East of England Radiotherapy Network:

Head and Neck Protocol V3.0

Contents

This protocol covers the following tumour sites:

1. Oral Cavity – C02 oral tongue, C03 Gum, C04 Floor of mouth, C05 Hard palate, C06 other and unspecified parts of mouth, C10 oropharynx

2. Oropharynx – C01 base of Tongue, C05 Soft palate/Uvula/other, C09 Tonsil, C10 oropharynx

3. Larynx – C32

4. Hypopharynx - C12 Pyriform sinus, C13/C14 Hypopharynx

5. Nasopharynx- C11

6. Unknown primary neck H&N cancer – HPV-positive (C10.9) or HPV-negative (C77.0)

For information about other HN sites such as salivary gland or sinonasal tumours please refer to local protocols though the principles of HN radiotherapy are likely to be very similar for all subsites

1.0 Indications and patient population

1.1 This protocol covers treatment in the following situations:

a. Curative radiotherapy + concomitant SACT* for squamous cell carcinoma for the above ICD codes

b. Curative radiotherapy for squamous cell carcinoma for the above ICD codes

c. Post-operative radiotherapy + concomitant SACT* for squamous cell carcinoma for the above ICD code

d. Post-operative radiotherapy for squamous cell carcinoma for the above ICD codes

e. Palliative radiotherapy for squamous cell carcinoma for the above ICD codes

1.2 Curative treatment eligibility

1.2.1 Inclusion criteria

- Localised squamous cell carcinoma with no evidence of metastases [1].

- Consider high dose palliation for local control in selected patients with an incurable disease [2].
- Adequate performance status and functional reserve ECOG 0-1.

* Concomitant SACT although not routinely recommended in patients older than 70, could be considered at the discretion of treating oncologist following discussion with patients.

1.2.2 Exclusion criteria

- Inadequate cardiovascular and respiratory function/reserve for safe delivery of radiotherapy and/or concomitant SACT.
- Not suitable for immobilisation required for the safe delivery of radiotherapy.

1.3 Palliative treatment eligibility

1.3.1 Inclusion criteria

- Locally advanced disease and unsuitable for curative radiotherapy.
- Metastatic disease.
- Poor performance status – e.g., ECOG 3-4.
- Patients who decline curative radiotherapy.

1.3.2 Exclusion criteria

- Inadequate cardiovascular or respiratory function/reserve for safe delivery of radiotherapy.
- Not suitable for immobilisation required for the safe delivery of radiotherapy.

1.4 Essential Pre-radiotherapy investigations for patients

1.4.1 Clinical requirements

- Discussion at the head and neck cancer MDT.
- Operation notes and relevant operative histology.
- Clinical examination by head and neck surgeon including Fibreoptic Nasendoscopy ** and EUA where appropriate.
- Histology and/or cytology confirmation of cancer.
- HPV test (p16 immunohistochemistry) on histology sample for oropharyngeal cancer [1].
- EBV test on histology sample and EBV DNA serum test for nasopharyngeal primary [3].
- Bloods – FBC, U&Es, LFT, Magnesium, as indicated for chemotherapy.

** H&N oncologist to be present where possible. Where this is not possible photographic information from the clinical examination should be made available

1.4.2 Imaging requirements

- Contrast MRI and/or CT scan of the primary site and neck [1].
- Contrast CT scan of chest for T3/4 or N+ disease [1].
- PET-CT scan for nasopharynx cancer and other locally advanced cancer (which can also aid target volume delineation) [1].
- USS ± FNA may be helpful to assess equivocal nodes seen on the radiotherapy planning scan [1].

1.4.3 Patient pre-treatment assessments

- Pre-treatment SALT and dietician review – weight loss management strategy and pre-treatment swallow and jaw exercises [1,4].
- Pre-treatment dental assessment– caries prevention strategy, extraction, dental restoration strategy (unless T1/T2N0 laryngeal cancer or palliative RT).
- Audiology, ophthalmology assessment as indicated.
- Smoking cessation advice/support and drug/alcohol service referral if indicated [5].

2.0 Localisation

Localisation	Notes	
Position	Supine, neutral neck with spinal cord, parallel to treatment couch, knee rest.	
Bolus	Appropriate bolus may be required when CTV close to or involving skin.	
Immobilisation and supports	5-point thermoplastic shell	Standard neck rest or customised neck rest. Consider mouth bite or separator for oral cavity tumour if need to move palate superiorly or tongue inferiorly
MRI/PETCT diagnostic scans	Consider co-registration of up-to-date and high-quality MRI and PET-CT scan if appropriate, especially if IV contrast is not used or significant dental amalgam noted.	
Contrast	IV contrast except for T1/T2N0 larynx and short course palliative radiotherapy	
CT acquisition	Slice thickness:	2mm-3mm
	Scanning limits upper	Vertex (for T1-T2 Larynx, superior limit Inferior orbital ridge could be considered)
	Scanning limits lower	Carina
*CT scans should ideally be done when the patient is not swallowing to avoid introducing systematic errors especially if the larynx is the target organ		

3.0 Dose prescription & chemotherapy

Intent	Dose (Gy)/#	#/ week	Technique	Chemotherapy
Oral Cavity, Oropharynx, Larynx (except T1/T2N0) and Hypopharynx				
Curative radiotherapy with concurrent chemotherapy T3/T4 and/or node positive	PTV_High: 65Gy in 30# PTV_Mid[5]: 60Gy in 30# PTV_Low: 54Gy in 30# [6]	5	**IMRT or VMAT**	Weekly Cisplatin or 3 weekly Cisplatin[1,4] [7,29,30] Or Weekly Carboplatin[2,4] (only when Cisplatin is contraindicated) [8] Or Weekly Cetuximab[3,4] (only when platinum treatment is contraindicated) [9]
	PTV_High: 70Gy in35# PTV_Mid[5]: 63Gy in 35# PTV_Low: 56Gy in 35# [10]	5		
Curative radiotherapy alone in those unsuitable for concomitant chemotherapy or with T1/2 N0 disease	PTV_High: 65Gyin 30# PTV_Mid[5]: 60Gy in30# PTV_Low: 54Gy in 30# [6]	5	**IMRT or VMAT**	
	PTV_High: 70Gy in35# PTV_Mid[5]: 63Gy in 35#	5		

Intent	Dose (Gy)/#	#/ week	Technique	Chemotherapy
	PTV_Low: 56Gy in 35# [10]			
	PTV_High: 55Gy in 20# PTV_Low 44 in20# [11] Only for small volume disease	5		
	DAHANCA PTV_High: 68Gy in 34# PTV_Mid: 60Gy in 34# PTV_Low: 50Gy in 34# [12]	5		
T1/T2N0 Larynx				
Curative radiotherapy	PTV: 55Gy in 20# [13] PTV: 50Gy in 16# [14]	5	**Conformal or IMRT or VMAT**	
Nasopharynx				
Curative radiotherapy with concurrent chemotherapy for Nasopharyngeal cancer For	PTV_High: 70Gy in 35# PTV_Mid[5]: 63Gy in 35#	5	**IMRT** **Or** **VMAT**	Weekly Cisplatin or 3 weekly Cisplatin[1,4] [7,29,30] Or

Intent	Dose (Gy)/#	#/ week	Technique	Chemotherapy

• Any T, N2-3
• all T3[15]
• Could be offered for
  ○ T1-2N1
  ○ T2N0 with bulky disease+/- adverse feature
	PTV_Low: 56Gy in 35# [15]			Weekly Carboplatin or 3 weekly Carboplatin[2,4] [16]

	PTV_High: 69.96 in 33# PTV_Mid[5]: 59.4Gyin 33# PTV_Low: 54Gy in 33# [17]	5		
	PTV-High: 65Gy in 30# PTV_Mid: 60Gy in 30# PTV_Low: 54Gy in 30# [18,19]	5		
Curative single modality radiotherapy For • T1-2, N0-1 [20] • any patient unsuitable for concurrent chemotherapy	PTV_High: 70Gy in 35# PTV_Mid[5]: 63Gy in 35# PTV_Low: 56Gy in 35#	5	**IMRT** **Or** **VMAT**	
	PTV_High: 69.96 in 33# PTV_Mid[5]: 59.4Gyin 33# PTV_Low: 54Gy in 33# [17]	5		
	PTV_High: 65Gy in 30#	5		

Intent	Dose (Gy)/#	#/ week	Technique	Chemotherapy
	PTV_Mid: 60Gy in 30# PTV_Low: 54Gy in 30#			
Post operative radiotherapy.				
Post operative adjuvant radiotherapy with concurrent chemotherapy. Positive margin and/or positive node with Extranodal Extension (ENE)	PTV_High[6]: 65Gy in 30# PTV_Mid: 60Gy in 30# PTV_Low: 54Gy in 30# [21,22,23]	5	**IMRT** **or** **VMAT**	Weekly Cisplatin or 3 weekly Cisplatin[1,4] [7,29,30] Or Weekly Carboplatin or 3 weekly Carboplatin[2,4] [8]
Post operative adjuvant single modality radiotherapy. High risk pathological features	PTV_High[6]: 65Gy in 30# PTV_Mid: 60Gy in 30# PTV_Low: 54Gy in 30# [21,22,23]	5	**IMRT** **Or** **VMAT**	
	PTV: 50Gy in 20# [24] OR PTV: 55Gy in 20# (If R1)	5	**IMRT or VMAT for small treatment volume**	
Oral cavity, Oropharyngeal, Larynx, Hypopharynx, Nasopharynx				
Palliative radiotherapy[7]	Single 8Gy	1	**V sim or conformal planning**	

Intent	Dose (Gy)/#	#/ week	Technique	Chemotherapy
	20Gy in 5# [25]	5	**V sim or conformal planning or IMRT/VMAT**	
	24Gy in 3# [26]	See comment	**V sim or conformal planning or IMRT/VMAT**	**Fraction 1 on Day 0, fraction 2 on Day 7 and fraction 3 on day 21**
	27Gy in 6 #	See comment	**V sim or conformal planning or IMRT/VMAT**	**3 fractions per week for 2 weeks or 2 fractions per week over 3 weeks**
	30Gy in 10# [27]	5	**V sim or conformal planning or IMRT/VMAT**	
[1] Weekly Cisplatin 40mg/m2 or 3 weekly Cisplatin 100mg/m2 [28,29,30]				
[2] Weekly Carboplatin AUC 1.5 or 3 weekly Carboplatin AUC 5 [8]				
[3] Weekly Cetuximab – Loading dose 400mg/m2, followed by 250mg/m2 [9]				
[4]Concurrent chemotherapy should ideally start on the first day of radiotherapy, but if not logistically possible can be given within 3 days of commencing radiotherapy				
[5]Intermediate dose levels (PTV_Mid) are frequently used at clinician's discretion, but are not mandatory				
[6]PTV_High can be added at the discretion of clinician to boost area with clinical/pathological high risk of local recurrence, e.g.R1 or R2 margin post operatively etc.				
[7]High dose palliative radiotherapy may be considered for selected cases to achieve more durable local disease control – please refer to dose fraction 'curative radiotherapy' section.				

4.0 Target volumes

4.1 For Oral cavity, Oropharynx, Larynx (except T1/T2N0), Hypopharynx and Nasopharynx

- **Unilateral radiotherapy for cancer of the oropharynx**
  - The treating clinician must define the laterality of the primary tumour.
  - Offer unilateral curative radiotherapy for lateralised T1-2 squamous cell carcinoma of tonsil in an N0 neck or with one involved ipsilateral neck node [31].
  - Consider unilateral curative radiotherapy for lateralised T1-2 squamous cell carcinoma of the tonsil with involved ipsilateral nodes but without *significant nodal burden** after discussing the benefit of reduced toxicity versus the possible risk of a contralateral neck recurrence with the patient.
  - The classification for lateralised and non-lateralised primary is as below.

CLASSIFICATION	TUMOUR CHARACTERISTICS [31]
LATERALISED	Tumour confined to palatine tonsil/tonsillar fossa/lateral pharyngeal wall, with greater than 10mm clearance from midline, not involving base of tongue or posterior pharyngeal wall and extending onto the adjacent soft palate by less than 10mm.
NON-LATERALISED	Tonsillar/lateral pharyngeal wall tumour that involves the adjacent base of tongue or involves the soft palate by greater than or equal to 10mm or with less than 10mm clearance from midline. Or a tumour that arises from a midline structure (base of tongue, soft palate, or posterior pharyngeal wall)

** RCR consensus statement on **significant nodal burden** – Many ipsilateral neck nodes (for example three or more) or large size (more than 3cm) or located in the levels other than II-III.*

- **Target volume definition**

Name	***Description***
GTVp	Primary GTV
GTVn	Nodal GTV
CTV_High	Primary and nodal CTV to receive a high dose
CTV_Mid	Primary and nodal CTV to receive an intermediate dose
CTV_Low	Nodal CTV to receive a low dose
PTV_High	Primary and nodal PTV to receive a high dose
PTV_Mid	Primary and nodal PTV to receive an intermediate dose

PTV_Low	Nodal PTV to receive a low dose

- Use standard nomenclature as per AAPM TG263
- https://www.aapm.org/pubs/reports/RPT_263.pdf

Curative radiotherapy GTV/CTV

GTV

- Gross tumour volume for primary tumour (GTVp) and involved nodes (GTVn), is defined by findings on clinical examination including findings on Fibreoptic nasendoscopy (FNE) and EUA, diagnostic contrast-enhanced CT, and/or MRI and/or PETCT scan [32].
- Lymph nodes should be presumed pathological and included in GTVn if any of the criteria below are fulfilled [31]:
  1. > 10mm in short axis (>5mm in short axis for retropharyngeal node)
  2. Node with central necrosis
  3. Demonstrate evidence of ENE
  4. Demonstrate increased uptake on PETCT.
  5. Any node that a head and neck radiologist/multidisciplinary team (MDT) feels is involved in the absence of the above criteria.

CTV

- Either 3 dose levels (CTV_High/CTV_Mid/CTV_Low) or 2 doses levels (CTV_High/CTV_Low) can be used [32].
- For centres using 2 levels of dose prescription, the CTV_Low for GTVp is associated with a prophylactic dose prescription (typically a dose equivalent to 50Gy in 2Gy per fraction over 5 weeks. For centres using 3 levels of dose prescription, CTV_Mid for GTVp is associated with an intermediate dose level (typically a dose equivalent to 60Gy in 2Gy per fraction over 6 weeks) [32].

CTV_High

Primary tumour outlining

- Use the '5+5' technique to generate CTV_High for well-defined primary tumour; A volumetric expansion of 5mm from GTVp to define the CTV_High [31,32].

- Consider using a larger margin from GTV (up to 10mm) if there are concerns regarding the certainty of GTVp determination based on the quality of imaging or clinical information [31,32].
- CTV_High should be edited to
    - Exclude air cavities.
    - Exclude structures limited by anatomical barriers that prevent microscopic disease extension boundaries (e.g., bone and fascia)
    - Include any other region at high risk of containing microscopic tumour.

Node outlining

- Expand GTVn by 5mm to form the CTV_High, editing from bone and air [31,33,34].
- Use a 10mm margin around GTVn with obvious extranodal extension (ENE) (e.g., into the sternocleidomastoid muscle) to form the CTV_High [31,33,34].

CTV_Mid and CTV_Low for centre using 3 dose levels.

Primary tumour outlining

CTV_Mid should include GTVp + 10mm isotropic margin, editing off anatomical barrier that prevent microscopic disease extension (e.g., air, bone, and fascia), as per Gregoire et al original 5+5 publication [31,32].

- Consider using a larger craniocaudal margin (e.g., 15mm) from GTVp for CTV_Mid in the case of hypopharyngeal posterior pharyngeal wall tumours, due to the risk of submucosal extension [31,32].
- CTV_Mid in nasopharyngeal cancer should include GTVp + margin less than 10mm when close to critical organ e.g., brainstem, could be used; CTV_Mid should also include at risk areas as per international guideline for nasopharyngeal outlining (2017) as well as ESMO-EURACAN clinical guideline (2020) [17].

Node outlining

- CTV_Mid for nodal disease without ENE should include GTVn + 10mm isotropic margin, editing to
    - exclude uninvolved muscle.
    - exclude uninvolved bone and air cavities.
- CTV_Mid for nodal disease with ENE, CTV_Mid for nodal disease should correspond to GTVn + 10mm isotropic margin including muscle above and below the site of infiltration [33,34].

- In cases of multiple indeterminate nodes within GTVn level, whole nodal level could be included in CTV_Mid [33,34].
- CTV_Low should include all remaining standard nodal levels at risk of harbouring microscopic disease as per international consensus guideline [33,34].

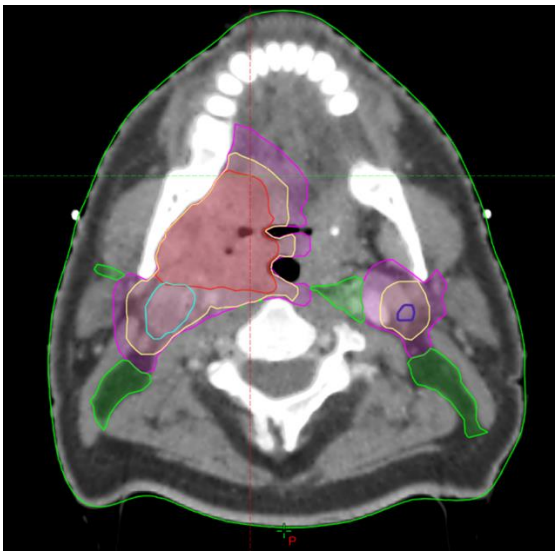
CTV_Low for centre using 2 dose levels.

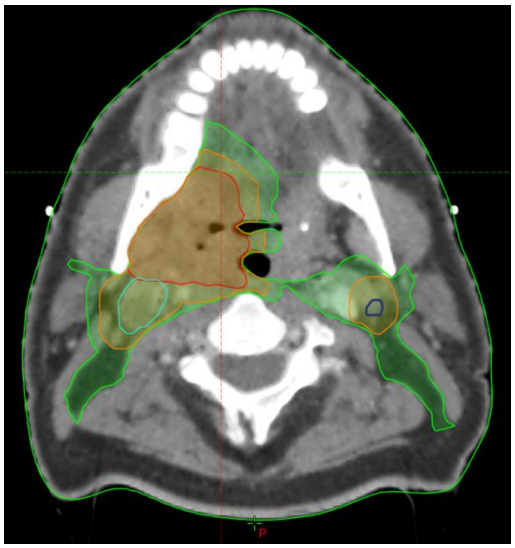
Primary outlining

- CTV_Low to primary is generated by isotropic expansion of GTVp by 10mm margin [31,32].
- Consider using a larger craniocaudal margin (e.g., 15mm) from GTVp for CTV_Low in the case of hypopharyngeal posterior pharyngeal wall tumours, due to the risk of submucosal extension [31,32].
- Consider a larger margin (up to 20mm) to include more of an involved muscle above and below the site of infiltration within CTV_Low [31,32].

Node outlining

- Delineate the rest of the involved nodal level to form part of the CTV_Low, extending at least 10mm craniocaudally from GTVn [33, 34].
- CTV_Low should also include all remaining standard nodal levels at risk of harbouring microscopic disease as per international consensus guideline [33, 34].





Example – Right oropharyngeal squamous cell carcinoma using 3 CTV dose levels. GTVp – red contour GTVn with ENE – blue contour GTVn without ENE – dark blue contour CTV_high – yellow segment CTV_int – purple segment CTV_low – green segment	Example – Right oropharyngeal squamous cell carcinoma using 2 CTV dose levels. GTVp – red contour GTV with ENE – blue contour GTV without ENE – dark blue contour CTV_high – orange segment CTV_low – green segment

RCR consensus statements recommend.

- Consider omitting the high-level II nodes from the elective target volume in an uninvolved contralateral neck when delivering radical or adjuvant radiotherapy for non-nasopharyngeal head and neck squamous cell carcinoma [31].
- Omit the contralateral retropharyngeal lymph nodes from the elective target volume when delivering radical radiotherapy for oropharynx cancer if all the following apply:
    - No involved nodes in the contralateral neck
    - No Ipsilateral involved retropharyngeal lymph nodes
    - GTVp does not involve the soft palate or posterior pharyngeal wall.

4.2 For T1/T2N0 Larynx cancer

- GTVp – include gross tumour as defined on clinical and radiological examination.
- Vocal cord can be usefully estimated on DRR as commencing anteriorly at intersection of ‘figure of 8 sign’ of thyroid cartilage and extends posteriorly to the most anterior component of the arytenoid cartilage as seen on axial slices.
- For T1N0 - CTV_High should include at least GTV+5- 10mm margin isotropically but exclude thyroid cartilage and air cavity [32].
- For T2N0 - CTV_High should include at least GTV + 10mm margin isotropically, may include thyroid cartilage but exclude cricoid cartilage and air cavity [32]
- In practice, the bilateral mucosal laryngeal surface axially is included as field change is common.
- Assessment of field borders on DRR could be carried out by oncologist, with superior field border typically at mid hyoid body and inferior field border typically at inferior margin of cricoid cartilage [13,14].
- Elective nodal irradiation is not usually recommended [13,14,32].

* When considering GTVp movement in the superior-inferior direction during treatment, Internal target volume (ITV) may be added CTV55 if clinician consider glottic movement during treatment may exceed PTV limits.

4.3 Adjuvant radiotherapy

Adjuvant radiotherapy with or without concurrent chemotherapy should be considered for patients with tumours that have involved margins and / or node(s) with extra-nodal extension.

Other pathological and clinical risk factors that could also be considered as indicators for recommending adjuvant radiotherapy [35]:

1. T3/T4 disease
2. close margins - usually <5mm
3. 2 or more involved nodes
4. Any lymph node > 30mm
5. Perineural and/or lymphovascular invasion

Adjuvant radiotherapy should commence as soon as it is clinically feasible, but ideally no longer than 6 weeks after surgery [35].

Treatment volume delineation should be guided by pre-operative imaging, panendoscopy reports, intra-operative findings, and post-operative pathology report [35,36].

As there is no clear international consensus in the radiotherapy CTV outlining for post operative radiotherapy (PORT), we recommend below reference papers for guidance:

- Radiotherapy Guideline 2020 DAHANCA Danish Head and neck Cancer Group
- Target delineation for postoperative treatment of head and neck cancer. M Evans, M Beasley. Oral Oncology 86 (2018) 288-295.
- Flap delineation guidelines in postoperative head and neck radiation. therapy for head and neck cancers. Guevelou JL, Bastit V, Marcy PY, et al. Radiotherapy and Oncology 151 (2020) 256–265.

GTVp and GTVn

- Consider using co-registration of pre-operative imaging to recreate GTVp and GTVn [35,36].

- Where co-registration of imaging is not possible, GTVp and GTVn could be recreated based on pathological findings and pre-operative clinical findings.

CTV_High

Primary tumour bed outlining

- CTV_High could be included at clinician's discretion for post operative patients with GTV visible on the RT planning scan or if there was an R1/R2 resection and the site ofninvolved margin can be contoured.
- For R1/R2 resection margin, CTV_High for primary tumour bed correspond to GTVp with concentrically isotropic margin of 5mm in all directions; though a larger isotropic margin for primary tumour bed should be used for poorly defined tumour and edited for un-involved anatomical barriers such as bone, fascia and air[37].

Node outlining

- When GTVn with gross ENE or invades a muscle not removed in the neck dissection, CTV_High could include GTVn plus 10mm or larger isotropic margin.

Considerations for surgical reconstruction

- Where flap reconstructions were used, review of operative notes, identification of type of reconstruction (site of anastomosis, flap component i.e., fat, fascia, skin, bone, muscle) and assessment of postoperative fibrosis and oedema are needed prior to delineation of CTV_High. Oncologist should confer directly with the surgeon to truly understand the surgical bed and locations of high risk / positive margins [36].
    - CTV_High should include GTVp and GTVn (recreated from co-registration of re-operative imaging) plus areas of high risk / positive margins, with isotropic margin of 10-20mm in all direction.

CTV_Mid

Primary tumour bed outlining

- After R0 resection margin, CTV_Mid for primary tumour bed correspond to GTVp with concentrically isotropic margin of 10mm in all directions [37].
- In case of R1/R2 resection, CTV_Mid include CTV_High with 5mm margin.

- The margin may be larger in case of poorly defined tumour and less if it extends into air or surpasses natural borders such as bone [37].

Node outlining

- CTV_Mid for nodal bed corresponds to pre-operative GTVn with concentrically isotropic margin of 10mm in all directions (edited for anatomical barriers such as bone, fascia, and air) plus the entire involved nodal level(s) [35].
- When a pathologically involved node is a boundary node, located between two contiguous nodal levels, both nodal levels should be included in CTV_Mid [35].
- When a pathological node abuts a muscle not removed in the neck dissection, this muscle may be included in the CTV_Mid, at least for the entire involved level [35].

Considerations for surgical reconstruction

- Where flap reconstructions were used, with R0 section margin, CTV_Mid should include GTVp and GTVn (recreated from co-registration of re-operative imaging) plus part or entire flap (after conferring with reconstructive surgeon), with isotropic margin of 5-10mm in all directions [36].

CTV_Low

Node outlining

- Prophylactic nodal irradiation should include all at risk uninvolved and/or undissected nodal levels [35].
- Extent of prophylactic nodal irradiation will vary depending on site of tumour, laterality of primary, extent of neck dissection [35].
- The general principle of prophylactic node level selection can be found in reference papers listed above.
- Offer contralateral neck prophylactic irradiation for oral tongue squamous cell carcinoma who had ipsilateral neck surgery if [31]:
  1. T3 or T4 tumour
  2. Primary within 10mm if midline
  3. 2 or more involved nodes in ipsilateral neck dissection
  4. Extracapsular spread in ipsilateral neck dissection
- Consider contralateral neck radiotherapy for patients having ipsilateral adjuvant radiotherapy for oral tongue squamous cell carcinoma who have had surgery to the primary site and an ipsilateral neck dissection if there is a single involved lymph node with no ENE in the ipsilateral neck [31].

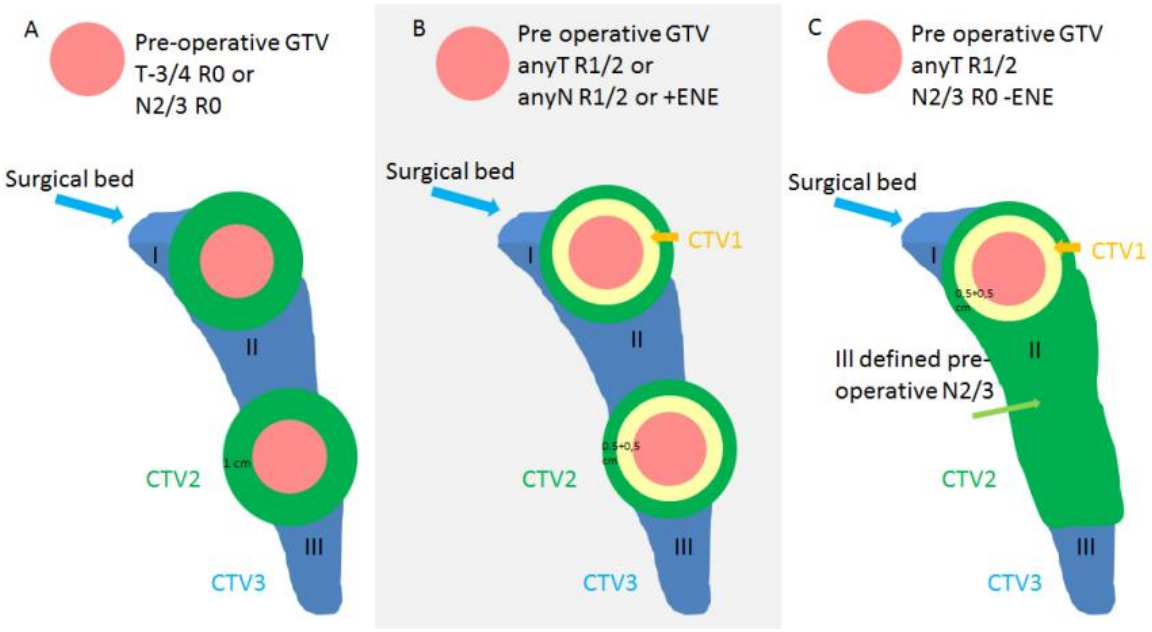


Diagram taken from Radiotherapy Guideline 2020 DAHANCA Danish Head and neck Cancer Group

Examples of postoperative radiotherapy scenarios. I, II, III refers to elective nodal regions. Scenario A: R0 PORT, thus no CTV_High (CTV1 in diagram) is present; Scenario B: Volumes with insufficient margins or ENE is included in CTV_High (CTV1); Scenario C: Well-defined pre-operative primary tumour GTV with R1 or R2 resection. Nodal areas with R0 resection and no ENE, but il defined (e.g., several smaller positive nodes).

4.4 Radical re-irradiation

- The risk benefit ratio of radical re-irradiation changes with time. Avoid re-irradiation in patients who have recurrence with a short latency period) e.g., within 6 to 12 months of completing radiotherapy) or significant late effects [31].

- Treat GTV with small margins (maximum GTV to CTV expansion of 5mm). The re-irradiation CTV should ideally be less than $50cm^3$ [31].

- Do not include elective nodal areas within re-irradiation treatment volumes [31].

- Keep the cumulative spinal cord and other important OAR as low as possible. Ensure a thorough radiobiology evaluation with advice from physicists had taken place with risks considered, discussed with patients, and documented [31].

- Given the additional risk associated with re-irradiation, we advise comprehensive review of the treatment planning in its entirety by a head and neck clinical oncologist either from

within the same SMDT or when necessary (e.g., lack of local expertise) from a head and neck clinical oncologist from another SMDT from within the East of England ODN.

4.5 Palliative radiotherapy

- GTV, CTV and PTV are usually defined as for curative treatment, however, to minimise normal tissue toxicity, smaller GTV to CTV margin can be used (e.g.,0-5mm).

5.0 Organs at risk

- The table below has been adopted from description from the Global Harmonization Group organ at risk consensus contouring guideline [38].
- CT-based delineation of organs at risk in the head and neck region could be found in the link below: **https://www.thegreenjournal.com/cms/10.1016/j.radonc.2015.07.041/attachment/e72aa779-d5af-4a36-a024-dea94798344f/mmc1.pdf**

Nomenclature	Description
SpinalCord¥	The spinal cord is contoured as true spinal cord, not spinal canal. Cranial border should be at the level of the tip of the dens of C2 and the caudal border 2.5cm below the most inferior slice of nodal PTV
Brainstem¥	The brainstem includes midbrain, pons, and medulla oblongata. Cranial border is the substantia nigra at the cerebral peduncle; the cranial aspect of the posterior clinoid process may be used as a bony landmark. Caudal border should be at the level of the tip of the dens of the C2 vertebra.
SpinalCord PRV¥ Brainstem PRV¥	Isotropic expansion of 3-5mm (depending on local practice and individual department data on accuracy of immobilisation).
Parotid_R¥ Parotid_L¥ Parotids¥	Each parotid gland should be contoured separately. The cranial border is the zygomatic arch and extends caudally to the angle of the mandible. The anterior border is the masseter muscle; in 20% of cases the parotid extends anteriorly over the surface of the masseter muscle. The posterior border is the anterior aspect of the sternocleidomastoid muscle. Laterally, it is confined by the platysma muscle and medially by posterior belly of the digastric muscle, styloid process and the parapharyngeal space. The retromandibular vein should be included in the parotid contour.

Parotid_sup_R¤ Parotid_sup_L¤	The superficial lobes of both parotid glands should be defined as separate contours. The medial edge of the superficial parotid gland extends from the posterior border of the mandible posteriorly.
Bone_Mandible¤	The mandible should be contoured in entirely from the temporomandibular junction to the symphysis menti. The teeth are excluded from the contour. Contour in bone windows.
OpticNrv_R¤ OpticNrv_L¤	Cranially below superior rectus muscle, caudally superior to the inferior rectus muscle; Anteriorly at the posterior edge of the centre of the globe; posteriorly at the optic canal
OpticChiasm¤	Caudally at the top of the suprasellar cistern, and the volume extend superiorly by 1-2 2mm slices; anteriorly optic canal and posteriorly infundibulum; Medially, internal carotid arteries and middle cerebral arteries
Lens_R¤ Lens_L¤	Contour the lens for each eye separately. The lens is a clearly visible biconvex avascular structure located between vitreous humour and the iris.
Eye_R¤ Eye_L¤	Contour entire orbital globe for each eye separately; it should include anterior and posterior segments of eye.
Eye_A_R¤ Eye_A_L¤	Each anterior segment of the eye should be contoured separately; the structure consists of the cornea, iris, ciliary body, and lens. Exclude the extra-ocular muscles.
Eye_P_R¤ Eye_P_L¤	Each posterior segment of the eye should be contoured separately. The posterior segment of the eye consists of the anterior hyaloid. membrane, vitreous humor, retina, and choroid. Exclude the optic nerve and extra-ocular muscles
Cochlea_R¤ Cochlea_L ¤ Cochlea¤	Each cochlea should be contoured separately. The cochleae appear as small curved or round lucencies in the petrous portion of the temporal bone. The cochleae lie caudal to the semi-circular canals, lateral to the internal auditory meatus, anterior to the vestibular apparatus, and medial to the middle ear. The structure is small and measures up to 0.6cc. Contour on CT using bone windows. Exclude the semi-circular canals. Cochlea is a summation of the right and left cochlea and may be used for dose reporting purposes.
Glnd_Submand_R¤ Glnd_Submand_L¤ Gland_Submands¤	Each submandibular gland should be contoured separately. The submandibular glands lie within the submandibular space and appear hypodense on CT compared to the surrounding structures. The submandibular glands are composed of a large superficial. lobe and a smaller deep lobe, which are continuous with each. other around the posterior border of the mylohyoid muscle.

	The cranial border is located at the caudal edge of the medial ptyergoid muscle at the level of the C3 vertebral body. Continue contouring caudally until fatty tissue appears. The lateral border is the platysma muscle and the mandibular surface. The medial border is the lateral surface of the mylohyoid muscle and the anterior belly of the digastric muscle. Glnd_Submands is a summation of the right and left. submandibular gland and may be used for dose reporting. purposes.
Musc_Constrict¤	The muscle constrictor structure encompasses the superior, middle, and inferior pharyngeal constrictor muscles in a single structure. Contour from the caudal tips of the pterygoid plates to the caudal limit of the arytenoid cartilages. The pre-vertebral muscle defines the posterior border. The lateral borders are the medial pterygoid muscle cranially and the hyoid and thyroid cartilages caudally. The anterior border at the cranial aspect is the pterygoid hamulus. The hyoid bone and posterior border of the thyroid cartilage define the anterior border for the middle and inferior pharyngeal. constrictor muscles.
Pituitary¤	The pituitary gland is best defined using sagittal viewing planes on brain soft tissue windows. The pituitary gland is oval shaped and lies in the sella turcica, measuring up to 12mm cranio-caudally. The pituitary gland is bordered laterally by the cavernous sinuses. The pituitary gland is connected to the hypothalamus by the pituitary stalk, which lies posterior to the crossing fibres of the optic chiasm. If the pituitary gland cannot be visualized on CT soft tissue windows consider MRI co-registration. Investigators may consider contouring the inner bony limits of the sella turcica, Fossa_Pituitary, as an alternative structure.
Glnd_Lacrimal_L¤ Glnd_Lacrimal_R¤	Each lacrimal gland should be contoured separately. The lacrimal gland lies in the cranio-lateral extraconal portion of the orbit, medial to the zygomatic process of the frontal bone. The structure is hyperdense when compared to the surrounding fat. The caudal border is at the level of the lateral rectus muscle; the superior rectus muscle lies laterally. The gland is almond shaped, concave against the eye and measures approximately 20 x 15 x 5mm. Contour on soft tissue windows
Hippocampus_L¤	Each hippocampus should be contoured separately. The

Hippocampus_R¤	hippocampus is a small, seahorse shaped, complex gray matter structure located in the medial temporal lobe. Delineation using co-registered T1-weighted MRI with use of sagittal viewing planes is essential. Hippocampal size (2.8-4.0cc) and location may vary. Begin the contour at the most caudal hypointense gray matter located medial to the cerebrospinal fluid hypointensity/temporal horn of the lateral ventricle. Continue to contour cranioposteriorly avoiding the amygdala and uncus, which are located anterior to the tip of the temporal horn of the lateral ventricle. The hippocampus terminates when the T1-hypointense structure no longer borders the lateral ventricle at the level of the pons and the pituitary gland. At this point, the crux of the fornix emerges anteriorly and the splenium of the corpus callosum can be visualized posteriorly. The medial border is the ambient and quadrigeminal cisterns.
Brain¤	The brain is the whole brain including the cerebellum, cerebrospinal fluid, and small brain vessels. Contour from the tentorium to the foramen magnum including the temporal lobes bilaterally. The brainstem, carotid canal, cavernous, sigmoid, transverse, and superior sagittal sinuses are excluded. Contour on brain soft tissue windows on CT. Use sagittal viewing planes and consider MRI co-registration to support identification of the cranial border of the brainstem.
BrachialPlex_L¤ BrachialPlex_R¤	Each brachial plexus should be contoured separately. The brachial plexus originates at the spinal nerve root foraminae C5, C6, C7, C8, and T1 and terminates at the medial limit of the second rib. Begin contouring with a 5mm diameter tool at the C5, C6, C7, C8, and T1 neural foramina and continue caudally, contouring the region from the lateral aspect of the spinal canal to the small space between the anterior and middle scalene muscles. At the levels where no neural foramina are present, contour the space or soft tissue between the anterior and middle scalene muscles. The middle scalene muscle, and therefore brachial plexus structure will terminate in the region of the subclavian neurovascular bundle one or two slices below the clavicular head. The first and second ribs serve as the medial limit of the brachial plexus contour. Co-registration with MRI and/or the use of intravenous contrast can help distinguish between nerves and vessels. Be aware that

	patient positioning may influence the position of the underlying anatomy and the brachial plexus
Bone_Mandible¤	The mandible should be contoured in entirety from the temporomandibular junction to the symphysis menti. The teeth are excluded from the contour. Contour on bone windows.
Larynx¤	The larynx is comprised of supraglottic and glottic components: epiglottis, supraglottic adductor muscles, aryepiglottic folds, arytenoid cartilages, and the true and false vocal cords. Contour from the tip of the epiglottis to the caudal edge of anterior part of the thyroid cartilage. The hyoid bone, preepiglottic space, and thyroid cartilage lie anteriorly. The inferior pharyngeal constrictor muscles, pharyngeal lumen, and cricoid cartilage define the posterior border. The thyroid cartilage is antero-lateral, and the pharyngeal lumen is medial to the structure.
¥ Mandatory OAR structures for all Head and neck radiotherapy planning **¤ Discretionary OAR structures for example in the planning of Nasopharyngeal tumour etc**	

- OAR auto-contouring, if available, should be completed before CTV contouring.
- All auto-contoured OARs must be reviewed and approved by clinicians involved in contouring and peer review of the radiotherapy treatment plan.

5.1 Constraints and objectives

Structure		2 Gy or 2.167 Gy per fraction		2.75 Gy per fraction*	
Name	Metric	Optimal	Mandatory	Optimal	Mandatory
SpinalCord_PRV	$D_{0.1cc}$	≤ 46Gy	≤ 50Gy (≤ 48Gy if concomitant chemo)	≤ 38Gy	≤ 42Gy (<40Gy if concomitant chemo)
SpinalCord~	$D_{0.1cc}$	≤ 44Gy	≤ 48Gy (≤ 46Gy if concomitant chemo)	≤ 37Gy	≤ 40Gy (≤ 38Gy if concomitant chemo)
Brainstem_PRV		$D_{0.1cc}$ ≤ 56Gy	V_{59Gy} < 10cc**	$D_{0.1cc}$ ≤ 47Gy	V_{49Gy} < 10cc**
Brainstem	$D_{0.1cc}$	≤ 54Gy		≤ 45Gy	
Lens_L/ Lens_R	$D_{0.1cc}$	≤ 6 Gy	≤ 10Gy	≤ 5Gy	≤ 8Gy
Eye_A_L / Eye_A_R	$D_{0.1cc}$	≤ 30Gy		≤ 25Gy	
Eye_A_L_PRV/ Eye_A_R_PRV	$D_{0.1cc}$	≤ 35Gy		≤ 29Gy	
Eye_P_L/ Eye_P_R	$D_{0.1cc}$	ALARP	≤ 45Gy	ALARP	≤ 37Gy
Eye_P_L_PRV/ Eye_P_R_PRV	$D_{0.1cc}$	ALARP	≤ 50Gy	ALARP	≤ 42Gy
Eye_L / Eye_R	$D_{0.1cc}$	ALARP	≤ 45Gy	ALARP	≤ 37Gy
Eye_L_PRV/ Eye_R_PRV	$D_{0.1cc}$	ALARP	≤ 50Gy	ALARP	≤ 42Gy
OpticNrv_L/ OpticNrv_R	$D_{0.1cc}$	ALARP	≤ 54Gy	ALARP	≤ 45Gy
OpticNrv_L_PRV/ OpticNrv_R_PRV	$D_{0.1cc}$	ALARP	≤55Gy	ALARP	≤46Gy

Structure		2 Gy or 2.167 Gy per fraction		2.75 Gy per fraction*	
Name	Metric	Optimal	Mandatory	Optimal	Mandatory
OpticChiasm	$D_{0.1cc}$	ALARP	≤ 54Gy	ALARP	≤ 45Gy
OpticChiasm_PRV	$D_{0.1cc}$	ALARP	≤55Gy	ALARP	≤46Gy
Brain	$D_{0.1cc}$	ALARP	≤ 60Gy	ALARP	≤ 50Gy
BrachialPlex_L/ BrachialPlex_R	$D_{0.1cc}$	ALARP	≤60Gy if low neck not involved ≤66Gy if low neck involved	ALARP	≤50Gy if low neck not involved ≤55Gy if low neck involved
Hippocampus_L/ Hippocampus_R		V_{20Gy} ≤20% $V_{7.3Gy}$ ≤40%		V_{16Gy} ≤20% V_{6Gy} ≤40%	
Pituitary	$D_{0.1cc}$ D_{mean}	≤ 50 Gy ≤20Gy		≤ 42Gy ≤16Gy	
Glnd_Lacrimal_L/ Glnd_Lacrimal_R	$D_{0.1cc}$	ALARP	≤ 40Gy	ALARP	≤ 33Gy
Glnd_Submand_L/ Glnd_Submand_R	D_{mean}	≤ 35Gy		≤ 29Gy	
Cochlea (IpsiLat)	D_{mean}	≤ 40Gy(≤35Gy if concomitant chemo)		≤ 33Gy (≤29Gy if concomitant chemo)	
Cochlea (ContraLat)	Dmean	≤ 10Gy		Dmean ≤ 8Gy	
Larynx	D_{mean}	≤ 40Gy		D_{mean} ≤ 33Gy	
Bone_Mandible	$D_{0.1cc}$	≤ 100% dose		$D_{0.1cc}$ ≤ 100% dose	
Parotid_L/ Parotid_R (IpsiLat)	D_{mean}	ALARP		ALARP	

Structure		2 Gy or 2.167 Gy per fraction		2.75 Gy per fraction*	
Name	Metric	Optimal	Mandatory	Optimal	Mandatory
Parotid_L/ Parotid_R (ContraLat)	D_{mean}	≤ 24Gy		D_{mean} ≤ 20Gy	
	D_{mean}	≤ 14Gy If unilateral		≤ 11Gy, If unilateral	
Parotid_sup_R Parotid_sup_L	D_{mean}	≤ 27Gy		D_{mean} ≤ 22Gy	
Musc_Constrict	D_{mean}	≤ 55Gy		D_{mean} ≤ 46Gy	

*Calculated using BED for 2Gy/fraction with α/β value of 2

**In cases where PTV overlap BrainstemPRV and PTV dose coverage couldn't be compromised

The above dose volume objectives are based on

1.QUANTEC - Marks LB, Yorke ED, Jackson A, Ten Haken RK, Constine LS, Eisbruch A, Bentzen SM, Nam J, Deasy JO. Use of normal tissue complication probability models in the clinic. Int J Radiat Oncol Biol Phys. 2010 Mar 1;76(3 Suppl):S10-9.

2.ADePT-DDR Radiotherapy and QA guidelines. Version: 1.0, 25th February 2021

3.Organs at risk in the brain and their dose-constraints in adults and in children: A radiation oncologist's guide for delineation in everyday practice. Radiotherapy and Oncology 114 (2015) 230–238

4.Radiotherapy Guidelines 2020 DAHANCA Danish Head and Neck Cancer Group. Version 1.0

While these objectives are based on the available guidelines, treatment plan should be optimised ALARP to the OARs.

6.0 Planning process/ technique

6.1 Planning Target Volumes

- All PTV volumes are defined by an isotropic margin added to each CTV, in line with ICRU 50, 62 and 83 recommendations and should not be edited.
- The magnitude of this margin will vary amongst difference radiotherapy centres and typically should be between 3-5mm.

6.2 Planning Technique

- All patients receiving curative radiotherapy should be planned using IMRT or VMAT
- Palliative radiotherapy could be treated with Vsim, conformal, IMRT or VMAT

6.3 Dose fractionation

- Please refer to table in section 3.0

6.4 Target volumes

- PlanPTV structures should be created for the purpose of assessing Target dose coverage.
- PlanPTVs are created by editing back the PTVs from the skin (or outer bolus surface if bolus is prescribed) by up to 5mm.
- Where the higher dose and lower dose PTVs overlap, the lower dose PlanPTVs should be edited off the respective higher dose PlanPTVs with 0mm margin.
- Dummy volumes, density override volumes and virtual bolus can be created to optimise a treatment plan (virtual bolus is applied only during optimisation; to produce a plan which gives dose coverage to PTV regions that overlap a lower density e.g. air).

6.5 Dose prescription and calculation

- Treatment dose should be prescribed to the PlanPTV rather than unedited PTV, to avoid the low dose build-up unbalancing the overall dose upon normalisation.

6.6 Plan evaluation

- Planning aims should be prioritised in the following order:

Critical organ constraints (cord/brainstem)>
high dose PTV>
low dose PTV>
non-critical organ objectives (e.g. parotids)>

other non-specific normal tissue objectives

* Non-critical organs could be prioritised over PTV(s) and/or critical organ(s) on a case-by-case basis; please consider adding planning comments on electronic system.

6.7 Target dose objectives

- All plans should be optimised to fulfil the target dose objectives detailed in the table below whilst respecting the structure priorities stated above.
- Hotspots in lower dose PTV volumes should be kept as low as possible.
- Final treatment plan dosimetry review must be visually appraised by responsible clinician prior to sign off.
- Deviations from stated constraints or objectives should be reported and justified. Planning objectives for IMRT/ VMAT are tabulated below.

Target Volume	Higher dose PlanPTV	Lower dose PlanPTV
99%	≥ 90%	≥ 90%
95%	Optimal ≥ 98% Mandatory ≥ 95%	Optimal ≥ 98% Mandatory ≥ 95%
50%	100%	100% + Centre dependent tolerance
5%	≤ 105%	-
2%	≤ 107%	-

*Centres may wish to set Target objectives exceeding those given in the table above.

7.0 Peer Review

- Prospective peer review (as per RCR guidance) should be carried out on all curative volumes before the start of treatment [39]. Consideration should be given to performing peer review across the East of England Radiotherapy Network if support is required, especially for rare tumour sites, for example nasopharynx.
- A description of the contouring (planning note) and of the peer review process including changes made should be saved in the patient record.

8.0 Target verification

- Treatment verification is an important component of radiotherapy to detect and minimise treatment delivery errors.

- Local protocol for target verification must adhere to recommendations set out in 'On target 2: updated guidance for image-guided radiotherapy' by the Radiotherapy Board. June

2021 publication by RCR, IPEM, and The College of Radiographer https://www.rcr.ac.uk/sites/default/files/radiotherapy-board-on-target-2-updated-guidance-image-guided-radiotherapy.pdf .

- As a minimum, images should be acquired for the initial three fractions and assessed off-line, with weekly images taken thereafter.

- More frequent volumetric imaging should be undertaken (i.e. daily imaging) where there are concerns of risk to critical structures due to the proximity of the high dose CTV(s).

- If a weekly image has an out of tolerance error, verification images should be repeated for the next 2 treatments to allow for calculation of a new systematic shift.

- Any systematic correction applied should be confirmed using imaging after being first applied.

- A local procedure should be in place to manage patient weight loss, tumour shrinkage and tissue oedema, and to enable early identification of patients that might require rescanning and/or replanning.

- For oropharyngeal and laryngeal tumours, patients should be asked to avoid swallowing during treatment if possible (dynamic IMRT) or to try and minimise this (static field IMRT).

- Adaptive planning based on soft tissues changes detected through three-dimensional imaging is permitted.

- All re-plans, as well as any re-evaluation during treatment should be reported with clear documentation on the reason for change.

9.0 Treatment gap management

The recommendations from RCR guidelines [40]:

- Unintended prolongation of curative radiotherapy treatment squamous cell carcinoma of head and neck (category 1) could lead to compromised treatment outcome or local tumour control rate.

- It is strongly recommended that all patients receiving radical radiotherapy for squamous cell carcinoma of head and neck should have the delivery of their treatment schedule audited.

- Prevention measures should be put in place to avoid unscheduled interruptions.

- Local strategies for compensation of treatment gap should be in place, and the strategies may include hyperfractionation, weekend treatment and/or increased total dose, if appropriate.

(Please refer to 'The timely delivery of radical radiotherapy: guideline for the management of unscheduled treatment interruptions' fourth edition, January 2019, RCR document)

10.0 Side effects

10.1a Possible early or short-term side-effects lower H&N sites	
Expected (50-100%)	**Management (if appropriate)**
Tiredness	
Skin soreness, itching, blistering and colour changes in treatment area	E45 cream, hydrocortisone cream, patient's current moisturiser along as it is Sodium Lauryl Sulphate (SLS) free; Flamigel RT / Flaminal Hydri/Forte
Thickened and tenacious secretions	Good oral hygiene, maintain good hydration, saline nebuliser, humidifier, Mucodyne (carbocisteine).
Dry mouth	Benzydamine hydrochloride mouthwash, salt water, bicarbonate of soda mouthwash
Oral ulcers	Benzydamine hydrochloride mouthwash, salt water, bicarbonate of soda mouthwash
Pain in the mouth and/ or throat which can cause problems with swallowing	Oral analgesia as per the WHO Analgesic Ladder, and topical analgesia for example aspirin gargles, lidocaine oral spray or mucilage
Loss or change of taste/ Loss of appetite/ Voice changes	Dietetic and SALT assessment and management
Cough	
Loss of appetite	
Hair loss in treatment area	
Anxiety, low mood, feeling fed-up or poor sleep	
Common (10-50%)	**Management (if appropriate)**
Blocked ear and/ or earache	
Mouth infections including oral thrush	Fluconazole 100mg /d for 7 days
Nausea/ Vomiting	Antiemetics

10.1a Possible early or short-term side-effects lower H&N sites	
Difficulty swallowing	May require placement of feeding tube at start of treatment or during to support nutrition and hydration
Less common (Less than 10%)	**Management (if appropriate)**
Chest infection	
Dehydration	
Laryngeal oedema	
Risk of hospital admission	
Lhermitte's sign	
Rare (Less than 1%)	**Management (if appropriate)**
Risk to life	

10.1b Possible late or long-term side-effects lower H&N sites	
Expected (50-100%)	**Management (if appropriate)**
Skin colour change in treatment area	
Lymphoedema	Referral to local lymphoedema service
Dry mouth	Artificial saliva and oral lubricants though these are often only effective for a very short time
Altered taste or loss of taste	
Hair loss in treatment area or patchy re-growth	
Common (10-50%)	**Management (if appropriate)**
Permanent skin texture changes in treatment area	
Telangiectasia in the treatment area	
Dental problems	Refer to restorative dentist
Trismus	SALT - Therabite
Voice changes	SALT referral
Hypothyroidism	Thyroid hormone replacement
Less common (Less than 10%)	**Management (if appropriate)**
Hearing loss or changes	Audiology assessment
Osteoradionecrosis of the jaw	Specialist OMFS referral assessment and management
Swallowing problems with risk of long-term/	Speech and swallow therapist and dietitian referral for assessment and exercise regimen

10.1b Possible late or long-term side-effects lower H&N sites	
permanent feeding tube requirement	
Laryngeal chondronecrosis	
Increased risk of stroke	
Rare (Less than 1%)	**Management (if appropriate)**
Permanent changes to brainstem, spinal cord and nerves to the face, arm, or hand	
A different cancer in the treatment area	
Risk to life	

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13.0 Amendment history

A record of changes in this document

Date	Updated version number	Previous version number	Page Number/ Section (updated version)	Details
01.04.23	V1.0			New Document
22.11.23	V2.0	V1.0	Pg 31	Skin side effects updated in line with updated RCR consent forms
07.10.24	V3.0	V2.0	Through out	Formatting updated
			Section 10	Side effects updated against current RCR consent form