







A Patient's Guide to **Endonasal Endoscopic Surgery** for **Pituitary Adenomas and Related Tumors**

PACIFIC PITUITARY DISORDERS CENTER

JOHN WAYNE CANCER INSTITUTE AT PROVIDENCE SAINT JOHN'S HEALTH CENTER



A PATIENT'S GUIDE TO ENDONASAL ENDOSCOPIC SURGERY FOR PITUITARY ADENOMAS AND RELATED TUMORS

DANIEL F. KELLY MD, GARNI BARKHOUDARIAN MD, CHESTER F. GRIFFITHS MD, FACS, KIAN KARIMI MD, PEJMAN COHAN, MD AND NILOUFAR ILANI, MD

Pacific Pituitary Disorders Center

John Wayne Cancer Institute at Providence Saint John's Health Center

The Pacific Brain Tumor Center and Pacific Pituitary Disorders Center at Providence Saint John's Health Center provides comprehensive care and minimally invasive surgery for patients with brain, pituitary and skull base tumors. With leading-edge technology and a proven track record in keyhole and endonasal endoscopic approaches, we make surgery safer, less invasive and more effective.

This brief guide provides an overview of the history, indications, advancements, surgical technique and post-operative care related to endonasal endoscopic surgery.

For more information or to set up an appointment go to: www.pacificpituitary.org or call 310-582-7450.



PACIFIC PITUITARY DISORDERS CENTER

AT PROVIDENCE SAINT JOHN'S HEALTH CENTER



The Pacific Pituitary Disorders Center (PPDC) is a Center of Excellence within the Pacific Neuroscience Institute (PNI). We provide comprehensive care, pituitary hormonal evaluations and minimally invasive endoscopic surgery for patients with pituitary and skull base tumors.

PATIENT-CENTERED FOCUS: A multidisciplinary team approach providing tailored diagnostic and treatment plans

EXPERIENCE, INNOVATION & RESEARCH: One of the largest series of pituitary surgeries world-wide; extensive academic publications in pituitary disorders; ongoing clinical trials and pituitary and brain tumor genomics research

TECHNOLOGY: State-of-the-art operating suite dedicated to endoscopic and keyhole neurosurgery

CONSISTENT QUALITY CARE: Providence Saint John's Health Center is the only hospital in California to receive Healthgrades® America's 50 Best Award™ 9 years in a row

COMMUNITY OUTREACH: Longest running Pituitary Patient Support Group nationwide established in 2000

PHYSICIAN EDUCATION: Regular symposia in pituitary tumor management and endoscopic skull base surgical techniques

DISORDERS WE TREAT

PITUITARY ADENOMAS

- Acromegaly
- Cushing's disease
- Endocrine-inactive adenoma
- Prolactinoma
- TSH-secreting adenoma
- Recurrent and residual adenoma
- Pituitary apoplexy

CRANIOPHARYNGIOMA

RATHKE'S CLEFT CYST

OTHER RELATED TUMORS & CYSTS

- Chordoma
- Meningioma
- Sellar arachnoid cyst
- Sinonasal carcinoma

PITUITARY FAILURE (HYPOPITUITARISM)

PITUITARY INFLAMMATION (HYPOPHYSITIS)

CEREBROSPINAL FLUID LEAKS

History: Evolution from Microscope to Endoscope

Pituitary surgery has evolved tremendously since it was first practiced in the early 20th century. Like all things in medicine, there is always room for improvement. Over the last 100 years, technological advancements, improvements in surgical instrumentation and better anatomical understanding have all helped revolutionize the transsphenoidal approach to the sella, pituitary gland and surrounding skull base. Although the operating microscope was used since the 1960s and was the standard visualization method for over 3 decades, in the last 15 years, the surgical endoscope has gradually become the viewing method of choice. Drs. Jho and Carrau in 1997 were the first to describe the fully endoscopic transsphenoidal approach in the treatment of a series of patients with pituitary adenomas. Since then, many if not most neurosurgeons around the world have transitioned from a traditional microscopic approach using one nostril to an endoscopic-assisted or to a fully endoscopic binostril approach.

At most centers, the endoscopic approach has become the method of choice for removal of pituitary adenomas and other tumors and cysts that arise around the pituitary and midline skull base including craniopharyngiomas, Rathke's cleft cysts, some midline meningiomas and clival chordomas. The microscopic approach however continues to be an effective approach in experienced hands, especially for smaller adenomas. Current indications for endonasal endoscopic surgery are shown in Figure 1. Importantly, some skull base and brain tumors may be better removed via a craniotomy such as the supraorbital eyebrow route or other minimally invasive approaches.

Indications for Endonasal Endoscopic Surgery

- · Pituitary Adenoma
 - Endocrine-active adenoma
 - Acromegaly
 - · Cushing's disease
 - · TSH-secreting adenomas
 - Prolactinoma (dopamine agonist cabergoline or bromocriptine usually tried before surgery)
 - Endocrine-inactive (non-secreting) adenoma
 - · Pituitary failure, visual loss, headaches
 - · Pituitary apoplexy (bleeding, tumor swelling)
 - Asymptomatic tumor with optic nerve or chiasm compression, tumor growth or prior bleeding
- · Other Skull Base & Brain Tumors:
 - Craniopharyngioma, Rathke's cleft cyst, arachnoid cyst, midline meningioma, clival chordoma, sino-nasal carcinoma

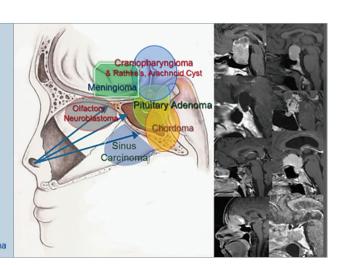


FIGURE 1

The transition from microscope to endoscope has occurred due to the simple fact that the endoscope affords a more panoramic and detailed view than the more restricted "tunnel vision" of the microscope; seeing better translates into better outcomes (Figure 2 & 3).

As shown in our recent publication, use of endoscopy allowed removal of additional tumor in one third of patients and in over half of patients with pituitary tumors 2 cm or greater in size (McLaughlin et al 2013). In the last 5 years, with development of high definition endoscopes and monitors as well as the initial creation of 3D endoscopes, the visual advantage of endoscopy is even greater.

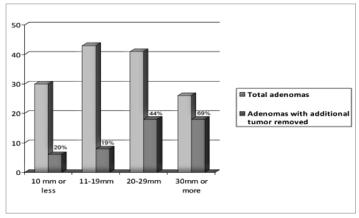
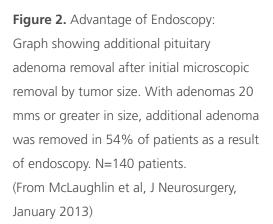


FIGURE 2



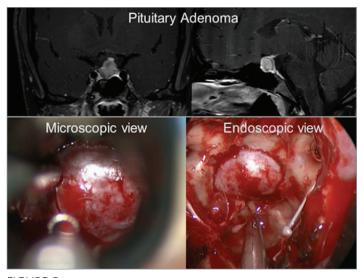


FIGURE 3

Figure 3. Intraoperative views during pituitary adenoma surgery. MRI of adenoma shown on top row. Bottom images show view of sella prior to dural opening: operating microscope view on left and high-definition endoscopic view on right. Note the more panoramic and brighter view with endoscopic view compared to relative tunnel vision view of the microscope.

Endoscopic Pituitary Surgery – Overview

Currently, as performed at our center and many centers around the world, the operation utilizes both nostrils with two surgeons operating together with three or four hands to hold the endoscope and surgical instruments (Figure 4). This binostril technique which incorporates a wide opening into the sphenoid sinus (sphenoidotomy), allows excellent instrument and endoscope maneuverability to remove pituitary adenomas and other types of skull base and brain tumors. The magnified visualization with the light source within the sphenoid sinus gives a high-definition display of the normal and pathological anatomy, improving the ability to remove both small tumors hidden within the gland and large tumors that extend into surrounding spaces such as the cavernous sinus.

This endoscopic approach also allows preservation of a great majority of the nasal mucosa which promotes rapid healing, preservation of sense of smell and a generally rapid recovery. This approach negates the use of relaxing incisions in the nostril. The incidence of lip and teeth numbness is essentially absent. Below we describe our team approach, pre-operative planning, operative technique and post-operative care for patients undergoing endonasal endoscopic surgery.

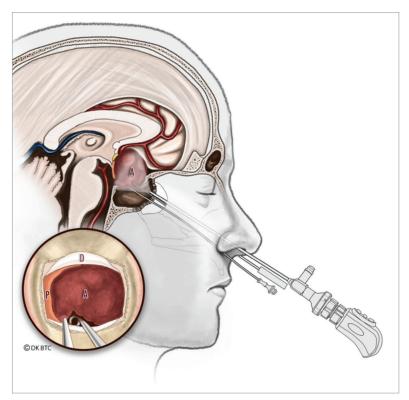


FIGURE 4

Figure 4. Diagram of the endonasal endoscopic transsphenoidal approach for pituitary tumors. A 4 mm high-definition endoscope is in the right nostril providing visualization and two working instruments are in the right and left nostrils. The insert view demonstrates endoscopic view of the sella and tumor with microsurgical instruments being used to remove the adenoma while preserving the normal pituitary gland. (A – adenoma, D – dura, P – pituitary gland)

Pre-operative Evaluation & Expectations



Pre-operative evaluation is essential to determine the likely diagnosis, whether surgery is indeed indicated and to define the surgical goals and expectations. Such pre-operative assessments typically include a pituitary MRI, pituitary hormonal blood (and sometimes urine) testing, evaluation by an endocrinologist (hormonal specialist) and in some cases by a neuro-ophthalmologist (visual assessment).

A complete pre-operative pituitary hormonal laboratory evaluation under the guidance of an endocrinologist is typically necessary to establish baseline pituitary function. In instances of functional pituitary tumors such as acromegaly, Cushing's disease and prolactinomas, this evaluation is critical to confirm the diagnosis. Perioperative corticosteroids and / or thyroid hormone may be necessary to supplement the patient's stress and metabolic response during surgery. A detailed vision examination with quantitated visual fields and optical coherence tomography (OCT) can be applicable for patients with vision loss and tumors compressing the optic nerves or optic chiasm.

Next surgical planning is critical for safe tumor removal, preservation of pituitary gland function and restoration or preservation of vision. Careful study of the MRI determines the possible tumor pathology, the location of normal surrounding structures (optic chiasm, pituitary gland, carotid arteries) and the need for further imaging such as cerebral angiograms or head CT. A pre-operative "navigational" MRI or CT scan is obtained in all patients and used as a "GPS" tool in the operating room to help confirm anatomical landmarks and further ensure the safety and effectiveness of the planned operation.

Endoscopic Surgical Technique

Endonasal endoscopic surgery to remove a pituitary adenoma or Rathke's cleft cyst generally takes approximately 2 to 4 hours. This time includes both the ENT and Neurosurgical portions of surgery. Any intranasal abnormalities are generally repaired or removed including septal deviations or nasal polyps. Larger tumors that extend further into the intracranial space such as craniopharyngiomas or meningiomas may take upwards of 6 to 8 hours to complete. Once in the operating room, approximately 45-90 minutes are spent getting the patient to sleep, positioning the patient, registering the neuro-navigation (GPS) system, and monitoring specific nerve function when applicable.

The initial phase of the operation to reach the sphenoid sinus is typically performed by the ENT surgeon. During the remainder of the procedure including exposure of the sella, tumor removal and skull base reconstruction, the ENT surgeon and neurosurgeon stand next to each other, looking at separate monitors showing the endoscopic image (Figures 5 & 6). This allows for ergonomic posture that decreases surgeon fatigue.

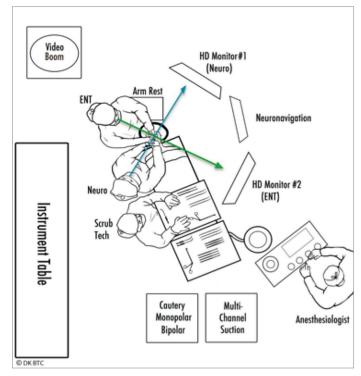


FIGURE 5

Figure 5. Layout of operating room with high-definition monitors and neuronavigation monitor. This setup promotes optimal ergonomics for maximizing surgeon maneuverability and dexterity while minimizing eye strain, neck and back strain as well as fatigue.



Figure 6. Intra-operative photograph demonstrating the ENT surgeon (left) and the neurosurgeon (right) looking at their respective monitors. The central monitor demonstrates the intraoperative neuro-navigation (GPS unit) identifying anatomical structures correlating with the patient's MRI.

FIGURE 6

During tumor removal, care is taken to protect the critical surrounding structures such as optic nerves and chiasm, carotid arteries, pituitary gland and pituitary stalk while aiming to safely remove as much tumor as possible. The carotid artery locations are verified with an intraoperative Doppler ultrasound. This technique also serves as a real-time confirmation of the accuracy of the navigation (GPS) system (Figure 7).

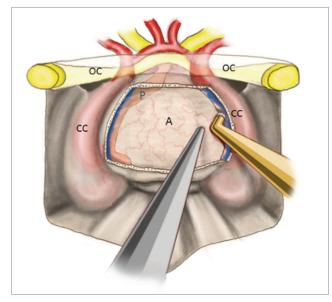


FIGURE 7

Figure 7. Diagram of Doppler ultrasound (right instrument) as it provides real-time audible pulse sound of the two paired carotid arteries during exposure of the sella and pituitary tumor. This technique helps prevents inadvertent damage to these critical arteries that supply blood to the brain. In this illustration, a large adenoma is shown pushing the normal pituitary gland to the patient's right side. (A – adenoma, CC – cavernous carotid arteries, OC – optic chiasm and optic nerves, P – pituitary gland)

Once the tumor is removed, the tumor resection cavity is thoroughly inspected with both straight and angled endoscopes to confirm that all tumor or the maximal amount of tumor possible has been removed. If a cerebrospinal fluid leak is identified, a small amount of fat is often harvested from the abdomen and placed in the sella to seal the leak. This repair is reinforced with a layer of collagen and often with a buttress of bone (harvested from the back of the nasal septum) or with an absorbable plate. The nasal mucosa is then re-approximated.

In patients requiring a larger endonasal skull base exposure to remove a brain tumor such as a craniopharyngioma, meningioma or chordoma, nasal mucosa from one side of the nasal septum can be elevated and rotated back to the skull base to cover the bony defect. Such nasal-septal flaps are highly effective in preventing post-operative cerebrospinal fluid leaks and minimizing the risk of meningitis in these types of cases.

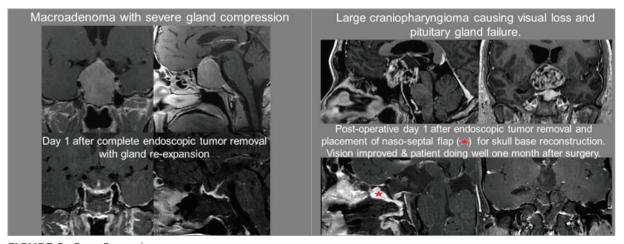


FIGURE 8. Case Examples

Post-operative Care, Return to Normal Activity & Long Term Follow-up



Following surgery for a pituitary adenoma or Rathke's cleft cyst, most patients spend one to two nights in the hospital. A pituitary MRI is usually performed on the first post-operative day. On the first post-operative morning, patients are generally sitting up, eating breakfast comfortably and begin walking. We monitor fluid balance, electrolytes and specific hormones routinely following surgery. For patients with acromegaly, Cushing's disease, or a prolactinoma, GH, cortisol/ACTH and prolactin levels (respectively) are followed on postoperative days 1 and 2 to document early remission. The most common hormones replaced after surgery include cortisol and ADH (vasopressin) which may be only needed temporarily or in some instances permanently along with other hormones such as thyroxin.

Longer hospital stays may be necessary for patients undergoing surgery for larger brain tumors. Before discharge from the hospital, the patient is evaluated for fluid and electrolyte imbalance as well as post-operative CSF leaks. Patients are discharged on a short course of antibiotics to prevent sinusitis. An assessment for blood sodium and cortisol levels is schedule for approximately 5-7 days following surgery since delayed hyponatremia (low sodium) can occur in approximately 5% of patients during this time period.

Regarding physical activity, patients are instructed to avoid heavy lifting, bending over and blowing the nose for the first week post-surgery. They are then allowed to gradually increase activity including vigorous exercising generally by 3-4 weeks post-surgery. Airplane travel is generally allowed within 7-10 days of surgery.

The patient is instructed to perform routine post-operative nasal care including irrigation with nasal sprays and nasal lavage starting after the fifth post-operative day. The ENT surgeon performs routine nasal debridments at least three times within the first 6 weeks of surgery to prevent crusting and scarring of the nasal structures.

Endocrinological evaluation is typically performed at 4-6 weeks following surgery and scheduled at various intervals depending on the pituitary gland function and pre-operative hormonal status.

Occasionally, stress dose steroids are prescribed during surgery and are tapered off during the week following surgery. If long-term steroids are administered, the endocrinologist will determine when and how they can be tapered. There is a small risk of diabetes insipidus following surgery (excessive thirst and urination, and elevated sodium levels); this is usually temporary, but can require prolonged therapy. The synthetic version of ADH, DDAVP or desmopressin, is prescribed according to the symptoms of the patient. For patients with functional pituitary adenomas including acromegaly, Cushing's disease, prolactinomas and TSH-secreting adenomas, long-term hormonal follow-up is required to confirm remission and monitor for possible recurrence.

Long term imaging follow-up is also typically continued for years. After the in-hospital MRI, another pituitary MRI is typically performed at 3 months after surgery and then at 6 to 12 month intervals for at least 5 to 10 years depending upon the clinical situation.

The endonasal endoscopic approach offers advantages for improved outcomes in the removal of pituitary adenomas, and select midline skull base and brain tumors. These advantages include:

- Superior panoramic and up-close high-definition views allowing for maximal tumor removal
- Better visualization of the normal pituitary gland and stalk helps reduce risk of pituitary gland damage and post-operative hormonal dysfunction
- Early identification of the normal anatomical structures including the carotid arteries and the optic nerves help prevent severe complications such as stroke or visual loss
- Expertise of 2 surgeons (4 hands) collaborating together to maximize safety and effectiveness of surgery

Notably, for some brain and skull base tumors, a trans-cranial keyhole approach such as the supraorbital eyebrow route or a more traditional craniotomy may be required

Additional technical advances to make surgery safer and more effective:

- Surgical navigation (GPS system) based on patients' pre-operative MRI or CT scan
- High definition endoscopes providing superior clarity and detail with variable angled lenses (0 degree, 30 degree, 45 degree views) to allow greater tumor visualization and removal
- Doppler ultrasound for carotid artery localization to minimize risk of blood vessel injury
- Graded repair protocol for cerebrospinal fluid leaks
- Post-operative care by ENT surgeon to promote rapid healing of nose and sinuses

In summary, the endonasal endoscopic transsphenoidal approach for pituitary tumor removal is generally a safe and highly effective alternative to the previously utilized microscopic-based surgical approaches. The endoscopic approach provides superior visualization of the pituitary and parasellar anatomy and allows for a wider exposure and increased degrees of freedom for tumor removal. In general endoscopy allows greater extent of tumor resection especially for larger and more invasive tumors. The incidence of complications is low provided that operations are performed by an experienced pituitary surgery team at a facility that performs a relatively high volume of pituitary tumor operations.

Endocrinology	Neurosurgery	Head & Neck Surgery (ENT)
Neuroradiology	Neuro Ophthalmology	Neuro Pathology
Neuro Anesthesia	Radiation Oncology	Patient Support and Education
TEAM APPROACH TO PITUITARY DISORDERS		

FIGURE 9

Given the complexities of pituitary tumors and related hormonal disorders, patients ideally should seek out a center that utilizes a multi-disciplinary approach to the diagnosis, treatment and long-term management of these problems (Figure 9).

PATIENT HANDBOOK

Contact Us

For more information on pituitary tumors, skull base and brain tumors, hormonal disorders, endoscopic

surgery and other keyhole surgical approaches, please visit the Pacific Pituitary Disorders Center website at

www.pacificpituitary.org.

You can also go to our Patient Resources pge for more FAQs.

To arrange a consultation with Dr. Kelly, Dr. Barkhoudarian or with one of our other specialists, call the Pacific

Pituitary Center office at 310-582-7450. Please provide us with your most recent relevant medical records

including diagnostic imaging (e.g., MRI, CT), blood tests and prior consultations.

Your information can be faxed, emailed or mailed to our office as shown below. If some tests have not been

done, our Clinical Coordinator Maricela Sandoval can help you arrange these as well.

Maricela Sandoval

Pacific Brain Tumor Center Coordinator

Office of Daniel F. Kelly, MD

Providence Saint John's Health Center & John Wayne Cancer Institute

2200 Santa Monica Blvd

Santa Monica, CA, 90404

Phone: 310-582-7450

Fax: 310-582-7495

Email: Sandovalm@jwci.org

14

Our Expert Team & Staff



DANIEL F. KELLY, MD

Director, Pacific Brain Tumor Center & Pituitary Disorders Program 2200 Santa Monica Santa Monica, CA 90404 Phone: 310-582-7450 Fax: 310-582-7495

KellyD@JWCI.org

GARNI BARKHOUDARIAN, MD

Director, Skull-Base and Endoscopic Microdissection Laboratory Faculty Neurosurgeon Pacific Brain Tumor Center and Pituitary Disorders Program 2200 Santa Monica

Santa Monica, CA 90404

Phone: 310-582-7450 Fax: 310-582-7495

BarkhoundarianG@JWCI.org

CHESTER F. GRIFFITHS, MD

Head & Neck Surgery & Endoscopic Skull Base Surgery, BTC Pacific Eye & Ear Specialists 11645 Wilshire Blvd. 6th Floor Los Angeles, CA 90025 Phone: 310- 477-5558 Fax: 310-477-7281 info@pacificspecialists.com

KIAN KARIMI, MD

Head & Neck Surgery & Endoscopic Skull Base Surgery, BTC Pacific Eye & Ear Specialists 11645 Wilshire Blvd, 6th Floor Los Angeles, CA 90025

Phone: 310-477-5558 Fax: 310-477-7281

www.pacificspecialists.com

PEJMAN COHAN, MD

Neuro-Endocrinology 150 N Robertson #210 Beverly Hills, CA 90211

Phone: 310-657-3030 Fax: 310-657-9777

PCohan@mednet.ucla.edu

NILOUFAR ILANI, MD

Neuro-Endocrinology 2021 Santa Monica Blvd, Suite 337 E Santa Monica, CA 90404

20911 Earl Street Suite 450 Torrance, CA 90503

Phone: 310-371-4543 Fax: 310-371-4635

HOWARD KRAUSS, MD

Neuro-Ophthalmology, BTC Pacific Eye & Ear Specialists 11645 Wilshire Blvd. 6th Floor Los Angeles, CA 90025 Phone: 310 477-5558 Fax: 310-477-7281 info@pacificspecialists.com

SANTOSH KESARI, MD, PHD

Director, Neuro-oncology and Neurotherapeutics John Wayne Cancer Center 2200 Santa Monica Boulevard Santa Monica, CA 90404 Phone: 310-829-8265 KesariS@JWCI.org

GEORGE P. TEITELBAUM, MD

Interventional Neuroradiology Garden Level of the Howard Keck Center Providence Saint John's Health Center Phone 818-847-4835 Fax 818-847-4842 http://newstjohns.org/BTC_Our_Expert_Team.aspx#George

LISA CHAIKEN, MD AND ROBERT WOLLMAN, MD

Radiation Oncology & Radiosurgery Garden Level of the Howard Keck Center Providence Saint John's Health Center Phone 310-829-8913 Fax 310-315-6168 http://newstjohns.org/BTC_Our_Expert_Team.aspx#Lisa http://newstjohns.org/BTC_Our_Expert_Team.aspx#Wollman

AMY A. EISENBERG, MSN, ARNP, CNRN

Nurse Practitioner

Pacific Brain Tumor Center and Pituitary Disorders Program Phone: 310-582-7450 Fax: 310-582-7495

eisenberga@jwci.org

MARICELA SANDOVAL

Patient Care Coordinator Pacific Brain Tumor Center and Pituitary Disorders Program Phone: 310-582-7450 Fax: 310-582-7495 sandovalm@jwci.org

MARILOU LORETO

Financial Counselor Pacific Brain Tumor Center and Pituitary Disorders Program Phone: 310-559-8276 Fax: 310-559-8263

mbmg97@aol.com

ANNIE HENG, RN

Research Nurse Coordinator Pacific Brain Tumor Center and Pituitary Disorders Program Phone: 310-582-7457 Fax 310-582-7495 annie.heng@providence.org

SHARMYN MCGRAW

Patient Advocate Hormones411 3857 Birch Street #453 Newport Beach, CA 92660 Phone: 949-515-9595 Fax: 888-410-3334 www.hormones411.org Sharmyn@hormones411.org

References

- 1. Jho HD, Carrau RL. Endoscopic endonasal transsphenoidal surgery: experience with 50 patients. J Neurosurg 1997; 87: 44-51
- 2. McLaughlin N, Eisenberg A, Cohan P, Chaloner C, Kelly DF: The value of endoscopy for maximizing tumor removal in endonasal transsphenoidal pituitary adenoma surgery: In press. J Neurosurgery, January 2013
- 3. McLaughlin N, Laws ER, Oyesiku NM, Katznelson L, Kelly DF. Pituitary centers of excellence. Neurosurgery. 2012 Nov;71(5):916-26: 10.1227/NEU.0b013e31826d5d06.



Helpful Links to Find Additional Medical Information

American Association of Neurological Surgeons

American Brain Tumor Association

Biology On-Line

Brain Tumor Foundation

Chordoma Foundation

Congress of Neurological Surgeons

E-Medicine

MedicineNet.com

MedicineTerms.com

Medline Plus (National Library of Medicine)

Musella Foundation For Brain Tumor Research & Info

National Brain Tumor Society

National Cancer Institute

PubMed Search Engine

National Library of Medicine

Pituitary Network Association

Pituitary Society

Up To Date Patient Information

Web MD

Patient Support and Advocacy Sites:

Acromegaly Community

American Brain Tumor Association

Brain Tumor Foundation

Chordoma Foundation

Cushings-Help

Endo.org

Hormones 411

National Brain Tumor Society

National Cancer Institute

Pituitary Network Association

Pituitary Society

Since its founding in 1942 Providence Saint John's Health
Center has been providing the patients and families of Santa
Monica, West Los Angeles and ocean communities with
breakthrough medicine and inspired healing. Providence
Saint John's provides a spectrum of treatment and diagnostic
services with distinguished areas of excellence in cancer,
spine, orthopedics, neurosurgery, women's health, cardiac and
specialized programs such as the internationally acclaimed
John Wayne Cancer Institute. Providence Saint John's is
dedicated to bringing to the community the most innovative
advances in medicine and technology.

