Comprehensive Treatment for Major Salivary Gland Carcinoma Based on Intensity-Modulated Radiotherapy with or without Radical Surgery

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Research

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Abstract

Background

The present study aimed to determine a treatment strategy and Intensity-Modulated Radiotherapy (IMRT) target volume for major salivary gland carcinoma (SGC).

Methods

Patients with SGC treated at our cancer center between August 2009 and August 2020 were retrospectively reviewed.

Results

The following primary tumor sites were identified: parotid gland in 61 (69.3%) patients, submandibular gland in 21 (23.9%) patients, and sublingual gland in six (6.8%) patients. Lymphoepithelial carcinoma (LEC) was the most common tumor subtype that accounted for 23.9% of cases. A total of 80 (90.9%) patients received radical surgery combined with postoperative radiotherapy. Eight patients (9.1%) received definitive radiotherapy: six patients with advanced-stage disease received induction chemotherapy (IC) combined with concurrent chemoradiotherapy (CCRT), and two patients with early-stage disease received CCRT. Complete response was observed in these eight patients after treatment completion. The median follow-up time of all patients was 42 months (range: 4–129 months). No patient developed local recurrence. The 5-year overall survival, regional failure-free survival, distant metastasis-free survival, and progression-free survival probabilities were 84.1%, 95.6%, 75.3%, and 75.7%, respectively. Distant metastasis was observed in 18 (20.5%) patients, followed by regional 2 (2.3%) recurrence. Permanent facial nerve injury was confirmed in 31 patients by follow-up. None of the patients experienced facial nerve paralysis in the definitive radiotherapy group.

Conclusions

LECs may be sensitive to chemoradiotherapy, which may achieve a radical effect and avoid unnecessary surgical injury. IC combined with CCRT is expected to become a new treatment strategy for advanced LECs. The IMRT target volume delineation according to the surgical principles may be a more promising method with good clinical efficacy that is worthy of further study.

Background

Salivary gland carcinomas (SGCs) are malignant neoplasms that account for approximately 1.0–8.5% of all head and neck cancers [1][2]. Recent studies have shown that the incidence of SGC is increasing every year, while the age of onset is decreasing [3][4]. Guidelines from the National Comprehensive Cancer Network (NCCN) recommend surgery as the primary treatment for SGCs and postoperative radiotherapy for patients with advanced-stage disease or high-risk factors [5]. The major complications of surgery include facial nerve injury, with reported incidence of 12–40% [6].

According to previous literature, lymphoepithelial carcinomas (LECs) are malignancies that have morphological features similar to those of undifferentiated nasopharyngeal carcinomas (NPCs) and occur in areas outside the nasopharynx, such as in the salivary gland, lung, and stomach [7][8][9][10]. NPCs are sensitive to chemotherapy and radiotherapy, and a radical effect can be achieved by chemoradiotherapy [11]. However, there are few reports on major salivary LECs. Radical surgery is also the primary treatment for this tumor subtype according to the NCCN guidelines. In addition, LECs often invade the facial nerve due to a high malignancy degree. For this reason, some surgical scholars believe that facial nerve preservation will affect the safety of surgery and thus advocate for the removal of the involved facial nerve to reduce local recurrence [12]. In short, surgery will likely cause permanent damage to the facial nerve in addition to disfigurement, which might affect patients' quality of life and self-confidence.

Intensity-modulated radiotherapy (IMRT) has become the standard treatment technique for head and neck cancer. However, there are few studies on target volume delineation for SGCs. Previous recommendations have determined the IMRT target volume based on the “tumor bed”, “surgical bed”, or even “parotid bed” [13][14][15]. However, our prior study suggests that these recommendations may not consider individual subtleties associated with the exact location of the primary lesion [16]. They also did not make full use of the IMRT advantage, which is that the high-dose areas conform closely to the three-dimensional shape and scale of the tumor.

Based on these considerations, the present retrospective study summarized the clinical characteristics of SGCs and analyzed failure patterns in patients treated with IMRT to provide a reference for individualized SGC treatment.

Methods And Materials

Patients

A total of 96 patients with SGCs were retrospectively evaluated between August 2009 and August 2020. The patients were restaged according to the 8th edition of the American Joint Committee on Cancer (AJCC) staging system for major salivary glands. The exclusion criteria were as follows: (1) evidence of distant metastasis before treatment, secondary malignancy, or both; (2) non-epithelial tumors. The ethics committee of Sun Yat-sen University Cancer Center approved the study protocol.

Diagnosis

All patients underwent a comprehensive exam and evaluation that included computed tomography (CT) or magnetic resonance imaging (MRI) of the head and neck, chest radiography, abdominal ultrasonography, emission computed tomography, or positron emission tomography-computed tomography. Some patients also underwent color Doppler ultrasound imaging of the salivary glands. The final diagnosis was based on histopathology or cytopathology results. Due to the histological finding similarity, distinguishing LECs from lymph nodes containing NPC metastases was especially important. Nasopharyngoscopy was conducted in all patients in order to make a correct diagnosis.

Chemotherapy

The induction chemotherapy (IC) regimen was a combination of taxanes, cisplatin, and fluorouracil (TPF), comprising intravenous infusion of docetaxel at a dose of 50 mg/m^2 on day 1, intravenous infusion of cisplatin at a dose of 60 mg/m^2 on day 1, and continuous intravenous infusion of 5-fluorouracil at a dose of 500 mg/m^2/day on days 1–5 for 120 h, three times per week, for a total of four cycles. If tumor shrinkage achieved a partial response (PR) or above after two cycles of IC, patients continued IC for up to four cycles and were administered concurrent chemoradiotherapy (CCRT). Otherwise, the patients received CCRT after two cycles of IC or were reconsidered for surgery. CCRT treatment prescribed cisplatin at a dose of 30 mg/m^2 of intravenous infusion on day 1, for 4–6 cycles weekly [17].

Radiotherapy

Definitive radiotherapy: prior to radiotherapy, patients were immobilized with head-and-neck thermoplastic masks in a supine position. A CT simulation was then performed using 3-mm slices of the head and neck within 1–2 weeks after IC [17].

Postoperative radiotherapy: postoperative MRI of the head and neck was performed 3 weeks after surgery when the wound had healed. The patients were immobilized in a supine position with a head-and-neck thermoplastic mask [16].

Some patients were immobilized with a bolus to the skin if necessary.

Target volume delineation

Definitive radiotherapy: gross tumor volume of primary site/regional lymph node (GTVp/nd) was defined as the volume of the primary tumor including lymph node metastasis. Medium risk clinical tumor volume (CTV1) was defined as GTVp/nd plus a

0.5- to 1.0-cm margin. Low-risk CTV (CTV2) was defined as CTV1 plus a 5-mm margin together with the regional selective lymph drainage areas. According to prior studies, ipsilateral level Ib–Va and □–□ should be included in parotid gland cases, ipsilateral level I–Va should be included in submandibular gland cases, and bilateral level I–Va should be included in sublingual gland cases [18][19][20]. For patients with advanced-stage disease, the GTVp/nd was contoured according to the tumor regression after IC [17].

Postoperative radiotherapy: among the reserved tissues, those located <5 mm from the invasive tumor edge before surgery were defined as high-risk CTV (CTV-HD); those located <10 mm away were defined as CTV1; and those located 10–20 mm away together with the regional selective lymph drainage areas were defined as CTV2 [16]. Examples of target volume delineation are presented in Figure 1.

Normal structures, including the mandible, brainstem, temporal lobe, oral cavity, middle ear, and spinal cord, were also contoured slice-by-slice in the treatment-planning CT scans [17].

Planning target volumes (PTV) were generated by addition of a 3–5-mm margin to all GTV/CTV values [17]. Table 1 summarizes the target volume definitions.

Table 1. Target volume specification for definitive and postoperative IMRT

Target	Definitive IMRT	Postoperative IMRT
GTV/CTVHD	Gross tumor and positive lymph node after IC	Reserved tissues around the margin of resection that were less than 5 mm from the invasive tumor edge before surgery
CTV1	GTV plus a 5- to 10-mm margin together with the primary tumor region before IC	Reserved tissues around the margin of resection that were less than 10 mm from the invasive tumor edge before surgery
CTV2	CTV1 plus a 5-mm margin together with the elective nodal regions	Elective nodal regions and reserved tissues around the margin of resection that were less than 20 mm from the invasive tumor edge before surgery

Abbreviations: IMRT = intensity-modulated radiotherapy; GTV = gross tumor volume; CTV = clinical target volume; IC = induction chemotherapy

Dose prescription and delivery

All patients enrolled since September 2015 were treated with adaptive re-planning intensity-modulated radiotherapy (AR-IMRT) after 25 fractions, while the rest of the patients were treated with one-course IMRT. The prescribed doses were GTV, 68–70 Gy; CTV-HD and CTVnd, 63–65 Gy; CTV1, 59–61 Gy; and CTV2, 45–54 Gy. The aim was to achieve 95% of any PTV at or above the prescription dose. IMRT was given once daily, 5 days per week with no treatment break [48].

Follow-up

The follow-up time was until August 2021 or the date of death. Treatment failure was confirmed by biopsy. Failure was defined in accordance with the definition provided by Chao et al. [21].

Statistical analysis

Estimates of overall survival (OS), regional failure-free survival (RFFS), distant metastasis-free survival (DMFS), and progression-free survival (PFS) were obtained using the Kaplan-Meier method. Statistical calculations were performed using SPSS version 25.0 (IBM SPSS Statistics for Windows, Armonk, NY, USA).

Results

Patient characteristics

Eight patients were excluded from the analysis due to development of distant metastases during treatment or diagnosis of non-epithelial tumors. As a result, a total of 88 patients with SGCs were selected for analysis of clinicopathological profiles: 33 females (37.5%) and 55 males (62.5%). The onset age ranged from 18 to 77 years, and the median age was 45 years. The primary tumor sites were as follows: parotid gland in 61 (69.3%) patients, submandibular gland in 21 (23.9%) patients, and sublingual gland in six (6.8%) patients. LEC was the most common tumor subtype (23.9%). The type of surgery was determined by surgeons. A total of 80 (90.9%) patients received radical surgery with or without neck dissection combined with postoperative radiotherapy. Eight patients (9.1%) received definitive radiotherapy: six patients with advanced-stage disease received IC combined with concurrent CCRT, and two patients with early-stage disease received CCRT. The details of patient and tumor characteristics are summarized in Table 2.

Table 2
Clinical characteristics

	Patients (N=88)	Definitive IMRT (N=8)	Postoperative IMRT (N=80)
Primary site			
Parotid gland	61	6	55
Submandibular gland	21	2	19
Sublingual gland	6	0	6
Age, y (range)	Median, 45 y (18–77 y)	Median, 47.5 y (27–61 y)	Median, 45 y (18–77 y)
< 60	63	7	56
≥ 60	25	1	24
Sex			
Male	55	5	50
Female	33	3	30
Disease presentation			
Primary	74	8	66
Recurrent	14	0	14
Histology			
Lymphoepithelial carcinoma (23.9 %)	21	6	15
Adenoid cystic carcinoma (20.5%)	18	0	18
Mucoepidermoid carcinoma (15.9%)	14	0	14
Salivary duct carcinoma (15.9%)	14	0	14
Acinic cell carcinoma (9.1%)	8	0	8
Squamous cell carcinoma (8.0%)	7	2	5
Other (6.8%)	6	0	6
Surgery type			
Total parotidectomy	23	0	23
Superficial parotidectomy	23	0	23
Submandibular gland excision	19	0	19
Sublingual gland excision	5	0	5
Unoperated	8	8	0
Not Available*	10	0	10
Treatment type			

Abbreviations: IMRT = intensity-modulated radiotherapy; IC = induction chemotherapy; CCRT = concurrent chemoradiotherapy; S = surgery; RT= radiotherapy; AR-IMRT = adaptive re-planning intensity-modulated radiotherapy

*Patients received surgery in another center and their operation records could not be found.

	Patients (N=88)	Definitive IMRT (N=8)	Postoperative IMRT (N=80)
IC+CCRT	6	6	0
CCRT	2	2	0
S+CCRT	62	0	62
S+RT	18	0	18
Radiotherapy type			
One-course	40	2	38
AR-IMRT	48	6	42

Abbreviations: IMRT = intensity-modulated radiotherapy; IC = induction chemotherapy; CCRT = concurrent chemoradiotherapy; S = surgery; RT= radiotherapy; AR-IMRT = adaptive re-planning intensity-modulated radiotherapy

*Patients received surgery in another center and their operation records could not be found.

Efficacy

After completion of definitive radiotherapy, complete response (CR) was observed in all of the patients. Table 3 summarizes clinical characteristics and outcomes of these eight patients. Cases 1–3 have been previously described by our team [22]. Updated follow-up data showed that Cases 1 and 2 were still alive without evidence of disease, while Case 3 died of distant metastasis. Case 6 was a 52-year-old man who achieved a PR after IC. After completion of definitive radiotherapy, CR was observed via MRI, and the patient showed no evidence of disease until the last follow-up (2021-8). Details of Case 6 are presented in Figure 2.

Table 3
Details of patients received definitive IMRT

	Case1	Case2	Case3	Case4	Case5	Case6	Case7	Case8
Primary site	Parotid gland	Parotid gland	Submandibular gland	Parotid gland	Parotid gland	Parotid gland	Parotid gland	Submandibular gland
Age, y	27	33	52	61	44	52	37	54
Sex	Male	Male	Male	Male	Female	Male	Female	Female
Histology	LEC	LEC	LEC	LDSCC	LDSCC	LEC	LEC	LEC
Stage	T4N3M0	T4N3M0	T4N2M0	T4N2M0	T4N2M0	T4N2M0	T1N0M0	T1N0M0
Regimen	TPF for 4 cycles plus DDP CCRT				DDP CCRT			
RT type	AR-IMRT	AR-IMRT	AR-IMRT	One-course	AR-IMRT	One-course	AR-IMRT	AR-IMRT
Overall survival time, m	28+	73+	15 Died of distant metastasis	100+	79+	35+	20+	20+
Progression-free survival time, m	28+	73+	13	100+	79+	35+	20+	20+

Abbreviations: LEC = lymphoepithelial carcinoma; LDSCC = low differentiated squamous cell carcinoma; TPF = taxanes, cisplatin and fluorouracil; DDP = cisplatin; CCRT = concurrent chemoradiotherapy; RT= radiotherapy; AR-IMRT = adaptive re-planning intensity-modulated radiotherapy

The median follow-up time for SGC patients was 42 months (range: 4–129 months). During follow-up, primary recurrence included local recurrence in 0 (0.0%) patients and regional recurrence in two (2.3%) patients. Distant metastasis was observed in 18 patients (20.5%). The five-year OS, RFFS, DMFS, and PFS rates were 84.1%, 95.6%, 75.3%, and 75.7%, respectively (Figure 3).

Clinical characteristics of the two patients with regional failure are summarized in Table 4.

Table 4
Details of patients with regional failure

Primary site	Histology	Stage	Surgery type	Failure site	Patterns of failure	Isodose (Gy)	Disease-free time, m
Parotid gland	SCC	T4bN2M0	Total parotidectomy	Ipsilateral level	PCTV2/50	55.29	62
Submandibular gland	SCC	T2N2M0	Submandibular gland excision	Ipsilateral level II	PCTV2/45	54.77	13

Abbreviations: SCC = squamous cell carcinoma

Supplementary Table 1. Comparison of tumor volume before and after IC

The pre-RT MRI showed an insignificantly enlarged lymph node that did not meet the diagnostic criteria in both cases, which were contoured in CTV2 (Figure 4–5).

Treatment Toxicity

Thirty-one patients who received surgery experienced peripheral facial paralysis. The relationship between facial paralysis and SGC subtypes is shown in Figure 6. LECs with facial paralysis accounted for 7/12 patients (58.3%), and other pathological types accounted for 19/63 patients (30.2%). Eight patients without surgery had an intact facial nerve and a normal appearance without reconstruction. In addition, Case 2 was a 33-year-old man who was admitted with a slowly growing mass in the left periauricular region and facial paresis. Six months after definitive radiotherapy, the patient's facial nerve function was fully recovered.

During IC (N=6), only one patient developed Grade 3 leukopenia. CCRT (N=70) induced several severe toxic effects, such as Grade 3 dermatitis (2/70, 2.8%), Grade 3 mucositis (5/70, 7.1%), Grade 3 xerostomia (3/70, 4.3%), and Grades 3–4 leukopenia (10/70, 14.3%). None of the patients experienced cholesteatoma otitis media, trismus, skin ulceration, mandibular osteoradionecrosis, or radiation encephalopathy.

Discussion

Histological classification of SGCs is very demanding and 24 subtypes have been specified according to the World Health Organization classification of malignant salivary gland tumors [23]. In 666 patients with SGCs in a study performed in the Netherlands, for which the pathology results were revised, adenoid cystic carcinoma (27%) was the most frequently diagnosed, followed by mucoepidermoid carcinoma (16%) and acinic cell carcinoma (14%) [24]. No satisfactory chemoradiotherapy method for the above tumor subtypes has been reported, while surgery was considered to be a more effective treatment [5][25]. High local failure rates of approximately 40% for parotid and 60% for submandibular tumors were observed with surgery alone [26]. Patients with advanced-stage disease or high-risk factors were recommended for postoperative radiotherapy [5][25]. IMRT has become the standard technique for SGC radiotherapy, enhancing local control by 80–95% [18][27][28][29]. However, surgery is likely to cause permanent damage to facial nerve function in addition to disfigurement, which could affect the patients' quality of life and self-confidence. Facial paralysis accounted for 31/80 patients (35.2%) in the present study, which is similar to a previous report [6]. In addition, LEC with facial paralysis accounted for 7/12 patients (58.3%), suggesting that LECs often invade the facial nerve due to a high malignancy degree.

LEC has distinct racial and regional characteristics and is well known to occur in a limited number of patients in the localized regions of Southwest Asia, southern parts of China, and the Arctic Circle [30][31]. In 235 patients with SGCs in a study performed in China, LECs were diagnosed in 21.2% of the cohort, which is a much higher rate than the reported average incidence of this disease in the western world [32]. Results of the present study are similar to this previous report (21/88, 23.9%). LEC is a undifferentiated carcinoma, which lacks obvious cell differentiation [7]. And LECs have similarities to NPCs in histological appearance, relationship with Epstein-Barr virus and race, and response to treatment [33][34][35]. Chemoradiotherapy is considered to be the first choice of treatment for NPCs. According to prior literature, IC plus CCRT in locoregionally advanced NPC showed a remarkable 5-year PFS (77.4%), OS (85.6%), DMFS (88.0%), and locoregional failure-free survival (90.7%). LEC is a rare malignant tumor that is typically treated with surgery according to previous recommendations. Although few clinical trials have been designed to investigate the efficacy of systemic therapy because of the rarity of the disease, some scholars have suggested that chemotherapy and radiotherapy may be of benefit as well. Praveen et al. have suggested that systemic therapy was a reasonable approach for patients who presented with regional adenopathy because they have a relatively high rate of distant metastasis [36]. There are also few chemotherapy regimens available for LEC treatment [37][38][39]. The present study reviewed the literature concerning LEC in the salivary gland and found two reports of patients treated without surgery. Kaidar-Person et al. have reported a case of LEC in the parotid gland that was effectively treated with a single cycle of chemotherapy followed by radiotherapy, with no evidence of disease 4 years after treatment [40]. Maeda et al. have reported a case of LEC in the parotid gland that was effectively treated with CCRT, with no evidence of disease 5 years after treatment [41].

The present study included 21 LEC cases. Influenced by the NCCN guidelines, surgical cases accounted for 15/21 patients (71.4%). Only six patients with LECs and two patients with low differentiated squamous cell carcinomas received definitive chemoradiotherapy. CR was observed in these eight cases, and all of these patients had an intact facial nerve. Consequently, to avoid facial nerve injury, chemoradiotherapy is a better choice for SGCs with poor differentiation, especially LECs.

There is still confusion concerning the optimal radiation target volume for SGCs. As reported previously, the present study relied on surgical principles to determine the IMRT target volume [16]. The 5-year OS, RFFS, DMFS, and PFS were 84.1%, 95.6%, 75.3%, and 75.7%, respectively. No patient developed local recurrence, and the main cause of failure within the study cohort was distant metastasis, which suggested that the method was reasonable and worthy of further research.

The present study included 14 patients with recurrent SGCs after primary surgery. In general, the first treatment plays a major role in cancer. But perhaps because of the special anatomic location of the salivary glands, secondary operation plus postoperative radiotherapy for recurrent SGCs also showed good clinical outcomes. Consequently, patients with recurrent SGCs are expected to strive for radical treatment.

The pre-RT MRI showed an insignificantly enlarged lymph node that did not meet the diagnostic criteria for both regional failures, which were contoured in CTV2 (Figure 4–5). According to a previous report, high rates of implicit metastasis of approximately 12–45% were observed for lymph nodes in SGCs cases, suggesting that it is very important in clinical practice to determine whether the lymph nodes have been spared or not [42][43]. However, the optimal treatment for risky lymph nodes that do not meet the diagnostic criteria remains to be determined. Guidelines from the NCCN recommend prescription doses of 44–50 Gy and 54–63 Gy for low and intermediate risk sites of suspected subclinical spread, respectively [5]. In addition, recurrence observed in a previous study occurred in a cervical lymph node that was not significantly enlarged, but was probably involved, and received a radiation dose of about 64 Gy [44]. Consequently, to control the more than microscopic disease, a dose of 63-65 Gy has been irradiated for the risky lymph nodes in the following treatment.

The present study has some limitations. First, it was a retrospective study from a single center, and further prospective multicenter studies are needed. Second, patients without surgery received lesion site fine needle aspiration biopsy in our study. According to previous reports, fine needle aspiration biopsy showed a sensitivity and a specificity of 41.7–92.8% and 93.9–98.5%, respectively [45][46][47]. Whether intraoperative frozen sections should be performed to obtain more pathological information is need to be studied further.

Conclusions

LECs may be sensitive to chemoradiotherapy, which may achieve a radical effect and avoid unnecessary surgical injury. IC combined with CCRT is expected to become a new treatment strategy for advanced LECs. The IMRT target volume delineation according to the surgical principles may be a more promising method with good clinical efficacy that is worthy of further study.

Abbreviations

IMRT: intensity-Modulated Radiotherapy, SGC: major salivary gland carcinoma, LEC: lymphoepithelial carcinoma, IC: induction chemotherapy, CCRT: concurrent chemoradiotherapy, NCCN: National Comprehensive Cancer Network, NPC: nasopharyngeal carcinoma, AJCC: American Joint Committee on Cancer, CT: computed tomography, MRI: magnetic resonance imaging, TPF: taxanes, cisplatin, and fluorouracil, GTVp/nd: gross tumor volume of primary site/regional lymph node, CTV1: medium risk clinical tumor volume, CTV2: low risk clinical tumor volume, CTV-HD: high-risk clinical tumor volume, PTV: planning target volumes, OS: overall survival, RFFS: regional failure-free survival, DMFS: distant metastasis-free survival, PFS: progression-free survival, CR: complete response, PR: partial response

Declarations

Ethics approval and consent to participate: This study was approved by the Medical Ethics Committee of Affiliated Hospital of Sun Yat-sen University Cancer Center, and the need for written informed consent was waived.

Consent for publication: Not applicable.

Availability of supporting data and materials: All data generated or analyzed during this study are included in this published article.

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Authors' Contributions: ZQ YS: conception and design; ZQ WC FL SL XL: data collection, statistical analysis; ZQ ZW: manuscript preparation; ZW LW DX: manuscript editing; YT YS: quality control of data and manuscript review; MW JH: radiation therapy planning.

All authors read and approved the final manuscript.

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Supplementary Table

Supplementary Table 1. Comparison of tumor volume before and after IC

	GTV-PRE (cm^3)	GTV-POST (cm^3)	GTV shrinkage	GTVnd-PRE (cm^3)	GTVnd-POST (cm^3)	GTVnd shrinkage
Case1	174.879	74.871	57.2%	26.961	6.072	77.5%
Case2	36.369	18.744	48.5%	22.659	9.741	57.0%
Case3	140.092	71.627	49.2%	30.102	11.940	60.3%
Case4	99.72	46.027	46.4%	22.707	6.918	69.5%
Case5	34.833	21.741	37.6%	8.913	2.925	67.2%
Case6	129.972	52.812	59.4%	27.669	8.940	67.7%

Abbreviations: GTV-PRE = gross tumor volume before induction chemotherapy; GTV-POST = gross tumor volume after induction chemotherapy; GTVnd-PRE = gross tumor volume of regional lymph node before induction chemotherapy; GTVnd-POST = gross tumor volume of regional lymph node after induction chemotherapy

Supplementary Table 2. AJCC 8th stage distribution of 88 patients

	Patients (N=88)	Definitive IMRT (N=8)	Postoperative IMRT (N=80)
T Classification (N=66)			
T1	10	2	8
T2	22	0	22
T3	13	0	13
T4	21	6	15
N Classification (N=66)			
N0	15	2	13
N1	14	0	14
N2	30	4	26
N3	7	2	5
Not Available*	22	0	22

*In total of 22 patients received surgery in another center and their preoperative CT could not be found.

Figures

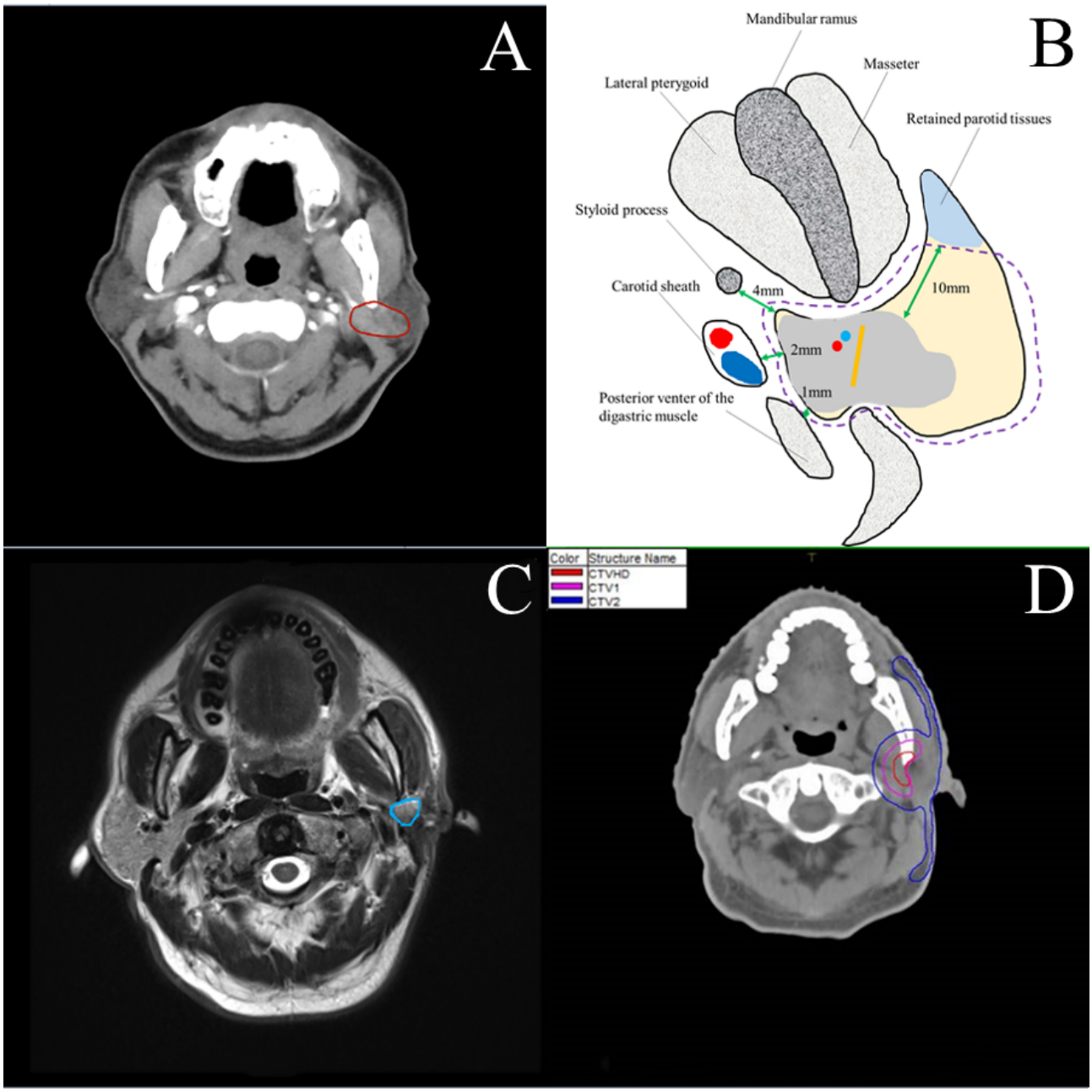

Figure 1

Target volume delineation of postoperative radiotherapy for salivary gland cancer patients. (A) Preoperative CT showed that the tumor (redline) crossed the deep lobe and the isthmus of the parotid gland and was adjacent to posterior venter of the digastric muscle, carotid sheath, styloid process and mandibular branch; (B) Surgical records showed that the patient underwent partial parotidectomy and facial nerve dissection. The purple dotted line showed the extent of surgical resection; (C) Postoperative MR showed that the reserved tissues included the retained parotid tissues (blue line), posterior venter of the digastric muscle, carotid sheath, styloid process and mandibular branch. (D) Posterior venter of the digastric muscle, carotid sheath, styloid process and mandibular branch were all less than 5 mm from the primary tumor edge, so they were very likely to be invaded, as delineated in the CTV-HD area. The retained parotid tissues were more than 10 mm away from the primary tumor edge, so they were delineated in the CTV2 area.

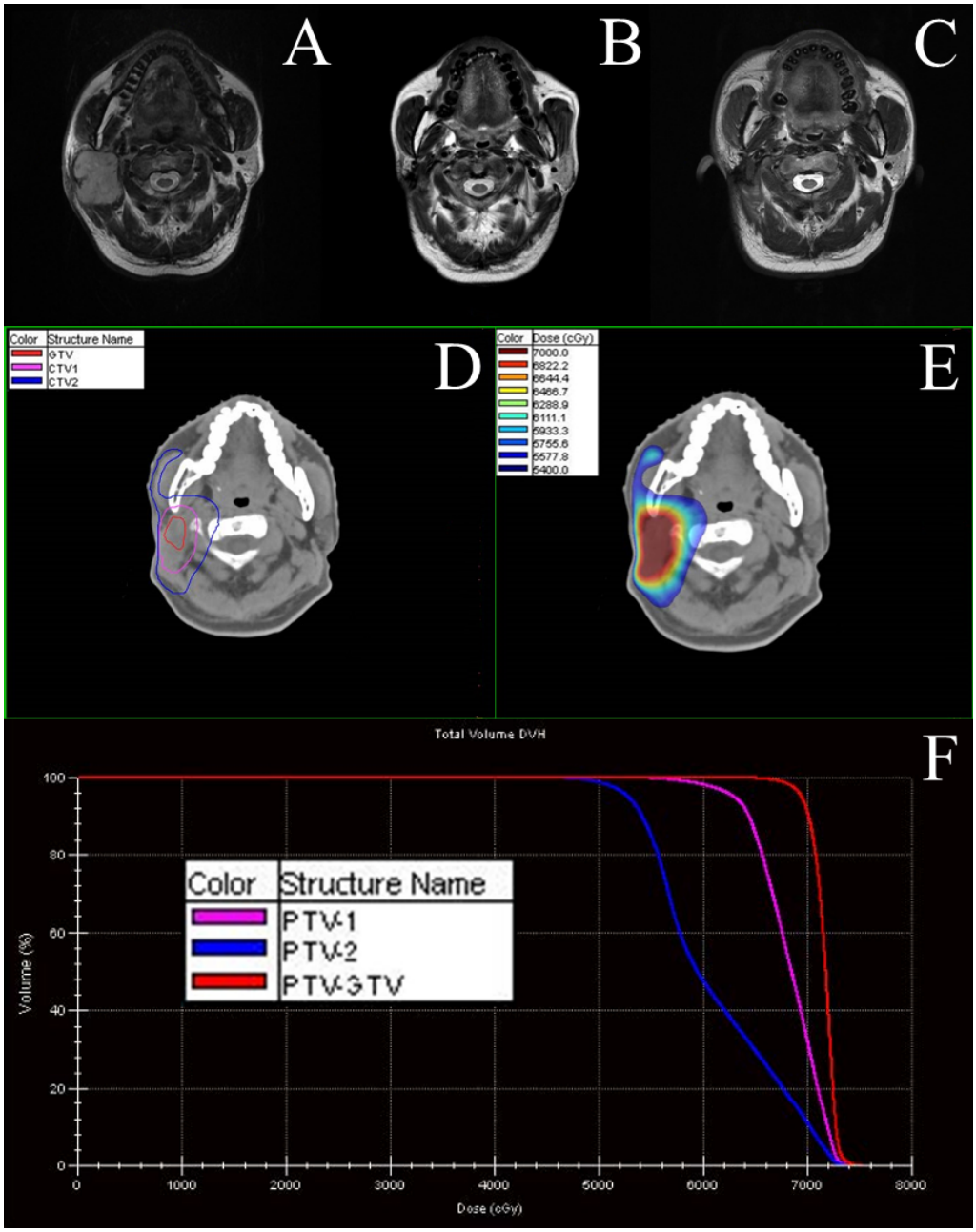

Figure 2

Details of Case 6. (A) Before induction chemotherapy (IC); (B) After IC, partial response was achieved; (C) After chemoradiotherapy, complete response was achieved; (D) Target volume delineation of definitive radiotherapy for Case 6; (E) Dose color wash; (F) DVH.

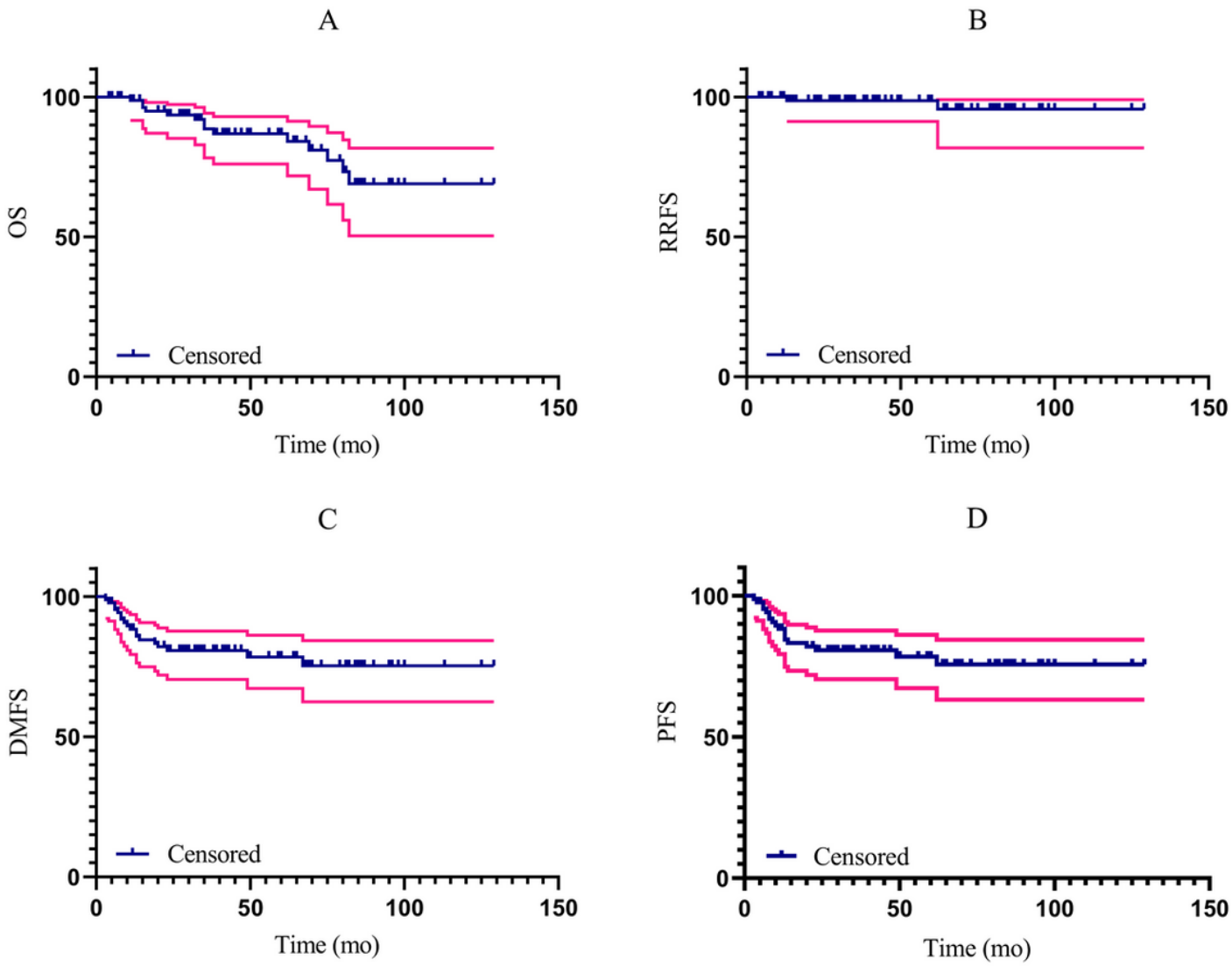

Figure 3

(A) Kaplan-Meier estimates of overall survival (5-year OS, 84.1%; 95% CI, 95.05 to 116.37); (B) Kaplan-Meier estimates of regional failure-free survival (5-year RFFS, 95.6%; 95% CI, 120.55 to 130.34); (C) Kaplan-Meier estimates of distant metastasis-free survival (5-year DMFS, 75.3%; 95% CI, 91.63 to 113.39); (D) Kaplan-Meier estimates of progression-free survival (5-year PFS, 75.7%; 95% CI, 91.66 to 113.39).

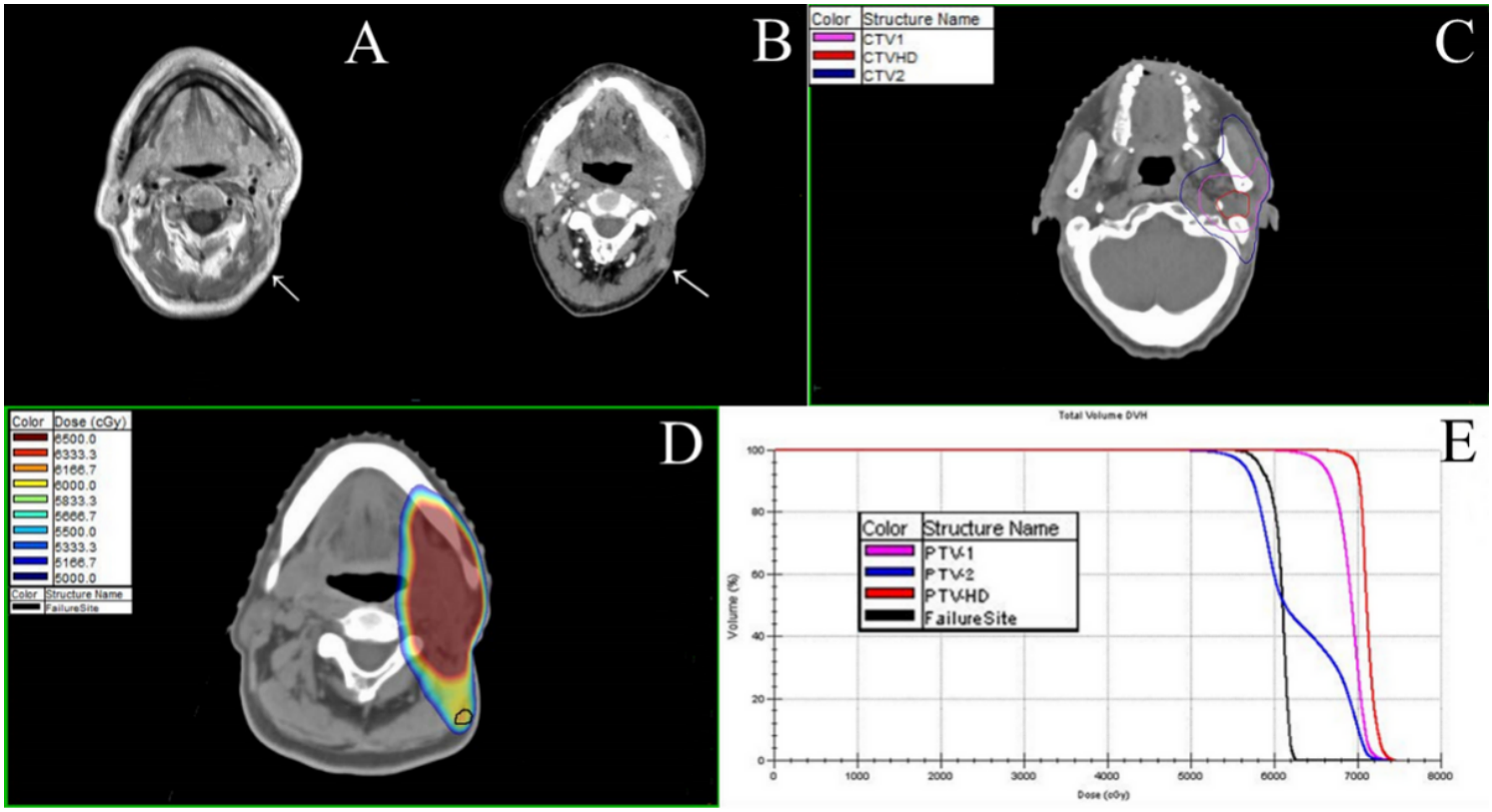

Figure 4

(A) Postoperative MR showed a lymph node measuring 6 mm; (B) The patient complained of a palpable node after 5 years, and regional recurrence was finally diagnosed; (C) Target volume delineation of postoperative radiotherapy; (E) Dose color wash; (F) DVH.

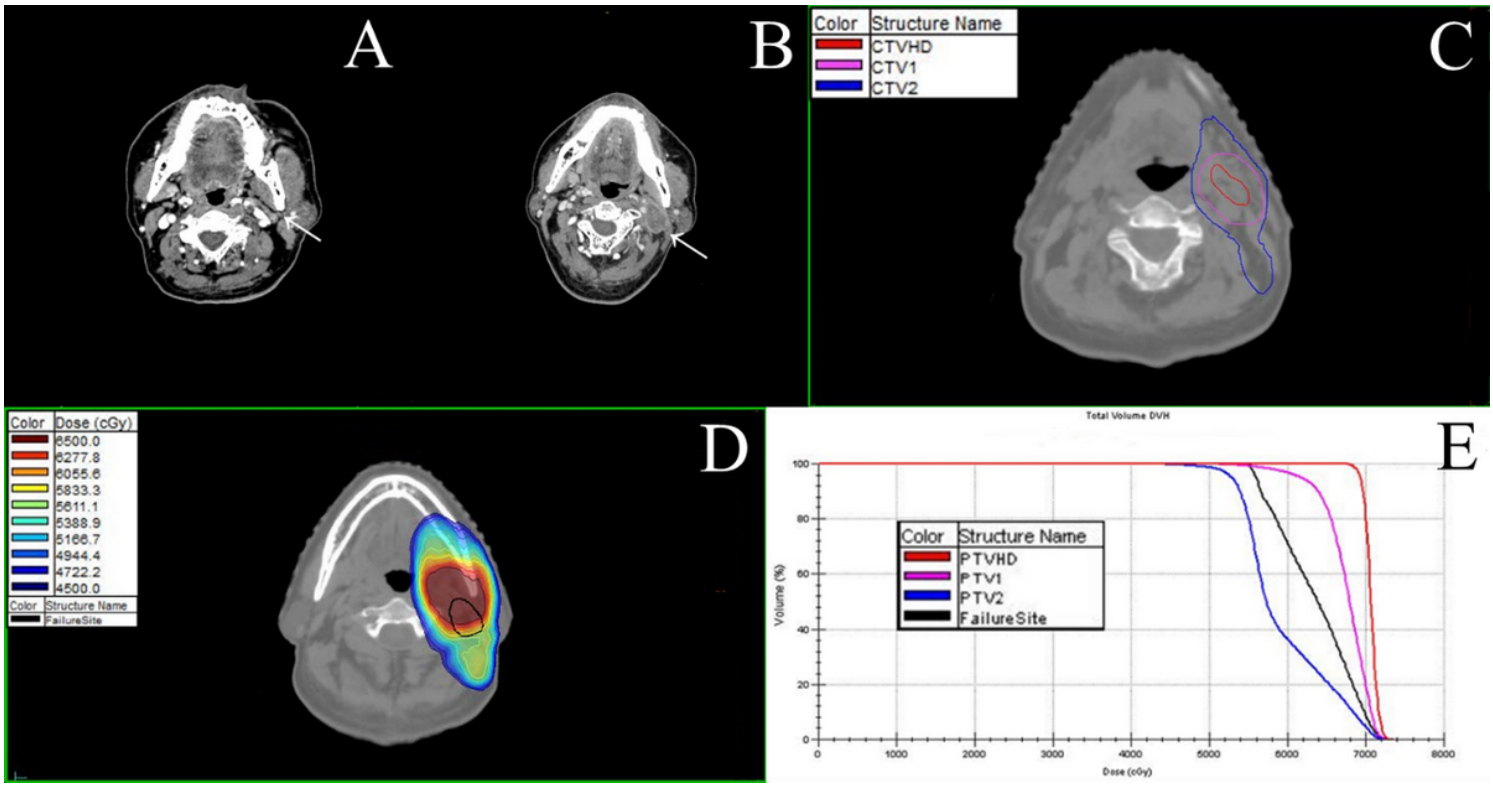

Figure 5

(A) Postoperative CT showed a lymph node measuring 4 mm; (B) Regional recurrence was finally diagnosed by CT after 2 years; (C) Target volume delineation of postoperative radiotherapy; (E) Dose color wash; (F) DVH.

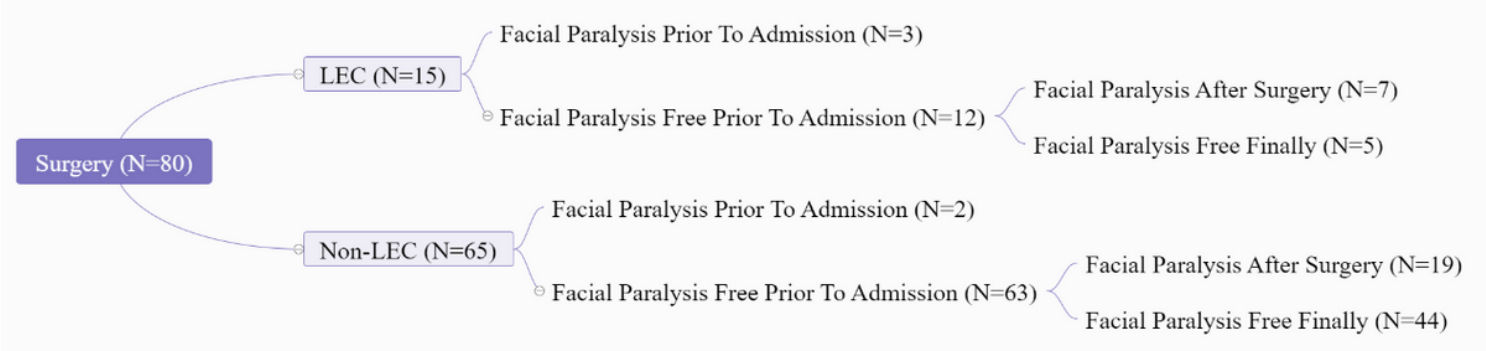

Figure 6

The relationship between facial paralysis and SGCs subtypes. Abbreviations: LEC = lymphoepithelial carcinoma

Supplementary Files

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- SupplementaryFigure1.png