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Effects of Radiotherapy to the Jaws 1: The Scale of the Problem

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Abstract - *Cancer care has become one of the main targets of the National Health Service in England and with cancer patients surviving longer, it is likely that head and neck cancer patients will make up a large proportion of patients seen within secondary care settings in the future. The management of these patients can be very difficult for a number of reasons. Part one of this paper attempts to highlight the major oral health problems encountered by these patients during and after their cancer treatment and supported by the current literature. Part two of this series will address the dental management of head and neck oncology patients undergoing radiotherapy with particular attention of possible improvement to current management strategies for these patients.*

KEYWORDS: Head and neck oncology, cancer, radiotherapy, dental complications, mucositis, taste loss, xerostomia, radiation caries, periodontal disease, osteoradionecrosis, trismus, implants

INTRODUCTION

Cancer of the oral cavity related structures has a global incidence of approximately 400,000 new cases each year[1] and is on the increase[2]. The mortality rate is high with a 5-year survival of 60%[2]. The focus initially is on prompt cancer treatment[3-6] however after recovery, these patients often want to return to their pre-disease appearance and function[7], indicating the importance of post-oncology rehabilitation in relation to quality of life. As patients survive longer, late effects of cancer treatment and survival are coming to light.

Surgery alone can be debilitating, and its effects can be further exacerbated by adjunctive radiotherapy. The deoxyribonucleic acid (DNA) of rapidly dividing cells is damaged by radiotherapy leading to the failure of the normal mechanisms of DNA repair causing cell death. This process is increased in cancer cells because the mechanisms of DNA repair are usually less effective and there is an increased rate of cell turnover[8]. Other normal tissues that have a high turnover (such as the oral mucosa) will be affected in a similar manner to the cancer cells.

Radiotherapy leads to hypovascularity, hypocellularity and hypoxia of the tissues, with a reduced capacity to remodel[9]. This may increase the risk of infection and necrosis[10]. Mucocutaneous tissues that are irradiated show increased vascular permeability, fibrin deposition, collagen formation and eventually fibrosis[11]. The extent to which normal tissues are affected is dependent on the total volume irradiated, the depth and intensity of the irradiation and the total dose of irradiation. Other factors that influence the effects of irradiation include: the fractionation schedule, previous surgery, genetically determined sensitivity to radiation, smoking, alcohol and nutrition. Some patients develop severe toxicity, which is not always predictable at the outset[12-14]. Human Papilloma Virus (HPV) positive squamous cell carcinomas (SCCs) of the oral cavity are more sensitive to cytotoxic chemotherapy and therefore potentially to chemo-radiotherapy[15] (with better outcomes expected in comparison to HPV negative SCCs[16]). However adjunctive chemotherapy can increase the general radiosensitivity of the patient[17-19].

Restorative Dentistry is an integral part of the multidisciplinary care team responsible for head and neck oncology patients. This includes treatment planning at the time or very soon after diagnosis of oral cancer, care during surgical phases/chemotherapy/radiotherapy, rehabilitation following the completion of oncology treatment, and beyond[20]. Numerous guidelines have discussed the importance of timely management of head and neck oncology patients by a multidisciplinary team, including a dentist with suitable training[3-5].

In an idealistic care pathway (Figure 1) for head and neck cancer patients, the first definitive treatment may include curative or palliative radiotherapy. If so, during the thirty-one days from making the decision to treat to the first definitive oncology treatment, radiotherapy planning and concurrent dental risk assessment and treatment must take place. It has been shown that only 11-20% of this group of patients do not need dental treatment prior to radiotherapy[21,22].

THE PROBLEM

Difficult dilemmas exist when proposing treatment plans for patients about to undergo radiotherapy, especially when end goals are to prevent future dental problems. These patients present with a number of dental issues such as retained roots, periodontally involved teeth, carious teeth, teeth that have been endodontically treated and sound teeth in the potential radiation field. Although it is obvious

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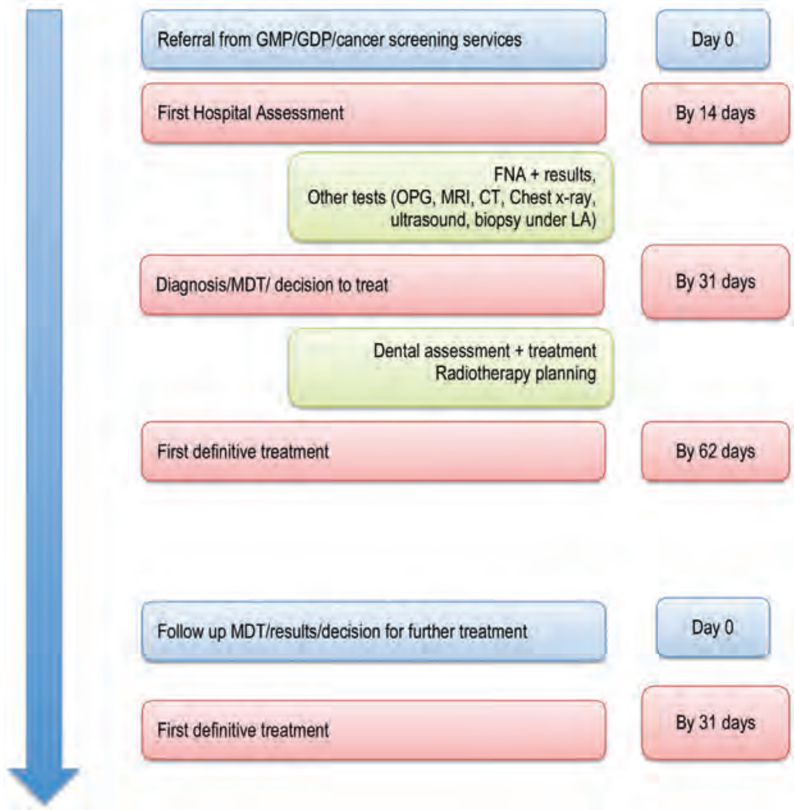

Figure 1. *Ideal head and neck cancer care pathway.*

that diseased teeth require treatment or extraction, what should be done with sound teeth in the radiation field and endodontically treated teeth exhibiting no obvious signs of infection at the time of assessment, is less clear. The question is do all patients undergoing radiotherapy suffer from increased dental complications during and following radiotherapy? If so, can a blanket protocol be applied?

It is very difficult to predict both the type and severity of the patients' reactions to radiotherapy. The effects may be dose and frequency dependent[23-28], which may be relatively straightforward to investigate. However, the effects may also be related to the patient's genetic ability to repair and recover following such treatment, which is likely to be more difficult and costly to study. TNM staging may additionally have an effect on dental management, for example, local tumour resections may be organ sparing with a better prognosis, warranting maintaining teeth to improve the quality of life of the patient.

Oral management of head and neck oncology patients is challenging and multifaceted due to a number of treatment related complications including: mucositis, reduced salivary gland function, taste loss, reduced tongue movement, difficulties with speech and swallowing, radiation caries, scarring leading to trismus, and the potential for osteoradionecrosis following radiotherapy[28-34]. Any one of these and facial disfigurement can have a significant impact on the patients' quality of life[32, 35-37]. Worst still a number of these complications are seen in the same patient. Frequently, patients are overwhelmed by the difficulties encountered during the recovery and rehabilitative period. It is not always easy to prepare patients for these eventualities or the fact that some effects may be life long.

It is worth remembering the psychological upheaval patients experience from the initial time of diagnosis, through surgery and radiotherapy and then ultimately coming to terms with the outcome of treatment. Patients need to take on board that they may never be the same as they were before the cancer diagnosis and this can be difficult to convey. This end position may be at variance with preconceived ideals they had hoped for. Conversations with these patients have highlighted to the authors the patient concerns regarding recurrence of the disease, function as a 'normal' person and desire for psychological support during this vulnerable time. These concerns may not be limited to patients, but also their families, friends, carers and dependents.

MUCOSITIS, LOSS OF TASTE, HYPOSALIVATION AND RADIATION CARIES

A variety of side effects of radiotherapy lead to deterioration of the dentition. Mucositis is often transient and can begin after the first week of radiotherapy persisting for 2-3 weeks following completion of radiotherapy[38]. Patients may experience pain, burning and discomfort as a result. This is caused due to the thinning of the epithelium, dilatation of the vasculature with inflammation and oedema of the submucosa[33].

Radiotherapy affects salivary gland function, which can be reduced by 50-60% within the first week of radiotherapy and then reduced to 20% of normal salivary gland function at 5-6weeks of radiotherapy[39]. Minor salivary glands have greater resistance to radiotherapy and ability to recover than parotid glands[40]. The effect on salivary glands can be acute and transient, or delayed and lifelong following radiotherapy. Variations in severity occur from patient to patient[34, 35].

In partially or fully edentulous patients, the lack of salivary lubrication may render dental prostheses difficult or impossible to tolerate. It must be borne in mind that salivary lubrication is also required for speech, chewing and swallowing comfortably which will all affect the wellbeing of the individual. The saliva is often thick with a low PH and increased salivary sediment[39]. Some recovery may occur in the first five years following radiotherapy completion; however there may never be a return to normal function[39]. Gomez et al (2011) found that a mean parotid dose of more than 26Gy was predictive of subsequent dental caries when intensity-modulated radiation therapy (IMRT) was used[41].

Radiation caries can develop suddenly with fast progression to decoronation of the teeth. Possible reasons may be a reduction in pH of the oral environment from 7.0 to 5.0 post-radiotherapy, a lowered salivary buffering capacity, a hampered remineralisation capacity, a reduced salivary flow rate, a change in the oral microflora to more cariogenic bacteria and alteration of the diet. Throughout radiotherapy the feeding can be via a nasogastric (NG) tube, a percutaneous endoscopic gastrostomy (PEG) tube or oral. If feeding is not oral, patients and carers may neglect brushing the teeth[34,42, 43]. Radiation can have an effect on the micro hardness of dentine (reducing its ability to act as a shock absorber). The disruption of the dentine enamel junctions and obliteration of the dentine tubules is also possible. This can lead to fracture and loss of the enamel[44, 45]. The loss of the protective salivary layer may result in hypersensitivity of the teeth, worsened if the protective layer of enamel is also lost. This may prevent patients from carrying out oral hygiene regimes[46]. A number of patients can go on to develop radiation caries despite best efforts with a preventative regime[47]. Caries therefore, may be inevitable, especially in patients with low compliance to maintaining good oral hygiene, or using topical fluoride applications[29, 34]. Compounded by mucositis, xerostomia and areas of plaque induced gingival inflammation a certain number of patients may be highly resistant to addressing the initial stages of plaque control due to the discomfort caused when brushing, especially as it comes at a time when they may be physically and emotionally drained.

Wang et al (2008) reported on caries rates in a retrospective case series, where 181 patients were observed before and after linear accelerator based radiotherapy to the head and neck (follow up of 3-12months, 54% lost to follow up). Patients received either 1.23% acidulated phosphate sodium fluoride (APF) or 2% sodium fluoride (NaF) in custom trays daily for 4 minutes. The mean number of carious lesions was significantly higher during and post-radiotherapy (7.18 +/- 7.10) compared to pre-radiotherapy (2.45 +/- 2.85)[48]. Jham et al found that 11% of patients (12 of 109) observed in a retrospective case series developed radiation caries with a mean development time of 1.38 years post-radiotherapy[49]. Schuurhuis et al (2011) reported that 13 of 80 (16%) patients with oral cavity and oropharyngeal cancer, developed one or more carious lesions within 2 years following radiotherapy (all were advised the topical application of 1% sodium fluoride in custom trays)[50].

The patients general well being, as well as their physical ability to move their shoulder following neck dissection, and to move their hand following a radial forearm free flap may also affect their ability to perform good oral hygiene. If family members or carers are aiding with brushing, there may be a reluctance to perform effective oral hygiene when the patient is clearly in discomfort.

During the acute phases of radiation-induced mucositis, taste disturbances and/or xerostomia can occur; relief may be sought with strongly flavoured sugary drinks (such as frequent sips of strong lemon squash, sweet tea) and/or lozenges. If these contain fermentable sugars, caries can progress quickly due to the hyposalivation and the diminished capacity for any remaining saliva to neutralise acids. Combined with a reluctance to use toothpastes and fluoride rinses due to their uncomfortable feeling, the caries can progress at an alarming rate (Figure 2). Long-term dental maintenance may also be affected by hyposalivation/altered oral flora (increased cariogenic bacteria and fungal infections[51]) and those patients who have ignored, forgotten or not received advice regarding caries prevention in the dry mouth may be at particular risk as they may not realise the long term effects.

Radiation caries often involves smooth surfaces including cusp tips and incisal edges, with circumferential spread of caries around the gingival margins, which can lead to decoronation of the tooth. Restoration of teeth with radiation caries can be difficult and unpredictable. De Moor et al reported on a prospective cohort study placing Glass Ionomer Cement (GIC) restorations, Resin Modified Glass Ionomer Cement (RMGIC) restorations and composite restorations in 35 patients (with concurrent use of 1% NaF gel in custom trays daily, loss to follow up of 8 patients at 24 months). The restorations were placed an equal number of times in anterior, middle and posterior tooth positions. Failure rates were higher with conventional GIC, followed by RMGIC and then composite (cumulative failures of 96%, 77% and 48% respectively)[52]. Therefore restoration of radiation caries with adhesive systems is not always predictable but composite restorations may be the better of existing materials.

There is little in the literature regarding the number of irradiated teeth that develop apical areas. Schuurhuis et al (2011) found that 10% of patients developed apical areas as seen on radiographs post-irradiation, which were not present at the time of pre-irradiation assessment[50]. Although the presence of a radiographic periapical area may be a good indicator of periapical pathosis, a lack of a radiographic periapical area is not a good indicator of

Figure 2. *Deterioration of the dentition following radiotherapy.*

health especially in mandibular molars and the palatal roots of upper molars[53, 54]. The lesion must break the bony cortex to be visible on radiographs and large lesions within cancellous bone may not be seen on radiographs[53, 54]. The fate of decoronated teeth is not known and in the authors experience some appear to be associated with profound pulpal sclerosis. Pulpal pain may be less severe due to decreased vascularity and increased fibrosis within the pulp following radiotherapy[34].

PERIODONTAL DISEASE

The loss of teeth may not always be as a result of the deterioration of the coronal portion of the teeth, but due to the breakdown of the periodontal architecture. In an observational prospective cohort study of 10 patients who received external beam radiation (4550-6000cGy) to unilateral fields (some with additional surgery or interstitial radiation), 86 teeth were left in situ within a high radiation dose area and 144 teeth outside high radiation dose areas. Sodium fluoride gel in customs trays was suggested for those with a dry mouth. During the follow up time of 3.25-10.75yrs, more teeth needed extraction due to periodontal disease in the irradiated region (mean total attachment loss of 2.81mm) compared to non-irradiated regions (mean total attachment loss of 1.43mm)[43]. Breakdown of the periodontal support may be as a result of poor oral hygiene or potential direct effects of radiotherapy on the periodontium. A change in the oral flora following radiotherapy, in favour of periodontal pathogens has not been demonstrated[55].

Schuurhuis et al (2011) reported periodontal pocket progression in 18% of their study population following radiotherapy, all of which occurred where there were pre-irradiation pockets that were 4mm or deeper (with the majority occurring where the pre-irradiation pocket depths were 6mm or deeper). The pre-irradiation treatment involved a combination of extractions with or without periodontal therapy. The radiotherapy began before reassessment following periodontal treatment[50]. Therefore the outcome of the periodontal treatment could not be assessed prior to commencing radiotherapy as a minimum of one to three months is recommended following periodontal treatment before re-probing, to allow undisturbed healing[56]. There is the possibility that radiotherapy interfered with healing following periodontal treatment or that the periodontal treatment was unsuccessful in the first instance. If this was known prior to radiotherapy, the tooth may have been extracted instead of remaining within the radiotherapy field.

TRISMUS AND REDUCTION OF ORAL APERTURE SIZE

The ability to treat post-radiotherapy dental complications is directly affected by the access into the oral cavity. Limited mouth opening hampers access. The reported incidence of trismus in head and neck cancer patients varies from 5% to 38%, with the definition of trismus varying from a mouth opening of 18mm to a mouth opening of 40mm[32, 57]. The normal range of mouth opening may vary from 40mm to 60mm[32, 57].

Median mouth opening has been associated with clinical tumour stage: Tis/T1-2 resulted in mouth opening of 35mm and T3-4 resulted in mouth opening of 24mm. Radiotherapy reduced median mouth opening with a mouth opening of 27mm in those who received radiotherapy compared with a mouth opening 38mm in those who did not receive radiotherapy. The type of primary surgery also affected median mouth opening: primary closure/laser/split skin graft lead to a mean mouth opening of 38mm, soft tissue flaps lead to a mean mouth opening of 30mm, and composite flaps lead to a mean mouth opening of 24mm[32]. However linear regression methods failed to find radiotherapy or tumour staging as predictors of mouth opening[32]. Tumours in the region of the mouth opening musculature and radiation to the temporomandibular joints (TMJs) or muscles of mastication can affect mouth opening[57]. An observational prospective cohort study on 58 patients, measuring mouth opening before and after radiotherapy to the jaws (0-6830cGy to the TMJs and pterygoid muscles) showed that the maximum vertical dimension reduced with increasing dose to TMJ and pterygoids. Radiation to the TMJs and/or pterygoid muscles reduced mouth opening by 18% (s.d. 17% and follow up of 6-12 months)[57]. Mandibular 'dysfunction' scores increased with increasing radiation dose to pterygoid muscles but not to the TMJs[27].

A large tumour in the posterior oral cavity requiring surgery and radiotherapy, with masticatory muscles in the irradiated field is likely to cause some trismus[32]. Tumour invasion of particular sites (e.g. the medial pterygoid muscle) can in itself restrict mouth opening. Scarring of the skin and lips following surgery and/or radiotherapy can also restrict the oral aperture (Figure 3). Patients may suffer from progressive trismus 4-5 years post-radiotherapy[28, 58]. Reduction of beyond 24mm mean even soft foods cannot be chewed[32].

When mouth opening is limited, it is not surprising that patients trying to maintain good oral hygiene encounter difficulties. Treatment of the teeth may be impossible and the options are to allow the teeth to disintegrate or extract the offending teeth. Trismus has particular pertinence to restorative dentistry as is can make treatment of posterior teeth (or even premolars) very difficult if not impossible especially if the patient has a marked Angle's class 2 division II malocclusion (deep overbite as shown in Figure 4). What may be a small area of caries in a molar, which would normally be amenable to simple restoration, can

Figure 3. *Reduced mouth opening*

Figure 4a – 4d. *In patients with a deep overbite (Angle's Class 2 division 2) even significant mouth opening may not necessarily give good access into the oral cavity*

Figure 5. *Difficult to treat teeth with significant root curvature as endodontic treatment can be difficult and atraumatic extraction may not be possible*

become a significant technical challenge to treat safely and effectively. If these teeth are left in situ they may lead to infection of the bone and osteoradionecrosis (ORN). It may be equally challenging to carry out atraumatic extraction of the teeth in post-radiotherapy patients with severely reduced opening. The potentiated risk of ORN leaves extraction an undesirable option[29]. In some cases both endodontic treatment and extraction may be equally challenging (Figure 5).

OSTEORADIONECROSIS

ORN is perhaps the most serious of the complications, although soft tissue necrosis can also occur following radiotherapy[59, 60]. ORN is a late complication of radiotherapy. It is due to inadequate repair and repopulation of the Haversian bone system and vessels following radiotherapy. The incidence of ORN following head and neck radiotherapy varies from 0.4% to 38%[55]. The current view is that the incidence of ORN is reducing[61]. The mandible is worst affected with a mandible to maxilla ratio of 24:1[62]. The buccal cortex of the molar and premolar regions is most vulnerable as it is thick and avascular by nature. These areas may receive larger doses of radiation[66]. The reported risk of ORN in the mandible is variable: ranging from 5% to 15%[63, 64]. ORN can develop at any time following radiotherapy but 70-94% occur in the first few years following completion of treatment, and half of these patients have surgical resection of the mandible as a result[23, 30]. ORN will have an impact on the patient's quality of life. The risk of ORN is dose dependent and the doses are higher if external beam irradiation and interstitial brachytherapy are combined[23, 30].

Dental extractions have been thought to increase the risk of ORN, especially if timed incorrectly[62, 65]. There are reports that ORN associated with post-radiation extractions require radical resection more often than pre-radiation extractions: 45.4% vs. 11.7% in a study of 70 patients who developed 83 episodes of ORN[66]. There has been some evidence to suggest that the extraction of teeth post-radiotherapy leads to a relatively low risk of ORN development if the exodontia is performed by experienced dentists[67] and that extractions undertaken during radiotherapy are detrimental due to the potential increased risk of ORN[65]. Others have found that the rates of ORN in those who underwent dental extractions prior to radiotherapy and post-radiotherapy are not markedly different[68]. It is very difficult to associate the ORN with dental extractions alone as not all patients who undergo extractions in the irradiated fields develop ORN.

Figure 6 is a summary of the finding relating to extractions and ORN. Of 53 studies looking at dental outcomes in head and neck cancer patients, 27 studies described in some detail the proportion of cases of ORN attributed to a variety of dental issues. As can be seen the rates of ORN related to dental extractions can be as high as 1 in 5 patients, however ORN due to caries, periodontitis and apical pathology or ORN due to other non dental reasons can also be high. The studies are heterogeneous, dating from 1972-2011 with marked variation in:

- patient characteristics
- pre-operative dental status
- smoking status
- alcohol status
- mode and dose of radiotherapy
- adjunctive surgery and chemotherapy
- extractions protocol (antibiotic cover, post operative antibiotic regimes, hyperbaric oxygen therapy, use of local anaesthesia without adrenaline, alveolotomies, primary closure and healing time from extractions to radiotherapy and after radiotherapy to extractions)
- decision making regarding the state of teeth to be left in situ vs. those to be extracted pre-radiotherapy
- maintenance of the dentition with various fluoride application protocols
- the definition of ORN.

It is difficult to be definite about the causes of ORN using the currently available literature. General trends are that ORN occurs in those with poor oral hygiene, bone loss of >60% & periodontal pockets >5mm[50, 69, 70]. Increase in dose of radiation and mode of radiation increases the risk of ORN with the vast majority of ORN cases occurring spontaneously or related to tumour regression[30, 66, 70-77]. Tumour surgery, chemotherapy, 'inadequate' dental assessments, nutrition, smoking and alcohol status are possible predisposing factors[78].

Curi et al (1997) found that there were two peaks in the onset of ORN following radiotherapy: the first peak was within the first 12 months thought to be due to tumour size and surgery, with little difference between the patients who were given pre-radiation oral care and those that were not (16% of ORN cases were related to factors originating from oral and dental infections). Second peak was between 24 and 60 months. In this group 60% of ORN cases were related to oral and dental infections with exodontias performed by GDPs. Pre-radiotherapy oral care was said to have an important role in preventing trauma induced ORN during the second peak[70].

Factors other than dental extractions are being linked to the development of ORN[79, 80]. Monnier et al (2011) found the incidence of mandibular ORN to be 40% (at 5 years in 73 patients), with oral cavity tumours, bone invasion, any surgery prior to radiotherapy and 'bone surgery' being important risk factors for the development of ORN. Age, sex, oral hygiene, alcohol and tobacco abuse, dental extractions, cardiovascular risk factors, induction and/or concomitant chemotherapy, total radiation dose, brachytherapy dose, and tumour stage were not significant risk factors for ORN[79]. Lee et al (2009) reported on 198 patients, 13 of whom (6.6%) developed ORN and again mandibular surgery was implicated as the most significant factor for the development of ORN[80]. Schuurhuis et al (2011) found that those patients who presented with dental infections at the pre-radiotherapy assessment developed ORN following radiotherapy[50]. Those that did develop ORN were mainly smokers, those with periodontal disease (pockets deeper than 6mm) at dental screening. The periodontally susceptible patients in their cohort were at a higher risk of ORN, if they failed to receive 'aggressive' treatment for periodontal pockets that were 6mm or deeper[50]. Newer research is suggesting a genetic basis for the development of ORN[81].

Delayed healing post radiation to the jaws is possible[72, 82]. Extractions in an irradiated field under HBO therapy in 40 patients revealed that those who healed within 1 year of extraction had completed radiotherapy on average of 3.3 years prior to extraction. However, those that took longer than one year to heal were an average of 0.8 years since radiation[83]. Being edentulous for several years pre-radiotherapy appears to have a protective effect against ORN[23, 75].

	Range	Mean
No of patients in 27 studies[23, 25, 49, 50, 69, 71-73, 75, 76, 78, 82, 93-107]	39 - 2853 patients	313 patients
% ORN in patients who did not have extractions (3 studies)[23,101,105]	0.3 - 1.4%	0.8%
% ORN attributed to pre-RT extractions (17 studies)[23, 49, 50, 69, 71, 73, 93, 98-107]	0 - 20%	4.4%
% ORN attributed to post-RT extractions (16 studies)[23, 50, 72, 73, 82, 95, 96, 98-103, 105, 107]	0 - 14%	2.1%
% ORN attributed to pre & post-RT extractions (2 studies)[23, 50]	1 - 1.4%	1.2%
% ORN attributed to caries, periodontitis or apical pathology (4 studies)[76, 97, 99, 100]	0 - 17%	4.5%
% ORN attributed to denture irritation (6 studies)[25, 98-100, 106, 107]	0 - 7%	2.5%
% ORN due to other reasons (3 studies)[75, 78, 94]	1.6 - 22%	11.3%
Total % of ORN in 27 studies[23, 25, 49, 50, 69, 71-73, 75, 76, 78, 82, 93-107]	0 - 43%	8.5%

Figure 6. *Summary of published data on ORN of the jaws*

IMPLANT SURVIVAL IN IRRADIATED PATIENTS

Dental rehabilitation post head and neck cancer treatment can now also involve the placement of dental implants. Dental implants placed in irradiated and grafted bone can have a significantly lower survival rate[71, 84-88], although a recent reviews of the available literature show that good results have been achieved with quoted survival rates of 82% – 100% during follow up periods of 15-96 months[89, 90]. Implants placed at the time of resection (primary implant placement) may overcome some of the problems of osseointegration in irradiated bone. Considering the difficulty of achieving success with conventional prosthodontics in those left with significant oral and facial deformities following oral cancer treatment, even with a lower survival rate, implants play an important role in oral and facial rehabilitation. The factors related to the success of dental implants in irradiated patients has been summarised by Dholam et al (2012)[91]. Clinical trials on the use of hyperbaric oxygen treatment (HBOT) in irradiated patients requiring dental implants are scarce, however a Cochrane Review based on one randomised controlled trial involving 26 irradiated patients (13 received HBOT before and after implant therapy and 13 who did not) concluded that HBOT may not offer significant clinical benefit[92].

It is difficult to develop clear conclusions regarding implant placement in this patient group, and decisions need to be based on a risk-benefit analysis for each patient. Factors to consider include the pre-existing risk factors for implant failure such as smoking, poor oral hygiene, alcohol, nutrition and periodontal disease[90], the residual deformity, prognosis of the patient, cost effectiveness and the quality of life of the patient. Those with limited mouth opening may not permit the placement of implants nor be able to maintain good oral hygiene around the implants. Those that are unable to swallow and therefore taking non-oral feeds may only require a dentition for aesthetic purposes and hence the upper anterior teeth alone may be sufficient.

CONCLUSIONS

The barriers to maintenance and rehabilitation of the dentition post-radiotherapy make pre-radiotherapy decision making exceedingly important. Recognition of the potential problems caused by radiotherapy to the oral cavity is paramount in appreciating the advantages and disadvantages of extraction prior to radiotherapy.

Since there is limited good quality evidence in this area, a more standardized approach to treatment and data collection for this group of patients will allow for meaningful analysis of outcomes. As a randomised controlled trial for these patients is not possible, routine collection of data relating to the following factors may be beneficial:

- diagnosis
- tumour staging
- cancer prognosis
- smoking and alcohol status
- dental findings (including periodontal examination)
- mouth opening
- irradiation field
- dental treatment (preventative, periodontal, endodontic and dental extractions, including tooth notation or relation to irradiation field and healing time before commencing radiotherapy)
- complications during and post-radiotherapy (especially trismus and site of ORN in relation to dental treatment)

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REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 10 [Internet] Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr
2. National Institute of Dental and Craniofacial Research. Oral Cancer. National Cancer Institute's Survey (2004). Available from www.nidcr.nih.gov/DataStatistics/FindDataByTopic/OralCancer/.
3. National Health Service Improvement. Ensuring Better Treatment: Going Further on Cancer Waits. An improvement guide for supporting sustainable delivery. 2009. http://www.improvement.nhs.uk/cancer/CancerHome/UsefulResources/Publications/tabid/331/Default.aspx
4. National Institute of Clinical Excellence. Improving outcomes in head and neck cancer. 2004
5. Department of Health. Manual for Cancer Services 2004. http://www.dh.gov.uk/en/Healthcare/Cancer/Treatment/DH_101998
6. Scottish Intercollegiate Guidelines Network. Diagnosis and management of head and neck cancer: a national clinical guideline. 2006
7. Rogers SN, El-Sheikha J, Lowe D. The development of a Patients Concerns Inventory (PCI) to help reveal patients concerns in the head and neck clinic. Oral Oncol. 2009; 45: 555-561
8. Cancer Research UK 2009. http://info.cancerresearchuk.org
9. Marx RE. Osteoradionecrosis: a new concept of its pathophysiology. J Oral Maxillofac Surg. 1983;41(5):283-8.
10. Hancock PJ, Epstein JB, Sadler GR. Oral and dental management related to radiation therapy for head and neck cancer. Journal of the Canadian Dental Association. 2003;69:585-590
11. Cooper JS, Fu K, Marks J, Silverman S. Late effects of radiation therapy in the head and neck region. International Journal of Radiation Oncology. 1995;31(5):1141-1164
12. Multhoff G and Radons J. Radiation, Inflammation, and Immune Responses in Cancer. Front Oncol. 2012; 2: 58.
13. Hoff CM, Grau C, Overgaard J. Effect of smoking on oxygen delivery and outcome in patients treated with radiotherapy for head and neck squamous cell carcinoma – A prospective study. Radiotherapy & Oncology. 2012;103 (1):38-44
14. Andreassen CN, Alsner J. Genetic variants and normal tissue toxicity after radiotherapy: A systematic review. Radiotherapy and Oncology. 2009;92(3):299-309
15. Marur S, D'Souza G, Westra WH, Forastiere AA. HPV-associated head and neck cancerL a virus related cancer epidemic. Lancet Oncology. 2010;11:781-89
16. Smith EM, Rubenstein LM, Haugen TH, Pawlita M, Turek LP. Complex etiology underlies risk and survival in head and neck cancer; Human papillomavirus, tobacco and alcohol: a case for multifactor disease. Journal of Oncology. 2012;2012:571862
17. Merlano M, Benasso M, Corvd R, Rosso R, Vitale V, Blengio F, Numico G, Margarino G, Bonelli L, Leonardo Santi L. Five-Year Update of a Randomized Trial of Alternating Radiotherapy and Chemotherapy Compared With Radiotherapy Alone in Treatment of Unresectable Squamous Cell Carcinoma of the Head and Neck. Journal of the National Institute. 1996;88:583-9

18. Wendt TG, Grabenbauer GG, Rödel CM, Thiel HJ, Aydin H, Rohloff R, Wustrow TP, Iro H, Popella C and Schalhorn A. Simultaneous radiochemotherapy versus radiotherapy alone in advanced head and neck cancer: a randomized multicenter study. Journal of Clinical Oncology. 1998:16(4);1318-1324
19. Al-Sarraf M, LeBlanc M, Giri PG, Fu KK, Cooper J, Vuong T, Forastiere AA, Adams G, Sakr WA, Schuller DE and Ensley JF. Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized Intergroup study 0099. Journal of Clinical Cncology. 1998;16(4);1310-1317
20. Jansma J, Vissink A, Spijkervet FKL, Panders AK, Vermey A, Roodenburg JLN, et al. Protocol for the prevention and treatment of oral complications of head and neck radiotherapy. Cancer. 1992;70:2171-2180
21. Brown RS, Miller JH, Bottomley WK. A Retrospective Oral/Dental Evaluation of 92 Head and Neck Oncology Patients, Before, During and After Irradiation Therapy. Gerodontology. 1990;9(2);35-39
22. Lizi EC. A case for a dental surgeon at regional radiotherapy centres. British Dental Journal. 1992;173:24-26
23. Chang DT, Sandow PR, Morris CG, Hollander R, Scarborough L, Amdur RJ, Mendenhall WM. Do pre-radiation dental extractions reduce the risk of osteoradionecrosis of the mandible? Head & Neck 2007;6:528-536.
24. Bedwinek, J.M., and others. Osteonecrosis in patients with definitive radiotherapy for squamous cell carcinomas of the oral cavity and naso- and oropharynx. Radiology 1976;119:665-667
25. Beumer J, Harrison R, Sanders B, Kurrasch M. Irradiation dental extractions and the incidence of bone necrosis. Head and Neck Surgery. 1983;5:514-521
26. Ichimura K & Tanaka T. Trismus in patients with malignant tumours in the head and neck. J Laryngol Otol. 1993;107:1017-20
27. Goldstein M, Maxymiw W, Cummings B, Wood R. The effects of anti-tumour radiation on mandibular opening and mobility: a prospective study of 58 patients. Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontology. 1999;88:365-73
28. Yeh S, Tang Y, Lui C, Huang E. Treatment outcomes and late complications of 849 patients with nasopharyngeal carcinoma treated with radiotherapy alone. Int J Radiat Oncol Biol Phys. 2005;62:672-9
29. Vissink A, Burlage FR, Spijkervet FKL, Jansma J, Coppes RP. Prevention and treatment of the consequences of head and neck radiotherapy. Critical Reviews in Oral Biology & Medicine. 2003a;14(3):213-225
30. Oh H-K, Chambers MS, Garden AS, Wong P-F, Martin JW. Risk of osteoradionecrosis after extraction of impacted third molars in irradiated head and neck cancer patients. Journal of oral and Maxillofacial Surgery. 2004;62:139-144
31. Dijkstra PU, Sterken MW, Pater R, Spijkervet FKL, Roodenburg JLN. Exercise therapy for trismus in head and neck cancer. Oral Oncology. 2007;43;389-394
32. Scott B, Butterworth C, Lowe D, Rogers SN. Factors associated with restricted mouth opening and its relationship to health-related quality of life in patients attending a Maxillofacial Oncology clinic. Oral Oncology. 2008:44;430-438
33. Andrews N & Griffiths C. Dental complications of head and neck radiotherapy: part 1. Australian Dental Journal. 2001;46(2):88-94
34. Kielbassa AM, Hincelbein W, Hellwig E, Meyer-Luckel H. Radiation related damage to dentition. Lancet Oncology. 2006;7:326-335
35. Vissink A, Jansma J, Spijkervet FKL, Burlage FR, Coppes RP. Oral sequelae of head and neck radiotherapy. Critical Review in Oral Biology & Medicine. 2003b;14:199-212
36. Morton RP & Izzard ME. Quality of life outcomes in head and neck cancer patients. World J Surg. 2003;27:884-889
37. Epstein JB, Robertson M, Emerton S, Phillips N, Stevenson-Moore P. Quality of life and oral function in patients treated with radiation therapy for head and neck cancer. Head & Neck 2001;23:389-398
38. Million and Cassisi: The effect of radiation on normal tissues of the head and neck. Management of head and neck cancer: A multidisciplinary approach. Philadelphia: JP Lippincott. 1984:173-204
39. Porter SR, Fedele S, Habbab KM. Xerostomia in head and neck malignancy. Oral Oncology. 2010;46:460-463
40. Niedermeier W, Matthaeus C, Meyer C, Staar S, Muller RP, Schulze HJ. Radiation induced hyposalivation and its treatment with oral pilocarpine. Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics. 1998;86:541-549
41. Gomez DR, Estilo CL, Wolden SL, Zelefsky MJ, Kraus DH, Shaha AR, Shah JP, Mechalakos JG, Lee NY. Correlation of osteonecrosis and denta events with dosimetric parameters in intensity modulated radiation therapy for head and neck cancer. Int J Radiat Oncol Biol Phys. 2011:81(4):e207-13
42. Keene HJ, Daly T, Brown LR, et al. Dental caries and Streptococcus mutans prevalence in cancer patients with irradiation-induced xerostomia: 1-13 years after radiotherapy. Caries Research. 1981;15:416-427
43. Epstein JB, Chin EA, Jacobson JJ, et al. The relationship among fluoride, cariogenic oral flora and salivary flow rate during radiation therapy. Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontology. 1998;86:286-92
44. Kielbassa AM, Beetz I, Schendera A, Hellwig E. Irradiation effects on micro hardness of fluoridated and non-fluoridated bovine dentine. European Journal of Dental Science. 1997a;105:444-447
45. Grotz KA, Duschner H, Kutzner J, et al. Neue erkenntnisse zur atiologie der sogenannten strahlkenkaries. Strahlenther Onkol. 1997;173:668-676
46. Toljanic JA, Saunders VW. Radiation therapy and management of the irradiated patient. Journal of Prosthetic Dentistry. 1984;52:852-858
47. Spak CJ, Johnson G, Ekstrand J. Caries incidence, salivary flow rate and efficacy of fluoride gel treatment in irradiated patients. Caries Research. 1994;28:388-393
48. Wang C, Huang E, Esu H, Chen H, Fang F, Hsiung C. The degree and time course assessment of radiation induced trismus occurring after radiotherapy for nasopharyngeal cancer. The Laryngoscope. 2008;15:1458-60
49. Jham BC, Reis PM, Miranda EL, Lopes RC, Carvalho AL, Scheper MA, Freire AR. Oral health status of 207 head and neck cancer patients before, during and after radiotherapy. Clinical Oral Investigations. 2008;12:19-24
50. Schuurhuis JM, Stokman MA, Roodenburg JLN, Reintsema H, Langendijk JA, Vissink A, Spijkervet FKL. Efficacy of routine pre-radiation dental screening and dental follow-up in head and neck oncology patients on intermediate and late radiation effects. A retrospective evaluation. Radiotherapy and Oncology. 2011;1-1:403-409
51. Meurman JH & Gronroos. Oral and dental health care of oral cancer patients: hyposalivation, caries and infections. Oral Oncology. 2010;46:464-467
52. De Moor RJG, Stassen IG, van't Veldt Y, Torbeyns D & Hommez GMG. Two-year clinical performance of glass ionomer and resin composite restorations in xerostomic head- and neck-irradiated cancer patients. Clinical Oral Investigations 2011;15(1):31-8.
53. Bender IB, SeltzerS. Roentgenographic and direct observation of experimental lesions in bone I: JADA 62:26. 1961
54. Bender IB, SeltzerS. Roentgenographic and direct observation of experimental lesions in bone II: JADA 62:82. 1961
55. Al-Nawas B, Grotz KA. Prospective study of the long term change of the oral flora after radiation therapy. Supportive Care in Cancer. 2006;14:291-296
56. Cobb CM. Clinical significance of non-surgical periodontal therapy: an evidence based perspective of scaling and root planning. Journal of Clinical Periodontology. 2002:29(S2);6-16
57. Dijkstra PU, Kalk WWI, Roodenburg JLN. Trismus in head and neck oncology: a systematic review. Oral Oncology. 2004;40:879-889
58. Wang C, Huang E, Hsu H, Chen H, Fang F, Hsiung C. The Degree and Time-Course Assessment of Radiation-Induced Trismus Occurring After Radiotherapy for Nasopharyngeal Cancer. The Laryngoscope. 2005;115:1458–1460
59. Beumer J, Curtis TA, Hamson RE. Radiation therapy of the oral cavity: sequelae and management, part 1.Head Neck Surg 1979;1:301-12.
60. Beumer J, Curtis TA, Harrison RE. Radiation therapy of the oral cavity: sequelae and management, part 2. Head Neck Surg 1979;1~392-408.
61. Nabil S, Samman N. Risk factors for osteoradionecrosis after head and neck radiation: a systematic review. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. 2012:113(1):54-69
62. Jereczek-Fossa BA, Orecchia R. Radiotherapy-induced mandibular bone complications. Cancer Treatment Reviews. 2002;28:65-74
63. Balogh JM, Sutherland SE. Osteoradionecrosis of the mandible: a review. Journal of Otolaryngology 1989;18:245-250.

64. Mendenhall WM. Mandibular osteoradionecrosis. Journal of Clinical Oncology 2004;22:4867-4868.
65. Friedman RB. Osteoradionecrosis: causes and prevention. Journal of National Cancer Institute Monographs. 1990;9:145-148.
66. Beumer J, Harrison R, Sanders B et al. Osteoradionecrosis: predisposing factors and outcomes of therapy. Head and Neck Surg. 1984;6:819
67. Koga DH, Salvajoli JV, Alves FA. Dental extractions and radiotherapy in head and neck oncology: review of the literature. Oral Diseases. 2008;14(01):40-44.
68. Clayman L. Management of Dental Extractions in irradiated Jaws. A protocol without hyperbaric oxygen therapy. Journal of Oral and Maxillofacial Surgery. 1997;55:275-281
69. Katsura K, Sasai K, Sato K, Saito M, Hoshina H and Hayashi T. Relationship between oral health status and development of osteoradionecrosis of the mandible: A retrospective longitudinal study. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. 2008;105:731-738.
70. Curi MM & Lauria L. Osteoradionecrosis of the jaws: a retrospective study of the background factors and treatment in 104 cases. Journal of Oral and Maxillofacial Surgery 1997;55:540-544.
71. Studer G, Glanzmann C, Studer SP, Gratz KW, Bredell M, Locher M, Lutolf UM, and Zwahlen RA. Risk-adapted dental care prior to intensity-modulated radiotherapy (IMRT). Schweiz Monatsschr Zahnmed. 2011 121: (3) 216-29
72. Lye KW, Wee J, Gao F, Neo PSH, Soong YL and Poon CY. The effect of prior radiationtherapy for treatment of nasopharyngeal cancer on wound healing following extractions: incidence of complications and risk factors. Int. J. Oral Maxillofac. Surg. 2007;36:315-320.
73. Reuther T, Schuster T, Mende U and Kubler A. Osteoradionecrosis of the jaws as a side effect of radiotherapy of head and neck tumour patients — a report of a thirty year retrospective review. Int. J. Oral Maxillofac. Surg. 2003;32:289-295.
74. Niewald M, Barbie O, Schnabel K, Engel M, Schedler M, Nieder C and Berberich W. Risk factors and dose-effect relationship for osteoradionecrosis after hyperfractionated and conventionally fractionated radiotherapy for oral cancer. The British Journal of Radiology 1996;69(825):847-851. 31.
75. Morrish RB, Chan E, Silverman S, Meyer J, Fu KK and Greenspan D. Osteonecrosis in Patients Irradiated for Head and Neck Carcinoma. Cancer 1981;47(8):1980-1983.
76. Regezi JA, Courtney RM, Kerr DA. Dental management of patients irradiated for oral cancer. Cancer. 1976;8:994-1000
77. Thorn JJ, Hansen HS, Specht L and Bastholt L. Osteoradionecrosis of the Jaws: Clinical Characteristics and Relation to the Field of Irradiation. J. Oral Maxillofac. Surg. 2000;58:1088-1093
78. Kluth EV, Jain PR, Stuchell RN and Frich JC. A study of factors contributing to the development of osteoradionecrosis of the jaws. The Journal of Prosthetic Dentistry 1988;59(2):194-201.
79. Monnier Y, Broome M, Betz M, Bouferrache K, Ozsahin M, Jaques B. Mandibular Osteoradionecrosis in Squamous Cell Carcinoma of the Oral Cavity and Oropharynx: Incidence and Risk Factors Otolaryngology. Head and Neck Surgery. 2011;144:726
80. Lee JI, Koom WS, Lee CG, Kim YB, Yoo SW, Keum KC, Kim GE, Choi EC, Cha IH. Risk Factors and Dose–Effect Relationship for Mandibular Osteoradionecrosis in Oral and Oropharyngeal Cancer Patients. International Journal of Radiation Oncology * Biology * Physics. 2009;75(4):1084-1091
81. Lyons AJ, West CM, Risk JM, Slevin NJ, Chan C, Crichton S, Rinck G, Howell D, Shaw RJ. Osteoradionecrosis in head and neck cancer has a distinct genotype-dependent cause. International Journal of Radiation Oncology Biology Physics. 2012:82(4);1479-84
82. Carl W, Schaaf NG and Sako K. Oral surgery and the patient who has had radiation therapy for head and neck cancer. Oral Surgery. 1973;36(5):651-657
83. Chavez JA and Adkinson CD. Adjunctive Hyperbaric Oxygen in Irradiated Patients Requiring Dental Extractions: Outcomes and Complications. Journal of Oral Maxillofacial. Surgery. 2001;59:518-522
84. Fenlon MR, Lyons A, Farrell S, Bavisha K, Banerjee A, Palmer RM. Factors Affecting Survival and Usefulness of Implants Placed in Vascularized Free Composite Grafts Used in Post–Head and Neck Cancer Reconstruction. Clinical Implant Dentistry and Related Research. 2012;14(2):266-272
85. Sammartino G, Marenzi G, Cioffi I, Tete S, Mortellaro C. Implant therapy in irradiated patients. Journal of Craniofacial Surgery. 2011;22(2):443-445
86. Yerit KC, Posch M, Seemann M, Hainich S, Dörtbudak O, Turhani D, Özyuvaci H, Watzinger F, Ewers R. Implant survival in mandibles of irradiated oral cancer patients. Clinical Oral Implants Research. 2006;17(3):337–34
87. Visch LL, van Waas MAJ, Schmitz PIM & Levendag PC. A Clinical Evaluation of Implants in Irradiated Oral Cancer Patients. Journal of Dental Research 2002;81(12):856-859.
88. Jisander S, Grenthe B, Alberius P. Dental implant survival in the irradiated jaw: a preliminary report. Int J Oral Maxillofac Implants. 1997 Sep-Oct;12(5):643-8.
89. Barber AJ, Butterworth CJ, Rogers SN. Systematic review of primary osseointegrated dental implants in head and neck oncology. British Journal of Oral and Maxillofacial Surgery. 2011;49:29-36
90. Javed F, Al-Hezaimi K, Al-Rasheed A, Almas K, Romanos GE. Implant survival rate after oral cancer therapy: a review. Oral Oncology. 2010;46(12):854-859
91. Dholam KP, Gurav SV. Dental implants in irradiated jaws: A literature review. Journal of Cancer Research and Therapeutics. 2012:8(6);85-93
92. Esposito M, Grusovin MG, Patel S, Worthington HV, Coulthard P. Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants (Review). The Cochrane Library. 2008;4
93. Bonan PRF, Lopez MA, Pires FR, de Almeida OP. Dental management of low socioeconomic level patients before radiotherapy of the head and neck with special emphasis on the prevention of osteoradionecrosis. Brazil Dental Journal. 2006;17(4):336-342
94. Starcke EN and Shannon IL. How critical is the interval between extractions and irradiation in patients with head and neck malignancy? Oral Surg. 1977;43(3):333-337.
95. Tong AC, Leung AC, Cheng JC, Sham J. Incidence of complicated healing and osteoradionecrosis following tooth extraction in patients receiving radiotherapy for treatment of nasopharyngeal carcinoma. Australian Dental Journal. 1999;44(3):187-194
96. Maxymiw WG, Wood RE and Liu FF. Postradiation dental extractions without hyperbaric oxygen. Oral Surg. Oral Med. Oral Pathol. 1991;72(3):270-274.
97. Hariot JC, Bone MC, Ibrahim E, Castro JR. Systematic dental management in head and neck irradiation. International Journal of Radiation Oncology Biology Physics. 1983;7:1025-1029
98. Oh HK, Chambers MS, Martin JW, Lim HJ and Park HJ. Osteoradionecrosis of the Mandible: Treatment Outcomes and Factors Influencing the Progress of Osteoradionecrosis. Int. J. Oral. Maxillofac. Surg. 2009;67:1378-1386.
99. Koga DH, Salvajoli JV, Kowalski LP, Nishimoto IN, Alves FA. Dental extractions related to head and neck radiotherapy: ten year experience of a single institution. Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontics. 2008;105(5):e1-6.
100. Ben-David MA, Diamante M, Radawski JD, Vineberg KA, Stroup C, Murdoch-Kinch CA, Zwetchkenbaum SR and Eisbruch A. Lack of Osteoradionecrosis of the Mandible after Intensity-Modulated Radiotherapy for Head and Neck Cancer: Likely Contributions of both Dental Care and Improved Dose Distributions. Int. J. Radiation Oncology Biol. Phys. 2007;68(2):396-402.
101. Widmark G, Sagne S and Heikel P. 0steoradionecrosis of the jaws. Int. J. Oral Maxillofac. Surg. 1989;18:302-306.
102. Makkonen TA, Kiminki A, Makkonen TK and Nordman E. Dental extractions in relation to radiationtherapy of 224 patients. Int. J. Oral Maxillofac. Surg. 1987;16:56-64.
103. Epstein JB, Rea G, Wong FLW, Spinelli J and Stevenson-Moore P. Osteonecrosis: Study of the Relationship of Dental Extractions in Patients Receiving Radiotherapy. Head & Neck Surgey 1987;10:48-54.
104. Marciani RD and Ownby HE. Osteoradionecrosis of the Jaws. Int. J. Oral Maxillofac. Surg. 1986;44:218-223.
105. Coffin F. The incidence and management of osteoradionecrosis of the jaws following head and neck radiotherapy. The British Journal of Radiology 1983;56:851-857.
106. Beumer J, Curtis TA and Morrish RB. Radiation complications in edentulous patients. J. Prosthet. Dent. 1976;36(2):193-203.
107. Daly TE, Drane JB, MacComb WS. Management of problems of the teeth and jaws in patients undergoing irradiation. American Journal of Surgery. 1972;124:539-542