**Case 12: Node Out, About It? Consideration of Adjuvant Treatment of Oral Tongue Cancer**

A 32-year-old female nonsmoker with no known family history of cancer presented to her primary care physician after a nonhealing wound in her tongue for 5 months that did not respond to conservative measures. A computed tomography scan of the neck revealed a 0.8 cm enhancing mass within the right mid to posterior tongue. There was no palpable lymphadenopathy or enlarged nodes on imaging. The patient underwent a right partial glossectomy and right neck dissection of levels 2 through 4. Pathology revealed a 1.5 cm × 0.7 cm (DOI) keratinizing squamous cell carcinoma with areas of moderate dysplasia. The closest margin was 0.8 cm. No lymphovascular invasion or perineural invasion was seen histologically. Right neck dissection revealed one 1.1 cm right level 2 node out of a total of 22 nodes without extranodal extension.

**Expert 1: Don't Take the Bait, Radiate: Importance of Adjuvant Radiation Therapy for Oral Tongue Cancer**

This young patient with a lack of traditional risk factors for oral cavity cancer (OCC) presents with a pathologic T2N1 stage III squamous cell carcinoma (SCC) of the tongue. Given the patient's young age, the omission of adjuvant radiation therapy may seem compelling. However, she has 2 indications for adjuvant radiation therapy: a depth of invasion of ≥5 mm and a positive node. Although omission of adjuvant therapy could be considered for a similar stage low risk oropharynx SCC, OCC carries a worse prognosis. Furthermore, ipsilateral level IB, a potential first-echelon drainage site, was not dissected and may harbor microscopic disease.

We recommend postoperative radiation therapy with 60 Gy in 30 fractions to the primary site and ipsilateral levels IA through IV, with undissected regions receiving 54 Gy. We at minimum include contralateral level IB with submandibular gland sparing, a possible first-echelon contralateral drainage site. Primary tumor with several pathologic risk factors, approaching midline, or floor of mouth invasion necessitates comprehensive contralateral neck coverage.

Regarding systemic therapy, we favor clinical trial enrollment as this patient lacks the standard indication for concurrent chemotherapy: positive margin or extracapsular extension. RTOG 0920 investigated concurrent cetuximab for intermediate-risk postoperative head and neck SCC, as we know concurrent cetuximab improves survival compared with definitive radiation alone in non-OCC head and neck SCC, so we await the full results before implementing off trial. Neoadjuvant immunotherapy is also being investigated for locally advanced OCC; however, this patient was clinical T1N0 at presentation and would not qualify.

Lastly, it is important to recognize that in young patients without a history of smoking, alcohol use, or premalignant lesions, OCC has a poorly understood biological component. As radiation oncologists, we are appropriately concerned about the long-term effects of radiation therapy; however, the morbidity and mortality of recurrent OCC must not be underestimated.

**Expert 2: Young Patient, Old Evidence**

This young patient initially had clinical T1N0 (0.8 cm) oral tongue cancer, which after surgery was noted to be pathologic T2 by virtue of its size (1.5 cm) and depth of invasion (0.7 cm).

Additionally, the patient has a metastatic ipsilateral neck node (N1). Therefore, I would recommend adjuvant radiation therapy for this patient with a stage III squamous cell carcinoma of the oral tongue. Although there is no evidence of perineural or lymphovascular invasion, I would ask the pathologist to comment on the presence or absence of worst pattern of invasion 5 in the primary tumor specimen. The presence of this negative prognostic feature would further tilt the balance in favor of offering radiation therapy.

Her young age with no obvious predisposing etiologic factors may also be of concern. Epidemiologic studies reveal an increasing incidence of oral tongue cancer among young nonsmokers, and some evidence suggests that this demographic may have a more aggressive disease course with inferior prognosis compared with the traditional demographic of older men with a long history of tobacco abuse.

Historical studies by Rouviere and more recent imaging studies done as part of the sentinel lymph node trials unequivocally demonstrate the crossover of lymphatics in oral tongue and floor of mouth cancers.

Hence, I would treat the primary tumor bed and ipsilateral neck (levels 1-3) to a dose of 60 Gy while delivering 54 Gy to the ipsilateral level 4 and contralateral neck in the same 30 fractions using a simultaneous integrated boost technique.

Although the standard-of-care recommendation in this case would be external beam radiation therapy alone, I would also strongly consider enrolling the patient in clinical trials, such as Radiation Therapy Oncology Group study 0920 (now closed to accrual), EA 3132 study (Eastern Cooperative Oncology Group-American College of Radiology Imaging Network), or other novel immunotherapy trials, which are evaluating the role of treatment intensification in patients with intermediate-risk head and neck squamous cell carcinoma.

**Expert 3: Depth of Invasion in Oral Tongue Cancer and Risk of Regional Failure**

Treatment of a young, nonsmoking female patient with oral tongue cancer represents a well-recognized clinical challenge.

In this case, the patient presented clinically as T1N0M0. However, after partial glossectomy and elective neck dissection, pathology revealed a pT2N1 lesion that was upstaged based on a depth of invasion of 7 mm.

There is a temptation to consider treatment complete and spare this young patient the long-term morbidity of adjuvant radiation. However, the presence of occult nodal metastasis in T1-2 oral cavity cancer increases the risk of dying of disease. Moreover, for T1-2N0 oral tongue cancer in patients deemed low risk after partial glossectomy and negative neck dissection who were observed, the presence of a depth of invasion of 4 mm or greater predicted a >20% risk of regional failure.

Importantly, approximately 40% of the failures occurred in the contralateral neck. Of the patients who experienced failure, only approximately 1 in 3 could be salvaged. Given this significant rate of contralateral lymphatic drainage of even lateralized tongue cancer, we often recommend sentinel node mapping and excision at the time of surgery.

For this case, we would recommend adjuvant radiation to the bilateral neck and the primary site to include in-transit lymphatics. Treatment of the ipsilateral neck would encompass levels I-IV, prescribed to a dose of 60 Gy to levels I-III, 57 Gy to level IV, and 54 Gy to the retrostyloid nodes. Contralateral neck treatment would include elective treatment to levels IB-III to a dose of 54 Gy with sparing of the retrostyloid area.

With regard to brachytherapy for the treatment of early-stage tongue cancer, our group and others have shown excellent outcomes incorporating adjuvant brachytherapy as a boost or standalone treatment in patients with close/positive margins and/or focal perineural invasion at the primary site.

For this patient, the main risk of failure is regional; therefore, she would not benefit from brachytherapy.

Enrollment in a clinical trial would be ideal. However, this patient would have not been eligible for Radiation Therapy Oncology Group (RTOG) 0920, which required 1 “intermediate” risk factor (perineural invasion, lymphovascular invasion, a single lymph node greater than 3 cm or 2 lymph nodes involved, and/or close margins), nor would she have been eligible for the current neoadjuvant immunotherapy trial enrolling clinically node-positive patients. Future trials are needed to address this unique cohort of patients.

**Expert 4: Your First Shot Is Your Best Shot**

The case presented is of a T2N1M0 stage III oral tongue squamous cell cancer in a young, nonsmoking woman. This designation (young, nonsmoking woman with tongue cancer) immediately brings to mind those patients we have all had who had terribly aggressive disease courses despite ostensibly low- to moderate-risk pathology. In addition to this initial instinct to treat this patient with adjuvant radiation, T2N1 oral cavity cancer is typically more aggressive than T2N1 oropharynx or larynx cancer. A 7-mm-deep lesion that has already spread to the neck despite the lack of other adverse pathologic features (poor differentiation, lymphovascular invasion, perineural invasion) demonstrates the ability to behave more aggressively than one would expect and therefore warrants adjuvant therapy.

Moreover, salvage rates are less than ideal in these patients. Our group and others have found that a recurrent oral cavity tumor that is subsequently salvaged with high-quality surgery and multimodality therapy has inferior outcomes. As I frequently tell my patients, “Your first shot is your best shot.” Finally, modern planning techniques allow for incredible sparing of normal tissue, thereby minimizing the morbidity of such an approach. I would treat the tumor and ipsilateral level 2 nodal bed to 60 Gy in 30 fractions and the R levels 1b, 3 and 4 to an elective dose of 54 Gy. This seems like a well-lateralized lesion, and contralateral elective nodal radiation appears unnecessary.

ChatGPT’s initial recommendation

**Expert 5: Prioritizing Adjuvant Radiation in a Young Patient with Oral Tongue Cancer and Intermediate Risk Factors**

Based on the available information, the patient has a T1N1M0 (Stage III) oral cavity squamous cell carcinoma (SCC) according to the AJCC TNM staging system. The mainstay of treatment for oral cavity SCC is surgical resection followed by adjuvant therapy, if indicated.

The patient has already undergone a right partial glossectomy and right neck dissection. The closest margin was 0.8 cm, which is relatively close. In addition, one positive lymph node was identified out of the 22 nodes dissected. These factors increase the risk of recurrence.

Our recommendation for this patient is adjuvant radiotherapy (RT) with a consideration for concurrent chemoradiotherapy (CRT), based on the following reasoning:

* Positive lymph node: The presence of a positive lymph node increases the risk of recurrence and indicates a need for adjuvant therapy.
* Close surgical margin: Although there is no universally agreed-upon threshold, a margin of 0.8 cm is considered relatively close, increasing the risk of local recurrence. Adjuvant RT would help address any residual microscopic disease at the primary site.
* No lymphovascular or perineural invasion: These factors are associated with a higher risk of recurrence, but their absence in this case is encouraging. It suggests that adjuvant RT alone may be sufficient, but concurrent CRT could still be considered for a more aggressive approach.

The specific RT recommendation would be to deliver approximately 60 Gy in 30 fractions to the primary tumor bed and the right neck, with a potential boost to the positive level 2 lymph node area. If concurrent CRT is pursued, cisplatin-based chemotherapy would be a standard choice.

ChatGPT’s revised recommendation after seeing other human experts’ recommendations

**Expert 6: Balancing Risk and Treatment Intensity in a Young Patient with Oral Tongue Cancer**

This young patient presents with a pathologic T2N1 stage III squamous cell carcinoma of the oral tongue, highlighting the need for an optimal balance between aggressive treatment and minimizing long-term side effects. Given the higher risk of recurrence due to the positive lymph node and close surgical margin, adjuvant radiation therapy is recommended.

To address these concerns, we propose administering 60 Gy to the primary tumor bed and ipsilateral neck (levels 1-3), and 54 Gy to the ipsilateral level 4 and contralateral neck in 30 fractions using a simultaneous integrated boost technique. This approach takes into account the potential for contralateral lymphatic drainage in oral tongue cancer while maintaining a focus on minimizing treatment-related morbidity.

In addition to the radiation therapy, we strongly recommend considering enrolling the patient in clinical trials like RTOG 0920 or EA 3132. These trials evaluate the role of treatment intensification in patients with intermediate-risk head and neck squamous cell carcinoma, providing potential access to novel treatments or strategies and contributing to our understanding of optimal management for this patient population.