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# Treatment-related toxicity in head and neck cancer patients treated with proton therapy is less common than with conventional radiotherapy

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*Dear Editor,*

Chen and colleagues deserve commendation for their study, which aimed to evaluate health-related quality of life (HRQoL) in 119 head and neck cancer (HNC) patients receiving proton therapy (PT) [1]. This prospective cohort study employed questionnaires—the EORTC-QLQ-C30, EQ-5D, and EORTC-H&N-35—administered during the pre-treatment period and at 0, 6, 12, and 24 months post-treatment to evaluate the benefit-tradeoff and adverse effects of radiation-related toxicities. During the treatment period, symptom and function scores showed a deterioration of all reported functions, most of which recovered within six months and improved beyond the baseline levels. At the end of PT, the patients' utility decreased significantly (0.12 points) compared to the baseline but recovered after six months, with a further improvement one year after the treatment. The study offers valuable insights into PT's potential advantages in reducing radiation-induced toxicity and enhancing HRQoL in HNC patients. However, the study has two limitations that deserve further discussion.

First, the study's dependence on self-reported HRQoL questionnaires introduces subjectivity in assessing outcomes [2–4]. While these tools are widely accepted, the lack of objective biomarkers or clinician-assessed toxicity grades diminishes the reliability of the reported findings. In this context, integrating clinical evaluations, such as assessments of salivary gland function, dental health, and swallowing capabilities, could offer a more comprehensive and accurate understanding of the impact of PT [5]. While PT has been shown to reduce RT-induced toxicities, some late toxicities, like osteoradionecrosis (ORN) of jaws, continue to impair patients' oral functions and overall well-being [6]. For example, the study conducted by Singh et al. [6] found that the prevalence of ORN was 10.6 % after PT, highlighting that ORN remains a clinical challenge even in the era of PT. Therefore, additional assessments of long-term toxicities, such as ORN, may enhance the robustness of Chen and colleagues' study.

Second, Chen and colleagues' study encompasses a heterogeneous cohort of tumors, each potentially exhibiting distinct profiles of treatment-related toxicity and varying impacts on HRQoL measures. Compared to other HNC sites, oral and oropharyngeal cancers reside closer to the maxilla and mandible [7]. Consequently, there is a higher likelihood of complications such as osteoradionecrosis (ORN), tooth loss, and periodontal toxicities in patients diagnosed with these specific cancer types [7,8]. Hence, conducting a comprehensive analysis of a larger head and neck cancer (HNC) cohort or focusing on a particular tumor group by incorporating all potential late toxicities may provide valuable insights into the site-specific toxicities associated with PT. Furthermore, this approach could elucidate the distinctive effects of PT on HRQoL metrics on a tumor-specific basis.

In conclusion, while this study contributes valuably to the PT literature in HNC patients, its generalizability is limited by the absence of a control group, reliance on self-reported measures, and significant tumor heterogeneity. Additionally, excluding critical late toxicities, such as ORN, diminishes the study's ability to evaluate PT outcomes comprehensively. Therefore, future research should prioritize rigorous comparative designs and objective toxicity assessments to further validate the benefits of PT compared to conventional RT.

## CRediT authorship contribution statement

**Efsun Somay:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, Visualization, Investigation, Writing – review & editing. **Erkan Topkan:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, Visualization, Investigation, Writing – review & editing. **Ugur Selek:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, Visualization, Investigation, Writing – review & editing.

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## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## References


[1] Hsuan Chen Y, Kroesen M, Hoogeman M, Versteegh M, Uyl-de Groot C, Blommestein HM. Treatment-related toxicity, utility and patient-reported outcomes of head and neck cancer patients treated with proton therapy: a longitudinal study. Clin Transl Radiat Oncol 2025;51:100913. https://doi.org/10.1016/j.ctro.2025.100913.

[2] Devlin NJ, Brooks, Richard. EQ-5D and the EuroQol group: past, present and future. Appl Health Econ Health Policy 2017;15:5. https://doi.org/10.1007/s40258-017-0310-.

[3] Scott NW, Fayers PM, Aaronson NK, et al. EORTC QLQ-C30 Reference Values This manual presents reference data for the QLQ-C30 based upon data provided by EORTC Quality of Life Group Members and other users of the QLQ-C30 Sprangers on behalf of the EORTC Quality of Life Group EORTC Quality of Life Group. Published online 2008.

[4] Singer S, Arraras JI, Chie WC, et al. Performance of the EORTC questionnaire for assessing quality of life in head and neck cancer patients EORTC QLQ- H&N35: a methodological review. Qual Life Res 2013;22(8):1927–41. https://doi.org/10.1007/S11136-012-0325-1/FIGURES/3.

[5] Nishi H, Obayashi T, Ueda T, Ohta K, Shigeishi H, Munenaga S, et al. Head and neck cancer patients show poor oral health as compared to those with other types of cancer. BMC Oral Health 2023;23(1):647. https://doi.org/10.1186/s12903-023-03356-6.

[6] Singh A, Kitpanit S, Neal B, et al. Osteoradionecrosis of the jaw following proton radiation therapy for patients with head and neck cancer. JAMA Otolaryngol Head Neck Surg 2023;149(2):151–9. https://doi.org/10.1001/jamaoto.2022.4165.

[7] Topkan E, et al. Do irradiated head and neck cancer site or prescribed radiotherapy dose have notable impacts on the development of osteoradionecrosis of the jaws? A concise review. Acta Sci Cancer Biol 2024;8(11):18–27.

[8] Lajolo C, Gioco G, Rupe C, Troiano G, Cordaro M, Lucchese A, et al. Tooth extraction before radiotherapy is a risk factor for developing osteoradionecrosis of the jaws: a systematic review. Oral Dis 2020. https://doi.org/10.1111/odi.13485.



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