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## **Research Article**

Multimodality imaging based treatment volume definition for recurrent Rhabdomyosarcomas of the head and neck region: An original article

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## Abstract

**Objective:** Rhabdomyosarcomas are among the malignant soft tissue tumors which may originate from primitive mesenchymal cells. These tumors may also be located in the head and neck region and may behave locally aggressive with the invasion of nearby structures. Radiation therapy (RT) may play a role as part of initial management as adjunctive therapy, or for treatment of recurrent disease. Accuracy and precision in RT treatment volume definition have gained utmost importance for achieving optimal treatment results. Herein, we assess multimodality imaging-based RT treatment volume definition for irradiation of recurrent head and neck rhabdomyosarcomas.

Materials and methods: Multimodality imaging-based RT treatment volume definition for irradiation of recurrent head and neck rhabdomyosarcomas were evaluated in this study. RT target volume definition by incorporation of magnetic resonance imaging (MRI) or by computed tomography (CT)-simulation images only was assessed with comparative analysis for patients receiving RT for recurrent head and neck rhabdomyosarcomas.

Results: As the main outcome of this study, ground truth target volume has been found to be identical to treatment volume definition by CT-MR fusion-based imaging.

**Conclusion:** Optimal management of recurrent head and neck rhabdomyosarcomas may be improved by precise and accurate RT treatment volume determination. Within this context, the incorporation of MRI in the target and treatment volume definition process may be strongly recommended to achieve improved accuracy and precision in target and treatment volume determination despite the need for further supporting evidence.

## Introduction

Rhabdomyosarcomas are among the malignant soft tissue tumors with distinctive genetic characteristics which may originate from primitive mesenchymal cells, however, there may be diverse localizations for these tumors such as the urinary bladder, prostate, ear, and paratesticular region [1–9]. Rhabdomyosarcomas constitute a large category of soft tissue sarcomas in children and adolescents [10,11]. Rhabdomyosarcomas may be classified into alveolar, embryonal, spindle cell/sclerosing, and pleomorphic subtypes depending on their clinicopathological features and genetic abnormalities, with each subtype demonstrating distinctive morphology and unique genetic alterations [10,11].

These tumors may also be located in the head and neck region and may behave locally aggressive with the invasion of nearby structures. Management options include surgery, chemotherapy and Radiation Therapy (RT). Symptomatology primarily depends on lesion location and association with critical structures. RT may play a role as part of initial management as adjunctive therapy, or for treatment of recurrent disease. Recently, there has been a rising trend toward improving the toxicity profile of radiation delivery

by the incorporation of contemporary radiotherapeutic approaches. Within this context, accuracy and precision in RT treatment volume definition have gained utmost importance for achieving optimal treatment results. Herein, we assess multimodality imaging-based RT treatment volume definition for irradiation of recurrent head and neck rhabdomyosarcomas.

#### **Materials and methods**

Multimodality imaging-based RT treatment volume definition for irradiation of recurrent head and neck rhabdomyosarcomas was evaluated in this study. RT target volume definition by incorporation of magnetic resonance imaging (MRI) or by computed tomography (CT)-simulation images only was assessed with comparative analysis for patients receiving RT for recurrent head and neck rhabdomyosarcomas. The ground truth target volume was used as the reference for actual treatment and for comparison purposes and has been defined by board-certified radiation oncologists after thorough evaluation, colleague peer review, detailed discussion, and consensus. All patients have been meticulously evaluated by a multidisciplinary team of experts regarding the lesion size, location, and association with surrounding critical structures, symptomatology, and contemplated results of radiotherapeutic management. CT-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) has been used for RT simulation for treatment planning at our tertiary cancer center. Planning CT images were acquired and then sent to the delineation workstation (SimMD, GE, UK) for contouring of treatment volumes and surrounding critical structures. Either CT-simulation images only or fused CT and MR images were used for treatment volume definition for radiotherapeutic management. Treatment volume definition with CT only and with the incorporation of CT-MR fusion was assessed with comparative analysis. Synergy (Elekta, UK) linear accelerator (LINAC) has been utilized for precise delivery of irradiation with routine incorporation of Image-Guided Radiation Therapy (IGRT) techniques such as electronic digital portal imaging and kilovoltage cone-beam CT for treatment verification.

#### Results

Radiation treatment planning has been performed by the utilization of contemporary RT treatment planning systems at our tertiary referral institution. Priority was given to minimize exposure of surrounding normal tissues while maintaining optimal treatment volume coverage. Determination of ground truth target volume which was performed by board-certified radiation oncologists was based on collaborative thorough assessment, colleague peer review, detailed discussion and consensus to be used for actual treatment and comparative evaluation. Synergy (Elekta, UK) LINAC was used for treatment delivery by incorporating IGRT techniques including kilovoltage cone-beam CT and electronic digital portal imaging, and for treatment verification. Treatment volume determination by CT-only imaging and by CT-MR fusion-based imaging has been assessed with comparative analysis. As the main outcome of this study, ground truth target volume has been found to be identical to treatment volume definition by CT-MR fusionbased imaging.

Rhabdomyosarcomas belong to the group of malignant soft tissue tumors with distinctive genetic characteristics which originate from primitive mesenchymal cells, nevertheless, there may be different localizations for these tumors including the urinary bladder, prostate, ear, and paratesticular region [1-9]. Rhabdomyosarcomas typically comprise a large category of soft tissue sarcomas both in children and adolescents [10,11]. Rhabdomyosarcomas can be classified into alveolar, embryonal, spindle cell/sclerosing, and pleomorphic subtypes based on the clinicopathological features and genetic alterations, with each subtype showing unique morphology and distinctive genetic alterations [10,11].

Rhabdomyosarcomas may be locally aggressive soft tissue tumors that may result in significant morbidity due to invasion of surrounding critical structures in the head and neck region. Despite multimodality management, recurrent disease is not uncommon [12]. Management of recurrent rhabdomyosarcomas of the head and neck region poses a formidable challenge to the treating physicians due to critical lesion localization in the vicinity of important structures. RT has been utilized as a part of multimodality management of head and neck rhabdomyosarcomas for both children and adults and may play a critical role to achieve improved therapeutic outcomes [12-19]. A study by Wen et al. revealed that RT could improve overall survival and event-free survival of patients with head and neck rhabdomyosarcomas by improving local tumor control [19].

Nevertheless, the head and neck region contains critical parts with important functions and excessive exposure to critical structures may result in significant morbidity and deterioration in the quality of life. Within this context, precision in treatment volume definition has become an indispensable aspect of contemporary irradiation protocols with the incorporation of excellent RT delivery techniques and modalities. Precisely focused irradiation of well-defined targets has been achieved by utilization of radiosurgical techniques with robust stereotactic immobilization and image guidance, however, vigilance is required for improved precision and accuracy in treatment volume definition to avoid geographic misses, treatment failures, and radiation-induced adverse effects. While the definition of larger than actual target volumes may result in excessive exposure of neighboring normal tissues with untowards toxicity, determination of smaller than actual target volumes may lead to treatment failures. In this context, there is an apparent need for the optimization of treatment volume definitions. While IGRT techniques may offer improved target localization, utilization of matched CT and MR images may assist in accurate target volume definition for optimal irradiation. There has been accumulating evidence in support of multimodality imaging-based target volume definition for many indications [20-51]. Within this context, this study may add to the growing body of evidence supporting the utility of multimodality imaging-based treatment volume definition for radiotherapeutic management of recurrent head and neck rhabdomyosarcomas.

The introduction of innovatory technologies offers great potential for improving the toxicity profile of radiation delivery in the millennium era. Utilization of efficacious doses of radiation while maintaining optimal normal tissue sparing may contribute to achieving improved therapeutic outcomes for patients with recurrent head and neck rhabdomyosarcomas. Within this context, accuracy in target volume definition has been an indispensable part of contemporary irradiation strategies. Recent years have witnessed important advances with excellent improvements in the radiation oncology discipline by the introduction of modernized treatment equipment and adaptive irradiation strategies, IGRT, Intensity Modulated Radiation Therapy (IMRT), Adaptive Radiation Therapy (ART), Breathing Adapted Radiation Therapy (BART), molecular imaging methods, automatic segmentation techniques, and stereotactic irradiation [52-89].

In conclusion, optimal management of recurrent head and neck rhabdomyosarcomas may be improved by precise and accurate RT treatment volume determination. Within this context, the incorporation of MRI in the target and treatment volume definition process may be strongly recommended to achieve improved accuracy and precision in target and treatment volume determination despite the need for further supporting evidence.

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