DOI: 10.7860/JCDR/2025/74577.21955

Original Article

Dentistry Section

Photon versus Proton Therapy in the Management of Head and Neck Cancer: A Systematic Review

S SOWMYA[1], R SANGAVI[2], R AMRITHA SRIPOO[3]

ABSTRACT

Introduction: Head and Neck Cancers (HNC), particularly Head and Neck Squamous Cell Carcinoma (HNSCC), are major causes of cancer morbidity and mortality. Radiation therapy, commonly using photons, can damage surrounding healthy tissues. Proton Therapy (PT), with its ability to target tumours more precisely, may reduce toxicity and improve Quality Of Life (QOL). The present review compares the efficacy, toxicity, and QOL outcomes of proton versus photon therapies in HNSCC treatment.

Aim: To evaluate and compare PT versus photon therapy in terms of therapeutic efficacy, adverse effects, and QOL in the management of HNC.

Materials and Methods: A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Electronic searches were performed across PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar, including studies published from February 2016 to January 2024. Eligible studies involved adult patients diagnosed with HNSCC and compared PT with photon therapy. A total of five studies were included, and their quality was assessed using the Newcastle-Ottawa Scale. A narrative synthesis of findings was performed, focusing on QOL and toxicity profiles.

Results: The PT demonstrated a significant dosimetric advantage over photon therapy, particularly in reducing radiation exposure to critical structures such as salivary glands and the spinal cord. Patients receiving PT showed a 40-50% improvement in QOL, with fewer instances of xerostomia, dental problems, and head and neck pain. In comparison, photon therapy resulted in higher rates of acute and chronic toxicity, including greater feeding tube dependence and increased use of opioid medications. PT was also associated with a reduced incidence of weight loss and a decreased need for pain management compared to photon therapy.

Conclusion: The PT offers a significant dosimetric advantage over photon therapy, improving QOL and reducing toxicity in patients with HNC. While PT has shown promising results, further research with longer follow-up is needed to confirm its long-term benefits and refine treatment protocols. PT is a viable alternative to photon therapy and is recommended for patients with HNSCC, especially those requiring precise radiation delivers to critical structures.

Keywords: Acute disease, Chronic disease, Dose-response relationship, Quality of life, Radiation, Toxicity

INTRODUCTION

Squamous cells line the oropharynx, nasopharynx, and hypopharynx. With more than 878,000 new cases diagnosed each year, it is the seventh most prevalent cancer in the world [1]. HNSCC can be cured if it is detected early, but it is often diagnosed at a later stage when it is more difficult to treat. The management of malignancies involves a range of treatments such as surgery, radiotherapy, chemotherapy, or a combination of chemotherapy and radiotherapy. The choice of treatment depends on factors such as the type of cancer, tumour location, and the patient's overall health [2].

The most common radiation treatment method used in regular healthcare settings is photon therapy, which employs numerous X-ray beams to irradiate a target tumour; however, it inevitably deposits radiation in healthy tissues beyond the target, which can have negative consequences including secondary metastasis [3-5]. The clinical benefits of photon therapy in the treatment of head and neck carcinoma are well known; however, comprehensive nodal irradiation can lead to short-term and long-term toxicity [1,6]. The QOL for patients with HNC is affected by acute radiation toxicity, which can develop into chronic toxicity and makes it difficult for patients to navigate the rehabilitation phase, even with the most advanced Intensity-modulated Radiation Therapy (IMRT) [7-9].

One of the most recent developments in this field is PT, which allows for a significant improvement in radiation precision and conformity, thus dramatically reducing the burden on adjacent healthy organs and tissues [10,11]. Proton Beam Therapy (PBT) is an emerging field in cancer treatment that minimises the risk of secondary metastases and post-radiation effects. Protons are positively charged subatomic particles that are accelerated to high speeds in a particle accelerator. Protons exhibit unique physical beam characteristics, such as the Bragg peak, which allows for more precise delivery of radiation to the tumour while causing less damage to surrounding healthy tissues [7,12]. PBT, with its unique physical beam characteristics, particularly the Bragg peak, has consistently demonstrated improvements in dosimetry and sparing of normal tissue. The Bragg peak is defined as the maximum dose delivered at the site of the tumour, with a rapid dose fall-off distal and proximal to the tumour [13-15].

The present review aims to evaluate the literature regarding the advantages of PT over photon therapy in the management of HNC. The objective is to compare therapeutic efficacy, toxicity, and QOL outcomes between proton and photon therapy in patients with HNC. This study will help clarify the potential advantages of PT over photon therapy, focusing on improving patient outcomes and minimising adverse effects, thus contributing valuable insights to clinical decision-making in HNSCC management. Unlike existing studies, which often examine the therapies in isolation or only consider short-term effects, the present study takes a comprehensive approach by directly comparing photon and PT across both acute and long-term toxicity profiles and evaluating the impact on patients' overall QOL.

MATERIALS AND METHODS

The present study followed the PRISMA guidelines, which are a set of standards for reporting systematic reviews and meta-analyses.

The study was also registered with PROSPERO, Registration ID: (CRD42023458087), and the study period was from January 2024 to June 2024. An electronic search was conducted in the Cochrane Library, PubMed, Web of Science, and Google Scholar until November 2023. The search terms used were the same for both PubMed and Cochrane and included the title, abstract, and MeSH terms.

Research questions: The purpose of present review was to address the following question: a) Does PT for HNC yield maximum therapeutic benefits with minimal complications and improved QOL? This systematic review was conducted following the PICO framework (Population, Intervention, Comparison, Outcome) to ensure a structured and focused evaluation of the available evidence.

P (Population): Patients with Head and Neck Cancer (HNC)

I (Intervention): PT

C (Comparison): Photon therapy

O (Outcome): Improvement in post-radiation therapy and toxicity

Inclusion criteria: The PICO model was used to develop the inclusion criteria and search terms:

P (Population): HNC patients

I (Intervention): PT

C (Comparison): Photon therapy

O (Outcome): Improvement in post-radiation therapy and toxicity

S (Study Design): Prospective and retrospective studies published from 2015 to 2024, with a minimum follow-up of three months to one year

Exclusion criteria: The exclusion criteria for this systematic review included studies that; Focused on cancers other than head and neck carcinoma; Were published in languages other than English; Involved animal studies; Focused on artificial intelligence models.

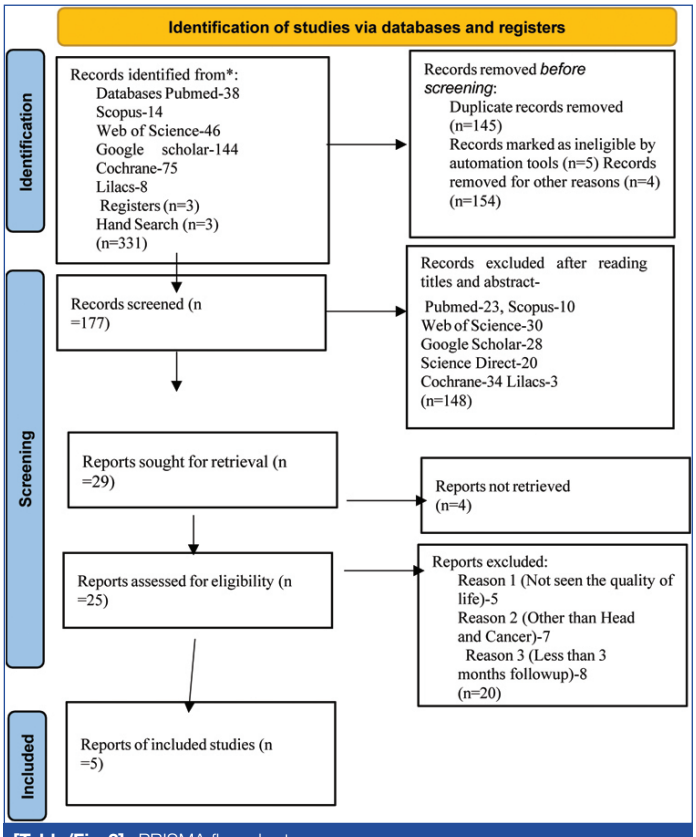
Primary outcome: The primary outcome is to assess the therapeutic and adverse effects of proton and photon therapy.

Secondary outcome: The secondary outcome is to assess which modality- proton or photon- improves the QOL.

The search strategy and study selection process were conducted in two stages. In the first stage, the primary author screened the search results and selected potentially eligible articles based on the title and abstract. In the second stage, the second author reviewed the same articles and agreed on the selection of potentially eligible studies. The full texts of the selected articles were then reviewed by both authors, leading to the identification and inclusion of five relevant studies in the systematic review [Table/Fig-1] [6,16-19]. The PRISMA flow diagram is depicted in [Table/Fig-2].

S. No	Type of database	Search terms	Articles extracted
1	PubMed	(Head and neck squamous cell carcinoma) OR (Squamous cell carcinoma of larynx) OR (Oral tongue squamous cell carcinoma) OR (Laryngeal squamous cell carcinoma) AND (Photon therapy) OR (Radiation therapy) OR (Photon Beam Therapy) AND (Proton therapies) OR (PBT) AND -(Life quality) OR (Health-related QOL) OR (Health-related QOL)	QOL of postoperative photon versus proton radiation therapy for oropharynx cancer [6].
2	PubMed	(Head and neck squamous cell carcinoma) OR (Squamous cell carcinoma of larynx) OR (Oral tongue squamous cell carcinoma) OR (Laryngeal squamous cell carcinoma) AND (Photon therapy) OR (Radiation therapy) OR (Photon Beam Therapy) AND (Proton therapies) OR (PBT) AND -(Life quality) OR (Health-related QOL) OR (Health-related QOL)	Acute toxicity in comprehensive head and neck radiation for nasopharynx and paranasal sinus cancers: cohort comparison of 3D conformal Proton Therapy (PT) and intensity modulated radiation therapy [16].
3	PubMed	(Head and neck squamous cell carcinoma) OR (Squamous cell carcinoma of larynx) OR (Oral tongue squamous cell carcinoma) OR (Laryngeal squamous cell carcinoma) AND (Photon therapy) OR (Radiation therapy) OR (Photon Beam Therapy) AND (Proton therapies) OR (PBT) AND -(Life quality) OR (Health-related QOL) OR (Health-related QOL)	Intensity-modulated PBT (IMPT) versus Intensity-modulated Photon Therapy (IMRT) for patients with oropharynx cancer: A case matched analysis [17].
4	PubMed	(Head and neck squamous cell carcinoma) OR (Squamous cell carcinoma of larynx) OR (Oral tongue squamous cell carcinoma) OR (Laryngeal squamous cell carcinoma) AND (Photon therapy) OR (Radiation therapy) OR (Photon Beam Therapy) AND (Proton therapies) OR (PBT) AND -(Life quality) OR (Health-related QOL) OR (Health-related QOL)	Intensity modulated PT versus intensity modulated photon radiation therapy for oropharyngeal cancer: first comparative results of patient-reported outcomes [18].
5	PubMed	(Head and neck squamous cell carcinoma) OR (Squamous cell carcinoma of larynx) OR (Oral tongue squamous cell carcinoma) OR (Laryngeal squamous cell carcinoma) AND (Photon therapy) OR (Radiation therapy) OR (Photon Beam Therapy) AND (Proton therapies) OR (PBT) AND -(Life quality) OR (Health-related QOL) OR (Health-related QOL)	PT reduces treatment-related toxicities for patients with nasopharyngeal cancer: A Case-match control study of intensity-modulated PT and intensity-modulated photon therapy [19].

[Table/Fig-1]: Article extracted from database.



[Table/Fig-2]: PRISMA flow chart.

Risk of bias: The present study employed the Newcastle-Ottawa Scale [20] for risk of bias assessment to evaluate the quality of the included studies. Based on the final evaluations, the studies were categorised as poor quality (scores 0-2), fair quality (scores 3-5), and good/high quality (scores 6-9) [21,22].

Agency for Healthcare Research and Quality (AHRQ) categorisation: The AHRQ categorisation was used for assessing the level of evidence of the included studies [23-25].

RESULTS

Description of Studies [Table/Fig-3] [6,16-19]: Sharma S et al., conducted a prospective study involving 64 participants, focusing on Oropharyngeal Squamous Cell Carcinoma (OPSCC), with a duration

of 12 months [6]. McDonald MW et al., carried out a retrospective study with 40 participants, investigating nasopharyngeal and paranasal sinus carcinoma, with a study duration of three months [16]. Blanchard P et al., also performed a prospective study involving 150 participants, focusing on oropharyngeal cancer, lasting for 32 months [17]. Sio TT et al., conducted a retrospective study with 149 participants, examining oropharyngeal cancer over a 24-month period [18]. Lastly, Holliday EB et al., performed a retrospective cohort study involving 30 patients with nasopharyngeal cancer, with a follow-up period of two years [19].

Participant Characteristics

The participant characteristics across the studies included patients diagnosed with oropharyngeal, nasopharyngeal, or paranasal sinus carcinoma, with sample sizes ranging from 30 to 150 individuals. The participants were primarily from the United States of America (USA) and their treatment involved either PT or photon therapy, which were compared in each study. The majority of the participants were adults undergoing radiation therapy as part of their treatment plan. Common characteristics included varying degrees of cancer severity, with many participants experiencing complications such as difficulty swallowing, weight loss, and the need for feeding tubes. These characteristics were important in evaluating the effectiveness and side effects of the treatment modalities.

Intervention Characteristics

Outcome measures: The outcome measures across the studies primarily focused on improvements in post-radiation therapy, particularly regarding QOL and the reduction of adverse effects commonly associated with radiation treatment. Key measures included the incidence of feeding tube usage, xerostomia (dry mouth), dental problems, head and neck pain, and the need for painkillers, as well as the occurrence of symptoms like difficulty swallowing, weight loss, and fatigue. In most cases, PT demonstrated lower toxicity rates, reduced dependence on feeding tubes, and fewer side effects, such as xerostomia and pain, leading to an overall improved QOL. In contrast, photon therapy was associated with higher rates of feeding tube dependency, weight loss, and other adverse effects, including increased use of pain medication.

Risk of Bias

For the included studies, the quality assessment was analysed using the Newcastle-Ottawa Scale. Based on the modified NOS scale, the quality of four studies was classified as good, while one study was rated as fair [Table/Fig-4] [6,16-19].

Based on AHRQ [23-25] categorisation, all the included studies were of grade 4 level of evidence [Table/Fig-5] [6,16-19].

S.no	Author	Year	Place of study	Sample	Group and treatment modality	Outcome measures	Treatment period	Response
1	Sharma S et al., [6]	2018	USA	64	Oropharyngeal Squamous Cell Carcinoma (OPSCC) Group 1 PT Group 2 photon therapy	Improvement in post radiation therapy	2013-2015	Group 1: Patient with 0% feeding tubes, 23.53% patient experienced xerostomia, 5.88% have dental problems, 8.33 % of patients have head and neck pain, and 17.65% of patients use painkillers to improve QOL. Group 2: Patients with 0% feeding tubes, 54.55% of patients experienced
2	Mc Donald MW et al., [16]	2016	USA	61	Nasopharyngeal and paranasal sinus carcinoma Group 1 PT Group 2 photon therapy	Improvement in post radiation therapy	2010-2014	Group 1: Improved No feeding tubes used, weight loss is less than 10%, opioids pain medication requirement is low (adverse effects of opioids such as nausea, somnolence, xerostomia, anorexia and constipation. Group 2: Feeding tube dependence is high, weight loss >10%, high use of opioid medication and more prone to adverse effects.
3	Blanchard P et al., [17]	2016	USA	150	Oropharyngeal cancer Group 1 PT Group 2 photon therapy	Improvement in post radiation therapy	2011-2014	Group 1: Use of feeding tubes is less, minimal acute, subacute and chronic toxicity and swallowing-related morbidity, increased QOL, patient goes through easy rehabilitation period, less mortality rate. Group 2: Difficulty in swallowing so, use of a feeding tube is more, fatigue, xerostomia, 21.21% had dental problems, 21.97% of patients had head and neck pain, and 36.36% of patients used painkillers, poor QOL.
4	Sio TT et al., [18]	2017	USA	149	Oropharyngeal cancer Group 1 PT Group 2 photon therapy	Improvement in post radiation therapy	2006-2015	Group 1: In the acute phase, both groups show no symptoms, In the subacute and chronic phase symptoms are comparatively less (taste sensation and mucus), improvement in the QOL, and 20% of patient use feeding tubes Group 2: Subacute and chronic phase symptoms are more, patient experiences difficulty in swallowing and poor appetite, and 46% of patient depends on feeding tubes, weight loss is reported
5	Holliday EB et al., [19]	2015	USA	30	Nasopharyngeal carcinoma Group 1: photon therapy Group 2: PT	Improvement in post radiation therapy	2011-2013	Group 1: Intensity Modulated Radiation Therapy (IMRT) The IMRT group had a toxicity rate of 90%, with 15% experiencing dysphagia and 25% developing dermatitis. Additionally, 65% required a G-tube. Group 2: PT In the PT group, toxicity was lower at 50%. There was no dysphagia, but 40% had dermatitis, and only 20% needed a G-tube.

[Table/Fig-3]: Data extraction of the included study [6,16-19].

Author	Selection				Comparability	Outcome			Score (9 points)
	Representation of cohort	Selection of non exposed cohort	Ascertainment of exposure	Demonstration of outcome of interest		Assessment of outcome	Was follow-up long enough for outcomes	Adequacy of follow-up of cohorts	
Sharma S et al., [6]	*	*	-	-	**	*	*	*	7
Mc Donald MW et al., [16]	*	*	-	-	**	-	-	*	5

Blanch ard P et al., [17]	*	*	*	*	* *	*	*	*	9
Sio TT et al., [18]	*	*	*	-	* *	*	*	*	8
Holliday EB et al., [19]	*	-	*	*	* *	*	-	-	6

[Table/Fig-4]: Quality assessment of included study [6,16-19].

S. no	Author	Year	Study design	Level of evidence
1.	Sharma S et al., [6]	2018	Cohort study	IV
2.	McDonald MW et al., [16]	2016	Cohort study	IV
3	Blanchard P et al., [17]	2016	Cohort study	IV
4	Sio TT et al., [18]	2017	Cohort study	IV
5	Holliday EB et al., [19]	2015	Cohort study	IV

[Table/Fig-5]: Evidence of included study [6,16-19].

DISCUSSION

The present systematic review compares post-radiation effects, toxicity, and quality of life in patients with head and neck carcinoma undergoing photon therapy versus PT. The review encompasses findings from five studies. While many studies aimed to assess toxicity rates and improvements in post-radiation outcomes, only a few successfully did so. The PT offers several advantages over photon therapy in terms of dosimetry, leading to reduced acute toxicity and greater efficacy in treating Head and Neck Malignancies (HNC) [13,16]. The precise delivery of protons to tumours, compared to photons, results in lower radiation exposure to surrounding healthy tissues while effectively targeting cancer cells. This precision is particularly beneficial for paediatric patients and individuals with tumours located in challenging anatomical regions [14,17].

The study conducted by Sharma S et al., used photon and PT in patients with OPSCC (n=64), estimating the toxicity and QOL. In Group 1, patients reported 0% feeding tube usage, 23.53% experienced xerostomia, 5.88% had dental problems, 8.33% reported head and neck pain, and 17.65% used painkillers, indicating an improved QOL. In contrast, Group 2 patients had 0% feeding tube usage, 54.55% experienced xerostomia, 21.21% had dental problems, 21.97% reported head and neck pain, and 36.36% used painkillers, suggesting a poorer QOL [6].

Another study by McDonald MW et al., found that Group 1 patients undergoing PT experienced weight loss of less than 10% in 2.8% of cases, with no feeding tube usage and low opioid pain medication requirements. Adverse effects associated with opioids, such as nausea, somnolence, xerostomia, anorexia, and constipation, were also reported. In Group 2, patients receiving photon therapy showed high feeding tube dependence, with 12.6% experiencing weight loss greater than 10%, increased use of opioid medication, and a higher incidence of adverse effects [16].

Blanchard P et al., conducted a study on patients with oropharyngeal carcinoma, comparing Intensity-modulated Proton Therapy (IMPT) with IMRT. The study included fifty IMPT patients and one hundred IMRT patients. Group 1 patients used fewer feeding tubes and experienced minimal acute, subacute, and chronic toxicity, as well as reduced swallowing-related morbidity. They also reported an improved QOL, had a smoother rehabilitation period, and exhibited a lower mortality rate. In contrast, Group 2 patients faced difficulties swallowing, leading to greater feeding tube usage, fatigue, and xerostomia, all of which negatively impacted QOL. Acute toxicity was reported more frequently in the photon therapy group, resulting in a comparatively higher mortality rate. There were no significant differences between IMPT and IMRT patients regarding severe dermatitis or mucositis (skin inflammation or mouth sores) in the first few months after treatment (p-value=0.15 and p-value=0.90, respectively). However, IMPT patients were less likely to report moderate or severe dry mouth three months after treatment than IMRT patients, with an odds ratio of 0.38 (95% CI: 0.18–0.79, p-value=0.009) [17].

According to the study conducted by Sio TT et al., they compared IMRT and IMPT. They found that patients who received IMRT experienced more difficulty swallowing and chewing at the start of the study than those who received IMPT. While the symptoms were similar in both groups during the acute phase of treatment, patients who received IMPT reported better taste and appetite during the subacute and chronic phases of treatment (mean of 5.15±2.66 for IMPT vs. 6.58±1.98 for IMRT; p=0.013) [18].

A study carried out by Holliday EB et al., in 2021 found that PT plans deliver less radiation to the oral cavity, spinal cord, salivary glands, and brain stem than IMRT plans for the treatment of cutaneous squamous cell carcinoma or major salivary gland malignancy. This results in significantly lower rates of severe side-effects, such as taste changes, mouth sores, and nausea. Similarly, patients who receive PT for oropharyngeal cancer report fewer side-effects than those who receive IMRT [Table/Fig-3] [19].

The present systematic review provides a preliminary overview of the toxicity profile of PT for HNC. It confirms that PT has outcomes similar to those of photon-based radiation therapy but with a significantly reduced risk of side effects. This is likely because PT can deliver more targeted radiation to the tumour while sparing healthy tissue. Further research is needed to better quantify the magnitude of this benefit.

Limitation(s)

The present review has a few limitations. First, it includes only a small number of studies, but this is not surprising because PT is a relatively new technology. Secondly, due to the heterogeneity in reporting results across the included articles, conducting quantitative analyses was challenging, and a meta-analysis was not performed. Third, the follow-up period was relatively short, so all the long-term adverse effects of PT could not be assessed.

CONCLUSION(S)

The PT is an effective and safe treatment for HNC. It has several advantages over photon therapy, including the ability to deliver a more precise radiation dose to the tumour while sparing nearby healthy tissues. This can lead to a lower risk of side effects, both during and after treatment. In order to fully understand the potential advantages of PT, which is still a relatively novel treatment for HNC, further research is required. However, the results thus far are encouraging, and PT is now considered a viable option for many patients with head and neck carcinoma.

REFERENCES

[1] Nuyts S, Bollen H, Ng SP, Corry J, Eisbruch A, Mendenhall WM, et al. Proton therapy for squamous cell carcinoma of the head and neck: Early clinical experience and current challenges. Cancers [Internet]. 2022;14(11):2587. Available from: http://dx.doi.org/10.3390/cancers14112587
[2] Baumann BC, Mitra N, Harton JG, Xiao Y, Wojcieszynski AP, Gabriel PE, et al. Comparative effectiveness of proton vs photon therapy as part of concurrent chemoradiotherapy for locally advanced cancer. JAMA Oncol. 2020;6(2):237-46.
[3] Atwell D, Elks J, Cahill K, Hearn N, Vignarajah D, Lagopoulos J, et al. A review of modern radiation therapy dose escalation in locally advanced head and neck cancer. Clin Oncol . 2020;32(5):330-41.
[4] Kim JK, Leeman JE, Riaz N, McBride S, Tsai CJ, Lee NY. Proton therapy for head and neck cancer. Curr Treat Options Oncol. 2018;19(6):28.
[5] Majeed H, Gupta V. Adverse effects of radiation therapy. 2020; Available from: https://europepmc.org/article/nbk/nbk563259.
[6] Sharma S, Zhou O, Thompson R, Gabriel P, Chalian A, Rassekh C, et al. QOL of postoperative photon versus proton radiation therapy for oropharynx cancer. Int J Part Ther. 2018;5(2):11-17.

[7] Park SG, Ahn YC, Oh D, Noh JM, Ju SG, Kwon D, et al. Early clinical outcomes of helical tomotherapy/intensity-modulated proton therapy combination in nasopharynx cancer. Cancer Sci. 2019;110(9):2867.
[8] Mohamed N, Lee A, Lee NY. Proton beam radiation therapy treatment for head and neck cancer. Precis Radiat Oncol. 2022;6(1):59-68.
[9] Gordon KB, Smyk DI, Gulidov IA. Proton therapy in head and neck cancer treatment: State of the problem and development prospects (review). Sovrem Tekhnologii Med. 2021;13(4):70-80.
[10] Li X, Lee A, Cohen MA, Sherman EJ, Lee NY. Past, present and future of proton therapy for head and neck cancer. Oral Oncol. 2020;110:104879.
[11] Liu H, Chang JY. Proton therapy in clinical practice. Chin J Cancer. 2011;30(5):315-26. Doi: 10.5732/cjc.010.10529. PMID: 21527064; PMCID: PMC4013396.
[12] Holliday EB, Kocak-Uzel E, Feng L, Thaker NG, Blanchard P, Rosenthal DI, et al. Dosimetric advantages of intensity-modulated proton therapy for oropharyngeal cancer compared with intensity-modulated radiation: A case-matched control analysis. Med Dosim. 2016;41(3):189-94.
[13] Chen Z, Dominello MM, Joiner MC, Burmeister JW. Proton versus photon radiation therapy: A clinical review. Front Oncol. 2023;13:1133909.
[14] Otero J, Felis I, Ardid M, Herrero A, Merchán JA. Acoustic Bragg peak localization in proton therapy treatment: Simulation studies. Proc AMIA Annu Fall Symp. 2019;42(1):71.
[15] Langendijk JA, Boersma LJ, Rasch CRN, van Vulpen M, Reitsma JB, van der Schaaf A, et al. Clinical trial strategies to compare protons with photons. Semin Radiat Oncol. 2018;28(2):79-87.
[16] McDonald MW, Liu Y, Moore MG, Johnstone PAS. Acute toxicity in comprehensive head and neck radiation for nasopharynx and paranasal sinus cancers: Cohort comparison of 3D conformal proton therapy and intensity modulated radiation therapy. Radiat Oncol. 2016;11:32.
[17] Blanchard P, Garden AS, Gunn GB, Rosenthal DI, Morrison WH, Hernandez M, et al. Intensity-modulated proton beam therapy (IMPT) versus intensity-modulated photon therapy (IMRT) for patients with oropharynx cancer- A case matched analysis. Radiother Oncol. 2016;120(1):48-55.
[18] Sio TT, Lin HK, Shi Q, Gunn GB, Cleeland CS, Lee JJ, et al. Intensity modulated proton therapy versus intensity modulated photon radiation therapy for oropharyngeal cancer: First comparative results of patient-reported outcomes. Int J Radiat Oncol Biol Phys. 2016;95(4):1107-14.
[19] Holliday EB, Garden AS, Rosenthal DI, Fuller CD, Morrison WH, Gunn GB, et al. Proton therapy reduces treatment-related toxicities for patients with nasopharyngeal cancer: A case-match control study of intensity-modulated proton therapy and intensity-modulated photon therapy. Int J Part Ther. 2015;2:19-28.
[20] Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: Advantages and limitations of the Newcastle Ottawa Scale. World Journal of Meta-Analysis. 2017;5(4):80-84.
[21] New ottava scale reference- Newcastle-Ottawa Quality Assessment Form for Cohort Studies [Internet] Available from: https://www.ncbi.nlm.nih.gov/books/NBK115843/bin/appe-fm3.pdf.
[22] Forte AJ, Guliyeva G, McLeod H, Salinas M, Avila FR, Perlman A. The impact of optimism on cancer-related and postsurgical cancer pain: A systematic review. Journal of Pain and Symptom Management. 2022;63(2):e203-11.
[23] Clair JS. A new model of tracheostomy care: Closing the research–practice gap. In: Henriksen K, Battles JB, Marks ES, et al., editors. Advances in Patient Safety: From Research to Implementation (Volume 3: Implementation Issues). Rockville (MD): Agency for Healthcare Research and Quality (US); 2005 Feb. Table 1, AHRQ scale of research grades and levels. Available from:
[24] Saragossi J. Research & Subject Guides: Evidence-Based Medicine: Home. 2011 Mar 4 [cited 2025 Mar 3]; Available from: https://guides.library.stonybrook.edu/evidence-based-medicine. Available from: https://guides.library.stonybrook.edu/evidence-based-medicine/levels_of_evidence.
[25] Owens DK, Lohr KN, Atkins D, Treadwell JR, Reston JT, Bass EB, et al. AHRQ series paper 5: Grading the strength of a body of evidence when comparing medical interventions--agency for healthcare research and quality and the effective health-care program. J Clin Epidemiol. 2010;63(5):513-23. Doi: 10.1016/j.jclinepi.2009.03.009.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Student, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, Tamil Nadu, India.
2. Senior Lecturer, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, Tamil Nadu, India.
3. Research Scholar, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. R Sangavi,
Senior Lecturer, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospital, Poonamalle High Road, Velapanchavadi,
Chennai-600077, Tamil Nadu, India.
E-mail: sangaviramesh12@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 30, 2024
- Manual Googling: Apr 07, 2025
- iThenticate Software: May 12, 2025 (13%)

ETYMOLOGY: Author Origin

EMENDATIONS: 9

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jul 29, 2024**
Date of Peer Review: **Dec 05, 2024**
Date of Acceptance: **May 14, 2025**
Date of Publishing: **Nov 01, 2025**