

**Ipsilateral Radiation for Squamous Cell Carcinoma of the Tonsil
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
1. Mendenhall WM, Morris CG, Amdur RJ, et al. Definitive radiotherapy for tonsillar squamous cell carcinoma. <i>Am J Clin Oncol</i> 2006; 29(3):290-297.	3a	503 total patients 198 patients underwent a planned neck dissection and 57 patients received induction	To update experience with definitive RT for carcinoma of the tonsillar area.	<ul style="list-style-type: none"> • The 5-year local control rates were as follows: T1, 88%; T2, 84%; T3, 78%; and T4, 61%. • Multivariate analysis revealed that local control was significantly influenced by T stage, primary site, and fractionation. • Local control after RT for early stage cancers was higher for tonsillar fossa/posterior pillar tumors than for those arising from the anterior tonsillar pillar. • The 5-year cause-specific survival rates were as follows: I, 100%; II, 86%; III, 84%; IVA, 73%; and IVB, 46%. • Multivariate analysis revealed that cause-specific survival was significantly influenced by T stage, overall stage, neck dissection, race, and gender. The incidence of severe late complications was 9%. • Based on the data and a review of the literature, definitive RT provides cure rates that are as good as those after surgery, and is associated with a lower rate of severe complications. Patients with lateralized tumors may be safely treated with ipsilateral field arrangements. The limited experience with intensity modulated RT suggests that it is as efficacious as conventional RT. 	2

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2. Perez CA, Patel MM, Chao KS, et al. Carcinoma of the tonsillar fossa: prognostic factors and long-term therapy outcome. <i>Int J Radiat Oncol Biol Phys</i> 1998; 42(5):1077-1084.	3a	384 patients 154 treated with RT alone (55-70 Gy) 144 with preoperative RT (20-40 Gy) 86 with PORT (50-60 Gy)	To identify prognostic parameters and evaluate the therapeutic outcomes for patients with carcinoma of the tonsillar fossa treated with three treatment modalities.	<ul style="list-style-type: none"> • Actuarial 10-year DFS rates were 65% for patients with T1 tumors, 60% for T2, 60% for T3, and 30% for T4 disease. • Patients with no cervical lymphadenopathy or with a small metastatic lymph node (N1) had better DFS (60% and 70%, respectively) at 5 years than those with large or fixed lymph nodes (30%). • Primary tumor recurrence (local, marginal) rates in the T1, T2, and T3 groups were 20%-25% in patients treated with RT and surgery and 31% for those treated with RT alone (difference not statistically significant). • In patients with T4 disease treated with surgery and PORT, the local failure rate was 32% compared with 86% with low-dose preoperative RT and 47% with RT alone (P=0.03). • The overall recurrence rates in the neck were 10% for N0 patients, 25% for N1 and N2, and 35%-40% for patients with N3 cervical lymph nodes, without significant differences among the various treatment groups. The incidence of contralateral neck recurrences was 8% with the various treatment modalities. • On multivariate analysis the only significant factors for local tumor control and DFS were T and N stage (P=0.04-0.001). • Fatal complications were noted in 7/144 (5%) patients treated with preoperative RT and surgery, 2/86 (2%) of those receiving PORT, and 2/154 (1.3%) patients treated with RT alone. • Other moderate or severe nonfatal sequelae were noted in 30% of the patients treated with preoperative RT and surgery, in 53% treated with PORT, and in 19% receiving RT alone. 	2

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3. Levendag P, Nijdam W, Noever I, et al. Brachytherapy versus surgery in carcinoma of tonsillar fossa and/or soft palate: late adverse sequelae and performance status: can we be more selective and obtain better tissue sparing? <i>Int J Radiat Oncol Biol Phys</i> 2004; 59(3):713-724.	3a	190 total patients 104 brachytherapy 86 surgery and PORT	To validate the use of a more selective clinical target volume in conjunction with highly conformal RT techniques to better spare the surrounding normal tissues.	Excellent locoregional control was obtained in T1-T3 tonsillar fossa and/or soft palate tumors. The rate at 10 years was 84% (brachytherapy group) vs 78% (surgery group). However, adverse late side effects were not negligible. In addition to modality-specific side effects (ulcer/trismus), both treatment groups were significantly affected by xerostomia. Only 6 recurrences (4%) were observed in the 149 electively treated contralateral necks, and no relapses were seen in the 29 untreated contralateral necks. Suggested that it is not necessary to treat the contralateral neck, unless the tumor extends beyond the midline of the soft palate (uvula) or beyond the lateral one-third of the ipsilateral base of the tongue. Moreover, with the currently available CT-based neck level definitions, more conformal contours (ie, tighter boundaries) around the clinical target volume can be designed. In this way, critical structures such as the temporomandibular joint and part of the pterygoid muscles can be avoided more easily. Also, when using highly conformal treatment techniques (eg, intensity-modulated RT), one can further reduce the dose to the major salivary glands and oral mucosa. We believe these measures will lead to less trismus and less xerostomia.	2

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4. Murthy AK, Hendrickson FR. Is contralateral neck treatment necessary in early carcinoma of the tonsil? <i>Int J Radiat Oncol Biol Phys</i> 1980; 6(1):91-94.	4	57 total patients	To review the records of patients with carcinoma of the tonsil to determine if contralateral neck treatment is necessary in the early stages.	<ul style="list-style-type: none"> • Among patients with T1 lesions, 1 patient of 9 in whom failure occurred in the primary as well as in the neck was salvaged. • Both of the N0 failures in the neck only were in the ipsilateral treated necks and neither was salvaged. • In only 1 patient with N1 disease did failure occur in the opposite neck, this patient was salvaged with further RT. • In none of the 20 patients with N0 or N1 disease did failure occur in the opposite neck only. • Failure only in the untreated opposite neck is uncommon in patients with early carcinoma of the tonsil. Xerostomia is a distressing complication of radiation when both parotid glands are treated. This can be reduced if radiation is limited to the primary and ipsilateral neck. This would not result in an unacceptable failure rate in the opposite neck. The rare patients who do fail in the opposite neck can be salvaged by further RT or surgery and thus reduce the distressing symptom of xerostomia. 	2

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5. Vergeer MR, Doornaert PA, Jonkman A, et al. Ipsilateral irradiation for oral and oropharyngeal carcinoma treated with primary surgery and postoperative radiotherapy. <i>Int J Radiat Oncol Biol Phys</i> 2010; 78(3):682-688.	3a	123 total patients	To evaluate the contralateral nodal control in postoperative patients with oral and oropharyngeal cancer treated with ipsilateral RT of the neck and primary site. Late radiation-induced morbidity was also evaluated.	<ul style="list-style-type: none"> • The 5-year actuarial contralateral nodal control was 92%. • The number of lymph node metastases was the only significant prognostic factor with regard to contralateral nodal control. • The 5-year contralateral nodal control was 99% in N0 cases, 88% in N1 or N2a cases, and 73% in N2b cases (P=0.008). • Borderline significance (P=0.06) was found for extranodal spread. Successful salvage could be performed in 71% of patients with contralateral metastases. • The prevalence of Grade 2 or higher xerostomia was 2.6% at 5 years. • Selected patients with oral or oropharyngeal carcinoma treated with primary surgery and postoperative ipsilateral RT have a very high contralateral nodal control with a high probability of successful salvage in case of contralateral metastases. However, bilateral RT should be applied in case of multiple lymph node metastases in the ipsilateral neck, particularly in the presence of extranodal spread. The incidence of radiation-induced morbidity is considerably lower as observed after bilateral RT. 	2
6. Bachar GY, Goh C, Goldstein DP, O'Sullivan B, Irish JC. Long-term outcome analysis after surgical salvage for recurrent tonsil carcinoma following radical radiotherapy. <i>Eur Arch Otorhinolaryngol</i> 2010; 267(2):295-301.	4	175 patients	Retrospective review to report the long-term outcomes of salvage surgery following local and/or regional failure of tonsillar carcinoma treated with standard fractionation RT.	5-year OS rate was 23%. The 5-year cause-specific survival was 40%. The probability of death due to disease was higher than the probability of death due to other causes. Both N-classification and T-classification were found to be significant predictors of time to death. Study shows the poor prognosis of recurrent disease. Despite the poor prognosis, 20% of patients will be alive at 5 years and therefore salvage surgery should be considered when possible.	2

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7. Selek U, Garden AS, Morrison WH, El-Naggar AK, Rosenthal DI, Ang KK. Radiation therapy for early-stage carcinoma of the oropharynx. <i>Int J Radiat Oncol Biol Phys</i> 2004; 59(3):743-751.	3a	175 patients	To evaluate the outcomes of RT treatment of patients with stage I and II SCC of the oropharynx and discover adverse prognostic factors that may help select a subgroup of patients for a different management approach.	<ul style="list-style-type: none"> • The median follow-up for all patients was 76 months (range, 2-302 months). • The actuarial 5-year local control, regional control, locoregional control, and DFS rates were 85%, 93%, 81%, and 77%, respectively. • T-stage classification was statistically significant (P=0.03) in univariate analysis for actuarial 5-year locoregional control, 88% for stage I vs 72% for stage II. • The 5- and 10-year disease-specific survival rates were 85% and 79%, respectively, while the actuarial 5- and 10-year OS rates were 70% and 43%, respectively. 51 patients (29%) developed second primary tumors, 86% of which were cancers of the upper aerodigestive tract. Heavy alcohol consumption was associated with both an increased risk of disease recurrence and development of a second cancer of the upper aerodigestive tract. • Patients with early-stage oropharynx cancer have high rates of disease control when treated with radiation. Lymphatic and hematogenous metastases are uncommon. Surgical salvage of disease recurrence is successful in approximately one-third of patients. As the majority of recurrences occur within the first 2 years from treatment, close observation during this time period is important. The development of second primary tumors of the upper aerodigestive tract adversely impacts survival in these patients to as great a degree as the index cancer. 	2

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8. Beeken L, Calman F. A return to "normal eating" after curative treatment for oral cancer. What are the long-term prospects? <i>Eur J Cancer B Oral Oncol</i> 1994; 30B(6):387-392.	4	25 patients interviewed	Retrospective investigation of the incidence of side-effects affecting eating and their effect upon quality of life more than 1 year after treatment, was undertaken to evaluate long-term patient rehabilitation.	<ul style="list-style-type: none"> • 72% of patients required modifications of dietary consistency. Energy and protein intakes decreased with increasing degrees of dietary modification. • Side-effects affecting eating persisted in 23/25 patients, with 80% still having a dry mouth at a mean of 3.5 years post-treatment. 40% had not regained weight lost during treatment. • The top ranked side-effects perceived to be of greatest importance to quality of life all related to the ability to eat. A return to "normal eating" is not possible in all patients. 	3
9. Bjordal K, Kaasa S, Mastekaasa A. Quality of life in patients treated for head and neck cancer: a follow-up study 7 to 11 years after radiotherapy. <i>Int J Radiat Oncol Biol Phys</i> 1994; 28(4):847-856.	3a	204 patients 103 conventional RT (2 Gy, 5 days-a-week) 101 hypofractionated regimen (2.35 Gy, 4 days-a-week)	To compare HRQoL factors in 845 head and neck cancer patients randomized to receive either conventional RT (2 Gy, 5 days-a-week) or a hypofractionated regimen (2.35 Gy, 4 days-a-week), a follow-up study was carried out 7 to 11 years after treatment in the surviving patients, representing 30% of the original patient number.	<ul style="list-style-type: none"> • Unexpectedly, patients in the hypofractionated group reported similar or better quality of life compared to patients in the conventional fractionated group. • Patients in both groups described a high level of symptoms, like dryness in the mouth and mucus production. • Clinical and sociodemographic variables did not explain variance in social function, emotional function or fatigue, except for the type of surgery performed, which significantly influenced the patients' emotional function. • Long-term survivors of head and neck cancer reported a high level of disease and treatment related symptoms. Emotional function was significantly influenced by the type of surgical procedure. Strategies for future trials in head and neck cancer should continue to attempt to stress conservative surgical approaches and coordinated adjuvant therapy to maximize local regional control and quality of life. Functional and emotional outcome are important parameters which should prospectively be evaluated in future clinical trials in head and neck cancer. 	2

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10. Cooper JS, Fu K, Marks J, Silverman S. Late effects of radiation therapy in the head and neck region. <i>Int J Radiat Oncol Biol Phys</i> 1995; 31(5):1141-1164.	7	N/A	Review on the late effects of RT in the head and neck region.	Irradiated mucocutaneous tissues demonstrate increased vascular permeability that leads to fibrin deposition, subsequent collagen formation, and eventual fibrosis. Irradiated salivary tissue degenerates after relatively small doses, leading to markedly diminished salivary output. This, in turn, effects the teeth by promoting dental decay which, in turn, effects the integrity of the mandible. Details of these changes are presented, including their pathophysiology, clinical syndromes, and potential treatment.	4
11. Garg AK, Malo M. Manifestations and treatment of xerostomia and associated oral effects secondary to head and neck radiation therapy. <i>J Am Dent Assoc</i> 1997; 128(8):1128-1133.	7	N/A	Review on the manifestations and treatment of xerostomia and associated oral effects secondary to head and neck RT.	Because xerostomia resulting from RT may be of a more permanent nature than xerostomia resulting from other causes, treatment is typically more extensive. Numerous regimens treat symptoms of xerostomia and associated caries and mucositis. Among them is the daily application of a fluoride gel, recommended to prevent or minimize dental caries. For patients with severe, chronic xerostomia who have some residual salivary tissue, the use of a sialagogue can promote an increased flow of saliva and treat the symptoms.	4
12. Langendijk JA, Doornaert P, Verdonck-de Leeuw IM, Leemans CR, Aaronson NK, Slotman BJ. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. <i>J Clin Oncol</i> 2008; 26(22):3770-3776.	4	425 disease-free patients	To investigate the impact of treatment-related toxicity on HRQoL among patients with HNSCC treated with RT either alone or in combination with chemotherapy or surgery.	Late radiation-induced toxicity, (RTOG (swallowing) and RTOG (xerostomia)), has a significant impact on the more general dimensions of HRQoL.	2
13. Scully C, Epstein JB. Oral health care for the cancer patient. <i>Eur J Cancer B Oral Oncol</i> 1996; 32B(5):281-292.	7	N/A	To discuss the aetiopathogenesis and current means available for preventing, ameliorating and treating these complications, as well as indicating research directions.	Orofacial complications are common after RT to the head and neck, and after chemotherapy for malignant disease. Mucositis is the most frequent and often most distressing complication, but adverse reactions can affect all other orofacial tissues.	4

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14. Vissink A, Burlage FR, Spijkervet FK, Jansma J, Coppes RP. Prevention and treatment of the consequences of head and neck radiotherapy. <i>Crit Rev Oral Biol Med</i> 2003; 14(3):213-225.	7	N/A	In this review, the various possibilities for prevention and/or treatment of radiation-induced changes in healthy oral tissues and their consequences are discussed.	<ul style="list-style-type: none"> • The clinical sequelae of the radiation treatment include mucositis, hyposalivation, and loss of taste, osteoradionecrosis, radiation caries, and trismus. • These sequelae may be dose-limiting and have a tremendous effect on the patient's quality of life. Most treatment protocols to prevent these sequelae are still based on clinical experience, but alternatives based on fundamental basic and clinical research are becoming more and more available. Many of these alternatives either need further study before they can be incorporated into the protocols commonly used to prevent and treat the radiation-related oral sequelae or await implementation of these protocols. 	4
15. Galati LT, Myers EN, Johnson JT. Primary surgery as treatment for early squamous cell carcinoma of the tonsil. <i>Head Neck</i> 2000; 22(3):294-296.	4	162 patients 84 treated with surgery	To evaluate primary surgery as treatment for early squamous cell carcinoma of the tonsil.	<ul style="list-style-type: none"> • Follow up from 2 to 15 years. • Of the 9 patients with stage I disease, 89% are without evidence of recurrent disease and 91% of patients with stage II tonsil cancers are also disease free. • The survival rates for stage III and stage IV cancer patients are 79% and 52%, respectively. • The data suggest that patients with early tonsil cancer can be effectively treated with surgery. Surgery allows pathologic staging so that patients with advanced tumors can be treated with adjuvant therapy. 	2

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16. Hicks WL, Jr., Kuriakose MA, Loree TR, et al. Surgery versus radiation therapy as single-modality treatment of tonsillar fossa carcinoma: the Roswell Park Cancer Institute experience (1971-1991). <i>Laryngoscope</i> 1998; 108(7):1014-1019.	3c	239 total patients 90 had tonsillar carcinoma 76 of these patients received either 56 surgery 20 RT	To compare the efficacy and treatment outcomes in patients with tonsillar fossa cancer using surgery or RT as a single modality therapy.	<ul style="list-style-type: none"> • 63% of the surgery and 80% of the RT treatment groups presented with either stage III or IV disease (P≤.05). • 47% of the surgery group and 52% of the RT patients had clinically positive regional disease at initial presentation. • There was a predictable pattern of nodal presentation, with level II, the most frequently involved region. • The rate of occult metastasis was 27% and was evenly distributed between T1 and T4 disease. • The overall local control rate in the surgery group was 75%, compared with 60% in the RT group (P value was not significant). • The disease-specific survival (all stages) was 61% in the surgery group and 37% in the RT group (P≤.05). • The DFS for stage III and stage IV disease in the surgery group was 47% and in the RT group 27% (P≤.05). Survival measured against clinical response to RT, in complete responders (all stages) was 83%; by contrast there were no survivors past 24 months in the partial response group (P≤.001). • The results from this study suggest that for early disease (stage I/II), surgery or RT as single-modality treatment is equally effective. For advanced disease RT is inferior to surgery as a single-modality treatment, as measured by ultimate survival and the local control of disease. There is, however, a subset of patients with advanced disease who respond to RT and whose survival is equivalent to our surgical cohort of patients. 	2

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17. Shin HA, Lim YC, Jeong HM, Choi EC. Role of primary surgery for early-stage (T1-2N0) squamous cell carcinoma of the oropharynx. <i>Oral Oncol</i> 2009; 45(12):1063-1066.	3a	46 consecutive cases 12 patients T1 34 patients T2	Retrospective analysis to evaluate treatment outcomes and the role of primary definitive surgery for T(1-2), clinically N(0) oropharyngeal SCC patients.	<ul style="list-style-type: none"> • The 5-year disease-specific survival rate was 83%: 100% for clinical stage I (T(1)N(0)) and 74% for clinical stage II (T(2)N(0)). • The 5-year disease-specific survival rate of patients with surgery alone was 86%. 13/14 patients (93%) treated with conservative surgery alone without mandible-splitting or adjuvant radiotherapy attained disease-free status. • In addition, 25/40 patients (63%) with disease-free status were treated with surgery alone. • Almost 30% of all patients may be candidates for adjuvant chemotherapy through histopathologic analysis according to the National Comprehensive Cancer Network (2007) guidelines. • The results of the present study demonstrate excellent oncologic outcomes with primary surgery for the treatment of early-stage oropharyngeal SCC and suggest that surgery offers the best opportunity to identify patients in whom adjuvant radio- or chemotherapy may be most appropriately applied. 	2

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18. Foote RL, Schild SE, Thompson WM, et al. Tonsil cancer. Patterns of failure after surgery alone and surgery combined with postoperative radiation therapy. <i>Cancer</i> 1994; 73(10):2638-2647.	3a	72 total patients 56 underwent surgery alone 16 surgery and postoperative adjuvant RT	To determine the patterns of treatment failure in patients treated with surgery alone or surgery combined with postoperative RT for SCC of the tonsil.	<ul style="list-style-type: none"> • The main pattern of treatment failure was above the clavicles. It occurred in 39% of patients treated with surgery alone and was significantly related (P=0.002) to the overall clinical TNM stage. • Disease recurrence above the clavicles occurred in 31% of patients undergoing surgery and postoperative adjuvant RT, despite their more advanced neck disease. • 5-year OS for patients with clinical stage III and IV disease who were treated with surgery and postoperative adjuvant RT was 100% and 78%, respectively. 5-year OS for patients treated with surgery alone that had clinical stage III, IVA, or IVB disease was 56%, 43%, and 50%, respectively. • Postoperative adjuvant RT is recommended for patients with clinical stage III or IV SCC of the tonsil who have undergone complete surgical resection because this appears to improve control of disease above the clavicles and OS. 	2

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19. Lim YC, Lee SY, Lim JY, et al. Management of contralateral N0 neck in tonsillar squamous cell carcinoma. <i>Laryngoscope</i> 2005; 115(9):1672-1675.	3a	43 N0-3 tonsillar cancer patients	A retrospective analysis to evaluate the management of contralateral N0 neck in tonsillar SCC.	<ul style="list-style-type: none"> • The follow-up period ranged from 2 to 120 (mean 38) months. • Clinically negative, but pathologically positive, contralateral lymph nodes occurred in 16% (7/43). • Of the 33 cases with an ipsilateral node positive neck, contralateral occult lymph node metastases developed in 21% (7/33), in contrast with 0% in ipsilateral N0 necks. • On the basis of the clinical staging of the tumor, 5% (1/22) of the cases showed lymph node metastases in T2 tumors, 36% (5/14) in T3, and 25% (1/4) in T4. None of the T1 tumors (3 cases) had pathologically positive lymph nodes (T1 + T2 vs T3 + T4, P<.05). Patients with no evidence of contralateral nodal cancer had significantly improved disease-specific survival over patients with any pathologically positive nodes (5 year disease-specific survival rate 92% vs 28%, P<.05). • The risk of contralateral occult neck involvement in above T3 staged tonsillar SCC with unilateral metastases was high (approximately 21%), and patients who present with a contralateral metastatic neck have a worse prognosis than those who are staged as N0. Therefore, we advocate an elective contralateral neck treatment in tonsillar SCC patients with ipsilateral node metastases. 	2
20. Olzowy B, Tsalemchuk Y, Schotten KJ, Reichel O, Harreus U. Frequency of bilateral cervical metastases in oropharyngeal squamous cell carcinoma: a retrospective analysis of 352 cases after bilateral neck dissection. <i>Head Neck</i> 2011; 33(2):239-243.	4	352 patients	A retrospective chart review to determine the frequency of histologically unveiled bilateral neck metastases.	Carcinomas of the tonsillar fossa starting with a T2 classification and carcinomas of the soft palate, base of tongue, and pharyngeal wall at any stage showed a high frequency of bilateral metastases. Bilateral neck dissection should be recommended for all but T1 and selected cases of T2 carcinomas of the tonsillar fossa.	2

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21. Cho KJ, Joo YH, Sun DI, Kim MS. Management of cervical lymph node metastasis in tonsillar squamous cell carcinoma: Is it necessary to treat node-negative contralateral neck? <i>Auris Nasus Larynx</i> 2011; 38(4):501-507.	3a	49 patients	To retrospectively investigate the appropriate management of cervical lymph node metastasis in patients with tonsillar SCC.	<ul style="list-style-type: none"> • Among the 49 ipsilateral neck dissection specimens, 34 neck specimens (69%) were pN+. • Out of 17 cases that underwent ipsilateral elective neck dissection, 4 cases (24%) were found to have pN+ necks. • The disease-specific survival of the 34 patients with pN+ necks and 4 patients with occult metastases was worse than that of the remaining patients with pN0 necks and without occult metastasis, respectively (P=0.049 and P=0.023, respectively). • All cases (100%) that underwent contralateral therapeutic neck dissection had pN+ findings. 2/21 cases (less than 10%) that underwent contralateral elective neck dissection turned out to have pN+ necks and did not show any difference in survival compared to the 19 cases with pN0 necks. The degree of differentiation was associated with contralateral nodal metastasis. • Patients with tonsillar SCC require thorough ipsilateral neck treatment because of the high probability of nodal metastasis and the close association between lymph node metastasis and survival. The contralateral cN+ neck should also be treated; however, the contralateral cN0 neck might be preserved with caution on the cases with poorly differentiated primary tumors and/or ipsilateral cN+ necks. 	2

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22. O'Sullivan B, Warde P, Grice B, et al. The benefits and pitfalls of ipsilateral radiotherapy in carcinoma of the tonsillar region. <i>Int J Radiat Oncol Biol Phys</i> 2001; 51(2):332-343.	3a	228 total patients	To evaluate the risk of failure in the opposite neck in cases selected for unilateral RT over a 21-year period.	<ul style="list-style-type: none"> • Mean follow-up was 7 years. • Cases tended to be T1 and T2, with N0 disease. • The 3-year actuarial local control rate was 77% and cause-specific survival was 76%. • Opposite neck failure was seen in 8 patients (crude rate of 3.5%). • In the earlier period of the study, primary coverage was problematic in a proportion of cases and resulted in higher rates of local failure. • Appropriately selected cases of carcinoma of the tonsil show minimal risk of failure in the opposite neck with ipsilateral techniques. Patients should undergo CT planning to ensure adequate target coverage. 	2
23. Cerezo L, Martin M, Lopez M, Marin A, Gomez A. Ipsilateral irradiation for well lateralized carcinomas of the oral cavity and oropharynx: results on tumor control and xerostomia. <i>Radiat Oncol</i> 2009; 4:33.	3a	20 consecutive patients	To evaluate the morbidity and tumor control for patients with well lateralized SCC of the oral cavity and oropharynx treated with ipsilateral RT.	At a median follow-up of 58 months, 5-year OS and loco-regional control rates were 82.5% and 100%, respectively. No local or contralateral nodal recurrences were observed. Mean dose to the contralateral parotid gland was 4.72 Gy and to the contralateral submandibular gland was 15.30 Gy. Mean score for dry mouth was 28.1 on the 0-100 QLQ-H&N35 scale. According to CTCAE v3 scale, 87.5% of patients had grade 0-1 and 12.5% grade 2 subjective xerostomia. The unstimulated salivary flow was >0.2 ml/min in 81.2% of patients and 0.1-0.2 ml/min in 19%. None of the patients showed grade 3 xerostomia. In selected patients with early and moderate stages, well lateralized oral and oropharyngeal carcinomas, ipsilateral RT treatment of the primary site and ipsilateral neck spares salivary gland function without compromising loco-regional control.	3

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24. Kagei K, Shirato H, Nishioka T, et al. Ipsilateral irradiation for carcinomas of tonsillar region and soft palate based on computed tomographic simulation. <i>Radiother Oncol</i> 2000; 54(2):117-121.	3a	32 patients	To reduce xerostomia in selected patients with carcinomas of the tonsillar region and soft palate.	<ul style="list-style-type: none"> • The median follow-up was 44 months. • 5-year overall, cause-specific survival, local control, and regional control rate was 64%, 79%, 74% and 81%. • No failure at the contralateral neck occurred. Moderate or severe symptomatic xerostomia was seen in 3 (9%) patients and osteo-radionecrosis requiring surgery occurred in one (3.3%) of 32 patients. • It is suggested that the ipsilateral technique is indicated in patients who had a unilateral tonsillar region or soft palate carcinoma that did not cross midline and have no contralateral neck lymph node metastasis. 	2
25. Rusthoven KE, Raben D, Schneider C, Witt R, Sammons S, Raben A. Freedom from local and regional failure of contralateral neck with ipsilateral neck radiotherapy for node-positive tonsil cancer: results of a prospective management approach. <i>Int J Radiat Oncol Biol Phys</i> 2009; 74(5):1365-1370.	4	20 patients	To review the outcomes of a prospective management approach using ipsilateral neck RT in the treatment of node-positive SCC of the tonsil with a well-lateralized primary lesion.	<ul style="list-style-type: none"> • The nodal disease was stage N1 in 4 patients, N2a in 3 patients, and N2b in 13 patients. • At a median follow-up 19 months (range, 12-40), no in-field or contralateral nodal recurrences had been observed. • The 2-year freedom from distant metastasis rate was 87.4%. • The actuarial 2-year disease-free and OS rates were both 79.5%. • Late Radiation Therapy Oncology Group grade 2 xerostomia occurred in 1 patient (5%). • No late Grade 3 or greater toxicity was observed. No patient was feeding tube dependent at their last follow-up visit. • In carefully selected patients with node-positive, lateralized tonsillar cancer, treatment of the ipsilateral neck and primary site does not appear to increase the risk of contralateral nodal failure and reduces late morbidity compared with historical controls. Although the outcomes with ipsilateral RT in the present series were promising, these findings require longer follow-up and validation in a larger patient cohort. 	3

**Ipsilateral Radiation for Squamous Cell Carcinoma of the Tonsil
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
26. Jackson SM, Hay JH, Flores AD, et al. Cancer of the tonsil: the results of ipsilateral radiation treatment. <i>Radiother Oncol</i> 1999; 51(2):123-128.	3a	271 patients	To analyze the survival and recurrence rates and sites of recurrence in a group of patients with carcinoma of the tonsil treated with ipsilateral techniques.	<ul style="list-style-type: none"> • The disease specific survival for all patients treated by radical radiation treatment was 61% at 5 years. • For the 178 patients who received ipsilateral radiation treatment the overall primary tumor control rate by ipsilateral radiation treatment alone was 75% and for T1 and T2 tumors 84%. • 8 (7.5%) of 101 of these patients with N0 nodes at presentation and without prior failure at the primary site, developed nodal recurrence (four within the initially radiated high dose volume). • Two developed contralateral nodes, and two developed field edge nodal recurrence, one cured by surgery. • In 54 patients with N1 disease, five developed nodal recurrence, two within field, two contralateral, one of whom was cured by surgery, and one at field edge. • In 23 patients with N2a, N2b or N3 disease node control was achieved from radiation treatment in 11 and two more were cured by surgery. All nodal failures were within the radiated volume. • Overall, 10/25 patients with nodal failure were cured by subsequent surgery. • Ipsilateral treatment of patients with carcinoma of the tonsil gives survival results that are at least as good as those reported with bilateral treatment with fewer side effects and a very low risk of failure in the contralateral neck. 	2

**Ipsilateral Radiation for Squamous Cell Carcinoma of the Tonsil
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
27. El-Mofty SK, Lu DW. Prevalence of human papillomavirus type 16 DNA in squamous cell carcinoma of the palatine tonsil, and not the oral cavity, in young patients: a distinct clinicopathologic and molecular disease entity. <i>Am J Surg Pathol</i> 2003; 27(11):1463-1470.	3b	33 cases	To investigate a possible relationship between tonsillar tumors and HPV.	The 12 HPV-positive tumors, 11 were HPV16 and 1 was HPV31. HPV-positive tumors had distinct nonkeratinizing basal cell morphology, they stained diffusely and strongly with p16 antibodies, had higher Ki-67 and lower p53 staining scores as compared with the conventional keratinizing HPV-negative carcinomas. It is concluded that in young patients, high-risk HPV, particularly HPV16, is strongly associated with tonsillar SCC and some cases of laryngeal, but not oral, tumors. The HPV-positive carcinomas have a distinct histopathologic and immunophenotypic features.	2
28. Klussmann JP, Gultekin E, Weissenborn SJ, et al. Expression of p16 protein identifies a distinct entity of tonsillar carcinomas associated with human papillomavirus. <i>Am J Pathol</i> 2003; 162(3):747-753.	3b	34 tonsillar carcinomas	To analyze p16 protein expression in tonsillar carcinoma for correlation to HPV status and load of viral DNA.	<ul style="list-style-type: none"> • 56% of all tumors tested were immunohistochemically positive for the p16 protein. • In 16/18 of the HPV-positive carcinomas diffuse p16 expression was observed. • In contrast, only one of the HPV-negative carcinomas showed focal p16 staining (P<0.001). • As determined by laser-assisted microdissection and quantitative real-time polymerase chain reaction, p16 expression correlated with the presence of HPV-DNA in the individual tumor specimens. Clinical outcome analysis revealed significant correlation of p16 expression with increased DFS (P=0.02). • These data indicate that p16 is a technically simple immunohistological marker, applicable for routine pathological histology, and its prognostic value for survival is fully equivalent to HPV-DNA detection. 	2

**Ipsilateral Radiation for Squamous Cell Carcinoma of the Tonsil
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
29. Vidal L, Gillison ML. Human papillomavirus in HNSCC: recognition of a distinct disease type. <i>Hematol Oncol Clin North Am</i> 2008; 22(6):1125-1142, vii.	15	N/A	To review HPV in HNSCC as a distinct disease type.	Strong epidemiologic and molecular data now support the conclusion that HPV infection is responsible for a distinct form of HNSCC, independent from the traditional risk factors of tobacco and alcohol use. Patients with HPV-positive HNSCC have a different clinical presentation and better clinical outcomes than those with HPV-negative HNSCC. A diagnosis of HPV-positive HNSCC is associated not only with therapeutic relevance, but also has important implications for future prevention and screening strategies.	4
30. Shoushtari AN, Meeneghan M, Treharne GC, et al. Clinical nodal staging of T1-2 tonsillar squamous cell carcinoma stratified by p16 status and implications for ipsilateral neck irradiation. <i>Cancer J</i> 2010; 16(3):284-287.	4	41 patients	Retrospective study to analyze the nodal staging of T1-2 tonsillar SCC stratified for p16 status, a marker of human papillomavirus positivity.	<ul style="list-style-type: none"> • 28 (68.2%) had p16+ tumors and 13 (31.7%) had p16- tumors. • 7 patients (17.0%) presented with contralateral cervical nodal disease, all of whom had p16+ tumors. • Furthermore, 25.0% of patients with p16+ tumors presented with contralateral cervical nodal disease compared with 0% of patients with p16- tumors. • Patients with p16+ T1-2 tonsillar SCC present with a higher incidence of contralateral nodal spread than those patients with p16- disease. This may have clinical implications when determining which patients are good candidates for ipsilateral cervical nodal RT. 	2

Evidence Table Key

Study Type Key

Numbers 1-7 are for studies of therapies while numbers 8-15 are used to describe studies of diagnostics.

1. Randomized Controlled Trial — Treatment
2. Controlled Trial
3. Observation Study
 - a. Cohort
 - b. Cross-sectional
 - c. Case-control
4. Clinical Series
5. Case reviews
6. Anecdotes
7. Reviews

8. Randomized Controlled Trial — Diagnostic
9. Comparative Assessment
10. Clinical Assessment
11. Quantitative Review
12. Qualitative Review
13. Descriptive Study
14. Case Report
15. Other (Described in text)

Strength of Evidence Key

- Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.
- Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.
- Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.
- Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

Abbreviations Key

CT = Computed tomography

DFS = Disease-free survival

HNSCC = Head and neck squamous-cell carcinoma

HPV = Human papilloma virus

HRQoL = Health-related quality of life

OS = Overall survival

PORT = Postoperative radiotherapy

RT = Radiation therapy

SCC = Squamous cell carcinoma