

RESEARCH ARTICLE

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Assessment of Radiation Dose and Volume Changes in the Masticatory Apparatus and their Clinical Correlation with Trismus in Oral Cavity Cancer Patients

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Abstract

Objective: To investigate the radiation dose–volume effects on the masticatory apparatus and determine their correlation with trismus severity and muscle atrophy in patients with oral cavity squamous cell carcinoma (OSCC). **Methods:** This prospective observational study was conducted at a tertiary care oncology center, involving 30 patients undergoing adjuvant external beam radiotherapy for OSCC. Trismus was assessed using the maximal incisor distance (MID) at baseline and three months post-radiotherapy. The masseter, medial and lateral pterygoid, and temporalis muscles were contoured on planning and follow-up CT scans, and muscle volumes were calculated. Mean radiation doses were extracted from dose–volume histograms (DVHs). Statistical analyses, including paired t-tests and Pearson’s correlation, were performed to evaluate the relationships between dose, volume loss, and functional decline. **Results:** Post-radiotherapy, a significant reduction in MID was observed ($p = 0.001$), and all patients demonstrated either persistence or progression of trismus. Significant volume loss occurred in all ipsilateral muscles ($p < 0.001$), particularly the temporalis (mean loss, 3.32 cm^3) and masseter (mean loss, 2.49 cm^3). Radiation dose significantly correlated with volume reduction in the ipsilateral masseter ($r = 0.511$, $p = 0.004$) and pterygoids ($r = 0.448$, $p = 0.013$). Furthermore, worsening trismus was strongly associated with volume loss in the ipsilateral masseter ($r = -0.464$, $p = 0.010$) and temporalis ($r = -0.533$, $p = 0.002$). Age > 50 years and buccal mucosa primary sites were identified as significant clinical predictors of severe trismus. **Conclusion:** Radiation-induced trismus is driven by dose-dependent atrophy of the masticatory muscles, specifically the ipsilateral masseter and temporalis. Consideration of radiation dose to the masticatory muscles during treatment planning may be important for minimizing functional morbidity.

Keywords: Trismus- oral cavity cancer- radiotherapy- masticatory muscles- dose-volume analysis- muscle atrophy

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Introduction

Head and neck squamous cell carcinoma (HNSCC) represents the sixth most prevalent malignancy globally, with more than 90% of these cases arising from the squamous epithelium [1-3]. Within the demographic landscape of Pakistan, oral cavity squamous cell carcinoma (OSCC) is the most frequent subtype, ranking as the leading cancer in males and the second most common in females [4]. According to the American Joint Committee on Cancer, head and neck oncology encompasses a broad spectrum of malignancies, including the oral cavity, pharynx, larynx, paranasal sinuses, and salivary glands [5]. The standard of care for oral cavity cancers typically involves surgical resection followed by adjuvant radiotherapy, with or without concurrent chemotherapy for high-risk or locally advanced presentations [6, 7].

While radiation therapy is instrumental in enhancing local control and overall survival, it is frequently associated with late-stage toxicities, most notably the induction of fibrosis within the masticatory musculature [8]. This fibrotic process leads to trismus, a condition defined by a pathological restriction in mouth opening, colloquially termed “lockjaw.”

The etiology of trismus is multifactorial, potentially stemming from direct tumor infiltration, surgical trauma, or radiation-induced tissue scarring. It is estimated to affect between 5% and 38% of patients undergoing treatment for head and neck cancer, significantly compromising essential functions such as speech, mastication, deglutition, and oral hygiene maintenance, while often predisposing patients to chronic pain and unintended weight loss [9,10]. Despite the recognition of trismus as a common functional complication, the

precise radiation-induced volumetric alterations within the masticatory apparatus remain insufficiently characterized, particularly within the South Asian population. There is a critical need to quantify the dose–volume effects on the masticatory muscles to establish predictive thresholds that may inform future contouring strategies and dose constraint protocols. Consequently, this study aims to evaluate the association between the radiation dose delivered to the masticatory apparatus and post-radiotherapy trismus grading in oral cavity cancer patients. Furthermore, this research investigates the volumetric changes in masticatory muscles following radiotherapy to correlate these anatomical shifts with delivered dose parameters and to identify whether specific muscle dose thresholds can predict the onset of clinically significant trismus.

Materials and Methods

This prospective observational study was conducted at the Section of Radiation Oncology, Department of Oncology at a tertiary care hospital in Pakistan, following approval from the Institutional Ethics Review Committee (ERC Number: 2023-8704-25484). The study duration spanned six months post-approval, utilizing a non-probability consecutive sampling technique to enroll patients. While no formal sample size calculation was performed, the study duration was predefined, and all consecutive cases meeting inclusion criteria were included. Eligible participants included those undergoing adjuvant external beam radiotherapy for histologically confirmed oral cavity squamous cell carcinoma. To ensure a homogenous study population and minimize confounding variables, patients presenting with distant metastasis, those receiving definitive radiotherapy, and individuals with a prior history of head and neck irradiation and flaps were excluded from the analysis.

The primary clinical focus of this investigation is trismus, operationally defined as a painful limitation in mouth opening where the maximal incisor distance (MID) is less than 35 mm, a threshold that typically interferes with essential activities such as mastication, speech, and oral hygiene [11]. The masticatory apparatus under investigation encompasses the masseter muscles, the medial and lateral pterygoid muscles, the temporalis muscles). Muscle volume change is calculated as the numerical difference between the initial volume measured on the planning CT and the volume observed on a follow-up CT scan performed three months post-treatment.

Data collection procedures begin with a baseline assessment conducted on the day of CT simulation, where the MID is measured to establish pre-treatment trismus status. During the treatment planning phase, the components of the masticatory apparatus, including the masseter, pterygoids, and temporalis muscles—are contoured on the planning CT scan using the ARIA 15 radiation therapy planning software. To minimize inter-observer variability, a standardized contouring protocol was followed: [12], all contours were initially delineated by a single radiation oncologist trained in head and neck anatomy; uniform anatomical boundaries

and window-level settings were applied across all cases; and all contours were subsequently reviewed and verified in consensus with a diagnostic radiologist. For each of these structures, the mean radiation dose is extracted from the respective dose–volume histograms (DVH). Subsequent reassessments of trismus are performed on the day of the first follow-up visit. At 3 months post-radiation, follow-up CT scans were obtained. The same muscles were contoured and volumetric measurements compared with baseline.

The primary endpoint of this study was the correlation between the mean radiation dose delivered to each masticatory muscles and the subsequent change in trismus severity. Secondary endpoints include the percentage of muscle volume loss and its specific correlation with various dose parameters. Statistical analysis was performed using SPSS version 22. Quantitative variables, including radiation dose, muscle volume, and MID, are presented as mean $\pm$ standard deviation, while qualitative variables are reported as frequencies and percentages. To evaluate associations between categorical variables, Chi-square test was employed. Comparison between pre- and post-treatment muscle volumes was conducted using the paired t-test or the Wilcoxon signed-rank test, depending on the normality of the data distribution. The relationship between dose, volume, and trismus severity was assessed using Pearson or Spearman correlation coefficients, with a p-value of less than 0.05 considered statistically significant.

Ethical integrity was maintained throughout the study by ensuring that all patient data is strictly anonymized and de-identified to protect confidentiality. The research protocol complies with the ethical standards set forth by the Ethics Review Committee (ERC).

Results

The study included 30 patients with oral cavity cancer, predominantly male 29 (96.7%), with a mean age of 51.7 ± 10.07 years. Most tumors arose from the buccal mucosa (83.3%), and lesions were more commonly left-sided (76.7%). Radiotherapy regimens were split between two standard curative schedules, with 60% receiving 70 Gy in 35 fractions and 40% receiving 66 Gy in 33 fractions, while concurrent chemotherapy was administered to the majority (83.3%). Disease staging demonstrated substantial heterogeneity, spanning from early-stage pT1 to advanced pT4 categories, with pT4 representing the most frequent individual stage (23.3%) (Table 1).

Baseline maximal incisor distance (MID) ranged from 8 to 31 mm. There was a statistically significant reduction in mouth-opening measurements following radiotherapy, with mean MID decreasing from 21.8 mm pre-treatment to 19.6 mm post-treatment ($p=0.001$). The mean change of 0.22 (95% CI: 0.14–0.29) indicates a consistent and clinically meaningful decline in mandibular opening across the cohort, reflecting the measurable impact of radiation on masticatory function (Table 2).

The greatest reductions were observed in patients with advanced tumor stage 4 and higher ipsilateral muscle

Table 1. Demographic & Clinical Characteristics of Patients (n=30)

Variable	Frequency (%)
Gender	
Female	1 (3.3)
Male	29 (96.7)
Age (Years)	
Mean $\pm$ SD	51.73 $\pm$ 10.07
Age Group	
30 – 50 Years	14 (46.7)
> 50 Years	16 (53.3)
Subsite	
Buccal Mucosa	25 (83.3)
Tongue	05 (16.7)
Laterality	
Right	07 (23.3)
Left	23 (76.7)
Radiotherapy Dose	
66 Gy in 33 fractions	12 (40.0)
70 Gy in 35 fractions	18 (60.0)
Chemotherapy	
Yes	25 (83.3)
No	5 (16.7)
T-Stage	
pT1	04 (13.3%)
pT2	02 (6.7%)
pT3	08 (26.7%)
pT4	16 (53.3%)
N-Stage	
pN0	15 (50.0%)
pN1	09 (30.0%)
pN2a	02 (6.7%)
pN2b	03 (10.0%)
pN3b	01 (3.3%)

doses. The ipsilateral pterygoid, masseter, and temporalis muscles received mean doses of 66.53 ± 2.57 Gy, 62.06 ± 11.07 Gy, and 32.18 ± 13.66 Gy, respectively, while the contralateral pterygoid, masseter, and temporalis muscles received 45.61 ± 12.98 Gy, 30.30 ± 10.68 Gy, and 10.68 ± 2.94 Gy, respectively. Pre-radiation CT measurements showed ipsilateral muscle volumes of 13.39 ± 3.19 cc for the pterygoid, 17.27 ± 5.73 cc for the masseter, 20.43 ± 5.31 cc for the temporalis, whereas contralateral volumes were 13.65 ± 2.51 cc, 18.42 ± 3.58 cc, and 20.82 ± 5.46 cc, respectively. At 3 months post-radiation, a decrease in muscle volumes

Table 2. Changes in Pre & Post Radiation Trismus (n=30)

Trismus	Mean	$\pm$ SD	Change (95% C.I.)	P-Value
Pre-Treatment	2.18	± 0.65	0.22 $\pm$ 0.19	0.000
Post-Treatment	1.96	± 0.60	(0.14----0.29)	

Paired Sample t-test, Level of Significance (P=0.000), C.I. (Confidence Interval)

was observed, with ipsilateral pterygoid, masseter, and temporalis measuring 11.11 ± 3.42 cc, 14.78 ± 5.01 cc, and 17.11 ± 3.78 cc, and contralateral pterygoid, masseter, and temporalis measuring 12.27 ± 2.53 cc, 16.83 ± 2.88 cc, and 18.98 ± 4.37 cc, respectively. The mean volume reductions were greatest in the ipsilateral temporalis muscle (3.32 cc), followed by the ipsilateral masseter (2.49 cc) and ipsilateral pterygoid (2.28 cc). Contralateral reductions were comparatively smaller, measuring 1.59 cc for the masseter, 1.84 cc for the temporalis, and 1.38 cc for the pterygoid.

Significant positive correlations were observed between radiation dose and volume loss in the ipsilateral pterygoid ($r=0.448$, $p=0.013$) and ipsilateral masseter muscles ($r=0.511$, $p=0.004$), indicating greater atrophy with higher doses. No meaningful associations were found for the ipsilateral temporalis or contralateral pterygoid and temporalis muscles. A modest but significant negative correlation was noted for the contralateral masseter ($r = -0.374$, $p=0.042$), suggesting a small inverse relationship between dose and volume change.

A significant association was observed between radiation dose to the ipsilateral masseter and worsening of trismus, with higher doses correlating with greater reduction in mouth opening ($r = -0.402$, $p = 0.028$).

Muscle volume loss showed significant correlations with worsening trismus for the ipsilateral masseter ($r = -0.464$, $p = 0.010$) and ipsilateral temporalis ($r = -0.533$, $p = 0.002$), indicating that greater atrophy of these muscles was associated with increased trismus severity. In contrast, changes in the ipsilateral pterygoid and all contralateral muscle groups demonstrated no meaningful relationship with trismus progression. Overall, trismus deterioration was most closely linked to volume loss in the ipsilateral masseter and temporalis muscles (Table 3).

Patients older than 50 years had significantly higher trismus severity both before ($p=0.011$) and after treatment ($p=0.009$). Similarly, buccal mucosa primaries were associated with greater post-treatment trismus compared with tongue lesions ($p=0.023$). Gender, laterality, radiotherapy dose group, and chemotherapy status did not

Table 3. Correlation between Muscle Volume and Changes in Trismus (n=30)

Correlation	Mean	$\pm$ SD	Correlation (r)	P-Value
Change in Ipsilateral Pterygoid Volume	2.28	± 1.49	-0.087	0.649
Change in Ipsilateral Masseter Volume	2.49	± 1.85	-0.464	0.010
Change in Ipsilateral Temporalis Volume	3.32	± 2.56	-0.533	0.002
Change in Contralateral Pterygoid Volume	1.37	± 1.40	-0.100	0.601
Change in Contralateral Masseter Volume	1.59	± 1.47	-0.158	0.405
Change in Contralateral Temporalis Volume	1.84	± 2.70	-0.238	0.205
Change in Trismus	0.22	± 0.19	-	-

Pearson's Correlation test, P-Value (Level of Significance)

significantly influence trismus severity at either timepoint.

Discussion

This study evaluates the association between radiation dosimetry, masticatory muscle changes, and trismus in oral cavity cancer patients. Our findings demonstrate a significant and progressive deterioration in trismus following radiotherapy, underpinned by measurable muscle atrophy that correlates with specific dosimetric parameters. By quantifying these changes, this research provides a clearer understanding of the dose–volume effects that contribute to one of the most debilitating late-stage toxicities in head and neck oncology.

The results of this study highlight the persistent and progressive nature of radiation-induced trismus. A significant worsening of trismus grades was observed across the entire cohort, with the mean maximal incisor distance (MID) declining from 21.8 mm to 19.6 mm within just three months of treatment completion. Notably, no patients demonstrated improvement in their trismus grade; instead, those with moderate baseline impairment frequently deteriorated into more severe categories. This aligns with existing literature suggesting that radiation-induced fibrosis is a dynamic, evolving process rather than a static injury [13]. Pathophysiology involves a cascade of chronic inflammation, fibroblast activation, and excessive collagen deposition within the masticatory muscles and the temporomandibular joint (TMJ) capsule [14]. Unlike surgical trauma, which may resolve with physical therapy, radiation-induced trismus often exhibits a late-onset progression that can continue for years post-treatment, significantly impacting the quality of life by hindering nutrition and speech [15].

A key finding of this investigation is the correlation between higher radiation doses and subsequent volume loss in the ipsilateral masseter and pterygoid muscles. Specifically, the ipsilateral masseter showed a strong correlation ($r=0.511$) between mean dose and volume reduction, reinforcing the hypothesis of a dose-dependent atrophic effect. Radiation therapy induces microvascular damage and direct myocyte injury, leading to a loss of muscle fibers and replacement with non-contractile fibrotic tissue [16]. Our data showed that the ipsilateral pterygoid and masseter muscles received substantial mean doses (66.52 Gy and 62.05 Gy, respectively), which were significantly associated with muscle thinning. This dose–volume relationship suggests that these muscles are particularly sensitive to high-dose radiation, and that exceeding specific dosimetric thresholds often cited as a mean dose of 40–50 Gy in literature leads to irreversible structural changes [17]. The observed atrophy in the contralateral muscles, though less severe, further suggests that even lower doses or systemic factors may contribute to bilateral muscle volume loss [18].

The clinical significance of this atrophy is highlighted by the strong correlations between volume loss in the ipsilateral masseter ($r=-0.464$) and temporalis ($r=-0.533$) with the worsening of trismus. These findings suggest that muscle volume reduction serves as a direct precursor to functional limitation. While many studies focus

solely on the pterygoids, our data emphasizes the role of the masseter and temporalis as key components of the masticatory pump that are vulnerable to radiation [19]. The temporalis muscle showed the greatest mean volume decrease (3.32 cm³), and its correlation with trismus severity indicates that it may be a critical imaging biomarker for predicting functional decline. These anatomical shifts, detectable on post-treatment scans, reflect the internal scarring that restricts the translation and rotation of the mandible [20].

Beyond dosimetry, our analysis identified older age (>50 years) and buccal mucosa tumor subsite as significant clinical predictors of trismus severity. Patients with buccal mucosa primaries exhibited greater post-treatment trismus, likely due to the anatomical proximity of the tumor to the masseter and the primary surgical site, which often necessitates more aggressive resection and higher localized radiation doses [21]. Interestingly, factors such as gender, laterality, and chemotherapy status did not show significant associations, suggesting that the individual fibrotic response and baseline muscle condition may play more dominant roles. The multifactorial etiology of trismus is evident here: the final functional outcome is a product of surgical scarring, radiation-induced vascular compromise, and the patient's inherent biological susceptibility to fibrosis [8, 14]. This complexity explains why some patients develop severe trismus even at lower dose ranges, while others remain relatively functional despite high-dose exposure.

The findings of this study have direct implications for the refinement of radiotherapy planning protocols. Given the clear correlation between masseter and pterygoid dose and trismus progression, there is a compelling argument for the routine contouring of these structures as Organs at Risk (OARs). Implementing stringent dose constraints, particularly using Intensity-Modulated Radiotherapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT), could spare the masticatory apparatus without compromising target coverage [12]. Our data suggests that prioritizing the sparing of the ipsilateral masseter may yield the highest functional benefit. Future research should focus on developing multi-variable predictive models that integrate dosimetric data with baseline functional status and genetic markers of fibrosis. Longitudinal studies with longer follow-up periods are also necessary to determine if early muscle volume changes can reliably predict the long-term “plateau” of trismus severity.

While this study provides important insights into the dose–volume effects on masticatory muscles and trismus, certain limitations should be acknowledged. The sample size and single-center design, though sufficient to demonstrate statistically significant associations, highlight the need for larger multicenter validation to strengthen generalizability.

The three-month follow-up captures early post-treatment changes, but further longitudinal studies are essential to characterize long-term functional outcomes. Muscle delineation was performed using standardized protocols with expert review, ensuring methodological rigor; Although CT was used for muscle delineation, MRI

would have provided superior soft-tissue contrast; this may modestly limit volumetric precision.

In conclusion, this study demonstrates that trismus in oral cavity cancer patients is a progressive functional impairment intrinsically linked to radiation-induced atrophy of the masticatory apparatus. Our data highlights a definitive dose–volume relationship, where elevated radiation doses to the ipsilateral masseter and pterygoid muscles lead to significant volumetric reduction. The strong correlation between volume loss in the masseter and temporalis muscles and the deterioration of mandibular mobility identifies these structures as critical determinants of post-treatment function.

The findings suggest that clinical factors, including older age and buccal mucosa tumor subsite, further compound this risk, emphasizing the multifactorial nature of the condition. Limiting the mean dose to the masticatory muscles in cases where they are not directly involved may reduce treatment-related morbidity. Future prospective trials with extended follow-up are warranted to establish precise dosimetric thresholds and evaluate the efficacy of early rehabilitative interventions in mitigating this debilitating complication.

Author Contribution Statement

All authors contributed equally in this study.

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