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Scientific Article

Refining Target Volume Coverage After Parotidectomy for Cutaneous Squamous Cell Carcinoma: Omission of the Cervical Neck From the Radiation Field

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Purpose: For patients without pathologic evidence of cervical disease after neck dissection for cutaneous squamous cell carcinoma involving the parotid region, inclusion of the ipsilateral cervical neck in the postparotidectomy radiation volume is routinely performed. We report our experience with selective avoidance of the ipsilateral neck for patients undergoing postoperative radiation to the parotid bed.

Methods and Materials: From January 2014 to December 2023, a total of 30 consecutive patients underwent postoperative radiation after parotidectomy for cutaneous squamous cell carcinoma involving the parotid area. All patients had previously had a neck dissection confirming pathologic N0 disease. Treatment was delivered using intensity modulated radiation therapy to a median dose of 60 Gy (range, 56-66 Gy). The radiation target volumes included the parotid bed only, with deliberate avoidance of the ipsilateral cervical neck. The median pathologic tumor size of the parotid tumor was 3.3 cm (range, 0.2-9.4 cm). Final pathologic evaluation showed positive microscopic margins in 8 patients (27%), perineural invasion in 17 patients (57%), and facial nerve involvement in 6 patients (20%).

Results: There were no isolated nodal failures. One patient developed an ipsilateral neck recurrence approximately 8 months after completion of radiation therapy. This occurred 2 months subsequent to the development of local recurrence. The 5-year actuarial rates of local (parotid) control, neck control, and overall survival were 87%, 97%, and 76%, respectively.

Conclusions: Omission of the ipsilateral neck from the parotid volume does not compromise disease control for pathologically N0 patients undergoing postoperative radiation for cutaneous squamous cell carcinoma involving the parotid region. Practical implications are discussed.

Introduction

Surgical resection with postoperative radiation therapy constitutes the standard of care for cutaneous squamous cell carcinomas involving the parotid region of the head and neck.[1-3] Regardless of whether these represent primary

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lesions arising from the temporal skin surface or alternatively periparotid metastasis from cutaneous cancers arising from other sites, parotidectomy followed by radiation to the operative bed is routinely recommended. Although the use of elective neck dissection to address potential occult disease is more variable, it is often included as part of the surgical procedure for clinically node-negative (N0) patients.[4] In the postoperative setting, inclusion of the ipsilateral cervical neck in the postparotidectomy radiation volume is routinely performed. For those without pathologic evidence of cervical neck disease after surgery, however, the utility of ipsilateral elective neck irradiation (ENI) is questionable. The purpose of this study was to therefore report our single-institutional experience with the omission of ENI for patients undergoing postoperative radiation to the parotid bed for cutaneous squamous cell carcinoma.

Methods and Materials

Patients

This study was approved by our institution's committee on human research. The medical records of all patients treated with radiation therapy for squamous cell carcinoma involving the parotid region from primary skin cancer of the head and neck from January 2014 to December 2022 were reviewed. These included all patients with pathologically confirmed metastasis involving the intrafascial and intraparenchymal parotid lymph nodes as well as the extrafascial preauricular lymph nodes. No patient had evidence of distant metastasis. All patients had axial imaging with either computed tomography (CT) or magnetic resonance imaging at diagnosis. Positron emission tomography was performed in all patients.

The initial review identified 85 consecutive patients with cutaneous squamous cell carcinoma involving the parotid area lymph nodes, clinically N0 necks, and no evidence of disease elsewhere. Among these, a total of 70 patients were treated with radiation after parotidectomy with ipsilateral neck dissection showing no pathologic cervical lymph node disease. Forty of these patients received postoperative radiation to the parotid bed and ipsilateral cervical neck. The 30 patients who underwent radiation therapy to the parotid bed without elective neck irradiation comprised the study population. The median age was 69 years (range, 49-96 years). Twelve patients (40%) had a previous history of cutaneous squamous cell carcinoma of the face.

Treatment

All patients were treated with initial surgery consisting of gross tumor resection of the parotid area tumor. The extent of surgery was at the discretion of the surgeon but generally based on the extent and location of disease. Sixteen (53%) and fourteen (47%) patients had total and superficial parotidectomy, respectively. Sacrifice of the facial nerve was not performed unless grossly involved by tumor intraoperatively or radiologically. Nearly all patients had a selective (supraomohyoid) neck dissection (26 patients), with the remaining having a modified radical neck dissection (4 patients). The median number of lymph nodes removed was 12 (range, 5-35). Radiation therapy was delivered to the ipsilateral parotid area using intensity modulated radiation therapy (IMRT) techniques with megavoltage equipment. The beam arrangements varied at the discretion of the treating physician but generally was designed to cover the parotid region with 2- to 3-cm margins. Clinical target volume delineation considered the preoperative volume of disease and generally included the anatomic region defined by the masseter muscle, mastoid tip, zygomatic arch, parapharyngeal space, and posterior belly of the digastric muscle. In cases of clinical or pathologic involvement of the facial nerve, the stylomastoid foramen was encompassed in the target volume. A circumferential expansion of 3 mm was placed on the clinical target volume to generate a planning target volume. None of the patients received ENI. Treatment was by continuous-course radiation with once-daily treatment using conventional fractionation and daily volumetric image guidance. Median radiation dose for all patients was 60 Gy (range, 56-66 Gy). The goal was to deliver the prescribed dose to 95% of the planning target volume. Twelve patients (40%) received concurrent cisplatin chemotherapy. Figure 1 illustrates a representative IMRT plan for a patient undergoing postoperative radiation to the parotid region. Organs at risk delineated included the spinal cord, brain stem, ocular structures, pharyngeal constrictor muscles, oral cavity, contralateral parotid gland, submandibular glands, lips, temporomandibular joints, cochlea, larynx, true vocal cords, cricopharyngeal inlet, cervical esophagus, and mandible. Table 1 outlines the dosimetric constraints typically used and the prioritization for IMRT planning.

Statistical analysis

The primary endpoint measured was regional (neck) control, which was attained if there was no evidence of disease recurrence based on clinical and radiographic findings. The secondary endpoints included local (parotid) control and overall survival. All events were measured from the last day of radiation therapy. The median follow-up was 37 months (range, 6-73 months). Follow-up was reported to the date last seen in the clinic. Actuarial rates were calculated using the Kaplan-Meier method with comparisons among groups performed using 2-sided log-rank tests.[5]

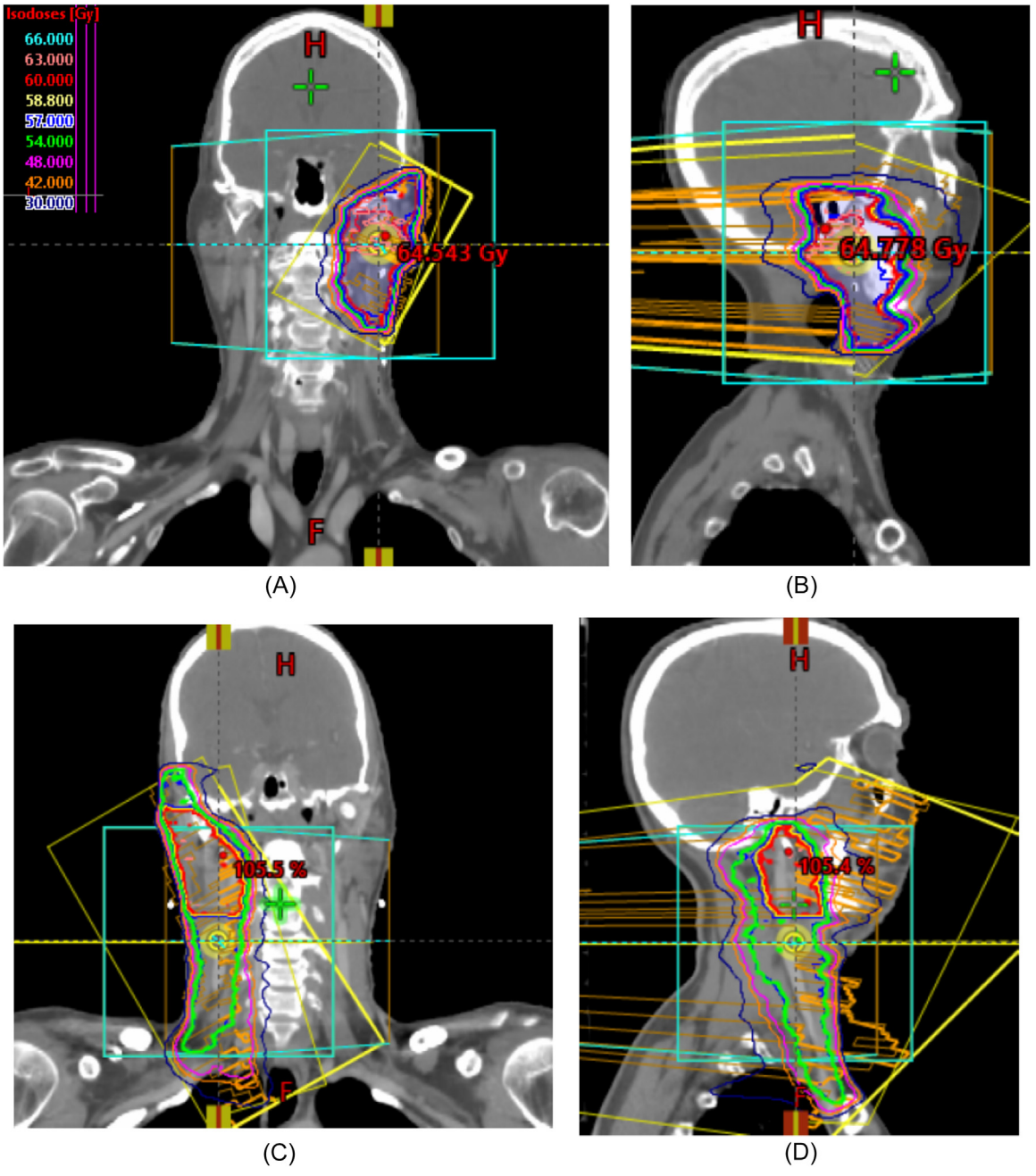

Figure 1 Radiation treatment plan, illustrated in the (A) coronal and (B) sagittal views for a patient who is status post-right-parotidectomy for a single 3-cm parotid metastasis from primary cutaneous squamous cell carcinoma. Ipsilateral neck dissection revealed 15 lymph nodes positive for disease. The patient was treated to 60 Gy in 30 fractions to the right parotid bed and is clinically without evidence of disease at approximately 50 months after completion of care. In comparison, the radiation treatment plan, illustrated in the (C) coronal and (D) sagittal views for a patient who is similarly status post-right-parotidectomy for a single 3-cm parotid metastasis from primary cutaneous squamous cell carcinoma and received 60 Gy to the right parotid bed and 54 Gy to the elective ipsilateral neck.

Results

Disease characteristics

The median pathologic tumor size of the parotid tumor was 3.3 cm (range, 0.2-9.4 cm); 5 patients had multifocal disease (17%). Final pathologic evaluation showed positive microscopic margins in 8 patients (27%), perineural invasion in 17 patients (57%), and facial nerve involvement in 6 patients (20%). Seven patients had bony invasion (23%). Table 2 outlines patient and disease characteristics. The P stages were P1 (5 patients), P2 (15

Table 1 Clinical and disease characteristics

Characteristic	No.	%
Age, y	3	10
<50	5	17
50-60	8	27
60-70	14	47
>70		
Sex		
Male	20	67
Female	10	33
Location		
Superficial lobe	23	77
Deep lobe	7	23
Surgical margins		
Positive	8	27
Negative	22	73
Multifocality		
No	25	83
Yes	5	17
Perineural invasion		
No	13	43
Yes	17	57
Lymphovascular invasion		
No	21	70
Yes	9	30
Facial nerve involvement		
No	24	80
Yes	6	20
Bony invasion		
No	23	77
Yes	7	23
Soft tissue invasion		
No	19	63
Yes	11	37
P stage		
P0	5	17
P1	15	50
P2	10	33

patients), and P3 (10 patients) using criteria classified by O'Brien et al.[6]

Local control

Among the 30 patients treated using surgery and postoperative radiation therapy, 4 patients experienced local recurrence at a median time of 9 months (range, 6-13 months), resulting in 3- and 5-year local (parotid) control rates of 87% and 87%, respectively, as shown in Fig. 2. Two of these local recurrences were isolated first events, and the remaining 2 recurred concurrently with the development of lung metastasis. None of the disease characteristics analyzed including tumor size, margin status, perineural invasion, facial nerve involvement, or bone invasion predicted for local survival ($P > .05$ for all).

Regional control

No patient developed an isolated neck recurrence. One patient, who had undergone total parotidectomy, lateral temporal bone resection, and ipsilateral neck dissection (with 0 of 15 lymph nodes removed from nodal stations I-IV) for a 6-cm tumor with invasion of the skull base, facial nerve, and stylomastoid foramen with positive microscopic margins, developed ipsilateral neck recurrence at level II and III approximately 8 months after completion of radiation therapy. This occurred 2 months after the development of local recurrence. Dosimetric analysis determined that the amount of radiation delivered to the foci of recurrences in the neck was negligible. This patient was found to have lung metastasis 1 month later. The prior neck dissection for this patient had removed a total of 8 lymph nodes. As shown in Fig. 3, the 3- and 5-year actuarial rates of regional (neck) control was 97% and 97%, respectively.

Overall survival

Twenty-three patients were alive at the time of this analysis. As shown in Fig. 4, the overall survival rate for the entire patient population at 3 and 5 years was 86% and 76%, respectively. None of the disease characteristics analyzed including tumor size, margin status, perineural invasion, facial nerve involvement, or bone invasion predicted for overall survival ($P > .05$ for all). There were no treatment-related deaths.

Toxicity

The most common acute reaction was related to skin toxicity, with 30 of 30 patients (100%) experiencing erythema with or without desquamation at the treated site. There were no reported cases of skin ulceration or necrosis. Acute dermal changes were managed successfully using conservative care and resolved after completion of treatment in all cases. The incidence of acute grade 3 or greater toxicity was 0. Eight patients (27%) reported mild odynophagia, but none required the use of prescription analgesics including opioids. Fifteen patients (50%)

Table 2 General dose constraints for intensity modulated radiation therapy planning (postoperative parotid bed)

Structure	Recommended constraint	Priority
Spinal cord	Max < 42 Gy	High
Brain stem	Max < 50 Gy	High
Temporal brain	Max < 60 Gy	High
Optic chiasm	Max < 45 Gy	High
Optic nerve	Max < 50 Gy	High
Cochlea	Mean < 45 Gy	Intermediate*
Parotid gland (contralateral)	Mean < 8 Gy or max < 10 Gy	Intermediate
Submandibular gland (contralateral)	Mean < 10 Gy or max < 12 Gy	Intermediate
Submandibular gland (ipsilateral)	Mean < 39 Gy	Intermediate
Larynx	Mean < 15 Gy	Intermediate
True vocal cords	Mean < 10 Gy	Intermediate
Oral cavity (minus PTV)	Mean < 15 Gy	Intermediate
Pharynx (uninvolved)	Mean < 20 Gy	Intermediate
Temporo-mandibular joints	Mean < 45 Gy	Low
Lips	Mean < 10 Gy	Low
Mandible	Max < 66 Gy	Low
Cricopharyngeal inlet	Mean < 15 Gy	Low
Cervical esophagus	Mean < 10 Gy	Low

Abbreviations: max = maximum; PTV = planning target volume.
*Exceeding this constraint permissible if constraint otherwise results in undercoverage of PTV.

reported noticeable dysgeusia. However, no patient experienced weight loss exceeding 5% of baseline. All acute symptoms resolved within 3 months of completion of radiation. No patient developed clinically evident hearing loss, chronic otitis media, vestibular dysfunction, or brain necrosis as a result of treatment. Two patients sought physical therapy for lymphedema after treatment, but both had physical symptoms before beginning radiation. There was 1 reported case of osteoradionecrosis involving the temporal bone, which was managed with surgical debridement, antibiotics, and hyperbaric oxygen.

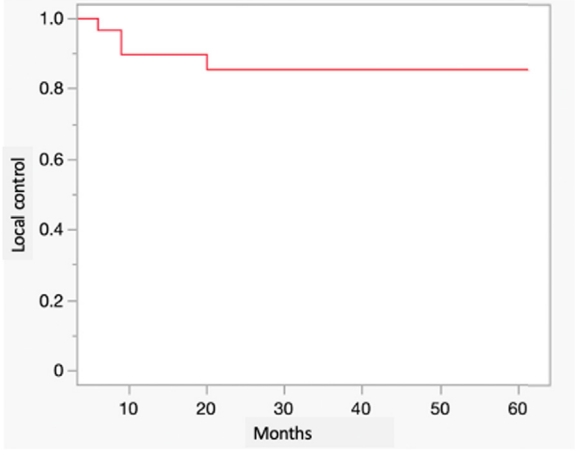

Figure 2 Local (parotid) control of the entire patient population.

Discussion

The results of the present series demonstrate that the selective avoidance of neck radiation is feasible for patients without pathologic evidence of cervical lymph node disease for cutaneous squamous cell carcinoma of the parotid area. Since the ipsilateral neck is traditionally encompassed within the radiation field together with the parotid bed after surgery, our data are thus valuable because it suggests that a modification in practice pattern can be considered. Although a recent practice guideline issued by the American Society of Radiation Oncology addressed the issue of elective nodal irradiation by conditionally recommending this in high-risk cases where targeting of the primary site is believed to result in "overlap of the adjacent nodal basin," it did not specifically state whether this was applicable in the postlymphadenectomy setting.[7]

Notably, the strategy of eliminating elective nodal irradiation in this setting did not compromise disease control for patients undergoing postoperative radiation. As importantly, this approach was exceptionally well-tolerated with minimal reports of toxicity. These results are relevant because postoperative radiation to the parotid

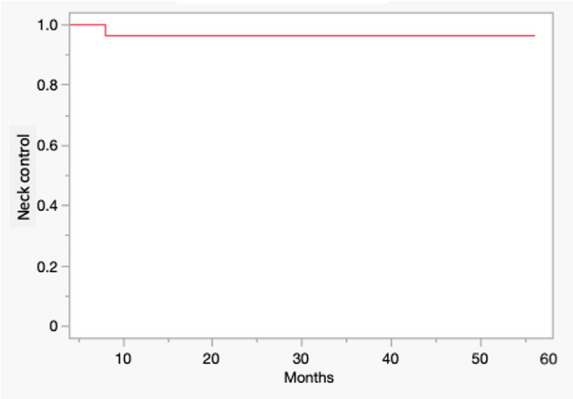

Figure 3 Regional (neck) control of the entire patient population.

bed has been shown to dramatically decrease the odds of local recurrence and is routinely recommended.[8]

For patients treated by surgery and postoperative radiation for parotid tumors, the toxicity is largely dependent on the volume of tissue irradiated.[9] For those receiving radiation to the parotid bed and ipsilateral neck, commonly reported side effects include dysphagia, mucositis, and dysgeusia. Due to exposure of radiation to such anatomic structures as the oral cavity, pharyngeal constrictor muscles, and larynx, among others, the treatment can be taxing on quality of life both in the acute and late settings.

Lymphedema is another well-described adverse effect of lymphatic radiation, particularly after nodal dissection.[10] Although it can be difficult to quantify the severity of lymphedema in the neck, studies have shown that the incidence is related the volume of tissue in the neck exposed to radiation.[11] Others have shown that lymphedema in conjunction with fibrosis can affect cervical range of motion and impair shoulder function thereby detrimentally affecting quality of life.[12,13]

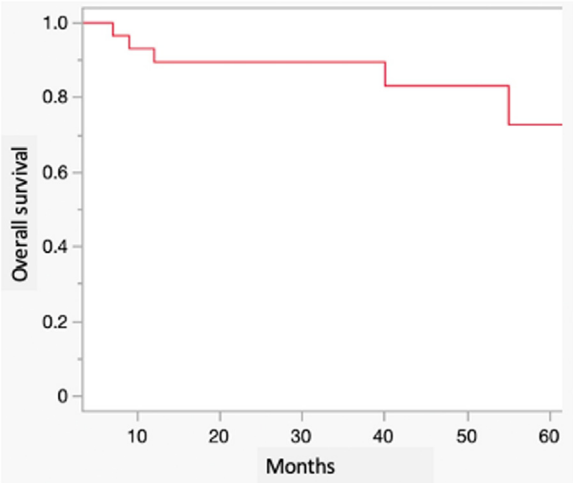

Figure 4 Overall survival of the entire patient population.

An increase in the incidence of stroke has also been shown to be observed in patients receiving radiation to the neck.[14] Radiation-induced toxicities to the carotid artery such as atherosclerosis, arterial stiffness, and arterioradionecrosis have all been described and are generally related to the dose to which areas of the large vessel are exposed.[15] Given that the dose to the carotid artery is dramatically reduced with omission of the ipsilateral neck from the postparotidectomy radiation target volume, the potential benefits may be significant. Although serious vascular events are generally thought to be multifactorial and cannot be singularly pinpointed on radiation, the lowering of any risk might be particularly relevant with the relatively elderly patient population who present with this disease.

It should be highlighted that the side effect profile described in the present series was relatively mild. Very few patients complained of severe toxicity and any observed grade 3 adverse events were likely due to exposure to normal structures near the parotid region such as the cochlea. With respect to swallowing, all patients were able to maintain their normal diet, and the incidence of gastrostomy-tube placement was 0. In the late setting, the incidence of soft tissue fibrosis, a commonly reported side effect for patients receiving cervical lymph node irradiation, was 0.

It is notable that the incidence of neck recurrence was low, even for patients with adverse risk features such as larger tumors, perineural invasion, positive margins, and bone involvement. This seems to suggest that surgery is generally adequate at clearing nodal disease in the neck for this disease. However, the fact that the 1 recurrence occurred in a patient with less than the median number of lymph nodes removed suggests that the likelihood of an adequate dissection decreases with the number of lymph node sampled. This is consistent with data from other sites in which the adequacy of a lymph node dissection is commonly used to guide decisions on subsequent radiation.[16-18] Although the relatively small sample size in the present series of patients who skipped neck irradiation precluded subset analysis to identify those at highest risk for recurrence, we nevertheless urge caution in applying this approach when concerns exist regarding the adequacy of neck dissection. Another consideration is that even when the ipsilateral neck is specifically excluded from the postoperative radiation volume, a measurable amount of dose still inadvertently encompasses the level II nodal region due to the proximity of the parotid tail to the parapharyngeal space.[19]

The accurate staging of disease both preoperatively and pathologically is paramount to the success of this strategy. It must be recognized that all patients were staged before surgery with CT and positron emission tomography. This is important to ensure that patients were clinically N0 and that appropriate treatment was used to address any suspicious deposits in the cervical neck. Lastly, the accuracy of a negative pathologic specimen may also depend on the scrutiny and meticulousness of the specimen processing. Standardized methods have been described which

make the likelihood of sampling error and/or false negatives low.[20] Given the potential consequences herein, utmost attention should be focused on accurate pathologic interpretation.

Although other studies have shown that the strategy of omitting radiation to a dissected neck is feasible for primary mucosal lesions of the head and neck, the present study is the first to analyze this issue for cutaneous squamous cell carcinoma involving the parotid area. In a single-arm phase 2 trial in which postoperative radiation was eliminated to the node-negative neck after surgical dissection for primary squamous cell cancers of the mucosal axis, only 2 of 73 patients experienced treatment failure in the pN0 unirradiated neck resulting in a 5-year unirradiated neck control of 94%.[21] Notably, quality of life outcomes did not significantly differ at various points in follow up compared with baseline. Similar to the present series, this was a single-center academic experience which might raise questions as to the applicability of this practice to the larger community.

The role of postoperative concurrent chemotherapy is controversial for patients with cutaneous squamous cell carcinoma and is largely extrapolated from its use in the treatment of mucosal head and neck cancers where it is generally recommended in the setting of positive margins and/or extracapsular soft tissue extension. Although the intent of chemotherapy is to potentiate the effects of radiation, the data supporting chemoradiation is limited to relatively small, single-institutional experiences.[22,23] More recently, the Trans-Tasman Radiation Oncology Group conducted a phase 3 study randomizing patients with high-risk cutaneous squamous cell carcinoma to postoperative radiation with or without concurrent carboplatin and showed no difference in outcome between the 2 arms.[24] The 2- and 5-year freedom from local-regional relapse rates were 88% and 83%, respectively, for radiation alone and 89% and 87%, respectively, for chemoradiation. Notably, these study results were not published until halfway through the years included in our analysis, which might possibly explain why 40% of our population received chemotherapy.

Conclusion

The avoidance of elective neck irradiation to the ipsilateral pathologic N0 did not compromise outcomes and seemingly improved tolerability for patients undergoing postoperative radiation for squamous cell carcinoma involving the parotid region. Further studies are warranted to validate the findings in this report.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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