ONLINE FIRST

This is a provisional PDF only. Copyedited and fully formatted version will be made available soon.

REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY

ISSN: 1507-1367

e-ISSN: 2083-4640

Radiation induced brachial plexopathy in head and neck cancer patients treated with definitive radiotherapy and correlation with disease characteristics and dosimetric parameters

Authors: Hadrian Noel Alexander F, Nirmala Srikantia, Sandeep Muzumder, Avinash H Udayashankara, John Sebastian MG, Deepu C Tom, R.P. Kathiressan, John Michael Raj

DOI: 10.5603/rpor.101097

Article type: Research paper

Published online: 2024-06-19

Radiation induced brachial plexopathy in head and neck cancer patients treated with definitive radiotherapy and correlation with disease characteristics and dosimetric parameters

10.5603/rpor.101097

Hadrian Noel Alexander F[1], Nirmala Srikantia[1], Sandeep Muzumder[1], Avinash H Udayashankara[1], John Sebastian MG[1], Deepu C Tom[1], R.P. Kathiressan[1], John Michael Raj[2]

[1]*Radiation Oncology, St John's Medical College Hospital, Bangalore, India*
[2]*Biostatistics, St John's Medical College Hospital, Bangalore, India*

Corresponding Author: Hadrian Noel Alexander F, St John's Medical College Hospital, Radiation Oncology, Sarjapur Road, Bengaluru, 560034 Bangalore, India; e-mail: dr.hadrian27@gmail.com

Abstract

Background: Definitive concurrent chemoradiotherapy (CRT) is the standard of care in advanced stages of head and neck cancer (HNC). With evident increase in survival rate there is also simultaneous increase in toxicity affecting the quality of life. One of the less researched late toxicity is radiation induced brachial plexopathy (RIBP). In this dosimetric study we intent to contour the brachial plexus (BP) as an organ at risk (OAR) and determine the factors that contribute to dose variations to BP, and clinically evaluate the patients for RIBP during follow-up using a questionnaire.

Materials and methods: 30 patients with HNC planned for CRT from September 2020 to June 2022 were accrued. Patients were treated to a dose of 6600 cGy with intensity modulated radiotherapy using the simultaneous integrated boost technique. From dose-volume histogram (DVH) statistics the BPvolume, Dmax and other parameters like V66, V60 were assessed and was correlated with respect to primary tumour and nodal stage.

Results: On corelation more than T stage, N stage and primary tumour location had a significant impact on Dmax. With a median follow-up of 17.9 months, the incidence of RIBP is 6.67%. The 2-year disease free survival and 2-year Overall Survival are 53.7% and 59.4%, respectively.

Conclusions: In oropharyngeal/hypopharyngeal primaries and in advanced nodal disease, BP receives higher doses contributing to RIBP. Primary tumor and nodal stage also impacted V60 and V66 of BP. Hence, contouring of BP as an OAR becomes imperative, and respecting the DVH parameters is essential.
Key words: head and neck neoplasms; radiation induced brachial plexopathy; chemoradiotherapy; quality of life; radiation tolerance; organs at risk

Introduction

Head and neck cancers (HNC) comprise nearly one-third (29.3%) of all cancers across various anatomic sites in India [1]. A majority of HNC patients (60–70%) present with locoregionally advanced disease (stage III, IVA and IVB), which carries a poor overall survival of less than 40% [2]. So, to optimize the chances for long term disease control, the modern standard of care is chemo-radiotherapy (CRT) [3]. CRT has shown a significant increase in survival rate. However, this approach goes with increased toxicity. Therefore, both the disease and its treatment affect the quality of life (QoL) [4]. As a result, considering the QoL of long-term survivors is crucial during the treatment of HNC patients [5]. The common acute toxicities that worsen QoL include xerostomia, mucositis, dysphagia, dysgeusia, dermatitis, and aspiration [6]. The conformal radiotherapy techniques, such as Intensity-Modulated Radiotherapy (IMRT), have shown promising outcomes in managing these toxicities [7]. For instance, parotid sparing IMRT has significantly reduced xerostomia, which is the most common late toxicity [8]. Additionally, there are less-researched late toxicities that may manifest months to years after treatment completion like subcutaneous fibrosis, thyroid function impairment, hearing impairment, and brachial plexopathy.

One of the known late toxicities in HNC is radiation-induced brachial plexopathy (RIBP), where RT can lead to direct axonal injury or damage the vasa nervorum, resulting in axonal ischemia and multifocal denervation. RIBP typically manifests with hypoesthesia, paraesthesia, and weakness in the affected limb and shoulder [9]. Due to these vague symptoms, RIBP diagnosis is often challenging during follow-up. Moreover, there is a paucity of literature on RIBP, and the reported incidence varies due to the lack of routine contouring of the brachial plexus (BP) as an organ at risk (OAR). Since RIBP is a late toxicity, the follow-up period required for symptom manifestation remains uncertain. Therefore, this study aims to report dose received by the BP in patients with HNC receiving radical radiotherapy, the factors contributing to dose variations in the BPs, and evaluate patients developing RIBP after CRT.

Materials and methods

Study design and setting

After obtaining Institutional Ethical Clearance, a prospective descriptive study was planned to analyse HNC patients who were scheduled for definitive CRT using the IMRT technique at the Department of Radiation Oncology, **XXXXXXXXXXXXXX**, from September 2020 to June 2022. A sample size of 30 was obtained using convenience sampling for the pilot study [10] and written informed consent was acquired from all the study patients. All HNC patients aged from 18–70 years with histo-pathologically proven cancer receiving radical radiotherapy with concurrent chemotherapy were included in the study. Patients who had undergone previous HNC surgery were excluded from the study. Post-operative patients were excluded from the study due to challenges in contouring the BP in post-operative necks, which can undergo anatomical disfiguration. Additionally, nerve-related issues, such as pain, in these patients may hinder the accurate assessment of RIBP.

Radiation therapy

All patients were treated with the IMRT technique on the Elekta Synergy linear accelerator. All OARs (except BP) were contoured following the Consensus Guidelines in the head and neck region [11]. BP was contoured as an OAR, as per the Hall et al. guidelines [12]. Contouring begins with identification of C4 and T2 vertebrae in the sagittal section (Fig. 1A). Bilateral anterior and middle scalene muscles from the level of C4 vertebra to its insertion on the first rib were marked (Fig. 1B). BP was contoured using a 2.5 mm brush tool from the neural foramina of C4 vertebra. Laterally, the contours were extended into the narrow space between the anterior and middle scalene muscles (Fig. 1B and 1C) till T2 vertebra. The volumes of interest include the gross disease and gross lymph nodes. For well-lateralized tumours of buccal mucosa only the ipsilateral neck nodes was included in the treatment field. In central lesions (tumours of soft palate, base of tongue, tip of tongue, larynx, hypopharynx, and nasopharynx) and in all other cases bilateral neck nodes were encompassed in the treatment field, following the consensus guidelines by Gregoire et al. [13]. As per our institutional protocol, a 3 mm planning target volume (PTV) margin was given for all cases [14]. Patients were treated using the simultaneous integrated boost (SIB) technique with a two-volume approach. The gross disease and neck nodes were treated to a total dose of 66 Gy in 30 fractions (2.2 Gy per fraction), while the clinical target volume (CTV) received a total dose of 54 Gy in 30 fractions (1.8 Gy per fraction). All patients received 5 fractions per week over 6 weeks. An optimal IMRT plan was generated using Monaco software version 6. The

planned objective was to ensure that 95% of the PTV would receive more than 95% of the prescribed dose. Additionally, it was aimed that not more than 10% and 1% of the volume should receive 107% and 110% of the planned dose, respectively. No dose constraints were imposed on BP and even if the PTV overlapped with the BP contour, priority was given to cover the target volume.

Chemotherapy

All patients received concurrent weekly Cisplatin chemotherapy. Cisplatin was administered at a dose of 40 mg/BSA per week. The number of chemotherapy cycles was titrated based on patient tolerance. Hydration, anti-emetics, and dose modifications were done according to the department protocol. Chemotherapy was not given after the completion of RT.

Study outcome

The primary objective of the study was to assess the radiation dose received by BP in patients with HNC treated with IMRT, and to correlate the dose received by BP with factors like location of primary, T and N categories. Using Dose-Volume Histograms (DVH), the BP volume in cc, Dmax, Dmean and D0.03 received by the BP were obtained. Similarly, the BP volume receiving 66 Gy (V66) and 60 Gy (V60) were acquired. The secondary outcome was to clinically evaluate for symptoms of RIBP, and to report overall survival (OS) and disease free survival (DFS). The RIBP was evaluated with a questionnaire during the follow-up visits. The study patients were evaluated once every three months for symptoms of RIBP using the symptomatic questionnaire which was modified by Chen at al. (15) from a previously validated instrument [16]. The questionnaire comprised the following 5 basic questions, requiring a “yes” or “no” answer:

1. Do you have any pain in your arm or hand?
2. Do you have any numbness or tingling of the hand or fingers?
3. Do you have any problems carrying and lifting objects with your arm?
4. Do you have any problems with your fingers, such as with writing or unscrewing a bottle?
5. Are there any contributory factors for the above-mentioned complaints?

In the event of a patient developing symptoms of RIBP, the corresponding doses to the Brachial Plexus (BP) were correlated. OS was defined as the period from the time of diagnosis to death due to any cause. DFS was defined as the period from the time of diagnosis to any disease event, such as recurrence (locoregional or distant), progression, or death due to any cause.

Statistical analysis

Data was analysed using SPSS v.24. All categorical data was summarized using frequency and percentages, all continuous data was described using mean and standard deviation or median and inter quartile range based on the distribution. ANOVA or Kruskal Wallis test was applied to study the correlation of dose (Dmax, V66 and V60) with tumour and nodal factors. P-value was considered significant at 5% level of significance for all comparisons. Both OS and DFS were analysed with Kaplan-Meier survival methods.

Results

A total of 30 histologically proven HNC patients consecutively treated with definitive radiation using IMRT with concurrent chemotherapy from September 2020 to June 2022 in Department of Radiation Oncology of our institute were prospectively analysed. The median follow-up time was 17.9 months. Baseline characteristics of the patients were summarised in Table 1. The median age group of our patients is 58 years [interquartile range (IQR): 44.25–62]. Among the study population, 70% of the patients were diagnosed with Stage IV disease. The location of the primary tumor was predominantly in the oral cavity (33.33%), followed by the larynx (30%) and oropharynx (26.67%). Twelve patients had bilateral gross lymph nodes and more than 70% of the patients had received at least 4 cycles of concurrent chemotherapy with weekly cisplatin. All patients received the prescribed dose of 66 Gy.

BP was contoured as an OAR in all 30 patients bilaterally, resulting in a total of 60 BP contours. The BP volume, Dmax, BP mean, D0.03, V66, and V60 dose received by the right and left BP are shown in Table 2. The Dmax dose received by the right and left BP was 62.594 Gy ± 4.65 Gy and 60.97 Gy ± 10.95 Gy, respectively. The proportion of patients receiving Dmax doses of ≤ 60 Gy, 61-65 Gy, and > 65 Gy are 43.33%, 26.67% and 30%, respectively, to the right BP and, 36.67%, 30% and 33.33%, respectively, to the left BP.

Factors affecting dose to BP

The Dmax, V66 and V60 were analysed in relation to T-category, N-category and primary tumor location (Tab. 3). The initial analysis revealed a significant difference in mean Dmax dose received by different T category. The mean dose was higher in lower T stage compared to higher T stage. When the mean Dmax dose was correlated with the location of the primary tumor using ANOVA analysis, a significant difference ($p = 0.02$) was observed. The BP received a higher dose in patients with N3b disease compared to those with lower nodal stages; however, the difference was not statistically significant. BP in patients with oropharyngeal/hypopharyngeal cancers had received a higher dose (66.24 Gy) compared to

other primary tumours. Correlation analysis using the Kruskal-Wallis test, as shown in Table 3, revealed that primary location, tumour and nodal stage had a significant impact on both V60 and V66.

Radiation induced brachial plexopathy — clinical outcome

With a minimum follow up of 16 months and maximum follow up of 32 months, only 2 patients reported symptoms related to RIBP based on the questionnaire administered during the 3-monthly follow-up after completion of treatment. One patient had right shoulder pain 25 months after completing treatment, with a Dmax dose to the right BP of 60.43Gy. The pain persisted for 3 months. Another patient developed right upper limb weakness and tingling sensation 21 months after treatment, with a Dmax dose to the right BP of 58.63Gy. These symptoms persisted for 8 months. Both patients were treated conservatively.

Survival outcome

After a median follow-up of 17.9 months, 19 patients were alive, 10 patients had locoregional progression and 1 patient was diagnosed with secondary malignancy. The 2-year DFS was 53.7% [35.3–81.59%, 95% confidence interval (CI)] (Fig. 2). Among the 11 deaths, 7 were attributed to cancer progression, 1 to heart failure, 1 to secondary cancer and the cause of death was unknown for 2 patients. The median survival was not achieved for the study cohort, and the 2-year OS was 59.4% (43–81.3%, 95% CI) (Fig. 3).

Discussion

In our study the mean brachial plexus volume was 12.62 cc. After a median follow-up of 17.9 months, 2 year DFS and 2 year OS were 53.7% and 59.4%, respectively. Recent systematic review and meta-analysis by Yan et al. suggested that the current BP constraints of 60–66 Gy are safe [17]. In 60% of our patients, BP received doses higher than 60 Gy, influenced significantly by N category and primary tumor location rather than T staging. Similar studies with the incidence and dose to BP along with the instrument used to determine the RIBP are presented in Table 4.

ANOVA analysis showed that patients with N3b disease had a higher mean Dmax (64.18 Gy) compared to those with N0 disease (59.79 Gy), but this difference was not statistically significant ($p = 0.35$). Similar findings were reported by Prakash et al. [18] who observed a statistically significant difference in BP dose with N category, with an average of 4.2 Gy

higher doses in patients with advanced nodal stage. Truong et al. [19] also reported an increased dose of 8.1 Gy to the BP in advanced stage nodal disease.

In the study by Prakash et al. [18], patients with T4 tumours received a significantly higher dose to the BP compared to patients with T1 disease. In our study, when Dmax was correlated to the T category, a significant difference ($p = 0.0007$) was also observed. However, on subgroup analysis, the mean Dmax dose in patients with T4b tumours was found to be lower than in patients with T1 disease. This disparity can be attributed to the prevalence of T3 and T4 lesions, primarily affecting the oral cavity/nasopharynx, while laryngeal/hypopharyngeal lesions, often in proximity to the brachial plexus, are mainly T1 or T2 diseases. This factor might have influenced the relationship between the T stage and the Dmax dose. In addition, the N stage might also have influenced the observed inverse relationship as the analysis was only a univariate analysis.

As mentioned earlier, the dose to the neck region is relatively small in cases of oral cavity and nasopharynx primary lesions, as the gross disease is located away from the brachial plexus. However, in patients with oropharyngeal or laryngeal disease, the primary tumor itself receives a dose of 6600 cGy and is in close proximity to the BP. So, on correlating the primary tumor with Dmax using ANOVA analysis, a statistically significant difference with higher dose deposition in patients with oropharyngeal and hypopharyngeal cancers was observed.

The highest recorded Dmax dose was 73.68 Gy (0.001 cc) in a patient with oropharyngeal malignancy, with a T stage of T1 and N stage of N3b. This suggests that besides the T category and primary location of the tumor, the N staging and its location also influence the dose to the brachial plexus.

Thomas et al. [20], in a retrospective analysis of 68 head and neck squamous cell carcinoma (HNSCC) patients who received definitive or adjuvant RT, observed that tumour and nodal stage had significantly influenced both V50 and V60 values. In our study, we correlated the median values of V60 and V66 parameters and found a statistically significant difference with primary tumour, T stage, and N stage. However, to determine the correlation of V60 and V66 parameters with the incidence of RIBP, a longer follow-up is needed.

In the present study, only two patients (6.67%) developed symptoms of RIBP during the median follow-up of 17.9 months. Despite a modest 7% incidence rate of RIBP, contouring the BP in HNC cases is essential because its impact on QoL remains less explored unlike the common late side effects like xerostomia, mucositis and dysphagia. By implementing BP contouring with imposed constraints, we have the opportunity to mitigate the 7% toxicity

associated with RIBP which may significantly improve the patient outcomes and overall QoL. Treatment-related factors, such as post-surgery and chemotherapy, have been known to contribute to the incidence of RIBP according to previous studies [20, 21]. However, in our study, we only included patients receiving definitive radiation with concurrent chemotherapy. Therefore, these factors will not be considered as confounders in our analysis. As this is a prospective study, we could administer the questionnaire at 3 monthly intervals during the follow-up period to assess the development of symptoms of RIBP.

Limitations of the present study

Our study has its own limitations. Firstly, the RIBP incidence rate of 6.67% is based on a median follow-up of only 17.9 months. So there is need for longer follow up as long term studies had demonstrated higher incidence rates. Secondly, inherent bias might be associated with our study design; but we have tried to overcome this by including all the consecutive patients treated at our institution. Lastly, the sample size of 30, while deemed sufficient for a pilot study, may warrant consideration for a larger scale study in the future.

Conclusion

The primary tumor and nodal stage also impacted V60 and V66 of the brachial plexus. Oropharyngeal and hypopharyngeal primaries and advanced nodal disease led to higher doses to the brachial plexus, potentially contributing to radiation-induced brachial plexopathy. Contouring the brachial plexus as an OAR and respecting dose volume parameters like Dmax, V60, and V66 becomes essential. During our study with a median follow-up of 17.9 months, the incidence of RIBP was only 6.67%, indicating the need for longer follow-up to determine RIBP incidence accurately.

Statement of ethics

The study was approved by the Institutional Ethics Committee of St. Johns Medical College, Bangalore, with IEC reference No: 336/2020 and informed consent was obtained from all study participants.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgement

The first author is grateful to Mrs. Karthika (Medical Physicist), Mrs. Swetha Natanam and Ms. Kiruba (Medical Physicist) for their unlimited support during this entire study. I am also

grateful to my junior colleagues for the extended co-operation during the analysis of the patients.

Financial support

Nil

Author contributions

Study concepts: H.N.A.F., N.S., S.M.; study design: H.N.A.F., N.S., S.M.; data acquisition: H.N.A.F., D.C.T., S.M., J.S.MG, N.S., R.P.K.; quality control of data and algorithms: H.N.A.F., N.S., S.M.; data analysis and interpretation: H.N.A.F., N.S., S.M., J.S.MG; statistical analysis: J.M.R.; manuscript preparation: H.N.A.F., S.M., N.S., A.H.U.; manuscript editing: H.N.A.F., S.M., N.S., A.H.U.; manuscript review: H.N.A.F., S.M., N.S., A.H.U.

Data availability

The data that support the findings of the current study are available from the corresponding author upon reasonable request.

1. **References**Sathishkumar K, Chaturvedi M, Das P, et al. Cancer incidence estimates for 2022 & projection for 2025: Result from National Cancer Registry Programme, India. Indian J Med Res. 2022; 156(4&5): 598–607, doi: 10.4103/ijmr.ijmr_1821_22, indexed in Pubmed: 36510887.
2. Monnerat C, Faivre S, Temam S, et al. End points for new agents in induction chemotherapy for locally advanced head and neck cancers. Ann Oncol. 2002; 13(7): 995–1006, doi: 10.1093/annonc/mdf172, indexed in Pubmed: 12176777.
3. Givens DJ, Karnell LH, Gupta AK, et al. Adverse events associated with concurrent chemoradiation therapy in patients with head and neck cancer. Arch Otolaryngol Head Neck Surg. 2009; 135(12): 1209–1217, doi: 10.1001/archoto.2009.174, indexed in Pubmed: 20026818.
4. Rathod S, Gupta T, Ghosh-Laskar S, et al. Quality-of-life (QOL) outcomes in patients with head and neck squamous cell carcinoma (HNSCC) treated with intensity-modulated radiation therapy (IMRT) compared to three-dimensional conformal radiotherapy (3D-CRT): evidence from a prospective randomized study. Oral Oncol. 2013; 49(6): 634–642, doi: 10.1016/j.oraloncology.2013.02.013, indexed in Pubmed: 23562564.
5. Funk GF, Karnell LH, Christensen AJ. Long-term health-related quality of life in survivors of head and neck cancer. Arch Otolaryngol Head Neck Surg. 2012; 138(2): 123–133, doi: 10.1001/archoto.2011.234, indexed in Pubmed: 22248560.
6. Trotti A, Bellm LA, Epstein JB, et al. Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review. Radiother Oncol. 2003; 66(3): 253–262, doi: 10.1016/s0167-8140(02)00404-8, indexed in Pubmed: 12742264.
7. Lee NY, Le QT. New developments in radiation therapy for head and neck cancer: intensity-modulated radiation therapy and hypoxia targeting. Semin Oncol. 2008; 35(3): 236–250, doi: 10.1053/j.seminoncol.2008.03.003, indexed in Pubmed: 18544439.

8. Gupta T, Kannan S, Ghosh-Laskar S, et al. Systematic review and meta-analyses of intensity-modulated radiation therapy versus conventional two-dimensional and/or or three-dimensional radiotherapy in curative-intent management of head and neck squamous cell carcinoma. PLoS One. 2018; 13(7): e0200137, doi: 10.1371/journal.pone.0200137, indexed in Pubmed: 29979726.

9. Schierle C, Winograd JM. Radiation-induced brachial plexopathy: review. Complication without a cure. J Reconstr Microsurg. 2004; 20(2): 149–152, doi: 10.1055/s-2004-820771, indexed in Pubmed: 15011123.

10. Golzar J, Noor S, Tajik O. Convenience Sampling. Int J Educ Lang Stud. 2022; 1(2): 72–77, doi: 10.22034/ijels.2022.162981.

11. Brouwer CL, Steenbakkers RJ, Bourhis J, et al. CT-based delineation of organs at risk in the head and neck region: DAHANCA, EORTC, GORTEC, HKNPCSG, NCIC CTG, NCRI, NRG Oncology and TROG consensus guidelines. Radiother Oncol. 2015; 117(1): 83–90, doi: 10.1016/j.radonc.2015.07.041, indexed in Pubmed: 26277855.

12. Hall WH, Guiou M, Lee NY, et al. Development and validation of a standardized method for contouring the brachial plexus: preliminary dosimetric analysis among patients treated with IMRT for head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2008; 72(5): 1362–1367, doi: 10.1016/j.ijrobp.2008.03.004, indexed in Pubmed: 18448267.

13. Biau J, Lapeyre M, Troussier I, et al. Selection of lymph node target volumes for definitive head and neck radiation therapy: a 2019 Update. Radiother Oncol. 2019; 134: 1–9, doi: 10.1016/j.radonc.2019.01.018, indexed in Pubmed: 31005201.

14. Chen AM, Farwell DG, Luu Q, et al. Evaluation of the planning target volume in the treatment of head and neck cancer with intensity-modulated radiotherapy: what is the appropriate expansion margin in the setting of daily image guidance? Int J Radiat Oncol Biol Phys. 2011; 81(4): 943–949, doi: 10.1016/j.ijrobp.2010.07.017, indexed in Pubmed: 20932680.

15. Chen AM, Wang P, Daly ME, et al. Dose–Volume Modeling of Brachial Plexus-Associated Neuropathy After Radiation Therapy for Head-and-Neck Cancer: Findings From a Prospective Screening Protocol. Int J Radiat Oncol Biol Phys. 2014; 88(2): 771–777, doi: 10.1016/j.ijrobp.2013.11.191, indexed in Pubmed: 24606846.

16. Hoeller U, Rolofs K, Bajrovic A, et al. A patient questionnaire for radiation-induced brachial plexopathy. Am J Clin Oncol. 2004; 27(1): 1–7, doi: 10.1097/01.coc.0000107891.65644.46, indexed in Pubmed: 14758125.

17. Yan M, Kong W, Kerr A, et al. The radiation dose tolerance of the brachial plexus: A systematic review and meta-analysis. Clin Transl Radiat Oncol. 2019; 18: 23–31, doi: 10.1016/j.ctro.2019.06.006, indexed in Pubmed: 31309161.

18. Prakash BB, Yathiraj PH, Sharan TK, et al. Dosimetric analysis and clinical outcomes of brachial plexus as an organ-at-risk in head-and-neck cancer patients treated with intensity-modulated radiotherapy. J Cancer Res Ther. 2019; 15(3): 522–527, doi: 10.4103/jcrt.JCRT_959_17, indexed in Pubmed: 31169214.

19. Truong MT, Romesser PB, Qureshi MM, et al. Radiation dose to the brachial plexus in head-and-neck intensity-modulated radiation therapy and its relationship to tumor and nodal stage. Int J Radiat Oncol Biol Phys. 2012; 84(1): 158–164, doi: 10.1016/j.ijrobp.2011.10.079, indexed in Pubmed: 22300574.

20. Thomas TO, Refaat T, Choi M, et al. Brachial plexus dose tolerance in head and neck cancer patients treated with sequential intensity modulated radiation therapy. Radiat Oncol. 2015; 10: 94, doi: 10.1186/s13014-015-0409-5, indexed in Pubmed: 25927572.

21. Metcalfe E, Etiz D. Early transient radiation-induced brachial plexopathy in locally advanced head and neck cancer. Contemp Oncol (Pozn). 2016; 20(1): 67–72, doi: 10.5114/wo.2015.55876, indexed in Pubmed: 27095943.

Figure 1. Delineation of brachial plexus (BP). **A.** Identification of C4, T1, and T2 vertebral levels in sagittal section; **B.** Axial section at the level of neural foramina; **C.** Axial section where there is no neural foramina. (*Green* — right anterior scalene muscles, *Violet* — right middle scalene muscles, *Blue* — left anterior scalene muscles, *Yellow* — left middle scalene muscles, *Cyan* — right BP, *Pink* — Left BP); **D.** Three dimensional reconstruction of BP

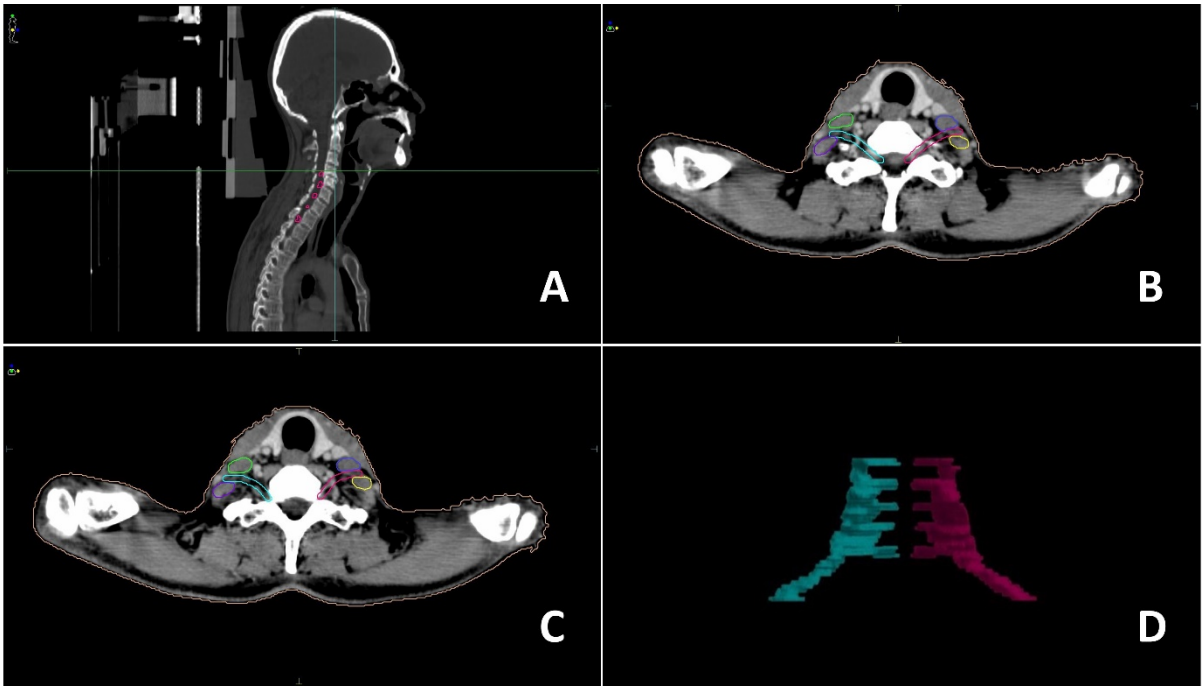


Figure 2. Kaplan Meier Survival curve of disease free survival

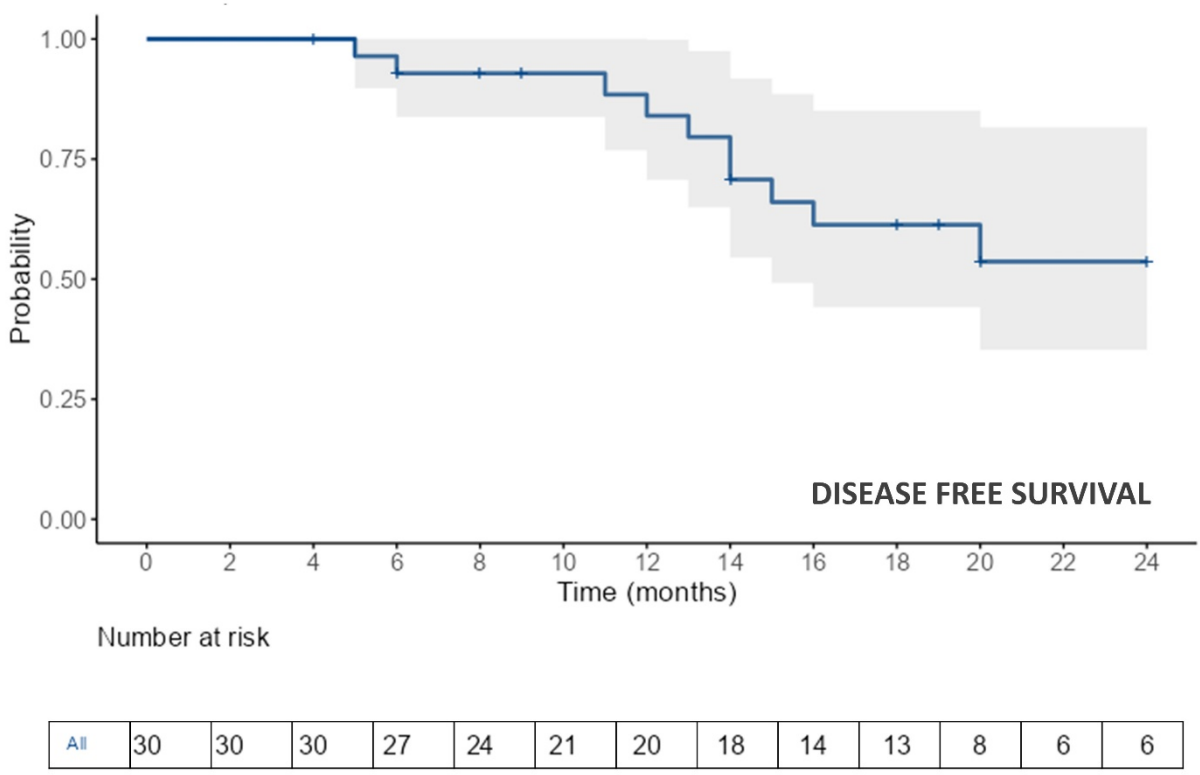
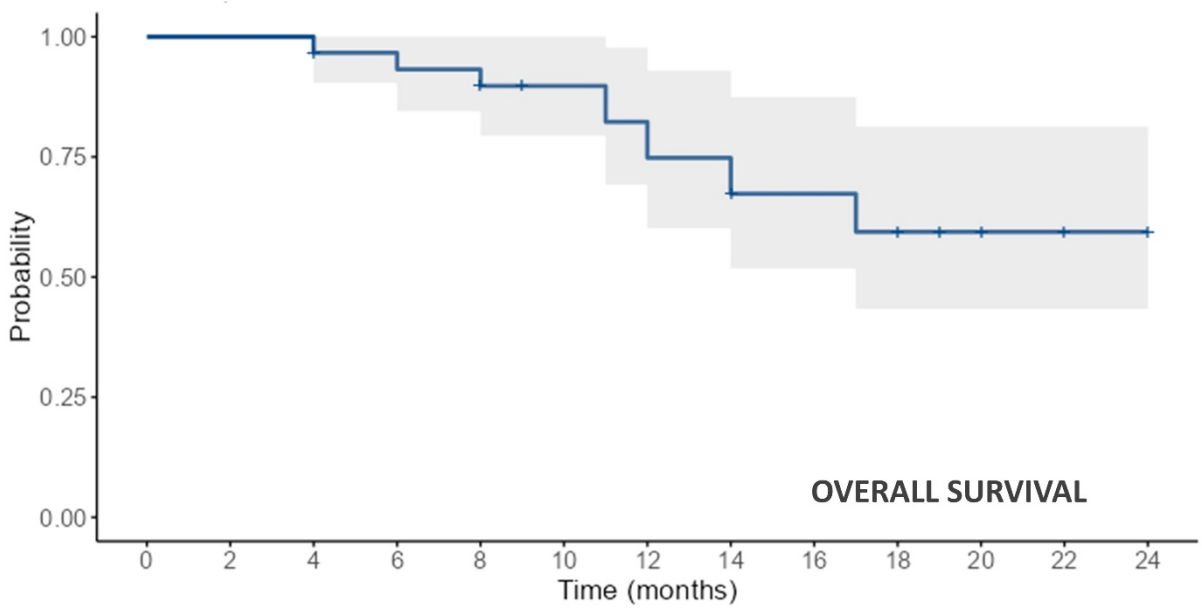


Figure 3. Kaplan Meier survival curve of overall survival



Number at risk

All	30	30	30	28	27	24	22	20	17	15	10	9	7