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LETTER TO THE EDITOR

WILEY

# Comment on "Ipsilateral neck radiotherapy in N2b well-lateralized tonsil cancer—Approach with caution"

To the Editor,

Maskell et al[1] report their long-term outcomes utilizing an ipsilateral radiotherapy protocol for well-lateralized tonsil cancers, the vast majority of whom had human papillomavirus (HPV)-associated disease. The report specifically focuses on the contralateral neck recurrence (CNR) rate in patients with N2b staged disease (American Joint Committee on Cancer Staging manual [ACC] 7th edition;[2] 4 of 28; 14%). The authors' conclusions were to recommend caution in offering ipsilateral treatment to this group of patients, offering bilateral treatment as a safe alternative. We offer a contrary interpretation of their results.

The majority of the 53 patients included were staged as N2b (28, 53%), and all four cases of CNR occurred in patients with p16+ T1N2b disease. Of these four CNRs, two patients ultimately died of recurrent disease following contralateral neck salvage, one as a consequence of a tongue recurrence (raising the possibility of a second primary), and the other from metastatic disease. This pattern of failure does not necessarily indicate that bilateral treatment *ab initio* would have definitely prevented either death. The remaining two patients were successfully salvaged. Although the first instinct is to consider any recurrence a treatment failure, this series should be viewed as successful from a rational treatment paradigm viewpoint. The successful salvage of two CNFs resulted in delivery of contralateral neck treatment to those ultimately requiring it, while sparing the majority (24/28; 86%) the toxicity of unnecessary bilateral irradiation. Maskell et al concluded that there was a "high rate" (14%) of CNR in their patients with N2b disease. However, a 14% risk of disease remains below the standard threshold for prophylactic irradiation. More importantly, we would suggest that "unsalvageable CNF" is a more appropriate endpoint in assessing the efficacy of ipsilateral treatment protocols. In this series, it is 7% at worst, and when the uncertainty of the two deaths is considered, it could be as low as 0%. In contrast to the authors' decision to treat all patients with N2b disease with bilateral treatment, our alternate interpretation would be that ipsilateral radiation in well-lateralized patients with N2b disease is an appropriate and effective approach. These rates are acceptably low when one considers the benefits of sparing the vast majority the toxicity of contralateral neck treatment.

A number of retrospective reviews have reported their outcomes when adopting an ipsilateral approach for well-lateralized tonsil cancers. The majority of reports predate routine p16/HPV testing and have not included a high proportion of patients with N2b disease, suggesting there is significant selection bias in those included in these series. In a systematic review of published ipsilateral outcomes, Al-Mamgani et al reported a CNF rate of 4.8% (9 of 186) for the N2b subgroup.[3] The Marsden ipsilateral series, which included the largest number of N2b cases (n = 55) in the literature to date, reported that all isolated CNFs (n = 6) occurred in patients with N2b disease, however, all were successfully salvaged.[4]

The approach by Maskell is in accordance with the current American Society for Radiation Oncology (ASTRO) clinical practice guidelines which recommend ipsilateral treatment only in well-lateralised T1-T2 tumors with a single involved lymph node ≤3 cm.[5] Although most treatment strategies in early stage HPV-associated oropharyngeal cancer are focusing on finding the most appropriate and safe form of de-escalation, ipsilateral treatment remains an underutilized deintensification treatment strategy. We need to focus on the ultimate patient outcomes, not just the isolated CNF rate. It is time for a rationale and prospective approach to assess elective treatment volumes in oropharyngeal cancers to spare the majority considerable and unnecessary morbidity while reserving the toxicity of bilateral treatment for those who definitely need it.

## ORCID

*Lachlan McDowell* https://orcid.org/0000-0002-4268-3079

Lachlan McDowell MB BS[1]

June Corry MD[2]

[1]*Department of Radiation Oncology, Peter Macallum Cancer Centre, Melbourne, Victoria, Australia*

[2]*GenesisCare Radiation Oncology, Division Radiation Oncology, St. Vincent's Hospital, Melbourne, Australia*

  

**Correspondence**

*Lachlan McDowell, Department of Radiation Oncology, Peter Macallum Cancer Centre, Melbourne, Victoria, Australia.*

*Email: lachlan.mcdowell@petermac.org*

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