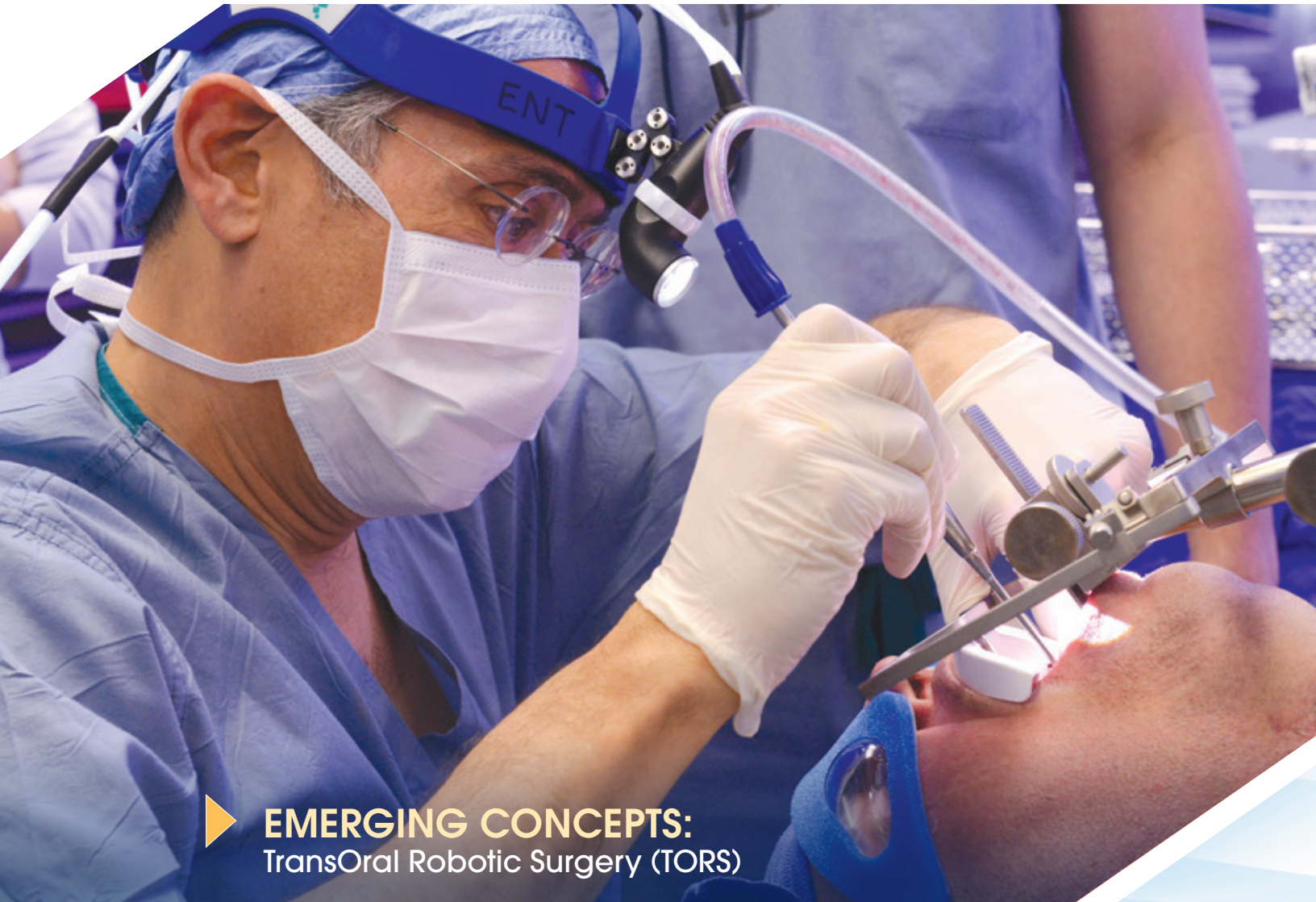


# PENN OTORHINOLARYNGOLOGY

## HEAD AND NECK SURGERY



▶ **EMERGING CONCEPTS:**  
TransOral Robotic Surgery (TORS)

INSIDE

- 2 ▶ Letter from the Chair
- 3 ▶ Emerging Concepts:  
TransOral Robotic Surgery (TORS):
  - Unknown Primary Detection
  - Nasopharyngeal Carcinoma Resection
  - Obstructive Sleep Apnea Treatment
  - Limited Post-Operative Radiation Treatment
- 7 ▶ Inaugural International TORS Conference
- ▶ Penn Honors Tony Horton as Health Care Innovator

# LETTER FROM THE CHAIR



**Bert W. O'Malley, Jr., MD**

*Gabriel Tucker Professor and Chair*

*Department of Otorhinolaryngology - Head and Neck Surgery  
Associate Vice President, University of Pennsylvania Health System*

## #3 in the Nation

Penn Otorhinolaryngology – Head and Neck Surgery at the hospitals of the University of Pennsylvania – Penn Presbyterian was **ranked #3** among the top Ear, Nose, and Throat departments in the nation by *U.S. News & World Report* for 2014.



## Dear Colleagues,

It is my honor to present the 2014 Penn Otorhinolaryngology – Head and Neck Surgery Newsletter. This issue details the growing number of emerging concepts evolving from TransOral Robotic Surgery (TORS) research and the increasing surgical applications for TORS. Among these are:

- **Expansion of diagnostics for unknown primary cancer sites in patients with human papilloma virus (HPV).** TORS-assisted endoscopy has been used to identify the primary tumor site, permitting subsets of patients to avoid radiation or chemotherapy.
- **Resection of recurrent nasopharyngeal carcinoma.** TORS is being investigated as a surgical option for patients with recurrent nasopharyngeal cancers, malignancies considered among the least accessible to surgical resection.
- **Treatment of obstructive sleep apnea (OSA).** OSA has proved amenable to a combination of TORS surgeries.
- **Reduction in the need for adjuvant radiotherapy in patients with head and neck cancer.** Researchers at Penn have begun a series of studies to investigate ways to diminish radiation toxicity in patients treated with TORS for oropharyngeal cancer.

As the birthplace of TORS and the world's leading source of TORS innovation, Penn Otorhinolaryngology recently hosted the Inaugural International TransOral Robotic Surgery Conference. At that event, world-renowned fitness expert Tony Horton (creator of P90X) was awarded the first Chevalier Jackson Health Care Innovator Medal. This annual award is presented to a non-physician each year who has worked to positively impact the health and well-being of their communities.

It's my hope that you find this issue of the Penn Otorhinolaryngology – Head and Neck newsletter informative and enlightening. For additional information, please visit us at [PennMedicine.org/ent](http://PennMedicine.org/ent).

Best Regards,

A handwritten signature in blue ink that reads "Bert W. O'Malley, Jr." The signature is fluid and cursive.

**Bert W. O'Malley, Jr., MD**

*Gabriel Tucker Professor and Chair, Department of Otorhinolaryngology – Head and Neck Surgery  
Associate Vice President, University of Pennsylvania Health System*

# EMERGING CONCEPTS IN TRANSORAL ROBOTIC SURGERY

TransOral Robotic Surgery (TORS) was developed at Penn Medicine in 2004 by Bert W. O'Malley, Jr., MD and Gregory S. Weinstein, MD. A dramatic leap forward, TORS enabled minimally invasive access to the confined spaces of the head and neck via slender, articulate robotic instruments as an alternative to the disfiguring incisions typical of traditional open surgery. TORS was approved in 2009 for the surgical treatment of selected malignant lesions (and all benign lesions) of the throat and larynx, and continues to be the fulcrum for a wide-ranging series of studies and emerging clinical concepts at Penn Medicine.

“Robotic surgery is the perfect combination of minimally invasive surgery and outstanding outcomes for patients.”

Gregory S. Weinstein, MD, FACS

*Vice Chairman, Department of Otorhinolaryngology – Head and Neck Surgery | Director, Head and Neck Surgery Division and Head and Neck Surgery Clinic  
Co-Director, Center for Head and Neck Cancer | Director, Head and Neck Oncology Fellowship | Professor of Otorhinolaryngology – Head and Neck Surgery*

TORS incorporates three-dimensional visualization, light-intensive magnification and robotic laparoscopic tools. As a surgical modality, TORS is thus ideally suited to surgical applications and tumor resections in areas of the head and neck and skull base that previously proved challenging to access.

At Penn, emerging applications for TORS include its use in the expansion of diagnostics for unknown primary cancer sites; resection of previously unresectable nasopharyngeal carcinoma; treatment for obstructive sleep apnea; and in the attenuation of adjuvant radiotherapy. These concepts are indicative of the evolving TORS program and its goals in that each seeks to improve upon current standard approaches to treating head and neck tumors. The following are highlights of these new concepts in detail.

## TORS-Assisted Endoscopy for Head and Neck Carcinoma of Unknown Primary Origin

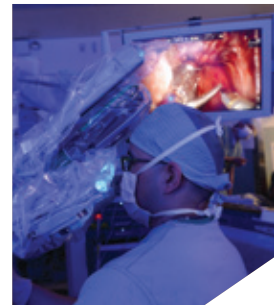
In clinical reports, the use of TORS in patients with head and neck carcinoma of unknown primary origin has led to positive identification of the primary cancer in 82% of patients, compared to 60% using traditional diagnostic methods alone.

Although head and neck carcinomas of unknown primary origin (HNCHUP) are rare, the standard treatment often includes comprehensive radiation with or without chemotherapy to the entire

*Anesthesiologist prepares patient for TORS*



(Continued on page 4)



*Left: Bert W. O'Malley, Jr., MD, and Gregory S. Weinstein, MD, examine a resected TORS specimen.*

*Middle: Dr. Weinstein positions the retractor prior to TORS.*

*Right: Bedside assistant during TORS resection.*

(Continued from page 3)

bilateral pharyngolarynx with devastating quality of life outcomes for our patients. Cancers of unknown primary are defined as metastatic cancers diagnosed by biopsy for which a primary location cannot be identified with classic diagnostic efforts. Traditional unknown primary diagnostics include fine needle aspiration, PET CT and other directed biopsies.

The inability to locate the primary cancer can have a profound influence on subsequent treatment. In patients with HNCUP, clinicians have traditionally been obliged to abandon safe and efficacious targeted therapies in favor of widespread radiation therapy, often with concurrent chemotherapy. Although generally successful, conventional radiotherapy results in grade 2 or worse toxicity in two-thirds of patients with head and neck cancers. In addition, esophageal stricture with associated swallowing and pharyngeal dysfunction with the need for a feeding tube can be seen in up to 40% of cases. Thus, the ability to locate the primary lesion in patients with head and neck cancer prior to treatment has both therapeutic and quality of life benefits.

With respect to a surgical approach to HNCUP, TORS has distinct advantages. In a TORS approach to HNCUP, surgeons are often able to see previously undetected surface changes and small ulcers or signs of a primary cancer using the high-definition,

high-magnification, three-dimensional optics of the robotic surgical system. TORS surgeons use the delicate and precise robotic instruments to perform a minimally invasive surgical resection of high risk sites or regions of subtle change within oropharynx while avoiding classic surgical complications including damage to cranial nerves and vessels.

With this foundation, TransOral Robotic Surgery was the subject of a retrospective clinical trial at Penn Medicine to determine its efficacy in the identification of HNCUP in patients with human papilloma virus (HPV), which often has a small primary site. Because the vast majority of HPV-associated oral cancers are found in the oropharynx (~70%), the presence of p16 in the needle aspiration of the neck node indicates that a primary lesion will most likely occur in the oropharynx.

In addition to the identification of p16-positive HNCUP, the trial at Penn assessed whether pathologic staging cervical disease during simultaneous cervical lymphadenectomy would allow for significant deintensification of radiotherapy.

TORS-assisted endoscopy identified the primary mucosal tumor site in 9 of 11 patients (81.8%). Neck dissection at the time of endoscopy provided detailed pathological staging of the cervical neck disease, which allowed four patients to avoid radiation and eight patients to avoid chemotherapy.

## TransOral Robotic Resection of Nasopharyngeal Carcinoma

In collaboration with Raymond Tsang, MD, Drs. Gregory Weinstein, Christopher Rassekh and Bert O'Malley, Jr., have developed a transoral robotic surgical approach to treat recurrent nasopharyngeal carcinoma. The advantages of TORS in the treatment of recurrent nasopharyngeal carcinoma (NPC) include the modality's capacity to visualize and maneuver within the deep skull.

Radiotherapy (66-70 Gy) is the standard first-line approach for early (stage I and IIA) NPC. Patients with locally advanced disease (stage IIB) are treated with combined chemotherapy–radiotherapy. Despite generally good five-year outcomes, up to 58% of patients having first-line therapy for NPC will have residual disease and/or recurrence.

Surgeons at Penn Medicine are exploring the use of TORS to eliminate residual cancer in patients with recurrent NPC and improve the efficacy of initial surgery. Located deep within the skull base, the nasopharynx is a challenging region to access.

The management of recurrent NPC is particularly challenging. NPC lesions appearing after initial radiation often exhibit extensive tissue involvement for which retreatment with standard therapy offers meager benefit (20% average 5-year overall survival). Surgery for recurrent NPC has been reserved for salvage therapy; until recently, however, salvage for recurrent nasopharyngeal carcinoma (NPC) exhibiting advanced tissue involvement was considered impossible.

The traditional exclusion of surgery for recurrent NPC has its foundation in the potential for intraoperative damage to the maxillofacial bony structures, cranial nerves, and major vessels. Distortion and trauma to the bony structures and injury to these key craniofacial nerves can cause facial disfigurement and functional deficits that are potentially devastating to a patient's quality of life. Injury to major vessels within the region of the nasopharynx may be life threatening.

In light of these circumstances, investigators worldwide have begun a search for alternative treatments for recurrent NPC. TORS is among the treatments under investigation. Drs. Weinstein, Rassekh, O'Malley and Tsang have initiated a clinical trial to investigate TORS for the treatment of recurrent NPC. The key to their approach involves the modality's capacity

---

Surgeons at Penn Medicine are exploring the use of TORS to eliminate residual cancer in patients with recurrent NPC and improve the efficacy of initial surgery.

---

for excellent lateral access to the nasopharynx, an approach that permits more efficacious tumor resection via a lateralized palatal and parapharyngeal incision. The benefit of these incisions is their potential to minimize dehiscence, fistula and other palate complications.

The clinical trial will also examine the potential of TORS as a first line modality in nasopharyngeal benign and malignant tumors.

Dr. Tsang is affiliated with the Division of Head and Neck Surgery at the University of Hong Kong Medical Centre. Southern China and southeast Asia have the world's highest concentration of nasopharyngeal carcinoma.

## TransOral Robotic Surgery for Obstructive Sleep Apnea

Researchers at Penn Medicine recently demonstrated the efficacy and safety of TORS as an alternative to traditional surgery for combined uvulopalatopharyngoplasty /lingual tonsillectomy in patients with obstructive sleep apnea.

Obstructive sleep apnea (OSA) is now recognized as an important contributor to cardiovascular morbidity (including hypertension, congestive heart failure and atrial fibrillation) and mortality risk. Moderate to severe OSA has an independent association with increased mortality risk; severe OSA raises the risk of death by approximately 45%. Among middle-aged adults, the condition affects 9% of women and 25% of men.

The present TORS treatment of OSA often combines three procedures, uvulopalatopharyngoplasty (UPPP), targeted tongue base resection, and limited lateral pharyngectomy. While neither procedure is particularly effective alone, the combination of these surgeries has been shown to ameliorate OSA in a majority of our patients.

(Continued on page 6)

TORS incorporates three-dimensional visualization, light-intensive magnification and robotic laparoscopic tools. As a surgical modality, TORS is thus ideally suited to surgical applications and tumor resections in areas of the head and neck and skull base that previously proved challenging to access.

(Continued from page 5)

Drs. Erica Thaler, Bert O'Malley, Jr., and Gregory Weinstein conducted a clinical trial to evaluate TORS for OSA in patients who were noted to have tongue base obstruction and pharyngeal collapse during a diagnostic sleep endoscopy procedure.

At this time, 65% of patients had responded to surgery. A significant decline in apnea-hypopnea index occurred (56.7%;  $p < 0.001$ ) and there were significant improvements in mean preoperative to postoperative minimum arterial oxygen saturation values (75.8% to 81.7%;  $p = 0.013$ ). In addition, a significant improvement in the Epworth Sleepiness Scale score occurred, from 13.4 to 5.9 ( $p = 0.003$ ).

Future directions included expanding the scope of the study and evaluating follow-up to assess the potential for lymphoid tissue regrowth and the long-term impact of the TORS surgical procedures.

On the basis of this and other studies, an indication submission has been filed with the Food and Drug Administration to obtain an approved indication for the TORS surgical procedures utilized in the treatment of OSA. Although TORS was approved in 2009 for the resection of selected malignant lesions as well as all benign disease, it is recommended that the non-FDA approved procedures be performed within the context of research protocols.



### Limited Radiation Clinical Trial

Standard options for advanced-stage, HPV-positive, oropharyngeal squamous cell carcinoma (SCCA) include either definitive chemoradiation or surgery followed by adjuvant radiation therapy (RT), with or without chemotherapy. Chemoradiation is associated with several significant concerns. Definitive chemoradiation can result in long-term feeding tube use in 8 to 35% of patients.

To address the serious side effects associated with definitive chemoradiation, researchers at Penn Medicine have initiated a series of studies to investigate approaches that would diminish radiation toxicity in patients having TORS for oropharyngeal cancer.

These trials follow upon an earlier study at Penn that demonstrated a local control rate of 97% in patients with oropharyngeal cancer who chose to forego adjuvant RT after surgery (TORS + selective neck dissection, or SND). Using this trial as a precedent for further investigation, a phase II study was initiated in completely resected patients with locally advanced, HPV-positive SCCA of the oropharynx to examine TORS alone for the primary tumor and SND followed by adjuvant RT (+/- chemotherapy) for the regional nodes.

The primary objectives of the study are to determine two-year local control at the primary tumor site and acute and long-term toxicity rates post-TORS among patients receiving adjuvant RT, omitting the primary tumor bed.

This study will allow for radiation therapy to be given with either Intensity-Modulated Radiation Therapy (IMRT) or pencil-beam proton therapy. Initial patient experience with pencil-beam proton therapy reveals significant decreases in doses to critical organs at risk with no differences in coverage of radiation dose to at-risk tumor sites. At Penn, radiation doses delivered to the oral cavity have consistently been reduced 10-fold with proton therapy compared to IMRT, with patients reporting no changes in taste sensation near the end of their proton course. ▲



## INAUGURAL INTERNATIONAL TORS CONFERENCE

### TransOral Robotic Surgery (TORS) Specialists Worldwide Gather at Penn Medicine for 1st International Conference

The 1st international TransOral Robotic Surgery (TORS) Conference took place in Philadelphia in July 2014 at Penn Medicine’s Smilow Center for Translational Research. Presented by Penn Otorhinolaryngology - Head and Neck Surgery and directed by Drs. Bert O’Malley, Jr. and Gregory Weinstein, the conference offered didactic presentations, TORS cadaver dissections, live TORS surgery and expert panel discussions. The event was a tremendous success, with a soldout audience of 240 attendees from around the globe along with a collection of highly-regarded guest specialists from Europe, South America and Asia, including Raymond King-Yin Tsang, MD, of the University of Hong Kong, Mohssen Ansarin, MD, of the European Institute of Oncology, and Georges Lawson, MD, of University Hospital of Louvain at Mont-Godinne, among others.

Meeting presentations focused upon TORS for benign and malignant lesions of the pharynx and larynx including cancers provoked by the human papilloma virus (HPV); TORS for parapharyngeal space and skull base lesions; the indications and contraindications for TORS; indications and contraindications to surgery; patient selection; and the latest techniques and approaches in TORS for tongue-base resection in sleep apnea. The cadaver dissection portion of the conference was particularly well received. The second day of the meeting, and the highlight of the event, featured live TORS surgery performed by Drs. O’Malley and Weinstein. ▲

## PENN HONORS TONY HORTON AS HEALTH CARE INNOVATOR

### Tony Horton, Creator of P90X, Awarded Inaugural Chevalier Jackson Health Care Innovator Medal for Outstanding Contributions to Physical Fitness

The inaugural Chevalier Jackson Health Care Innovator Medal has been awarded to Tony Horton, an international fitness and nutrition expert. Recognized for his work in creating P90X, a scientifically-based exercise regimen, Mr. Horton has helped many reach their diet and fitness goals and improve their overall health and wellness. Named for an early pioneer in endoscopy at the University of Pennsylvania, the medal was presented by the Penn Otorhinolaryngology – Head and Neck Surgery and the Penn Center for Head and Neck Cancer at the 1st International Transoral Robotic Surgery Conference in Philadelphia.

“The spirit of this award is to honor a member of the lay public for their outstanding efforts in championing a cause that could impact the health and well-being of their communities,” said Bert W. O’Malley, Jr., MD. “In the light of the current obesity epidemic in the United States, Mr. Horton’s efforts in the area of fitness and nutrition make him an excellent recipient of the Medal.” ▲



Tony Horton (center) receiving the inaugural Chevalier Jackson Health Care Innovator Medal, presented by Gregory S. Weinstein, MD, (left) and Bert W. O’Malley, Jr., MD (right).



## TRANSORAL ROBOTIC SURGERY (TORS) TEAM



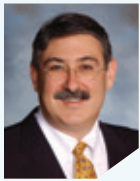
▶ **Bert W. O'Malley, Jr., MD**

Gabriel Tucker Professor and Chair,  
Department of Otorhinolaryngology –  
Head and Neck Surgery  
Co-Director, Center for Head and Neck Cancer  
Associate Vice President,  
University of Pennsylvania Health System



▶ **Jason G. Newman, MD**

Director, Head & Neck Surgery, Pennsylvania Hospital  
Co-Director, Skull Base Center  
Associate Professor of Otorhinolaryngology –  
Head and Neck Surgery



▶ **Gregory S. Weinstein, MD, FACS**

Vice Chairman, Department of Otorhinolaryngology –  
Head and Neck Surgery  
Director, Head and Neck Surgery Division  
and Head and Neck Surgery Clinic  
Co-Director, Center for Head and Neck Cancer  
Director, Head and Neck Oncology Fellowship  
Professor of Otorhinolaryngology –  
Head and Neck Surgery



▶ **Erica R. Thaler, MD**

Director, Division of General Otorhinolaryngology  
Director, Otorhinolaryngology, Penn Medicine Radnor  
Professor of Otorhinolaryngology –  
Head and Neck Surgery



▶ **Steven B. Cannady, MD**

Assistant Professor,  
Clinical Otorhinolaryngology –  
Head and Neck Surgery



▶ **Christopher H. Rassekh, MD**

Associate Professor,  
Clinical Otorhinolaryngology –  
Head and Neck Surgery



▶ **Ara A. Chalian, MD**

Director, Facial Plastic Reconstruction  
Patient Safety Officer  
Director, Microvascular Lab  
Professor of Otorhinolaryngology –  
Head and Neck Surgery

## Penn PhysicianLink<sup>®</sup>

Consults • Referrals • Transfers

For more information on how to make **Penn PhysicianLink** work for your practice and your patients, call **877.937.PENN (7366)** or visit [PennMedicine.org/PhysicianLink](http://PennMedicine.org/PhysicianLink).