



Research Article

Volume 32 Issue 4 - August 2026
DOI: 10.19080/CTOIJ.2026.32.556345

Cancer Ther Oncol Int J

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Assessment of Target Volume Determination for Alveolar Rhabdomyosarcoma of the Eye: The Impact of Multimodality Imaging

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Submission: July 31, 2026; Published: August 11, 2026

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Abstract

Objective: The present study aimed to evaluate target volume definition for radiotherapy of ocular/orbital alveolar rhabdomyosarcoma by comparing computed tomography (CT)-based contouring with multimodality imaging-guided target delineation incorporating magnetic resonance imaging (MRI) and other available diagnostic imaging.

Materials and Methods: This retrospective study was conducted at the Department of Radiation Oncology, University of Health Sciences, Gulhane Medical Faculty, a tertiary referral institution with extensive experience in multidisciplinary oncologic management, pediatric and young adult malignancies, radiotherapy applications, and advanced image-guided treatment techniques. Initial gross tumor volumes were contoured on CT simulation images alone by experienced radiation oncologists familiar with head and neck radiotherapy planning. Subsequently, MRI and other available pretreatment imaging datasets were incorporated into the contouring workflow, and target volumes were re-evaluated and modified where appropriate based on improved soft-tissue visualization, lesion conspicuity, anatomical correlation, and delineation of tumor interfaces with critical orbital structures.

Results: Integration of multimodality imaging resulted in clinically meaningful modifications of target volumes in a substantial proportion of evaluated cases. Compared with CT-only contouring, incorporation of MRI improved visualization of tumor boundaries and facilitated more confident differentiation between tumor tissue, adjacent orbital soft tissues, and treatment-related or nonspecific anatomical changes.

Conclusion: Multimodality imaging substantially improves the precision and confidence of target volume delineation for ocular/orbital alveolar rhabdomyosarcoma compared with CT-based planning alone.

Keywords: Alveolar Rhabdomyosarcoma; Eye; Radiotherapy; Target Definition; Computed Tomography; Emission Tomography

Abbreviations: IMRT: Intensity-Modulated Radiotherapy; VMAT: Volumetric Modulated Arc Therapy; IGRT: Image-Guided Radiotherapy; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography

Introduction

Rhabdomyosarcoma is the most common soft-tissue sarcoma of childhood and represents an important malignant tumor in pediatric oncology because of its potential for local invasion, regional dissemination, and distant metastasis [1,2]. Although rhabdomyosarcoma may arise in a variety of anatomical locations, tumors involving the head and neck represent a particularly important clinical subgroup because of the complex anatomy and the proximity of the primary lesion to critical functional structures. Orbital involvement is an uncommon but clinically distinctive presentation and may be associated with characteristic

patterns of local extension and favorable opportunities for organ-preserving treatment when appropriately diagnosed and managed [2]. Among the histological subtypes of rhabdomyosarcoma, alveolar rhabdomyosarcoma is characterized by aggressive biological behavior and may demonstrate a greater propensity for regional and distant dissemination than some other pediatric rhabdomyosarcoma subtypes [2].

Consequently, management generally requires coordinated multimodality therapy incorporating systemic chemotherapy and definitive local treatment with radiotherapy, surgery, or

selected combinations of these approaches [2]. Radiotherapy plays an important role in local disease control for patients with rhabdomyosarcoma, particularly when preservation of critical anatomical structures is prioritized. In ocular and orbital disease, the therapeutic objective is particularly challenging because adequate treatment of the primary tumor must be balanced against the risk of radiation-induced injury to the eye and surrounding structures. The orbit contains multiple radiosensitive tissues with important visual, endocrine, neurological, and cosmetic functions, including the globe, lens, retina, optic nerve, optic chiasm, extraocular muscles, lacrimal apparatus, and adjacent brain structures. These anatomical considerations make accurate target volume delineation a fundamental component of radiotherapy planning for ocular/orbital rhabdomyosarcoma.

Inaccurate definition of the primary tumor may result in geographic miss and inadequate local treatment, whereas unnecessarily extensive target volumes may expose normal ocular and neurological structures to avoidable radiation. The importance of precise target definition is further amplified when highly conformal treatment techniques are employed, because steep dose gradients can make relatively small contouring uncertainties clinically relevant. The anatomical complexity of the orbit also creates significant challenges for conventional CT-based target delineation. Simulation CT provides reliable geometric information and remains an essential component of radiotherapy planning and dose calculation. However, the relatively limited soft-tissue contrast of CT may make it difficult to distinguish tumor tissue from normal orbital structures, particularly when the lesion is small, infiltrative, irregularly shaped, or closely associated with extraocular muscles, the optic nerve, orbital apex, or other soft-tissue structures.

Magnetic resonance imaging (MRI) provides superior soft-tissue contrast and multiplanar anatomical characterization and is therefore particularly valuable for assessment of orbital malignancies. T1-weighted and T2-weighted sequences, contrast-enhanced imaging, and diffusion-weighted sequences can provide complementary information regarding tumor morphology, tissue characteristics, anatomical extension, and relationships with adjacent structures. MRI may consequently improve identification of the true extent of disease beyond that appreciated on CT simulation images alone. In addition to MRI, other diagnostic imaging modalities may provide complementary information during the pretreatment evaluation of rhabdomyosarcoma. Positron emission tomography/computed tomography (PET/CT), when clinically indicated, may contribute information regarding regional or distant disease. Ophthalmologic examination and dedicated ocular imaging may also provide clinically relevant information regarding involvement of the globe and adjacent ocular structures. Integration of these complementary datasets may therefore improve confidence in the definition of the primary treatment target.

The importance of multimodality imaging may be particularly pronounced in patients who receive systemic chemotherapy before definitive local treatment. Rhabdomyosarcoma frequently demonstrates substantial treatment-related changes in tumor size and morphology following induction therapy. Distinguishing residual tumor from treatment-related changes may be difficult on individual imaging modalities, and comparison with pretreatment imaging may therefore be essential for accurate target definition. Modern radiotherapy technologies have further increased the relevance of high-quality multimodality imaging. Intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), proton therapy, image-guided radiotherapy (IGRT), stereotactic techniques in selected circumstances, and adaptive radiotherapy permit increasingly conformal dose delivery [3-100]. These techniques can reduce radiation exposure to adjacent normal tissues, but their effectiveness depends critically on accurate identification of the target and reliable characterization of the surrounding anatomy.

In ocular and orbital rhabdomyosarcoma, this issue is particularly important because the tumor may lie near structures for which even relatively modest radiation exposure may result in clinically meaningful toxicity. Depending on tumor location, relevant organs at risk may include the lens, globe, retina, optic nerve, optic chiasm, lacrimal gland, extraocular muscles, brain, pituitary gland, and other structures of the skull base and central nervous system. Despite increasing recognition of the value of MRI and multimodality imaging in head and neck radiotherapy, the specific contribution of multimodality imaging to target volume determination in ocular/orbital alveolar rhabdomyosarcoma remains incompletely characterized.

Limited information is available regarding the extent to which MRI and complementary imaging modalities modify CT-based target contours and whether these modifications have potential implications for treatment planning. Accordingly, the present study aimed to evaluate target volume definition for radiotherapy of ocular/orbital alveolar rhabdomyosarcoma by comparing CT-based contouring with multimodality imaging-guided target delineation. The study further sought to characterize the anatomical situations in which additional imaging information most substantially influenced target definition and to explore the potential implications of multimodality imaging for individualized radiotherapy planning.

Materials and Methods

This retrospective study was conducted at the Department of Radiation Oncology, University of Health Sciences, Gulhane Medical Faculty, a tertiary referral institution with extensive experience in multidisciplinary oncologic management, pediatric malignancies, sarcoma treatment, and advanced image-guided radiotherapy techniques. Patients with histopathologically confirmed alveolar rhabdomyosarcoma involving the eye/orbit who underwent radiotherapy planning at our institution were retrospectively

evaluated. Eligible patients had pretreatment diagnostic imaging and a dedicated CT simulation dataset suitable for target delineation analysis. Patients were included if sufficient imaging information was available to permit comparative assessment of target volume definition using CT alone and CT supplemented by MRI and other clinically available imaging studies. Patients with incomplete imaging documentation, inadequate image quality, or insufficient information for reliable target delineation were excluded from the analysis.

All cases were evaluated within a multidisciplinary clinical framework involving radiation oncology, pediatric oncology/medical oncology, radiology, pathology, ophthalmology, and other relevant specialties when clinically indicated. The pretreatment evaluation included review of clinical findings, pathological diagnosis, disease stage, treatment history, and available diagnostic imaging. Particular attention was directed toward the anatomical location of the primary lesion, laterality, involvement of the globe and orbital structures, extension toward the orbital apex or skull base, and relationship with the optic nerve and other critical structures. Where available, pretreatment MRI examinations were reviewed together with CT, PET/CT, ophthalmologic imaging, and other diagnostic examinations relevant to characterization of the primary tumor. Systemic treatment administered before radiotherapy was also reviewed when applicable because treatment-induced changes in tumor dimensions and morphology may influence the interpretation of post-treatment imaging.

CT simulation was performed using a dedicated radiotherapy CT simulator. Patients were positioned using individualized immobilization techniques appropriate for head and neck radiotherapy. Reproducible head positioning was emphasized because of the small treatment volumes and the close proximity of the target to critical ocular and neurological structures. Thin-slice CT images were obtained for treatment planning and target delineation. Intravenous contrast was administered when clinically appropriate to improve visualization of tumor tissue, vascular structures, and relevant anatomical interfaces. The CT dataset served as the reference dataset for the initial contouring analysis and subsequent image registration. MRI examinations were performed using dedicated head and orbital imaging protocols when available.

MRI datasets included sequences selected to optimize visualization of the primary lesion and surrounding orbital structures. Depending on clinical availability, imaging included T1-weighted, T2-weighted, fat-suppressed, contrast-enhanced, and diffusion-weighted sequences. Particular attention was directed toward visualization of tumor extension within the orbit, relationships with the globe and extraocular muscles, optic nerve involvement, orbital apex extension, and possible extension toward adjacent skull-base or intracranial structures. Additional imaging examinations, including PET/CT and dedicated

ophthalmologic imaging, were reviewed when clinically available and relevant to the assessment of disease extent. MRI and other diagnostic imaging datasets were registered with the planning CT dataset using available image-registration techniques to facilitate anatomical correlation.

Initial gross tumor volumes were contoured on CT simulation images alone by experienced radiation oncologists with expertise in head and neck and pediatric radiotherapy. At this stage, the radiation oncologists were asked to define the gross tumor volume based exclusively on the CT simulation dataset and available clinical information according to the institutional contouring approach. Following completion of the CT-only contouring process, MRI and other relevant imaging datasets were incorporated into the delineation workflow. The gross tumor volume was subsequently reassessed and modified where appropriate according to the additional anatomical information provided by multimodality imaging.

Attention was directed toward:

- Definition of the superior and inferior tumor boundaries
- Medial and lateral tumor extension
- Anterior and posterior orbital extension
- Relationship with the globe
- Extraocular muscle involvement
- Optic nerve proximity or involvement
- Orbital apex extension
- Skull-base relationships
- Intracranial extension
- Involvement of adjacent soft tissues
- Distinction between tumor and normal orbital structures

The CT-only and multimodality imaging-based contours were subsequently compared to characterize changes in target volume definition. Where applicable, clinical target volume and planning target volume expansions were generated according to institutional protocols. Organs at risk were delineated with particular attention to structures whose radiation exposure may influence visual, neurological, endocrine, or cosmetic outcomes.

These included the:

- Globe
- Lens
- Retina
- Optic nerves
- Optic chiasm
- Lacrimal glands

- Extraocular muscles
- Brain
- Pituitary gland
- Other relevant skull-base and intracranial structures

The relationship between the target volume and these organs at risk was assessed before and after incorporation of multimodality imaging. Treatment plans were generated using the institutional treatment planning system. Where appropriate, plans based on CT-only contours were compared with plans generated following multimodality imaging-guided contour refinement. Dosimetric evaluation focused on target coverage, target volume, conformity, dose gradients, and radiation exposure to adjacent organs at risk. Dose-volume histogram analyses were performed when applicable. The potential impact of altered target contours on dose distribution and normal tissue sparing was assessed. Qualitative assessment of contouring confidence and anatomical visualization was also performed.

The reviewers evaluated whether incorporation of MRI and complementary imaging improved:

1. Identification of tumor boundaries;
2. Confidence in distinguishing tumor from normal orbital structures;
3. Recognition of subtle tumor extension;
4. Characterization of tumor relationships with critical organs at risk; and
5. Overall confidence in the final target definition.

Results

Patients with pathologically confirmed ocular/orbital alveolar rhabdomyosarcoma who fulfilled the predefined eligibility criteria were included in the analysis. Integration of multimodality imaging resulted in clinically meaningful modifications of target volume definition in a substantial proportion of evaluated cases. Compared with CT-only contouring, incorporation of MRI provided improved visualization of the primary tumor and facilitated more confident delineation of its boundaries. The benefit of MRI was particularly apparent in areas where the tumor demonstrated limited contrast relative to surrounding orbital soft tissues on CT imaging. In several cases, CT-only imaging resulted in uncertainty regarding the precise extent of the lesion, particularly at interfaces with the globe, extraocular muscles, optic nerve, orbital apex, and adjacent skull-base structures.

Following incorporation of MRI, these anatomical relationships could be more clearly characterized, resulting in modification of the gross tumor volume. MRI also facilitated differentiation between tumor tissue and adjacent normal orbital structures. This was particularly relevant in regions where small

differences in tissue contrast could influence the interpretation of tumor extension. In selected cases, multimodality imaging demonstrated areas of suspected tumor extension that were not clearly appreciated on CT simulation imaging alone. Conversely, improved anatomical characterization also allowed some regions initially considered suspicious on CT to be excluded from the final target volume when MRI demonstrated a more likely normal anatomical structure or nonspecific change.

The magnitude and direction of contour modifications varied according to tumor location, size, morphology, and relationship with adjacent orbital structures. Multimodality imaging was particularly valuable in anatomically complex lesions involving or approaching the orbital apex, optic nerve, extraocular muscles, globe, or skull base. Modification of target contours following multimodality imaging resulted in corresponding changes in treatment planning parameters. In cases in which MRI allowed more precise definition of tumor boundaries, target volumes could be refined without compromising the intended anatomical extent of treatment. More accurate delineation also improved characterization of the spatial relationship between the target and adjacent organs at risk. In selected cases, multimodality imaging-guided contour refinement resulted in reduction of unnecessary irradiation of adjacent normal tissues while maintaining appropriate target coverage. Overall, the imaging findings demonstrated that incorporation of MRI and complementary imaging information substantially influenced target volume determination in ocular/orbital alveolar rhabdomyosarcoma.

Discussion

Rhabdomyosarcoma of the orbit represents a distinctive clinical entity in which successful treatment requires precise local control while preserving visual function and minimizing treatment-related morbidity [2]. The anatomical complexity of the orbit and the close proximity of the primary tumor to multiple radiosensitive structures make accurate target delineation particularly important. The present study evaluated the contribution of multimodality imaging to target volume determination and demonstrated that incorporation of MRI and complementary imaging information can meaningfully modify CT-based target definition. The principal finding of this analysis was that multimodality imaging improved visualization of the primary tumor and increased confidence in delineating its anatomical boundaries. Compared with CT-only contouring, MRI provided superior soft-tissue discrimination and allowed more detailed assessment of tumor relationships with adjacent orbital structures.

This finding has relevance in ocular/orbital rhabdomyosarcoma because the difference between tumor and normal tissue may be difficult to appreciate on CT alone. The orbit contains a complex arrangement of muscles, nerves, vessels, fat, connective tissues, and the globe, all of which may contribute to uncertainty when

defining a relatively small tumor volume. MRI offers important advantages in this setting because of its superior soft-tissue contrast and multiplanar capability. Tumor extension involving the extraocular muscles, orbital apex, optic nerve region, and adjacent soft tissues can be more readily characterized on MRI than on CT in many clinical circumstances. Another important aspect of target delineation in rhabdomyosarcoma is the potential impact of systemic therapy before radiotherapy. Patients may undergo substantial tumor regression during induction chemotherapy, resulting in changes in tumor dimensions and morphology.

However, radiographic reduction does not necessarily imply complete elimination of viable tumor. Therefore, target definition should incorporate both pretreatment disease extent and the post-treatment anatomical appearance. Multimodality imaging may be particularly valuable in this setting because it permits direct comparison of the original tumor with the post-treatment anatomy. MRI may help distinguish residual tumor from treatment-related edema, fibrosis, necrosis, or other nonspecific changes. Such distinctions can be clinically important when defining the final treatment volume. The implications of accurate target delineation are particularly significant for radiotherapy of orbital tumors. The primary tumor may be located only millimeters from highly radiosensitive structures, and unnecessary expansion of the treatment volume may increase the radiation dose received by the lens, retina, optic nerve, optic chiasm, lacrimal gland, and other critical tissues.

Conversely, inadequate target definition may result in geographic miss and compromise local control. Thus, the central challenge is not simply to create the smallest possible treatment volume but rather to define the most anatomically accurate volume that adequately represents the true extent of disease. The present findings suggest that multimodality imaging may improve this balance. By providing additional anatomical information, MRI can help refine the target contour and potentially reduce unnecessary inclusion of adjacent normal tissue. In selected cases, this may translate into improved dose conformity and more favorable organ-at-risk exposure. Modern radiotherapy technologies further amplify the importance of accurate imaging. IMRT, VMAT, proton therapy, IGRT, and other highly conformal techniques allow radiation dose to be shaped closely around the target. However, the benefit of these technologies is inherently dependent on the accuracy of the target volume. A highly conformal treatment plan based on an inaccurate contour may simply deliver an inaccurate dose distribution with greater geometric precision.

Therefore, multimodality imaging should be regarded as an integral component of advanced radiotherapy rather than an optional diagnostic supplement. The findings also support the potential role of MRI in image-guided and adaptive radiotherapy workflows. MRI-guided radiotherapy systems provide superior soft-tissue visualization compared with conventional image guidance and may allow more reliable assessment of anatomical

changes during treatment. Although online MRI-guided adaptive radiotherapy is not currently standard for all patients with orbital rhabdomyosarcoma, the conceptual advantages are important. Changes in tumor volume, patient anatomy, treatment response, or positioning could potentially be incorporated into individualized treatment adaptation in appropriately selected cases. Another important consideration is the complementary nature of different imaging modalities. CT remains essential for radiotherapy simulation and dose calculation, whereas MRI provides superior soft-tissue characterization.

PET/CT may provide additional information regarding metabolically active disease when clinically indicated, while ophthalmologic assessment can provide direct information regarding ocular involvement that may not be fully captured by conventional radiotherapy imaging. Accordingly, multimodality imaging should not be interpreted as a competition between imaging techniques. Rather, each modality provides complementary information that can contribute to a more comprehensive representation of disease extent.

The anatomical complexity of orbital rhabdomyosarcoma also highlights the importance of multidisciplinary interpretation. Radiologists, radiation oncologists, ophthalmologists, pediatric oncologists, surgeons, and other specialists may interpret different aspects of the available imaging data. Integration of these perspectives may reduce uncertainty and improve the reliability of final target definition.

The dosimetric consequences of contour modification are potentially clinically important. Even modest changes in target volume can alter dose distributions when critical structures are located immediately adjacent to the tumor. More accurate contours may permit reduction in unnecessary irradiation of normal tissue while maintaining appropriate target coverage. However, the clinical significance of improved contouring precision should not be overstated. A change in target volume does not necessarily translate directly into improved local control or reduced toxicity. Prospective studies correlating multimodality imaging-based contouring with treatment outcomes, visual function, endocrine effects, late toxicity, and local tumor control are needed.

Future studies should investigate standardized multimodality imaging protocols, quantitative MRI parameters, diffusion-weighted imaging, PET/MRI where appropriate, deformable image registration, and longitudinal assessment of treatment-related anatomical changes. Integration of advanced imaging with radiomics and artificial intelligence-assisted segmentation may represent another potentially important direction. Automated or semi-automated segmentation tools could assist with delineation of complex orbital structures, although their reliability will ultimately depend on the quality and consistency of the underlying imaging data. In addition, prospective evaluation of MRI-guided adaptive radiotherapy may determine whether

daily anatomical information can be translated into clinically meaningful reductions in radiation exposure to critical ocular and neurological structures.

Overall, the present findings emphasize that accurate target delineation is a central component of radiotherapy for ocular/orbital alveolar rhabdomyosarcoma and that multimodality imaging can provide important anatomical information beyond CT simulation alone. Multimodality imaging, particularly the integration of MRI with CT-based radiotherapy planning, improves visualization and delineation of ocular/orbital alveolar rhabdomyosarcoma and can result in clinically meaningful modifications of target volume definition. The greatest benefit appears to occur in anatomically complex lesions involving or approaching the globe, extraocular muscles, optic nerve, orbital apex, and adjacent skull-base structures.

Improved target characterization may facilitate more precise radiotherapy planning, maintain adequate target coverage, and potentially reduce unnecessary radiation exposure to critical visual and neurological structures. These findings support the incorporation of multimodality imaging into the target delineation workflow for ocular/orbital alveolar rhabdomyosarcoma. Prospective studies incorporating standardized imaging protocols, quantitative imaging biomarkers, dosimetric endpoints, visual and neurological outcomes, and long-term tumor control are warranted to further establish the clinical value of multimodality imaging and to define its role in MRI-guided and adaptive radiotherapy.

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DOI: [10.19080/CTOIJ.2026.32.556345](https://doi.org/10.19080/CTOIJ.2026.32.556345)

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