Spectral Dual Energy CT and Textural Radiogenomic Analysis for Optimal Tumor Delineation, Patient Staging and Biomarker for Head and Neck Squamous Cell Carcinoma

Reza Forghani, MD, PhD; Maryam Bayat, MD; Léon van Kempen, PhD; Michael Hier, MD; Alex Mlynek, MD, MSc; Louise Rochon, MD; Sabrina Da Silva, PhD; Mark Levental, MD; Khalil Sultanem, MD; George Shenouda, MD; Benoit Gallix, MD

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INTRODUCTION

Imaging is essential for accurate determination of the anatomic extent and stage of head and neck squamous cell carcinomas (HNSCC). Currently, the information on CT and MRI scans is mainly used for the evaluation of anatomic extent and stage of tumor. There is increasing evidence that dual-energy CT (DECT), an advanced CT technique, can improve diagnostic evaluation of HNSCC. There is also increasing interest in evaluation of tumour texture, known as radiomic analysis, using advanced software in order to derive additional clinically relevant information such as predicting molecular composition, prognosis, and response to treatment, providing an additional step towards personalized therapy.

OBJECTIVES

Objective 1: Prospectively evaluate and demonstrate that DECT improves assessment and hence local staging of HNSCC compared to conventional CT equivalent (65 keV) images. Comparison will also be made to MRI (current gold standard imaging with the greatest soft tissue contrast – will also be used as standard in non-surgical cases) and surgical-pathologic findings (absolute gold standard, used for surgical cases).

Objective 2: Perform advanced tumor texture analysis and correlate with the tumor gene expression profile in order to identify a radiogenomic signature as a biomarker for different HNSCC subtypes. This type of image analysis and phenotype-genotype correlation has the potential, in the future, to provide additional information on the tumor that currently is only available by invasive tissue biopsy and molecular analysis beyond current standard of care.

METHODS / INTERVENTIONS

35 HNSCC patients will be prospectively recruited: oral cavity (surgical, n = 10), oropharyngeal tumors planned for TORS (surgical, n = 10), and larynx (surgical or non-surgical, n = 10) and will be followed up for a minimum of 5 years. All patients will undergo a DECT scan of the neck and an MRI. The following will be evaluated in a blinded fashion independently by at least 3 different head and neck radiologists: (1) 65 keV virtual monochromatic images (VMIs) - equivalent to single energy CT acquisition, (2) DECT set (65 keV, 40 keV, 95 keV, and 140 keV VMIs; iodine overlay map), and (3) MRI.

Tumor visibility, image quality, diagnostic confidence, and radiologic T and N stage will be validated.

Validation will be done by confirmation of 3 to 5 predetermined landmarks during surgery as well as on histopathological evaluation. The process will also be used to direct specimen collection from the tumors for gene expression analysis using the NanoString™ nCounter® Analysis System. Texture analysis will be performed using a commercial software (TexRAD).

RESULTS

Current Status – Patient Recruitment

We have so far enrolled 11 eligible patients, all of them in the surgical category. The DECT-DECT-MRI comparison is done in blinded fashion and will be revealed at a later time point. An example of DECT improving tumor visibility from our earlier work is provided in Figure 1. The molecular gene expression analysis will be done in batches. We will be conducting the first batch analysis soon.

Figure 1. Example of tumor appearance on 40 keV and 65 keV VMIs from a patient with a small tumor involving the anterior commissure of the larynx. (A) 65 keV (similar to low-kV dual energy CT) and (B) 40 keV VMIs are shown. Note the increased tumor visibility on the 40 keV VMIs.

Procedure

A rigorous process for correlation of imaging, surgical, and pathologic findings as well as biobank specimen harvesting is key for this project. Preoperatively, 3-5 landmarks are selected in conjunction with the surgery team that are then validated in the OR and on pathology.

In addition, members of the imaging team present to the pathology area at time of harvesting of biobank specimen for “narrowing” the radiomic target corresponding to the resected specimen. This is assisted with 3D models and video recordings.

The radiomic analysis pipeline for spectral/multienergy analysis has been set up and tested using a retrospective dataset (Figure 3).

Figure 2. Example of an oral tongue SCC hemiglossectomy specimen (double arrowheads). A 3D “mold” (arrow) is used to orient and help identify the site of biopsy specimen resection for future radiomic analysis. This was assisted by video recordings (not shown). inset shows an image of the tumor post biobank sample harvesting. Note the defect (arrowhead) at site of resection.

Figure 3. Set up of texture/radiomic analysis pipeline. The analysis pipeline has been set up using a retrospective dataset of HNSCC patients. In the example shown in a preliminary dataset, texture features of the primary tumor are used to predict the presence of lymphadenopathy. Note relatively high accuracy as well as improved performance of multimodality dataset compared to conventional single energy CT equivalent 65 keV reconstructions alone.

Figure 4. ROC - Lymphadenopathy Untreated - 65 keV

False positive rate
True positive rate
0.0 0.2 0.4 0.6 0.8 1.0
0.0 0.2 0.4 0.6 0.8 1.0

PATIENT IMPACT

Patients enrolled in this study are receiving state-of-the-art work-up using the most advanced imaging techniques and exemplary multidisciplinary evaluation. The results of this study have the potential to enhance non-invasive diagnostic work-up of head and neck cancer patients and generate new imaging biomarkers with the potential to predict molecular composition, treatment response, and outcome, further helping advance personalized cancer therapy.

CONCLUSION

This investigation represents a fusion of state of art approaches for diagnostic evaluation of HNSCC patients.

First, the study will prospectively evaluate and compare DECT with conventional single energy CT equivalent reconstructions and MRI for initial work-up of HNSCC. So far, retrospective data suggest that there is added value of DECT and we expect this to be shown as well in this prospective, blinded study.

The second part of the study will use advanced image texture/radiomic analysis and correlate with the gene expression profile and outcomes. The aims of this part of the study are to determine unique non-invasive tumor radiogenomic signatures that can potentially be used as a biomarker to predict tumor behavior, prognosis, and even guide individualized therapy.

Successful completion of this project has the potential to enable the use of information available on medical images to predict, at least in part, tumor gene expression profiles that would otherwise only be possible by invasive tissue biopsy and extensive and costly gene expression analysis. Preliminary analysis of spectral texture analysis using a retrospective dataset is promising and supports the viability of this approach.

The stratification of HNSCC using radiogenic signatures can potentially be used to predict response to treatment and help guide therapy, enhancing the value of imaging for phenotype-genotype correlation and individualized therapy.

TRANSLATION ACROSS THE RCN

If the value of DECT for HNSCC evaluation is confirmed prospectively, then this may be used for future resource planning, making sure that the technology is available and used at major cancer centers for work-up of HNSCC patients. Successful completion of the radiogenomic part of this study may provide the basis for implementation and development of a multidisciplinary radiomic group involving the Department of Radiology and other interested departments at McGill wide research support and potentially clinical applications in the future.