In Response to Letter to the Editor, Regarding Adjuvant Radiation for T2N0 Oral Tongue Cancer
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We thank Varvares et al for their comments on our study evaluating the survival impact of adjuvant radiation for pathologic-stage T2N0 oral tongue cancer (American Joint Committee on Cancer [AJCC], seventh edition). In our study, an overall survival benefit was not demonstrated for patients who received postoperative radiation therapy (PORT) versus surgery alone, irrespective of depth of invasion (DOI). We presented a multivariate analysis adjusting for differences in patient factors and clinicopathologic factors, such as DOI and tumor differentiation. Varvares et al eluded to the importance of other clinicopathologic factors, such as perineural invasion and lymphovascular invasion (LVI), which were not accounted for in our study, as they were not available or were missing for a large percentage of patient population. Therefore, we agree with the authors that our results should be carefully interpreted and seen in the context of available information.

DOI was not included in the seventh edition of AJCC staging manual and was incorporated into the eighth edition only because of its prognostic value as it relates to occult lymph node involvement at neck dissection. It is acknowledged that lymph node involvement for oral tongue cancer is a poor prognostic sign and results in worse survival than lymph node–negative status. We aimed to determine if DOI alone, without the involvement of lymph nodes or positive surgical margins, benefited from PORT in terms of overall survival. While we were unable to demonstrate a survival advantage to PORT in the node and margin-negative setting, we understand the limitations that local control or regional control benefit with PORT could not be addressed by this study. We also used a cutoff of ≤5 mm versus >5 mm, which is different from criteria used in AJCC eighth edition. In a recent multicenter institutional study by Ebrahimi et al of 1409 patients with oral squamous cell carcinoma of tumor size ≤4 cm treated between 1990 and 2011, patients without any other adverse factors (including nodal metastases or involved margins) were evaluated with and without PORT. For patients who underwent surgery alone, the 5-year disease-specific mortality was 10% with DOI ≥10 mm, 8% with DOI 5 to <10 mm, and 6% with DOI <5 mm (P = .169), yielding an absolute risk difference of 4%. The authors concluded that an increased DOI reflects an association with other pathologic risk factors (nodal metastases, close or positive margins) and that PORT based on DOI alone should not be an indication.

In light of this letter, we have reanalyzed the National Cancer Database with updated data from 2004 to 2015. A total of 1169 patients with T2N0 oral tongue cancer (AJCC seventh edition) with negative surgical margins were identified with inclusion criteria similar to those used in our published study. In addition to conducting an analysis comparing surgery alone versus surgery + PORT, we included LVI and recategorized DOI into the following groups, to be consistent with the staging system of the AJCC eighth edition: ≤5 mm, >5 to ≤10 mm, and >10 mm. We would like to clarify that LVI and DOI information was available in the National Cancer Database mostly from 2010 onward.

In our updated analysis, median follow-up was 36.9 and 41.8 months in all and surviving patients, respectively. There were 312 deaths reported during the follow-up period, with a median survival of 135.8 months and with 3- and 5-year actuarial survival rates of 79.0% and 70.8%, respectively. The corresponding 3- and 5-year survival rates were 80.4% and 71.3% for surgery only (median survival, 119.7 months) and 75.7% and 69.7% for surgery + PORT (median survival, 135.8 months; P = .722).

On multivariate analysis (adjusting for patient age, sex, race, Charlson-Deyo score, adjuvant chemotherapy, primary site, tumor grade, and propensity scores generated from other patient factors) for the whole cohort without DOI, there was no difference observed between surgery only and surgery + PORT (hazard ratio [HR], 1.18; 95% CI, 0.85-1.63, P = .336; Table 1). When DOI data were incorporated into the model, the results remained insignificant (HR, 1.13; 96% CI, 0.72-1.80; P = .593).

We then performed a multivariate analysis stratified by DOI. Compared with surgery only, surgery + PORT yielded HRs (95% CI) of 1.04 (0.57-1.88, P = .909), 0.94 (0.31-2.84, P = .915), and 0.72 (0.16-3.20, P = .661) for the ≤5-mm, >5- to ≤10-mm, and >10-mm groups, respectively. Finally, 770 patients had information available on LVI, and only 61 (7.9%) reported LVI. Compared with surgery only, surgery + PORT yielded HRs (95% CI) of 0.99 (0.62-1.58, P = .970) and 0.50 (0.14-1.74, P = .278) in patients without and with LVI, respectively.

In summary, when overall survival outcomes were evaluated between PORT and no PORT for T2N0 oral tongue cancer (AJCC seventh edition), no statistically significant difference was noted between the treatment groups. Furthermore, similar nonsignificant results were observed when relationship was explored by DOI size and LVI status. Ideally, a prospective study incorporating all clinicopathologic factors would be needed to answer this question. Based on our current analysis, PORT based on DOI alone should not be an indication.
on our previous and current analysis, no statistically significant survival advantage was observed for PORT, a result that should be interpreted with caution.

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References

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