The historical evolution of transsphenoidal surgery: facilitation by technological advances

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Over the past century, pituitary surgery has undergone multiple evolutions in surgical technique and technological advancements that have resulted in what practitioners now recognize as modern transsphenoidal surgery (TSS). Although the procedure is now well established in current neurosurgical literature, the historical maze that led to its development continues to be of interest because it allows a better appreciation of the unique contributions by the pioneers of the technique, and of the innovative spirit that continues to fuel neurosurgery. The early events in the history of TSS have already been well documented. This paper therefore summarizes the major early transitions along the timeline, and then further concentrates on some of the more recent advancements in TSS, such as the surgical microscope, fluoroscopy, endoscopy, intraoperative imaging, and frameless guidance. The account of each of these innovations is unique because they were each developed as a response to certain historical needs by the surgeon. An understanding of these more recent contributions, coupled with the early history, provides a more complete perspective on modern TSS. (DOI: 10.3171/2009.6.FOCUS09119)

Key Words • history of neurosurgery • pituitary surgery • transsphenoidal surgery • fluoroscopy • operating microscope • endoscopy • imaging-guided surgery

The historical development of TSS is a complex tale of innovative ideas coupled with periods of extensive surgical experimentation and even complete rejection of the technique. Summaries of the historical movements that have resulted in its adoption as the preferred approach to tumors of the hypophysis have already been well documented (Fig. 1). However, within this history there exist some significant evolutions in technique and technology that have further advanced the utility of this operation and that merit further study. The first of these evolutions was in surgical technique, with the introduction of sublabial and transnasal approaches to the pituitary. Then, with the introduction of intraoperative image intensification by Gerard Guiot and colleagues in 195820 and the surgical microscope by Jules Hardy in 1967,24 many of the technical difficulties faced by pioneers such as Harvey Cushing could be circumvented. This laid the foundation for the advances that now shape modern TSS, including the use of endoscopy, intraoperative imaging, and frameless guidance.

Abbreviation used in this paper: TSS = transsphenoidal surgery.
mann Schloffer in Innsbruck. He performed a lateral rhinotomy, turning the entire nose toward the right side, and removed the nasal septum, turbinates, medial wall of the orbit, and maxillary sinus. Postoperatively, the patient suffered from a brief period of CSF rhinorrhea and died 2 months later from acute intracranial hypertension. Autopsy revealed that a majority of the tumor remained, and that it had occluded the foramen of Monro. Neither preoperative neurological examination nor skull radiographs revealed the true magnitude of the lesion, and unfortunately it would not be until 1919, with Dandy’s introduction of pneumoencephalography, that imaging techniques started to achieve the level of accuracy that Schloffer required.

Between 1907 and 1912, many general surgeons, otorhinolaryngologists, and neurosurgeons were attempting to develop innovative ways to approach the pituitary from below while trying to minimize the incidence of meningitis and maximize the preservation of vision. European general surgeons were among the first to approach the pituitary transnasally. However, because of their inexperience with illumination and depth of field in such a restricted surgical space, they performed unnecessarily large external nasal openings. This procedure was soon replaced in favor of less invasive techniques. One of the first steps was taken by Ottakar Chiari in 1912, with a superior transethmoidal approach through the medial aspect of the orbit. However, risk of damage to the anterior ethmoidal artery and the carotid siphon led to the abandonment of this approach, except by a few otorhinolaryngologists of the time.

During 1909 and 1910, multiple variations of inferior transnasal exposures of the pituitary were being developed simultaneously in both America and Europe. Allen Kanavel and Albert Halstead first introduced an infranasal approach and subsequently a gingival approach, which were quickly adopted by Harvey Cushing in Baltimore. Cushing performed his first pituitary operation in 1909, and over the next 30 years, in an era before the development of steroids and antibiotics, sustained a remarkable mortality rate of 5.6% (Fig. 2). At about the
same time, a Viennese otolaryngologist, Oscar Hirsch, introduced the technique that is still in use today in a modified form. He incised the columella between the nares, and using a nasal speculum to keep the operative field open, he performed a submucosal resection of the entire nasal septum, opened the sphenoid sinus, resected the sphenoid septum, and finally perforated the floor of the sella turcica and the basal dura mater. Hirsch performed hundreds of these operations, first in Vienna until 1938, and then for another 20 years in Boston. Cushing’s sublabial approach and Hirsch’s transnasal approach became the 2 most popular methods of TSS. According to Rosegay, however, after gaining operative experience in both transcranial and transsphenoidal approaches, Cushing gradually began to favor the former technique, and by 1929 he had completely abandoned the transsphenoidal approach. His rationale was that reoperations on transsphenoidal cases were more difficult than those on transcranial cases, and that the transcranial operations had a higher percentage of visual restoration. Additionally, he found that many of the pituitary lesions were in fact not adenomas (or were adenomas with significant suprasellar extension) and were much easier to treat transcranially under direct vision. There remains much debate as to the true statistical validity of Cushing’s remarks, but at the time a majority of neurosurgeons followed his example, abandoning the transsphenoidal approach.

For the next quarter century, the transsphenoidal approach remained essentially forgotten except by a handful of neurosurgeons. Among them was Norman Dott, a pupil of Cushing, who in turn taught the technique to Guiot in Paris in 1956, and began a revival of interest in transnasal pituitary surgery that quickly spread abroad. For many years afterward, the sublabial transsphenoidal approach that Cushing had once taught was the preferred inferior nasal approach. However, over the past few decades the transnasal approach, similar to the Hirsch method, has once again regained its popularity.

**Fluoroscopy and the Microscope**

Multiple innovations during the 1950s served as catalysts for the new interest in TSS. With the introduction of cortisone and antibiotic therapy, total hypophysectomy was widely performed, with a significantly reduced mortality rate and long-term success. Additionally, soon after performing his first transnasal resection, Guiot introduced intraoperative image intensification and fluoroscopy, allowing the surgeon for the first time to visualize the depth and positioning of surgical instruments intraoperatively. Regarding fluoroscopy, Jules Hardy recently remarked, “…the major advantage of fluoroscopy was the monitoring of the instrumental maneuvers on the television screen while removing large pituitary tumors with suprasellar extension. Intermittent views during the progressive descent of the tumor dome, monitored by air injection through the lumbar route or by direct visualization with contrast solution perfusion, afford immediate intraoperative live imaging of the tumor removal.” This real-time visualization revolutionized the technical aspects of pituitary surgery and set the stage for subsequent innovations in intraoperative image guidance.

By the later 1950s, the basic techniques necessary to perform TSS had been well established. What were required to improve outcomes and expand the versatility of the technique were advances in visualization of the operative field and tumor bed. Adequate illumination of the operative field had always been a limitation of the transsphenoidal technique. Cushing had used a headlamp, otolaryngologists such as Hirsch had operated with the otolaryngological mirror, and Dott tried to improve illu-
mination by attaching small light bulbs near the tip of the blade.\textsuperscript{41} Although otolaryngologists had used the operating microscope since the 1920s for otologic surgery, its applications to TSS were pioneered by Hardy in Montreal many years later. In 1965 he first used the operating microscope for a total hypophysectomy for metastatic breast cancer and for a selective anterior hypophysectomy for diabetic retinopathy.\textsuperscript{56} The microscope and the specialized new instruments were inserted via a midline oronasal approach (Fig. 3). Not only did it improve illumination, it also added magnification and stereoscopic visualization to the operation, and reports quickly propagated in the literature, with these advances becoming an essential part of transsphenoidal approaches to the pituitary. Hardy is credited with developing the fundamental principles and tools of pituitary surgery, which are still used in current neurosurgical practice.\textsuperscript{44} He dedicated his neurosurgical practice to pituitary surgery and published an eminent

Evolution of transsphenoidal surgery: technological advances

paper in 1971 describing his surgical technique in total hypophysectomy, resection of pituitary adenomas, cranioopharyngiomas, and chordomas and meningiomas of the clivus (Fig. 4).44

Development of Endoscopy

Fluoroscopy and the operating microscope greatly expanded the versatility of the transsphenoidal approach but also clearly demonstrated the growing need for even greater accuracy and visualization. According to histories by Doglietto et al.13 and Prevedello and colleagues,30 the first endoscope was invented by Philipp Bozzini in 1806. The “lichtleiter” comprised an eyepiece and a container for a candle, which when lit was reflected by a mirror through a tube. Nearly a century later, Hirschman, an otolaryngologist, was the first to use a cystoscope to inspect the maxillary sinus, and thus interest in nasal endoscopy began. Walter Dandy, considered to be the father of neuroendoscopy, introduced the endoscope to neurosurgery in 1922, as has been detailed in various articles on the history of neurosurgery.13,43,50 Until recently, however, its use had been primarily limited to intraoperative operations. Gerard Guiot and colleagues,21 in 1963, were the first to report the use of an endoscope during sublabial TSS. Due to poor visualization, however, this method was abandoned.

Technical improvements of the endoscope facilitated the resurgence of endoscopy. In 1957, a gastroenterologist, Basil Hirschowitz,13 introduced an endoscope with flexible glass-coated fibers, the “fiberscope.”13,49,50 In 1965, Karl Storz, added light transmission to the glass-coated fibers of the fiberscope, resulting in a fiberoptic scope that significantly improved visualization.13,50 These technological advances yielded a smaller, more flexible endoscope with improved optics, illumination, and visualization. A camera was added to the endoscope in 1969 by Bell Laboratories.13,50

As previously noted, the microscope was applied to TSS by Jules Hardy in 1967. Even with the operating microscope, visualization during pituitary surgery was limited to a straight and narrow view at the sella. Angled mirrors were required to visualize landmarks outside of the line of sight. In 1977 Apuzzo et al.2 and in 1978 Bushe and Halves1 described using the endoscope as an adjunct to the microscope in tumors with extrasser extension. The endoscope offered visualization of anatomical landmarks and degree of tumor resection/extension, particularly in tumors with extrasellar extension. In the 1990s, multiple reports of endoscopy as an adjunct to the microscope confirmed the initial reports of Apuzzo and Bushe and Halves. The endoscope improved visualization of the pituitary gland, the surrounding structures, and anatomical landmarks outside of the microscopic view.2,3,5,22,32,50 Fries and Perneckzy,13 pioneers of endoscopy-assisted microsurgery, reported on 380 cases, 49 of which involved the sella. They concluded that the endoscope afforded better visual control with less retraction during tumor resection, and “...helps to increase the visual field of the operating microscope and light intensity within the surgical field.”71

With the use of the endoscope as an adjunct to the microscope, lesions outside of the sella became accessible via the transsphenoidal route. The ability to look around corners and obtain a panoramic view with the endoscope was paramount in developing extended transsphenoidal approaches. In 1987, Weiss described the first to describe the extended transsphenoidal procedure for suprasellar lesions. This approach included extending the removal of the sellar floor anteriorly to include the tuberculum sellae and the posterior part of the planum sphenoidale. This approach was the stepping-stone for many variations of the extended transsphenoidal approach. In 1995, Fraioli et al.33 described a transsphenoidal approach with the addition of a maxillary osteotomy to gain access to the cavernous sinus. Five years later, Sabit et al.32 described the transmaxillary-transsphenoidal approach, with which they achieved distant lateral, inferomedial access to the cavernous sinus. The transethmoid-transsphenoidal approach to the cavernous sinus was initially described by Laws et al.44 in 1979 for access to a carotid-cavernous fistula, and was revisited by Kitano and Taneda in 2001, when it was applied to pituitary adenomas with cavernous sinus invasion. In 2004, Couldwell et al.8 reported on 105 patients undergoing extended transsphenoidal approaches in which access was gained to the cavernous sinus, suprasellar region, and clival region. They were able to demonstrate that extended transsphenoidal approaches are a safe alternative to cranial approaches. As recently as 2008, Almefty et al.1 reported on 43 patients undergoing extended transsphenoidal approaches to the clivus for lesions in the clivus and anterior to the brainstem. They noted that the use of the endoscope as an adjunct to the microscope “enhances the safety of the procedure and facilitates its undertaking.” The boundaries for expanded transsphenoidal cases now include lesions extending anteriorly to the cribiform plate, superiorly into the suprasellar cistern, laterally into the cavernous sinus, and inferiorly into the clivus and foramen magnum.12,44

The pure endoscopic transsphenoidal technique, in which the endoscope is used alone for visualization without an accompanying microscope or transsphenoidal retractor, was described in the 1990s, with the collaboration of otolaryngologists and neurosurgeons, namely Jankowski et al.30 Sethi and Pillay,54 Jho and Carrau,32 and Cappabianca et al.6 In 1992, Jankowski et al. were the first to report on 3 cases in which the sublabial pure endoscopic approach to the sella turcica was used.13,30,50 Three years later, Sethi and Pillay described the pure endoscopic endonasal transsphenoidal approach. Jho and Carrau, regarded as the pioneers of the pure endoscopic endonasal approach, reported on 46 patients treated via the pure endoscopic approach in 1997.13,31,50 The term “functional endoscopic pituitary surgery,” or “FEPS,” was introduced by Cappabianca et al. in 1998. In historical reviews of TSS, these authors have been attributed as significantly contributing to the endoscopic instrumentation, technical improvements, scientific basis, and critical assessment of the pure endoscopic technique.13,50 Due to the collaboration of otolaryngologists and neurosurgeons, the use of endoscopy as a stand-alone instrument for pituitary surgery is becoming increasingly popular in the neurosurgical armamentarium. The work of these pioneers culmi-
nated in the First World Congress of Endoscopic Surgery, which was held in Pittsburgh, Pennsylvania in 2005.6,13,31

The principles of expanded transsphenoidal approaches are now being applied to pure endoscopic techniques. Otolaryngology and neurosurgery teams continue to advance the field of endoscopic neurosurgery, with such leaders as Kaptain et al.,34 Frank and Pasquini,16 and Kassam and colleagues.35–38 Thanks to these pioneers, the current boundaries for endoscopic TSS continue to expand. The anteriormost border allows access to the olfactory groove by removing the ethmoid roof.14,36,50 The clivus, ventral brainstem, and foramen magnum may be accessed by removing the sphenoidal floor and clivus, and with further inferior dissection, the C-1 ring and odontoid process may be accessed endoscopically.35,37,38,50 The lateralmost extent currently described includes the foramen ovale.16,38,50

Advantages of the pure endoscopic technique include the endoscope’s angled telescopes that allow for visualization of otherwise blind corners, and the ability to change perspectives between close-up and panoramic views. Wide visualization allows identification of anatomical landmarks, and it places the observer close to the target, inside the anatomy.11 By identifying normal anatomy with the endoscope, fluoroscopy can be avoided, along with unnecessary radiation. Additionally, the instruments may be used with a wider range of movement, which was previously encumbered by the retractor. Endoscopy may also have applications in the excision of recurrent and residual sellar masses in which the anatomy is distorted by the first operation or by radiation therapy.5 Disadvantages of the pure endoscopic approach include a steep learning curve and added operating time while on the learning curve. Also, the endoscope produces 2D images and subsequently loss of depth of field perception, compared with the stereoscopic, 3D images from the microscope. Last, but not least, complications such as bleeding from the carotid artery are very difficult to control with the use of the endoscope, often times requiring conversion to the microscope to ameliorate the situation.

The future of endoscopy is full of potential. Previous approaches thought accessible only with a microscope are now being performed safely and in larger numbers via the pure endoscopic technique. With the development of improved technology allowing better illumination, resolution, and stereoscopic vision, the limits continue to expand.

**Intraoperative Imaging and Frameless Guidance**

In addition to the challenges of illumination, the pioneers of pituitary surgery also faced significant difficulties in adequately imaging the region. Schloffer, using only plain lateral skull films, attempted the first transsphenoidal operation in 1907, with disappointing results because he was unable to assess the gross extent of the tumor. The pneumoencephalogram, first introduced in 1919, partially addressed the need for better imaging and was in use until the modern sectional imaging techniques of CT and MR imaging became available in the 1970s. These newer modalities offered the neurosurgeon unprecedented visualization of the pituitary, allowing for more accurate preoperative planning as well as postoperative follow-up. Over the past decade, further advancements in imaging protocols have allowed for the use of intraoperative imaging techniques that may potentially replace radiofluoroscopy in the coming years.

Radiofluoroscopy, an established standard in pituitary surgery, when combined with contrast medium can demonstrate the shape and size of the sella turcica and outline the suprasellar extension of the tumor mass in the lateral view. Additionally, serial images obtained during tumor removal document the descent of the tumor dome, and this method thus provides “immediate intraoperative live imaging...”.7 However, radiofluoroscopy is unable to demonstrate adequately the lateral extension of the tumor, and it fails to define essential topographic relationships of adjacent structures, such as the carotid artery and the optic chiasm.

Multiple studies in the current literature have described intraoperative CT and MR imaging as the solution to the shortcomings of radiofluoroscopy.46–48 Theoretically, by being able to obtain serial images of the operative region during surgery, a more complete resection is possible. However, despite the possible advantages of these modalities, their popularity remains limited because of the high cost and specialized operating suites required for their implementation as well the extended operating time required to accommodate the repeated scans.

In addition to serial intraoperative imaging, the multiple-image guidance systems now available have been applied to TSS. By registering the preoperative CT or MR images, these systems allow for 3D localization during the surgical approach and resection. However, as with intraoperative imaging, these image guidance systems are expensive and increase operating time. Additionally, these images do not provide real-time pictures; thus, when the suprasellar mass moves into the sella during surgery, tumor extension can no longer be judged based on preoperative images. The eventual utility of these systems probably lies in cases in which a repeat operation is performed or when there is significant destruction of bone landmarks so that the neurosurgeon can no longer rely on traditional localization methods.14

**Conclusions**

At its beginning, TSS started as a quickly proliferating innovation with a multitude of technical variations, most of which have been long abandoned. During this period, the sublabial and transnasal approaches gained prominence, and the latter technique eventually became the standard. The establishment of a single, universally accepted technique was one of the first major transitions in the development of TSS. During the revival of the approach in the 1950s, radiofluoroscopy and the operating microscope once again quickly advanced the field by greatly improving illumination and intraoperative imaging. Innovations in technology soon offered even more advanced methods to visualize the operative field through endoscopy, either as an adjunct to the microscope or by itself. Because of its ability to visualize otherwise blind corners within the operative field, and to provide a vari-
Evolution of transsphenoidal surgery: technological advances

ty of panoramic and close-up views, it has become very popular over the past decade and reports on its use are currently being expanded in the literature.

In conjunction with advances in operative visualization, there have been 2 major, historically important developments in intraoperative imaging for pituitary surgery. The first is intraoperative CT and MR imaging, which now offer the surgeon an unprecedented ability to determine the immediate extent of resection and the exact location of important anatomical structures. More recently, the allure of real-time intraoperative imaging has led to the explosion in frameless guidance systems that can allow for exact instrument and anatomical localization throughout the operation. Each of these major historical transitions has helped to define modern TSS. The surgical technique itself has been concretely established, but some debate continues in regard to the true utility and applications of the more recent technological innovations. This debate, however, instead of stifling the growth of these advances, will undoubtedly fuel the same innovative spirit that first drove the pioneers in our specialty, and will lead to new evolutions in TSS.

Disclosure

Dr. Prestigiacomo is a consultant for Boston Scientific, Aesculap, and Terumoetux, Inc. He is a stockholder in Micrus Endovascular.

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C. D. Gandhi et al.