Réseau de cancérologie Rossy
Rossy Cancer Network

# Marching Ahead: Imaging Biomarkers, a New Revolution in Patient Management and Care for Human Papilloma Virus (HPV) Positive Oropharyngeal Cancer

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## INTRODUCTION

Squamous cell carcinoma (SCC) of the head and neck region is the sixth most common cancer diagnosed worldwide. There is an increasing incidence of Human Papilloma Virus (HPV)-related Oropharyngeal Squamous Cell Cancer (OPSCC) especially in the younger patient population. HPV-positive OPSCC is a distinct clinic-pathological entity associated with better prognosis than HPV-negative OPSCC.

Texture Imaging, which evaluates the gray-level intensity, position of the pixels, and arrangement and interrelation among voxel intensities could potentially be used to differentiate between P16 positive and negative OPSCCC and their subtypes

## OBJECTIVES

The purpose of this study is to develop a mathematical texture model based on Texture Imaging for oropharyngeal cancer to categorize patients into P16 positive and P16 negative and their subtypes which would enable us to modify/plan/individualize treatment.

## METHODS

**Patient Cohort:.**

Subsequent to research ethics board (REB) approval 40 patients between 18-90 years of age with newly diagnosed biopsy proven stage III or IV HPV-positive Oropharyngeal Squamous Cell Cancer referred for treatment to the McGill University teaching hospitals –McGill University Health Centre (MUHC) and Jewish General Hospital (JGH) are being recruited into our study.

**Imaging Techniques:**

i) CT examination: Examination will be performed on 64 slice GE CT scanner at the MUHC or JGH. Axial 4mm images will be obtain from the skull base to the thoracic inlet with patient in supine position and quiet breathing after intravenous injection of contrast. Reformatted sagittal and coronal images would also be obtained.

ii) MRI examination: Examination will be performed on 3Tesla Siemens MRI scanner at MUHC using neck array coils. Exam will include T1 and T2 weighted, Turbo Spin Echo (TSE sequence) followed by an echo-planar Diffusion weighted Imaging sequence before injection of contrast. The echo planar Diffusion weighed sequence will have b values of 0, 500 and 1000s/ mm2.All axial sequences will be performed from base of the skull to the supraclavicular region covering the primary tumor and the different nodal groups.

Dynamic Contrast Enhanced (DCE) Perfusion will be done after infusion of contrast followed by T1WTSE sequence in the axial, sagittal and coronal planes. Post- processing of the images would be done to obtain Apparent Diffusion Co-efficient (ADC) and perfusion maps.

Follow-up MRI would be done after 6 months of treatment to access response to therapy.

**Tumor Volume Definition:**

Contours defining the 3D tumour region for each patient were manually drawn slice-by-slice on T2W images using FDA approved ”OsiriX MD” software on an iMac by an experienced Neuroradiology fellow which was then assessed independently by a fellowship trained experienced Neuroradiologist.

## METHODS / INTERVENTIONS

**Image Data Pre-Processing and Texture Extraction:**

Prior to texture analysis MRI DICOM data were transferred into MATLAB (The Math Works Inc., Natick, MA) format using the software CERR. All subsequent analyses were performed in MATLAB. MRI scans were kept in raw data form, and voxels within the tumour region with intensities outside the range $\mu \pm 3\sigma$ were rejected and not considered in subsequent texture computations.

Forty-two textures (3 global and 39 high order features) were extracted at 4 different resolutions (0.5 mm,1 mm, 2 mm, 3 mm), using 4 different number of gray-levels (8, 16, 32, 64) from contoured tumor region on the CT/MRI images.

The construction of prediction models for prediction of P16 positive or negative status from the combination of different textural features was performed using 100 bootstrap samples (100 training and testing sets) and logistic regression.

## RESULTS

**”Study in Recruiting Phase”. Ten patients have been recruited for the study till date.**

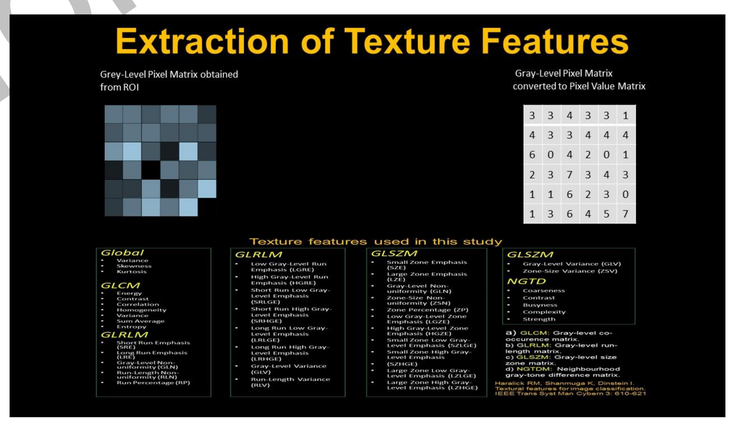
Texture features would be incorporated into multivariate logistic regression (LR) models for prediction of P16 positive and negative status using the equation;

$$P(y_i = 1|\mathbf{x}_i) = \frac{\exp[g(\mathbf{x}_i)]}{1+\exp[g(\mathbf{x}_i)]}, \qquad g(\mathbf{x}_i) = \beta_0 + \sum_{j=1}^{p} \beta_j x_{ij},$$

**probability of the outcome status**

$$\text{for } i = 1, 2, \ldots, N,$$

where the vector of input variables (imaging data) of the I th patient is xi = {xij ∈ R : j = 1, 2,..., p}, for a number N of patients.




## PATIENT IMPACT

In patients with P16 positive tumors, based on subtype, the amount of radiation dose administered could be scaled down significantly without hampering prognosis. Since most of these patients are young with severe toxicity from chemotherapy and radiotherapy, this would help them to lead better quality of life. The treatment for P16 positive tumors is considerably less aggressive than that for P16 negative tumors.

In P16 negative patients, where more aggressive treatment is warranted, radiotherapy and chemotherapy protocols can be modified depending on the various different “texture subtypes” which shall be discovered with the maturation of this new imaging technique. If texture imaging is able to subdivide P16 negative tumors into further subtypes, each tumor subtype can be treated in a tailored fashion. This promises to better individualize therapy in the future, and spare patients unnecessary toxic treatments.

## CONCLUSION

Texture imaging, a novel imaging technique, has the potential to be a non-invasive alternative to biopsy in the determination of P16 status. It has wide reaching implications for patient care, particularly given the increasing incidence of HPV positive Oropharyngeal Cancer in the past decade.

The ultimate objective of “Personalized Medicine” in Head and Neck Oncology care can be achieved by the application of a mathematical “texture model” prospectively in a large multicenter clinical trial in an attempt to tailor therapy, based on gene expression decoded by texture signature.

Questions

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