Predicting and Managing Oral and Dental Complications of Surgical and Non-Surgical Treatment for Head and Neck Cancer

A Clinical Guideline

RD-UK
Consultant & Specialist Group
Informing, Educating & Inspiring

British Association of Head and Neck Oncology Nurses

BAHNO
BRITISH ASSOCIATION OF HEAD AND NECK ONCOLOGISTS

ROYAL COLLEGE OF SPEECH & LANGUAGE THERAPISTS

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KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1^{++} High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTS with a very low risk of bias

1^{+} Well conducted meta-analyses, systematic reviews of RCTS, or RCTs with a low risk of bias

1 Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias

2^{++} High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2^{+} Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2^{-} Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3 Non-analytic studies, eg case reports, case series

4 Expert opinion

GRADES OF RECOMMENDATION

Note: the grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A At least one meta-analysis, systematic review of RCTs, or RCT rated as 1^{++} and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population and demonstrating overall consistency of results

B A body of evidence including studies rated as 2^{++}, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1^{++} or 1^{-}

C A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2^{++}

D Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2^{+}

GOOD PRACTICE POINTS

✓ Recommended best practice based on the clinical experience of the guideline development group

1 Introduction

1.1 THE NEED FOR A GUIDELINE

Approximately 9200 patients with new cancers of the head and neck are registered in the UK each year. The incidence of this disease has tended to increase with age and in the UK, 85% of cases occur in people over the age of 50. There is now evidence that the incidence of head and neck cancers is increasing among young people of both sexes. This may be in association with Human Papilloma Virus (HPV) induced cancers. Head and neck cancer tends to be a disease associated with deprivation and the risk of developing the disease is four times greater in men living in the most deprived areas.

Approximately 90% of patients presenting with head and neck cancer have dental disease and the treatment of head and neck cancer produces significant oral/dental side effects.

More people are retaining teeth into old age. The Adult Dental Health Survey 2009 published in 2011 looked at the dental health of the UK apart from Scotland[1]. This showed that 94% of the combined populations of England, Wales and Northern Ireland were dentate (that is had at least one natural tooth). The proportion of adults in England who were edentulous had fallen from 28% in 1978 to 6% in 2009.

Consequently, the oral and dental management of head and neck cancer patients is complex and will become an increasing challenge as patients retain their teeth longer. These issues are managed by the Consultant in Restorative Dentistry: a core member of the head and neck cancer multidisciplinary team[2].

There are UK guidelines for the management of head and neck cancers which outline oral rehabilitation[2,3,4]. Detailed guidelines for management of oral rehabilitation for head and neck cancer patients are lacking.

1.2 REMIT OF THE GUIDELINES

The guidelines address issues relating to oral and dental care at the pre-, peri- and post-treatment stages. They examine the quality of evidence for managing oral and dental complications from an holistic, pathway-based and multidisciplinary team-based approach. Opportunities for minimising these complications are considered.

The guidelines will be of interest to all healthcare professionals working with patients with head and neck cancers including restorative dentistry consultants, maxillofacial surgeons, ear, nose and throat surgeons, plastic surgeons, clinical oncologists, cancer nurse specialists, dental therapists, dietitians and speech and language therapists.

1.3 STATEMENT OF INTENT

These guidelines are not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technological advances and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the appropriate healthcare professional(s) in light of the clinical data and patient preferences. However, it is advised that significant departures from the national guidelines or any local guidelines derived from them should be fully documented in the patient's case notes at the time the relevant decision is taken.

1.4 REVIEW AND UPDATING

These guidelines were issued in 2016 and will be considered for review in three years.

2. The impact of head and neck cancer treatment on oral health.

The overall aim of treatment for head and neck cancer is to maximize locoregional control and survival with minimal resulting damage to function and form. Treatment of the primary tumour and neck may involve surgical resection with or without reconstruction or radiotherapy with or without chemotherapy. Adjuvant radiotherapy or chemoradiotherapy may be required following surgical resection. These treatment modalities can result in adverse short- and long-term oral, facial and dental complications. Surgical tumour resection can produce alterations to the normal anatomy which adversely affect function and outward appearance. Radiotherapy causes unavoidable radiation damage to normal tissues surrounding the tumour, affecting the function of these tissues both in the short-term (during and immediately after treatment) and long-term (for months and years after treatment or lifelong). Chemotherapy causes acute mucosal and haematological toxicity, with the former being accentuated if chemotherapy is delivered concurrently with radiation therapy. Thus, head and neck cancer treatment can have adverse effects on respiration, mastication, swallowing, speech, taste, salivary gland function, mouth opening and the outward appearance of the head and neck region. The complications of treatment need to be anticipated and managed by the multidisciplinary team with the input of the restorative dentistry consultant who is a core member of the head and neck cancer multidisciplinary team. Older patients increasingly have a greater proportion of retained, often heavily restored teeth. Oral rehabilitation and maintenance is therefore complex and lifelong, often continuing well beyond discharge from cancer follow up.

2.1 ORAL COMPLICATIONS OF TREATMENT

2.1.1 SHORT-TERM:

- Oral Mucositis: This is inflammation and ulceration of the mucosal lining of the oral cavity and oropharynx. This complication affects most patients having radiotherapy or chemoradiotherapy to the head and neck. It may be severe, requiring opioid analgesia to alleviate pain and impairs quality of life. Painful swallowing (odynophagia) caused by mucositis can markedly impair the intake and enjoyment of food and is a significant factor associated with difficulties eating and drinking and sustaining weight. Many centres across the UK plan nutritional management with prophylactic tube placement in anticipation of this symptom. Oral mucositis may inhibit or completely prevent oral hygiene and dental disease prevention measures due to inability to tolerate the physical trauma of toothbrushing or the strong flavours of toothpastes and mouthwashes. Onset of mucositis is within the first two weeks of treatment and usually resolves by six weeks after treatment.

- Infection: Chemotherapy-induced neutropenia renders the patient susceptible to bacterial, viral, and fungal infections. Oral candidal infections are extremely common following chemotherapy or radiotherapy. Antifungal drugs absorbed or partially absorbed from the gastrointestinal tract prevent oral candidiasis in patients receiving treatment for cancer. They are significantly better at preventing oral candidiasis than drugs not absorbed[5] .
- Trismus: This is restricted or limited mouth opening and mandibular hypomobility. This can be due to either active spasm (tonic contraction) of the muscles of mastication (also described as reflex guarding) or it can be due to physical restriction of the muscles of mastication and/or temporomandibular joint (TMJ) capsule. In relation to head and neck cancer, this physical restriction can be due to the presence of tumour, post-surgical inflammation or can be due to fibrosis of those tissues as a result of chemotherapy and radiotherapy. Following surgery and chemotherapy trismus may be reversible. However, trismus that follows radiotherapy can occur rapidly over the first 9 months after treatment[6], tends to be progressive and may be irreversible. Mandibular hypomobility ultimately results in both muscle and TMJ degeneration. If muscles do not move through their range of motion atrophy is evident within days. Immobilised joints quickly show signs of degeneration. Restricted mouth opening causes problems with eating, speaking, laughing, yawning, sexual intimacy, access for oral self care and access for oral care by any dental professional. This can result in social isolation and have an adverse effect on quality of life[7].
- Salivary hypofunction: This is defined as reduced resting salivary flow rate below 0.2ml per minute or stimulated salivary flow rate of less than 0.7 ml per minute. It is caused by ionising radiation damage to salivary tissue in the radiotherapy fields. In the acute phase, saliva thickens and stringy mucous is common. There is also a qualitative change in saliva with a change in consistency, reduced buffering effect, reduced clearance and reduced pH. The oral microflora is altered to favour cariogenic bacteria. Xerostomia, the subjective feeling of a dry mouth, is a consequence of hyposalivation. These changes lead to problems with speech, mastication, swallowing and increased risk of dental caries.
- Aguesia/Dysguesia (taste loss/altered taste): this is usually reversible. It can cause reduction in appetite due to loss of pleasure in eating.

2.1.2 LONG-TERM:

- Altered anatomy/impaired function and appearance: Surgical ablation and reconstruction can cause permanent changes in facial and oral anatomy. There may be significant difficulties with speech, mastication and swallowing if there are surgically produced intra-oral defects or alterations to anatomy. Examples include maxillectomy, soft palate defect or alteration, tongue defect or alteration or loss of significant numbers of opposing pairs of teeth. Facial appearance may be significantly adversely affected. Prosthetic rehabilitation is often difficult after surgery and sometimes impossible, especially where rehabilitation is not planned with the restorative dentistry consultant ahead of ablation.
- Trismus (as above)
- Salivary hypofunction (as above)

- Radiotherapy-associated dental caries: This is an indirect effect of non-surgical treatment (chemotherapy and radiotherapy). Radiation associated caries can develop as a result of reduced salivary flow and altered saliva function in combination with the high protein and calorie diet. This includes sucrose and glucose dense nutrition and 'little and often' dietary approach frequently necessary and advocated, within the context of appropriate nutritional management, by dietitians. This effect can be compounded by reduced tolerance to caries prevention measures at this phase in treatment. Rapidly developing, widespread caries can result that is often circumferential around the teeth and may affect incisal edges. Nutritional supplements are often necessary. Some nutritional supplements are particularly cariogenic due to their sucrose and glucose content, sticky texture and frequent intake. Particular care is needed at this time if caries is to be avoided and close, joint supervision of the patients by dietitians and restorative dentistry consultants is essential.
- Osteoradionecrosis (ORN): This entity is defined as an area of exposed bone of at least three months duration in an irradiated site and not due to tumour recurrence. This may cause long-term significant morbidity.

2.2 MODERN RADIOTHERAPY SCHEDULES:

There is a correlation between the volume of parotid gland irradiated to 25-30Gy and the long-term recovery of salivary function [8,9].

Intensity Modulated Radiotherapy (IMRT) reduces the dose delivered to the parotid gland. It is complex to plan and deliver but it achieves a better balance between target coverage and normal tissue avoidance than conventional radiotherapy[10].

Sparing the parotid glands with IMRT significantly reduces the incidence of xerostomia in patients with oropharyngeal and hypopharyngeal tumours[11] 1++ and in nasopharyngeal tumours[12,13]1+ and leads to recovery of saliva secretion over time and improvements in associated quality of life. IMRT may be associated with a less frequent prevalence of trismus but this needs further study[14]. The weighted prevalence for ORN with IMRT is 5.2% compared with 7.3% for conventional radiotherapy but it is not clear if this is clinically significant[15] 3.

HPV-associated oropharyngeal cancers often occur in younger, relatively healthy patients with, possibly, healthy dentition. They may, therefore, experience late complications for many years. It is possible that treatment for such cancers may be de-escalated with a resultant reduction in late complication risk. However there is no firm evidence for this as yet and it remains controversial.

B IMRT has been shown to reduce long-term xerostomia and should be offered to all appropriate patients

3. Oral and dental management prior to treatment

3.1 AIMS OF PRE-TREATMENT MANAGEMENT

- The restorative dentistry consultant will identify those patients who need pre-treatment assessment at the multidisciplinary team meeting. This will generally include: patients requiring an assessment to consider oral rehabilitation, particularly those planned for surgical intervention that will alter oral anatomy, dentate patients requiring radiotherapy where the treatment field includes any part of the maxilla, mandible or salivary glands, patients with specific dental concerns

Aims:

- To avoid unscheduled interruptions to primary treatment as a result of dental problems
- To ensure the patient understands the nature and implications of the short- and long-term oral complications. Excellent communication skills are required as this is a time of immense anxiety for patients. Patients report that having access to combined, comprehensive MDT services on one site is an important advantage. Excellent communication by the Restorative team with the MDT is essential.
- To carry out appropriate dental treatment informed by assessment of individual risk of development of post treatment oral complications and taking into account the overall prognosis.
- To plan post-treatment prosthetic oral rehabilitation

Treatment planning at this stage is based around assessment of the risk of developing post-treatment long-term complications: altered anatomy, trismus, hyposalivation, radiotherapy associated caries and ORN. Patients whose oral cavity, teeth, salivary glands and jaws will be affected by radiotherapy to the oropharynx, nasopharynx, maxilla, mandible and parotid glands should have assessment and appropriate management as early as possible after the cancer treatment plan is made to allow time for any necessary dental treatment. This should render patient dentally fit before treatment and ensure the oral cavity can be rehabilitated and maintained after treatment. In the case of adjuvant radiotherapy, assessment may be prior to surgery and again prior to radiotherapy.

Potential for altered anatomy: Joint planning consultation with maxillofacial surgeons and restorative dentistry consultants may be required where patients are planned for surgery which will alter the oral cavity or cause microstomia and access difficulties. This is particularly true where maxillectomy procedures or primary implants are required.

Trismus risk: lack of uniform criteria to define trismus in the literature makes evaluation of study outcomes difficult when assessing risk[16] 2++. Criteria vary from less than 20mm of mouth opening to less than 40mm of mouth opening. Others give a graded rather than dichotomous definition. An inter-incisal distance of 35 mm or less as the cut-off point has been suggested[17]. Combining this with a subjective measurement of patient perception of change in mouth opening since treatment has also been advocated[7]. Reported prevalence rates for trismus are as follows: 25.4% for patients receiving conventional radiotherapy, 5% for those receiving IMRT and 30.7 % for radiotherapy and chemotherapy 2++. The risk of developing trismus as a result of radiotherapy to the head and neck appears to be dose dependent. Levels in excess of 60 Gy are more likely to result in trismus[18]. IMRT may be associated with less frequent incidence of trismus but this needs further study[14]. Risk seems to be greater when the TMJs and pterygoid muscles are exposed to ionizing radiation[19]. This is most likely in tumours of parotid gland, nasopharynx, oropharynx and posterior oral cavity. There is higher risk when pretreatment function is poor and for T3/T4 tumours. Chemoradiotherapy may be associated with an increased prevalence of trismus. Following development, restriction may be irreversible. Exercises early in the course of treatment may be of benefit. Some patients may be genetically predisposed to fibrosis. Transforming Growth Factor β1 (TGFβ1) is the major cytokine responsible for the regulation of fibroblast proliferation and differentiation. The development of ORN may be related to the presence of the T variant allele within the TGFβ1 gene [20]. Trismus may be overlooked by patients and clinicians and patients may assume it is 'normal' or will resolve. Onset of trismus is progressive and, if patients are on a feeding tube or liquid diet, this may not be evident until there is an attempt to resume normal oral intake.

Hyposalivation risk: See section 2.2

ORN risk: the reported incidence of ORN development following extraction of teeth from irradiated regions of the jaws is low. The total incidence is 7%[21]. The extraction of mandibular teeth within the radiation field in patients who have received a radiation dose higher than 60Gy represents a higher risk of ORN[21] 2++.

C Pre-radiotherapy extractions may be required especially where teeth are of doubtful long term prognosis and are in an area of mandible which will receive > 60 Gy

✓ **Patients deemed at risk of trismus should have instruction on home exercise and this should continue for 9 months following the start of radiotherapy.**

✓ **Inter-incisal distance should be monitored and sensitive anatomical structures should be protected during radiotherapy.**

✓ **If patients are deemed at risk of trismus they should be warned and the progressive and potentially irreversible nature explained.**

3.2 PRE-TREATMENT ASSESSMENT

Full history and clinical examination should be carried out:

This should cover:
Presenting concerns, relevant medical history: including TNM staging and cancer treatment plan, whether treatment will be curative or palliative and the overall prognosis for the patient. Information regarding nutritional intake should also be discussed with the dietitian in order to gauge caries risk.
Dental history: this should include patient motivation or anxiety and attitude to treatment
Social history: including smoking and alcohol intake, domestic situation and current and past employment status

Extra-oral examination: This should include assessment of cervical lymph nodes, temporomandibular joints, salivary glands and measurement of mouth opening ability.
Intra-oral examination: soft tissues (lips, buccal mucosa, floor of mouth, tongue, hard and soft palate, oropharynx), periodontal tissues (oral hygiene, periodontal probing depths, bleeding on probing, supra- and sub-gingival calculus, recession, mobility), dentition (teeth present, caries, tooth wear, presence and quality of restorations, occlusion) and any existing fixed or removable prostheses.
Radiographic examination: Panoramic radiograph, periapicals and bitewings as appropriate.
Special investigations: sensitivity testing, salivary flow rates

3.3 PRE-TREATMENT MANAGEMENT

3.3.1 PREVENTIVE MANAGEMENT

Note: current recommended methods of caries prevention[22] may not be tolerable for some patients during (chemo)radiotherapy due to acute toxicity. Prevention and management of mucositis, trismus and xerostomia will, therefore, contribute indirectly to caries prevention.

This should include:

- Instruction on maintenance of good oral hygiene; effective toothbrushing and interdental cleaning.
- Dietary advice with regard to caries prevention in conjunction with dietitians. Working jointly with dietitians allows optimisation of nutritional status to be balanced with prevention of dental caries. Management of nutritional supplements should be discussed specifically with regard to cariogenic potential and frequency and method of intake.
- Daily topical fluoride application (Duraphat 5000ppm fluoride toothpaste for adults at risk of radiation associated caries) in custom-made trays or brush-on.
- Daily 0.05% sodium fluoride mouthrinse.
- Daily use of GC Tooth Mousse ^{TM} containing free calcium for patients at risk of radiation associated caries

- Saliva replacement therapy/use of frequent saline rinses
- Advice on active jaw exercises in conjunction with the speech and language therapists from the outset of treatment to reduce or prevent trismus for patients at risk of trismus.
- Written information regarding the above should be given to the patient.

✓ **The benefits of caries prevention when cariogenic substances are taken by enteral tube should be considered alongside the importance of maintaining nutritional status, avoidance of feeding tube dependency and maintenance of swallowing function**

✓ **Where caries preventative measures are not tolerated the patient should be referred to the dietitian for appropriate nutrition support methods and guidance for the intake of cariogenic food and drinks**

3.3.2 IMPRESSIONS FOR STUDY MODELS

Dental impressions prior to cancer treatment allow for the construction of plaster models of the upper and lower teeth and hard palate. They provide a record of the pre-treatment tooth position and size which can be used for reference in post-surgical prosthetic rehabilitation. They are also required for:

- Primary implant planning
- Obturator construction
- Customised fluoride tray construction
- Where it is considered that post treatment impressions may be difficult or impossible due to trismus or microstomia

3.3.3 RESTORATION OF TEETH

- Required where restorations are failing or have the potential to traumatise soft tissues/flap
- Required where there is caries

3.3.4 EXTRACTION OF TEETH

- Extraction is required for teeth which are of doubtful prognosis, are unrestorable or at risk of dental disease in the future and are in an area deemed to be at risk of ORN. This includes grossly carious teeth, retained roots, teeth with apical pathology, mobile teeth, teeth associated with tumour, periodontally involved teeth, non-functional teeth, teeth close to osteotomy cuts, inaccessible teeth (or those predicted to be inaccessible after treatment)[23].
- There are no randomised controlled trials to assess the effect of extracting teeth prior to radiotherapy compared to leaving teeth in the mouth during radiotherapy to the jaws[24]2++. There are no randomised controlled trials regarding the minimum time recommended between dental extractions and the onset of radiotherapy. There is little evidence in the literature regarding pre-radiotherapy extractions and the prevention of ORN. There is lack of consistency in criteria for defining ORN compared with delayed healing. There is lack of detail in description of the precise

nature and level of surgical intervention involved in dental extraction and lack of detail regarding reason for extraction. Decisions are, therefore based on clinical experience and expert Restorative Dentistry Consultant opinion rather than on evidence base[25].

✓ **Extractions should be carried out as early as possible to maximise time for healing.**

✓ **Where it is known that adjuvant radiotherapy will be given, extractions should take place at primary surgery to maximise the time for healing and minimise the number of surgical events for patients.**

4. Oral and dental management during treatment

4.1 ORAL MUCOSITIS

This condition usually begins around 1-2 weeks after onset of treatment and can last around six weeks after treatment is complete. Severe pain produced by mucositis may inhibit oral hygiene measures. This means patients may stop toothbrushing and use of fluoride products. Toothbrushing and fluoride application should be resumed as soon as comfort permits. Basic oral care including dental care before during and after cancer treatment should improve oral comfort[26] 4. Chlorhexidine mouthwash should not be used to prevent oral mucositis in patients receiving radiation care for head and neck cancer. There may be other indications for its use, for example where there are difficulties with mechanical plaque control[26] 3.

Various preventive and management methods for oral mucositis have been advocated including neutral supersaturated calcium phosphate mouthrinse (Caphosol), polyvinyl pyrrolidine/sodium hyaluronate gel (Gelclair), mucoadhesive oral rinse (Mugard), soluble aspirin, benzydamine hydrochloride (Difflam)[27,28] 1, low level laser therapy[27,29] 3 and Zinc supplements [27,30] 3.

A Benzydamine mouthwash (Difflam) can prevent oral mucositis in patients having radiotherapy to the head and neck receiving moderate dose radiotherapy (up to 50 Gy) . This dose, however, would only be used for lymphoma.

D Low level laser therapy (wavelength around 632.8nm) may be used to prevent oral mucositis in patients undergoing radiotherapy without concomitant chemotherapy for head and neck cancer

D Zinc supplements administered orally may help prevent oral mucositis in oral cancer patients receiving radiotherapy or chemotherapy

✓ Basic oral care including use of bland rinses such as normal saline and sodium bicarbonate and dental professional care during treatment is of benefit

4.2 INFECTION

Oral candidal infections are common and there is strong evidence that some antifungal drugs prevent oral candidiasis caused by cancer treatment, but nystatin does not appear to be effective. Chlorhexidine gluconate has antifungal and antibacterial properties in addition to antiplaque effects; however, its value is still unconfirmed. Its tendency to stain teeth and its alcohol content, which can irritate inflamed tissues, are other potential drawbacks

4.3 HYPOSALIVATION (XEROSTOMIA)

4.3.1 PREVENTION

- Parotid sparing techniques

Sparing the parotid glands with IMRT significantly reduces the incidence of xerostomia in patients with oropharyngeal and hypopharyngeal tumours[11] 1++ and in nasopharyngeal tumours[12,13]1+ and leads to recovery of saliva secretion over time and improvements in quality of life.

- Cytoprotection
  Amifostine is a hydrophilic compound whose active metabolite, WR-1065 is selectively taken up by normal tissues. It is preferentially accumulated in certain tissues including salivary glands. WR-1065 acts as a radioprotectant by acting as a free radical scavenger for patients receiving radiotherapy. There is, however, question regarding the potential tumour protective effect and it has significant side effects including hypotension, nausea, vomiting, allergic reactions and severe toxic epidermonecrolysis (Steven-Johnson syndrome). There is no benefit shown from the use of amifostine in patients having concurrent chemoradiotherapy [31,32] 2++.
  There is no indication for routine use of pilocarpine in xerostomia prevention[31].

- Surgical transfer of the submandibular gland
  Transfer of the submandibular gland to the submental space can preserve its function and has been shown to prevent development of radiation induced xerostomia[31,32]4. The submandibular gland, however, will always be removed at neck dissection with lymph glands at level 1b for oral cavity disease. This technique, therefore, has limited applicability.

- Salivary Stimulants
  Pilocarpine HCl, a cholinergic parasympathomimetic agent can enhance salivary secretions in patients who have some functional salivary gland tissue preserved following radiotherapy. Oral administration of pilocarpine HCl 5mg three times daily is effective in the treatment of radiation-induced xerostomia in patients with head and neck cancer. The improvement declines after the cessation of treatment and therefore has to be administered lifelong[31,32,33]2++. Adverse effects include sweating, headache and urinary frequency. The use of pilocarpine is contraindicated in patients with a history of bronchospasm, severe COPD, congestive heart disease, angle closure glaucoma, uncontrolled asthma and gastric ulcers. Pilocarpine HCl suspended in a pastille or lozenge or administered as a mouthwash is also effective in improving xerostomia. Cevimiline is a muscarinic agonist which acts mainly on M1 and M3 muscarinic receptors and do not have the respiratory and cardiac side effects of pilocarpine [31,33]. Stimulation of residual function can also be achieved by chewing sugarless gum or lozenges.

- Acupuncture may be of benefit but further studies are required[31,32].

B Pilocaprine use is recommended, where appropriate, following radiotherapy in head and neck cancer for the improvement of xerostomia but this improvement may be limited.

4.3.2 TREATMENT

- Oral mucosal lubricants/Saliva substitutes

Xerostomia symptoms may be relieved by sipping sugarless fluids frequently but this results in polyuria. Several saliva substitutes are available including AS Saliva Orthana® (AS Pharma), Biotene Oralbalance Gel® (GSK), Saliveze® (Wyvern), Xerotin® (SpePharm) and Glandosane® (Fresenius Kabi). They all offer limited relief and are of relatively short duration. They are more effective than a placebo but no specific mucosal lubricant is recommended[31] 1++. Biotene Oralbalance Gel® (GSK) may be the most accepted by patients because of its extended duration of effect. Acidic salivary replacements such as Glandosane® should not be used by dentate patients as they can cause erosive damage to the teeth.

Mucin base saliva substitutes have higher clinical acceptance than carboxymethylcellulose-based. From limited evidence, linseed based saliva substitutes are also effective. Product families (e.g. Biotene or BioXtra ranges) appear to be effective in treatment of xerostomia but with no evidence of their performance compared to saliva substitutes. Gels may have better substantivity[34] 1.

C Oral mucosal lubricants/saliva substitutes are recommended for short-term improvement in xerostomia following radiation therapy.

4.4 TRISMUS

Various preventive/treatment strategies have been advocated[35]. An understanding of the pathogenesis is essential in order to develop efficacious treatment.

4.4.1 NON-PHARMACOLOGICAL TREATMENT

These include jaw exercises , Therabite™, DTS Dynasplint, Corkscrew devices, stacked tongue depressors and microcurrent[35] .

Jaw exercises and the use of devices such as the Therabite™ during radiotherapy and for the first 9 months after completion of head and neck cancer treatment may limit the severity of trismus but they will not mobilize fibrosis once fully established. These techniques may help surgically-induced trismus (as may coronoidectomy).

Exercises may be active, where movement is driven by musculature around the joint or passive which occurs when an external force is applied.

Pain from oral mucositis may have an inhibitory effect on exercise and use of devices.

These interventions appear to be effective in the short term but no long-term data is available[16] 2++.

4.4.2 PHARMACOLOGICAL TREATMENT

Pentoxyfylline. One pilot trial treating twenty patients showed a modest effect[36] 3.

Botulinum toxin. This was effective in pain reduction but has no beneficial effect on trismus[14] 2++.

D Regular jaw exercises should continue during and after radiotherapy

✓ Patients should have the support of a dental therapist during treatment

✓ Liaison between restorative dentistry consultant, speech and language therapist and dietitian is essential

5. Oral and dental management following treatment

As early as possible following primary treatment patients will be reassessed by the restorative dentistry consultant. Information on oral intake, as assessed by the dietitian and speech and language therapist, will be gained. Regular care by the hygienist/therapist will be continued as patients who have been fed via gastrostomy tube progress to oral intake, especially if nutritional supplements are prescribed orally. For patients who have been unable to tolerate oral hygiene and caries prevention methods, these will be re-introduced as mucositis subsides and comfort improves. Patients will be assessed regarding their maxillofacial prosthetic needs and for the presence of trismus, xerostomia, radiotherapy associated caries and osteoradionecrosis. Dental work that was deferred during radiotherapy should be completed. If adjuvant radiotherapy is prescribed following surgery, the patient will be assessed again by the restorative dentistry consultant prior to radiotherapy commencing.

5.1 ALTERED ANATOMY/IMPAIRED FUNCTION

Oral rehabilitation with prostheses may be required to replace missing hard and soft tissue and teeth in order to restore appearance and function. These may be implant-supported or non implant-supported conventional prostheses.

5.1.1 ORAL REHABILITATION USING OSSEOINTEGRATED IMPLANTS

Osseointegrated implants allow effective oral and facial rehabilitation following cancer treatment including radiotherapy. They are used to support oral or facial prostheses. Appropriate detailed planning and patient selection are important prior to proceeding with treatment.

Primary dental implants [37]

The placement of intra-oral and extra-oral implants at the same time as tumour resection may be beneficial for carefully selected patients where there is continuity of the mandible, in patients who require the prosthetic obturation of significant maxillary defects where retention of the obturator is likely to be compromised or in patients undergoing rhinectomy or orbital exenteration. In patients having segmental resection and reconstruction of the mandible, implant survival and usefulness is improved by delayed placement after suitable prosthodontic planning. Where post-operative radiotherapy is certain, there is advantage in primary placement of implants, however time for planning ideal implant position may be compromised.

Secondary dental implants

For many patients, the placement of osseointegrated implants will be considered following cancer treatment in response to ongoing problems with oral function. A secondary approach allows a detailed assessment of the patient's overall prognosis, individual risk factors (alcohol, smoking, oral hygiene, radiotherapy etc.) as well as anatomical factors such as the presence of reconstructive hard and soft tissue grafts, metal hardware, tongue function and mouth opening.

Comprehensive prosthodontic planning should be undertaken prior to implant surgery and the use of computerised planning and surgical guide stent technology is often necessary.

It is possible to place implants in irradiated jaws but careful case selection is required. Failure rates are higher than in non-irradiated bone[38] 3 and higher in the maxilla than in the mandible. There is a risk of implant placement causing osteoradionecrosis. Failures are less likely with a radiation dose lower than 45Gy 3. A delay of one to two years after irradiation for implant placement and a further 6 months delay for abutment connection has been advocated but this is debatable[39] 3. There is no good quality evidence for the use of hyperbaric oxygen for patients who require implant placement in the irradiated jaws[40] 1.

Zygomatic implants

These may be used to retain obturators as an alternative to free flap reconstruction or conventional obturation.

In the non head and neck cancer patient zygomatic implants are usually combined with at least two conventional implants in the anterior maxilla. Alternatively if there is insufficient or no anterior maxillary bone in the head and neck cancer patient two or three zygomatic implants can be used in each upper quadrant. Placement is not straightforward and carries the risk of orbital trauma. Placement and abutment connection can be difficult or impossible if trismus is present. The efficacy of zygomatic implants in aiding maxillary obturation is not clear [41, 42, 43] 3.

Implants in vascularized grafts versus native bone

Implants can be place into vascularized grafts at primary surgery or secondarily into irradiated or non-irradiated grafts. There may be an increased risk of implant failure in free flap bone that has been irradiated[44, 45] 3

✓ **Implants should be considered for all patients having resection for head and neck cancer**

5.1.2 ORAL REHABILITATION USING CONVENTIONAL PROSTHESES

Where mandibular resection and reconstruction results in edentulous areas, these may be restored prosthetically with conventional full or partial dentures as an alternative to implant-retained prostheses. Joint discussion pre-operatively with the surgeon will help ensure soft tissue contours are optimized to allow prosthesis retention.

Maxillary and mid face defects can be reconstructed using surgery or obturated using a prosthesis. Surgical reconstruction can be achieved using non vascularised grafts, local flaps and regional flaps, however, restrictions exist regarding the availability of sufficient tissue and length of vascularised pedicle. Use of such techniques has been largely superseded by microvascular free tissue transfer which provides vascularised hard and soft tissue for reconstruction. Surgical reconstruction using free tissue transfer is often carried out at the time of tumour resection and often does not involve the patient undergoing additional surgical

procedures which are required following reconstruction with local and regional flaps.

Rather than reconstructing surgically, defects can be obturated using a removable prosthesis. Surgical obturators are provided for the patient at the time of tumour resection, however these require modification or replacement with an intermediate obturator during healing prior to the provision of a definitive obturator. Obturators can either be tissue and/or tooth-borne or supported and retained by osseointegrated dental and/or zygomatic implants. These prostheses are fabricated using a range of different materials and constructed in one piece or multiple parts. The anatomy of the defect and surrounding hard and soft tissues, status of the remaining dentition in addition to other systemic and patient factors all influence the decision making process regarding obturator design.

The level of evidence available to support surgical reconstruction using free flaps versus prosthetic obturation of maxillary and mid-face defects is low. Maxillectomy is a relatively uncommon operation so patient numbers are low and larger defects tend to be surgically reconstructed limiting the data available for prosthetic obturation. Multiple confounding factors exist including the size of defect, whether or not the patient received chemo and/or radiotherapy, what type of free flap has been used and the status of any existing natural dentition or dental prostheses. There is also a lack of consensus regarding standardisation and reporting of the size of maxillary defects and the most appropriate outcomes measures.

As the size of maxillary defect increases, so do the reported problems associated with Health Related Quality of Life (HRQOL) and function. There appears to be no difference in HRQOL outcomes between patients who received surgical reconstruction using microvascular free tissue transfer versus prosthetic obturation if the size of the defect is not controlled for[46] 3. If a maxillary defect involves at least half of the hard palate, or the anterior hard palate including the canines bilaterally, statistically significantly better functional outcomes for speech are identified in patients that have received surgical reconstruction using a free flap compared to prosthetic obturation[47]3. As the size of the maxillary defect increases, a higher number of patients receive surgical reconstruction using microvascular free tissue transfer/free flaps compared to prosthetic obturation[46,47] 3. There is no statistically significant difference between the time taken to diagnose a localized recurrence of a T4 squamous cell carcinoma of the maxillary gingiva/hard palate between patients who received surgical reconstruction using a free flap compared to prosthetic obturation[47] 3. The most significant predictor of obturator function is the size of the defect. Statistically better obturator function is associated with defects where resection of the soft palate is one third or less and resection of the hard palate is one quarter or less[46,48]Statistically significant higher obturator speech scores are achieved as the size of soft palate resection decreases[48] 3. The decision as to whether obturation or free flap reconstruction of maxillary and mid-face defects provides better oral rehabilitation is controversial. Patients may prefer to have a reconstruction which brings a sense of completeness rather than cope with a defect.

✓ **The decision to carry out obturation or free flap reconstruction of maxillary and mid-face defects should be discussed jointly with surgeons, restorative dentistry consultants and the patient to ensure optimal oral rehabilitation outcomes are considered and achieved.**

5.2 XEROSTOMIA

This is often a long-term, troublesome side effect and should continue to be managed as described in section 4.3

5.3 RADIOTHERAPY-ASSOCIATED DENTAL CARIES

Risk of caries development is removed when patients are exclusively fed via an enteral feeding tube. The high-risk time is when patients continue or recommence oral feed and have frequent intake of high calorie, sucrose or glucose containing foods and/or oral nutritional supplements. Close liaison with the dietitian at this time is key. Recommendation for nutritional intake and monitoring should be under the guidance of the dietitian to ensure consistent information is given to patients. In the early stages of the post radiotherapy phase patients often have very poor oral hygiene and poor tolerance for fluoride products. Caries management must be individualised and patients must be assessed at regular intervals to determine the caries risk and caries activity to provide guidance for maintenance of the dentition. Frequent visits to the dental therapist may be required during the first few weeks. Preventive advice should continue as described in section 3.3.1

5.4 TRISMUS

Jaw exercises should be continued as described in the recommendations in section 4.4.1

5.5 OSTEORADIONECROSIS

Prevention is best achieved by careful management prior to the treatment. Once osteoradionecrosis has developed, its management is controversial. Some advocate the use of hyperbaric oxygen but this is not supported by randomized controlled trials[49]. Surgical management may sometimes be required. The use of long-term pentoxyfilline, tocopherol and clodronate may be of benefit[50].

5.6 LONG-TERM FOLLOW UP

Implant-supported prostheses and complex conventional prostheses may need to be kept under long-term review by the restorative dentistry consultant. For the majority of patients with radiation-induced side effects, discharge to the care of a primary care practitioner should be possible when the initial side effects have settled, frequent intake of cariogenic food and drinks has been stopped, good oral hygiene is re-established and the use of fluoride products is comfortably tolerated. For these patients, their risk of caries development and ORN will mean that they should have more frequent follow up than other patients in the primary care

setting. Recall interval will be determined on an individual basis dependent on risk factors and the presence of active dental disease. Patients who continue long-term on an energy-dense diet including sucrose and glucose containing foods and supplements should be monitored closely for caries development.

6. Development of the guideline

6.1 Introduction

This guideline was developed by multidisciplinary groups of practicing clinicians using a standard methodology based on a systematic review of the evidence based on the methodology outlined in "SIGN 50; A Guideline Developer's Handbook" available at **www.sign.ac.uk**

6.2 Systematic Literature Review

The evidence base for this guideline was synthesized in accordance with SIGN methodology. The guideline development group is grateful to SIGN Evidence and Information Scientist, Juliet Brown, for carrying out the systematic literature review.

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9. KEY QUESTIONS

1. Does IMRT reduce the risk of xerostomia?
2. Does IMRT reduce the risk of osteoradionecrosis (ORN)?
2b. Does IMRT reduce the risk of trismus?
3a. Is ORN risk worse with any particular tumour site or staging?
3b. What is the minimum time between extraction and radiotherapy to avoid ORN?
3c. What is the minimum time between extraction and neo-adjuvant chemotherapy to avoid ORN?
3d. Extraction of which teeth is most likely to cause ORN
4. What are the risk factors for trismus development in patients who have radiotherapy for head and neck cancer?
5. Do interventions such as jaw exercises help reduce trismus?
6. What primary methods of dental disease prevention are effective in patients who have received radiotherapy?
7. Obturation vs free flap closure in maxillary and mid-face disease which is better for oral rehabilitation?
8. Does pre-treatment dental care reduce the incidence of mucositis and infection?
9. What is the most effective treatment for mucositis?
10. What is the most effective saliva replacement for patients with radiation induced xerostomia?
10b.Does pilocarpine reduce/prevent xerostmia?
11. What factors are significant when planning a head and neck cancer patient for implant treatment?
12. Which patients will benefit from the placement of primary implants?
13. Is the placement of zygomatic implants of benefit to maxillary obturation?
14. Does the success rate differ when implants are placed into vascularized bone grafts compared with native bone?
15. Does prophylactic HBO in irradiated patients affect implant survival?
16. How often should patients with radiation induced xerostomia have dental assessment? (xerostomia follow-up)