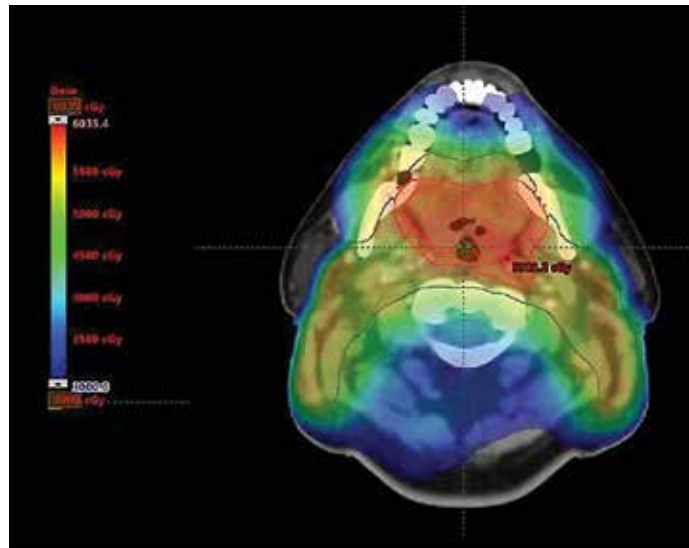


Quarterback 2: A Phase II Clinical Trial of Sequential Therapy and De-Intensified Chemoradiotherapy for Locally Advanced HPV-Positive Oropharynx Cancer

Marshall Posner, MD Professor, Director, Head and Neck Medical Oncology

The Quarterback trial is a radical, multidisciplinary research study to reduce short- and long-term side effects of radiation therapy in patients with locally advanced HPV-positive oropharynx cancer (HPVOPC). This is part of a broad clinical research effort at Mount Sinai's Head and Neck Cancer Research Program to create the safest and most effective therapies for patients with HPVOPC. It is known that locally advanced HPVOPC has a significantly better response, locoregional control and survival compared to non-HPVOPC after chemotherapy and radiotherapy.

The Quarterback trial compared reduced dose chemoradiation (rdCRT) after induction chemotherapy (IC) to standard dose CRT after IC in a randomized trial for advanced cancers not eligible



Example of reduced dose intensity modulated radiation plan for a patient enrolled in the Quarterback trial. The red area indicates higher doses delivered to the tumor, while the green and blue areas represent reduction of dosage to normal tissues.

for minimally invasive robotic surgery at Mount Sinai. Twenty volunteers were randomized, 8 to sdCRT with 7000 Gy and 12 to rdCRT with 5600cGy. As of June 2018, patients had been followed for a minimum of 3 years and an average >4 years. The progression free (PFS) and overall survival (OS) were stable after 2 years and were 87.5 percent for sdCRT (7/8) and 83.3 percent (log-rank test $p=0.85$) for rdCRT (10/12 patients) for both measures.

We performed quality of life (QOL) assessments, which demonstrated significantly better

QOL outcomes among the rdCRT patients compared to sdCRT. These results were reported in abstracts at the ASCO meetings in 2017 and 2018. We concluded that rdCRT had similar PFS/OS, compared to those receiving sdCRT. These results support the

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A Note from Department Chair Eric Genden, MD, MHA, FACS

This newsletter is focused on translating basic science research and novel treatment approaches into clinical practice. The Quarterback trial evaluating the de-intensification of chemoradiotherapy for locally advanced HPV-positive oropharynx cancer is the product of years of basic science research to understand the impact of radiation on cancer cells and the interaction of chemotherapeutic agents on radiation sensitization. Using technological advancements to accurately

locate thyroid metastasis or improve the accuracy of skull base surgery are just examples of the exciting work being done at Mount Sinai. These translational trials are changing the way we treat patients and offer reduced toxicity, smaller incisions, more rapid recovery, and in many cases, improved disease cure rates. Such research is impacting the care and quality of life of our patients. I hope that you will find value in our work and consider supporting our research mission.

Identification of Papillary Thyroid Cancer Micrometastases in Lymph Nodes Using a Multilevel Sectioning Protocol and the Potential Impact on Risk of Recurrence: **A Call for Standardization of Lymph Node Processing to The College of American Pathologists**

Mark Urken, MD, FACS, Co-Chief, Division of Head and Neck Oncology

The American Thyroid Association guidelines stratify patients based on various disease-related factors that predict their risk of recurrence. If classified as intermediate-risk, papillary thyroid cancer patients may be considered for further treatment with radioactive iodine, which carries multiple health risks. One classification factor for intermediate-risk of recurrence is the presence of micrometastases in greater than five lymph

nodes. However, determining the number of involved lymph nodes is not so simple and the extent of lymph node sectioning by a pathologist complicates this matter. Furthermore, there is no standard sectioning protocol for patients with papillary thyroid cancer on the cusp of intermediate-risk classification.

Mount Sinai researchers conducted a retrospective study to determine whether intensified, multilevel sectioning increases detection of micrometastases, thereby influencing the risk of recurrence and postoperative radioactive iodine decision-making. The study consisted of 17 patients who underwent total thyroidectomy for primary treatment of papillary thyroid carcinoma, from

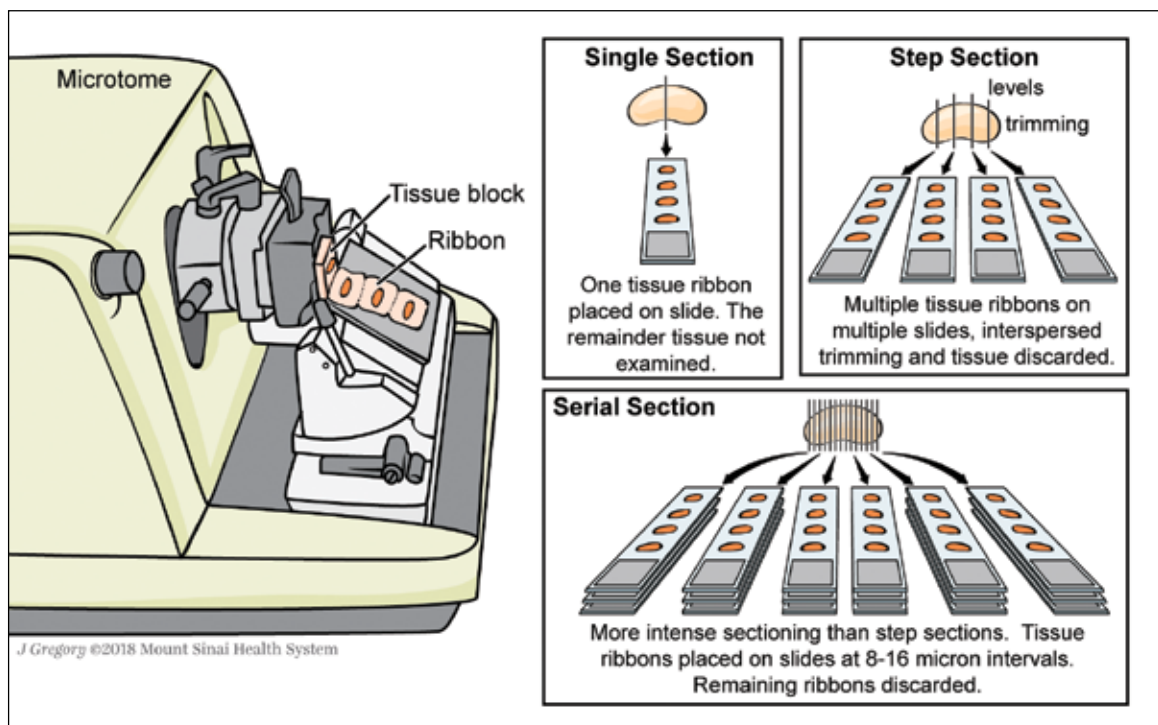


Figure 1. Diagrammatic representation of three histopathologic sectioning techniques: single, step and serial sections.

January 2010 to August 2017 at Mount Sinai Beth Israel with the following inclusionary criteria: a) ≥ 5 lymph nodes excised during thyroidectomy and b) ≤ 5 positive lymph nodes determined on initial pathologic analysis. Multilevel sectioning was performed on the original tissue blocks and reviewed by a senior pathologist.

Using the multilevel protocol, new lymph nodes were identified in 6 of 17 patients (35 percent). Multilevel sectioning yielded an additional 1.1 lymph node ± 0.9 SD per patient, compared to conventional sectioning (19.2 lymph nodes ± 14.9 SD vs. 18.1 lymph nodes ± 14.0 SD respectively; $p=0.03$, paired t-test). In total, we found 12 new lymph

nodes with metastatic disease. Six (50 percent) were found in newly identified lymph nodes and six (50 percent) were found in lymph nodes previously deemed negative by conventional sectioning. For three patients, the revised total number of positive lymph nodes was greater than five, thus reclassifying them as intermediate-risk of recurrence. Therefore, we propose that the multilevel sectioning method be adopted as the standard protocol for patients on the cusp of being upstaged, to ensure more consistent and accurate staging and risk stratification.

The role of 3D Printing and Immersive Simulation in the Surgical Planning of Skull Base Lesions in Endoscopic Endonasal Skull Base Surgery

Alfred Marc Calo Iloreta, MD, Rhinologist and Skull Base Surgeon

Surgical planning is crucial when using a minimally invasive approach, and appropriate and effective surgical planning done using 3D models may have the potential to decrease time under general anesthesia and allow surgeons to optimize their preoperative planning and surgical efficiency. The neurosurgery and otolaryngology teams at Mount Sinai's Skull Base Surgery Center have found success in using 3D models for surgical planning and image guidance for the endoscopic approach to complex skull base surgeries. Digital 3D models were used to highlight important bony landmarks and vessels in cases of odontoidectomy, Meckel's cave mass, and skull based adenoid cystic carcinoma. The models were used to validate future use of printed 3D models for tactile evaluation of surgical approach and adequate length of endoscopic tools.

Preoperatively, patient-specific segmented structures generated from radiological imaging and representative 3D models were printed within 72 hours. Structural models were printed at 1:1 scale in full color using a ProJet 660 3-D printer (Rockville, SC, 3D Systems). Costs for full-color models were less than \$500 per patient.

These models allowed surgeons to test various approaches, tools, and operative positioning in a patient-specific atmosphere. They could also be used as an instructional tool for teaching residents. Intraoperatively, Surgical Theater's 3D imaging technology, the Surgical Planner (SRP) and Surgical

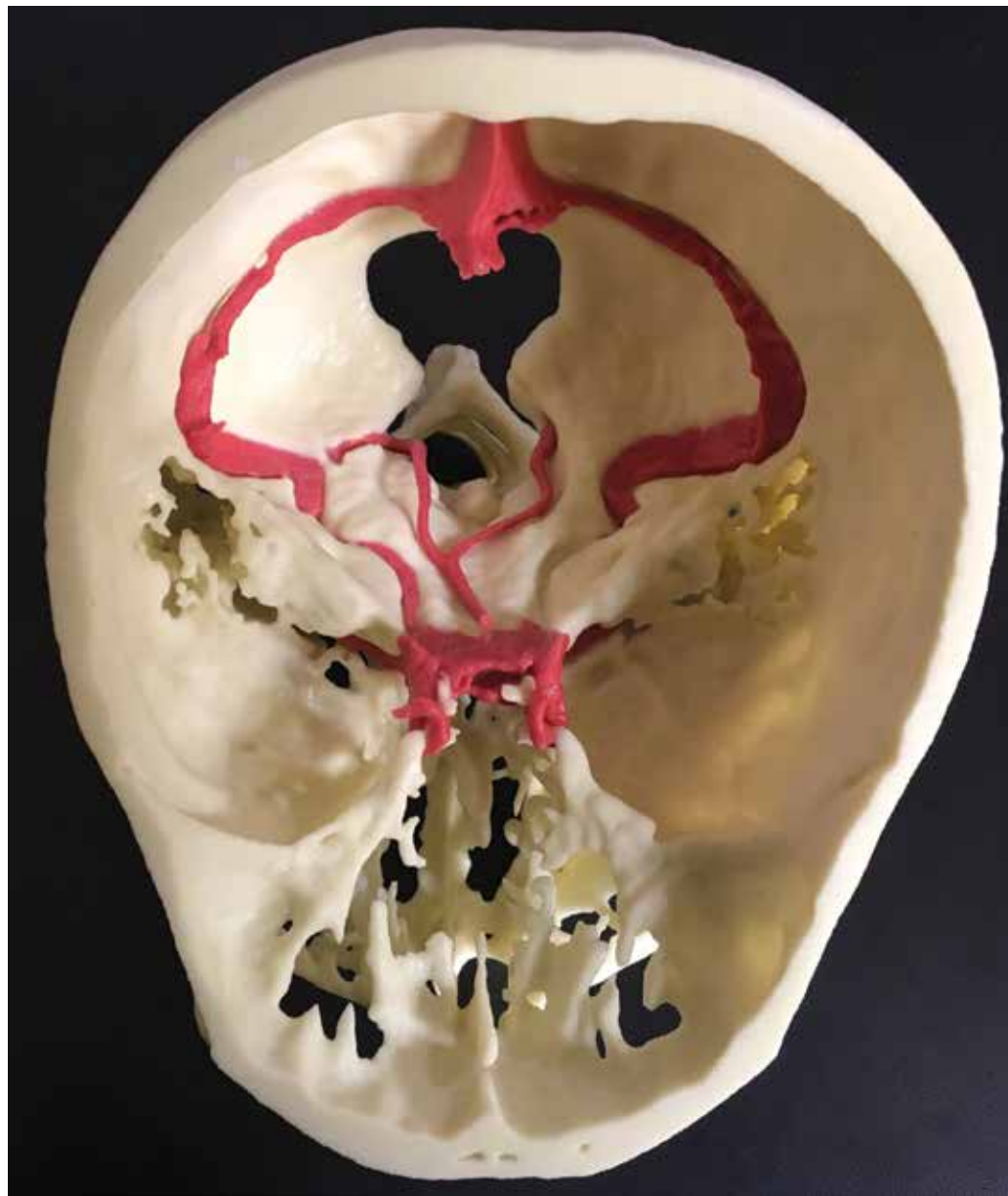


Figure 1. Surgical Theater 3D reconstruction images with neuronavigation and 3D printed model for endoscopic odontoidectomy.

Navigation Advanced Platform (SNAP) were used to create and simulate the otolaryngology and neurosurgical skull base approaches with a 3D model of the patient's anatomy and pathology.

As navigation with 3D imaging and 3D printing becomes more widely available, it may be considered in the surgical planning of endoscopic endonasal approaches to lesions associated with obscured or difficult anatomy.

Make a Gift...Make a Difference

The Head and Neck Cancer Research Program is designed to provide patients with access to cutting edge technology and state-of-the-art clinical trials. We need your help to continue pursuing our goals. Please select a sponsorship level and the study you wish to sponsor and make the check payable to: **Icahn School of Medicine at Mount Sinai**. Checks can be sent to:

Head and Neck Cancer Research Program

Attention: Leslie Waters-Martin
Research Program Manager
One Gustave L. Levy Place, Box 1189
New York, NY 10029

For questions, call **212-241-7107**
or email:
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- 1. Sinai Robotic Surgery Trial in HPV-Positive Oropharyngeal SCCA (SIRS) Trial
- 2. Role of Continuous Local Infusion of Ropivacaine for Postoperative Pain Management
- 3. Brief-Smell Identification Test Scores after Frontal Sinus Surgery: A Prospective Trial
- 4. Randomized, Placebo-Controlled Trial Looking at the Efficacy of Gabapentin for the Reduction of Pain after Uvulopalatopharyngoplasty (UPPP)
- 5. Epidemiologic Analysis of HPV-Related Head and Neck Cancer

1. Sinai Robotic Surgery Trial in HPV-Positive Oropharyngeal SCCA (SIRS) Trial

This non-randomized phase II de-escalation clinical trial aims to establish recurrence rates, site of recurrence, survival and quality of life outcomes for early T-stage HPV-positive oropharyngeal SCCA treated with upfront surgery.

Principal Investigators: Brett Miles, DDS, MD, FACS

2. Role of Continuous Local Infusion of Ropivacaine for Postoperative Pain Management in Patients Receiving Osseocutaneous Free Flaps

The goal of this study is to control donor site pain utilizing local, targeted analgesia to relieve discomfort at the donor site for osseocutaneous free flaps.

Principal Investigators: Brett Miles, DDS, MD, FACS

3. Brief-Smell Identification Test Scores after Frontal Sinus Surgery: A Prospective Trial

This activity aims to determine if frontal sinus surgery, including Draf IIa, Draf IIb, and Draf III, will increase nasal airflow to the olfactory epithelium, and, thus improve postoperative olfaction scores in patients with chronic rhinosinusitis.

Principal Investigator: Alfred Marc Ilorete, MD

4. Randomized, Placebo-controlled Trial Studying the Efficacy of Gabapentin for the Reduction of Pain After Uvulopalatopharyngoplasty (UPPP)

The goal of this study is to determine whether giving Gabapentin versus placebo for one week preoperatively and two weeks postoperatively will decrease the amount of pain experienced after UPPP.

Principal Investigator: Fred Lin, MD

5. Epidemiologic Analysis of HPV-related Head and Neck Cancer

This research is being conducted to further understand the role of the human papillomavirus (HPV) in people with head and neck cancer, as its role in other head and neck squamous cell cancers (HNSCC) are unclear.

Principal Investigator: Brett Miles, DDS, MD

Quarterback 2: A Phase II Clinical Trial of Sequential Therapy and De-Intensified Chemoradiotherapy for Locally Advanced HPV Positive Oropharynx Cancer *(continued from page 1)*

clinical benefit of rdCRT as a treatment option with comparable survival to the sdCRT with better QOL. All eligible patients are now being treated via a second study, Quarterback 2, with rdCRT, and our researchers are planning modifications of this trial in the future to explore even lower dose rdCRT and proton beam technology.

The results of this work indicate that we can achieve high survival rates in advanced HPV-related head and neck cancer, while minimizing the toxicity of therapy and long-term side effects for patients. All of this within the setting of the rigorous monitoring of a clinical trial. In the future, we hope to study biologic and genetic markers from the patients entered on these trials to predict which patients would benefit from reduced radiation and which patients require more aggressive therapy in order to improve outcomes.

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