EJMO

DOI: 10.14744/ejmo.2024.45801
EJMO 2024;8(3):336–340

Research Article

Dosimetric Evaluation of Cervical Oesophagus as an Organ at Risk in Breast Cancer Radiotherapy

Naveen Thimmaiah,[1] Nithin Bhaskar,[1] Ayushee Saini,[1] Rashmi Shivananjappa,[1] Tanvir Pasha,[1] Sathiyaraj Palanivel,[2] Nikhila Radhakrishna[1]

[1]Department of Radiation Oncology, Kidwai Memorial Institute of Oncology, Bangalore, India
[2]Department of Radiation Physics, Kidwai Memorial Institute of Oncology, Bangalore, India

Abstract

Objectives: The current study intends to analyze dose-volume parameters of the cervical oesophagus (CO) as an organ at risk (OAR) during radiotherapy (RT) to the supraclavicular fossa (SCF) in breast cancer (BC) patients.

Methods: Plans of 97 consecutive BC patients receiving 40 Gy/15 fractions were reviewed. The CO was retrospectively contoured from the cricopharyngeal junction to the sternal notch. Dmax, Dmean, V10, V20, and V30 to the CO, as well as the RT technique, were noted.

Results: 53/97 patients had right BC, and 44/97 had left BC. 69/97, 17/97, and 11/97 were treated with 3DCRT, IMRT, and VMAT, respectively. Mean length of CO=8.3±1.3 cm; CO-Dmax=37.95±5.16 Gy; Dmean=17.48±7.7 Gy.

Mean V10=60.12±26%, V20=41.75±24%, V30=25.04±19.8%. Patients with right BC had a lower CO-Dmax of 36.45±6.9 Gy and lower Dmean=14.54±7.12 Gy to CO, compared to left BC with CO-Dmax=39.75±2.4 Gy (p=0.017), and Dmean=21.2±7.2 Gy (p=0.0001).

Conclusion: The cervical oesophagus receives significant doses in breast cancer patients during SCF irradiation, especially in left-sided breast cancer patients. Restricting and reporting doses to CO as an OAR must be adopted as a routine practice.

Keywords: Breast cancer, cervical oesophagus, supraclavicular fossa

Cite This Article: *Thimmaiah N, Bhaskar N, Saini A, Shivananjappa R, Pasha T, Palanivel S, et al. Dosimetric Evaluation of Cervical Oesophagus as an Organ at Risk in Breast Cancer Radiotherapy. EJMO 2024;8(3):336–340.*

Breast cancer (BC), being the leading cancer, represents 11.7% of the global cancer burden. Indian statistics reveal a steady rise of about 39% in the age-standardized incidence of BC over the last 26 years, accounting for 13.5% of all cancer cases. It has also been observed that a larger number of patients are presenting with BC at a younger age.[1] With improvements in diagnostic and treatment options for BC, the key focus has shifted towards improving the quality of life of survivors.

Adjuvant radiotherapy (RT) to the breast/chest wall, along with regional nodes (supraclavicular fossa (SCF)/axillary nodes), plays a significant role in the multimodality management of breast cancer (BC). Adjuvant RT reduces locoregional recurrence and offers improvement in overall survival after both breast conservation surgery and mastectomy.[2] The heart, lungs, and brachial plexus have been extensively studied as organs at risk (OARs) in breast/chest wall radiotherapy. However, the dose received by the cervical oesophagus (CO) during regional nodal irradiation (RNI) has been less commonly explored.

The CO lies in close proximity to the medial border of the supraclavicular field. A large part of the planning target

Address for correspondence: Nikhila Radhakrishna, MD. Department of Radiation Oncology, Kidwai Memorial Institute of Oncology, Bangalore, India
Phone: 09655403407 **E-mail:** dr.nikhilakmio@gmail.com

Submitted Date: November 17, 2023 **Revision Date:** January 21, 2024 **Accepted Date:** June 18, 2024 **Available Online Date:** September 10, 2024

volume (PTV) often overlaps the CO. Several patients receiving adjuvant radiotherapy involving regional nodes complain of acute odynophagia during weekly review. The incidence of esophagitis with regional nodal irradiation in breast cancer patients has been observed to be as high as 40-70%,[3,4] although not commonly reported. With hypofractionated radiotherapy of 40 Gy in 15 fractions becoming the standard of care both for the breast/chest wall and the regional nodes, the impact of this hypofractionation on doses to the CO requires further evaluation.[5,6] With progressively increasing overall survival in BC, patients receiving RT have been observed to have a higher incidence of secondary esophageal cancer compared to the general population (95% confidence interval 1.34–1.71, p<.05).[7] Journy et al.[8] observed 252 women who developed oesophageal cancer after breast cancer radiotherapy, suggesting that the risk of oesophageal cancer increases by 7.1% per Gy (95% confidence interval 1.9–20.6) median oesophagus dose.

The current study intends to document the dose-volume parameters of the CO as an organ at risk (OAR) during regional nodal irradiation in BC.

Aims and Objectives

To assess dose-volume parameters for the cervical oesophagus as an OAR during breast/chest wall radiation with regional nodal irradiation for locally advanced and node-positive breast cancers.

Methods

Records of 100 consecutive patients with BC treated between May 2021 and May 2023 were selected for the current study. All patients with T3-T4, N1-2 stages who received adjuvant RT to the breast or chest wall, along with the supraclavicular fossa, were selected for the study.

All patients were simulated in the supine position on a breast board with arms abducted overhead. A radio-opaque marker was used to delineate the palpable breast tissue circumferentially for cases with an intact breast. The scan extended from the mandible cranially to the 2nd lumbar vertebra with 0.3 cm CT slices. The head was either turned or kept straight during the simulation. Being a retrospective study, this factor could not be controlled and was therefore used as a factor to study the dosimetric differences with different neck positions.

Table 1. Dose volume parameters of cervical oesophagus for right sided versus left sided breast cancer

Parameter	Right Side (53)	Left Side (44)	p
D_{mean} (Gy)	14.54±7.12	21.2±7.2	0.0001*
D_{max} (Gy)	36.45±6.9	39.75±2.4	0.003*
V10 (%)	53.2±26.1	69.66±22.5	0.001*
V20 (%)	33.16±21.7	52.85±23.56	0.0001*
V30 (%)	16.83±15.19	34.92±20.61	0.0001*

* statistically significant.

Table 2. Dose volume parameters of cervical oesophagus for head straight versus head turned to opposite side during breast radiotherapy

Parameter	Head straight (72)	Head Turned (25)	p
D_{mean} (Gy)	16.47±7.9	20.25±7.09	0.04*
D_{max} (Gy)	37.57±6.4	39.14±2.10	0.24
V10 (%)	57.9±28.0	67.18±20.05	0.13
V20 (%)	38.79±24.62	50.94±24.04	0.03*
V30 (%)	22.29±18.0	34.57±22.72	0.008*

* statistically significant.

Target volume delineation of the breast/chest wall and supraclavicular nodal clinical target volume (CTV) was performed based on the Radiation Therapy Oncology Group (RTOG) guidelines. All T3-T4 or node-positive patients received radiation to the supraclavicular fossa. A PTV margin of 5 mm was used according to institutional protocol.

A standard dose of 40 Gy/15 fractions using 6 MV photon energy was planned and delivered for all patients. The planning technique used was either 3-dimensional conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), or volumetric modulated arc therapy (VMAT). Patients with breast conservation surgery received a lumpectomy cavity boost as per standard indications.

Contouring of Cervical Oesophagus

Upon the already planned and delivered cases, the cervical oesophagus (CO) was retrospectively contoured. According to the anatomical classification of the oesophagus in the American Joint Cancer Committee Cancer Staging Manual 8th Edition,[9] the cervical oesophagus lies in the neck, extending superiorly from the hypopharynx to the thoracic inlet inferiorly. Hence, the cranial-caudal extent of the CO was delineated from the cricopharyngeal junction to the sternal notch. The following dose-volume parameters received by the CO were documented: D_{max}, D_{mean}, V10, V20, V30, neck position, and length of the CO.

Results

100 patients were selected for this retrospective dosimetric study. 97/100 patients received RT to the breast/chest wall and supraclavicular nodal area. 53/97 patients had right BC, and 44/97 patients had left BC with dosimetric parameters

as elaborated in Table 1.

69/97, 17/97, and 11/97 were treated with 3DCRT, IMRT, and VMAT, respectively. 72 patients were treated with a straight neck, and 25 with the head and neck turned to the contralateral side with doimetric parameters as elaborated in Table 2. The mean length of the CO was 8.3±1.3 cm. The overall D_{max} of CO was 37.95±5.16 Gy, and the D_{mean} was 17.48±7.7 Gy. Mean V10=60.12±26%, V20=41.75±24%, V30=25.04±19.8%. Other DVH parameters have been elaborated in Table 3.

Discussion

As part of the multimodality management of breast cancer (BC), adjuvant radiotherapy is delivered to the breast/chest wall along with regional nodal irradiation (RNI) to the supraclavicular nodes alone or in combination with axillary RT.[10] RNI to the supraclavicular fossa (SCF) alone is indicated in all patients with four or more involved axillary nodes, Level III involved nodes, or stage III BC post-neoadjuvant chemotherapy. RT to the SCF nodes is also considered in patients with 1-3 positive nodes who have high-risk features such as grade 3, T3-T4 tumors, extranodal extension, or lymphovascular invasion.[10] Despite a significant overlap of the PTV over the cervical oesophagus in patients receiving RT to the SCF, very few breast cancer radiotherapy dosimetry studies, about 5% (42/831 studies), have reported doses to the oesophagus.[11]

The oesophagus has been elaborately evaluated as an OAR in lung cancer radiotherapy.[12] The maximum dose to the oesophagus has shown a significant correlation ($p \leq 0.05$) with severe esophagitis in lung cancer radiotherapy with conventional fractionation.[13] Some studies have demonstrated that other parameters, such as a mean dose <34 Gy[14] or the V20[15] and V35[16] or V60,[17,18] may be significant DVH parameters that correlate with esophagitis of Grade 2 and above. The current study has, therefore, evaluated V10, V20, and V30 to the CO, considering the total prescribed dose of 40 Gy/15 Fr.

Table 3. Dose volume parameters of cervical oesophagus for 3DCRT vs IMRT vs IMRT techniques

D_{max}	3DCRT	IMRT	VMAT	p (one way ANOVA)
N	69	17	11	
D_{max}	37.30	39.59	39.53	0.2
Std.Dev.	6.19	1.74	5.49	
D_{mean}	15.99	22.02	21.30	0.003*
Std.Dev.	7.91	5.77	5.55	
V10	54.29	84.38	69.90	0.0001*
Std.Dev.	23.09	17.44	26.45	
V20	39.37	52.46	48.10	0.10
Std.Dev.	24.27	25.44	18.26	
V30	25.03	27.78	23.09	0.81
Std.Dev.	21.20	19.32	11.20	

* statistically significant.

Dosimetric data of 414 breast cancer patients who received radiation doses incidentally to the oesophagus during breast radiotherapy between 1943-1996 in North America and Europe were extracted by Lamart et al.[19] SCF and internal mammary nodal fields had been used for 85% of patients by the 2-dimensional technique. The population median dose received by the cervical oesophagus was 38 Gy, mainly by the SCF field. The population median dose received by the upper and middle thoracic oesophagus was 32 Gy and 25 Gy, respectively, mainly contributed by the internal mammary fields. However, these are doses reconstructed on a computational phantom model of the human body.

Duane et al.[11] have highlighted the esophageal doses during various schedules of breast radiotherapy between 2010-2020. The CO received negligible doses of 0.2-1.8 Gy during partial breast RT or whole breast/chest wall RT with no SCF irradiation. However, the dose received by the CO during nodal irradiation ranged from 11.4 Gy to 34.4 Gy in the various schedules, with higher doses observed in the IMRT technique.[11] The studies in this review are a combination of those with and without regional nodal irradiation. The current study has considered only patients who have received RT to the SCF with or without axillary nodal RT.

West et al.[20] have reported the factors affecting radiation-induced esophagitis in patients with early breast cancer (EBC) receiving supraclavicular RT to a conventional dose of 50 Gy/25 Fr. They reported a higher incidence of grade 2 and above esophagitis for a mean esophageal dose of ≥31 Gy compared to CO D_{mean} <31 Gy (18/24 versus 6/24, respectively, p=0.025). They included the pharynx above the cricopharyngeal junction within the esophageal contour in patients whose SCF volumes extended beyond the cricoid cartilage. They reported higher esophageal doses with higher grade 2 toxicity in patients with at least 1 cm of the pharynx included in SCF fields (15/24 versus 9/24 (37.5%) p=0.0116). We, however, believe that the SCF fields should not be extended cranially beyond the level of the cricoid cartilage in BC patients. We have used the RTOG guidelines for nodal target volume delineation and hence have limited the cranial extent of the esophageal contours to the cricopharyngeal junction.

Left-sided BC patients consistently received higher doses to the CO compared to right-sided BC across multiple studies.[11,13,14,21] The same dosimetric observation was noted in the current study as well. Patients with right BC

had a statistically significant lower D_{max} of 36.43±7.8 Gy and D_{mean}=15.3±7.1 Gy to CO, compared to left BC with D_{max}=40.70±1.5 Gy (p=0.017), D_{mean}=23.4±5.8 Gy (p=0.0001) to CO. The current study has used a dose of 40 Gy/15 fractions and believes the effects of hypofractionation on the CO need further clinical evaluation. The 2 Gy equivalent dose (EQD2) D_{max} received by CO in right versus left-sided BC was 40.23±9.26 Gy versus 45.01±3.97 Gy, respectively, and D_{mean} of 12.21±7.12 Gy versus 19.18±8.04 Gy, respectively, calculated with an alpha/beta ratio of 3. Wang et al.[3] used 43.5 Gy/15 fractions and demonstrated a higher incidence of grade 2 and above esophagitis in patients with left-sided BC than in those with right-sided BC (52.3% vs. 29.7%; p<0.001) and among patients with CO V25>20% (35.9% vs. 60.9%; p=0.04).

No statistically significant differences were observed in the higher doses to CO with respect to the technique of RT planning used (3DCRT vs. IMRT) in this study. However, the low dose volume of the CO (V10) was significantly higher with IMRT and VMAT than 3DCRT. A higher incidence of grade 2 esophagitis was observed with IMRT versus 3DCRT by Yaney et al.[21] (23.6% vs. 10.9%; p<0.001), where 531 patients had been treated with 50 Gy/25 Fr. This could be attributed to the low-dose bath with multiple beam angles and the possible dose dumping during IMRT planning since the oesophagus is not routinely contoured as an OAR.

Radiotherapy to the SCF may be planned and delivered with the patient positioned with the head straight or turned to the contralateral side as per the conventional practice during 2D radiotherapy, as per clinical choice. A significantly higher Dmean, V20 (corresponding to the volume receiving an EQD2=17.3 Gy), and V30 (corresponding to the volume receiving an EQD2=30 Gy) were observed in patients with the head turned to the contralateral side (V20 - 51% versus 39%, p=0.03) and (V30 - 35% versus 22%, p=0.008) in comparison with the head positioned straight. A similar higher Dmean to the oesophagus has been observed by Pulickal et al.[22] in the tilted neck 22.94 (±9.53) Gy versus straight neck group 18.57 (±7.30) Gy and p=0.023. This suggests the convenience of treating breast cancer patients with the head and neck kept straight during RNI.

A large population-based study by Sun et al.[7] has investigated the risk of developing secondary esophageal cancer (SECs) in BC survivors between those who received adjuvant radiotherapy (2,55,135 patients) versus those who did not (2,68,367 patients) between 1975-2018. They identified adjuvant radiotherapy as a clear risk factor for the development of SECs. The BC patients receiving RT showed a greater standardized incidence ratio [1.52; 95% confidence interval [CI], 1.34–1.71, p<0.05)] for SECs. As prospective evaluations for the incidence of secondary esophageal cancer with such a large number of patients may not be practical, this study must be used to guide our steps to report esophageal doses during breast cancer radiotherapy and attempt to restrict the dose to the CO as an OAR.

The limitations of the current study are its retrospective dosimetric nature, as a result of which we are unable to propose a predictive dose cutoff for the development of radiation esophagitis.

Conclusion

The cervical oesophagus receives significant doses in breast cancer patients during SCF irradiation, especially in left-sided breast cancer patients. Restricting and reporting doses to the CO as an OAR must be adopted as a routine practice.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept: N.R., N.T.; Design: N.R., N.T.; Supervision: N.B., T.P.;.Materials: A.S., N.B., R.S., S.P.; Data Collection: A.S., R.S., N.B., N.R.; Literature search: A.S., N.B.; Writing: N.R., N.B., N.T.; Critical Review: All Authors.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209–49.
2. EBCTCG (Early Breast Cancer Trialists' Collaborative Group); McGale P, Taylor C, Correa C, Cutter D, Duane F, Ewertz M, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: Meta-analysis of individual patient data for 8135 women in 22 randomised trials. Lancet 2014;383:2127–35.
3. Wang DQ, Zhang N, Dong LH, Zhong YH, Wu HF, Zhong QZ, et al. Dose-volume predictors for radiation esophagitis in patients with breast cancer undergoing hypofractionated regional nodal radiation therapy. Int J Radiat Oncol Biol Phys 2023;117:186–97.
4. Zalfa Abdul A, Donald F, Sandesh BR, Krishnaraj H, Tony J, Lanisha SJ. Radiation-induced esophagitis in patients with breast cancer receiving supraclavicular nodal irradiation: A retrospective observational study. Cancer Res Stat Treat 2023;6:209–14.
5. Whelan TJ, Olivotto IA, Parulekar WR, Ackerman I, Chua BH, Nabid A, et al; MA.20 Study Investigators. Regional

nodal ırradiation in early-stage breast cancer. N Engl J Med 2015;373:307–16.
6. Haviland JS, Owen JR, Dewar JA, Agrawal RK, Barrett J, Barrett-Lee PJ, et al; START Trialists' Group. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. Lancet Oncol 2013;14:1086–94.
7. Sun Q, Chen Y, Li T, Ni B, Zhu X, Xu B, Li J. Risk and prognosis of secondary oesophagus cancer after radiotherapy for breast cancer. Sci Rep 2023;13:3968.
8. Journy N, Schonfeld SJ, Hauptmann M, Roberti S, Howell RM, Smith SA, et al. Dose-volume effects of breast cancer radiation therapy on the risk of second oesophageal cancer. Radiother Oncol 2020;151:33–9.
9. Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK, et al., editors. AJCC Cancer Staging Manual. New York: Springer International Publishing; 2017.
10. Northern Cancer Alliance. Breast cancer clinical guidelines. Available at: https://northerncanceralliance.nhs.uk/wp-content/uploads/2019/02/NCA-Breast-Cancer-Guidelines-v2-.10.pdf. Accessed Aug 14, 2024.
11. Duane FK, Kerr A, Wang Z, Darby SC, Ntentas G, Aznar MC, et al. Exposure of the oesophagus in breast cancer radiotherapy: A systematic review of oesophagus doses published 2010-2020. Radiother Oncol 2021;164:261–7.
12. Werner-Wasik M, Yorke E, Deasy J, Nam J, Marks LB. Radiation dose-volume effects in the esophagus. Int J Radiat Oncol Biol Phys 2010;76:S86–93.
13. Singh AK, Lockett MA, Bradley JD. Predictors of radiation-induced esophageal toxicity in patients with non-small-cell lung cancer treated with three-dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 2003;55:337–41.
14. Bradley JD, Bae K, Graham MV, Byhardt R, Govindan R, Fowler J, et al. Primary analysis of the phase II component of a phase I/II dose intensification study using three-dimensional conformal radiation therapy and concurrent chemotherapy for patients with inoperable non-small-cell lung cancer: RTOG 0117. J Clin Oncol 2010;28:2475–80.
15. Wei X, Liu HH, Tucker SL, Liao Z, Hu C, Mohan R, et al. Risk factors for acute esophagitis in non-small-cell lung cancer patients treated with concurrent chemotherapy and three-dimensional conformal radiotherapy. Int J Radiat Oncol Biol Phys 2006;66:100–7.
16. Belderbos J, Heemsbergen W, Hoogeman M, Pengel K, Rossi M, Lebesque J. Acute esophageal toxicity in non-small cell lung cancer patients after high dose conformal radiotherapy. Radiother Oncol 2005;75:157–64.
17. Palma DA, Senan S, Oberije C, Belderbos J, de Dios NR, Bradley JD, et al. Predicting esophagitis after chemoradiation therapy for non-small cell lung cancer: An individual patient data meta-analysis. Int J Radiat Oncol Biol Phys 2013;87:690–6.
18. Rodríguez N, Algara M, Foro P, Lacruz M, Reig A, Membrive I, et al. Predictors of acute esophagitis in lung cancer patients treated with concurrent three-dimensional conformal radiotherapy and chemotherapy. Int J Radiat Oncol Biol Phys 2009;73:810–7.
19. Lamart S, Stovall M, Simon SL, Smith SA, Weathers RE, Howell RM, et al. Radiation dose to the esophagus from breast cancer radiation therapy, 1943-1996: An international population-based study of 414 patients. Int J Radiat Oncol Biol Phys 2013;86:694–701.
20. West K, Schneider M, Wright C, Beldham-Collins R, Coburn N, Tiver K, et al. Radiation-induced oesophagitis in breast cancer: Factors influencing onset and severity for patients receiving supraclavicular nodal irradiation. J Med Imaging Radiat Oncol 2020;64:113–9.
21. Yaney A, Ayan AS, Pan X, Jhawar S, Healy E, Beyer S, et al. Dosimetric parameters associated with radiation-induced esophagitis in breast cancer patients undergoing regional nodal irradiation. Radiother Oncol 2021;155:167–73.
22. Pulickal SG, Bhaskaran R, Perumangat A, Reghu H, Moolath GB. Dosimetric evaluation of oesophagus in hypofractionated supraclavicular nodal irradiation in breast cancer- A retrospective observational study in a tertiary care cancer centre in Alappuzha, Kerala. J Evid Based Med Healthcare 2021;8:2974–9.