Clinical Trials Introduce Novel Treatments and Tailored Approaches to Care
Center specialists are leading numerous early-phase clinical trials, including new personalized approaches to care, in an effort to improve outcomes and long-term quality of life among patients.

Organ Preservation Techniques Improve Quality of Life for Patients
Advanced, multidisciplinary approaches employed by specialists in the Center aim to achieve the best functional outcome for each patient and include a combination of radiation and medical therapies, as well as new minimally invasive surgical techniques.

Innovative Radiation Techniques Enhance Outcomes and Minimize Toxicity
Radiation oncologists in the Center are offering new dosing strategies using intensity modulated radiation therapy (IMRT) and introducing stereotactic body radiation therapy (SBRT) for select patients with head and neck cancer.

Survivorship Studies Address Comprehensive, Long-term Patient Care
Survivorship efforts at the Center are addressing a wide range of short- and long-term effects of treatment for head and neck cancer.
Head and Neck Oncology Center

HIGHLIGHTS

Comprised of subspecialty experts in head and neck surgery, medical oncology, radiation oncology, pathology, and radiology, our multidisciplinary team:

- Provides advanced care for more than 600 patients each year, including patients with head and neck cancers, thyroid cancer, and salivary gland cancers;
- Delivers innovative multimodality techniques designed to achieve and maintain high cure rates, while preserving function;
- Leads an average of 15 clinical trials at a time, including trials that are rapidly expanding the availability of targeted therapies and changing the standard of care for many patients with head and neck cancers;
- Offers cutting-edge radiation therapies and planning techniques that maximize outcomes and minimize side effects;
- Pioneers research that is advancing the understanding of the development, prognosis, and prevention of head and neck cancers.

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Specialists in the Head and Neck Oncology Center are leading numerous early-phase clinical trials in an effort to improve outcomes and long-term quality of life among patients.

“As a multidisciplinary team, we collaborate in applying innovative techniques designed to achieve and maintain high cure rates, while minimizing impact on patient quality of life,” said Robert I. Haddad, MD, Center Director for the Head and Neck Oncology Center.

New Trials for HPV-related Head and Neck Cancers
Several current studies led by specialists in the Center are evaluating new approaches for patients with HPV-related head and neck cancers, which typically carry a better prognosis than patients with HPV-negative disease. Current trials include:

• Phase II Study of Docetaxel/Cisplatin/5-Fluorouracil (TPF) Induction Chemotherapy, Followed by Concurrent Chemoradiotherapy Using a Modified Radiation Dose in Patients with Newly Diagnosed, HPV positive, locally Advanced Squamous Cell Carcinoma of the Oropharynx – Robert I. Haddad, MD, is leading this novel trial for patients with HPV-positive locally advanced oropharyngeal cancer. The trial aims to decrease treatment side effects using a lower radiation dose while maintaining high cure rates;

• Randomized Phase II Trial Contrasting Weekly Paclitaxel, Carboplatin and Cetuximab (PCC) with Cetuximab, Docetaxel, Cisplatin and Fluorouracil (C-TPF) in Previously Untreated Patients with Locally Advanced Head and Neck Squamous Cell Carcinoma – The Center is one of only two centers nationwide to participate in this innovative trial comparing two novel induction chemotherapy regimens. Patients with locally advanced head and neck cancer are treated with high dose chemotherapy, followed by a chemoradiation approach that is tailored to their initial presentation and HPV status.

Treatment for Metastatic or Recurrent Disease
Medical Oncologist Sewanti A. Limaye, MD, is leading a multicenter Phase III study for patients with metastatic or recurrent squamous cell carcinoma of the head and neck who have progressed on or after platinum-based chemotherapy. The study is comparing overall survival, treatment response, and safety and tolerability of two treatment regimens: Reloxin in combination with paclitaxel and carboplatin versus paclitaxel and carboplatin alone.

Novel Agents for Thyroid Cancer
Center specialists are evaluating novel agents for patients with metastatic thyroid carcinoma. “Our team is tailoring treatments and developing new personalized approaches to care, including new trials based on characteristics of the patient’s disease,” said Jochen Lorch, MD, who leads translational research at the Center.

The Center is one of only four sites nationwide to offer a current Phase II trial using RAD001 (mTOR inhibitor everolimus) for patients with radioiodine refractory thyroid cancer. Initiated and led by Dr. Lorch, this study includes genetic screening of tumor samples in order to determine genetic markers of response.

Two additional trials led by Dr. Lorch include a Phase II study of the BRAF inhibitor RO5185426 in patients with metastatic or unresectable papillary thyroid cancer who are positive for the BRAF V600 mutation and resistant to radioactive iodine and a multicenter, placebo-controlled Phase III trial of E7080 in 131I-refractory differentiated thyroid cancer.

For additional information regarding trials and studies in the Head and Neck Oncology Center, please contact Clinical Research Manager Alyson B. Boulanger, MA, at (617) 632-6725 or aboulanger@partners.org, or Research Nurse Pamela Rothe, RN, BSN, OCN, at (617) 632-6817 or prothe@partners.org.

Enhancing the Understanding of Head and Neck Cancers
The Center is participating in several studies designed to advance the understanding of head and neck cancer development, including:

• HPV oral transmission – This study of the risk factors for oral HPV infection, persistence, and transmission is continued on page 7

Medical Oncologist Jochen Lorch, MD (right), is collaborating with Amin I. Kassis, PhD, Director of Radiobiology and Experimental Radionuclide Therapy at Harvard Medical School, in a first-of-its-kind study to create a test for cancer using circulating tumor cells and gene signatures found in patients’ white blood cells.
Organ Preservation Techniques Improve Quality of Life for Patients

Specialists in the Head and Neck Oncology Center are employing advanced multidisciplinary approaches to achieve the best functional outcome for each patient, including a combination of radiation and medical therapies, as well as surgery when necessary.

“Preserving function for our patients is extremely important, as we treat structures that are essential for eating, speaking, swallowing, and many other critical roles,” said Robert I. Haddad, MD, Center Director for the Head and Neck Oncology Center.

Novel approaches in the use of chemoradiation, including the use of lower doses of radiation and new chemotherapy agents, are designed to minimize side effects of curative therapy (see trials on Page 3). In addition, Center specialists are offering less invasive surgical treatment options and novel approaches to the management of surgical morbidities in order to maintain quality of life.

New Findings in Induction Chemotherapy

Specialists in the Head and Neck Oncology Center pioneered the use of induction chemotherapy with docetaxel, cisplatin, and fluorouracil (TPF) in head and neck cancers and led the Phase III study that resulted in the FDA approval of this regimen (N Engl J Med. 2007;357(17):1705-1715). In this study, more than 500 patients were enrolled worldwide, and a clear survival advantage was noted with TPF. This finding has resulted in a significant change in treatment of patients with head and neck cancer.

Jochen Lorch, MD, recently published the five-year survival update on this pivotal study and was able to show that the survival benefit of induction chemotherapy with TPF is maintained at five years (Lancet Oncol. 2011 Feb;12(2):153-9.). Median survival was 70.6 months in the TPF group versus 34.8 months in the PF group. Progression-free survival was also significantly better in patients treated with TPF (median 38.1 months) compared with PF (13.2 months).

TORS: A Revolutionary New Surgical Treatment

Dana-Farber/Brigham and Women’s Cancer Center surgeons Donald J. Annino, Jr., MD, DMD, and Tom Thomas, MD, MPH, perform TransOral Robotic Surgery (TORS) – an innovative new surgical treatment for oropharyngeal, pharyngeal, and laryngeal cancers. TORS offers many benefits compared with traditional surgery for head and neck cancers, including:

• No external incisions;
• No need for jaw splitting or tracheotomy;
• Faster recovery;
• Shorter hospital stay (three to four days compared with seven to 10 days);

Case Study: Pharyngeal Cancer Treated with Robotic Surgery

A 52-year-old woman was successfully treated for oral cavity cancer in October 2005, however, the treatment left her with scarring and limited ability to open her mouth (less than 3 cm).

In November 2010, a routine PET-CT scan revealed a lesion on the posterior pharyngeal wall which could not be treated with conventional surgery. She underwent transoral robotic surgery at Brigham and Women’s Hospital in January 2011 with complete excision of the 1.1 x 1.2 cm lesion. A total area of 3.3 x 3.0 cm was removed. Margins were negative. She was discharged home on the third day following the procedure with no dietary restrictions or swallowing or speech difficulties.

TORS also provides a minimally invasive treatment option for patients who have had previous treatment – including surgery, chemotherapy, and radiation, as well as those with recurrent or second primary disease.

“Conventional surgery and reconstruction for head and neck cancers, while effective, have the potential for a longer and more difficult recovery period, and possible external defor-
Innovative Radiation Techniques Enhance Outcomes and Minimize Toxicity

Specialists in the Head and Neck Oncology Center are evaluating new dosing strategies of intensity modulated radiation therapy (IMRT), currently the standard-of-care, and the use of stereotactic body radiation therapy (SBRT) in select patients with head and neck cancer.

“The newest approaches in radiation therapy involve looking at different treatment strategies based on the patient’s type of cancer and related prognosis,” said Roy B. Tishler, MD, PhD, Radiation Oncology Director for the Head and Neck Oncology Center.

SBRT Trial for HPV-negative Disease
Patients with HPV-negative head and neck cancers, who traditionally don’t respond as favorably to standard treatments, are being enrolled in a study using SBRT to provide a “boost” dose of radiation to the primary tumor and lymph nodes, while reducing risk of damage to normal surrounding tissues. SBRT is a cutting-edge technique that combines advanced radiation-delivery equipment with complex imaging technology to map precise tumor dimensions and location.

De-escalation Trial for HPV-associated Disease
Robert I. Haddad, MD, Center Director for the Head and Neck Oncology Center, and Dr. Tishler are leading this novel trial for patients with HPV-associated locally advanced oropharyngeal cancer. The trial, which aims to decrease treatment side effects while maintaining high cure rates, provides induction chemotherapy followed by chemoradiation using a lower radiation dose (see page 3 for more information);

Multi-Modality Treatments Result in Strong Outcomes
Specialists in the Center have published treatment results from various disease sites that demonstrate survival and cancer control benefits of radiation therapy combined with other treatment modalities. Dr. Tishler is senior author of several recent outcomes studies published in the International Journal of Radiation Oncology • Biology • Physics:

- Overall Survival (OS) and Locoregional Control (LRC) in Oral Cavity Squamous Cell Carcinoma (OCSCC) – A retrospective study of patients treated for oral cavity squamous cell carcinoma (OCSCC) with adjuvant or definitive IMRT found that postoperative IMRT is associated with promising LRC, OS, and lower late toxicity rates, and chemoradiotherapy is a successful treatment for patients with high-risk disease (Int J Radiat Oncol Biol Phys. 2011 Apr 29). Forty-two patients with OCSCC were included in the study. Thirty of these patients were initially treated with surgical resection.

- Efficacy and toxicity of chemoradiotherapy using IMRT for head-and-neck squamous cell carcinoma of an unknown primary (HNCUP) – A total of 24 patients with HNCUP were included in this study (Int J Radiat Oncol Biol Phys. 2011 Aug 1;80(5):1405-11). Of these patients, 22 had Stage N2 disease or greater. All patients underwent neck computed tomography, positron emission tomography-computed tomography, and examination under anesthesia with directed biopsies. Of the 24 patients, 22 received concurrent chemotherapy, and seven (29 percent) also underwent induction chemotherapy. The two-year actuarial overall survival and locoregional control rate was 92 percent and 100 percent, respectively.

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Survivorship Studies Address Comprehensive, Long-term Patient Care

Survivorship efforts at the Head and Neck Oncology Center are designed to address the short- and long-term effects of treatment for head and neck cancers.

“We have seen a major shift in the patient demographics for head and neck cancers, with the majority of newly-diagnosed patients being much younger and having different risk factors than we have seen in the past,” said Medical Oncologist Sewanti A. Limaye, MD. “This brings into play new considerations related to survivorship.”

Dr. Limaye is leading several studies addressing survivorship in patients with head and neck cancer and is establishing a new survivorship clinic within the Head and Neck Oncology Center. The Center’s survivorship clinic will integrate survivorship care with the Lance Armstrong Foundation Adult Survivorship Program at Dana-Farber Cancer Institute and provide disease-specific services designed to complement other services within the Head and Neck Oncology Center.

Survivorship studies in the Center include:

- **A Prospective Observational Study of Andropause in Male Patients Receiving Chemotherapy for Head and Neck Cancer** – This ongoing study is examining the effect of chemotherapy treatment on testosterone and other male hormone levels in head and neck cancer survivors. This study also will evaluate interpersonal wellbeing in these patients and hormonal variation as it applies to fatigue, fertility, and other aspects of quality-of-life;

- **Patient reported symptom-burden for patients with Head and Neck Cancer After Sequential Therapy or Primary Chemoradiotherapy, with or without salvage surgery** – This upcoming study will analyze survey responses of patients who are at least two years post-treatment for head and neck cancer.

This study will examine head and neck specific symptoms and quality of life parameters, including a screening tool assessing oral health and general health questions. The purpose of this study is to gauge the prevalence of late toxicities, including oral health issues in long-term survivors and physical, economic, and psychosocial effects of treatment for head and neck cancers;

- **A prospective integrated survivorship care study** – This upcoming prospective study, which will open for enrollment in early 2012, is comparing integrated survivorship care support in addition to standard care with standard care alone. Patients in the post treatment period, following imaging and determination of complete eradication of disease, are eligible to participate. This study includes a range of sub-specialists focused on survivorship issues who are familiar with the participants’ prior treatment and expected acute and chronic toxicities.

Other services provided through integrated survivorship care will include an oral health plan, rehabilitation therapies (such as speech and swallow therapy), lymphedema therapy, and physical therapy. The survivorship division also will help navigate patients for additional services needed.

For more information regarding any of these studies, please contact Principal Investigator Sewanti A. Limaye, MD, at (617) 632-3090 or slimaye@partners.org.

Medical Oncologist Sewanti A. Limaye, MD, is leading numerous studies that address short- and long-term survivorship issues in patients with head and neck cancer and is establishing a new survivorship clinic within the Head and Neck Oncology Center.

Easy Access to Consults and Specialists
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researching biomarkers for HPV-associated oral cancer and survival and is being conducted in conjunction with the Johns Hopkins Bloomberg School of Public Health. The study is evaluating patients and their partners or spouses and includes both patients with HPV-associated and HPV-unassociated disease. Couples are followed longitudinally and provide a repository of study samples;

- **Tracking circulating tumor cells** – Patients with locally advanced oropharyngeal cancer are being evaluated for the number of circulating tumor cells before, during, and after cancer treatment;

- **Head and neck cancer tumor bank** – Dr. Lorch and Guilherme Rabinowits, MD, are collecting tumor and blood samples from patients with cancer of the head and neck, salivary gland, thyroid and/or skin, or patients with benign head and neck disease to populate a tumor bank designed to support future immunohistochemical investigations of novel cancer therapies. Additionally, the bank is expected to be beneficial in microRNA (miRNA) profiling of biopsy samples.

**Evaluating Genetic Information in White Blood Cells**

Dr. Lorch and Amin I. Kassis, PhD, Director of Radiobiology and Experimental Radionuclide Therapy at Harvard Medical School, are collaborating in a first-of-its-kind study designed to create a test for cancer by assessing circulating tumor cells through gene signatures found in the patients’ white blood cells. The test may be used to detect cancer in patients without a definitive diagnosis, assess a patient’s response to treatment, and track patients for signs of recurrence.

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Novel Technique to Restore Esophageal Patency

Occasionally, patients present with complete esophageal stenosis following head and neck cancer treatment. Head and neck surgeon Laura Goguen, MD, FACS, and her head and neck surgical colleagues, collaborating with thoracic surgeon Michael Jaklitsch, MD, FACS, are among few in the nation to perform combined antegrade and retrograde esophageal dilation (CARD), including patients who are referred from other centers. A retrospective review of 45 patients who underwent CARD at the Center between May 2001 and September 2008 supports this procedure as a viable option for patients with complete esophageal stenosis and an alternative to chronic gastric tube dependence or laryngopharyngo esophagectomy (Laryngoscope. 2010 Feb; 120(2):261-6).

Intraoperative esophageal patency was obtained in 91 percent of patients and resumption of oral intake occurred in 80 percent of patients. The majority of patients had their gastric tubes removed and resumed a soft or regular diet. Minor complications occurred in 29 percent of CARD procedures, including eight pneumomediastinum, seven GT site problems, two esophageal perforations, and one pharyngeal infection. All complications resolved spontaneously or with minimal interventions.

Pre-emptive Approaches to Swallowing Issues

Speech and Swallow Specialists Elaine Burke, MS, CCC-SLP, and Maria Puglia, MA, CCC-SLP, provide education and swallowing therapy for patients. Prior to the start of treatment, and during and after therapy, these specialists prescribe exercises for the jaw, tongue, tongue base, and the posterior pharyngeal wall to combat the effects of chemoradiation on these structures. These exercises are designed to help stretch and strengthen muscles and maintain range-of-motion in the jaw, tongue, and tongue base.

“We have found that those patients who follow the exercises at the beginning and throughout treatment and continue to eat or drink even small amounts of liquid or pureed foods during treatment are able to reduce dependence on gastric tubes and have them removed much sooner than patients who do not continue to work these muscles,” said Elaine Burke, MS, CCC-SLP.

Strategies related to diet, developed in conjunction with nutritionists in the Center, help patients to reduce the risk of aspiration when consuming foods or liquids. These include modifying types of foods and head positioning during swallowing. Patients also are evaluated using video swallow studies and fiberoptic endoscopic evaluation of swallowing (FEES), which are used to identify issues related to various stages of the patient’s swallow. Video swallow studies also identify esophageal strictures that are referred for dilation.

Long-term Support for Treatment Toxicities

Long-term support for patients includes a range of efforts to address swallowing issues, hormone changes, cardiovascular toxicities, dental concerns, and other issues. Speech and swallow specialists continue to address swallowing issues that occur after treatment is concluded, sometimes several years or more following treatment.

Easy Access to Consultations and Specialists

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