Research in Oncology
2024; Vol. 20, No. 2: 33-39
DOI: 10.21608/resoncol.2024.285976.1209

Original Article

Is Volumetric Modulated Arc Radiotherapy a Good Choice in the Treatment of Early Glottic Cancer: A Dosimetric Study

Rabab A. Abdel Moneim [1] ✉, Hanan S. Darwish [1], Ahmed F. Elhaggar [2], Radwa T. Abdel Rahman [2], Khaled A. Khalil [1]

[1] Department of Clinical Oncology and Nuclear Medicine, Kasr Al-Ainy Faculty of Medicine, Cairo University, Cairo, Egypt; [2] Medical Physics, Department of Clinical Oncology and Nuclear Medicine, Kasr Al-Ainy Faculty of Medicine, Cairo University, Cairo, Egypt

Abstract

Background: The extended survival of patients with early glottic cancer has heightened concerns about the long-term side effects of radiation therapy, which may negatively impact quality of life and increase the risk of non-malignant mortality. This study evaluated whether volumetric modulated arc radiotherapy (VMAT) offers improved target volume coverage and better protection of organs at risk (OARs) compared to three-dimensional conformal radiotherapy (3D-CRT) in patients with early glottic cancer.
Methods: Computed tomography (CT) images from 13 patients with early glottic cancer were analyzed to compare the dosimetric plans of 3D-CRT and VMAT. Dose-volume histogram (DVH) parameters were assessed across 26 treatment plans, including the homogeneity index (HI) and conformity index (CI) for the planning target volume (PTV). Specific dose-volume metrics for OARs, such as the carotid arteries, thyroid gland, and spinal cord, were also compared between the two modalities.
Results: VMAT plans demonstrated significantly higher PTV mean dose, PTV maximum dose, and volume receiving 95% of the prescribed dose compared to 3D-CRT plans ($p = 0.047$, 0.045, and <0.001, respectively). VMAT also showed superior homogeneity and conformity indices for the PTV ($p = 0.003$ and 0.001, respectively). Additionally, the mean doses to the right and left carotid arteries and the thyroid gland were significantly lower with VMAT ($p = 0.009$, 0.03, and <0.001, respectively).
Conclusion: VMAT provides superior dose-volume parameters for target coverage, homogeneity, and sparing of OARs compared to 3D-CRT in the treatment of early glottic cancer. These advantages suggest that VMAT may be particularly beneficial for patients at increased risk of cerebrovascular complications.

Keywords: Early glottic cancer, dosimetric comparison, VMAT, 3D-CRT, carotid sparing

Corresponding author: Rabab A. M. Abdel Moneim, MD, Department: Clinical oncology and nuclear medicine- Kasr El- Ainy Faculty of Medicine, Cairo University; Email: dr.rababahmed2014@cu.edu.eg

Received: 28-April-2024, **Accepted:** 21-August-2024, **Published online:** 17-November-2024

Introduction

Laryngeal cancer is the second most common form of head and neck cancer, and its management requires a multidisciplinary approach to preserve organ function, improve survival, and enhance quality of life.[1] Advances in radiation therapy techniques have improved the therapeutic ratio by effectively controlling tumor volume while minimizing damage to nearby organs at risk. Radiation therapy has been shown to improve 5-year outcomes, preserving function as well as voice quality and overall quality of life.[2]

Anatomically, the larynx is surrounded by various normal tissues, including the thyroid gland (which regulates metabolism, heart rate, and body temperature), carotid arteries, pharyngeal constrictor muscles, and arytenoid cartilage (which facilitates vocal cord movement).

Early glottic cancer (T1, T2), involving the true vocal cords and the posterior and anterior commissures, presents challenges for long-term survival, raising concerns about the late effects of radiation therapy. These late effects can significantly impact quality of life, leading to complications such as changes in phonation, hypothyroidism, dysphagia, xerostomia, vascular events, and an increased risk of non-malignant deaths, including cerebrovascular accidents, which can adversely affect long-term outcomes.[3, 4] Therefore, selecting the optimal technique to reduce toxicity to organs at risk while achieving effective treatment remains a critical challenge.

Modern radiation techniques such as volumetric modulated arc radiotherapy (VMAT) and three-dimensional conformal radiotherapy (3D-CRT) offer improved dose distribution for the planning target volume (PTV) while sparing normal tissues adjacent to the larynx. The treatment of locally advanced cases continues to be the focus of ongoing research. In this study, we compared VMAT and 3D-CRT treatment planning techniques for early glottic cancer to determine whether VMAT offers superior target volume coverage and better sparing of organs at risk compared to 3D-CRT.

Methods

Patient Selection

This comparative dosimetric study included the computed tomography (CT) images of thirteen patients diagnosed with histologically confirmed early-stage glottic squamous cell carcinoma. These patients received 3D-CRT as definitive radiation therapy. Staging was performed using direct laryngoscopy, tissue biopsy, and neck CT with contrast or magnetic resonance imaging (MRI) of the head and neck. The study period spanned from January 2021 to December 2022.

Planning CT Simulation and Volume Definitions

Patients were immobilized in a supine position with maximum head extension, using a 5-point thermoplastic head-neck-shoulder mask to ensure stability. Treatment planning CT scans were acquired from the top of the skull to the lower neck, with a slice thickness of 2.5 mm. The image data for each patient were then transferred to the treatment planning system (Eclipse, version 16.1; Varian Medical Systems, Palo Alto, CA, USA), where the clinical target volume (CTV), PTV, spinal cord, thyroid gland, and carotid arteries were delineated. Target volumes and doses were defined following guidelines from the International Commission on Radiation Units (ICRU).

For all thirteen patients, two treatment plans were developed—one using 3D-CRT and the other using VMAT—resulting in a total of 26 plans. Each plan used a total dose of 66 Gy (2 Gy per fraction) with a photon energy of 6 MV. All plans were normalized to ensure that at least 95% of the PTV received 100% of the prescribed dose.

Volume Definitions

- **Gross Target Volume (GTV):** Defined based on visible tumor identified through radiological imaging and endoscopic findings. The aim of delineating the GTV is to ensure that the tumor lesion is fully encompassed within the CTV.
- **Clinical Target Volume (CTV):** Included the entire larynx, extending from the inferior border of the hyoid bone superiorly to the bottom of the cricoid cartilage inferiorly. It also covered the arytenoid cartilage and posterior commissure posteriorly, as well as the anterior commissure and the entire thyroid cartilage anterolaterally.
- **Planning Target Volume (PTV):** Created by adding a 5-mm margin around the CTV to account for patient movements, such as swallowing, during radiation therapy.
- **Organs at Risk (OAR):** The spinal cord, thyroid gland, and carotid arteries were delineated as organs at risk, with specific focus on minimizing radiation exposure to these structures.

Treatment Planning

For dosimetric comparison, VMAT plans for each patient were created using the Eclipse treatment planning system. Conventional 3D-CRT plans utilized two opposed-lateral wedged fields. The wedge angle was selected to achieve the most optimal dose distribution within the PTV. The arc of the VMAT plans used a 197° clockwise (CW) gantry rotation from 276° to 79°. In both techniques, treatment was conducted using 6-MV photon energy on a linear accelerator with the Millennium 120-leaf multi-leaf collimators (MLCs) system (Clinac unique; Varian Medical Systems Inc.) and RT doses of 66 Gy (2Gy/fraction) were applied.

Comparison of Dosimetric Characteristics

Dose-volume histogram (DVH) parameters for the 26 treatment plans, along with specific dose-volume parameters, were analyzed in collaboration with a medical physicist to achieve optimal dose distribution. Initially, minimum (Dmin), mean (Dmean), and maximum (Dmax) doses were evaluated for both the PTV and OARs.

The following parameters were compared for the PTV between the two treatment techniques:

- Dose and volume receiving 95% of the prescribed dose
- Volume receiving 98% of the prescribed dose
- Dose to 2% of the volume
- Homogeneity Index (HI)
- Conformity Index (CI)

The HI and CI were calculated using the following formulas:

- Conformity Index (RTOG): CI = VRI / TV, where VRI is the reference isodose volume and TV is the target volume. The range is 0–1, with 1 indicating high conformity.
- Homogeneity Index (RTOG): HI = Imax / RI, where Imax is the maximum isodose in the target, and RI is the reference isodose.

Additionally, specific dose-volume parameters were assessed and compared for the following OARs:

- Carotid Arteries: V35 and V50
- Thyroid Gland: V30 and V50
- Spinal Cord: Dmax

Statistical Analysis

Data were compiled using Microsoft Excel 2013, and comparisons were made between doses to OARs, tumor dose coverage, CI, HI, and minimum, mean, and maximum dose volumes for the target volume and OARs across the two dosimetric plans. A paired t-test was conducted to determine differences within each planning technique, with a p-value of <0.05 indicating statistical significance. Statistical analyses were performed using IBM SPSS version 22.0.

Results

Figure 1 shows an axial CT image with isodose lines from a VMAT plan for a patient with early stage glottic cancer.

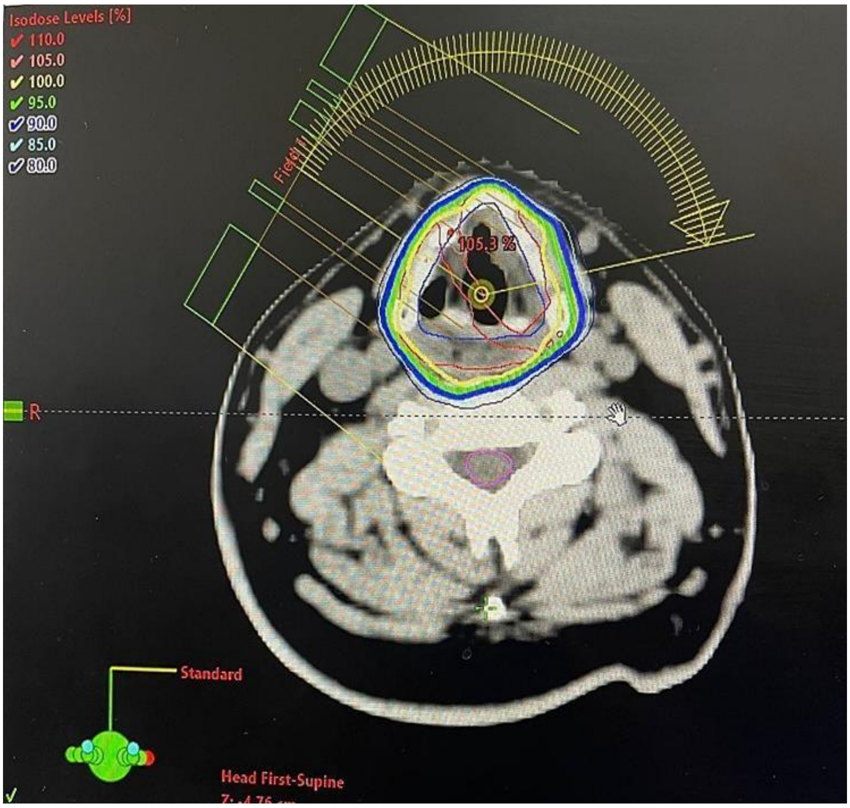

Figure 1. An axial CT image displaying isodose lines for a VMAT (Volumetric Modulated Arc Therapy) plan in the treatment of early stage glottic cancer

Target volume dose coverage

The results of the PTV comparison of the two techniques are shown in Table 1.

The mean PTV volume was 93.14 cm^3 (range: 45–171 cm^3), with variations reflecting differences in staging (T1 vs. T2 early glottic cancer). A statistically significant difference was found in the average mean doses for the PTV, with VMAT delivering a higher dose compared to 3D-CRT. Similarly, the maximum dose (Dmax) values were significantly higher for VMAT than for 3D-CRT, while the minimum dose (Dmin) showed no significant difference between the two plans.

Across all plans, 95% of each PTV was covered by 95% of the prescribed dose. The D95% values for both techniques ranged from 60 Gy to 70 Gy, with VMAT achieving higher values, which was statistically significant.

When assessing PTV volume in relation to D98%, VMAT performed significantly better than 3D-CRT. However, there was no statistically significant difference between the D2% values for the two techniques.

The HI for the PTV was significantly improved with VMAT compared to 3D-CRT. Additionally, the CI values indicated that VMAT was significantly superior to 3D-CRT.

Table 1. Comparison of dosimetric parameters for target volume between 3D-CRT and VMAT

Parameter	3D-CRT	VMAT	*p* value
	Mean ± SD	Mean ± SD	
PTV Dmean (Gy)	66.87 ± 2.85	67.92 ± 2.1	0.047
PTV Dmin (Gy)	50.77 ± 18.7	51.47 ± 15.5	0.816
PTV Dmax (Gy)	72.56 ± 10.3	74.23 ± 10.9	0.045
D2% (Gy)	69.80 ± 3.03	70.05 ± 2.25	0.666
D95 % (Gy)	64.08 ± 2.89	65.26 ± 2.46	0.041
D95% volume (cc)	86.70 ± 37.2	90.60 ± 40.7	0.0001
D98% volume (cc)	72.70 ± 30.6	83.40 ± 37.1	0.006
Homogeneity index (HI)	1.115 ± 0.031	1.089 ± 0.025	0.003
Conformity index (CI)	0.935 ± 0.012	0.970 ± 0.019	0.001

3D-CRT: Three-dimensional conformal radiotherapy, **VMAT**: Volumetric modulated arc radiotherapy, **PTV**: Planning target volume

Table 2. Comparison of dosimetric parameters for organs at risk between 3D-CRT and VMAT

Parameter		3D-CRT	VMAT	*p* value
		Mean ± SD	Mean ± SD	
Right carotid	**Dmean** (Gy)	45.73 ± 8.38	38.94 ± 7.01	0.009
	Dmin (Gy)	7.65 ± 9.27	16.20 ± 37.75	0.448
	Dmax (Gy)	61.49 ± 18.72	65.97 ± 3.60	0.369
	V35% (cc)	3.17 ± 1.49	2.99 ± 1.84	0.512
	V50% (cc)	2.20 ± 1.58	1.45 ± 1.23	0.065
Left carotid	**Dmean** (Gy)	44.55 ± 9.33	38.16 ± 10.66	0.03
	Dmin (Gy)	5.23 ± 8.71	3.39 ± 4.81	0.135
	Dmax (Gy)	67.61 ± 3.8	64.87 ± 12.44	0.428
	V35 % (cc)	3.07 ± 1.35	2.34 ± 1.49	0.0001
	V50% (cc)	2.07 ± 0.97	1.25 ± 1.2	0.0001
Thyroid gland	**Dmean** (Gy)	30.42 ± 12.06	24.88 ± 10.92	0.0001
	V30% (cc)	6.58 ± 3.27	5.03 ± 2.91	0.0001
	V50% (cc)	5.17 ± 2.63	3.42 ± 2.32	0.0001
Spinal cord	**Dmax** (Gy)	22.59 ± 5.10	24.37 ± 11.89	0.641

3D-CRT: Three-dimensional conformal radiotherapy, **VMAT**: Volumetric modulated arc radiotherapy

Dose distribution in organs at risk

The dosimetric parameters for OARs are listed in Table 2.

The carotid arteries were outlined only at the treatment site. Comparing 3D-CRT and VMAT, the latter demonstrated superior dose sparing for both the left and right carotid artery segments within the PTV region. The mean dose to the left and right carotid arteries was significantly lower with VMAT than with 3D-CRT. For volume-based criteria (V35% and V50%), VMAT also showed lower volumes compared to 3D-CRT, with mean reductions of 15% for the mean dose, 26% for V35%, and 40% for V50%.

The mean dose to the thyroid gland was significantly lower with VMAT. For volume-based metrics, VMAT plans had significantly lower V30% and V50% values compared to 3D-CRT, with mean reductions of 19% for the mean dose, 24% for V35%, and 34% for V50%.

No significant differences were observed in the average maximum dose values between the two techniques.

Discussion

For patients with early glottic cancer, radiation therapy is essential for preserving laryngeal function. Important factors in selecting a radiation therapy technique include achieving homogeneity within the target volume, minimizing toxicity to critical organs, and ensuring effective tumor control. Our dosimetric study compared two radiation therapy techniques—3D-CRT, the standard technique at our center, and VMAT—to determine which provides better PTV coverage and organ protection for thirteen patients with early glottic cancer. Although there have been concerns about potential geographic misses with newer radiation therapy techniques during planning or delivery, several studies have reported no statistically significant differences in local relapse rates between Intensity Modulated Radiation Therapy (IMRT) and VMAT compared to traditional 2D techniques. [3, 5, 6]

In our study, single-arc VMAT demonstrated significant improvements in target dose and volume coverage, specifically for D95%, D98%, and homogeneity, compared to 3D-CRT. These findings align with other dosimetric studies that have evaluated tumor target coverage using VMAT versus 3D-CRT in early glottic carcinoma, which generally show VMAT's superior dose distribution. [7, 8]

Conventional head and neck radiation therapy has been associated with atherosclerotic changes in the carotid arteries, stenosis, and an increased risk of ischemic brain injury, with incidences ranging from 18% to 38% compared to 0% to 9.2% in non-irradiated patients. [9, 10, 11] Additionally, RT for early glottic cancer has been linked to a higher incidence of stroke, rising to 2.8% at 15 years, compared to 1.5% after surgery. Our study showed that single-arc VMAT significantly outperforms 3D-CRT in sparing the carotid arteries. Specifically, the mean doses to the carotid artery segments within the PTV were reduced by 15% with VMAT compared to 3D-CRT ($p < 0.001$). This aligns with findings from Kim et al., who reported a significant reduction in mean dose for VMAT compared to 3D-CRT (22.2 Gy vs. 49 Gy, respectively, $p < 0.001$). [13]

Moreover, Berber and Demirhan observed that the mean carotid artery dose with 3D-CRT was significantly higher than with VMAT (61.99 Gy vs. 32.69 Gy, respectively, $p = 0.001$). [7] Our results are consistent with a recent retrospective dosimetric study comparing three RT techniques (3D-CRT, helical tomotherapy-intensity-modulated RT (HT-IMRT), and VMAT) in 28 patients with early glottic carcinoma. This study found that VMAT significantly reduced the mean dose to the carotid arteries compared to both HT-IMRT and 3D-CRT (20 Gy, 27.9 Gy, and 30 Gy, respectively, $p = 0.01$). [14]

Additionally, Martin JD et al. suggested that a dose of 35 Gy is a threshold for pathological wall abnormalities in the carotid artery. [15] In our study, the values of V35% and V50% were significantly reduced by 26% and 40%, respectively, with VMAT compared to 3D-CRT. This further emphasizes VMAT's advantage in minimizing radiation exposure to the carotid arteries, potentially reducing the risk of long-term vascular complications associated with head and neck radiation therapy.

The thyroid gland, located near the PTV, is another organ at risk during radiation therapy of early glottic cancer. Studies indicate that 6%–15% of patients receiving radiotherapy for head and neck cancer develop hypothyroidism, with radiation doses exceeding 30 Gy being a potential trigger for this condition. [8] In our study, VMAT demonstrated a 19% reduction in the mean dose to the thyroid gland compared to 3D-CRT, with an absolute dose reduction of 5.5 Gy. Additionally, VMAT significantly reduced the volume of the thyroid gland receiving radiation at the V30% and V50% dose levels compared to 3D-CRT. These results are consistent with findings from Kim and Yeo, who reported that VMAT substantially spares the thyroid gland compared to conventional radiotherapy, with reductions in mean dose, V30%, and V50% by 32.6%, 40.9%, and 46.0%, respectively. [16] Consequently, VMAT may offer a clinical advantage for patients with early glottic cancer by lowering the risk of hypothyroidism, a potential late effect of radiation treatment. Maintaining spinal cord doses within safe limits is also crucial in conventional radiotherapy for head and neck cancer to prevent severe adverse events.

Our study found that the maximum dose to the spinal cord with VMAT was slightly higher than with 3D-CRT, but this difference was not statistically significant ($p = 0.641$), and spinal cord doses remained within acceptable limits. This finding aligns with other dosimetric studies on early glottic cancer, which have shown that modern radiotherapy techniques, including VMAT, often result in higher spinal cord doses compared to 3D-CRT. For instance, Kim et al. reported significantly higher spinal cord doses with double-arc VMAT and 8-field IMRT compared to 3D-CRT and lateral parallel-opposed photon fields (36.7 and 36.3 Gy vs. 22.3 and 7.3 Gy, respectively). [13] Similarly, Ekici et al. observed significantly increased maximum spinal cord doses with modern techniques compared to 3D-CRT (28.27 Gy vs. 4.13 Gy, $p = 0.002$). [8] Another study by Berber and Demirhan also confirmed higher spinal cord doses with VMAT and IMRT compared to 3D-CRT (24.96 and 24.67 Gy vs. 4.23 Gy, respectively, $p < 0.001$). [7]

Our study's limitations include a small sample size, which may affect the generalizability of our results. Future studies with larger sample sizes are necessary to validate these findings. Additionally, the impact of organ movement during radiotherapy and potential geometric misses were not assessed due to the lack of image-guided radiotherapy systems at our center.

Conclusion

Compared to 3D-CRT for the treatment of early glottic cancer, VMAT demonstrates significantly superior dose-volume parameters. VMAT provides improved target coverage, greater homogeneity, and better conformity of dose distributions within the PTV while also sparing organs at risk. This leads to a reduction in radiation therapy-induced toxicities, which is particularly advantageous for managing the highly curable early glottic cancer.

Acknowledgments

Not applicable.

Authors' contribution

Conception & Design: Rabab Abdel Moneim & Hanan Darwish; Data Collection: Rabab Abdel Moneim & Khaled Khalil; Data Analysis & Interpretation: Hanan Darwish; Drafting the manuscript: Rabab Abdel Moneim & Khaled Khalil; Revising the manuscript: Hanan Darwish; Radiotherapy planning & dosimetric comparison: Ahmed Elhaggar & Radwa Abdel Rahman; Approval of the final version of the manuscript: All authors; Agreement to be accountable for all aspects of the work: All authors.

Conflict of interest

The authors declare that they have no conflict of interest to disclose.

Data availability

Anonymized data can be obtained from the corresponding author upon reasonable request.

Ethical considerations

This study was conducted in compliance with the principles outlined in the Declaration of Helsinki.

Funding

Not applicable.

Study registration

Not applicable.

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