type of tracking system will facilitate the combination of the techniques and increase its use.

Regarding intraoperative imaging, a growing number of centers are equipped with intraoperative MRI (iMRI) and use it among others during transsphenoidal pituitary surgery, mainly with the microscopic technique[20, 53]. However, if studies tend to demonstrate that iMRI probably increases resection rates for standard microscopic pituitary procedures, some authors consider that these improvements do not compare with those that can be achieved by the adoption of the endoscope with the extended approaches, a technique which does not increase operating time and thus consider that the considerable costs associated with this technique are at the present time not justified[331]. An alternative to iMRI is presented by intraoperative CT, but its application to neurosurgical procedures is not comparable to that of iMRI because of the much lower definition of soft tissues. However, its much more reasonable costs and the development of so called morphing software will eventually in a near future allow to produce "artificial" intraoperative MR images by using pre-operative fused CT and MRI images combined with the intraoperative CT (iCT) images. The iCT would then become a very attractive alternative modality of intraoperative imaging, not only because of its much lower costs and simpler application with less interruption of the surgical workflow, but also because the same installation could be used for other intraoperative imaging, as for example for control of screw placement in spinal fusion procedures, thus increasing the applications of the whole installation. Furthermore the installation of an iCT requires much less building modifications [247]. This kind of development would become more attractive for clinics working on soft and hard tissue and would allow for a much better return on investment.

Instrumentation improvements

The instruments dedicated to endoscopic applications are also under constant optimization. One of the main drawbacks of cerebral and intraventricular

neuroendoscopy is that the surgeon has to work into a rigid channel and thus most of the instruments will be rigid and neither angled nor rotatable. This will for example prevent the grasping of a structure not lying in the center of the vision field, in line with the working channel or will also not allow the relative positioning of one instrument as related to the other in the case of optics with 2 working channels.

At the moment with the exception of some bipolar probes as the one used in our department most of the other instruments are not steerable or rotatable. One rotatable biopsy forceps has been recently acquired in order to facilitate the separation of small biopsies with rotation of the tip of the forceps instead of tearing, thus reducing the risk of unwanted avulsions.

During a course on cerebral endoscopy in Gent (14th International Workshop on Endoscopic Neurosurgery, 7-10 December 2008) Professor Caemert presented a concept for steerable endoscopic instruments. These type of instruments work following diverse principles as for example the principle of the spatial parallelogram-

mechanism[29]. While the central part of the instrument remains rigid and is exactly the length of the working channel of the rigid endoscope, the proximal and distal extremities can be bended in such a way that when the proximal extremity is bent to the right or backwards, the distal extremity will bend forwards or to the left and vice versa. If such instruments are not yet at disposition it is foreseeable that they will soon belong to the standard armamentarium of neuroendoscopic procedures.

8. Conclusions

Within the last 15 years the use of the endoscope has been implemented progressively in the Department of Neurosurgery of the Cantonal Hospital in St Gall., The endoscopic third ventriculostomy for obstructive hydrocephalus has allowed the author to make his first steps with this new technology and has become the standard intraventricular procedure. During the observation period, increasing experience and assimilation of the continuous technical improvements as well as integration of other technologies, in particular the neuronavigation, has allowed for an extension of the indications to more rare pathologies such intraventricular tumors and cystic lesions.

In the field of transnasal procedures, the author has had the opportunity to collaborate with an experienced rhinologist which allowed for a safe and shorter learning period. The endoscopic transsphenoidal surgery has become the standard in the institution and has allowed to extend the indications to most of the procedures included in difficulty levels I to IV of the Kassam classification[192] with the exception of transclival procedures. The experiences with anterior skull base meningiomas have shown the feasibility of the procedures but the risk of CSF remains a concern and will limit the indications to processes where the anticipated resulting skull base defect remains clearly below 3 cm.

As endoscopic procedures are not as frequent as microscopic ones and often involve sensible regions, the teaching of these procedures to trainees submitted to strict work regulation policies will represent a challenge in the future and has already motivated some countries to develop "out of the theatre" training modules. Thus far these training programs rely on high technological and expensive systems. In order to offer today a training option for young neurosurgeons who are interested in endoscopic neurosurgery an affordable training model has been developed and evaluated. It offers a reasonable option until more sophisticated and affordable models will be on the market. It might even be sufficient for the training of basic skills as studies have demonstrated that there was no significant differences between expensive high sophisticated VR simulators and rather cheap physical models to transmit basic skills to early learners, and advanced neurosurgical trainees starting with pituitary endoscopic surgery are clearly endoscopic "beginners".

Even if neurosurgery was one of the last specialties to adopt it, the endoscope has unmistakably made its way into this discipline in the last 2 decades and the author encourages young trainees to make this tool one of their armamentarium in order to be in a position where they can offer their patient good options.

9. References

- 1. Abbot R, Abbott R (2004) History of neuroendoscopy. Neurosurg Clin N Am 15:1– 7
- van Aken J, Struys M, Verplancke T, de Baerdemaeker L, Caemaert J, Mortier C (2003) Cardiovascular changes during endoscopic third ventriculostomy. Minim Invasive Neurosurg 46:198–201
- 3. Alaraj A, Charbel F, Birk D, Al E (2013) Role of cranial and spinal virtual and augmented reality simulation using immersive touch modules in neurosurgical training. Neurosurgery 72(suppl 1:115–123
- 4. Alaraj A, Charbel F, Birk D, Tobin M, Luciano C, Banerjeee P, et al (2013) role of cranial and spinal virtual and augmented reality simulation using immersive touch modules in neurosurgical training. Neurosurgery (72 Suppl 1):115–23
- 5. Alaraj A, Luciano C, Bailey D, Elsenousi A, Roitberg B, Bernardo A, Banerjee P, Charbel F (2015) Virtual reality cerebral aneurysm clipping simulation with realtime haptic feedback. Neurosurgery 11 Suppl 2(Mar):52–8
- 6. Ali M, Usman M, Khan Z, Khan KM, Hussain R, Khanzada K (2013) Endoscopic third ventriculostomy for obstructive hydrocephalus. J Coll Physicians Surg Pak 23(5)(May):338–341
- 7. Ammirati M, Wei L, Ciric I (2012) Short-term outcome of endoscopic versus microscopic pituitary adenoma surgery: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. doi: 10.1136/jnnp-2012-303194
- 8. Anastakis D, Regehr G, Reznick R, et al (1999) Assessment of technical skills transfer from the bench training model to the human model. Am J Surg 177:167–70
- 9. Andolfi C, Plana A, Kania P, Banerjee P, Small S (2017) Usefulness of Three-Dimensional Modeling in Surgical Planning, Resident Training, and Patient Education. J Laparoendosc Adv Surg Tech A 27(5)(May):512–515
- 10. Aoun R, Hamade Y, Zammar S, Patel N, Bendok B (2015) Futuristic Three-Dimensional Printing and Personalized Neurosurgery. World Neurosurg 84(4)(Oct):870–1
- 11. Arita K, Kurisu K, Tomainaga A (1998) Trans-sellar color Dopp- ler ultrasonography during transsphenoidal surgery. Neurosurgery 42:81–86
- 12. Barahona M, Sojo L, Wägner A, Bartumeus F, Oliver B, Cano P, Webb S (2005) Determinants of neurosrugical outcome in pituitary tumors. J Endocrinol Invest 28:
- 13. Baykan N, Isbir O, Gerçek A, Dağçnar A, Ozek M (2005) Ten years of experience with pediatric neuroendoscopic third ventriculostomy: features and perioperative complications of 210 cases. J Neurosurg Anesth 17(Jan):33–7
- 14. Beijnum J Van, Hanlo P, Fischer K, Majidpour M, Kortekaas M, Verdaasdonk R, Vandertop W (2008) LASER-ASSISTED ENDOSCOPIC THIRD VENTRICULOSTOMY : LONG-TERM RESULTS IN A SERIES OF 202 PATIENTS.

Neurosrugery 62(2):437-444

- 15. El Beltagy M, Kamal H, Taha H, Awad M, El Khateeb N (2010) Endoscopic third ventriculostomy be- fore tumor surgery in children with posterior fossa tumors, CCHE experience. Childs Nerv Syst 26:1690–1704
- 16. Belykh E, Lei T, Safavi-Abbasi S, Yagmurlu K, Almefty R, Sun H, Al E (2016) Lowflow and high-flow neurosurgical bypass and anastomosis training models using human and bovine placental vessels: a histological analysis and validation study. J Neurosurg 125:915–928
- 17. Benzel EC, Orr RD (2011) A steep learning curve is a good thing! Spine J 11(2):131–2
- 18. Berci G, Forde K (2000) Berci G, Forde KA () History of endoscopy: what lessons have we learned from the past? Surg Endosc 7:14:5–15
- 19. Berhouma M, Baidya NB, Zhang J, Ammirati M (2013) Shortening the learning curve in endoscopic endonasal skull base surgery: A reproducible polymer tumor model for the trans-sphenoidal trans-tubercular approach to retro-infundibular tumors. Clin. Neurol. Neurosurg.
- 20. Berkmann S, Fandino J, Müller B, Remonda L, Landolt H (2012) Intraoperative MRI and endocrinological outcome of transsphenoidal surgery for non-functioning pituitary adenoma. Acta Neurochir (Wien) 154(4):639–47
- 21. Bernardo A (2017) Virtual Reality and Simulation in Neurosurgical Training. World Neurosurg 106(October):1015–1029
- 22. Bernardo A, Preul M, Zabramski J, Spetzler R (2003) A three-dimensional interactive virtual dissection model to simulate transpetrous surgical avenues. Neurosurgery 52:499–505
- 23. Biroli F, Esposito F, Fusco M, Bani G, Signorelli A, de Divitiis O, Cappabianca P, Cavallo L (2008) Novel equine collagen-only dural substitute. Neurosurgery 62(March):15–18
- 24. Bleier B, Palmer J, Gratton M, Al E (2008) Laser tissue welding in the rabbit maxillary sinus. Am J Rhinol 22:625–628
- Bleier B, Palmer J, Sparano A, Al E (2007) Laser assisted cerebrospinal fluid leak repair: an animal model to test feasibility. Otolaryngol Head Neck Surg 137:810– 814
- 26. Bohman L, Stein S, Newman J, Palmer J, Adappa N, Khan A (2012) Endoscopic versus open resection of tuberculum sellae meningiomas: a decision analysis. ORL J Otorhinolryngol Relat Spec 74:255–263
- Boogaarts HD, Decq P, Grotenhuis JA, Le Guérinel C, Nseir R, Jarraya B, Djindjian M, Beems T (2011) Long-term results of the neuroendoscopic management of colloid cysts of the third ventricle: a series of 90 cases. Neurosurgery 68(1):179–87
- 28. Bouras T, Sgouros S (2012) Complications of Endoscopic Third Ventriculostomy A Systematic Review. Acta Neurochir (Wien) 113:149–153
- 29. Breedveld P, Scheltes JS, Blom EM, Verheij JEI (2005) A New, Easily Miniaturized Steerable Endoscope. Eng Medicien Biol Mag (November/December):40–47
- 30. Breimer GE, Bodani V, Looi T, Drake JM (2015) Design and evaluation of a new

synthetic brain simulator for endoscopic third ventriculostomy. J Neurosurg Pediatr 15(1):82–88

- 31. Breimer GE, Haji FA, Bodani V, Lopez-Rios A-L, Okrainec A, Drake JM (2017) Simulation-based Education for Endoscopic Third Ventriculostomy: A Comparison Between Virtual and Physical Training Models. Neurosrugery 13(February):89–95
- 32. Bronstein MD, Musolino NR, Benabou S, Marino R (1989) Cerebrospinal fluid rhinorrhea occuring in long-term bromocriptine treatment for macroprolactinomas. Surg Neurol 32:346–349
- 33. Brown S, Tabaee A, Singh A, Schwartz T, Anand V (2008) Three-dimensional endoscopic sinus surgery: feasibility and technical aspects. Otolaryngol Head Neck Surg 138(3)(Mar):400–2
- 34. Bushe K, Halves E (1978) Modified technique in transsphenoidal operations of pituitary adenomas. Technical note. Acta Neurochir (Wien) 41(1-3):163–75
- 35. Buxton N, Vloeberghs M, Punt J (1998) Liliequist's membrane in minimally invasive endoscopic neuroendoscopy. Clin Anat 11:187–190
- 36. Campero A, Ajler P, Goldschmidt E, Bendersky D (2012) Tension sellar pneumocele: A case report and review of the literature. Surg Neurol Int 8;3(Suppl(Dec):S395-9
- 37. Cappabianca P, Cavallo LM, de Divitiis E (2004) Endoscopic Endonasal Transsphenoidal Surgery. Neurosurgery 55(4):933–941
- 38. Cappabianca P, Cinalli G, Gangemi M, et al (2008) Application of Neuroendoscopy to Intraventricular Lesions. Neurosurgery 62(2):575–598
- 39. Cappabianca P, Esposito F, Cavallo L, Messina A, Solari D, di Somma L, de Divitiis E (2006) Use of equine collagen foil as dura mater substitute in endoscopic endonasal transsphenoidal surgery. Surg Neurol 65(2)(Feb):144–8
- 40. Carragee EJ, Michael HY, Suen WP, Kim D (2003) Lumbar Discectomy for Sciatica : The Effects of Fragment Type and Anular Competence. J bone Jt Surg 85(January):102–108
- 41. Carter B (1952) The fruition of Halsted's concept of surgical training. Surgery 32:518–27
- 42. Casal-Moro R, Castro-Menendez M, Hernandez-Blanco M, Bravo-Ricoy J, Jorge-Barreiro F (2010) Long-term outcome after microendoscopic diskectomy for lumbar disk herniation: a prospective clinical study with a 5-year follow-up. Neurosurgery 68 6:1568–75
- 43. Castelnuovo P, Pistochini A, Locatelli D (2006) Different surgical approaches to the sellar region: focusing on the "two nostrils, four hans technique". Rhinology 44:2–7
- 44. Caton R, Paul F (1893) Notes of a case of acromegaly trated by operation. Br Med J 2:1421–1423
- 45. Cavallo LM, Dal Fabbro M, Jalalod'din H, Messina A, Esposito I, Esposito F, de Divitiis E, Cappabianca P (2007) Endoscopic endonasal transsphenoidal surgery. Before scrubbing in: tips and tricks. Surg Neurol 67(4):342–7
- 46. Caversaccio M, Eichenberger A, Häusler R (2003) Virtual simulator as a training tool for endonasal surgery. Am J Rhinol 17(5)(Sep-Oct):283–90

- 47. Cawley C, Tindall G (1999) Transsphenoidal Surgery: Operative Techniques. In: Krisht A, Tindall G (eds) Pituit. Disord. - Compr. Manag. LIPPINCOTTWILLIAMS& WILKINS, Baltimore, pp 349–359
- 48. Chan S, Conti F, Salisbury K, Blevins N (2013) Virtual reality simulation in neurosurgery: technologies and evolution. Neurosurgery 72(suppl 1:154–164
- 49. Choudhury N, Gélinas-Phaneuf N, Delorme S, Del Maestro R (2013) Fundamentals of neurosurgery: Virtual reality tasks for training and evaluation of technical skills. World Neurosurg 80(5)(5):9–19
- 50. Choudhury N, Gélinas-Phaneuf N, Delorme S, Del Maestro R (2013) Fundamentals of neurosurgery: virtual reality tasks for training and evaluation of technical skills. World Neurosurg 80(5):e9–19,
- 51. Cinalli G, Cappabianca P, de Falco R, Spennato P, Cianciulli E, Cavallo LM, Esposito F, Ruggiero C, Maggi G, de Divitiis E (2005) Current state and future development of intracranial neuroendoscopic surgery. Expert Rev Med Devices 2:351–373
- 52. Ciric L, Ragin A, Baumgartner C, Pierce D (1997) Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. Neurosurgery 40(Feb):225–36
- 53. Coburger J, König R, Seitz K, Bäzner U, Wirtz C, Hlavac M (2014) Determining the utility of intraoperative magnetic resonance imaging for transsphenoidal surgery: a retrospective study. J Neurosurg 120(Feb):346–56
- 54. Cohen A (1993) Images in clinical medicine. Endoscopic laser third ventriculostomy. N Engl J Med 328:552
- 55. Colpan M, Slavin K, Amin-Hanjani S, Calderon-Arnuphi M, Charbel F (2008) Microvascular anastomosis training model based on a Turkey neck with perfused arteries. Neurosurgery 62(5 Suppl(May):ONS407-10; discussion ONS410-1
- 56. Costello R (1936) Subclinical adenoma of the pituitary gland. Am J Pathol 12:205–216
- 57. Couldwell W, Weiss M, Rabb C, Liu J, Apfelbaum R, Fukushima T (2004) Variations on the standard transsphenoidal approach to the sellar region, with emphasis on the extended approaches and parasellar approaches: surgical experience in 105 cases. 23. Neurosurgery 55(3)(Sep.):539–47
- 58. Crockard H (1995) Transoral surgery: some lessons learned. Br J Neurosurg 9:283–293
- 59. Curey S, Derrey S, Hannequin P, Hannequin D, Fréger P, Muraine M, Castel H, Proust F (2012) Validation of the superior interhemispheric approach for tuberculum sellae meningioma: clinical article. J Neurosurg 117(6):1013–21
- 60. Cushing H (1932) Intracranial tumors. Notes upon a series of two thousand verified cases with surgical mortality percentages pertaining thereto. Springfield: Ch C Thomas:
- 61. D'Haens J, Van Rompaey K, Stadnik T, Haentjens P, Poppe K, Velkeniers B (2009) Fully endoscopic transsphenoidal surgery for functioning pituitary adenomas: a retrospective comparison with traditional transsphenoidal microsurgery in the same institution. Surg Neurol 72(4):336–40
- 62. Daltroy L, Cats-Baril W, Katz J, Fossel A, Liang M (1996) The North American spine

society lumbar spine outcome assessment Instrument: reliability and validity tests. Spine (Phila Pa 1976) 21 6:741–9

- 63. Dandy W (1918) Ventriculography following the injection of air into the cerebral ventricles. Ann Surg 68:5–11
- 64. Dandy W (1922) Cerebral ventriculoscopy. Bull JohnsHopkins Hosp 33:189–190
- 65. Dandy W, Blackfan K (1913) An experimental and clinical study on internal hydrocephalus. JAMA 61:2216–2217
- 66. Davis (1936) Neurological Surgery. Philadelphia: Lea & Febiger.
- 67. Decq P (2009) Endoscopic management of colloid cysts. In: Sindou M (ed) Pract. Handb. Neurosurg. Thieme, Wien/NewYork, pp 275–285
- 68. Decq P, Le Guerinel C, Brugieres P, Djindjian M, Silva D, Keravel Y, Melon E, Nguyen J (1998) Endoscopic management of colloid cysts. Neurosurgery 42:1288–1296
- 69. Decq P, Le Guerinel C, Palfi S, Djndjian S, Kéravel Y, Ngyen J (2000) A new device for endoscopic third ventriculostomy. J Neurosurg 93:509–512
- 70. Decq P, Schroeder HWS, Fritsch M, Cappabianca P (2013) A history of ventricular neuroendoscopy. World Neurosurg 79(2 Suppl):S14.e1-6
- 71. Delorme S, Laroche D, Diraddo R, F. Del Maestro R (2012) NeuroTouch: A physicsbased virtual simulator for cranial microneurosurgery training. Neurosurgery 71(SUPPL.1):32–42
- 72. Dereymacker A, VonDenBergh R, Stroobandt G (1961) Experiences personnelles dans le traitement d'une centaine d'enfants hydrocéphales. ActaNeurolPsychiatr Belg 61:373–382
- 73. Derome P (1995) Transbasal approach to tumors invading the skull base, chapter 36. In Schmidek H, Sweet WH (Eds). Operative neurosurgical techniques. WB Saunders Co, 427.
- 74. Deschler D, Gutin P, Mamelak A, McDermott M, Kaplan M (1996) Complications of anterior skull base surgery. Deschler DG, Gutin PH, Mamelak AN, McDermott MW, Kaplan MJ. Skull Base Surg 6 (2):113–8
- 75. DeVille K, Goldberg D, Hassler G (2011) Malpractice risk according to physician specialty. N Engl J Med 17(Nov):365(20):1939; author reply 1940
- 76. Diao Y, Liang L, Yu C, Zhang M (2013) Is There an Identifiable Intact Medial Wall of the Cavernous Sinus? Macro- and Microscopic Anatomical Study Using Sheet Plastination. Neurosurgery 73(September):106–110
- 77. de Divitiis E, Esposito F, P C, LM C (2008) Tuberculum sellae meningiomas: high route or low route? A series of 51 consecutive cases. Neurosurgery 62:556–563
- 78. Divitiis E De, Ii F, Stella L, Al DIET (2007) EXTENDED ENDOSCOPIC TRANSSPHENOIDAL APPROACH FOR TUBERCULUM SELLAE MENINGIOMAS OBJECTIVE: Neurosurgery 61(November):23–26
- 79. Dumont A, Kanter A, Jane J, Laws E (2006) Extended Transsphenoidal Approach Laws ER Jr, Sheehan JP (eds). Pituit. Surg. - A Mod. Approach. Karger: Basel, pp 29–45
- 80. Duntze J, Litré C, Graillon T, Maduri R, Pechgourg G, Rakotozanany P, Gras R,

Dufour H (2012) [Cerebrospinal fluid rhinorrhea following endocopic transsphenoidal pituitary surgery: Experience from 337 patients] (French). Neurochirurgie 58(4)(Aug):241–5

- 81. Durnford AJ, Kirkham FJ, Mathad N, Sparrow OCE (2011) Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus: validation of a success score that predicts long-term outcome. J Neurosurg Pediatr 8(5):489–93
- 82. Dusick JR, Esposito F, Malkasian D, Kelly DF (2007) Avoidance of carotid artery injuries in transsphenoidal surgery with the Doppler probe and micro-hook blades. Neurosurgery 60(4 Suppl 2):322-8-9
- 83. Duz B, Harman F, Secer HI, Bolu E, Gonul E (2008) Transsphenoidal approaches to the pituitary: a progression in experience in a single centre. Acta Neurochir (Wien) 150(11):1133-8-9
- 84. El-Ghandour NMF (2009) Endoscopic treatment of third ventricular colloid cysts: a review including ten personal cases. Neurosurg Rev 32(4):395–402
- 85. Elias W, Chadduck J, Alden T (1999) Frameless stereotaxy for transsphenoidal surgery. Neurosurgery 45:271–277
- 86. Ericsson K (1996) The acquisition of expert performance: an introduction to some of the issues. In: Ericsson K (ed) road to Excell. Acquis. Expert Perform. arts Sci. Sport. games. Mahwah, NJ: Lawrence Erl- baum, Mahwah, NJ, pp 1–50
- 87. Ericsson K (1996) The acquisition of expert performance: an introduction to some of the issues. In: The road to excellence: the acquisition of expert per- formance in the arts and sciences, sports, and games. Associates, Lawrence Erl-baum, Mahwah, NJ
- 88. Erşahin Y, Arslan D (2008) Complications of endoscopic third ventriculostomy. Childs Nerv Syst 24(8):943–8
- 89. Esposito F, Dusick JR, Fatemi N, Kelly DF (2007) Graded repair of cranial base defects and cerebrospinal fluid leaks in transsphenoidal surgery. Neurosurgery 60(4 Suppl 2):295-303-4
- 90. Esposito F, Di Rocco F, Zada G, Cinalli G, Schroeder HWS, Mallucci C, Cavallo LM, Decq P, Chiaromonte C, Cappabianca P (2013) Intraventricular and Skull Base NeuroEndoscopy in 2012: A Global Survey of Usage Patterns and the role of intraoperative neuronavigation. World Neurosurg. doi: 10.1016/j.wneu.2013.05.011
- 91. Estridge M, Smith R (1967) Transoral fusion of odontoid fracture: Case report. J Neurosurg 27:462–465
- 92. Ezzat S, Asa S, Couldwell W, Barr C, Dodge W, Vance M, McCutcheon I (2004) The prevalence of pituitary adenomas: a systematic review. Cancer 101(3):613–619
- 93. Fabiano A, Doyle K, Grand W (2010) Delayed stoma fail- ure in adult communicating hydrocephalus after initial successful treatment by endoscopic third ven- triculostomy: case report. Neurosurgery 66:E1210–E1211
- 94. Fatemi N, Dusick JR, Mattozo C, McArthur DL, Cohan P, Boscardin J, Wang C, Swerdloff RS, Kelly DF (2008) Pituitary hormonal loss and recovery after transsphenoidal adenoma removal. Neurosurgery 63(4):709-18–9
- 95. Fay T, Grant F (1923) Ventriculoscopy and intraventricular photography in
internal hydrocephalus. Report of case. JAMA 80:461-463

- 96. Feld M (1958) Le ventriculoscope coagulant. Nouveaux perfectionnements. Neurochirurgie 4:130
- 97. Filho FVG, Coelho G, Cavalheiro S, Lyra M, Zymberg ST (2011) Quality assessment of a new surgical simulator for neuroendoscopic training. Neurosurg Focus 30(4):E17
- 98. Fitts P, Posner M (1967) Human performance., Brooks/Col. Belmont, CA
- 99. Fitts P, Posner M (1967) Human perfor- mance. Belmont, CA
- 100. Fournier J-Y, Yetimoglu C, Lange H, Huscher K, Hildebrandt G, Tasman J, Engel D Endoscopic versus microscopic transsphenoidal resection of pituitary adenomas: new and learning against the expert. Submitted
- 101. Francis H, Masood H, Laeeq K, Bhatti N (2010) Defining milestones toward competency in mastoidectomy using a skills assessment paradigm. Laryngoscope 120(7):1417–1421
- 102. Frank G, Pasquini E, Farneti G, Mazzatenta D, Sciarretta V, Grasso V, Faustini Fustini M (2006) The endoscopic versus the traditional approach in pituitary surgery. Neuroendocrinology 83(3–4):240–8
- 103. Frank G, Sciarretta V, Calbucci F, Farneti G, Mazzatenta D, Pasquini E (2006) The endoscopic transnasal transsphenoidal approach for the treatment of cranial base chordomas and chondrosarcomas. Neurosurgery 59 (1 Supp(Jul):ONS50-7
- 104. Frazier C (1913) Lesions of the hypophysis from the viewpoint of the surgeon. . Surg Gynecol Obs 17:724–736
- 105. Frazier C (1919) Choice of method in operations upon the pituitary body. Surg Gynecol Obs 29:9–16
- 106. Fried MP, Sadoughi B, Gibber MJ, Jacobs JB, Lebowitz R a, Ross D a, Bent JP, Parikh SR, Sasaki CT, Schaefer SD (2010) From virtual reality to the operating room: the endoscopic sinus surgery simulator experiment. Otolaryngol Head Neck Surg 142(2):202–7
- 107. Froelich SC, Abdel Aziz KM, Cohen PD, van Loveren HR, Keller JT (2008) Microsurgical and Endoscopic Anatomy of Liliequist's Membrane. Neurosurgery 63(July):0NS1-0NS9
- 108. Fukushima T, Ishijima B, Hirekawa K (1973) Ventriculofiberscope: a new technique for endoscopic diagnosis and operation. J Neurosurg 38:251–256
- 109. Gaab M, Schroeder H (1998) Neuroendoscopic approach to intraventricular lesions. J Neurosurg 88:496–505
- 110. Gallagher AG (2012) Metric-based simulation training to proficiency in medical education:- what it is and how to do it. Ulster Med J 81(3):107–13
- 111. Gangemi M, Maiuri F, Naddeo M, Godano U (2008) Endoscopic third ventriculostomy in idiopathic normal pressure hydrocephalus: an italian multicenter study. Neurosurgery 63(1):62–69
- 112. Gangemi M, Mascari C, Maiuri F, Godano U, Donati P, Longatti P (2007) Long-term outcome of endoscopic third ventriculostomy in obstructive hydrocephalus. Minim Invasive Neurosurg 50(5)(Oct):265–9

- 113. Gangemi M, Mascrari C, Maiuri F, Godano U, Donati P, Longatti P (2007) Longterm outcome of endoscopic third ventriculostomy in obstructive hydrocephalus. Minim Invasive Neurosurg 50(5)(Oct):265–9
- 114. Gardner P a, Kassam AB, Snyderman CH, Carrau RL, Mintz AH, Grahovac S, Stefko S (2008) Outcomes following endoscopic, expanded endonasal resection of suprasellar craniopharyngiomas: a case series. J Neurosurg 109(1):6–16
- 115. Gardner P, Vescan A, de Almeida J, Janjua A, Kassam A, Prevedello D, Carrau R, Snyderman C (2012) Endoscopic Endonasal Approach for Olfactory Groove Meningiomas. Endosc. approaches to skull base. , pp 76–86
- 116. Garg B, Nagraja U, Jayaswal A (2011) Microendoscopic versus open discectomy for lumbar disc herniation: a prospective randomised study. J Orthop Surg (Hong Kong) 19 1:30–4
- 117. Gasco J, Holbrook T, Patel A, et al (2013) Neurosurgery simulation in residency training: feasibility, cost, and educational benefit. Neurosurgery 73(Suppl 1:39–45
- 118. Gautschi OP, Smoll NR, Kotowski M, Schatlo B, Tosic M, Stimec B, Fasel J, Schaller K, Bijlenga P (2014) Non-assisted versus neuro-navigated and XperCT-guided external ventricular catheter placement: a comparative cadaver study. Acta Neurochir (Wien) 156(4):777–85
- 119. Ghobrial G, Anderson P, Chitale R, Campbell P, Lobel D, Harrop J (2013) Simulated spinal cerebrospinal fluid leak repair: an educational model with didactic and technical components. Neurosurgery 73(Suppl 1:111–115
- 120. Giordano D (1897) Compendia di chirurgia operatoria. UTET, Torino, Italia:
- 121. Glastonbury CM, Osborn MAG, Karen L (2011) Masses and Malforma- tions of the Third Ven- tricle : Normal Anatomic Relationships and Differ-. RadioGraphics 31:1989–2011
- 122. Goel A, Bhatjiwale M, Desai K (1998) Basilar invagination: A study based on 190 surgically treated patients. J Neurosurg 88:962–968
- 123. Goodmann R (1993) Magnetic resonance imaging directed stereotactic endoscopic third ventriculostomy. Neurosurgery 32(6):1043–7
- 124. Goodrich J (2000) Reprint of the operative treatment of communicating hydrocephalus by Walter E. Dandy, MD. 1938. Childs Nerv Syst 16:545–550
- 125. Gragnaniello C, Nader R, van Doormaal T, Kamel M, Voormolen EHJ, Lasio G, Aboud E, Regli L, Tulleken C a F, Al-Mefty O (2010) Skull base tumor model. J Neurosurg 113(5):1106–11
- 126. Gragnaniello C, Nader R, van Doormaal T, Kamel M, Voormolen EHJ, Lasio G, Aboud E, Regli L, Tulleken C a F, Al-Mefty O (2010) Skull base tumor model. J Neurosurg 113(5):1106–11
- 127. Grant J (1996) Victor Darwin Lespinasse: a biographical sketch. Neurosurgery 39:1232–2133
- 128. Grantcharov T, Kristiansen V, Bendix J, Bardram L, Rosenberg J, Funch-Jen- sen P (2004) Randomized clinical trial of virtual reality simulation for laparoscopic skills training. Br J Surg 91:146–50
- 129. Gray S, Wu A (2013) Pathophysiology of iatrogenic and traumatic skull base injury. In: Randolph G (ed) Benjamin S. Bleier Compr. Tech. CSF leaf repair skull

base Reconstr., Karger., pp 12–23

- 130. Griffith H (1975) Technique of fontanelle and persutural ventriculoscopy and endoscopic ventricular surgery in infants. Child Brain 1:359–363
- 131. Griffith H (1977) Endoneurosurgery: endoscopic intra- cranial surgery. Proc R Soc L B 195:261–268
- 132. Grober E, Hamstra S, Wanzel K, et al (2004) The educational impact of bench model fidelity on the acquisition of tech- nical skill: the use of clinically relevant outcome measures. Ann Surg 240:374–81
- 133. Grotenhuis J (1999) How to avoid complications of endoscopic third ventriculostomy? In: Ferrer E (ed) Minim. invasive neurosurgery., Monduzzi. Bologna, pp 3–7
- 134. Grunert P, Charalampaki P, Hopf N, Filippi R (2003) The role of third ventriculostomy in the management of obstructive hydrocephalus. Minim Invasive Neurosurg 46(1)(Feb):16–21
- 135. Guiot G (1973) Ventriculo-cisternostomy for stenosis of the aqueduct of Sylvius. Puncture of the floor of the third ventricle with a leucotome under television control. Acta Neurochir (Wien) 28:275–289
- 136. Guiot Gérard, J. Rougerie, M Fourestier, A. Fournier, C. Comoy, J. Vulmiere RG (1963) Une nouvelle technique endoscopique. Explorations endoscopiques intracraniennes 92914-0001.pdf. Presse Med 71(24):1225–1228
- 137. Hadad G, Bassagasteguy L, Carrau RL, Mataza JC, Kassam A, Snyderman CH, Mintz A (2006) A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. Laryngoscope 116(10):1882–6
- 138. Hader WJ, Walker RL, Myles ST, Hamilton M (2008) Complications of Endoscopic Third Ventriculostomy in Previously Shunted Patients. Neurosurgery 63(July):0NS168-0NS175
- 139. Hajek M (1904) Zur Diagnose und intranasalen chirurgischen Behandlung der Eiterung der Keilbeinhöhle und des hinteren Siebbeinlabyrinthes. Arch Laryngol Rhinol 16:105
- 140. Haji F, Clarke D, Matte M, et al (2015) Teaching for the Transition: the Canadian PGY-1 Neurosurgery "Rookie Camp". Can J Neurol Sci 42(1)(Jan):25–33
- 141. Haji F a, Dubrowski A, Drake J, de Ribaupierre S (2013) Needs assessment for simulation training in neuroendoscopy: a Canadian national survey. J Neurosurg 118(2):250–7
- 142. Halstead A (1910) Remarks on the operative treatment of tumors of the hypohysis: with the report of two cases operated on by an oronasal method. Trans Am Surg Assoc 28:73–93
- 143. Hamlat A, Pasqualini E, Askar B (2004) Hypothesis about the physiopathology of acute deterioration and sudden death caused by colloid cysts of the third ventricle. Med Hypotheses 63:1014–1017
- 144. Hankinson T, Grunstein E, Gardner P, Spinks T, Anderson R (2010) Transnasal odontoid resection followed by posterior decompression and occipitocervical fusion in children with Chiari malformation Type I and ventral brainstem compression. J Neurosurg Pediatr 5(6)(Jun):549–53

- 145. Hardy J (1969) Transsphenoidal microsurgery of the normal and pathological pituitary. Clin Neurosurg 16:185–217
- 146. Hardy J (2010) Historique de la chirurgie hypophysaire. Neurochirurgie 56:358– 362
- 147. Hardy J, Ciric I (1968) Selective anterior hypophysectomy in the treatment of diabetic retinopathy. A transsphenoidal microsur- gical technique. JAMA 203:73– 78
- 148. Hardy J, Wigser S (1965) Trans-sphenoidal surgery of pituitary fossa tumors with televised radiofluoroscopic control. J Neurosurg 23:612–619
- 149. Harris AE, Hadjipanayis CG, Lunsford LD, Lunsford AK, Kassam AB (2005) Microsurgical Removal of Intraventricular Lesions Using Endoscopic Visualization and Stereotactic Guidance. Neurosurgery 56(January):125–132
- Harrop J, Lobel D, Bendok B, Sharan A, Rezai A (2013) Developing a neurosurgical simulation-based educational curriculum: an overview. Neurosurgery 73 Suppl 1(Oct):25–9
- 151. Hayashi N, Endo S, Hamada H, Shibata T, Fukuda O, Takaku A (1999) Role of midsagittal resonance imaging in endoscopic third ventriculostomy. Minim Invasive Neurosurg 42:79–82
- 152. Hayashi N, Kurimoto M, Hamada H, Kurosaki K, Endo S, Cohen A (2008) Preparation of a simple and efficient laboratory model for training in neuroendoscopic procedures. Childs Nerv Syst 24:749–751
- 153. Hellwig D, Bauer B, Schulte M, Gatscher S, Riegel T, Bertalanffy H (2003) Neuroendoscopic treatment for colloid cysts of the third ventricle: The experience of a decade. Neurosurgery 52:525–533
- 154. Hellwig D, Benes L, Bertalanffy H, Bauer B (1997) Endoscopic stereotaxy—an eight year experience. Stereotact Funct Neurosurg 68:90–97
- 155. Hellwig D, Giordano M, Kappus C (2013) Redo third ventriculostomy. World Neurosurg 79(2 Suppl(Feb):S22.e13-20
- 156. Hellwig D, Grotenhuis J, Tirakotai W, Riegel T, Schulte D, Bauer B, Bertalanffy H
 (2005) Endoscopic third ventriculostomy for obstructive hydrocephalus. Neurosur Rev 28(1):1–34
- 157. Hellwig D, Haag R, Bartel V, Riegel T, Eggers F, Becker R, Bertalanffy H (1999) Application of new electrosurgical devices and probes in endoscopic neurosurgery. Neurol Res 21:67–72
- 158. Hellwig D, Schulte M, Tirakotai W (2006) Surgical management of arachnoid, suprasellar, and Rathke's cleft cysts. In: Schmidek H, Roberts D (eds) Schmidek Sweet Oper. Neurosurg. Tech., Saunders E. Philadelphia, pp 455–76
- 159. Heuer GG, Dandy W (1918) A new hypophysis operation. Johns Hopkins Hosp Bull 29:154–155
- 160. Hildebrandt G, Surbeck W, Stienen MN (2012) Emil Theodor Kocher: the first Swiss neurosurgeon. Acta Neurochir (Wien) 154(6):1105–15; discussion 1115
- 161. Hirayama R, Fujimoto Y, Umegaki M, Kagawa N, Kinoshita M, Hashimoto N, Yoshimine T (2013) Training to acquire psychomotor skills for endoscopic endonasal surgery using a personal webcam trainer. J Neurosurg 118(May):1120–

1126

- 162. Hirsch O (1910) Endonasal method of removal of hypophyseal tumors. JAMA 55:772–774
- 163. Hirsch O (1958) Hypophysentumoren Ein Grenzgebiet. Acta Neurochir (Wien) 5:1–10
- 164. Hoh BL, Neal DW, Kleinhenz DT, Hoh DJ, Mocco J, Barker FG (2012) Higher complications and no improvement in mortality in the ACGME resident duty-hour restriction era: An analysis of more than 107 000 neurosurgical trauma patients in the nationwide inpatient sample database. Neurosurgery 70(6):1369–1381
- 165. Hopf N, Grunert P, Darabi K, Busert C, Bettag M (1999) Frameless neuronavigation applied to endoscopic neurosurgery. Minim Invasive Neurosurg : 42:187–193
- 166. Hopf N, Grunnert P, Fries G, Resch K, Perneczky A, Grunert P (1999) Endoscopic Third Ventriculostomy: Analysis of 100 consecutiv procedures. Neurosurgery 44(April):795–804
- 167. Hopkins H (1976) Optical principle of endoscope.In: Endoscopy, edited by Berci G. New York: Appleton-Century-Crofts.
- 168. Horn EM, Feiz-Erfan I, Bristol RE, Lekovic GP, Goslar PW, Smith K a, Nakaji P, Spetzler RF, Ph D (2007) Treatment options for third ventricular colloid cysts: comparison of open microsurgical versus endoscopic resection. Neurosurgery 60(4):613–620
- 169. Horsley V (1906) On the technique of operations on the central nervous system. Br Med J 2:411–423
- 170. Hsu H, Chang S, Yang S, Chai C (2011) Learning curve of full-endoscopic lumbar discectomy. Eur Spine J 22 4:727–33
- 171. Hsu W, Li K, Bookland M, Jallo G (2009) Keyhole to the brain: Walter Dandy and neuroendoscopy. J Neurosurg Pediatr 27:439–442
- 172. Hwang G, Oh C, Park S, Sheen S, Bang J, Kang H (2010) Comparison of different microanastomosis training models: Model accuracy and practicality. Korean Neurosurg Soc 47:
- 173. Iannelli A, Lenzi R, Muscatello L (2014) A useful maneuver to simplify sellar floor repair following endoscopic transnasal pituitary surgery. J Neurol Surg A Cent Eur Neurosurg 75 (2)(Mar):158–60
- 174. Iplikcioglu A, Bek S, Bikmaz K, Basocak K (2003) Tension pneumocyst after transsphenoidal surgery for Rathke's cleft cyst: case report. Neurosurgery 52(Apr):960–2
- 175. Jack C, Kelly P (1989) Stereotactic third ventriculostomy: assessment of patency with MR imaging. Am J Neuroradiol 10:515–522
- 176. Jagannathan J, Laws E, Jane J (2012) Advantage of the endoscope and transitioning from the microscope to the endoscope for endonasal approaches. Kassam AB, Gardner PA (eds). Endosc. Approaches to Skull Base. Karger: Basel, pp 7–20
- 177. Jain K (1984) Sutureless extra-intracranial anastomoses by laser. Lancet 324:816– 817
- 178. Jakimovski D, Bonci G, Attia M, Shao H, Hofstetter C, Tsiouris A, Anand V, Schwarz T (2013) Incidence and Significance of Intraoperative CSF leak in Endoscopic

Pituitary Surgery Using Intrathecal Fluorescein. World Neurosurg.

- 179. Jallo G, Kothbauer K, Abbott I (2005) Endoscopic Third Ventriculostomy. Neurosurg Focus 19(6)(6):E11
- 180. Jane J, Han J, Prevedello D, Jagannathan J, Dumont A, Laws E (2005) Perspectives on endoscopic transsphenoidal surgery. Neurosurg Focus 19(6):1–10
- 181. Jane J, Thapar K, Kaptain G (2002) Pituitary surgery: transsphenoidal approach. Neurosurgery 51:435–442
- 182. Jenkinson MD, Hayhurst C, Al-Jumaily M, Kandasamy J, Clark S, Mallucci CL (2009) The role of endoscopic third ventriculostomy in adult patients with hydrocephalus. J Neurosurg 110(5):861–6
- 183. Jhala A, Mistry M (2010) Endoscopic lumbar discectomy: Experience of first 100 cases. Indian J Orthop 44 2:184–90
- 184. Jho H-DD, Carrau RL (1997) Endoscopic endonasal transsphenoidal surgery: experience with 50 patients. J Neurosurg 87(1):44–51
- 185. Jho H, Carrau R, Ko Y, Daly M (1997) Endoscopic pituitary surgery: an early experience. Surg Neurol 47:213–22
- Jones R, Kwok B, Stening W, Vonau M (1994) The current status of endoscopic third ventriculostomy in the management of non-communicating hydrocephalus. 35. Minim Invasive Neurosurg 37:28–36
- 187. Jones R, Stening W, Brydon M (1990) Endoscopic third ventriculostomy. Neurosurg Rev 26:86–91
- 188. Joswig H, Richter H, Haile SR, Hildebrandt G, Fournier JY (2016) Introducing Interlaminar Full-Endoscopic Lumbar Diskectomy: A Critical Analysis of Complications, Recurrence Rates, and Outcome in View of Two Spinal Surgeons' Learning Curves. J Neurol Surgery, Part A Cent Eur Neurosurg 77(5):406–415
- 189. Kadrian D, van Gelder J, Florida D, Jones R, Vonau M, Teo C, Stening W, Kwok B (2005) Long-term Reliability of Endoscopic Third Ventriculostomy. Neurosurgery 56(6):1271–1278
- 190. Kanner A, Hopf NJ, Grunert P (2000) The "optimal" burr hole position for endoscopic third ventriculostomy: results from 31 stereotactically guided procedures. Minim Invasive Neurosurg 43:187–189
- 191. Kassam AB, Carrau RL, Snyderman CH, Thomas A, Vescan A, Prevedello D, Mintz A, Gardner P (2008) Endoscopic Reconstruction of the Cranial Base Using a Pedicled Nasoseptal Flap. Neurosurgery 63(July):ONS44-ONS53
- 192. Kassam AB, Prevedello DM, Carrau RL, et al (2011) Endoscopic endonasal skull base surgery: analysis of complications in the authors' initial 800 patients. J Neurosurg 114(6):1544–68
- 193. Kassam AB, Snyderman C, Gardner P, Carrau R, Spiro R (2005) The Expanded Endonasal Approach: A Fully Endoscopic Transnasal Approach and Resection of the Odontoid Process: Technical Case Report. Neurosurgery 57(Supplement 1):E213
- 194. Kassam A, Snyderman C, Mintz A, Carrau R (2005) Expanded endonasal approach: the rostrocaudal axis. Part I. Crista galli to the sella turcica. Kassam A, Snyderman CH, Mintz A, Gardner P, Carrau RL. Neurosurg Focus 15(Jul):19(1):E3

- 195. Kawamata T, Kubo O, Hori T (2005) Surgical removal of growth hormonesecreting pituitary adenomas with intensive microsurgical pseudocapsule resection results in complete remission of acromegaly. Neurosurg Rev 28:201– 208
- 196. Kestle JRW, Drake JM, Cochrane D, Milner R, Walker M, Abbott R, Boop F (2003) Lack of benefit of endoscopic ventriculoperitoneal shunt insertion: a multicenter randomized trial. J Neurosurg 98:284–290
- 197. Key E, Retzius M (1875) Anatomie des Nervensystems und des Bindegewebes. Samson and Wallin, Stockholm
- 198. Kim K-T, Lee D-H, Cho D-C, Sung J-K, Kim Y-B (2015) Preoperative Risk Factors for Recurrent Lumbar Disk Herniation in L5–S1. J Spinal Disord Tech 28(10):E571– E577
- 199. King W, Ullman J, Frazee J, Post K, Bergsneider M (1999) Endoscopic resection of colloid cysts: Surgical considerations using the rigid endoscope. Neurosurgery 44:1103–1111
- 200. Kirkman MA, Ahmed M, Albert AF, Wilson MH, Nandi D, Sevdalis N (2014) The use of simulation in neurosurgical education and training. J Neurosurg 121(2):228– 246
- 201. Klein I, Steger U, Timmermann W, Thiede A, Gassel H (2003) Microsurgical training course for clinicians and scientists at a German University hospital: a 10-year experience. Microsurgery 23:461–465
- 202. Knosp E, Steiner E, Kitz K, Matula C (1993) Pituitary adenomas with invasion of the cavernous sinus space: a magnetic resonance imaging classification compared with surgical findings. Neurosurgery 33(October):610–618
- 203. Kocher T (1909) Ein Fall von Hypohpysis Tumor mit operativer Heilung. Deutsch Z Chir 100:13–37
- 204. Kockro R, Hwang P (2009) Virtual temporal bone: An interactive 3-dimensional learning aid for cranial base surgery. Neurosurgery 64 Suppl 2:
- 205. Kockro R, Serra L, Tseng-Tsai Y, Chan C, Yih-Yian S, Gim-Guan C (2000) Planning and simulation of neurosurgery in a virtual reality environment. Neurosurgery 46:118–135
- 206. Komotar R, Starke R, Raper D, Anand V, Schwartz T (2012) Endoscopic skull base surgery: a comprehensive comparison with open transcranial approaches. Br J Neurosurg 26 (5)(Oct):637–48
- 207. Komotar RJ, Starke RM, Raper DMS, Anand VK, Schwartz TH (2012) Endoscopic endonasal compared with microscopic transsphenoidal and open transcranial resection of craniopharyngiomas. World Neurosurg 77(2):329–41
- 208. Konakondla S, Fong R, Schirmer CM (2017) Simulation training in neurosurgery: advances in education and practice. Adv Med Educ Pract Volume 8:465–473
- 209. Kono Y, Prevedello DM, Snyderman CH, Gardner P a, Kassam AB, Carrau RL, Byers KE (2011) One thousand endoscopic skull base surgical procedures demystifying the infection potential: incidence and description of postoperative meningitis and brain abscesses. Infect Control Hosp Epidemiol 32(1):77–83
- 210. Kopta J (1971) The development of motor skills in orthopaedic education. Clin Or-

thop 75:80-5

- 211. Koutourousiou M, Gardner P a, Fernandez-Miranda JC, Paluzzi A, Wang EW, Snyderman CH (2013) Endoscopic endonasal surgery for giant pituitary adenomas: advantages and limitations. J Neurosurg 118(3):621–31
- 212. Krause F (1912) Surgery of the brain and spinal cord based on personal experience, vol 1 translated by HA Haubold. New York: Rebman. Comp.
- 213. Kulkarni A V, Drake JM, Mallucci CL, Sgouros S, Roth J, Constantini S (2009) Endoscopic third ventriculostomy in the treatment of childhood hydrocephalus. J Pediatr 155(2):254–9.e1
- 214. Kulwin C, Schwartz TH, Cohen-Gadol A a (2013) Endoscopic extended transsphenoidal resection of tuberculum sellae meningiomas: nuances of neurosurgical technique. Neurosurg Focus 35(6):E6
- 215. Kumar A, Maartens N, Kaye A (2003) Reconstruction of the sellar floor using Bioglue following transsphenoidal procedures. J Clin Neurosci 10:92–95
- 216. Kwiek S, Kocur D, Doleżych H, Suszyński K, Szajkowski S, Sordyl R, Ślusarczyk W, Kukier W, Bażowski P (2012) Endoscopic technique in the treatment of patients with colloid cysts of the third ventricle. Report based on over a decade of experience. Polish J Neurol Neurosurg 3:216–223
- 217. Landolt AM, Dott N (1999) Development of Pituitary Adenoma Treatment A critical Essay. Pituitary 2:103–112
- 218. Laws EJ (1996) Comment on Rodziewicz GS, Kelley RT, Kellman RM: Transnasal endoscopic surgery of the pituitary gland: technical note. Neurosurgery 39:189– 193
- 219. Laws EJ (1997) Comment on Jho HD, Carrau RL, Ko Y Endoscopic pituitary surgery: an early experience. Surg Neurol 47:213–223
- 220. Leach D (2004) A model for GME: shifting from process to outcomes a progress report from the Accreditation Council for Graduate Medical Education. Med Educ 38:12–4
- 221. Lee EJ, Ahn JY, Noh T, Kim SH, Kim TS, Kim SH (2009) Tumor tissue identification in the pseudocapsule of pituitary adenoma: should the pseudocapsule be removed for total resection of pituitary adenoma? Neurosurgery 64(3 Suppl):ons62-9; discussion ons69-70
- 222. Leng LZ, Brown S, Anand V, Schwartz T (2008) "Gasket-seal" watertight closure in minimal access endoscopic cranial base surgery. Neurosurgery 62(May):ONSE342-ONSE343
- 223. Lewis A, Crone K, Taha J, van Loveren H, Yeh H, Tew JJ (1994) Surgical resection of third ventricle colloid cysts. Preliminary results comparing tran- scallosal microsurgery with endoscopy. J Neurosurg 81:174–178
- 224. Liliequist B (1956) The anatomy of the subarachnoid cisterns. Acta Radiol 46:61– 71
- 225. Limbrick DD, Darcey RG (2013) Simulation in Neurosurgery: Possibilities and Practicalities: Foreword. Neurosurgery 73(4):1–3
- 226. Liu JKC, Kshettry VR, Recinos PF, Kamian K, Schlenk RP, Benzel EC (2015) Establishing a surgical skills laboratory and dissection curriculum for

neurosurgical residency training. J Neurosurg 123(November):1-8

- 227. Lobosky J, Vangilder J, Damasio A (1984) Behavioural manifestations of third ventricular colloid cysts. J Neurol Neurosurg Psychiatry 47:1075–1080
- 228. Locatelli D, Canevari F, Acchiardi I, Castelnuovo P (2010) The endoscopic diving technique in pituitary and cranial base surgery: technical note. Neurosurgery 66(2)(Feb):E400-1
- 229. Longatti P, Godano U, Gangemi M, et al (2006) Cooperative study by the Italian neuroendoscopy group on the treatment of colloid cysts. Childs Nerv Syst 61:1263–1267
- 230. Longatti P, Martinuzzi A, Moro M, Fiorindi A, Carteri A (2000) Endoscopic Treatment of Colloid Cysts of the Third Ventricle : 9 Consecutive Cases. Minim Invasive Neurosurg 43:118–123
- 231. Loris MD, Ph D (1999) A Set of Coaxial Microneurosurgical Instruments. Neurosurgery 45(December):1492–3
- 232. Louis R, Pouratian N, Jane J (2012) Endoscopic approach for pituitary tumors. In: Kassam A, Gardner P (eds) Endosc. Approaches to Skull Base., Karger. Basel, pp 60–75
- 233. Luginbuhl A, Campbell P, Evans J, Rosen M (2010) Endoscopic repair of high-flow cranial base defects using a bilayer button. Laryngoscope 120(5)(May):876–80
- 234. Luther N, Cohen A, Souweidane M (2005) Hemorrhagic sequelae from intracranial neuroendoscopic procedures for intraventricular tumors. Neurosurg Focus 19:
- 235. Madan A, Frantzides C, Tebbit C, Quiros R (2005) Participants' opinions of laparoscopic training devices after a basic laparoscopic training course. Am J Surg 189(6)(Jun):758–61
- 236. Maeder P, Gudinchet F, Meuli R, Fankhauser F (1998) Dynamic MRI of cerebrospinal fluid flow in endoscopic percutaneous ventriculostomy. Br J Neurosurg 12:18–22
- 237. Mahapatra A, Mehr S, Singh D, Tandon M, Ganjoo P, Singh H (2011) Ostomy closure and the role of repeat endoscopic third ventriculostomy (re-ETV) in failed ETV procedures. Neuro India 59(6)(Nov-Dec):867–73
- 238. Di Maio S, Cavallo LM, Esposito F, Stagno V, Corriero OV, Cappabianca P (2011) Extended endoscopic endonasal approach for selected pituitary adenomas: early experience. J Neurosurg 114(2):345–53
- 239. Mantur M, Łukaszewicz-Zając M, Mroczko B, et al (2011) Cerebrospinal fluid leakage--reliable diagnostic methods. Clin Chim Acta 12;412(11-(May):837–40
- 240. Matsumoto E, Hamstra S, Radom-ski S, Cusimano M (2002) The effect of bench model fidelity on endourological skills: a randomized controlled study. J Urol 167:1243–7
- 241. Mattei T, Frank C, Bailey J, Lesle E, Macuk A, Lesniak M, Patel A, Morris M, Nair K, Lin J (2013) Design of a synthetic simulator for pediatric lumbar spine pathologies. J Neurosurg Pediatr 12(2)(Aug):192–201
- 242. Mattula CW, Steiger CN (2005) Hemostasis and fleece-bound sealing in neurosurgery, Thieme. Stuttgart New York
- 243. McArthur (1912) An aseptic surgical access to the pituitary body and its

neighborhood. JAMA 58:2009–2011

- 244. Meier J, Bleier B (2013) Anteriorly based pedicled flaps for skull base reconstruction. Adv Otorhinolaryngol 74:64–70
- 245. Melmed S, Colao A, Barkan A, et al (2009) Guidelines for acromegaly management: an up- date. J Clin Endocrinol Metab 94:1509–1517
- 246. Messerer M, De Battista JC, Raverot G, Kassis S, Dubourg J, Lapras V, Trouillas J, Perrin G, Jouanneau E (2011) Evidence of improved surgical outcome following endoscopy for nonfunctioning pituitary adenoma removal. Neurosurg Focus 30(4):E11
- 247. Mezger U, Jendrewski C, Bartels M (2013) Navigation in surgery. Langenbecks Arch Surg 398(4):501–14
- 248. Mixter W (1923) Ventriculoscopy and puncture of the floor of the third ventricle. Bost Med Surg J 188:277–278
- 249. Moeller C, Welch K (2010) Prevention and management of complications in sphenoidotomy. Otolaryngol Clin North Am 43(4)(Aug):839–54
- 250. Moonesinghe S, Lowery J, Shahi N, Millen A, Beard J (2011) Impact of reduction in working hours for doctors in training on postgraduate medical education and patients' outcomes: systematic review. BMJ 22(Mar):342:d1580, 36.
- 251. Moorthy R, Rajshekhar V (2011) Endoscopic third ventriculostomy for hydrocephalus: a review of indications, outcomes, and complications. Neurol India 59 (6)(Nov-Dec):848–54
- 252. Morfeld M, Kirchberger I, Bullinger M (2011) SF-36. Fragebogen zum Gesundheitszustand. Deutsche Version des Short Form-36 Health Survey., Hogrefe Ve. Göttingen
- 253. Morota N, Watabe T, Inukai T, Hongo K, Nakagawa H (2000) Anatomical variants in the floor of the third ventricle ; implications for endoscopic third ventriculostomy. J Neurol Neurosurg Psychiatry 1:531–534
- 254. Mugamba J, Stagno V (2013) Peer-Review Reports Indication for Endoscopic Third Ventriculostomy. 19–23
- 255. Naftel RP, Reed GT, Kulkarni A V, Wellons JC (2011) Evaluating the Children's Hospital of Alabama endoscopic third ventriculostomy experience using the Endoscopic Third Ventriculostomy Success Score: an external validation study. J Neurosurg Pediatr 8(5):494–501
- 256. Neubauer A, Wolfsberger S (2013) Virtual endoscopy in neurosurgery: a review. Neurosurgery 72 Suppl 1(January):97–106
- 257. Nishihara T, Teraoka A, Morita A, Ueki K, Takai K, Kirino T (2000) A transparent sheath for endoscopic surgery and its application in surgical evacuation of spontaneous intracerebral hematomas. Technical note. J Neurosurg 92:1053–1055
- 258. Nowitzke A (2005) Assessment of the learning curve for lumbar microendoscopic discectomy. Neurosurgery 56 4:755–62
- 259. O'Malley BW, Grady MS, Gabel BC, Cohen M a, Heuer GG, Pisapia J, Bohman L-E, Leibowitz JM, Surgery N (2008) Comparison of endoscopic and microscopic removal of pituitary adenomas: single-surgeon experience and the learning curve.

Neurosurg Focus 25(6):E10

- 260. Ogino-Nishimura E, Nakagawa T, Sakamoto T, Ito J (2012) An Endoscopic Endonasal Surgery Training Model Using Quail Eggs. Laryngoscope 122:2154– 2157
- 261. Oi S, Shimoda M, Shibata M, Honda Y, Togo K, Shinoda M, Tsugane R, Sato O (2000) Pathophysiology of long-standing overt ventriculomegaly in adults. J Neurosurg 92:933–940
- 262. Oka K, Ohta T, Kibe M, Tomonage M (1990) A new neurosurgical ventriculoscopetechnical note. Neurol Med Chir Tokyo 30:77–79
- 263. Okuda T, Kataoka K, Kato A (2010) Training in endoscopic endonasal transsphenoidal surgery using a skull model and eggs. Acta Neurochir 152(10)(Oct):1801–4
- 264. Oliveira M, Araujo A, Nicolato A, Prosdocimi A, Godinho J, Valle A, Al E (2016) Face, content and construct validity of brain tumor microsurgery simulation using a human placenta model. Neurosrugery 12:61–67
- 265. Osborne A (2010) Primary nonneoplastic cysts. In: Osborne A, Salzmann K, Barkovich A (eds) Anne Osborne Diagnostic imaging. Brain, Amirsys. Altona, Canada, p I.7.6-I.7.9
- 266. Ou Y, McGlone E, Camm C, Khan O (2013) Does playing video games improve laparoscopic skills? Int J Surg 11(5):365–369
- 267. Paladino J, Rotim K, Stimac D, Pirker N, Stimac A (2000) Endoscopic third ventriculostomy with ultrasonic contact microprobe. Minim Invasive Neurosurg 43:132–134
- 268. Palter VN (2011) Comprehensive training curricula for minimally invasive surgery. J Grad Med Educ 3(3):293–8
- 269. Paluzzi A, Fernandez-Miranda JC, Tonya Stefko S, Challinor S, Snyderman CH, Gardner PA (2013) Endoscopic endonasal approach for pituitary adenomas: a series of 555 patients. Pituitary. doi: 10.1007/s11102-013-0502-4
- 270. Paraskevopoulos D, Biyani N, Constantini S, Beni-Adani L (2011) Combined intraoperative magnetic resonance imaging and navigated neuroendoscopy in children with multicompartmental hydrocephalus and complex cysts: a feasibility study. J Neurosurg Pediatr 8(3):279–88
- Pascal-Vigneron V, Leclère J (1993) Rhinorrhea and otorrhea: rare complication of medical treatment for invasive prolactinomas.pdf. Ann Endocrinol (Paris) 54:347– 351
- 272. Pasztor E, Vajda J, Piffko P (1980) Horvath M: Transoral surgery for basilar impression. Surg Neurol 14:473–476
- 273. Pawar SJ, Sharma RR, Mahapatra a K, Dev EJ (2001) Giant ependymal cyst of the temporal horn -- an unusual presentation. Case report with review of the literature. Pediatr Neurosurg 34(6):306–10
- 274. Payr E (1908) Drainage der Hirnventrikel Mittelst frei Transplantirter Blutgefässe; Bemerkungen ueber Hydrocephalus. Arch Klin Chir 87:801–885
- 275. Peretta P, Ragazzi P, Galarza M, Genitori L, Giordano F, Mussa F, Cinalli G (2006) Complications and pitfalls of neuroendoscopic surgery in children. J Neurosurg

105:187-193

- 276. Persaud T (1997) A History of Anatomy: The Post-Vesalian Era., Springfiel. Illinois
- 277. Pichierri A, Frati A, Santoro A, Lenzi J, Delfini R, Pannarale L, Gaudio E, D'Andrea G, Cantore G (2009) How to set up a microsurgical laboratory on small animal models: organization, techniques, and impact on residency training. Neurosurg Rev 32(1)(Jan):101–10; discussion 110
- 278. Pierre-Kahn A, Renier D, Bombois B, Askienasy S, Moreau R, Hirsch J, van Veelen MLC (1975) Place de la ventriculo-cisternostomie dans le traitement des hydrocephalies non-communicantes. Neurochirurgia (Stuttg) 21:557–559
- 279. Pinto FCG, Saad F, de Oliveira MF, et al (2013) Role of Endoscopic Third Ventriculostomy and Ventriculoperitoneal Shunt in Idiopathic Normal Pressure Hydrocephalus: Preliminary Results of a Randomized Clinical Trial. Neurosurgery 72(5):845-53-4
- 280. Piquer J, Qureshi MM, Young PH, Dempsey RJ (2015) Neurosurgery Education and Development program to treat hydrocephalus and to develop neurosurgery in Africa using mobile neuroendoscopic training. J Neurosurg Pediatr 15(6):552–559
- 281. Placantonakis D, Tabaee A, Anand V, Hitzlik D, Schwartz T (2007) Safety of low dose intrathecal fluorescein in endsoscopic skull base surgery. Neurosurgery 61:161–165
- 282. Ploch CC, Mansi CS, Jayamohan J, Kuhl E (2016) Using 3D Printing to Create Personalized Brain Models for Neurosurgical Training and Preoperative Planning. World Neurosurg 90(June):668–674
- 283. Pollock B, Shreiner S, Huston J (2000) A theory on the natural history of colloid cysts of the third ventricle. Neurosurgery 46:1077–1083
- 284. Potts J 3rd (2006) Core training in surgery: what does it need to include? Semin Vasc Surg 19(4):210–213
- 285. Powell M, Torrens M, Thomson J, Horgan J (1983) Isodense colloid cysts of the third ventricle: A diagnostic and therapeutic problem resolved by ventriculoscopy. Neurosurgery 13:234–237
- 286. Prevedello DM (2012) Transsphenoidal approaches to the sellar and parasellar area. In: Edward R. Laws JS (ed) Ed.R. Laws, Sheehan J.P. Sellar parasellar tumors. Thieme, New York, pp 177–186
- 287. Prickett K, Wise S (2013) Grafting materials in skull base reconstruction. In: G. Randolph BM (ed) BenjaminS. Bleier Compr. Tech. CSF leaf repair skull base Reconstr., Karger. , pp 24–32
- 288. Purcell Jackson G, Tarpley J (2009) How long does it take to train a surgeon? BMJ 5(nov):339:b4260
- 289. Putnam T (1934) Treatment of hydrocephalus by endoscopic coagulation of the choroid plexus. N Engl J Med 210:1373–1376
- 290. Rachinger W, Grau S, Tonn J (2010) Different microsurgical approaches to meningiomas of the anterior cranial base. Acta Neurochir (Wien) 152:931–939
- 291. Radetzky A, Rudolph M, Starkie S, Davies B, Auer L (2000) ROBO-SIM: A simulator for minimally invasive neurosurgery using an active manipulator. Stud Health Technol Inform 77:1165–1169

- 292. Raithatha R, McCoul E, Woodworth G, Schwartz T, Anand V (2012) Endoscopic endonasal approaches to the cavernous sinus. Int Forum Allergy Rhinol 2(1)(Jan-Feb):9–15
- 293. Ray W, Ganju A, Harrop J, Hoh D (2013) Developing an anterior cervical diskectomy and fusion simulator for neurosurgical resident training. Neurosurgery 73(Suppl 1:100–106
- 294. Raymond J, Hardy J, Czepko R (1997) Arterial injuries in transsphenoidal surgery for pituitary adenoma; the role of angiography and endovascular treatment. Am J Neuroradiol 18(Apr):655–665
- 295. Reznick R, MacRae H (2006) Teaching surgical skills—changes in the wind. N Engl J Med 355:2664–2669
- 296. Reznick R, Regehr G, MacRae H, Martin J, McCulloch W (1997) Testing technical skill via an innovative "bench station" examination. Am J Surg 173(3):226–230
- 297. Rhode V, Behm T, Ludwig H, Wachter D, Rohde V (2012) The role of neuronavigation in intracranial endoscopic procedures. Neurosurg Rev 35(3):351–358
- 298. Rhoton AL (2002) Chapter 6: anterior and middle cranial base. Neurosurgery 51(October):S1-273-S1-301
- 299. Rhoton AL (2002) Chapter 5: Latera and 3d ventricles. Neurosurgery 51(October):207–271
- 300. Rhoton AL (2002) Chapter 4: Cerebral veins. Neurosurgery 51(October):159–205
- 301. Richard K.Reznick HM (2006) Teaching Surgical Skills Changes in the wind. N Engl J Med 355:2664–9
- 302. Riegel T, Alberti O, Hellwig D, Bertalanffy H (2001) Operative management of third ventriculostomy in cases of thickened, non-translucent third ventricular floor: technical note. Minim Invasive Neurosurg 44:65–69
- 303. Robison R, Liu C, Apuzzo M (2011) Man, mind, and machine: the past and future of virtual reality simulation in neurologic surgery. World Neurosurg. doi: 10.1016/j.wneu
- 304. Di Rocco C, Cinalli G, Massimi L, Spennato P, Cianciulli E, Tamburrini G (2006) Endoscopic third ventriculostomy in the treat- ment of hydrocephalus in pediatric patients. Adv Tech Stand Neurosurg 31:119–219
- 305. Roitberg B, Banerjee P, Luciano C, Matulyauskas M, Rizzi S, Kania P, Gasco J (2013) Sensory and motor skill testing in neurosurgery applicants: a pilot study using a virtual reality haptic neurosurgical simulator. J Neurosurg 73 Suppl 1(Oct):116– 21
- 306. Rong L, Xie P, Shi D, Dong J, Liu B, Feng F, Al. E (2008) Spinal surgeons' learning curve for lumbar microendoscopic discectomy: a prospective study of our first 50 and latest 10 cases. Chin Med J (Engl) 121 21:2148–51
- 307. Rosseau G, Bailes J, Del Maestro R, et al (2013) The Development of a virtual simulator for training neurosurgeons to perform and perfect endoscopic endonasal transsphenoidal surgery. Neurosurgery 73(SUPPL. 4):85–93
- 308. Rosser J, Lynch P, Duddihy L, Gentile D, Klonsky J, Merrell R (2007) The impact of video games on training surgeons in the 21st century. Arch Surg 142(2):181–186,

discusssion 186

- 309. Rotenberg B, Tam S, Ryu WH a, Duggal N (2010) Microscopic versus endoscopic pituitary surgery: a systematic review. Laryngoscope 120(7):1292–7
- 310. Ruetten S, Komp M, Merk H, Godolias G (2007) Use of newly developed instruments and endoscopes: full-endoscopic resection of lumbar disc herniations via the interlaminar and lateral transforaminal approach. J Neurosurg Spine 6(6):521–530
- 311. Ruetten S, Komp M, Merk H, Godolias G (2008) Full-endoscopic interlaminar and transforaminal lumbar discectomy versus conventional microsurgical technique: a prospective, randomized, controlled study. Spine (Phila Pa 1976) 33 9:931–9
- 312. Ruiz-Juretschke F, Mateo-Sierra O, Iza-Vallejo B, Carrillo-Yagüe R (2007) Intraventricular tension pneumocephalus after transsphenoidal surgery: a case report and literature review. Neurocir (Astur) 18(2)(Apr):134–7
- 313. Ryder J, Kleinschmidt-DeMasters B (1986) Sudden deterioration and death in patients with benign tumors of the third ventricle area. J Neurosurg 64:216–224
- 314. Sacko O, Boetto S, Lauwers-Cances V, Dupuy M, Roux F-E (2010) Endoscopic third ventriculostomy: outcome analysis in 368 procedures. J Neurosurg Pediatr 5(1):68–74
- 315. Sano T, Yamada S (1994) Histologic and immunohistochemical study of clinically non-functioning pituitary adenomas: special reference to gonadotropin-positive adenomas. Pathol Int 44:697–703
- 316. Satyarthee G, Mahapatra A, Satyarthe G (2003) Tension pneumocephalus following transsphenoid surgery for pituitary adenoma report of two cases. J Clin Neurosci 10(4)(Jul):495–7
- 317. Sawka A, Aniszewski J, Young WJ, Nippoldt T, Yanez P, Ebersold M (1999) Tension pneumocranium, a rare complication of transsphenoidal pituitary surgery: Mayo Clinic experience 1976-1998. J Clin Endocrinol Metab 84(12)(Dec):4731–4
- 318. Sayers M, Kosnik E (1976) Percutaneous third ventriculos- tomy: experience and technique. Childs Brain 2:24–30
- 319. Scarff J (1952) Non obstructive hydrocephalus: Treatment by endoscopic cauterization of choroid plexus. Long term results. J Neurosurg 9:164–176
- 320. Schaberg MR, Anand VK, Schwartz TH, Cobb W (2010) Microscopic versus endoscopic transnasal pituitary surgery. Curr Opin Otolaryngol Head Neck Surg 18(1):8–14
- 321. Schirmer CM, Elder JB, Roitberg B, Lobel DA (2013) Virtual reality-based simulation training for ventriculostomy: An Evidence-based approach. Neurosurgery 73(SUPPL. 4):66–73
- 322. Schirmer CM, Elder JB, Rotberg B, Lobel DA (2013) Virtual Reality Based Simulation Training for Ventriculostomy: An Evidence-Based Approach. Neurosurgery 73(4):66–73
- 323. Schlickum M, Hedman L, Enochsson L, Kjellin A, Felländer-Tsai L (2009) Systematic video game training in surgical novices improves performance in virtual reality endoscopic surgical simulators: a prospective randomized study. World J Surg 33(11):2360–2367

- 324. Schloffer H (1906) Zur Frage der Operationen an der Hypophyse. Bruns Beitr Klin Chir 50:767–817
- 325. Schloffer H (1907) Erfolgreiche Operation eines Hypophysentumors auf nasalem Wege. Wien Klin Wochenschr 20:621–624
- 326. Schloffer H (1907) Weiterer Bericht über den Fall von operiertem Hypophysentumor: Plötzlicher Exitus letalis 2 ½ Monate nach der Operation. Wien Klin Wochenschr 20:1075–1078
- 327. Schoffl H, Hager D, Hinterdorfer C, Dunst K, Froschauer S, Steiner W, Kwasny O, Huemer G (2006) Pulsatile perfused porcine coronary arteries for microvascular training. Ann Plast Surg 57(2)(Aug):213–6
- 328. Scholtes F, Signorelli F, McLaughlin N, Lavigne F, Bojanowski MW (2011) Endoscopic endonasal resection of the odontoid process as a standalone decompressive procedure for basilar invagination in Chiari type I malformation. Minim Invasive Neurosurg 54(4):179–82
- 329. Schroeder HW, Niendorf W, Gaab M, Schreoder H, Hiendorf W (2002) Complications of endoscopic third ventriculostomy. J Neurosurg 96:1032–40
- 330. Schulz M, Bohner G, Knaus H, HaBerl H, ThoMale U (2010) Navigated endoscopic surgery for multiloculated hydrocephalus in children. J Neurosurg Pediatr 5:434– 442
- 331. Schwarz T (2014) Intraoperative magnetic resonance imaging and pituitary surgery. Editorial. J Neurosurg 120(2):342–45
- 332. Seeger W (2006) Endoscopic anatomy of the third ventricle. Microsurgical and endoscopic approaches., Springer. Wien/NewYork
- 333. Segal S (1998) Anatomy for neurosurgical endoscopic procedures. In: Jimenez D (ed) Intracranial Endosc. Neurosurg. Thieme/AANS, pp 39–90
- 334. Sekhar LN, Tariq F, Ferreira M (2012) What is the best approach to resect an anterior midline skull base meningioma in 2011? Microsurgical transcranial, endonasal endoscopic, or minimal access cranial? World Neurosurg 77(5–6):621–2
- 335. Selden N, Origitano T, Hadjipanayis C, Byrne R (2013) Model-based simulation for early neurosurgical learners. Neurosurgery 73 Suppl 1(Oct):15–24
- 336. Service PH, Services H (2004) National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 32(8):470–485
- 337. Seymour N, Gallagher A, Roman S, et al (2002) Virtual reality training improves operating room performance: results of a randomized, double-blinded study. Ann Surg 236:458–63
- 338. Shah J (2002) Endoscopy through the ages. BJU Int 89:645–652
- 339. Shah S, Har-El G Diabetes insipidus after pituitary surgery: incidence after traditional versus endoscopic transsphenoidal approaches. Am J Rhinol 15(6):377–9
- 340. Shah RN, Leight WD, Patel MR, Surowitz JB, Wong Y-T, Wheless S a, Germanwala A V, Zanation AM (2013) A controlled laboratory and clinical evaluation of a threedimensional endoscope for endonasal sinus and skull base surgery. Am J Rhinol

Allergy 25(3):141-4

- 341. Shaun J, Mclaughlin N, Bojanowski MW, Lavigne F (2010) Extracranial Complications of Endoscopic Transsphenoidal Sellar Surgery. J Otolaryngol Neck Surg i(3):309–314
- 342. Shimon I, Cohen Z, Ram Z, Hadani M (2001) Transsphenoidal surgery for acromegaly: endocrinological follow-up of 98 patients. Neurosurgery 48:1239– 1243
- 343. Skerbinjek Kavalar M, Kavalar R, Strojnik T (2005) A colloid cyst of the third ventricle -- the cause of episodic headache and sudden unexpected death in an adolescent girl. Wien Klin Wochenschr 117:837–840
- 344. Snyderman C (2007) Who is the skull base surgeon of the future? Skull Base-an ... 1(212):353–355
- 345. Snyderman CH, Kassam AB, Carrau R, Mintz A (2007) Endoscopic Reconstruction of Cranial Base Defects following Endonasal Skull Base Surgery. 1(212):73–78
- 346. Snyderman C, Pant H, Gardner P, Carrau R, Prevedello D, Kassam A (2012) Management of complications of endonasal cranial base surgery. In: Kassam A, Gardner P (eds) Endosc. approaches to skull base, Karger. Lunsford LD, Basel, pp 182–190
- 347. Sonnenburg R, White D, Ewend M, Senior B (2004) The learning curve in minimally invasive pituitary surgery. Am J Rhinol 18(4):259–263
- 348. Spencer WR, Das K, Nwagu C, Wenk E, Schaefer SD, Moscatello A, Couldwell WT (1999) Approaches to the Sellar and Parasellar Region : Anatomic Comparison of the Microscope Versus Endoscope. Lancet (May):791–794
- 349. Spetzler RF, Sanai N (2012) The quiet revolution: retractorless surgery for complex vascular and skull base lesions. J Neurosurg 116(2):291–300
- 350. Stankiewicz J, Lal D, Connor M, Welch K (2011) Complications in endoscopic sinus surgery for chronic rhinosinusitis: a 25-year experience. Laryngoscope 121(12)(Dec):2684–701
- 351. Steinmeier R, Fahlbusch R, Ganslandt O (1998) Intraoperative magnetic resonance imaging with the magnetom open scanner: concepts, neurosurgical indications, and procedures: a prelimi- nary report. Neurosurgery 43:739–747
- 352. Stelter K, Tsekhmistrenko V, Ledderose G, Rachinger W, Thon N, Betz C (2013) Mentale Arbeitsbelastung und Ergonometrie bei endoskopischen Nasennebenhöhlen- und Schädelbasiseingriffen. 21. Jahrestagung der Gesellschaft für Schädelbasischirurgie. Tübingen, p 46
- 353. Suh J, Ramakrishnan V, DeConde A (2012) Nasal floor free mucosal graft for skull base reconstruction and cerebrospinal fluid leak repair. Ann Otol Rhinlo Laryngol 121:91–95
- 354. Tabaee A, Anand VK, Barrón Y, Hiltzik DH, Brown SM, Kacker A, Mazumdar M, Schwartz TH (2009) Endoscopic pituitary surgery: a systematic review and metaanalysis. J Neurosurg 111(3):545–54
- 355. Tabaee A, Anand VK, Brown SM, Lin JW, Schwartz TH (2007) Algorithm for reconstruction after endoscopic pituitary and skull base surgery. Laryngoscope 117(7):1133–7

- Tabaee A, Anand V, Fraser J, Brown S, Singh A, Schwartz T (2009) Threedimensional endoscopic pituitary surgery. Neurosurgery 64(5 Suppl(May):288– 93
- 357. Tasman Abel-Jan, Stammberger Heinz kolling g. (1998) Is monocular perception of depth through the rigid endoscope a disadvantage compared to binocular vision through the operating microsope in paranasal sinus surgery ? Am J Rhinol 12:87–91
- 358. Tasman Abel-Jan, Wallner F., Kolling G.H. .. (1996) Wie gut ist die räumliche Orientierung durch die starre Optik? HNO 44:73–77
- 359. Taussky P, Kalra R, Coppens J, Mohebali J, Jensen R, Couldwell W (2011)
 Endocrinological outcome after pituitary transposition (hypophysopexy) and adjuvant radiotherapy for tumors involving the cavernous sinus. J Neurosurg 115 (1)(Jul):55–62
- 360. Telera S, Carapella CM, Caroli F, Crispo F, Cristalli G, Raus L, Sperduti I, Pompili A (2012) Supraorbital keyhole approach for removal of midline anterior cranial fossa meningiomas : a series of 20 consecutive cases. Neurosurg Rev 35:67–83
- 361. Temple J (2010) Time for Training. A Review of the Impact of the European Working Time Directive on the Quality of Training. London
- 362. Teo C, Kadrian D, Hayhurst C (2013) Endoscopic management of complex hydrocephalus. World Neurosurg 79(2 Suppl(Feb):S21.e1-7
- 363. Teo C, Nakaji P (2004) Neuro-oncologic applications of endoscopy. Neurosurg Clin N Am 15:89–103
- 364. Ting J, Metson R (2013) Free graft techniques in skull base reconstruction. In: G. Randolph BM (ed) Benjamin S. Bleier Compr. Tech. CSF leak repair skull base Reconstr., Karger. , pp 33–41
- 365. Turillazzi E, Bello S, Neri M, Riezzo I, Fineschi V (2012) Colloid cyst of the third ventricle, hypothalamus, and heart: a dangerous link for sudden death. Diagn Pathol 18(Oct):144
- 366. Valentine R, Athanasiadis T, Moratti S, Hanton L, Robinson S, Wormald P (2010) The efficacy of a novel chitosan gel on hemostasis and wound healing after endoscopic sinus surgery. Am J Rhinol Allergy 24(1)(Jan-Feb):70–75
- 367. Valentine R, Boase S, Jervis-Bardy J, Dones Cabral J, Robinson S, Wormald P (2011) The efficacy of hemostatic techniques in the sheep model of carotid artery injury. Int Forum Allergy Rhinol 1(2)(Mar-Apr):118–22
- 368. Valentine R, Wormald P-J (2011) Carotid artery injury after endonasal surgery. Otolaryngol Clin North Am 44(5):1059–79
- 369. Vance M (1987) Prolactinomas. Endocrinol Metab Clin North Am 16:731–753
- 370. Vance M (1999) Growth Hormone-Secreting Adenomas. In: Krisht A, Tindall G (eds) Pituit. Disord. Compr. Manag., LIPPINCOTT. Baltimore, pp 235–242
- 371. Varoquier M, Hoffmann CP, Perrenot C, Tran N, Parietti-Winkler C (2017) Construct, Face, and Content Validation on Voxel-Man® Simulator for Otologic Surgical Training. Int J Otolaryngol 2017:1–8
- 372. Vincenzo J Di, Gaab MR, Schroeder HWS, Oertel JMK (2012) Endoscopic Third Ventriculostomy : Preoperative Considerations and Intraoperative Strategy Based

on 300 Procedures. J Neurol Surg A

- 373. Voelcker-Rehage C (2008) Motor-skill learning in older adults—a review of studies on age-related differences. Eur Rev Aging Phys Act 5(1):5–16
- 374. Volkmann J (1923) Ueber Versuche zur unmittelbaren Besichtigung der Gehirnkammern(Enzephaloskopie). Münchener Med Wochenschr 46:1382
- 375. Volkmann J (1924) Das Enzephaloskop. Sonderabdruck. Zentralbl Chir 23:1233– 1234
- 376. Vons J, Velut S (2008) André Vésale. Résumé de ses livres sur la fabrique du corps humain, traduction et commentaires., Les Belles. Paris
- 377. Vries J (1978) An endoscopic technique for third ventricu- lostomy. Surg Neurol 9:165–168
- 378. Walker M (2001) History of ventriculostomy. Neurosurg Clin N Am 12(1):101– 105
- 379. Wang L, Kim J, Heilman C (1999) Intracranial mucocele as a complication of endoscopic repair of cerebro-spinal fluid rhinorrhea: case report. Neurosurgery 45:1243–1245
- 380. Wang C, Liu C, Xiong Y, Han G, Yang H, Yin H, Wang J, You C (2013) Surgical treatment of intracranial arachnoid cyst in adult patients. Neuro India 61(1)(Jan-Feb):60–4
- 381. Wang B, Lu G, Patel A, Ren P, Cheng I (2011) An evaluation of the learning curve for a complex surgical technique: the full endoscopic interlaminar approach for lumbar disc herniations. Spine J 11 2:122–30
- 382. Wang B, Lü G, Patel A a, Ren P, Cheng I (2011) An evaluation of the learning curve for a complex surgical technique: the full endoscopic interlaminar approach for lumbar disc herniations. Spine J 11(2):122–30
- 383. Wang B, Lü G, Patel A, Ren P, Cheng I (2011) An evaluation of the learning curve for a complex surgical technique: the full endo- scopic interlaminar approach for lumbar disc herniations. Spine J 11(2):122–130
- 384. Waran V, Narayanan V, Karuppiah R, et al (2014) Injecting realism in surgical training – Initial simulation experience with custom 3D models. J Surg Educ 71(2):193–197
- 385. Warf B, Kulkarni A (2010) Intraoperative assessment of cerebral aqueduct patency and cisternal scarring: impact on success of endoscopic third ventriculostomy in 403 African children. J Neurosurg Pediatr 5:204–209
- 386. Warren W, Medary M, Dureza C, Bellotte J, Flannagan P, Oh M, Fukushima T (2000) Dural Repair Using Acellular Human Dermis: Experience with 200 Cases: Technique Assessment. Neurosurgery 46:1391–1396
- 387. Weigl M, Stefan P, Abhari K (2015) Intra-operative disruptions, surgeon's mental workload, and technical performance in a full-scale simulated procedure. Surg Endosc 30:559–566
- 388. Weinstock P, Rehder R, Prabhu SP, Forbes PW, Roussin CJ, Cohen AR (2017) Creation of a novel simulator for minimally invasive neurosurgery: fusion of 3D printing and special effects. J Neurosurg Pediatr 20(1):1–9
- 389. Xu H, Liu X, Liu G, Zhao J, Fu Q, Xu B (2014) Learning curve of full-endoscopic

technique through interlaminar approach for L5/S1 disk herniations. Cell Biochem Biophys 70(2):1069–1074

- 390. Yadav YR, Madhariya S, Parihar V, Namdev H, Bhatele P (2013) Endoscopic
 Transoral Excision of Odontoid Process in Irreducible Atlantoaxial Dislocation :
 Our Experience of 34 Patients. J Neurol Surg A 74:162–167
- 391. Yadav Y, Parihar V, Namdev H, Agarwal M, Bhatele P (2013) Endoscopic Interlaminar Management of Lumbar Disc Disease. J Neurol Surg A Cent Eur Neurosurg 74 2:77–81
- 392. Yang Isaac, Wang Marilene B., Bergsneider Marvin .. (2010) Making the Transition form Microsurgery to Endoscopic Trans-Sphenoidal Pituitary Neurosurgery. Neurosurg Clin N Am 21:643–651
- 393. Yaniv E, Rappaport Z (1997) Endoscopic transseptal transsphenoidal surgery for pituitary tumors. Neurosurgery 40:944–946
- 394. Yasuda A, Campero A, Martins C, Rhoton AL, Ribas GC, Al ET (2004) The Medial Wall of the Cavernous Sinus: Microsurgical Anatomy. Neurosurgery 55(1):179– 190
- 395. Yorgason J, Arthur A, Orlandi R, Apfelbaum R (2004) Endoscopic decompression of tension pneumosella following transsphenoidal pituitary tumor resection. Pituitary 7(3):171–7
- 396. Young W, Scheithauer B, Kovacs K, Horvath E, Davis D, Randall R (1996)
 Gonadotroph adenoma of the pituitary gland: a clinicopathologic analysis of 100
 cases. Mayo Clin Proc 71:649–656
- 397. Zada G, Du R, Laws ER (2011) Defining the "edge of the envelope": patient selection in treating complex sellar-based neoplasms via transsphenoidal versus open craniotomy. J Neurosurg 114(2):286–300
- 398. Zada G, Liu C, Apuzzo MLJ (2012) "Through the looking glass": optical physics, issues, and the evolution of neuroendoscopy. World Neurosurg 77(1):92–102
- 399. Zanation A, Carrau R, Snyderman C, Kassam A, Gardner P, Prevedello D, Mintz A (2012) Endoscopic reconstruction of anterior skull base defects. In: Kassam AB, Gardner PA: In: Kassam A, Gardner P (eds) Endosc. approaches to skull base, Karger. Basel, pp 168–181
- 400. Zhang L, Kamaly I, Luthra P, Whitfield P (2016) Simulation in neurosurgical training: a blueprint and national approach to implementation for initial years trainees. Br J Neurosurg 30(5):577–581
- 401. Zuccaro G, Ramos J (2011) Multiloculated hydrocephalus. Child's Nerv Syst 27(10)(Oct):1609–19
- 402. (1993) Council Directive 93/104/EC. Off J Eur Communities L307:18-24