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Optimising volumetric arc radiotherapy for dental rehabilitation in oropharynx cancer – A retrospective dosimetry review and feasibility planning study

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ABSTRACT

Purpose: To assess the dosimetry to dentally relevant substructures within the mandible/maxilla, establish the predictors of increased mean anterior mandible dose and assess the feasibility of rationale optimisation of dose to the anterior mandible (AM) volume to aid reconstructive dental surgery planning, where the AM is a critical structure.

Materials and methods: In a cohort of radically treated oropharynx cancer patients we conducted a retrospective dosimetry analysis of mandible/maxilla volumes, created using a published atlas. Comparisons of mean AM dose and clinical parameters between groups were tested using Wilcoxon rank-sum and Kruskal-Wallis tests. A multivariate linear regression model was created to assess independent predictors of increased mean AM dose. Patients with a mean AM dose over 37.5 Gy were included in feasibility planning study to test the hypothesis that it is possible to safely limit the dose whilst maintaining dose tolerances for other organs at risk.

Results: 57 patients were included. Median AM mean dose was 32.2 Gy (IQR 27.7–38.7). T stage, N stage and inclusion of Level 1B were significantly associated with increased mean AM dose. Only T stage ($p = .0132$) and Level Ib inclusion ($p = .018$) remained significant in the linear regression model. 88% of plans, all of which included Level Ib, were successfully re-optimised without breaching accepted constraints.

Conclusions: Oropharynx cancer patients with advanced T stage and who require Level Ib treatment receive increased mean AM dose, potentially limiting surgical dental rehabilitation options. The majority of patients can be optimised safely with appropriate AM contouring.

Introduction

Squamous cell carcinomas (SCC) of the oropharynx are potentially curable cancers with surgery, radiotherapy, chemoradiotherapy or a combination of the same [1]. Three year survival rates up to 82% are reported, and are best in Human Papilloma Virus (HPV) related disease [2], meaning that survivorship issues are now increasingly important. In a UK head and neck cancer follow up clinic almost 30% of patients complained of ongoing dental issues relating to pain as well as poor functional dental consequences, reported by both dentate and edentulous patients [3]. These effects are confirmed in long term follow up of those who have survived 5 years or more from their diagnosis and can affect many aspects of their quality of life [4].

Successful dental rehabilitation is possible as part of a holistic multidisciplinary approach involving Radiation Oncologists and Restorative Dentists. The oral environment is often compromised by radical treatment which results in altered anatomy, trismus and xerostomia, all of which complicate successful dental rehabilitation. The anterior aspect of the mandible and maxilla is particularly important for existing or planned edentulous patients. For edentulous patients there is now clear guidance that dental implants strategically placed in the anterior mandibular are the standard of care [5]. High retention rates, excellent life span and improved quality of life all indicate that dental implants should now be considered for all patients. Randomised clinical trials have shown that patient reported outcomes in general and oral related quality of life outcomes are improved [6,7]. However failure rates of the implants are a legitimate concern, particularly in areas which have received doses in excess of 50–60 Gy [8–10].

At our centre, all patients who undergo radical head and neck radiotherapy are evaluated by a Consultant in Restorative Dentistry.

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Patients with poorly controlled primary dental disease (dental caries and periodontal disease) in areas expected to receive doses of 60 Gy or more are advised to have dental extractions. At presentation, it is difficult to predict where high dose areas will fall as this is before the radiotherapy treatment volumes are created, the plan optimised and the dose distribution finalised. Therefore, patients can have significant dental interventions planned based on dose estimations which may be inaccurate.

The most consistent recommended dose constraint is a maximum dose of 70 Gy to any point in the whole mandible [11] but there is no evidence for a dose constraint when the mandible is a planned surgical field. Furthermore Restorative Dentists are more concerned with the dose to the subsections where reconstructive implants will be inserted, namely the anterior mandible. Previous studies have attempted to address this by publishing retrospective dose distributions on either a tooth-by-tooth basis or a mandibular volume basis [12–15]. Whilst useful, they lack a shared definition of regions of interest, in particular the anterior mandible. They also combine tumour sub-sites, dose prescriptions and dose solutions [Intensity Modulated Radiotherapy (IMRT) and Volumetric Arc Therapy (VMAT)] making general conclusions difficult.

One small study suggested that it is dosimetrically possible to spare the anterior mandible using an IMRT solution [16]. However their dosimetry (D_{max} and D_{mean}) is based on five point estimates in the region between the left and right mental foramen, with no orientation in three dimensional space such as distance from the crest or information about dose in between these points. In addition, no information is provided on where the 'spared' dose has been pushed to following the reduction in the anterior mandible and the consequent increase in doses to other organs at risk (OAR).

We first aim to describe the distribution of dose to relevant tooth-bearing and potentially implant-bearing volumes of the maxilla and the mandible [17] in a radically treated oropharyngeal population. Secondly we undertook a feasibility planning optimisation study. In the absence of an accepted standard volume based constraint, we chose published dose parameters which suggest an lower risk of osteoradionecrosis (ORN) in patients who received a mandible V50 of 30.8% and a mean dose of 37.5 Gy [18]. These rates are further supported by data from post radiation dental lesions which showed that rates of moderate/severe damage were 2–3 times higher following 30–60 Gy, but this effect was most significant above 40 Gy [19].

We hypothesise it is possible to safely limit the dose administered to an anterior mandible volume with rational optimisation of the radiotherapy treatment plans whilst maintaining dose tolerances for other organs at risk.

Methodology

Audit

A retrospective audit was approved by Oxford University NHS Foundation Trust. We reviewed all radically treated head and neck patients from March 2014 until March 2015. The inclusion criteria were patients over the age of 18, with an oropharyngeal primary squamous cell carcinoma, who had completed treatment with radiotherapy to dose of 65 Gy in 30 fractions. Only patients treated using a VMAT dose solution were included. Treatment records were reviewed for age, primary site, tumour size, nodal stage, whether dentate or edentulous, p16 status, inclusion of level 1b in the planning target volume (PTV), whether ipsilateral or bilateral radiotherapy was used and, finally, use of cisplatin or cetuximab.

The CT dataset was modified to included six new structures. The volumes were outlined using published guidelines [17] and standard CT bone window settings (width 1600, length 800HU). All outlining was performed by a single researcher to minimise inter-observer error. The first five consecutive patients' volumes were reviewed with the Restorative Dentist to ensure anatomical boundaries were correctly identified on computed tomography and clinical relevance of the structures. Four separate data points were recorded for each of the mandible and maxilla sextants; maximum dose (D_{max}), mean dose (D_{mean}), volume receiving 50 Gy (V_{50}) and the volume receiving 60 Gy (V_{60}) for each patient.

Areas treated to 65 Gy included the gross tumour volume (GTV) of the primary disease and involved lymph nodes. The clinical target volume (CTV) treated to 65 Gy included the GTV primary with 1 cm geometric expansion, edited for anatomical boundaries and the GTV lymph nodes with a 1 cm geometric expansion, including the entire nodal level and edited for anatomical boundaries. Nodal levels deemed at risk of microscopic spread were treated to 54 Gy. All nodal delineation followed international consensus guidelines [20]. Following summation of all volumes to be treated a 5 mm geometric expansion for PTV was added. Patients were treated in chin neutral position, immobilised in a thermoplastic shell. All tongue base patients receive bilateral neck radiotherapy per protocol. Tonsil patients with well lateralised tumours more than 1 cm from the midline had ipsilateral neck radiotherapy. Otherwise they received bilateral neck treatment.

Planning study

The prospective *in silico* research planning study was sponsored by the Oxford University Hospitals NHS Foundation Trust and approved by the West Midlands Research Ethics Committee *(REC reference 16/WM/0115)*. CT datasets were anonymised and allocated a study number. Radiotherapy planning was performed on Varian Eclipse RapidArc© v11 [21] and calculated using Varian's Analytical Anisotropic Algorithm (AAA) 10.0.28. Two rotational arcs with 6 MV photons were used. Prescription dose was 65 Gy in 30 fractions with simultaneous integrated boost (SIB) technique, normalised to median dose.

The primary outcome for the study was the proportion of patients whose radiotherapy plans could be optimised to limit the dose to the anterior mandible to D_{mean} of less than 37.5 Gy and/or a V_{50} of less than 30.8% [18]. These optimisation constraints were set a lower priority than all pre-existing constraints for Organs at Risk (OAR) in head and neck planning (see Table 1). The OAR of interest were spinal cord, brainstem, left parotid, right parotid, cerebellum and lips. Acceptable plans had equivalent PTV coverage to the original plan. All plans were approved by a Consultant Clinical Oncologist specialising in Head and Neck cancer.

Statistical analysis

All data was assessed for normality of distribution. Descriptive statistics are provided for the maximum dose (D_{max}), mean dose (D_{mean}), volume receiving 50 Gy (V_{50}) and volume receiving 60 Gy (V_{60}) for each of the sextants. Dosimetric parameters between left tonsil, right tonsil and tongue base tumours were compared using the Kruskal Wallis test. Wilcoxon rank sum test was used to compare groups of two. A multivariate linear regression model was constructed to assess for independent predictors of mean anterior mandible dose. In the planning study changes to OAR between the original plan and the re-plan were compared using the Wilcoxon signed-rank test for matched pairs. The level for significance for all analyses is < 0.05, two sided. All analyses were performed using R (version 3.3.1) [22].

Results

Patient characteristics

A total of 57 patients were included. The median age was 59 years (range 40–80). 91% (N = 52) of patients were dentate or partially dentate. There were approximately equal numbers' of left tonsil, right tonsil and tongue base cancers (20, 19, 18 respectively). The patient