Taipei Veterans General Hospital Practices Guidelines Oncology

Oral Cavity Cancer

2022.06.06 修訂

Definition of oral cavity cancer:

Cancers arising from:

The buccal mucosa, the lip mucosa, the anterior two thirds of the tongue, the upper and lower gingiva, the floor of the mouth, the hard palate, and the retromolar trigone.

Cutaneous squamous cell carcinoma of the vermilion lip is not included.

Indications of radiation therapy

- **Definitive radiotherapy**
  - Early stage (T1-2N0)disease
  - Selected T4a patients who decline surgery (NCCN V1.2022)
  - T4b
  - Clinical trial
- **Adjuvant radiotherapy**
  - Risk factors: positive surgical margin, close surgical margin(< 5 mm), extranodal extension (ENE) of metastatic lymphadenopathy, perineural invasion, vascular invasion, lymphatic invasion, tumor emboli, pT3 or pT4 primary, N2 or N3 nodal disease, nodal disease in levels IV or V.

Principles of patient simulation

- Patients must have an immobilization device (e.g., aquaplast mask) made prior to treatment planning CT scan.
- Shoulder fixation is recommended, esp. with IMRT technique.
- A cork or tongue depressor can be used to depress the tongue for tongue, floor of mouth or hard palate cancer.
- The treatment planning CT scan can be performed with *IV contrast so that the major vessels* of the neck are easily visualized. The treatment planning CT scan must be performed with the immobilization device and in the treatment position. Slice thickness should be at most 0.3 cm.

Principles of Radiation Therapy

- **Radiation technique:**

  – **Intensity-Modulated Radiotherapy (IMRT)**

  IMRT has been shown to be useful in reducing long-term toxicity in oropharyngeal, nasal cavity, paranasal sinus, and nasopharyngeal cancers by reducing the dose to salivary glands, temporal lobes, auditory structures (including cochlea), and optic structures. The application of IMRT to other sites (eg, oral cavity, larynx, hypopharynx, salivary glands) is evolving and may be used at the discretion of treating physicians. Helical tomotherapy and VMAT (volumetric modulated arc therapy) are advanced forms of IMRT.

  – **IMRT and Fractionation**

  A number of ways exist to integrate IMRT, target volume dosing, and fractionation. The **Simultaneous Integrated Boost (SIB)** technique uses differential "dose painting" (66-74 Gy to gross disease; 50-63 Gy to subclinical disease) for each fraction of treatment throughout the entire course of radiation. SIB is commonly used in conventional (5 fractions/week) and the "6 fractions/week accelerated" schedule.

  Sequential (SEQ) IMRT technique typically delivers the initial (lower dose) phase (weeks 1-5) followed by the high-dose boost volume phase (weeks 6-7) using 2-3 separate dose plans, and is commonly applied in standard fractionation and hyperfractionation.

Principles of Radiation Therapy

- **Definitive radiotherapy**
  - Primary and gross adenopathy:
    - Conventional fractionation: 66-74 Gy (2.0-2.2 Gy/fraction; daily)
    - Altered fractionation:
      - 6 fractions/week accelerated: 66-74 Gy to gross disease.
      - Concomitant boost accelerated RT: 72 Gy/6 weeks (1.8 Gy/fraction, large field; 1.5 Gy boost as second daily fraction during last 12 treatment days)
      - Hyperfractionation: 81.6 Gy/7 weeks (1.2 Gy/fraction, twice daily)
  - Subclinical primary disease and uninvolved nodal stations
    - 50-63 Gy (1.6-2.0 Gy/fraction)

Principles of Radiation Therapy

- **Postoperative radiotherapy**
  - Preferred interval between resection and postoperative RT is ≤ 6 weeks.
  - Primary: 60 Gy (2.0 Gy/fraction) for free margins; 63-66 Gy (2.0-2.2 Gy/fraction) for positive or close margins.
  - Neck
    - Nodal stations with ENE: 63-66 Gy (2.0-2.2Gy/fraction)
    - Other nodal stations: 50-63 Gy (1.6-2.0 Gy/fraction)

References

Table 2. IMRT target delineation for oral cavity cancer

Variable	Dose (Gy)/fractions	Primary site	Nodal volume
Gross positive margins or gross residual disease	70/2.0	Gross PTV	—
Microscopic positive margins	66/2.0	Microscopic PTV	—
Negative margins, high-risk disease	60/2.0 or 59.4–63/1.8	High-risk PTV	High-risk PTV
Negative margins, low-risk/contralateral disease	54/1.8	Low-risk PTV	Low-risk PTV

Abbreviations: IMRT = intensity-modulated radiotherapy; PTV = planning target volume.

MSKCC. post-OP RT. 2000/9~2006/12. NO.=35
Int J Radiat Oncol Biol Phys. 2009 Mar 15;73(4):1096-103.

All patients were irradiated with IMRT. Three clinical target volumes (CTVs) were typically defined. CTV1 was defined as the preoperative tumor bed with margin (1–2 cm). CTV2 was defined as the operative bed exclusive of CTV1, and CTV3 was defined as subclinical sites at risk not operated. Doses prescribed to these 3 targets were 60, 57, and 54 Gy, respectively; treatment was delivered in 30 fractions. Occasionally a high-risk volume was identified that received higher dose (63–66 Gy) typically in cases of extracapsular nodal extension (ECE), positive margin or questionable margin status. Dosing was individualized for patients that were found to have recurrent disease at the start of their radiation.

MD Anderson. post-OP RT. 2000~2012. NO.=289
Oral Oncol. 2017 Sep;72:90

the working station for RT planning. The prescribed dose was 1.8–2 Gy/fraction/day, given 5 days per week. In general, the total

chiasm were also contoured on the treatment plan. The prescribed doses to the high-risk, intermediate-risk, and low-risk CTV/PTV were 66–70.2, 59.4–61.2, and 50.4–54 Gy, respectively.

NCKU.post-OP RT. 2005/1~2008/9. NO.=131
Oral Oncol. 2012 Aug;48(8):747-52.

(PTVs), which were PTV-H, PTV-M, and PTV-L. Generally, for patients with positive surgical margins or ECS, 66 Gy was used for CTV-H, 59.4 Gy for CTV-M and 50.4 Gy for CTV-L. Patients with free margin and without ECS were prescribed 60 Gy, 54–60 Gy, and 50 Gy to CTV-H, CTV-M, and CTV-L, respectively. The fraction size was 1.8–2 Gy, and the fraction was delivered once per day, 5 days per week.

VGHTPE. post-OP RT. 2002/11~2012/5. NO.=150 (buccal)
J Chin Med Assoc. 2017 Sep;80(9):569-574.

Dose prescription. Patients undergoing definitive chemoradiation received 66 Gy at 2.2 Gy per fraction to the high-risk PTV, 54 Gy at 1.8 Gy per fraction to the standard-risk PTV, and 50–52 Gy at 1.67–1.73 Gy per fraction to the low-risk PTV. Among postoperative patients, those with positive surgical margins or ECE received 66 Gy at 2.2 Gy per fraction to the high-risk PTV, 54 Gy at 1.8 Gy per fraction to the standard-risk PTV, and 50–52 Gy at 1.67–1.73 Gy per fraction to the low-risk PTV. Patients with negative margins and no ECE received 60–60.2 Gy in 2- to 2.15-Gy fractions to the high-risk PTV, 54 Gy in 1.8-Gy fractions to the intermediate-risk PTV, and 50–52 Gy in 1.67- to 1.73-Gy fractions to the low-risk PTV. Seven patients with no prior neck dissection

Stanford University Medical Center.
Definitive + post-OP RT.
2002/10~2009/6. NO.=7 + 30
Int J Radiat Oncol Biol Phys. 2011 Aug 1;80(5):1412-22.

The median radiation dose prescribed to the postoperative bed was 60 Gy (2 Gy/fraction). The postoperative bed and dissected neck routinely received (at least) 60 Gy in 30 fractions, and any low risk (i.e. undissected) neck sites received (at least) 54 Gy in 30 fractions. If high risk sites were present (i.e. microscopically involved margins or pathological node(s) with extracapsular extension [ECE]), these sites received 66 Gy in 33 fractions while the remaining postoperative bed and dissected neck received 60 Gy in 33 fractions and low risk neck sites received 56 Gy in 33 fractions.

Princess Margaret Hospital, University of Toronto.
post-OP RT.
2005~2010. NO.=180
Oral Oncol. 2013 Mar;49(3):255-60.

IMRT was delivered by 6 MV photon beams on a Varian linear accelerator with sliding window technique. The technical solution of choice was a 5 field arrangement ('class solution') for all patients. 70 Gy or 69.6 Gy in 35 and 33 fractions was administered for definitive IMRT; one patient received 74 Gy. IMRT treatment was delivered using a simultaneously integrated boost (SIB) technique in all patients; details on SIB are reported elsewhere [7]. The dose in electively irradiated regions was 54 Gy in 33 fractions (range 50–56).

University Hospital Zurich.
Definitive + post-OP RT.
2002/10~2011/6. NO.= 44 + 116
Radiat Oncol. 2012 Jun 11;7:84.

Principles of Target volume delineation

- **Gross Target Volume (GTV) delineation**
  - –defined as tumor detected on physical examination or imaging studies. In postoperative cases, the GTV was defined as the preoperative gross tumor volume.
- **Clinical Target Volume (CTV) delineation**
  - –included all potential areas at risk for microscopic tumor involvement by either direct extension or nodal spread.
  - –Including volumes 4-5 mm around GTV.
- **Planning Target Volume (PTV) delineation**
  - –including a margin for patient motion and setup errors.
  - – 3 to 5 mm margin is usually added to CTV.

Contouring guideline

- Image registration of CT, MRI, or PET (if available) should be done for GTV delineation.
- **Adequate coverage of infratemporal fossa is necessary for upper gingival or retromolar trigone cancer.**
- For oral cavity cancer, adjacent level Ia and Ib of neck are usually included, except for early retromolar trigone tumors (only Ib). Level II to V should be covered for LN (+) cases.
  - Level V could be omitted if only levels I to II are involved
- Lateral retropharyngeal LN (of Rouviere, level VIIb) are rarely involved by oral cavity cancer. (Only few case reports exist).
- The following lymph nodes are not included :
  - **Level VIa**: Lymph nodes in the prelaryngeal area of the neck.
  - **Level VIb**: Lymph nodes in the paratracheal area of the neck and upper mediastinum.

CTV: unilateral or bilateral neck? Summary of Recommendations

- **Ipsilateral neck irradiation:**
  - Stage I-II buccal, gingival, retromolar cancer
- **Bilateral neck irradiation:**
  - ***midline tumors***: tongue, floor of mouth and hard palate and any tumors with involvement of these structures.
  - Contralateral positive nodes.
- **Both of the above are acceptable:**
  - All others
- Risk factors for contralateral neck recurrence: locally advanced primary disease, multi-involvement of ipsilateral neck nodes, ENE, high pathological grading are associated with contralateral neck lymph node metastasis.

TABLE 3 Multivariate analyses of risk factors associated with the 5-year contralateral neck recurrence rate (patients with tongue cancer with local control, $n = 310$)

Characteristic (n)	P value	HR (95% CI)
Differentiation	0.012	
Well/moderate (284)		Reference category
Poor (26)		1.058 (1.013–1.106)
Perineural invasion	0.001	
No (228)		Reference category
Yes (82)		4.343 (1.781–10.594)
Level IV or V metastases	0.042	
No (301)		Reference category
Yes (9)		1.036 (1.001–1.072)

HR hazard ratio; *CI* confidence interval

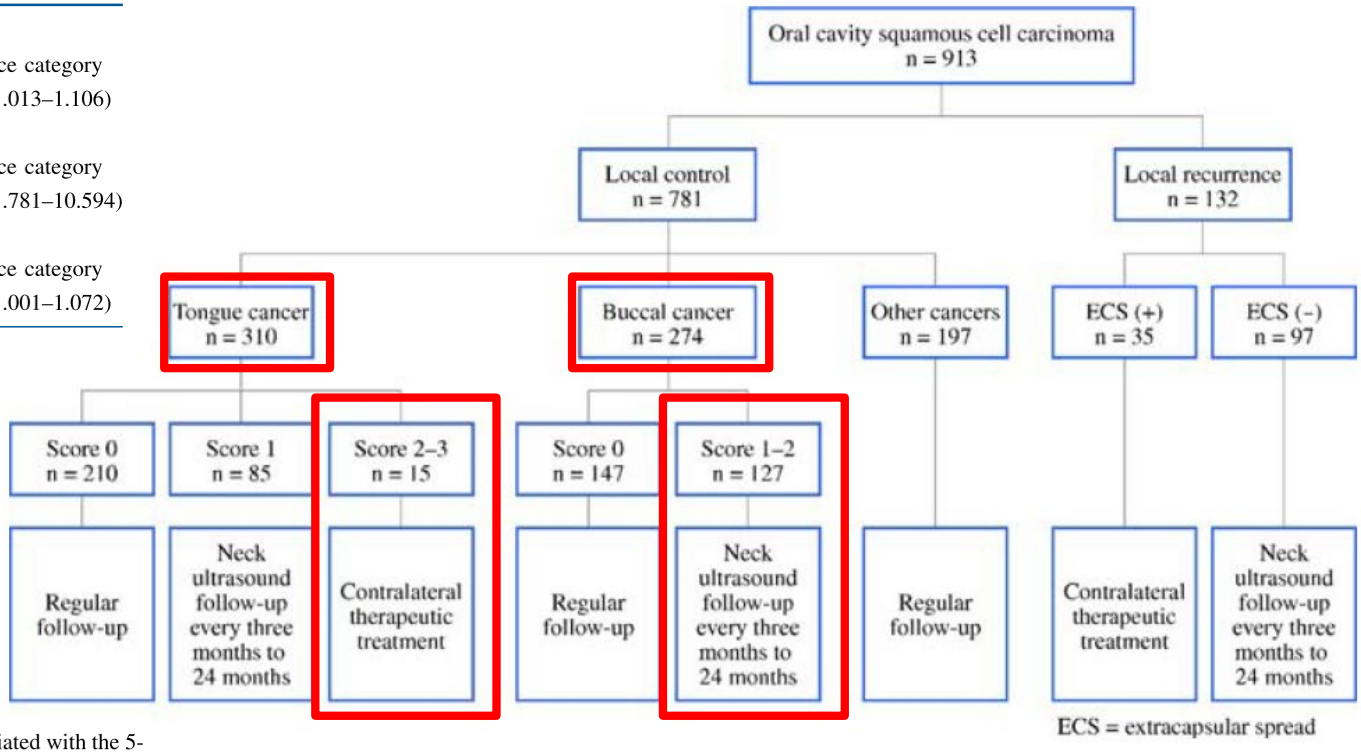


TABLE 4 Multivariate analyses of risk factors associated with the 5-year contralateral neck recurrence rate (patients with buccal cancer with local control, $n = 274$)

Characteristic (n)	P value	HR (95% CI)
Differentiation	0.022	
Well/moderate (257)		Reference category
Poor (17)		1.088 (1.012–1.169)
Pathological T status	0.024	
T1–2 (155)		Reference category
T3–4 (119)		3.325 (1.175–9.414)

HR hazard ratio; *CI* confidence interval

Ann Surg Oncol. 2009 Jan;16(1):159-70.

CTV: unilateral or bilateral neck?

- For salvage irradiation after local (regional) recurrence, contralateral neck treatment might be considered for patients with extracapsular spreading initially.
  Ann Surg Oncol. 2009 Jan;16(1):159-70.
- For buccal cancer, locoregional control might not differ between patients undergoing unilateral or bilateral neck treatments
  Int J Radiat Oncol Biol Phys. 2008 Apr 1;70(5):1373-81.

- **DAHANCA guidelines:**
  Lateral tumours: buccal mucosa, gingiva and retromolar trigone, with no involvement of contralateral nodes.
  Midline tumours: tongue, floor of mouth and hard palate and any tumours with involvement of these structures.

- **Radical Radiotherapy**:
  Midline tumours are treated with bilateral elective regions and lateral tumours with ipsilateral elective regions. Elective nodal regions are:
  - N0: level I, II, III
  - N1-3: level I, II, III. Elective regions are extended at least 2 cm cranially and caudally of GTV-N.
- **Postoperative radiotherapy**:
  Midline tumours are treated with bilateral elective regions and lateral tumours are treated with ipsilateral elective regions. Elective nodal regions are
  - pN0: level I, II, III. In case of involvement of macroscopic cranial nerve, the nerve is included to the base of skull.
  - pN1-3: level I, II, III. Elective regions are extended at least 2 cm cranially and caudally of GTV-N. If extension to nearby muscle involvement is suspected the entire muscle is included at least 2 cm above and below GTV-N.

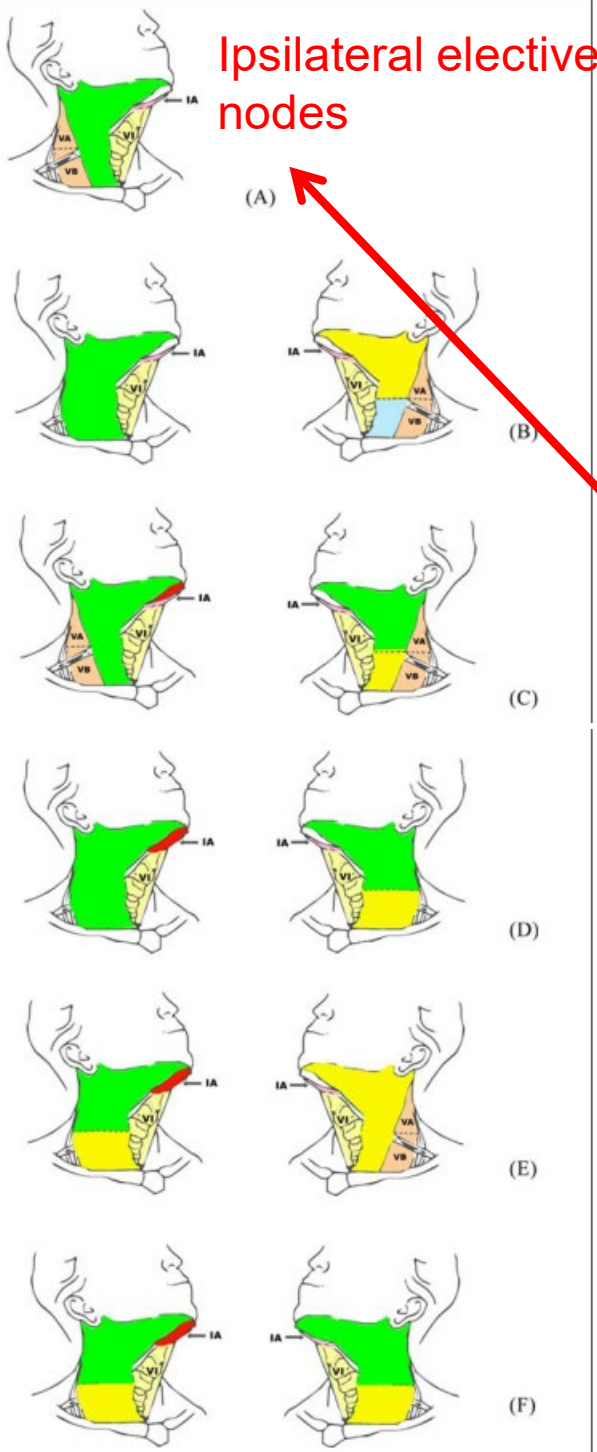


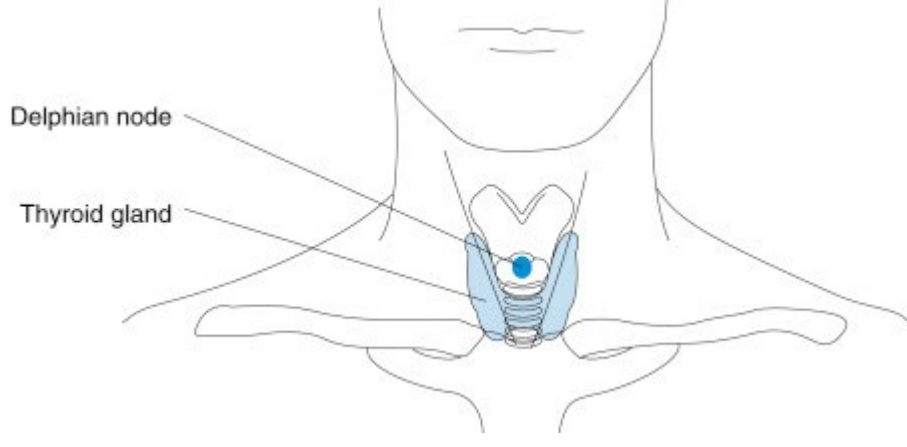
FIGURE 1. Most common delineations and dose specifications for nodal clinical target volume (CTV).
CTV2 is shown in green and
CTV3 in yellow.
Level Ia neck is included in floor of mouth and anterior tongue lesion and is shown in red.
(A) Buccal/gingival/retromolar trigon without cross midline lesion - pT1–2N0.
(B) Buccal/gingival/retromolar trigon without cross midline lesion pT3–4N0.
(C) Tongue/mouth floor/hard palate or with cross-midline lesion - pT1–2N0.
(D) Tongue/mouth floor/hard palate or with cross-midline lesion - pT3–4N0.
(E) Any T with positive ipsilateral node.
(F) Any T with positive contralateral node.

Head Neck. 2015 Jul;37(7):933-9.

CTV: Necessity to cover the unusual sites of recurrence?

- Parotid (~1%):
  - May be included for ipsilateral buccogingival cancer or advanced level I/II LAPs
- Retropharyngeal nodes
  - Bilateral RP nodes are at risk
  - May be included for advanced level I/II LAPs
  - May be included for tumor invading nasal cavity, hard palate, nasopharynx, and oropharynx

  Int J Oral Maxillofac Surg. 2009 Sep;38(9):1004-8.
  Int J Radiat Oncol Biol Phys. 2004 May 1;59(1):28-42.
- Prelaryngeal nodes (Delphian node)



https://www.sciencedirect.com/topics/neuroscience/thyroid-isthmus

TABLE 3 Characteristics of oral cavity cancer with unusual neck recurrent sites (n = 26)

No.	Age (years)	Site	Pathologic stage	Primary treatment	Unusual sites of neck recurrence	Interval between primary surgery and the event						
						Tumor recurrence (M)	Neck recurrence (M)		Distant metastases (M)	Tumor salvage	Neck salvage		Died of disease (M)
							Uual	Unusual			Usual	Unusual	
1	34	Buccal	T2N2b	S + RT	Delphine	–	–	9	9			–	9
2	55	Gum	T4N2b	S + RT	Delphine[a]	4	4	4	–	–	–	–	5
3	52	Gum	T2N0	S	Delphine	33	–	41	–	+		+	53
4	27	Mouth floor	T1N2b	S + CCRT	Delphine[a]	–	3	4	5		–	–	7
5	46	Tongue	T2N2b	S + RT	Delphine[a]	–	5	5	–		+	+	10
6	67	Gum	T4N1	S	Parotid[a]	–	16	16	–		–	–	18
7	52	Buccal	T1N2b	S + CCRT	Parotid[a]	–	4	4	–		–	–	7
8	53	Gum	T2N2b	S + CCRT	Parotid	–	–	4	–			–	7
9	36	Buccal	T2N0	S	Parotid	–	–	3	–			+	8
10	66	Gum	T4N0	S + RT	Parotid	–	–	4	–			–	9
11	29	Buccal	T3N2b	S + CCRT	Parotid	–	–	7	–			+	13
12	39	Tongue	T1Nx	S	Parotid[a]	–	4	5	7		+	–	8
13	39	Lip	T3N2c	S + RT	Parotid	8	–	10	12	+		+	14
14	41	Tongue	T2N0	S + RT	Parotid[a]	36	39	39	–	+	+	+	43
15	48	Buccal	T1N1	S + CCRT	Parotid[a]	34	34	37	39	+	+	–	40
16	47	Tongue	T4N1	S + CCRT	Parotid	30	–	44	–	+		+	51
17	40	Buccal	T4N2b	S + CCRT	Parotid[a]	–	1	1	6		+	+	9
18	44	Hard palate	T4N0	S + RT	Parotid	101	–	105	105	+		–	119
19	46	Tongue	T1N1	S + CCRT	RP[a]	14	14	14	–	–	–	–	15
20	68	Tongue	T4N2c	S + CCRT	RP[a]	–	5	5	–		–	–	6
21	46	Buccal	T2N2b	S + CCRT	RP[a]	–	4	4	4		–	–	8
22	39	Buccal	T3N2b	S	RP[a]	4	4	4	–	–	–	–	8
23	59	Retromolar	T2N2b	S + RT	RP	16	–	16	–	–		–	21
24	55	Retromolar	T4N2b	S + CCRT	RP	–	–	3	–			–	6
25	62	Hard palate	T2N0	S	RP	–	–	7	–			+	11
26	41	Gum	T4N0	S + RT	RP	23	–	23	–	+		+	37

M months, *S* surgery, *RT* radiation therapy, *CCRT* concurrent chemoradiation, *RP* retropharyngeal

[a] Patients 2, 4, 5, 6, 7, 12, 14, 15, 17, 19, 20, 21, and 22 also had neck metastases at usual sites

CGMH 204/1480 neck recurrence, 26 unusual group.
Ann Surg Oncol. 2013 Jan;20(1):257-66.

5 at the prelaryngeal
13 at the parotid
8 at the retropharyngeal

TABLE 2. Baseline data, treatments, and prognoses of patients with oral squamous cell carcinoma with neck recurrence in unusual sites ($n = 24$).

Patient #	Age, y	Sex	Site	pTNM classification	Pathological grade	Growth pattern	Tobacco use	Alcohol use	Primary neck treatment	Recurrence sites	Recurrence time, mo	Salvage treatment	Censor (mo)
1	64	M	Tongue	T2N1	II	Infiltrative	Yes	No	S	Inferior parotid	17	S + RT	Death (167)
2	68	F	Lower gingival	T1N0	I	Exophytic	No	No	S	Inferior parotid + neck	2	S + RT	Death (45)
3	58	F	Floor of mouth	T1N0	II	Ulcerative	No	No	S	Parotid	115	S	Survival (148)
4	50	F	Tongue	T2N0	I	Exophytic	No	No	S	Inferior parotid + neck	9	S + CCRT	Death (20)
5	37	M	Tongue	T2N0	I	Infiltrative	Yes	Yes	S	Lateral retropharyngeal	6	RT	Death (11)
6	46	F	Buccal	T3N2b	II	Ulcerative	Yes	No	S + RT	Parotid	4	S	Survival (99)
7	72	M	Upper gingival	T1N1	I	Exophytic	No	No	S	Lateral retropharyngeal + neck	13	S + RT	Death (59)
8	52	M	Lower gingival	T4N2c	I	Infiltrative	Yes	Yes	S + RT	Inferior parotid	9	S	Death (18)
9	65	F	Tongue	T3N0	I	Ulcerative	No	No	S	Prelaryngeal	9	S + RT	Survival (86)
10	62	M	Tongue	T1N0	I	Ulcerative	Yes	Yes	S + RT	Prelaryngeal	7	S	Survival (66)
11	68	M	Upper gingival	T3N1	II	Infiltrative	No	No	S + RT	Parotid	8	Quit	Death (24)
12	58	M	Tongue	T2N2b	I	Infiltrative	Yes	Yes	S + RT	Prelaryngeal + neck	8	S + CT	Death (15)
13	62	M	Lower gingival	T3N0	I	Exophytic	No	No	S	Parotid + distance	18	RT	Death (24)
14	32	M	Tongue	T2N1	I	Ulcerative	Yes	Yes	S + RT	Prelaryngeal	3	S	Death (9)
15	50	M	Tongue	T1N2b	II	Infiltrative	Yes	Yes	S + RT	Prelaryngeal + neck	8	Quit	Death (11)
16	55	M	Tongue	T2N2c	III	Infiltrative	Yes	Yes	S + RT	Lateral retropharyngeal + neck	18	Quit	Death (25)
17	63	M	Tongue	T4aN2c	II	Infiltrative	Yes	Yes	S + RT	Inferior parotid	16	RT	Survival (24)
18	67	M	Buccal	T2N0	I	Exophytic	No	No	S	Inferior parotid	30	RT	Death (35)
19	59	M	Buccal	T4aN2b	II	Infiltrative	Yes	No	S + RT	Parotid	3	Quit	Death (5)
20	68	F	Tongue	T2N1	I	Exophytic	No	No	S + CCRT	Parotid	6	Quit	Death (8)
21	78	M	Lower gingiva	T4aN0	I	Exophytic	No	Yes	S + RT	Parotid	14	CT	Death (15)
22	43	M	Tongue	T4N2b	II	Infiltrative	Yes	Yes	S + RT	Parotid	8	Quit	Survival (27)
23	50	M	Tongue	T3N2b	II	Infiltrative	Yes	Yes	S + RT	Inferior parotid	3	S	Lost to follow-up
24	77	M	Buccal	T2N2b	I	Ulcerative	Yes	Yes	S	Parotid + neck	9	CCRT	Death (15)

Abbreviations: S, surgery; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; CT, chemotherapy.

Beijing 24/1658 unusual site recurrence
Head Neck. 2016 Apr;38 Suppl 1:E680-6.

4(0.2%) at the prelaryngeal
17(1.0%) at the parotid
3(0.2%) at the retropharyngeal

CTV: Flap Coverage?

- Flap delineation guidelines in postoperative head and neck radiation therapy for head and neck cancers
  Radiother Oncol . 2020 Oct;151:256-265

- Patterns of local recurrence
  – Most recurrences developed at the anastomosis marginal site
  Head Neck . 2019 Nov;41(11):3916-3923.

CTV: Flap Coverage?

Item	Proposals established by a GORTEC steering committee and present at:	GORTEC Rating Committee		External Review group
		Round 1	Round 2	Round 3
Tumor spread pattern in a flap				
18	Coregistration of the preoperative imaging with the postoperative CT scan should be performed systematically to define the postoperative CTV	NC [8]	RA [8]	NC
19	Coregistration uncertainties (of the preoperative imaging with postoperative planning CT) should be compensated by expanding larger margins (than recommended for postoperative radiotherapy) around the preoperative GTV	NC [6]	NC [5]	
20	"Direct" postoperative modifications (edema, hematoma, lymphocele) of the flap should be included in the CTV	NC [7]	SA [7]	NC
21	The risk of microscopic tumor spread is centrifugal from the junction area to the depth of the remaining native tissues	NC [7]	SA [8]	NC
22	The risk of spreading microscopic disease is centrifugal from the junction area to the "mucous or cutaneous" surface of the flap	NC [4.5]	NC [5]	
23	The risk of microscopic diffusion into the flap may vary depending on the histology (squamous cell carcinoma and variants, adenoid cystic carcinoma, adenocarcinoma...)	NC [5]	NC [6]	
24	The risk of microscopic diffusion into the flap may vary depending to the tumor location (parotid vs pharynx vs sinus)	NC [6.5]	NC [6]	
25	The junction area between the native tissues (remaining after tumor resection) and the deep part of the flap is an area at higher risk of cancer	SA [8]		FR
26	The junction area is an area of the order of 6 mm thick in the depth of the flap as described by Bittermann (2015)	NC [6]	RA [7]	NC
27	The junction area at risk is about 10 mm thick in the depth of the flap	NC [5.5]	NC [5]	
28	The junction area varies in thickness depending on the nature of the components of the flap (mucosa/skin, fat, muscle/fascia, bone)	NC [7]	SA [7]	NC
29	The body of the flap (including all the rest of the flap beyond the junction area) should be irradiated entirely in the low-risk area	NC [4]	NC [3]	
30	When the flap is very large, some of the flap body may not be included in the low-risk area	NC [6.5]	SA [8]	NC
31	The delineation uncertainties are so great in the postoperative situation that it is better to irradiate wide even if it means including the entire flap	NC [4.5]	NC [7]	
32	For pedicled flaps, it is not useful to include the vascular pedicle in the CTV. Its tumor colonization is unlikely, and its distal part is far from the operating bed of the primary patient	NC [4.5]	NC [7]	
33	For free flaps, vascular anastomosis is not a way of tumor dissemination	NC [5]	NC [7]	
34	The dose level delivered to the junction area corresponds to primary low-risk CTV if the resection is R0	NC [7.5]	RA [8]	NC
35	The dose level delivered to the junction area corresponds to primary high-risk CTV if the final quality of the resection is dubious R0 or R1 or R2	SA [8]		FR

SA strong agreement, RA relative agreement, NC no consensus, FR final recommendation

A GORTEC internationally-reviewed HNCIG-endorsed consensus
Radiother Oncol . 2021 Jul;160:140-147

CTV: Flap Coverage?

Item	Proposals established by a GORTEC steering committee and present at:	GORTEC Rating Committee Round 1	GORTEC Rating Committee Round 2	External Review group Round 3
Functional flap outcomes				
36	Flap necrosis occurs in early postoperative (vessel quality, morbidity, technical procedure) and radiotherapy does not induce any specific risk	NC [7]	SA [8]	FR
37	Irradiation of the vascular pedicle of a flap induces a risk of necrosis of the flap that is negligible (=unlikely) (strong agreement)	NC [7]	SA [8]	FR
38	The dose received at the vascular anastomosis is not correlated with an increased risk of vascular thrombosis	NC [7]	RA [8]	FR
39	Irradiation of the vascular pedicle from a free flap is at higher risk of necrosis than irradiation of a vascular pedicle from a pedicled flap (no consensus)	NC [5]	NC [5]	
40	Radiotherapy alters the flexibility of the flap	NC [7]	SA [8]	FR
41	Radiotherapy can alter the functional results (swallowing, phonation) of the flap	NC [7]	SA [7]	FR
42	Irradiation of a bone flap is at risk of radionecrosis of the flap	NC [7]	SA [8]	FR
43	Atrophy of the fat flaps is possible spontaneously even in the absence of radiotherapy	NC [7]	SA [8]	FR
44	The risk of atrophy of the flap fat increases with radiotherapy	NC [8]	SA [8]	FR
45	Flap fat atrophy is associated with deterioration of functional results	NC [5.5]	NC [5]	
46	Flap fat atrophy MUST BE anticipated by surgeons by overcompensating tissue/flap thickness	NC [7]	NC [7]	
47	The radiation-induced atrophy of the fatty component of the flaps is related to the dose received	NC [5]	NC [7]	
48	Fibrosis changes of flaps are possible spontaneously even in the absence of radiotherapy	NC [6]	RA [7]	FR
49	Fibrosis of the muscle flap component can be favored by radiotherapy (significantly more than surgery alone)	NC [7]	SA [7]	FR
50	Radiation-induced flap fibrosis increases with dose	NC [7]	SA [7]	FR
Technical IMRT feasibility (dose painting for structure avoidance)				
51	For thin flap, it may not be possible to achieve sufficiently steep gradients to spare the flap of the part	NC [7.5]	SA [8]	FR
52	Limiting the average dose to the flap could limit the risk for fatty atrophy and muscle fibrosis	NC [6]	RA [7]	FR
53	Limiting the average dose to the bone of the flap could limit the risk for flap osteoradionecrosis	NC [7]	RA [7]	FR
54	Limiting the maximum dose to the bone flap could limit the risk for osteoradionecrosis	NC [8]	SA [8]	FR
55	In the case of a bone flap, the presence of titanium, or other metal, in the irradiation area induces an increased risk of osteoradionecrosis	NC [7.5]	NC [6]	
56	In the case of a bone flap, avoid irradiating the titanium plate fixing the flap allows to reduce the risk of osteoradionecrosis	NC [4.5]	NC [3]	
57	In the case of a bone flap, titanium-type materials must be substituted to reduce the risk of osteoradionecrosis	NC [4.5]	NC [5]	
58	Limiting the maximum dose (hot spots) to the vascular pedicle seems feasible technically if the pedicle is delineated	NC [7]	SA [7]	FR
59	Limiting the maximum dose (hot spots) to the vascular pedicle would reduce the risk of necrosis of the flap	NC [5]	NC [6]	

SA strong agreement, RA relative agreement, NC no consensus, FR final recommendation

A GORTEC internationally-reviewed HNCIG-endorsed consensus
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