ORIGINAL ARTICLE

LARYNGEAL MOVEMENT IN THE ERA OF PRECISION RADIATION THERAPY IN LARYNGEAL CARCINOMA

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ABSTRACT

OBJECTIVE: To report laryngeal movement during simulation for radiation treatment planning in patients with laryngeal carcinoma. **METHODS AND MATERIALS:** A retrospective review of patients diagnosed with laryngeal carcinoma treated with radiation therapy was done. Movement of the larynx in cephalo-caudal direction was noted with help of fluoroscopic images taken during resting and deglutition phases. Information of variables such as patient s age, gender, tracheostomy status, stage of disease and sub-site of disease were recorded. Simple linear regression was used to assess the linear relationship between laryngeal movement and different variables. **RESULTS:** A total of 47 patients were identified between February 2006 and December 2017 whose laryngeal movement was documented during simulation. About half of the patients had stage I disease (n = 22 [46.8%]). In majority of the patients, the disease originated in glottis (n = 37 [78.7%]). The mean laryngeal movement was noted to be 0.96 cm (SD of 0.392, range: 0.5-2.0cm). There was no linear association observed between laryngeal movement and age (p = 0.239), gender (p = 0.369), tracheostomy status (p = 0.664), stage of disease (p = 0.322) or sub-site of disease (p = 0.761). **CONCLUSION:** In this era of precision, recording laryngeal movement and incorporating in contouring remains important because it can lead to geometrical miss of target volume during radiation delivery. Our study shows a physiological motion of nearly 1 cm in a cephalo-caudal direction. We conclude that a cautious margin of planning target volume (PTV) should be considered and incorporated during radiation planning of laryngeal cancers.

Key Words: Laryngeal Cancer; Precision Radiation Therapy, Laryngeal movement, PTV margins, Advanced Radiation Techniques

Introduction

Laryngeal cancer consists of about 2% of the total cancer risk and has been reported to be among the two most common sites of head and neck cancers in Karachi.[1] The ratio of glottic to supraglottic carcinoma

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mentioned in international literature is approximately 3:1 but according to a study done in Pakistan 56% are supraglottic, 34% are glottic and 10% are of glottic origin.[2] Radiation therapy (RT), is effective, curative and organ preservation treatment for early, moderately advanced and advanced laryngeal cancers. Cure rates of 95% and 80% are documented for T1 & T2 glottic cancer with RT alone respectively.[3] Like other head and neck cancer sites, during the RT of the laryngeal tumor, patients are immobilized via customized thermoplastic masks to minimize geometric uncertainties daily throughout the treatment. These uncertainties may be due to setup errors during patient s positioning and internal organ motion. These errors are reduced by adding a setup margin and an internal margin to the planning target volume (PTV) during contouring based on the magnitude of movement.[4] The setup variation for head-and-neck cancer has been determined in several studies.[5,6] The larynx is a mobile organ which normally moves during deglutition. Even when the patient's head is immobilized, the movement of the larynx can occur during radiation treatment delivery and is associated with swallowing. The larynx moves in cephalo-caudal direction during deglutition. Tumor and normal structure movement during deglutition in real-time needs to be considered before executing the RT plans.[7] With the advancements of conformal techniques such as intensity-modulated radiotherapy (IMRT), more focus is set on sparing normal structures along with delivering adequate dose to PTV. With IMRT, it is possible to selectively give a high dose to the larynx and spare its substructures as organs at risk (OARs), thereby reducing the risk of speech and swallowing dysfunction.[8] However, the risk of marginal miss increases with high conformity through contouring errors and organ motion. This study was designed to determine planning target volume (PTV) margins to incorporate the laryngeal tumor in resting state and deglutition for patients with laryngeal cancer treated with curative and definitive radiation therapy. The objective of this study was to measure laryngeal movement in cephalo-caudal direction during the simulation for definitive radiation therapy planning of patients with squamous cell carcinoma of the larynx.

Material & Methods

All patients who received definitive radiation therapy for biopsy-proven squamous cell carcinoma of the larynx at our university hospital from February 2006 till December 2017 were included in the study. The research protocol was reviewed and permission was granted by ethical review committee (ERC) of our university. Hospital information management system (HIMS) and radiation oncology record were sought to identify patients who received definitive radiation therapy for laryngeal cancer. Laryngeal movement is noted routinely during simulation using fluoroscopy by asking the patients to swallow saliva and recorded in centimeters (cm) in the patient's charts. Movement of the larynx in cephalo-caudal direction is noted in centimeters (cm) by comparing the resting and deglutition fluoroscopic images, taken during a real-time simulation at the time of radiation therapy treatment planning as per departmental protocol. Varian Acuity™ simulator has been used for fluoroscopic imaging during RT planning simulation at our centre since its inception in February 2006. A retrospective review of patient s simulator images was done and laryngeal movement was recorded by two physicians. Patient charts and radiotherapy database was reviewed to identify patients meeting inclusion criteria and data was collected for baseline characteristics including age, gender, sub-site of larynx and tumor, node metastasis.

Patients, less than 18 years of age were excluded. Mean with standard deviation (SD) was reported for age and laryngeal movement. Frequencies and percentages for gender, tracheostomy status, stage and sub-sites of the disease were calculated. Simple linear regression was used to assess the linear relationship between laryngeal movement and age, gender, tracheostomy status, stage and sub-site of disease. All data were analyzed by the Statistical Package for Social Sciences (SPSS) version 19.

Results

Medical record and radiation treatment charts were reviewed for a total of 47 patients meeting the inclusion criteria. The details of patient s and disease characteristics are shown in (Tab.1). Regarding planning

technique, 29 (61.7%) patients were treated with 3DCRT, while 12(25.5%) and 6 (12.8%) were treated with IMRT and 2D techniques respectively.
The mean laryngeal movement was noted to be 0.96 cm with a SD of 0.392 (Range: 0.5-2.0cm). There was no linear association observed between laryngeal movement and age (p-value = 0.239), gender (p-value = 0.369), tracheostomy status (p-value = 0.664), stage of disease (p-value = 0.322) and sub-site of disease (p-value = 0.761).

Characteristics	No. (%)
Age in years (Mean ± SD)	59 ± 9.908
Gender	
Male	44 (93.6)
Female	03 (06.4)
Tracheostomy Status	
Yes	06 (12.8)
No	41 (87.2)
Stage of Disease	
Stage I	22 (46.8)
Stage II	08 (17.0)
Stage III	11 (23.4)
Stage IV	06 (12.8)
Sub-Site of Disease	
Supra Glottis	10 (21.3)
Glottis	37 (78.7)
Sub Glottis	00 (0.00)
Treatment technique	
IMRT	12 (25.5)
3DCRT	29 (61.7)
2D	6 (12.8)

Table 1: Frequencies of Patients and Disease Characteristics

Discussion

Management of laryngeal cancer aims to achieve cure with the best functional outcome and minimum risk of adverse complications. Treatment of laryngeal cancers involves a multidisciplinary team approach, with Head and Neck Surgeon, Pathologist, Radiologist, Radiation Oncologist and Medical Oncologist as core members of the tumor board meetings.[9]
Historically, radiation therapy has been used as a definitive modality in the treatment of laryngeal cancers for more than 50 years. Conventional methods of delivering radiation via two parallel opposed portals expose adjacent normal tissues to higher doses of radiation.[10] Over the years, radio-therapeutic techniques have evolved and nowadays highly conformal techniques are employed to adequately cover the target volume with sparing of normal tissues.
Simultaneously, patient immobilization and set up reproducibility are of paramount importance in the context of precision radiation. Any inaccuracy in patient positioning can lead to geometrical miss of the planned target volume. Probability of tumor control is not the only parameter that is affected due to geometrical miss but the volume of normal tissue that is irradiated is also increased which can raise the likelihood of treatment-related complications.
Several devices and methods have been described to minimize positioning uncertainties and to increase the reproducibility of patient setup during every single fraction.[11,12] The ultimate goal is to increase the chances of local tumor control by precisely modelling the dose distribution. However, like incorporating organ motion in curative radiation for other sites including prostate for prostate cancer, respiratory motion for breast cancer and thoracic radiation (lung, lymphoma etc.), this poses a unique challenge when dealing with normal unavoidable physiological organ motion which might result in underdosing of the target volume.
Conformal radiation techniques are associated with a greater time and there are high chances of larynx moving out of the radiation field. Literature has shown variation in results. In a study, Van Asselen et al reported that although the displacement of the larynx can be large due to swallowing, the incidence of such movement was less for most of the patients (on average 0.45% of the irradiation time).[13] Therefore, it was concluded that there was no need to adjust the PTV margins around the CTVs to consider these displacements. Other motions occur with a magnitude smaller than that caused by swallowing. For instance, the tip of the epiglottis moves within a range of 7.1 mm 95% of the time, in the cranial-caudal direction. In another study by Hamlet et al on non-tracheostomized adults,[7] the reported frequency of swallowing was once every 1 2 min and they stated laryngeal movement in the craniocaudal direction approximately 2 cm during a swallow and less than 1 cm anteriorly.

They found that during radiation therapy treatment, the length of the treatment is a crucial component as the probability of swallowing movement occurring during a radiotherapy treatment fraction is dependent on it. The ratio of the number of swallows to the number of intervals was 0.27 if radiation treatment time less than 2 min long. For irradiation intervals between 2 3 min long, the ratio was 1.76. Based on careful estimates of laryngeal movement, field dimensions, and incidence of swallowing, the decrease in the prescribed dose of radiation-related to swallowing during treatment was expected to be approximately 0.5%. Considering these results, they stated that with small fields, the total dose is decreased by 0.5% only with swallowing, so the variation in the total dose is not significant.

However, in an editorial published in 2007, Feigenberg advised about the cautious use of IMRT in this setting14 as reflected by the experience of the author and his colleagues in assessing "several patients for laryngectomy for radiation failures in early-stage glottic cancer who were treated with IMRT". They raised the concern that marginal misses, specifically for tumors with the involvement of anterior commissure, could be particularly prevalent with IMRT planning. They emphasized on the point that IMRT takes approximately 20 min to deliver, compared with just a few minutes for conventional RT technique. The increase in time of treatment delivery led to concerns that laryngeal motion with swallowing during this prolonged treatment delivery time may reduce the total prescribed target dose resulting in under coverage of target volume.

In our study, the maximal movement of the larynx caused by swallowing in craniocaudal direction is 2cm (range 0.5cm 2cm). During the simulation, the movement of the larynx was noted by documenting the drive of hyoid bone with x-ray fluoroscopy. Our observation of maximum laryngeal motion which is consistent with the published literature.[7,15] Our experience shows that the larynx may not always be in the same position based upon the swallowing movement observed on fluoroscopy in simulation. This can have implications especially in those patients in which radiation treatment delivery time is longer or more conformal RT technique like IMRT is used. However, the present study has limitations. Firstly, does such a movement impact the dose distribution, resulting in hot or cold spots within the irradiated volume? Secondly, does the frequency of motion during a single fraction lead to any change in dosimetry affecting the local control? Another limitation of our study is that we did not observe the real-time laryngeal movement during radiation treatment delivery.

Conclusion

In this era of precision radiotherapy, documenting the laryngeal movement and its implication during contouring is still an important step because it can lead to geometrical miss of target volume during radiation delivery as increased conformity increases the risk of marginal misses through contouring errors and organ motion. A balanced careful approach between precision and under dosage of target volume should be considered. Our study shows a physiological motion of approximately 1 cm in cephalo-caudal direction during voluntary deglutition. We suggest that expansion of PTV margins based upon individual's laryngeal movement should be carefully considered during contouring of laryngeal cancers in this era of highly conformal radiation therapy because it can lead to marginal miss and under dosage of target volume.

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