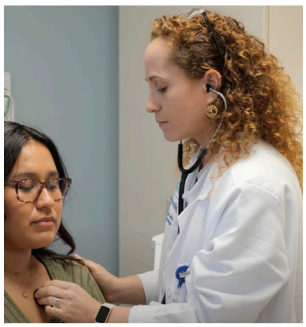
Endoscopic Endonasal Surgery for

Pituitary Adenomas and Related Tumors



Patient Guide

PacificPituitary.org | 310-582-7450

PACIFIC
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INSTITUTE®

Pacific Pituitary Disorders Center

With one of the world's largest experiences in endonasal endoscopic surgery for pituitary adenomas, craniopharyngiomas, chordomas and meningiomas, and an extensive track record in pituitary hormonal evaluation and replacement, our specialists at the Pituitary Disorders Center provide comprehensive care to patients suffering from all types of pituitary disorders. Our multidisciplinary approach provides tailored diagnostic and treatment plans for each patient.

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

For an appointment or second opinion:

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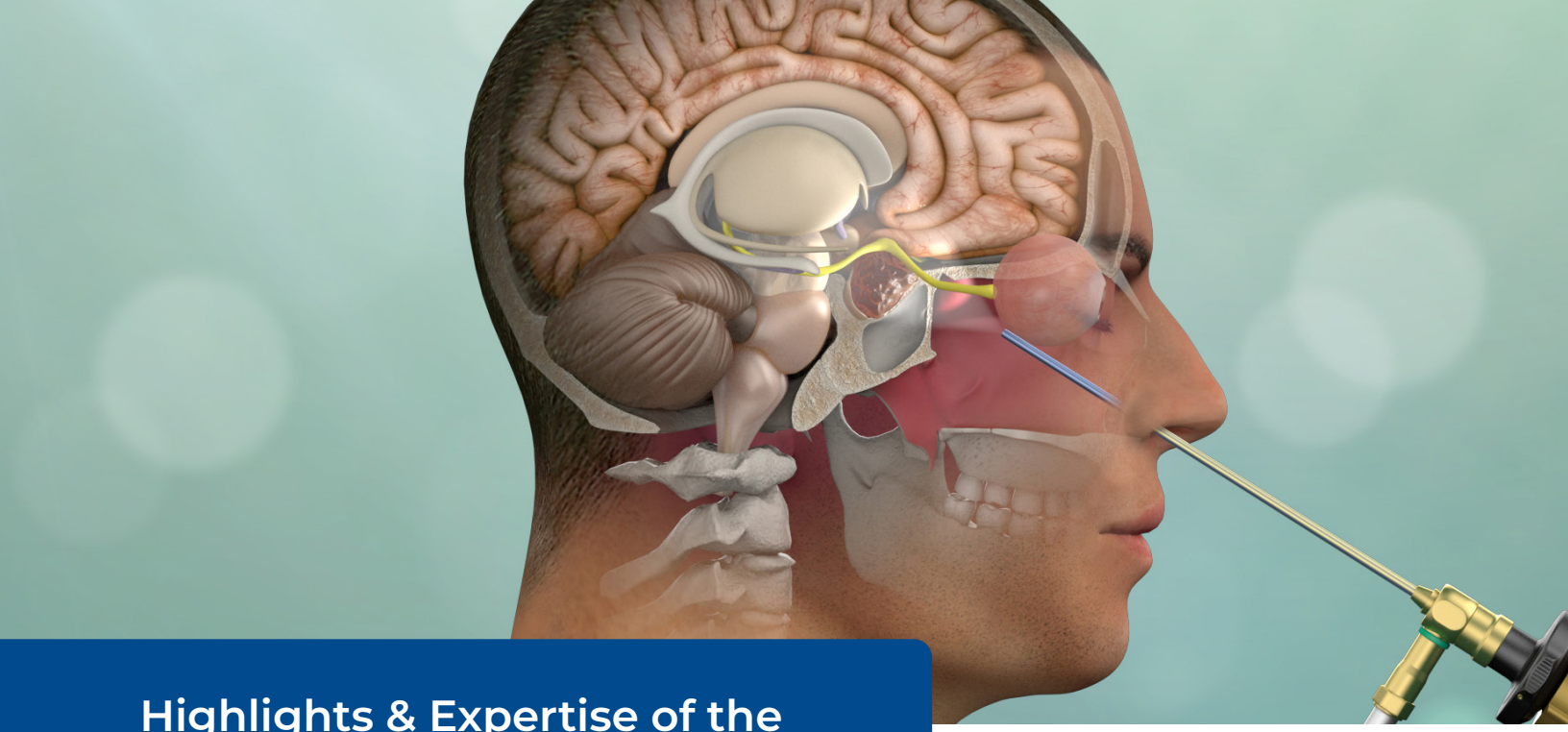


Highlights & Expertise of the Pacific Pituitary Disorders Center

- One of the longest running pituitary centers of excellence in the nation
- One of the most experienced surgical teams in the nation performing over 1000 endoscopic endonasal surgeries with some of the highest effectiveness and lowest complication rates published.
- Outstanding collaboration between specialists in neurosurgery, endocrinology, ENT, neuro-ophthalmology, neuro-oncology, radiation oncology and neuropathology Endocrine-inactive adenoma
- Long academic track record in pituitary medicine and endoscopic skull base surgery:
    - Over 80 peer-reviewed publications focused on pituitary disorders including pituitary tumors and related skull base tumors, pituitary gland hormonal function
    - Regular symposia and talks by PNI Faculty at national and international symposia, including hands-on courses teaching the nuances and indications of endoscopic and keyhole surgery
    - Over a decade of neurosurgical fellowship training in endoscopic pituitary, skull base and keyhole brain tumor surgery

Disorders We Treat

Pituitary Adenomas

- Acromegaly
- Cushing's disease
- Non-functional / 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 hormone deficiency (pituitary failure / hypopituitarism)

Pituitary inflammation (hypophysitis)

Cerebrospinal fluid leaks

Team Approach to Pituitary Disorders

- Endocrinology
- Neurosurgery
- Head & Neck Surgery (ENT)
- Neuroradiology
- Neuro Ophthalmology
- Neuro Pathology
- Neuro Anesthesia
- Radiation Oncology
- Patient Support and Education

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

Expert Team

Our multi-disciplinary team of specialists work collaboratively to ensure you receive the highest levels of care. You will often be seen by multiple specialists all in one visit in a single convenient location.

Daniel F. Kelly, MD

DIRECTOR, PACIFIC NEUROSCIENCE INSTITUTE

Dr. Kelly is an internationally recognized neurosurgeon with a focus in the field of endoscopic and keyhole brain, skull base and pituitary surgery. He treats a wide range of tumors including pituitary adenomas, meningiomas, craniopharyngiomas, chordomas and metastatic brain tumors. *pacificneuro.org/kelly*

Chester Griffiths, MD

DIRECTOR, EYE, EAR & SKULL BASE CENTER

Dr. Griffiths has an extensive over 35-year experience as a sino-nasal endoscopic surgeon. He is co-surgeon in endonasal endoscopic pituitary and skull base surgery, and provides post-operative sinus care. *pacificneuro.org/griffiths*

Howard Krauss, MD

DIRECTOR, EYE, EAR & SKULL BASE CENTER

Dr. Krauss is specialized in diagnostic neuro-ophthalmology, including visual field analysis and ocular coherence tomography, as well as strabismus, orbital and anterior skull base surgery. *pacificneuro.org/krauss*

Noa Tal, MD

ENDOCRINOLOGIST

Dr. Tal is an experienced endocrinologist specializing in the diagnosis and treatment of pituitary hormone abnormalities in adults, including Cushing's disease, prolactinomas, acromegaly, sellar masses and other pituitary tumors. *pacificneuro.org/tal*

Garni Barkhoudarian, MD

CMO; DIRECTOR, PITUITARY DISORDERS CENTER

Dr. Barkhoudarian is a neurosurgeon specializing in skull base and minimally invasive endoscopic surgery, particularly pituitary and parasellar tumors, intra-ventricular brain tumors, trigeminal neuralgia, hemifacial spasm, other cranial nerve syndromes and hydrocephalus. *pacificneuro.org/barkhoudarian*

Michael Yong, MD, MPH, MBA

OTOLARYNGOLOGY - HEAD & NECK SURGEON

Dr. Yong has expertise in sinonasal and skull base disorders using minimally invasive techniques to treat nasal obstruction, smell disorders, rhinitis, facial pain, sinusitis, nasal polyps, and tumors of the sinonasal cavities. *pacificneuro.org/yong*

Alexander Solomon, MD

NEURO-OPHTHALMOLOGIST

Dr. Solomon specializes in advanced adult strabismus diagnosis and treatment, thyroid eye disease, cranial nerve palsies, and orbital disease, as well as visual field analysis and optical coherence tomography interpretation. *pacificneuro.org/solomon*

Michelle Holmes, OD

NEURO-OPTOMETRIST

Dr. Holmes is board certified and TLG licensed to treat and manage ocular disease. She specialiizes in neuro-optometry, ocular disease, and visual rehabilitation. She also participates in clinical research & studies. *pacificneuro.org/holmes*

Full team directory on page 16

Patient Support

The Pacific Pituitary Disorders Center Patient Support Group is moderated by PNI experts. The aim of the group is to provide education, support and empowerment for those dealing with neurological challenges due to pituitary disease. Through our guest speakers and educational support, we strive to help patients and their families cope with and ultimately conquer their illnesses. Our support group is for patients, their family members, and friends.

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 and saliva) 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 hormonal evaluation is critical to confirm the diagnosis. A detailed vision examination with quantitated visual fields and optical coherence tomography (OCT) is generally indicated 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 (and sometimes CT of the sinuses) 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 Endonasal Surgery

Pituitary surgery has evolved tremendously since it was first practiced in the early 20th century. Over the last century, technological advancements, improvements in surgical instrumentation and better anatomical understanding have all helped revolutionize the transsphenoidal approach to the midline skull base including the 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 20 years, the surgical endoscope has gradually replaced the microscope for visualization at most pituitary centers, and is 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

Currently, at Pacific Pituitary Disorders Center and many centers around the world, endoscopic endonsal surgery is performed by two surgeons (a neurosurgeon and ENT surgeon) working together through the natural corridors of the nostrils (Figure 1). 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 (Figure 2). After pituitary adenoma surgery, most patients can be discharged home after only one or two nights in the hospital. Below we describe our team approach, pre-operative planning, operative technique, and post-operative care for patients undergoing endonasal endoscopic surgery.

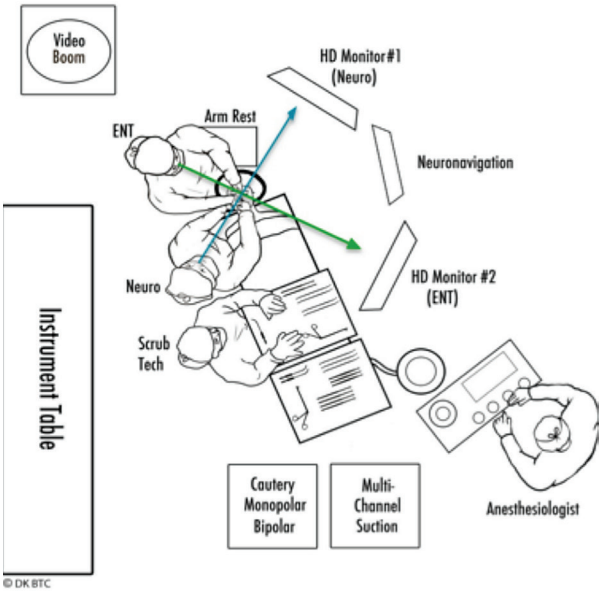
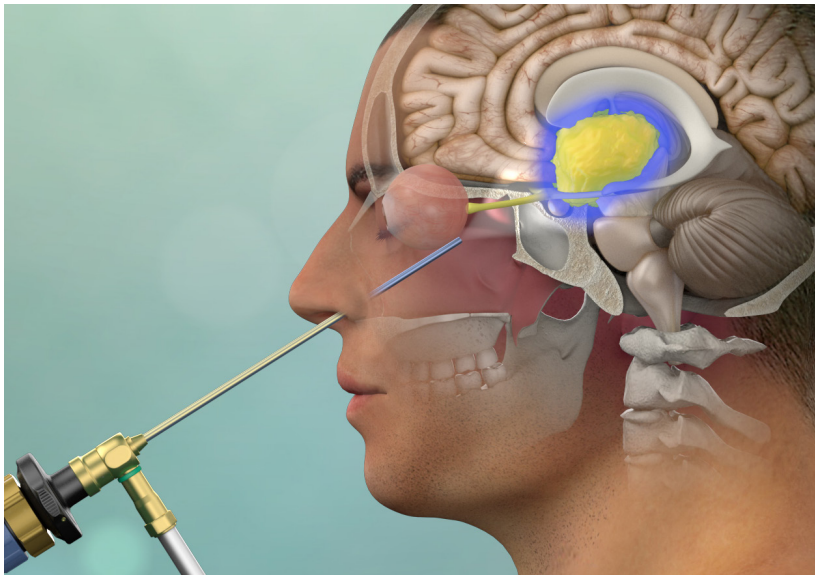


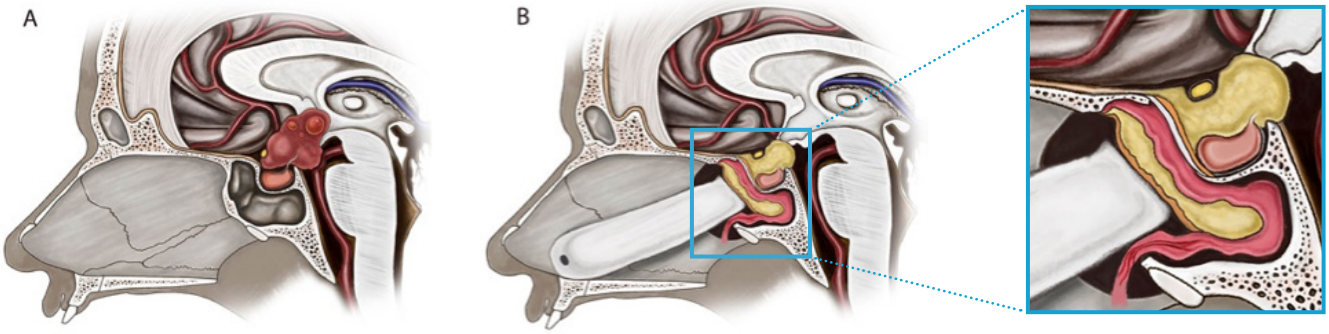
Figure 1

Layout of operating room with high-definition monitors and neuro-navigation 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 2

Endoscopic endonasal approach for craniopharyngioma. A 4 mm high-definition endoscope is in one nostril providing visualization and two working instruments are placed in the right and left nostrils. A.The tumor impacts the pituitary gland and surrounding structures. B. After tumor removal, the skull base is reconstructed. The insert view demonstrates the preservation of the pituitary gland.





Endoscopic endonasal surgery for pituitary adenoma or Rathke's cleft cyst generally takes approximately 3 to 4 hours. This time includes both the ENT and Neurosurgical portions of surgery. Any significant intranasal abnormalities are generally repaired or removed including severe septal deviations. 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 45-60 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 who makes relaxing incisions in the mucosa of the nasal cavity and enlarges the natural openings at the back of the nasal cavity to reach the sphenoid sinus. Great care is taken to preserve the normal mucosa and olfaction fibers of the nose.

During the remainder of the procedure, including exposure of the sella, tumor removal and skull base reconstruction, the ENT surgeon and neurosurgeon stand side-by-side, looking at separate monitors showing the endoscopic image (Figure 3), allowing for an ideal ergonomic posture that decreases surgeon fatigue

Figure 3

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.

Tumor removal is performed with a variety of specialized micro-instruments including curettes, microscissors, grasping instruments and gentle suction, depending upon the texture and toughness of the tumor tissue. Great care is taken to protect the critical surrounding structures such as carotid arteries, optic nerves and chiasm, the 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 4).

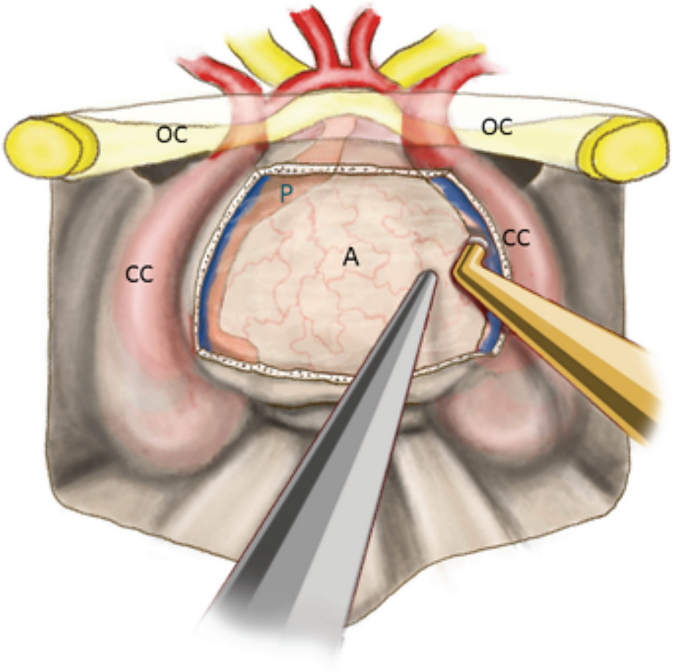


Figure 4

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 maximal safe tumor removal has been achieved. If a cerebrospinal fluid leak is identified, a small amount of fat is often harvested from the abdomen and placed in the sella to help seal the leak. This repair is reinforced with a layer of collagen and tissue glue, and often with a buttress of bone (harvested from the back of the nasal septum). The nasal mucosa is then re-approximated. In some instances, a nasal tampon is placed through one nostril as a soft temporary buttress to help hold the fat graft and collagen in ideal position (usually for 5 days) to prevent a post-operative CSF leak.

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 "nasoseptal flaps" are highly effective in preventing post-operative cerebrospinal fluid leaks and minimizing the risk of meningitis in these types of cases where a larger opening into the skull base is required for tumor removal.

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. Many patients can be discharged to home on post-operative day 1. Most patients are sent home with a water bottle to limit their fluid intake for the 1st week until the labs are drawn.

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 early after surgery are cortisol (with hydrocortisone - a steroid) and vasopressin (with DDAVP), which in most patients are only needed temporarily but in some cases may require long-term or even permanent replacement.

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 sometimes discharged on a short course of antibiotics to prevent sinusitis if a nasal tampon is in place. 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.

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 driving after two weeks and exercising by 3 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 debridements (cleanings) typically 2-3 times within the first 6 weeks of surgery to prevent crusting and scarring of the nasal structures.

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

Endocrinological evaluation is typically performed at 6-8 weeks following surgery for reassessment of all pituitary hormones and then is scheduled at various intervals depending on pituitary gland function and pre-operative hormonal status. 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 to12 month intervals for at least 5 to 10 years depending upon the clinical situation.



The endoscopic endonasal approach offers the following advantages for improved outcomes:

- 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 to maximize safety and effectiveness
- 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
- 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, endoscopic endonasal surgery for pituitary adenoma and related tumors is generally safe and highly effective when performed by an experienced endoscopic skull base surgery team at a facility performing a high volume of such operations.

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 pacificpituitary.org.

To arrange a virtual or office consultation with our neurosurgeons or with one of our other specialists, call the Pacific Pituitary Disorders 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 Coordinators can help you arrange these as well.

International & Out-Of-State Patients

For patients living outside the United States, our physicians can provide a prompt review of imaging and other tests. We can suggest a recommendation about the optimal treatment options with no charge for such initial evaluations and preliminary reviews.

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Key Publications

1. McLaughlin N, Laws ER, Oyesiku NM, Katznelson L, Kelly DF: Pituitary Centers of Excellence. Neurosurgery. Nov;71(5):916-26, 2012
2. Barkhoudarian G, Cutler AR, Yost S, Lobo B, Eisenberg A, Kelly DF. Impact of selective pituitary gland incision or resection on hormonal function after adenoma or cyst resection. Pituitary. 2015 Dec;18(6):868-75. PubMed PMID: 26115709.
3. Sivakumar W, Barkhoudarian G, Lobo BM, Zhang X, Zhao F, Eisenberg A, Kesari S, Krauss H, Cohan P, Griffiths C, Wollman R, Chaiken L, Kelly DF. Strategy and technique of endonasal endoscopic bony decompression and selective tumor removal in symptomatic skull base meningiomas of the cavernous sinus and Meckel's cave. World Neurosurg. 2019 Jun 18 [Epub ahead of print] PubMed PMID: 31226453.
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7. "Transsphenoidal endoscopic skull base surgery: state of the art and future perspectives" Aaron Cutler, Garni Barkhoudarian, Chester Griffiths, Daniel Kelly, Innovative Neurosurgery 1(1), 15-35, 2013
8. Griffiths, Chester F., Aaron R. Cutler, Huy T. Duong, Gal Bardo, Kian Karimi, Garni Barkhoudarian, Ricardo Carrau, and Daniel F. Kelly. "Avoidance of postoperative epistaxis and anosmia in endonasal endoscopic skull base surgery: a technical note." Acta Neurochirurgica (2014): 1-9.
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10. Barkhoudarian, Garni, Aaron R. Cutler, Sam Yost, Bjorn Lobo, Amalia Eisenberg, and Daniel F. Kelly. "Impact of selective pituitary gland incision or resection on hormonal function after adenoma or cyst resection." Pituitary(2015): 1-8.
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12. Barkhoudarian, Garni, Sheri K. Palejwala, Ronke Ogunbameru, Hua Wei, Amalia Eisenberg, and Daniel F. Kelly. "Early recognition and initiation of temozolomide chemotherapy for refractory, invasive pituitary macroprolactinoma with long-term sustained remission: a case report." World neurosurgery 118 (2018): 118-124
13. Burke, William T., David L. Penn, Joseph P. Castlen, Daniel A. Donoho, Caroline S. Repetti, Sherry Iuliano, Garni Barkhoudarian, and Edward R. Laws. "Prolactinomas and nonfunctioning adenomas: preoperative diagnosis of tumor type using serum prolactin and tumor size." Journal of neurosurgery 1, no. aop (2019): 1-8.
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Helpful Links to Find Additional Medical Information

PNI Video Library | Pacific Pituitary Disorders Center

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