

Head and Neck Oncology

Head & Neck Oncology Research

Danny Enepekides, Kevin Higgins, Antoine Eskander

The Sunnybrook Health Sciences Centre Head and Neck Oncology Division had a productive year with several clinical trials and research projects currently underway. The division has launched a research project in collaboration with the Department of Dentistry (Dr. Eszter Somogyi-Ganss) and Craniofacial Prosthetics Unit to create a survey on the satisfaction and use of craniofacial prosthetic devices.

This year, the department was also very pleased to welcome medical oncologist Dr. Martin Smoragiewicz to our team who will assist in overseeing several head and neck oncology clinical trials. Among those include a multicentre study which will explore the effects of high vs. low-dose cisplatin and N-acetyl cysteine (NAC) on ototoxicity for locally advanced head and neck squamous cell carcinomas (HNSCC). An exciting upcoming trial for first-line treatment in recurrent/metastatic HNSCC will examine a novel immunomodulatory agent in combination with Pembrolizumab and chemotherapy.

A few clinical trials have achieved successful recruitment this year in HPV-associated oropharyngeal SCC; most notably ORATOR II and HN.10 (EVADER), which examine de-escalation radiotherapy vs. trans-oral surgery, and de-escalation radiotherapy, respectively.

We are pleased to announce that Dr. Antoine Eskander received the New Investigator Award from the Terry Fox Research Institute and Canadian Institute of Health Research (CIHR). Dr. Eskander will receive \$445,000 over three years to conduct an exciting new research project that aims to explore symptoms in increasingly younger patients with HPV-related head and neck cancers as predictors of various factors including survival, cost of care,

emergency room visits and unplanned hospitalizations. Dr. Eskander has formal graduate appointment status and is on several thesis committees at the Institute of Health Policy, Management and Evaluation including co-supervision with Dr. Natalie Coburn of one of our own residents, Dr. Christopher Noel, on his PhD thesis.

Additional research projects under Dr. Eskander's care include a funded study examining self-harm and psychological distress in cancer patients, prediction of locoregional failure in patients with T3 larynx cancer, and several studies at ICES looking to assess the impact of COVID-19 on the cancer system.

Additional research under Dr. Kevin Higgins includes the creation of a surgical database, compiling the surgeries that included the use of free tissue transfer flaps into a singular dataset to better link the types of surgeries and free-flaps used in these procedures. Between July 1st, 2019 to June 30th, 2020, a total of 97 of these surgeries were performed at Sunnybrook. Another prospective research study examining the use and healing rates of Cytal™ Wound Matrix on skin graft donor sites following free-flap procedures is currently in progress.

Head & Neck Surgical Research

David Goldstein, Ralph Gilbert, Patrick Gullane, Dale Brown, Jonathan Irish, John de Almeida

The 2019–2020 academic year has been another productive and successful research year for the Wharton Head and Neck Cancer Surgery research program at the University Health Network. During this academic year the UHN surgeons had over 70 peer-reviewed publications accepted or in-press as well as authored nine book chapters. This past year also saw a number of successful grants being obtained by our UHN head and neck faculty, as either principal investigator or co-investigator, in the

amount of almost 3 million dollars, including two CIHR project grants, one CIHR operating grant and one CCS innovation to impact grant. Many local, national and international research collaborations continue in the areas of clinical and translational research.

There have been a number of notable research activities to report for this past academic year. The Finding/identifying primaries with neck disease (FIND) trial has successfully completed recruitment and closed, as has the multicentre study on comparison of quality of life between open vs endoscopic skull base using the Skull-base Inventory. We have completed a pilot window of opportunity study of immunotherapy prior to oral cancer surgery, the SNOW trial, with ten patients accrued. The Guided Therapeutics program also has a number of notable achievements that is presented separately.

The SELECT trial: A phase III randomized trial investigating the role of lymphatic mapping for management of the neck in oropharynx cancer was approved by the Canadian Cancer Trials Group and the EORTC to move forward with the study development. The Toronto Active Surveillance in low risk thyroid cancer study has been successfully recruiting and expected to complete accrual by December 2020. The CIHR and CCSRI sponsored Pan-Canadian Active Surveillance study has been initiated with representation of study sites across Canada, in addition to continued participation and collaboration from the many sites within and outside of the Greater Toronto Area.

We have continued active efforts in the assessment and rehabilitation of oral cavity cancer patients. We are piloting a biofeedback program at UHN using electropalatography to aid in oral rehabilitation of patients in their home through a computer link. There have been five patients who have completed the protocol and 4 patients actively enrolled. In a separate effort, we are tracking the speech and swallowing outcomes of patients who have undergone surgery, involving the oral cavity, to develop metrics that could guide oral cavity

reconstruction. There have been 60 patients that have completed the protocol and 18 patients enrolled. A pilot study evaluating the microbiome in oral cavity cancer patients to see if there is an association with an inflammatory response at the invasive front has been initiated with currently 19 people who are enrolled in the study.

Lastly, we want to highlight and acknowledge two very generous donations to support the head and neck cancer research program at the UHN. Firstly, the Shen Family Charitable Foundation support to develop a head and neck surgical database which will prospectively collect outcomes on surgical patients to complement the Anthology of Outcomes Head and Neck Database. The other is the Robertson Foundation donation to support the development of a head and neck surgical oncology trials program at the UHN.

The ORATOR trial led out of Western University by Dr. A Nichols and Dr. D Palma was presented at ASCO with the UHN site being one of the centres of accrual, been successfully recruiting, as well as being expanded to other Ontario centres. At the recent American Head and Neck Society and Triologic Society Meeting in Austin this year the UHN head and neck surgical team had 5 podium presentations and 7 research poster presentations. Dr. Mirko Manojlovic-Kolarski (PGY4) won a poster prize for best value poster for his poster titled “Cost-Effectiveness of Salvage Laryngectomy Closure Techniques”, Dr. Carissa Thomas (Head & Neck Fellow) won best poster for the AHNS for “Decision Regret in Older Patients Undergoing Head and Neck Surgery”, and Dr. David Goldstein won the *Harris P. Mosher Triologic Society Award* for excellence in a clinical thesis on “Frailty as a Predictor of Outcomes in Older Patients Undergoing Major Head and Neck Surgery”. Dr. Xiao Zhao (PGY5) successfully completed his PhD under supervision of Dr. Fei-Fei Liu, evaluating the role of metabolic regulation in the development of radiation induced fibrosis. This work resulted in a first-authored publication by Dr. Zhao in the very prestigious journal *Nature Metabolism*.

David Goldstein and Anna Sawka were awarded a CIHR Project Grant for Active Surveillance or Surgery for Primary Management of Very Low Risk Papillary Thyroid Cancer for (\$1,013,625); a CIHR Grant for planning a Prospective Active Surveillance Study for Low Risk Papillary Thyroid Cancer (\$10,000); and a Princess Margaret Department of Surgical Oncology Education grant to support a knowledge translation event on over diagnosis and overtreatment of Low Risk Papillary Thyroid Cancer (\$30,000).

Head & Neck Oncology Research

Ian Witterick, Christina Macmillan, David Fu, Ron Chazen, Anne Hsieh, Jeremy Freeman, Eric Monteiro, Allan Vescan

This year has been difficult because of the pandemic. However, we continue to focus on a number of clinical and basic science research projects. Clinical research projects focus on thyroid cancer outcomes. Basic science projects focus on molecular oncology to identify predictive/prognostic molecular signatures, their biological functional roles and signaling pathways that drive thyroid and head & neck cancers.

We use high throughput automated robotic screens to identify novel anti-cancer small molecules/compounds, and characterize their potential therapeutics. Integrating a variety of disciplines, we develop molecular biomarkers at microRNA, mRNA, DNA and/or protein levels through molecular analysis of human cancer tissues or biopsies. We aim to establish early diagnostic assays for identifying pre-cancer patient and prognostic assays for objectively evaluating the patient's overall outcome, and investigate novel therapeutic approaches that transform laboratory discoveries into improving cancer patient care for thyroid cancer and oral cancers.

Current projects this year included developing a molecular assay for detection and quantification of the BRAF mutation in residual tissue from thyroid FNA specimens and investigating Galactin-3 in distinguishing invasive encapsulated carcinoma from noninvasive follicular thyroid neoplasms with

papillary-like nuclear features (NIFTP).

Head & Neck Translational Program

Fei-Fei Liu

The Head and Neck Cancer (HNC) Translational Research Program at the Princess Margaret strives for a future where HNC can be cured without toxicity. This program has three main goals: 1) To understand HNC biology at the molecular, cellular, and tumour levels; 2) To elucidate the molecular and genetic bases of treatment toxicities in response to radiation, with or without chemotherapy; and, 3) To train young scientists and physicians in the scientific pursuits of understanding HNC. Our research team comprises of over 80 clinicians, scientists and research personnel, collectively working on several projects, including: tumour initiating cells, genetic determinants of outcome, biomarkers & novel drug discovery, proteomic studies, treatment of human papilloma virus (HPV) associated oropharynx cancer, and prognostic value of imaging-omic data.

Each year, our team publishes over 100 peer-reviewed publications in leading scientific journals. This year has seen numerous advances in HNC research. First, I would like to congratulate the Princess Margaret HN.10 Team on winning the highly prestigious 2020 CCTG Phase III Team Award for excellent accrual metrics including local activation time, and excellent compliance. HN.10 is an innovative, multi-institutional Phase II single arm trial that evaluates the effectiveness of elective volume adjusted de-escalation radiotherapy in patients with low-risk HPV-related oropharyngeal squamous cell carcinoma. Led by Dr. Scott Bratman, the multi-disciplinary and multi-professional team includes: Drs. Andrew Bayley, John Cho, Meredith Giuliani, Ezra Hahn, Andrew Hope, Ali Hosni, John Kim, Jolie Ringash, John Waldron, Andrea McNiven, Aaron Hansen, Lillian Siu, Anna Spreafico, John de Almeida, Eugene Yu, Ur Metser, as well as Pat Merante, Masoud Mohammadi, Andrei Rotarescu, Rehab Chahin, Jesse Abed, Maria Braganza, Zoe Doyle, Sarah Ramotar, and Vanessa Speers.

Next, congratulations to Dr. Brian O'Sullivan,

former Bartley-Smith Wharton Chair in Radiation Oncology (2009-2019) and renowned HNC researcher, on receiving the 2020 American Society for Radiation Oncology (ASTRO)'s Gold Medal Award! The Gold Medal is the society's highest honour, which recognizes individuals who have made exceptional contributions and impact within the field of Radiation Oncology through their research, clinical care, teaching and service.

Finally, a research team led by Drs. Fei-Fei Liu, Xiao Zhao (former head-and-neck surgery resident) and

Jennifer Kwan (radiation oncology resident) published a high impact review in *Nature Reviews Drug Discovery*, which discusses evidence to date on targeting metabolic dysregulation for fibrosis therapy and describes novel opportunities for drug discovery and therapeutic development. Radiation-induced fibrosis is a long-term side effect that can significantly compromise patients' quality of life, particularly for HNC patients. The team also received an Innovation to Impact Grant from the Canadian Cancer Society to develop anti-fibrosis treatments to improve cancer survivorship.