

**American College of Radiology
ACR Appropriateness Criteria®**

IPSILATERAL RADIATION FOR SQUAMOUS CELL CARCINOMA OF THE TONSIL

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Summary of Literature Review

Introduction

Treatment of early- and intermediate-stage carcinoma of the palatine tonsil with primary radiotherapy (RT) has a high success rate [1]. The well-lateralized location of the tonsils means that squamous cell carcinomas (SCCAs) arising in this region rarely metastasize to lymph nodes in the contralateral hemineck [2]. Because of this finding, multiple reports have questioned the need to electively irradiate the clinically negative contralateral hemineck in selected patients [3-5]. Controversy exists, however, as to the specific criteria for selecting patients for ipsilateral RT (defined as radiation to the primary site and ipsilateral regional nodes only). Important factors in determining the appropriateness of ipsilateral radiation are T stage, N stage, and the extent of invasion of the soft palate and base of tongue. Appropriate patient selection is a critical issue, as regional recurrences are rarely successfully salvaged [6,7]. The benefit of limiting radiation to the ipsilateral hemineck is decreasing the rate of permanent xerostomia, a condition that often results in poor nutrition and accelerated tooth decay, as well as decreased quality of life [8-14]. This article specifically discusses the appropriate RT volume without addressing the role of systemic chemotherapy concurrent with radiation.

Results from Surgical Literature

Although there are multiple reports on the outcome of tonsillar carcinoma treated with primary surgery [15-17], only a few specifically address the rate of neck failure in the undissected and unirradiated contralateral neck. The Mayo Clinic published its results on 56 patients with stage T1-4 N0-2b SCCA of the tonsil who underwent surgery alone ([18]). Seventy-nine percent of patients were stage T1-2, and 88% were N0-1. All patients underwent resection of the primary tumor, and 75% underwent an ipsilateral neck dissection. No patient had a dissection of the contralateral neck. With a minimum follow-up of 3.5 years, 3 of the 56 patients (5%) failed in the contralateral neck, with control at the primary and ipsilateral neck.

Multiple pathologic studies have shown that, for tonsillar primaries, the risk of pathologically occult contralateral lymph nodes is about 15% overall, and depends on the extent of the primary tumor and clinical N stage. Patients with T1-2 N0-1 tonsillar cancers have an extremely low risk of pathologically positive contralateral nodes, supporting the use of ipsilateral RT techniques in these patients.

Lim et al [19] retrospectively analyzed 43 patients with SCCA of the tonsil who underwent elective dissection of the clinically negative contralateral hemineck. The rate of pathologically positive contralateral lymph nodes was 16% in the entire patient cohort, with none occurring in the 10 patients who were N0. Six of the seven patients with pathologically positive contralateral nodes were T3 or T4. No attempt was made to correlate the results with extent of soft palate or base of tongue invasion.

Olzowy et al [20] reviewed 197 patients with SCCA of the tonsil who underwent bilateral neck dissections and showed that 14.7% had pathologically positive contralateral lymph nodes, although the authors did not specify the clinical stage of the contralateral hemineck prior to neck dissection.

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A recent report from Korea [21] showed that 2 of 21 (9.5%) patients with SCCA of the tonsil who underwent an elective contralateral neck dissection in addition to resection of the primary and ipsilateral neck dissection had pathologically positive contralateral nodes. These 2 patients were clinically N+, but the report did not specify the exact N stage. None of the patients who were clinically N0 had pathologically involved contralateral nodes.

Extent of Soft Palate or Base of Tongue Invasion

The extent of invasion of the primary tonsillar tumor into the soft palate and base of tongue has been shown to be an important predictor of contralateral lymph node failure. As tumor approaches midline in the base of tongue or soft palate, the risk of contralateral nodal involvement increases.

The seminal study on ipsilateral RT for tonsillar carcinoma is a retrospective study from the Princess Margaret Hospital group [22] which reported the outcomes of 228 patients with carcinoma of the tonsil treated with ipsilateral RT techniques. All patients had a clinically negative contralateral hemineck. The majority of patients were treated to 50 Gy at 2.5 Gy per fraction using cobalt 60. Contralateral neck failure occurred in 8 (3.5%) patients, although only three occurred in patients with control at the primary site. Of the 3 patients who experienced failure in the contralateral neck with the primary controlled, all had significant soft palate involvement (to within 1 cm of midline in 2 cases, and involving the middle third of the palate hemistructure in the third case). Two of the 3 patients were T3, and one was T2. All 3 patients were also N1. No patient with T1 or N0 disease failed in the contralateral neck. The authors concluded that <1 cm of extension into the soft palate or base of tongue is associated with a low risk of occult contralateral nodal involvement and is appropriately treated with ipsilateral RT.

A much smaller study showed excellent contralateral neck control when patients with only minimal soft palate or base of tongue extension were selected for ipsilateral radiation. Cerezo et al [23] reported on 8 patients with tonsillar carcinoma who had <1 cm of tumor extension to the soft palate or base of tongue and were treated with ipsilateral RT to a total dose of 66-70 Gy at 2 Gy per fraction to the primary tumor. The nodal stage varied from N0-2b. No contralateral neck failures were detected at 5 years.

Other authors have demonstrated that even tumors with more extensive base of tongue or soft palate invasion are successfully treated with ipsilateral radiation. Kagei et al [24] reported on 32 patients with carcinoma of the tonsil or soft palate treated with ipsilateral RT. The only selection criterion was that the primary tumor did not cross midline. The stage varied from T1-4 and N0-3. Patients were treated to 65 Gy plus a 15 Gy boost, depending on clinical response, delivered at 2.5 Gy per fraction using cobalt 60. Eight node-positive patients received bilateral lower neck irradiation. Twelve patients received concurrent carboplatin. The authors found no isolated contralateral neck failures at a median follow-up of 44 months. (See [Variant 1](#), [Variant 2](#) and [Variant 3](#).)

Nodal Stage

The extent of ipsilateral nodal disease has also been correlated with the risk of contralateral nodal failure. Patients with lateralized tumors that are N0-1 have a very low risk of failure in the untreated contralateral hemineck. Controversy exists, however, over the risk for patients with N2 disease, especially N2b.

A prospective study was performed by Rusthoven et al [25] that specifically addressed the issue of the node-positive patient. Twenty patients with carcinoma of the tonsil with stage T1-3 N1-2b were treated with ipsilateral RT. Thirteen of 20 patients were stage N2b. Patients with any invasion of the soft palate or base of tongue were excluded. All patients underwent pretreatment scans with computed tomography (CT) and positron emission tomography using fluorine-18-2-deoxy-D-glucose tracer (FDG-PET) to rule out occult contralateral neck lymphadenopathy. Sixteen of the 20 patients were treated with a tonsillectomy with a resultant positive margin, and 14 had undergone ipsilateral neck dissection prior to ipsilateral RT. Four patients with N2a or large N2b disease were treated with neoadjuvant chemotherapy followed by a planned neck dissection. Nineteen of the 20 patients received chemotherapy, which was concurrent platinum-based chemotherapy in most cases. The total RT dose was 60-66 Gy to the primary tumor or tumor bed for patients treated post-operatively and 66-70 Gy for the four patients treated with primary RT. At a median follow-up of 19 months, there were no contralateral nodal failures.

Jackson et al [26] retrospectively reviewed the charts of 178 patients with carcinoma of the tonsil treated with ipsilateral RT. The majority of patients received 60 Gy at 2.4 Gy per fraction. In 155 patients with stage N0-1 and control at the primary site, only 4 (2.6%) had isolated contralateral nodal failures. The authors did not analyze the contralateral nodal failures in the small number of N2-3 patients. (See [Variant 4](#) and [Variant 5](#).)

Role of HPV Status

Human papilloma virus (HPV)-associated SCCA of the oropharynx is thought to be a distinct epidemiologic, clinical, and molecular entity from non-HPV-associated tumors [27-29]. Given these differences, specific attention has recently been given to determining if ipsilateral RT is appropriate in HPV-associated tonsillar tumors.

Shoushtari et al [30] reviewed the charts of 41 patients with T1-2 SCCA of the tonsil to assess the rate of radiographically positive contralateral nodes. Patients with any soft palate or base of tongue invasion were excluded. Of the 28 patients with p16+ tumors, 25% presented with contralateral nodal disease. None of the 13 patients with p16- tumors had contralateral nodal disease. The authors conclude that given the high rate of clinically involved nodes in patients with p16+ tumors, the subclinical rate of contralateral nodal involvement may be sufficiently high to warrant elective irradiation of the contralateral hemineck, even in early-stage disease with no extension to the base of tongue or soft palate. (See [Variant 6](#).)

Radiation Technique

Ipsilateral RT can be done with either a 3D-conformal wedge-pair photon beam technique or intensity-modulated radiation therapy (IMRT). Both techniques achieve a low mean dose to the contralateral parotid gland, which is the main benefit in using ipsilateral RT. The benefit of using a wedge-pair technique is that the contralateral parotid gland can usually be completely excluded. However, achieving adequate coverage of the primary tumor can be challenging. On the other hand, the benefit of IMRT compared to traditional 3D-conformal RT is the ability to sculpt the dose around the target, sparing the surrounding critical organs as much as possible. While IMRT is superior to 3D-conformal RT regarding dose conformity and homogeneity, RT delivery time is generally increased, as is the number of monitor units, resulting in a greater integral body dose.

Summary

- Extent of soft palate or base of tongue invasion: We recommend ipsilateral radiation when there is <1cm of tumor invasion into the soft palate or base of tongue. If there is extension of 1 cm or greater, then we recommend bilateral neck irradiation because of the increased risk of occult contralateral nodal involvement.
- Nodal stage: For nodal stage of N2b or greater, we recommend bilateral neck irradiation, regardless of the extent of soft palate or base of tongue invasion. For nodal stage N0-1, we recommend basing the decision about whether to use ipsilateral or bilateral neck irradiation on the extent of soft palate and base of tongue invasion.
- HPV status: The panel concludes that there are insufficient data at this time to alter treatment decisions based on HPV status. Our recommendation is to treat with ipsilateral neck irradiation if the patient is an appropriate candidate based on the factors listed above, regardless of the patient's HPV status.

Supporting Documents

- [ACR Appropriateness Criteria® Overview](#)
- [Evidence Table](#)

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Clinical Condition: **Ipsilateral Radiation for Squamous Cell Carcinoma of the Tonsil**

Variant 1: **50-year-old man with a T2N0 SCCA of the right tonsil, with tumor extending 0.5 cm onto the soft palate. There is no base of tongue involvement. HPV status is negative.**

Treatment	Rating	Comments
Radiation Therapy Volume		
Ipsilateral neck irradiation plus primary	8	
Bilateral neck irradiation plus primary	3	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 2: **50-year-old man with a T3N0 SCCA of the right tonsil, with tumor extending 1 cm onto the soft palate (2 cm from midline). There is no base of tongue involvement. HPV status is negative.**

Treatment	Rating	Comments
Radiation Therapy Volume		
Ipsilateral neck irradiation plus primary	3	
Bilateral neck irradiation plus primary	7	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 3: **50-year-old man with a T3N0 SCCA of the right tonsil, with tumor extending onto the soft palate to within 1 cm of midline. There is no base of tongue involvement. HPV status is negative.**

Treatment	Rating	Comments
Radiation Therapy Volume		
Ipsilateral neck irradiation plus primary	1	
Bilateral neck irradiation plus primary	8	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: Ipsilateral Radiation for Squamous Cell Carcinoma of the Tonsil

Variant 4: 50-year-old man with a T1N1 SCCA of the right tonsil, with no soft palate or base of tongue extension. There is a single positive node in right level II. HPV status is negative.

Treatment	Rating	Comments
Radiation Therapy Volume		
Ipsilateral neck irradiation plus primary	8	
Bilateral neck irradiation plus primary	5	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 5: 50-year-old with a T1N2b SCCA of the right tonsil, with no soft palate or base of tongue extension. There are two positive nodes located in right level II. HPV status is negative.

Treatment	Rating	Comments
Radiation Therapy Volume		
Ipsilateral neck irradiation plus primary	3	
Bilateral neck irradiation plus primary	7	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Variant 6: 50-year-old man with a T2N1 SCCA of the right tonsil, with no soft palate or base of tongue extension. HPV status is positive.

Treatment	Rating	Comments
Radiation Therapy Volume		
Ipsilateral neck irradiation plus primary	8	
Bilateral neck irradiation plus primary	5	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		