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Presenting pre-radiotherapy dental status of head and neck cancer patients in the novel radiation era

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Conflicts of interest statement

None declared

There are no conflicts of interest to declare by any of the authors for this submitted work.

Abstract

Objectives: Dental assessment remains a key intervention for head and neck (HNC) cancer patients pre-radiotherapy (RT). The purpose of this study was to identify the variation in dental status of patients pre-treatment with respect to population and oncological demographics.

Materials & methods: The study reviewed dental panoramic radiographs of HNC patients seen on a dedicated pre-RT dental clinic from 2011-2017. Only patients whom had undergone intensity modulated radiotherapy treatment were included within this study. Relevant dental and oncological data were collected.

Results: A total of 886 patients were included in this study with oropharyngeal cancer constituting 36% of the cohort. The average number of teeth in HNC patients was < 21 at the pre-RT phase, which is below the recognised threshold for a functional dentition. Smoking status has a significant impact on overall DMFT (decay/missing/filled teeth), severity of horizontal bone loss and the number of third molars present ($p<0.001$). In the latter, males had a higher mean number of third molars compared to females ($p<0.005$). Comparing dental status of patients based on their tumour sub-site identified significant ($p<0.0005$) variation in all aforementioned categories

Conclusion: There are distinct differences in the dental health of HNC patients due to commence RT compared to the general population. It varies by cancer sub-site and this should be taken into consideration at dental assessment to tailor a dental care plan to the needs of he individual. Consideration should be given to balancing masticatory function against the risks of osteoradionecrosis on the background of increasingly extended survivorship.

Keywords

DMFT, dental status, dentition, head and neck cancer, radiotherapy, osteoradionecrosis

Introduction

A generally accepted stereotype is that head and neck cancer (HNC) patients have sub-optimal dental status. Frydrych et al[1] reported most HNC patients had not visited a dentist in the year preceding diagnosis and the mean time to the last visit was 5.6 years. It is therefore not surprising that many suffer from both periodontal disease and caries.[2] This creates a challenge to achieve 'dental fitness' in the restricted time window provided before commencing radiotherapy (RT). The perceived threat of osteoradionecrosis (ORN) means carious and periodontally involved teeth particularly in 'at risk' ORN areas maybe sacrificed though potentially restorable. It is unclear what dental factors are pertinent in developing a dental oncology treatment plan for an individual partly because they have not been mapped against prognostic indices such as gender, age, smoking history, p16 status and stage of disease. Rather than persisting with an anecdotal approach to treatment planning the relevance of different dental components that together constitute dental status needs to be validated. Some factors have been shown to impact quality of life such as having > 8 teeth removed prior to starting RT.[3] The increasing number of long term survivors has brought to a focus the complex dynamics between dental status, tumour stage and patient demographics which needs to be understood when developing an oncological dental treatment plan.

With the changing pattern of HNC and a national improvement in dental health (Adult Dental Health Survey, 2009 [ADHS])[4] it remains unclear whether this improvement extends to the current cohort of HNC patients. The current study is an observational study to assess the dental status of HNC patients at the pre-RT phase and is the largest cohort of patients treated exclusively by intensity modulated radiation therapy (IMRT) currently reported in the literature

Material & method

The electronic appointments log for Guys & St Thomas' HNC pre-RT dental assessment clinic was retrieved for the period of March 2011 until December 2017. The log commenced at March 2011 following the introduction and routine use of IMRT for all HNC patients at the hospital. Internal yearly audit over the past 5 years has shown that 95-98% of HN RT patients had a dental assessment prior to commencing treatment. Reasons for missed assessment were failure to attend, urgent initiation of RT or patient infirmity. These patients were not captured in the current database.

The electronic out-patient appointments system yielded a total of 1360 new patient appointment. Inclusion criteria included biopsy proven HNC with curative intent requiring RT. A total of 474 patients were excluded (non-squamous cell HNC, distant metastases, RT with palliative intent, previous history of HNC). Edentulous patients were also excluded as not all these patients are routinely sent for pre-RT dental review. Following exclusions a total of 886 patients included in this retrospective study.

All data was collected using fixed options per category. The domains included patient demographics (gender, age, smoking status) and tumour demographics (sub-site, size, nodal involvement) using multi-disciplinary meeting records. The dental status of each patient was collected using their presenting dental panoramic tomograph (DPT), which is used as a primary screening image for all patients at their pre-RT dental assessment. Under the umbrella of dental status, data was collected under five domains; teeth present, carious or restored teeth, decayed/missing/filled teeth (DMFT) score and severity grading of horizontal bone loss (HBL). All of these excluded the presence and number of third molars for which the data was collected as a separate domain. Severity of HBL was graded as nil (0), mild (1), moderate (2), severe (3) for all 6 sextants with the sum providing an overall score for the patient. The total score provided a generalised severity grading (0: no generalised HBL, 1-6: mild, 7-12: moderate, 13-18: severe). The severity was judged on the basis of thirds along the tooth root length. This meant mild equated to a maximum of a third, moderate a maximum of two-thirds and severe beyond two-thirds HBL.

Data was retrospectively collected by 4 individuals (VP, DP, TB, SP). All data collectors were standardised by jointly carrying out data collection for the same 20 patients. In addition the author VP audited the data by assessing 87 (10%) random patients to check for standardisation.

Statistical analysis

The sample and outcome data were summarised using descriptive statistics. The mean dental status based on gender was compared using unpaired t-test. The dental statuses of the remaining categories (age, smoking, tumour stage, nodal status, sub-site) were compared using one-way ANOVA. Significance was assumed at the 5% level, and analyses included the use of IBM SPSS Statistics for Windows, version 23.0 (IBM Corp).

Results

A total of 886 patients were evaluated with males (n = 641, 72%) heavily dominating the cohort. The most common age group was 55-64 (n=295, 33%). Forty percent of patients were ex-smokers (n = 336, 37.9%) followed closely by current smokers (n = 321, 36%). Tumour demographics showed that oropharyngeal cancer (n = 320, 36%), T2 size tumours (n = 257, 29%) and N2 nodal status (n = 416, 47%) were the most populated indices. Table 1 provides the category breakdown.

With respect to dental status in this test cohort, significantly more ($p = 0.0037$) males retained their third molar teeth compared to females (Table 2) and in both dental health declined with age (Table 3). Smoking status (Table 4) had a negative impact in all dental parameters measured except caries/restoration ($p = 0.0814$). More caries/restorations ($p = 0.005$) and HBL ($p = 0.0373$) were associated with increasing tumour stage (Table 5) but paradoxically both number of teeth ($p = 0.0437$) and presence of third molars ($p = 0.0195$)

increased with nodal status peaking for N3 classification (Table 6). All tumour sub-sites (Table 7) showed a significant relationship to dental factors recorded in this study.

Discussion

The current study assessed the dental status in various formats of newly diagnosed HNC patients due to commence RT. To understand the implications of their dental status it is imperative to compare them to their demographic equivalents in the general population. The current ADHS (2009)[4] provides reliable oversight of dental status for the UK. Hence, we have compared and contrasted our data to this national population survey. The current study provides the most recent data on a changing pattern in both dental health and HNC placed against the introduction of IMRT (intensity modulated RT). Previous dental studies in HNC are either now historic and do no reflect these changes or have small numbers. This study is the largest HNC cohort study in this new dental and oncological era. What is novel is that this study relates dental status to HNC sub-sites.

The retention of 21 or more natural teeth is widely used to define the minimum number of teeth consistent with a functional dentition.[4] In the current study, the mean number of teeth in both genders fell short of this threshold at the time of their pre-RT dental assessment. Hence, further dental extractions are likely to directly impact on future oral function. Post-RT related changes such as xerostomia, dysphagia and trismus mitigate against simple dental rehabilitation with a denture. Dentures may complicate and exacerbate the problem. It is therefore a significant challenge to correctly balance between dental extractions, future dental function and risk of ORN at pre-RT oncological dental planning.

There is limited information regarding the dental status of HNC patients in the pre-RT phase of treatment. Historic studies do not pertain to RT provision in the

IMRT era and are inappropriate for modern oncological dental planning. This is evident when comparing the study by Guggenheimer et al[5] (1965-1990) with Critchlow et al[6] (2013). In the former population of 947 HNC patients, 59% were edentulous, 14% had a poor dentition and 18% an intact dentition[5] compared to the 2013 cohort where only 2% of HNC patients were edentulous.[6] This changing pattern of tooth retention is one confirmed by ADHS.[4] The current study shows that although dental health in the general population has improved (mean number of teeth 25.7)[4] HNC patients still lag behind with an average of only 19.8 teeth based on this study (Table 2). Critchlow et al[6] confirmed this point by showing only 64% of HNC patients were able to meet the functional 21 teeth threshold.

Another difference is the rate of dental caries. ADHS[4] reported 31% of the general population to have dental decay in contrast to 71% (Lockhart et al[7]) and 61% (Critchlow et al[6]) in the HNC population. The present cohort had a mean of 8.2 carious/restored teeth and a minimum of 41% (8.2/19.8 teeth) were potential candidates for extraction either pre- or post-RT with the risk continuing over time. The mean DMFT in the study population was 16.2, which was similar to that of Rouers et al[8] (DMFT 16.1) but less than that in earlier studies where values of 18.1 (Moraes et al[9]) and 19.6 (Tezal M et al[9]) were reported. The high DMFT scores reflect the current and historical burden of dental disease in the population.

The final component is periodontal disease which is prevalent in all studies reporting on HNC patients ranging from 40% (Niewald et al[10]) to 80% (Critchlow et al[6] & Moraes et al[10]). The present study assessed HBL from radiographs and moderate (7.4) alveolar bone loss was evident. Lockhart et al[7] reported bone loss of 66% in HNC patients compared to 45% in the general population[4] and the difference probably relates in part to smoking habits. The relevance of identifying periodontal disease is the increased risk of ORN.[11] If poor or hopeless teeth are not extracted then the incidence of ORN rises from

~7% to 33%.[11] The need for balance dental extractions in preparing the patient for treatment is obvious.

Gender

Data from the ADHS survey identifies men as having more natural teeth, dental caries and periodontal disease compared to females.[4] In the current cohort there were no significant differences in dental statuses by gender except for the presence of third molars. Males had 1.4 third molars compared to 1.1 in females. ORN, is more prevalent in men[21] with the most favoured site being the mandibular third molar region. Hence, non-ectopic impacted third molars should be considered for extraction at the pre-RT phase. In 2000, the national institute of clinical excellence (NICE) published guidance against the low threshold for third molar surgery.[12] The net result is that more third molars are being retained in the younger population. This is reflected in the current data where the age group 29-52y had the highest number of third molars. The concern regarding the retention of third molars is that they commonly succumb to dental disease[13] over time and their anatomical position in the jaws coincides with radiation hot spots and which leads to vulnerability to ORN.

Age

The number of teeth is strongly associated with age, reflecting the one-way nature of tooth loss and the accumulated effects of dental disease and treatment over the life course.[4] It is therefore not surprising that all the aforementioned dental parameters deteriorated with increasing age. Today adults < 65 years of age rarely lose all their natural teeth[4] but those >45y, carry the legacy of dental decay and heavily restored teeth which means fewer sound teeth in the mouth.[4] The reality is that post-RT teeth are vulnerable to dental disease and with it the risk of ORN. In this study, age appeared to be an important factor when considering the 21 natural teeth threshold for a functional dentition. A pivotal point of change was identified between age decade 45-54 and 55-64. Between these decades the mean number of teeth present shifted from 22.3 to 19.7 respectively. This finding is even more potent as the decade 55-64 was the peak age range for HNC diagnosis accounting for a third of the whole cohort.

With increasing age (≥45-54) there is an emergence of root caries[4] in the general population and this risk is accentuated by post RT xerostomia with radiation caries particular in root dentine. In the present study 35-53% of teeth in patients age 45-90 were either decayed or vulnerable to secondary decay at the pre-RT phase. What is clear is that in the 21st century patients aged 45-90 (82% of the cohort) present with complex dental issues that pose a real dilemma as to how to achieve optimum post-RT function and quality of life from a dental perspective.

Smoking status

Smoking has a significant role in HNC and in the current cohort 72% of patients were either smokers or ex-smokers. Smoking has strong links to oral health with dentate adults who had never smoked more likely to have excellent oral health compared to current or ex smokers.[4] In the study cohort smoking status was significantly inversely related to number of teeth present, DMFT score, HBL and third molars being present. Furthermore, smoking increases xerostomia, which invites caries.[14]

Tumour stage

For both caries/restorations and HBL a statistical relationship to tumour stage and the trends would suggest that higher stage patients correlated to irregular dental attendance or an unwillingness to address health issues. Therefore pre-RT preparation is likely to result in extraction rather restoration in the face of unrestorable teeth or periodontal disease.

Nodal stage

Enlarging nodal stage was associated with an increase in both mean number of teeth and third molar presence. This finding is likely linked to the increasing number of oropharyngeal cancer (OPC) patients which accounted for 36%

(320/886) of the cohort. OPC patients commonly present with painless neck lumps.[15,16] Ang et al[17] reported that over 66% (478/721) of patients presented with advanced classification (N2 or N3) nodal disease. Many of these patients do not have the conventional HNC risk factors of tobacco exposure and excessive alcohol use but rather related to human papilloma virus (HPV). Hence, the lack of traditional risk factors means the dentition does not reflect the 'stereotyped' HNC dentition and therefore the retention of more teeth. The immediate concern is a higher nodal staging encompasses a larger volume of tissue being irradiated involving a larger proportion of the dentition. This coupled with high cure rates in HPV positive OPC[17] could explain why this sub-group of patients are at a heightened risk of ORN. The presence third molars in higher nodal stage therefore requires meticulous assessment at the pre-RT phase. The radiation dose to this region in higher nodal stages is likely to be above the 40Gy threshold in developing ORN.

Sub-site

Differential appreciation of HNC sub-site is an essential factor during pre-RT dental assessment. Distinct differences in RT coverage for various sub-sites are recognised and should be considered during treatment planning. Tooth bearing areas in laryngeal cancers often receive less than 25Gy.[18] In contrast, tooth bearing areas in patients being treated with radiotherapy for OPC and hypopharyngeal cancers receive in excess of 50Gy.[18] While in nasopharyngeal cancers maxillary teeth have a higher dose of RT than the mandibular teeth.[18] However, though various groups have been deemed vulnerable to ORN, it is their dental status which drives the risk. The long-term presence of teeth, long-life expectancy and late effects of radiation-induced fibrosis encourage the development of ORN. It is on this principle patients with OPC and nasopharyngeal cancers have such an elevated risk. The clear difference in dental status by tumour sub-site is exposed in this study. Some tumour sites are associated with disproportionate consumption of excessive alcohol and tobacco and patients had on average < 20 teeth on presentation, whereas those sub-sites not dominated by these risk factors had >20 teeth on average. Compared to Maier et al[19] who reported on pre-RT status via sub-site, our study showed almost identical figures of carious and restored teeth for larynx, oral and hypopharynx patients. This finding would suggest a lack of change over the years in oral health priorities in tobacco and alcohol related HNC sub-sites. However, Maier et al[19] had also identified OPC attended with poor dental status. In contrast, this study showed OPC patients had a higher number of carious/restored teeth with the likelihood the number reflects more repaired teeth. A major change with OPC rising related to HPV over the last 2 decades has led to a differing population with a better dentition than the average HNC patient.

One very interesting finding in this study was the dental status of the 'unknown HNC primary'. Patients who had attended with a neck lump without an obvious primary tumour. It now transpires that these patient are likely to have micro-tumours in the oropharynx (tonsil or tongue base). In the current cohort 49 patients were deemed to have an unknown HNC primary. When assessing their dental status against the OPC group of 320 patients the pattern was almost identical with the standard deviations differences less than 1 tooth apart and points to the fact that the occult primary and the OPC patients co-localise.

The current population study reviewed all patients attending for a pre-RT dental assessment on a continuous basis from 2011-2017. Amongst this population OPC was the most populated group with over a third of all cases. If the unknown HNC primary group is amalgamated with OPC this equates to 42% of all cases. With the phenomenal rise of OPC with high cure rates[20] dental oncologists need to urgently re-evaluate dental management approach in this group. The balance of maintaining a functional dentition while avoiding ORN over an extended time period is a significant challenge. Equally, oncologists need to recognize the challenges faced by dental oncologists in this sub-group of patients and try tailor their radiation fields to minimize dental exposure to radiation in a changing oral health landscape.

Limitations

Though this study includes a large cohort of patients a number of limitations have been recognised. The study used radiographs alone to determine dental status without incorporating clinical examination data. Two main limitations have been identified. Firstly, radiographic HBL reflects historic periodontal disease and does not inform on current disease status. Secondly, third molars were recorded as present or absent on radiographs, as their eruptive status based on imaging only cannot be determined.

Tables

Table 1: Shows the current cohort of 886 patients sub-categorised via basic and oncological demographics.

Table 2: Shows the mean values for each dental domain with standard deviation in brackets based on gender. *Unpaired t-test with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

Table 3: Shows the mean values for each dental domain with standard deviation in brackets based on age decades. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

Table 4: Shows the mean values for each dental domain with standard deviation in brackets based on smoking status. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

Table 5: Shows the mean values for each dental domain with standard deviation in brackets based on tumour stage classification. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

Table 6: Shows the mean values for each dental domain with standard deviation in brackets based on nodal stage classification. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

Table 7: Shows the mean values for each dental domain with standard deviation in brackets based on head and neck cancer sub-sites. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

Ethics

19/EE/0224 - Dental status, radiotherapy doses and subsequent implications in head and neck cancer patients - A retrospective cohort study

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Demographics	Subcategories (N)
Gender	Male (641)
	Female (245)
Age Group	16-24 (2)
	25-34 (18)
	35-44 (58)
	45-54 (217)
	55-64 (295)
	65-74 (215)
	75-84 (76)
	85+ (5)
Smoking Status	Current (321)
	Ex-smoker (336)
	Never (229)
Tumour Site	Paranasal & Sinus (25)
	Salivary Glands (62)
	Unknown Primary (49)
	Hypopharynx (24)
	Nasopharynx (39)
	Oral Cavity (154)
	Larynx (192)
	Oropharynx (320)
	Other Head & Neck (21)
Stage	I (76)
	II (110)
	III (135)
	IV (509)
Tumour Size	T0 (56)
	T1 (166)
	T2 (257)
	T3 (182)
	T4 (225)
Nodal Size	N0 (345)
	N1 (85)
	N2 (416)
	N3 (40)

Table 1: Shows the current cohort of 886 patients sub-categorised via basic and oncological demographics.

	Overall (886)	Male (641)	Female (245)	p value
Teeth Present	19.8 (7.4)	20.1 (7.1)	19.5 (7.6)	**0.2703**
Caries/Restored	8.2 (5.3)	8.1 (5.1)	8.2 (5.4)	**0.7974**
DMFT	16.2 (7.1)	15.9 (7.1)	16.5 (7.1)	**0.2609**
Horizontal Bone Loss	7.4 (3.8)	7.5 (3.9)	7.3 (3.7)	**0.4889**
Third molars present	1.3 (1.4)	1.4 (1.4)	1.1 (1.3)	**0.0037*#**

Table 2: Shows the mean values for each dental domain with standard deviation in brackets based on gender. *Unpaired t-test with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

	16-24 (2)	25-34 (18)	35-44 (58)	45-54 (217)	55-64 (295)	65-74 (215)	75-84 (76)	85+ (5)	p value
Teeth Present	28 (0)	26.3 (2.7)	24.4 (4.9)	22.3 (6.0)	19.7 (7.4)	17.5 (7.7)	16.0 (6.6)	17.0 (4.4)	**0.0000*#**
Caries/Restored	0 (0)	2.7 (3.1)	6.0 (4.6)	7.9 (4.8)	8.8 (5.5)	8.5 (5.5)	8.0 (4.3)	9.0 (2.2)	**0.0000*#**
DMFT	0 (0)	4.3 (4.4)	9.6 (7.4)	13.5 (6.9)	17.0 (6.3)	18.8 (5.9)	19.8 (5.1)	19.8 (3.8)	**0.0000*#**
Horizontal Bone Loss	1.5 (2.1)	3.8 (2.6)	6.1 (3.3)	7.0 (4.1)	7.8 (3.8)	7.7 (3.7)	8.0 (3.0)	10.6 (2.5)	**0.0000*#**
Third molars present	3.0 (1.0)	1.9 (1.6)	1.8 (1.6)	1.4 (1.5)	1.3 (1.4)	1.1 (1.2)	0.9 (1.1)	1.2 (1.3)	**0.0005*#**

Table 3: Shows the mean values for each dental domain with standard deviation in brackets based on age decades. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

	Current (321)	Ex-smokers (336)	Never (229)	p value
Teeth Present	18.1 (7.8)	19.9 (7.1)	22.5 (5.9)	**0.0104***
Caries/Restored	7.6 (5.3)	8.3 (4.8)	8.5 (5.2)	**0.0814**
DMFT	17.4 (7.1)	16.3 (6.8)	13.8 (7.1)	**0.0000*#**
Horizontal Bone Loss	8.4 (4.0)	7.5 (3.7)	5.9 (3.3)	**0.0000*#**
Third molars present	1.2 (1.4)	1.2 (1.3)	1.6 (1.4)	**0.0007*#**

Table 4: Shows the mean values for each dental domain with standard deviation in brackets based on smoking status. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

	T0 (56)	T1 (166)	T2 (257)	T3 (182)	T4 (225)	p value
Teeth Present	21.5 (6.5)	20.2 (7.6)	20.5 (7.1)	19.2 (7.2)	19.2 (7.5)	**0.0763**
Caries/Restoration	8.7 (5.9)	8.5 (5.1)	8.9 (5.3)	7.3 (4.9)	7.5 (5.3)	**0.0050*#**
DMFT	15.2 (7.0)	16.1 (7.1)	16.2 (7.2)	15.9 (6.8)	16.2 (7.4)	**0.8951**
Horizontal Bone Loss	7.4 (4.1)	6.7 (3.5)	7.4 (3.8)	8.0 (3.9)	7.5 (3.9)	**0.0373***
Third Molars Present	1.5 (1.4)	1.2 (1.4)	1.3 (1.4)	1.3 (1.4)	1.3 (1.4)	**0.7407**

Table 5: Shows the mean values for each dental domain with standard deviation in brackets based on tumour stage classification. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

	N0 (345)	N1 (85)	N2 (416)	N3 (40)	p value
Teeth Present	19.1 (7.4)	19.9 (8.3)	20.5 (6.9)	21.1 (7.0)	0.0437*
Caries/Restorations	7.7 (5.1)	8.4 (6.0)	8.5 (5.2)	7.4 (4.9)	0.1444
DMFT	16.5 (7.4)	16.2 (7.3)	15.8 (6.7)	14.3 (7.2)	0.2205
Horizontal Bone Loss	7.6 (3.9)	6.7 (3.3)	7.4 (3.9)	7.8 (3.7)	0.2466
Third Molars Present	1.2 (1.3)	1.4 (1.4)	1.3 (1.4)	1.9 (1.6)	0.0195*

Table 6: Shows the mean values for each dental domain with standard deviation in brackets based on nodal stage classification. *One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*

Tumour Site	Teeth present	Carious or restored teeth	DMFT	Horizontal bone loss	Third molar present
Paranasal and sinus (25)	19.0 (6.9)	7.9 (4.5)	17.0 (7.3)	7.6 (3.8)	1.0 (1.2)
Salivary Gland (62)	22.1 (6.7)	8.6 (5.1)	14.3 (7.1)	5.4 (3.1)	1.1 (1.2)
Unknown primary (49)	21.1 (6.6)	8.8 (6.1)	15.7 (7.1)	7.7 (4.2)	1.4 (1.3)
Hypopharynx (24)	19.5 (7.6)	7.8 (4.7)	16.2 (5.6)	8.0 (3.5)	1.0 (1.0)
Nasopharynx (39)	23.7 (4.9)	5.1 (4.8)	9.0 (6.8)	6.6 (3.6)	2.2 (1.6)
Oral Cavity (154)	18.3 (7.7)	7.3 (5.5)	16.8 (7.6)	7.4 (3.8)	1.3 (1.3)
Larynx (192)	17.2 (7.5)	7.6 (4.8)	18.3 (6.4)	8.7 (3.7)	1.1 (1.3)
Oropharyngeal (320)	21.1 (6.9)	9.0 (5.1)	15.7 (6.7)	7.2 (3.8)	1.4 (1.5)
Other head & neck (21)	22.2 (5.7)	8.3 (6.0)	13.8 (7.0)	5.7 (4.2)	1.8 (1.7)
p value	**0.0000*#**	**0.0002*#**	**0.0000*#**	**0.0000*#**	**0.0004*#**

Table 7: Shows the mean values for each dental domain with standard deviation in brackets based on head and neck cancer sub-sites.
*One-way ANOVA with 95% confidence intervals with p values with those <0.05 marked by an *. Bonferroni correction (p<0.01) denoted as #*