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# Oral and Dental Management for Head and Neck Cancer Patients Treated by Chemotherapy and Radiotherapy

**Abstract:** The incidence of head and neck cancer is rising. The attendant oral complications of cancer management make oral health maintenance a lifelong challenge for these patients. Holistic management in the context of a core multidisciplinary team is essential in optimizing outcomes. Predicting the risk of adverse oral outcomes is difficult. Effective communication between healthcare professionals in the core and extended teams and with the patient is essential.

**Clinical Relevance:** Primary care dental teams will be involved in the long-term management of oral care for head and cancer patients. A broad understanding of the management of head and neck cancer, consequences of treatment and the need for good communication is key to good quality patient care.

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Cancers of the head and neck include those of the oral cavity, oropharynx, salivary glands, sinuses, nasopharynx, hypopharynx and larynx. There are approximately 6,700 new head and neck cancers diagnosed each year in England and Wales and approximately 1,100 in Scotland. Eighty-five percent of cases are in people aged over 50 years, however, there is evidence of increasing incidence in younger people.[1,2,3] There has been a more than 30% increase in oral cavity cancer between 1990 and 2006 and the incidence of oropharyngeal cancer has more than doubled.[1] There may be a change in the pattern of aetiology of oropharyngeal cancer, with human papilloma virus (HPV) rather than smoking and alcohol being the primary risk factor in a younger sub-population. Ninety percent of patients presenting with head and neck cancer have pre-existing dental disease. Many also have co-morbidities. These factors, together with the increasing retention of teeth into old age, result in significant challenges in the management of the oral and dental health for these patients.

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The management of head and neck cancers may include treatment by surgery or by chemotherapy and radiotherapy, or a combination of modalities. Care is delivered by multidisciplinary teams (MDTs) exercising shared decision-making under significant time pressures. These teams include maxillofacial, ENT and plastic surgeons, oncologists, radiologists, pathologists, speech and language therapists, cancer nurse specialists, dietitians and restorative dentists as core members. Extended team members include general dental practitioners, dental therapists and maxillofacial technologists.

The treatment of head and neck cancers may produce a number of complications. The primary treatment of oral cavity disease is surgery. Those complications resulting from surgery are discussed elsewhere in this issue (pp98–106). This article will describe the management of those complications produced by chemotherapy and radiotherapy.

Where surgery is not indicated as primary treatment for a head and neck cancer, chemotherapy may be given as primary treatment prior to chemo-radiotherapy (neo-adjuvant) or as part of concurrent primary chemo-radiotherapy. Where surgery has been the primary treatment, some cases require post-operative radiotherapy or chemo-radiotherapy (adjuvant treatment). Chemotherapeutic agents commonly used are 5-fluorouracil cisplatin and docetaxel. There is evidence that survival outcomes are improved when concomitant chemo-radiotherapy is used as an adjuvant treatment compared with adjuvant radiotherapy alone however, for some patients, co-morbidities may preclude the use of concomitant chemo-radiotherapy.[4]

## Oral and dental complications of chemotherapy and radiotherapy

The complications of chemo-radiotherapy vary between individuals and between different tumour sites and can be difficult to predict accurately. The effects are dose-related and are significant above an absorbed radiation dose of 60 Grays (Gy).

**Figure 1.** Radiation-associated caries.

**Figure 2.** Trismus.

Intensity modulated radiotherapy (IMRT) may reduce these side-effects but is more complicated and time consuming to plan and execute than conventional radiotherapy and is not available in all centres.[5] There is some emerging evidence that patients with HPV positive oropharyngeal cancer have improved survival outcomes.[6] The suggestion has followed that perhaps, in the future, less aggressive treatment could still be curative in this context. This is currently being investigated in a UK multicentre trial (DeESCALaTE).

There are early and late complications as follows.

**Early**

***Mucositis***

This is inflammation and ulceration of the upper aerodigestive tract mucosa and can cause severe pain necessitating opioid analgesia. It begins 1–2 weeks following the onset of chemotherapy or radiotherapy but usually resolves after treatment is completed. If mucositis is severe then swallowing may be inhibited to the extent that enteral feeding is required. This may be via nasogastric tube, percutaneous endoscopic gastrostomy tube (PEG) or radiologically inserted gastrostomy tube (RIG). Pain with mucositis can inhibit effective oral hygiene.

***Infection***

Chemotherapy can result in profound compromise to the immune system. Patients affected in this way are highly susceptible to fungal, bacterial and viral infections at this time.

***Taste disturbance***

This is due to a combination of xerostomia and direct damage to taste receptors. In some patients this will reduce over time.

***Dysphagia***

Difficulty with swallowing may be a short- and long-term problem and may mean that long-term use of enteral feed or nutritional supplements is required.

**Late**

***Xerostomia***

Dry mouth is both a short- and long-term effect. Salivary hypofunction is defined as resting salivary flow rate of less than 0.2 ml per minute or stimulated salivary flow rate of less than 0.7 ml per minute. This is caused by direct ionizing radiation damage to the cells of the saliva glands in the radiotherapy fields. Xerostomia can result in difficulties with swallowing, speaking, eating and in susceptibility to oral infections and dental caries development. IMRT may reduce the radiation dose to the parotid glands and surgical transfer of the submandibular saliva gland has been suggested as a method of prevention of xerostomia.[7]

***Radiation-associated caries (Figure 1)***

Lack of saliva results in reduced buffering effect, reduced clearance and alteration of oral microflora to favour cariogenic bacteria. Pain from mucositis can inhibit effective oral hygiene. Many patients will be prescribed liquid nutritional supplements which contain refined carbohydrate that can be either sucrose or glucose. These preparations are often of a consistency which favours adhesion to the oral surfaces. These factors, together with the high calorie/frequent intake diet advised by dietitians to promote maintenance of weight during and after treatment, can lead to rapidly developing widespread caries. Close liaison between dietitian, restorative dentist and dental hygienist is essential.

***Trismus (Figure 2)***

This is defined as mouth opening of less than or equal to 35 mm in the dentate patient.[8] Trismus is a consequence of fibrosis of the muscles of mastication following radiotherapy which has involved these muscles in the radiotherapy fields. The resultant fibrosis is irreversible. Most of the total reduction in mouth opening occurs over the first 9 months after radiotherapy. This can lead to problems with eating, communication, performing oral hygiene, denture wearing, and carrying out dental treatment. Access to the oral cavity can also be compromised by surgically induced microstomia as a result of treatment for lip or buccal mucosa cancer. This may be exacerbated by adjuvant radiotherapy.

***Osteoradionecrosis (ORN) (Figure 3)***

This is defined as exposed bone present for at least 3 months in an area which has been previously irradiated and does not represent a tumour recurrence. ORN is caused by trauma to the irradiated jaw (such as tooth extraction) but can also occur spontaneously. This condition can also arise as a result of inadequate healing time following pre-radiotherapy extractions. ORN carries risk of mortality and significant morbidity; intractable pain, pathological fracture and oro-cutaneous fistula may develop (Figure 4). It may be treated using hyperbaric oxygen (HBO) but evidence for this is not robust. A trial examining HBO in treatment of ORN is running across Europe currently (DAHANCA 21). The HOPON (Hyperbaric Oxygen for the Prevention of Osteoradionecrosis) multicentre trial currently running in the UK aims to clarify the effectiveness of HBO in preventing ORN in patients who have surgical procedures to the irradiated jaws.

## Pre-treatment assessment

This is carried out by a consultant in restorative dentistry. Patients whose oral cavity, teeth salivary glands and jaws will be affected by treatment should have assessment as early as possible to maximize the time available for treatment. Unfortunately, owing

**Figure 3.** Osteoradionecrosis.

**Figure 4.** Oro-cutaneous fistula as a result of osteoradionecrosis.

**Figure 5.** Use of tongue spatula bundles to address trismus.

**Figure 6.** Therabite® device.

to the complexities of cancer diagnosis and treatment planning and management, this is challenging. Patients may have multiple appointments to attend for assessments by all MDT members and can find the pace and volume of new and daunting information overwhelming. A full history and examination are carried out to elicit any existing oral and dental problems aside from the tumour itself. Appropriate radiographs and special investigations are performed.

The aims of pre-treatment assessment by the restorative dentist are as follows.

**Avoidance of unscheduled interruptions to primary treatment as a result of dental problems**

It is essential to elicit any dental problems which may interrupt or compromise the course of cancer treatment. There is evidence for reduced survival in patients who have interruption to treatment and therefore dental treatment to avoid this risk must be pro-active.[9] This is the main reason for extraction of teeth of uncertain prognosis prior to treatment. There is no point in saving a tooth if survival is compromised. This must be balanced against the need to optimize functional outcomes after treatment and decision-making at this point is therefore the role of the restorative consultant, who is a core member of the head and neck cancer MDT. These decisions are often complex and require an holistic approach to the individual patient informed by interaction with other MDT members.

**Minimization of post-treatment oral and dental complications**

This involves an assessment of the risk of long-term complications for individual patients. Pro-active dental treatment aimed at ensuring that the patient can achieve optimum and maintainable oral health following cancer management is balanced against carrying out overly aggressive treatment. This is often challenging as individual outcomes can be difficult to predict. There is some evidence that osteoradionecrosis and trismus risk may be genetically determined by alleles of the TGFβ1 gene.[10]

Decisions in pre-treatment oral management plans will be informed by discussions with other head and neck cancer MDT members at team meetings. Final plans must be communicated effectively with the rest of the MDT, particularly surgeons, oncologists and cancer nurse specialists.

## Pre-treatment management

**Preventive management and restorative care**

The oral and dental side-effects of cancer treatment are explained and preventive advice given.

Patients are given instruction on good oral hygiene and advice with regard to caries prevention. This is done in conjunction with head and neck cancer specialist dietitians.

Patients are prescribed high concentration fluoride toothpaste (Colgate Duraphat® 5000ppm toothpaste (1.1% sodium fluoride) and fluoride mouthrinse (0.05% sodium fluoride) for daily use, eg Colgate FluoriGard® or 0.2% sodium fluoride for weekly use, eg Duraphat® weekly dental rinse). Casein phosphopeptides – amorphous calcium phosphate (Recaldent™) in GC Tooth mousse® may be of benefit for remineralizing early carious lesions. Fluoride mouthrinse should be used at a different time from the toothpaste.

Trismus reduction exercises are recommended, especially for those who are to have surgery and/or radiotherapy in the region of the temporomandibular joints and the muscles of mastication. Exercise should involve vertical and horizontal range of motion exercises. Use of bundles of tongue spatulas (Figure 5), custom-made trismus screw or TheraBite® (ATOS Medical) device (Figure 6) have been advocated. The evidence for the effectiveness of these exercises is, however, limited.

Impressions may be taken for study models and fluoride applicator tray construction (and obturator construction and implant planning where appropriate).

Teeth which have failing restorations or caries but good overall prognosis and outwith proposed radiotherapy fields can be dressed or restored if time permits.

Xerostomia and mucositis can make denture-wearing difficult. Existing dentures are likely to be abandoned during treatment. Patients should be counselled appropriately.

**Pre-chemoradiotherapy extractions**

Teeth with doubtful long-term prognosis and which lie in the radiotherapy fields should be extracted. Extraction of these teeth following radiotherapy incurs high risk of ORN. Extractions should be carried out as early as possible: ideally at the time of primary surgery if adjuvant radiotherapy is planned and at least 10 days and, ideally, 21 days before radiotherapy begins. Atraumatic technique is essential and primary closure of surgical sites should be achieved wherever possible.

**Planning for prosthetic rehabilitation**

This is covered elsewhere in this issue (pp98–106).

## Oral and dental management during treatment

Ideally, patients should have regular contact with a dental hygienist if available at the cancer centre. If not, nursing staff can provide appropriate care. Various topical treatments for mucositis have been advocated, including ice chips prior to chemotherapy cycles, Benzydamine hydrochloride oral rinse (Difflam, Meda Pharmaceuticals),[11] *Caphosol* (EUSA Pharma) and Mugard® (Spepharma).

If pain from mucositis is severe, oral hygiene other than chlorhexidine gluconate rinse (sometimes diluted 50:50) at this stage may be virtually impossible. Some patients can only tolerate oral swabbing with a moist sponge. Manual toothbrushing should be resumed as pain subsides. Some patients are able to drink nutritional supplements which all contain refined carbohydrate (sucrose and/or glucose) and frequent small sips are taken. This, together with lack of good oral hygiene and poor tolerance to the strong flavours of fluoride toothpastes and mouthrinses, makes this a period of high risk for caries development. Close liaison with the dietitian and dental hygienist at this stage are critical. *OraNurse* unflavoured toothpaste (RIS Products Ltd) has 1450ppm sodium fluoride and may be useful at this time. Hard or spicy foods and extremes of temperature are avoided.

Chemotherapy can produce a profound reduction in immune function. Scaling and root planing are contra-indicated during chemotherapy owing to infection risk.

Candidiasis is common and may require treatment with systemic antifungals.


**Figure 7. (a, b)** Thirty-two year-old female patient with carcinoma ex PSA in lower right retromolar region treated by primary surgery with facial split access approach and reconstructed with radial forearm free flap. **(c)** Post-operative chemo-radiotherapy in the same patient as **(a, b)** has caused inflammatory changes in the skin in the radiotherapy field. Note healing surgical access scars in right side of neck. **(d, e)** Same patient 3 years post treatment. Healed flap visible at LR7 region. Excellent outcome due to optimum pre- peri- and post-treatment dental management despite the significant trismus and xerostomia now present.

## Oral and dental management after primary treatment

Follow-up will be frequent in the first few months after treatment. As post-treatment symptoms reduce, patients may be able to consume more food and drink orally. For some, a safe swallow never recovers and the necessity for tube-feeding persists long term. Some individuals may continue long term on oral nutritional supplements. Dietitians encourage small frequent meals and appetite can be poor at this stage. In consequence, a high calorie sweet diet may be encouraged for weight maintenance. This needs close supervision to ensure oral health is maintained. Patients are encouraged to return to fluoride mouthwash and high concentration fluoride toothpaste use and use of fluoride applicator trays if possible. In some cases, trismus precludes the use of fluoride trays. GC Tooth Mousse® may also be of benefit. Chlorhexidine gel applied using trays for 5 minutes each night for a 2-week period and repeated every 3 months may be helpful in reducing the dominance of cariogenic bacteria in the oral flora of xerostomic patients.[12]

Good oral hygiene is essential and the dental hygienist will help the patient adapt individual approaches as the outcomes of the effects of surgical and non-surgical cancer treatment become apparent.

Post-surgical prosthetic oral rehabilitation will be carried out if required.

If replacement dentures are required, construction is optimal around 4–6 months after completion of treatment.

The symptoms of xerostomia can be managed by the use of salivary stimulants and saliva substitutes.

### Salivary stimulants

Chewing sugar-free gum can stimulate saliva production via stimulation of oral chemoreceptors and mechanoreceptors (ie taste and chewing effect). Pilocarpine, a parasympathomimetic drug, may help with patients who have some residual salivary function following radiotherapy but has unpleasant side-effects.

The use of an intra-oral electrostimulating device has been reported in Sjögren's disease and is the subject of an ongoing randomized controlled trial soon to open in London and Bradford (Leonidas 2).[13]

#### Saliva substitutes

Frequent sipping of sugarless fluids can be used to alleviate dryness but the effect is short lasting and produces polyuria.

Saliva replacements currently approved for use by the Advisory Committee on Borderline Substances (ACBS) for patients who have dry mouth as a result of radiotherapy are:

- AS Saliva Orthana® (AS Pharma): a mucin (porcine) based spray which contains fluoride and has duration of effect of about 30 minutes. The spray should be directed towards the buccal sulcus and the ventral surface of the tongue.
- BioXtra® (RIS Products Ltd): a hydroxethylcellulose-based gel or spray. Has antimicrobial function based on lactoferrin, lysozyme, lactoperoxidase, immunoglobulins and colostrum extracts. The gel can be helpful at night.
- Salivese® (Wyrem Medical Ltd): an oral spray with carmellose sodium. It is an aqueous solution of electrolytes and has neutral pH.
- Glandosane® (Fresenius Kabi Ltd) has acidic pH (5.75) and should not be given to dentate patients.

Saliva replacements approved for use in any condition giving rise to a dry mouth include:

- Biotène Oral Balance® (GSK): hydroxethylcellulose-based gel and mouthrinse. These should be used with Biotène Oral Balance toothpaste® (GSK) as the sodium lauryl sulphate in ordinary toothpaste destroys the bulking agent in Oral Balance gel.
- Xerotin® (Spepharm)carboxymethylcellulose-based spray. Contains a formaldehyde releaser as a preservative so should be avoided in patients with allergy to formaldehyde and formaldehyde-releasing compounds.

## Long-term management

Xerostomia, trismus and risk of radiation caries and ORN are lifelong and patients require close follow-up long after being discharged from 5-year cancer follow-up. A combination of effective planning prior to cancer treatment and effective follow-up care should result in good functional and aesthetic oral and dental outcomes (Figure 7). Those worst affected by late complications may need extended follow-up by the specialist centre but others can be discharged to continuing primary care follow-up.

## The role of the primary care team

Many patients will have been referred by their GDP to the cancer team in the first place. The GDP may be asked to carry out urgent dental treatment prior to commencement of treatment for cancer. Pre-radiotherapy extractions are usually managed in the cancer centre. Many patients, however, do not have a regular GDP. Patients will be followed-up initially in the cancer centre but many will eventually be returned to primary care. All patients with late complications will remain highly susceptible to dental disease for life. The primary care dentist and team can help by providing regular follow-up and regular prescription of high concentration fluoride toothpaste and fluoride mouthwash. Close liaison with the cancer MDT and secondary care dental team is essential.

If a patient requires any extractions after radiotherapy he/she must be referred back to the cancer centre owing to the risk of ORN.

## Conclusions

The management of the oral health of head and neck cancer patients who have chemotherapy or radiotherapy as part of their cancer treatment is complex. The primary care team has a vital role to play in providing treatment in the wider context of the head and neck cancer multidisciplinary team and will be involved in lifelong patient care and consequent quality of life in conjunction with the restorative dentist. This teamwork is central to producing optimum functional aesthetic outcomes for this highly challenging patient group.

#### Acknowledgement

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#### Further Reading

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