Title: Is MRI a useful modality to measure pharyngeal oedema following chemoradiation?
Funded by the ANZHNCS foundation 2016
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Summary of Project

Internal lymphoedema of pharyngeal structures is a common sequela of head and neck cancer treatment impacting on short and long-term swallowing function. Our aim with this seed funding was to assess the utility of MRI in the evaluation of oedema severity and the resultant effect on swallowing function. While anatomical changes on MRI have now been documented including their relationship to dose, these anatomical changes have not been correlated with long-term swallow function. MRI anatomical changes were used to see if there is a dose relationship in the pharyngeal constrictors and determine a threshold dose above which changes appeared to be more pronounced. Further, using the Sydney Swallow Questionnaire (SSQ) and Functional Oral Intake Score (FOIS), we identified that important changes in swallow function that may relate to radiation related damage to the pharyngeal constrictors and cricopharyngeus as seen on MRI scans.

Method

Fifteen consecutive patients with biopsy proven squamous cell cancer of the head and neck treated with definitive radiotherapy, with or without chemotherapy were enrolled into this pilot study. Prior surgery was not an exclusion criteria, however, all patients had to be treated to a dose of 70Gy in 35 fractions. Patients were excluded if they could not undergo MRI scans for medical or personal reasons or if they could not complete the Sydney Swallow Questionnaire at 1 year. All patients were treated with IMRT or VMAT radiotherapy with areas of macroscopic disease were prescribed 70Gy in 2Gy per fraction. Areas of equivocal disease were treated to 63Gy and clinically uninvolved areas of the neck that were considered to be at risk of microscopic disease were given 56Gy. All but one patient was treated with concurrent chemotherapy (cisplatin) or biological therapy (cetuximab). Swallowing function was measured using the SSQ and the FOIS. Pre and post treatment MRI enabled accurate measurements of both the muscle/structure thickness and volume of both the pharyngeal constrictors and the epiglottis, structures critical to an effective and safe swallow.

Results

Pharyngeal Constrictors (PC) - Superior Pharyngeal Constrictors (SPC), Middle Pharyngeal Constrictors (MPC) and Inferior Pharyngeal Constrictors (IPC) and Cricopharyngeus (CP)

Dosimetry to swallowing structures The average mean doses to the swallowing structures were as follows – combined pharyngeal constrictors (SPC, MPC and IPC) = 60.68Gy (range 55.97-62.49Gy), SPC = 61.57Gy (range 53.52 – 64.62Gy), MPC = 60.13Gy (range 51.62 – 68.14Gy), IPC = 56.29Gy (range 50.43 – 67.33Gy), CP = 54.4Gy (range 44.46 – 59.82Gy) and epiglottis = 60.84Gy (range 50.84 – 71.34Gy).

Changes in muscle volume during treatment The volumes and thicknesses of SPCs and epiglottis were carried out in all 15 patients however, the MPCs were assessed in 12/15, the IPCs in 10/15 and the CP in 9/15 because the MRI studies did not cover the full extent of these structures in either the pre or post radiotherapy scans. All of the pharyngeal constrictor groups had significant increases in mean volume and mean thickness after radiotherapy treatment. The greatest volume differences were in the SPC with a mean increase of 5.9ml 95% CI [4.2, 7.6] ($p<0.00001$) and this was most likely due to the extended length of this structure compared to the other PCs.

Association between dose and change in muscle thickness The changes in mean thickness of all of the PCs was similar, between 1.9 - 2.6mm. Submucosal thickness was also increased in MPC and IPC by 3.2mm 95%CI [1.8, 3.5] and 1.4mm 95%[0.4, 2.3] respectively, but not in in CP, 0.5mm 95% CI [-0.3, 1.3] ($p = 0.183$). Interestingly, the epiglottis did not change significantly in mean thickness or volume

following radiotherapy. Qualitatively, however, the epiglottis changed shape after treatment, becoming shorter and wider, a feature not captured by volume and mean thickness measurements made in this analysis. The association between change in mean thickness and the mean dose received by the structures was evaluated, there was only a positive association in SPCs. For every 1Gy of dose, the mean SPCs thickness increased by 0.14mm [95% CI -0.002 to 0.29] (p=0.002). For MPCs, the inverse was observed with their thickness decreasing by 0.14mm 95% CI [-0.27, -0.013] (p=0.035) with every unit of dose. For the other structures there was no significant association between change in muscle thickness and dose.

Long term swallow function outcomes

At three months following radiotherapy, two patients were gastrostomy dependent with Functional Oral Intake Scale (FOIS) scores of 3. By 6 months after therapy, all patients were on an oral diet (FOIS 6-7), with only one patient requiring special food preparation. In our cohort, four patients had an abnormal SSQ score (>234) at 1-year post radiotherapy indicating some degree of swallow dysfunction and 3 patients had upper oesophageal strictures requiring dilatation. There was no significant correlation between 12month SSQ scores and the changes in thickness or volume of the swallowing structures in this study.

Discussion

In this retrospective analysis, we have identified that important anatomical changes occur to the PCs and CP following radiotherapy to the pharynx as seen on MRI scans. We suspect that early identification and acknowledgement of these changes could lead to beneficial early focused intervention. Whether this is in terms of intensive swallowing exercises, lymphoedema management, focus on reducing acute radiation mucositis or through early oesophageal dilatation is yet to be investigated. However, we believe that these are interesting and important avenues for exploration. The results of this study helped us to elucidate the methodological challenges related to using MRI as a measure of pharyngeal oedema. Moving forward, we propose to assess thicknesses and volumes of the PCs after radiotherapy prospectively, acquiring MRI scans that cover all of the organs of interest and scanning patients with immobilisation masks in the radiotherapy position. Importantly information obtained from the results funded through this research has been used to inform further grant writing for competitive grants from our unit.

Academic output: Oral presentation ANZHNCS ASM 2017; Results referenced in future grant writing;