The beginnings of transsphenoidal surgery date back over a century ago, when in 1907, Austrian neurosurgeon Dr. Hermann Schloffer carried out the first documented transnasal operation in a patient with a pituitary tumor. This procedure was subsequently performed by surgeons in Vienna, von Eiselsberg and Hochenegg, in 1908. A year later, in 1909, Theodor Kocher modified the transnasal approach by introducing submucosal resection for better visualization, and within the year, developed the lighted nasal speculum to provide better illumination in the narrow working area. Richard Pfeiffer, inspired by Dott, adopted his technique and used intraoperative radiofluoroscopic technique for image guidance. Hardy, a fellow of Guiot, from Montreal, Canada, revolutionized transsphenoidal microsurgery with the introduction of the binocular microscope and selective adenomectomy.

During a time when transsphenoidal surgery was on the brink of extinction, a critical lineage of 3 key surgeons—Norman Dott, Gerard Guiot, and Jules Hardy—would resurrect the art, each working to further improve the procedure. Dott, Cushing’s apprentice from 1923 to 1924, brought his experiences with transsphenoidal surgery to Edinburgh, Scotland, and along the way, developed the lighted nasal speculum to provide better illumination in the narrow working area. Guiot, inspired by Dott, adopted his technique and used intraoperative radiofluoroscopic technique for image guidance. Hardy, a fellow of Guiot, from Montreal, Canada, revolutionized transsphenoidal microsurgery with the introduction of the binocular microscope and selective adenomectomy.

The teachings of these pioneers have endured over time and are now widely used by neurosurgeons worldwide. In this paper, we review the lineage and contributions of Dott, Guiot, and Hardy who served as crucial players in the preservation of transsphenoidal surgery.
tion of tumors.\cite{7,11,14,45} In light of this, he decided to pursue the group of chiasmal and suprachiasmal lesions that he felt were better explored using a transcranial method, and therefore, abruptly transitioned to a purely transcranial practice.\cite{7,28,42,45} Subsequently, Hirsch, who had been exiled from Austria by the Nazis, joined Hannibal Hamlin, a neurosurgeon in Boston, and continued to use the transsphenoidal approach in their private practice with continued success.\cite{20,21,30,31,42,54} Nonetheless, Hirsch remained an "obscure voice in the wilderness," as described by Dr. Nicholas Zervas.\cite{54} By then, most neurosurgeons, influenced by Cushing's practice, also largely abandoned the use of the transsphenoidal approach.

Because of this transition from transnasal to transcranial surgery, the transsphenoidal operation fell out of favor for the majority of the neurosurgery community for nearly 35 years. However, it was the contributions of 3 key surgeons, whose lineage can be traced back to Cushing, who resurrected and preserved the transsphenoidal approach. Norman Dott, who learned the transsphenoidal operation from Cushing, introduced the method to Gerard Guiot, who in turn, passed it on to Jules Hardy.\cite{38,39,42,45,51} In this paper, we present a historical review of the resurrection and preservation of transsphenoidal surgery, specifically Harvey Cushing's legacy, with a focus on the lineage that extends from Dott to Guiot to Hardy into modern-day transsphenoidal surgery.

**Norman Dott of Edinburgh, Scotland**

Born on the southern outskirts of Edinburgh, Scotland in 1897,\cite{32} Norman McOmish Dott (Fig. 2) was integral in promoting transsphenoidal surgery in Europe. In his early life, Dott had been an engineering apprentice before attending medical school in Edinburgh in 1919. He became a resident in the Royal Infirmary of Edinburgh, where he was awarded the Fellowship of the Royal College of Surgeons in Edinburgh and undertook research that included the effects of pituitary ablation, which led to his earning the Rockefeller Fellowship. It was through this fellowship that Dott spent November 1923 to June 1924 as Harvey Cushing's assistant at the Peter Bent Brigham Hospital in Boston (Fig. 3).\cite{32,34,45,53} Interestingly, Dott was actually hesitant to go to Boston when given the opportunity to work with Harvey Cushing. At the time, he had just been newly appointed as Assistant Professor at the Chalmers and Deaconess Hospitals in Edinburgh and was establishing the beginnings of his career. In his words, "I had just put my plate up."\cite{47} It was due to Sir Walter Fletcher, secretary of the Medical Research Council in London, who convinced Dott that working with the great Harvey Cushing would be of benefit to him in the future, that Dott agreed to accept the Rockefeller Fellowship.\cite{47}

As Cushing's pupil, Dott observed and learned the transsphenoidal operation to access lesions of the pituitary fossa using the midline, oronasal-rhinoseptal route through a sublabial incision, originally developed by Harvey Cushing in 1910, which was later adopted by Dott, Guiot, and Hardy. Reprinted with permission from Hardy and Wigs: J Neurosurg 23:612-619, 1965.

**Fig. 1.** Anatomical illustration depicting the transsphenoidal approach to the pituitary fossa using the midline, oronasal-rhinoseptal route through a sublabial incision, originally developed by Harvey Cushing in 1910, which was later adopted by Dott, Guiot, and Hardy. Reprinted with permission from Hardy and Wigs: J Neurosurg 23:612-619, 1965.

**Fig. 2.** Photograph of Norman Dott, one of many in a series taken by one of his patients, Miss Grace Allison. Dott performed a transsphenoidal pituitary tumor resection on Miss Allison. Reprinted with permission from Rush C, Shaw JF: With Sharp Compassion. Norman Dott: Freeman Surgeon of Edinburgh. Edinburgh: Aberdeen University Press, 1990.
Resurrection of transsphenoidal surgery

In the early months of his fellowship, Dr. Eric Dott (Norman Dott’s brother) recollected Dott’s experience with Cushing:

“I remember him [Norman Dott] telling me that it seemed to go too slowly for him at first, there were too many showy, talkative young men there, who liked to push themselves into prominence, whereas Norman just worked quietly and patiently away. Cushing soon discovered his real talents though, and gave him work to do.”

Norman Dott’s learning experience with “The Chief,” as he referred to Harvey Cushing, was a unique one. According to Dott:

“He [Cushing] did no formal teaching of his staff. We learned from him by watching his face and hands and by absorbing his casual remarks. We learned so thoroughly that it amused and impressed the writer in later years to observe some of his disciples displaying unconsciously but most faithfully the Chief’s personal attitudes and characteristic utterances in their own operating rooms as well as observing his technical routines with religious exactitude—such was the imprint of the hero worship that he evoked.”

In 1925, Dott and Dr. Percival Bailey reported their review of Cushing’s 196 patients with pituitary tumors. Of these, 177 underwent transsphenoidal tumor removal and 19 underwent transfrontal resection. They concluded that

the object of this surgical procedure is not only to remove as much of the tumour as thought safe, but also to relieve the upward pressure of a lesion which cannot be removed entirely, and will inevitably continue to grow, by permitting the growth to enlarge downward. Only the operation from below can accomplish this object.

The recorded mortality rate in the patients who underwent transsphenoidal operations was 8.6%, and in those who underwent surgery by the transfrontal route, it was 5.2%. The authors mentioned that perhaps the smaller number of transfrontal cases confounded the comparability of the mortality rates. However, they stated that

... it is quite probable, nevertheless, that the transsphenoidal operation will always have a slightly higher operative mortality than the transfrontal procedure, from the occasional possibility of meningeal infection which it carries with it...the transfrontal operation can hold out little to a patient with an adenoma of pressure symptoms; and there is always the risk of further damage to the chiasm by direct trauma, which defeats the main purpose of the operation. The transsphenoidal procedure confers a large measure of relief whose duration is much longer, often extending over many years. When, therefore, a diagnosis of adenoma can be made with confidence, we believe there is no question that the first surgical step should be a sellar decompression with partial removal of the tumour from below.

Cushing had largely abandoned the use of the transsphenoidal approach by the late 1920s, because of its intrinsic difficulty and his growing interest in learning the transcranial avenues to the sella. In the meantime, Dott returned to Edinburgh at the end of his apprenticeship and introduced the transsphenoidal procedure to his neurosurgical practice. It has been reported that although Cushing trained Dott in his transsphenoidal procedure, he personally instructed Dott “not to teach it to anyone else.” In 1939, Henderson, Dott’s assistant in Edinburgh, compared the most common complications between the two procedures in a follow-up retrospective review of a series of 338 cases performed by Cushing. He concluded that there was “no essential difference in the operative mortality of the two procedures. The danger of meningitis after the transsphenoidal operation is counterbalanced by the slight risk of clot formation after the transfrontal operation.” This information seemed to reaffirm the integrity of the transsphenoidal operation for Dott, who thought that the approach had “fallen into rather undeserved neglect during recent years.” Professor Dott not only preserved and passed on Cushing’s teachings, but he further enhanced the approach by developing a lighted nasal speculum retractor to provide better illumination in the deep, dark, narrow surgical field. By 1956, Dott had performed 120 transsphenoidal surgeries, with a 0% mortality rate in the final 80 consecutive patients.

At the time of his death in 1973, in appreciation of Professor Dott, an observer remarked about the paucity of reports written by Dott regarding his scientific work because “his literary reticence was curious... he wrote well, and from his vast experience he certainly had much to write about...” Perhaps Dott wrote little about his experience with the transsphenoidal approach to respect his instructor’s wishes, given that Cushing had asked him to refrain from passing on his teachings. In addition, at that time, the vast majority of the neurosurgical community mirrored Cushing’s rejection of the transsphenoidal procedure as an accepted practice for chiasmal lesions. Conceivably, Dott did not want to undermine or insult Cushing’s practice guidelines by making such literature...
available that promoted the use of the transsphenoidal approach.

It has been postulated that perhaps Dott’s previous experience as a pediatric surgeon specializing in the correction of facial defects, such as the cleft palate, benefited him in improving the transsphenoidal approach. The skill set required in working on the delicate pediatric population afforded him the ability to work in the rather small, dark, and narrow operative corridor in transsphenoidal surgery. It can further be theorized that Dott’s background in engineering allowed him to possess the level of meticulous attention to detail required during these procedures to achieve tremendous results with his patients. It is no secret that the seamlessness of Dott’s surgeries and his postoperative results were both impressive and inspiring, especially to his Parisian student, Gerard Guiot.

Gerard Guiot of Paris, France

Gerard Guiot was a pioneering French neurosurgeon who promoted the revival of transsphenoidal surgery in France (Fig. 4). Guiot was born in Fourmies, a small town in northern France. After graduating from the Medical School of Paris in 1937, he became an assistant to Clovis Vincent, who had learned various procedures from Harvey Cushing in the US during the 1920s. It was through this relationship that Guiot received his place as Cushing’s “spiritual grandchild.” Impressions with Dott’s success with the transsphenoidal approach during his 2-week stay as a visiting observer at the Royal Infirmary in Edinburgh in 1956, Guiot reaffirmed the use of the transsphenoidal surgical approach in France. In 1957, Guiot began to use the transsphenoidal approach in Paris and introduced the x-ray film intensifier and fluoroscopy for intraoperative image guidance. These tools were among the most valuable contributions in the 1960s, because they allowed for improved delineation of the tumor contour and good visualization of instruments placed at the skull base.

In 1959, Guiot wrote, “It is perhaps surprising today to propose the transsphenoidal route to extirpate certain tumors of the hypophysis … In France, notably, the intracranial route is used exclusively … the transsphenoidal route is practically forgotten … its advantages should be reconsidered and its indications retained.” A year later, in a report of his experience with the transsphenoidal procedure, he further stated, “Shouldn’t one stop referring to this approach as ‘historic’ and ‘passé’? Isn’t it right to admit its advantages and retain its indications? Without doubt.”

In his practice, Guiot demonstrated with more than 1000 cases that the transsphenoidal approach was clearly statistically superior to the transcranial route for removal of pituitary adenomas. He was able to exhibit a lower rate of morbidity and better results with visual recovery in patients with suprasellar extension of their tumor. In his tribute to Guiot, Jules Hardy reported that Guiot was able to show that 90% of pituitary adenomas could be surgically removed via the transsphenoidal approach. In a separate oral presentation about the history of pituitary tumors and microneurosurgery, Hardy reflected upon the major challenges with pituitary surgery as described by his mentor, Gerard Guiot:

Although the complete removal of a pituitary adenoma might restore the previous hormonal deficit, one should agree this is rather exceptional. From this point of view one must say that the patient is rather endangered since the adenomatous tissue is not separable from the normal hypophyseal tissue and the attempt to perform a complete radical excision brings in the curettes the glandular tissue still functionally active. Therefore, this increases the hormonal deficit which can lead to a complete pituitary insufficiency following surgery.

It was partly in response to this dilemma that Jules Hardy contributed the next major advancement in transsphenoidal surgery, the surgical microscope.

Despite the setbacks he encountered, Guiot continued to innovate by expanding the indications for the transsphenoidal approach and also by experimenting with new technology. He extended the use of the transsphenoidal approach to the sella to resect other tumors such as craniopharyngiomas, clival chordomas, and other parasellar lesions. Gerard Guiot is also credited as the first neurosurgeon to use the endoscope for transsphenoidal surgery, having used it in 1961. Guiot’s endoscope was designed with an external light source that was supported in a rigid shaft. However, he abandoned its use because he felt that it did not provide adequate visualization during surgery. He did occasionally use the endoscope after removal of a tumor to examine the sellar floor for residual tumor tissue, a technique that Jules Hardy also adopted after training with Guiot at the Foch Hospital.
Little did Guiot know that this innovation would eventually transform transsphenoidal surgery in the modern era.

**Jules Hardy of Montreal, Canada**

Jules Hardy was born in Sorel, a small city in Quebec, in 1932. He graduated from medical school at the University of Montreal and went on to train in neurosurgery under Claude Bertrand, a leading founder of stereotaxic surgery in the 1950s. Through this connection, Hardy became a fellow of the McLaughlin Foundation in Toronto and received the opportunity to travel to France to study stereotaxic surgery under Gerard Guiot, a pioneer in the field (Figs. 5 and 6). In France, Hardy was primarily doing neurophysiology-related work until he stumbled upon and became involved in pituitary surgery. He was impressed with Guiot’s procedure and the excellent postoperative recovery of the patients. In an interview with Dr. Roy Selby, Hardy reflected on how he was introduced to the transsphenoidal approach:

> Back when I was in Paris with Guiot, he had just started to do transsphenoidal from a few years before in 1958. He went to Edinburgh where he learned that procedure from Dott, who learned from Cushing invariably. So, that was a third generation of professors, and I was very much influenced also. This is where I learned transsphenoidal by just watching as I was a senior resident, and Professor Guiot let me do several cases by myself...so when I came back to Montreal, I came back with ... the transsphenoidal approach, which was not a new method, it was an old traditional, classical Cushing’s operation.

In 1962, Hardy returned to Notre-Dame Hospital in Montreal and continued to use Guiot’s modified version of Cushing’s transsphenoidal hypophysectomy in conjunction with preoperative encephalography and intraoperative radiofluoroscopy (Figs. 7 and 8).

One of the many criticisms at the time about the transsphenoidal approach was that the surgical exposure was limited in its ability to allow adequate light and visualization by the surgeon, thereby preventing a complete or gross-total resection of tumors in the pituitary fossa. In 1965, Hardy and Wigser reported 20 cases of pituitary fossa tumors that were resected by means of a transsphenoidal approach to the sella using intraoperative televised radiofluoroscopy, which allowed complete removal of the tumor. They further described that with both preoperative and intraoperative diagnostic and radiological control, the removal of these tumors via the transsphenoidal route could result in good postoperative outcomes.
Hardy discovered that at a higher magnification, the surgeon could visualize the difference between the tumor and normal pituitary gland tissue. As described by Guiot, the inability to differentiate between normal and abnormal pituitary tissue had been one of the largest challenges at the time, as the treatment of pituitary lesions required total hypophysectomy (Fig. 11). Hardy stated that this problem was:

... upsetting to me so that when I decided to use the surgical microscope, I soon became aware of a new fact: at higher magnification I was able to distinguish in some cases the residual normal pituitary gland quite separate from the tumoral tissue. As a result I decided to make all effort to preserve the pituitary to prevent new deficits.22

In 1968, Hardy and his assistant, Dr. Ivan Ciric, described a series of 17 cases involving patients with diabetic retinopathy who underwent selective anterior hypophysectomy with transsphenoidal microsurgical technique. They emphasized the utility of the operative microscope in visualization of the pituitary gland and the ability to differentiate between the anterior and posterior lobes based on the difference in color. The ability to see the morphological variation between the two lobes allowed greater accuracy and precision in the selective removal of the anterior lobe of the pituitary gland. Perhaps one of the most important advantages the microscope conferred was that it allowed the surgeon to ensure gross-total resection of the particular tumor or lesion.26 Dr. Ciric brought his knowledge to Chicago, where he performed the first transsphenoidal pituitary surgery in the US in November of 1967, using the operating microscope at Evanston Hospital.59 Interestingly, in the same year of 1967, just as Ciric was finishing his fellowship with Hardy, Dr. Charles B. Wilson visited Guiot in Paris to learn the transsphenoidal approach in the resection of skull base lesions. Using both the operating microscope and intraoperative fluoroscopic guidance, he was not limited to performing total hypophysectomies, but could also attempt removal of microad-
nomas, craniopharyngiomas, sellar and clival chordomas, and in rare instances, sellar meningiomas, melanomas, and granular cell tumors. In fact, it was Hardy who coined the term pituitary “microadenoma” in 1968—also referring to the lesion as the “pimento in the olive.” At the time, he was met with great skepticism from the rest of the neurosurgical community as well as by endocrinologists for his conclusions.

Nevertheless, the transsphenoidal approach continued to be used over the next 40 years and was widely promulgated internationally. The approach has continued to evolve with the advent of technological innovations such as high-definition and 3D endoscopes, frameless stereotactic image-based guidance, intraoperative MRI, and extended transsphenoidal approaches to regions beyond the sella.

Conclusions

The transsphenoidal approach might have been lost if not for the work of Harvey Cushing’s dedicated disciple Norman Dott, who continued to use the approach and developed the lighted nasal speculum for its advancement. Dott’s excellent results inspired Gerard Guiot to emulate his technique and improve it with the utilization of radiofluoroscopy for intraoperative image guidance. Guiot’s fellow, Jules Hardy, avidly learned the approach and introduced the operative microscope, thus transforming the field with a new emphasis on microsurgery and selective adenomectomy. Through the work of these pioneer-
ing surgeons, the art of transsphenoidal surgery has been preserved and has continued to evolve with technological advances into the contemporary era. Today, it remains the preferred route to access sellar and parasellar lesions.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Fig. 10. Operative drawing illustrating Hardy’s selective removal of a pituitary microadenoma from the lateral wing of the gland in a patient with acromegaly. This operation involving selective removal of a pituitary microadenoma with preservation of the normal pituitary gland is perhaps one of Jules Hardy’s most recognized contributions to transsphenoidal surgery. Reprinted with permission from Hardy: J Neurosurg 34:582–594, 1971.

Fig. 11. Photograph from Jules Hardy’s personal collection showing Gerard Guiot (left) and Hardy (right) shaking hands. Guiot’s mentorship and his impact on Hardy’s neurosurgical practice is noteworthy. His guidance inspired Hardy to enrich the transsphenoidal operation with his own contributions. Reprinted from Neurosurg Clin N Am 14, Lanzino G, Laws ER Jr: Key personalities in the development and popularization of the transsphenoidal approach to pituitary tumors: an historical overview, pp 1–10, copyright 2003, with permission from Elsevier.
Resurrection of transsphenoidal surgery
