

# Radiation Therapy (RT) Target Volume Determination for Locally Advanced Pyriform Sinus Carcinoma: An Original Research Article Revisiting the Role of Multimodality Imaging

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**Keywords:** Pyriform Sinus Carcinoma; Radiation Therapy (RT); Magnetic Resonance Imaging (MRI)

**Abbreviations:** RT: Radiation Therapy; MRI: Magnetic Resonance Imaging; IGRT: Image Guided RT; ART: Adaptive RT; CT: Computed Tomography; AAPM: American Association of Physicists in Medicine; ICRU: International Commission on Radiation Units and Measurements

## ABSTRACT

**Objective:** The hypopharynx is a critical region of the head and neck including three primary anatomical subsites, namely the pyriform sinuses, the posterior pharyngeal wall, and the postcricoid area. Although comprising a relatively smaller proportion among all cancers, pyriform sinus carcinomas account for the majority of hypopharyngeal tumors. Radiation therapy (RT) plays a critical role for management of pyriform sinus carcinomas with encouraging therapeutic outcomes. Optimal target volume definition has been a more critical component of current RT protocols for pyriform sinus tumors. In this original research article, we shed light on this critical issue by assessment of multimodality imaging with incorporation of Magnetic Resonance Imaging (MRI) for RT target volume determination of locally advanced pyriform sinus carcinomas.

**Materials and Methods:** We have performed a comparative analysis of target volume definition for radiotherapeutic management of locally advanced pyriform sinus carcinomas based on Computed Tomography (CT) simulation images only or by incorporation of fused CT-MRI. Primary objective of the study was to assess the role of multimodality imaging for target volume determination along with other factors including critical organ delineation, interobserver and intraobserver variations.

**Results:** As the primary result, the ground truth target volume was found to be identical with fused CT-MRI based delineation for patients with locally advanced pyriform sinus carcinoma.

**Conclusion:** Multimodality imaging with incorporation of MRI in the RT planning procedure may be considered for patients with locally advanced pyriform sinus carcinomas.

## Introduction

The hypopharynx is a critical region of the head and neck including three primary anatomical subsites, namely the pyriform sinuses, the posterior pharyngeal wall, and the postcricoid area [1]. Although comprising a relatively smaller proportion among all cancers, pyriform sinus carcinomas account for the majority of hypopharyngeal tumors [2,3]. The hypopharyngeal region extends from superior border of epiglottis and the pharyngoepiglottic folds from the level of the hyoid bone above to the lower border of the cricoid cartilage below [1]. This critical part of the head and neck region is associated with critical body functions. Pyriform sinus carcinomas may differ from other head and neck cancers with their frequent presentation at relatively more advanced stages due to substantial tumor growth before onset of symptoms [4]. Patients with alcohol abuse history and medical comorbidities related to alcohol are more commonly diagnosed with pyriform sinus carcinomas [4]. These tumors have tendency for lymphatic and systemic spread which make the prognosis relatively poorer. Also, the critical localization of these tumors in intimate association with the hypopharynx and larynx poses an important concern for surgical management. Removal of the entire larynx may be required for surgical therapy which may lead to speech disruption. Radiation therapy (RT) plays a critical role for management of pyriform sinus carcinomas with encouraging therapeutic outcomes [4-9]. Improvements in surgical management strategies, RT, and systemic treatments have been reflected in longer life expectancy for patients with pyriform sinus carcinomas.

In this respect, adverse effects of treatment have been considered as a more important aspect of management in recent years. Indeed, radiotherapeutic strategies have evolved in the millenium era with introduction of sophisticated treatment techniques including Intensity Modulated RT (IMRT), Image Guided RT (IGRT), molecular imaging methods, automatic segmentation techniques, stereotactic RT, and adaptive RT (ART) [10-48]. These relatively never radiotherapeutic concepts have resulted in more precise and accurate targeting of tumors along with steeper dose gradients around the target volume for reduced normal tissue exposure. Decreased critical organ doses may allow for reduced treatment induced toxicity and target dose escalation which may lead to achieving an improved therapeutic ratio. Clearly, vigilance is required for implementation of these contemporary therapeutic approaches in clinical practice. Optimal target volume definition has been a more critical component of current RT protocols for pyriform sinus tumors. In the meantime, Computed Tomography (CT) simulation constitutes the backbone of RT planning in majority of cancer centers universally. CT may be considered as a feasible

technique for dose calculation purposes, however, integration of additional imaging modalities for RT planning may improve accuracy and precision in target volume determination. Several studies have addressed the utility of multimodality imaging for improved target definition [49-84]. In this original research article, we shed light on this critical issue by assessment of multimodality imaging with incorporation of Magnetic Resonance Imaging (MRI) for RT target volume determination of locally advanced pyriform sinus carcinomas.

## Materials and Methods

For many years, Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences has been serving as a tertiary cancer center of a referral institution for treatment of several indications. In the context of this study, we have performed a comparative analysis of target volume definition for radiotherapeutic management of locally advanced pyriform sinus carcinomas based on CT simulation images only or by incorporation of fused CT-MRI. Primary objective of the study was to assess the role of multimodality imaging for target volume determination along with other factors including critical organ delineation, interobserver and intraobserver variations. To be utilized for actual treatment and for comparison purposes, we have generated a ground target volume by the collaborative effort of board-certified radiation oncologists after meticulous consideration of all imaging and relevant data with colleague peer review and consensus. Radiotherapeutic management of patients has been decided following detailed individualized assessment by a multidisciplinary group of experts from relevant disciplines including surgical oncology and medical oncology. Specifically, patient, disease, and treatment characteristics have been evaluated on an individual basis by taking into account the age, symptomatology, performance status, previous therapies, lesion size, location and association with surrounding critical structures, contemplated outcomes of suggested therapies, patient preferences and logistical issues. Treatment delivery has been achieved by use of Synergy (Elekta, UK) linear accelerator (LINAC) with integration of IGRT techniques. CT simulation was performed by robust immobilization of the patients. After acquisition of high-quality RT planning images at the CT simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK), we have transferred the acquired RT planning images to the delineation workstation (SimMD, GE, UK) through the network for generation of individualized structure sets including the treatment volumes and critical structures. A comparative analysis has been conducted to assess target and critical organ definitions by use of either CT simulation images only or by fused CT-MRI.

## Results

In this original research article, multimodality imaging for target volume definition was assessed in patients referred for radiotherapeutic management of locally advanced pyriform sinus carcinoma at Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences. To evaluate the impact of multimodality imaging, we performed a comparative analysis of target and critical organ determination by utilization of either CT only imaging or by fused CT-MRI. Assessed tumor related parameters included the lesion size, location and association with surrounding normal tissues. As another aspect of management, we also considered individual patient symptomatology, age, performance status and logistical factors. Reports by American Association of Physicists in Medicine (AAPM) and International Commission on Radiation Units and Measurements (ICRU) have been taken into account in RT planning. RT plans have been generated by considerable input from expert radiation physicists with strict adherence to relevant guidelines. Electron density, tissue heterogeneity, CT number and HU values in CT images have also been considered. Primary objective of RT planning was to achieve optimal target coverage with minimal exposure of surrounding normal tissues. The ground truth target volumes have been vigilantly defined by the expert radiation oncologists after thorough evaluation, rigorous colleague peer review process, and consensus to be used for actual treatment and for comparison purposes. Also, IGRT techniques were utilized for setup verification. Precise delivery of irradiation was achieved by use of Synergy (Elekta, UK) LINAC available at our department. As the primary result, the ground truth target volume was found to be identical with fused CT-MRI based delineation for patients with locally advanced pyriform sinus carcinoma.

## Discussion

Hypopharyngeal region constitutes an important component of the head and neck site and contains three primary anatomical subsites, namely the pyriform sinuses, the posterior pharyngeal wall, and the postcricoid area [1]. While pyriform sinus carcinomas comprise a relatively smaller proportion of all cancers, they account for the majority of hypopharyngeal tumors [2,3]. The hypopharyngeal region extending from superior border of epiglottis and the pharyngoepiglottic folds from the level of the hyoid bone above to the lower border of the cricoid cartilage below is a critical subsite associated with critical body functions. Pyriform sinus carcinomas may differ from the other head and neck carcinomas due to more common presentation at relatively advanced disease stages and significant tumor growth before onset of symptoms [4]. History of alcohol abuse and medical comorbidities associated with

alcohol may be present in patients diagnosed with pyriform sinus carcinomas [4]. These tumors may have predilection for lymphatic and systemic spread with a relatively bad prognosis. Additionally, critical location of these tumors in close neighbourhood of the hypopharynx and larynx comprises a challenge for optimal surgical management. Complete surgical removal of the entire larynx might be needed which could consequently result in speech disruption. RT plays an eminent role in the management of pyriform sinus carcinomas, and treatment results are promising [4-9].

Advances in surgery, RT, and systemic treatments have led to longer life expectancy for patients with pyriform sinus carcinomas. With this regard, treatment induced toxicity may be considered as a critical aspect of contemporary management strategies. Admittedly, irradiation approaches evolved in the millenium era with introduction of contemporary treatment techniques such as IMRT, IGRT, molecular imaging methods, automatic segmentation techniques, stereotactic RT, ART [10-48]. State of the art RT concepts have allowed for more precise targeting of tumors accompanied by steep dose gradients around target volumes resulting in decreased exposure of normal tissues. Reduction in critical organ doses may improve the toxicity profile of radiation delivery, and also treatment dose escalation strategies may be considered for further improvements in treatment results. At this critical point, vigilance is warranted for integration of these sophisticated treatment strategies in clinical routine. Hereby, optimization of target volume definition became a very important aspect of recent irradiation protocols for pyriform sinus tumors. Currently, CT simulation remains to be the more commonly utilized procedure for RT planning purposes in a considerable proportion of cancer centers on a global scale. CT should be regarded as a reasonable technique for RT dose calculation purposes. Nevertheless, incorporation of other imaging modalities for improved RT planning may be considered. In the literature, many studies assessed the use of multimodality imaging [49-85]. Our study may add to the growing body of evidence supporting the utility of multimodality imaging for improved target definition. In conclusion, multimodality imaging with incorporation of MRI in the RT planning procedure may be considered for patients with locally advanced pyriform sinus carcinomas.

## Conflicts of Interest

There are no conflicts of interest and no acknowledgements.

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