Glucose Chemical Exchange Saturation Transfer (GlucoCEST) MRI in Human Papilloma Virus (HPV) positive oropharyngeal squamous cell carcinoma (SCC) treated with radical radiotherapy (RT)

Poster No.: C-3085
Congress: ECR 2018
Type: Scientific Exhibit
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Keywords: Cancer, Radiation effects, Imaging sequences, MR-Functional imaging, Head and neck
DOI: 10.1594/ecr2018/C-3085

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Aims and objectives

Imaging is a vital component of the head and neck cancer management pathway, used for diagnosis, staging, treatment planning and response assessment. In addition to anatomical MRI, FDG-PET is used routinely but it is time-consuming and involves ionising radiation. MRI is superior to other imaging modalities in terms of its ability to perform multiparametric tissue characterisation and in addition does not involve ionising radiation. Functional MRI, combining physiological information with anatomical detail, is ideally placed for use in adaptive radiotherapy planning, with further potential to assess the effects of treatment and evaluate the actions of targeted therapies.

Chemical exchange saturation transfer (CEST) MRI is a novel sequence which provides a means of inducing image contrast proportional to the local concentration of compounds through the saturation of off-resonant exchanging protons (1). This can be the result of either endogenous or exogenous agents, and provides a mechanism by which specific biomarkers of disease can be imaged (2). CEST imaging using glucose as a contrast agent (glucoCEST) was found by Walker-Samuel et al. (3) to be comparable to FDG-PET autoradiography in human colorectal tumour xenograft mouse models. CEST images have been successfully acquired in patients with head and neck cancer by Wang et al (4).

The aim of this single centre study is to evaluate the feasibility of using glucose CEST (glucoCEST) MRI to assess oropharyngeal carcinomas during radical radiotherapy.
Methods and materials

Patient population: A prospective, single-centre study is recruiting 20 patients with human papilloma virus (HPV) positive oropharyngeal squamous cell carcinoma undergoing radical radiotherapy (RT) +/- systemic therapy. An interim analysis was undertaken after 4 patients who underwent scans at baseline and after 2 weeks radiotherapy.

Data acquisition: All MRI examinations were performed using 3 Tesla GE Signa MRI scanner (GE, USA) with an 8 channel neurovascular coil receiver. A single slice CEST sequence through the tumour and/or involved node was acquired between ±5 ppm (glucose resonances oversampled at 1.2 and 0.8 ppm). Images were taken without contrast and during an 0.08 ml/s, 20% glucose infusion, preceded by a 50 ml, 50% glucose bolus.

Data analysis: The region of interest (ROI) was outlined by a radiologist specialising in head and neck cancers (NT) on ITK-SNAP (5) on T2-weighted axial images. Using custom scripts developed in MATLAB (Mathworks, USA) by AS and BB, the T2 image and ROI were transformed and registered to the CEST scans. CEST parameter maps for each voxel were generated and Mean Magnetisation Transfer Ratio (MTR) asymmetry was determined. Comparison between means was undertaken given the small sample size.
Results

Four patients with tonsillar primaries (T-stage 1-3, N-stage 1-3) were recruited. All four patients were male, with median age 54.5 (range 43-69). Four had baseline and three had on-treatment imaging with no adverse events reported. CEST imaging was not done on treatment for one patient due to software updates requiring reinstallation of the CEST sequence. All patients had stable or minor visible reduction of the ROI on anatomical imaging between baseline and week 2 RT.

At baseline, mean tumour MTR was 1.20 (Standard Deviation [SD] 0.95, n=2), which rose with glucose infusion to 1.94 (SD 1.03). However, for nodal disease, mean MTR fell with glucose from 1.08 (SD 1.23, n=2) to 0.80 (SD 0.49).

In one patient (Figures 1-3), mean tumour MTR fell after two weeks RT from 1.18 (SD 0.47) to 0.94 (SD 0.18). Similarly, with glucose infusion the mean MTR was 2.16 (SD 0.57) at baseline and 0.77 (SD 0.57) on treatment. FDG-PET uptake at baseline was visually comparable to glucoCEST.

However, another patient with bulky nodal disease showed no change in mean MTR of 0.90 between baseline (SD 0.88) and week 2 RT (SD 0.71). With glucose infusion, mean MTR rose from 0.75 (SD 0.66) to 1.06 (SD 0.8) during RT.

Blood glucose levels (mmol/L) were taken using a FreeStyle Optium Neo H meter (Abbott Laboritories, Maidenhead, UK). All patients had fasted for at least 4 hours before imaging. Mean pre-scan blood glucose was 5.4 (SD 0.6, n=4) at baseline imaging and 5.8 (0.6, n=3) for on RT scan. This rose to 10.4 (SD 1.4, n=4) and 11.8 (SD 2.5, n=3) following glucose bolus and infusion.
Images for this section:

Fig. 1: IDEAL T2 MRI with tumour ROI outlined in red

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**Fig. 2:** Baseline FDG-PET/CT scan

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Fig. 3: GlucoCEST MRI mean MTR* (%) of tumour at baseline and week 2 radiotherapy with and without glucose infusion

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Conclusion

The purpose of this study was to assess the feasibility of glucoCEST MRI in patients having radiotherapy for head and neck cancer, where PET scanning for staging and response assessment is becoming standard.

This interim review demonstrated that glucoCEST MRI was tolerated well by participants and there were no adverse effects secondary to the glucose infusion.

There was evidence of a change in CEST MTR from baseline to week 2 RT both without and with glucose infusion. The rise in mean MTR with glucose from baseline in one involved node may have been due to combining the rim of active tissue with necrotic core. Distribution of MTR rather than mean is being investigated.

Further work will include completing recruitment of a planned 20 patients and scanning patients post radiotherapy, which will be compared with FDG-PET/CT response assessment.
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