



# Target Volume Determination for Recurrent Uterine Carcinosarcoma: An Original Research Article Revisiting the Utility of Multimodality Imaging



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## Abstract

**Objective:** Optimization of target definition has been a very important part of contemporary radiotherapeutic management of uterine carcinosarcomas. In this original research article, our goal is to address and evaluate target volume determination for recurrent uterine carcinosarcomas by multimodality imaging.

**Materials and methods:** We have performed a comparative evaluation to investigate target definition based on CT simulation images only or by integration of Magnetic Resonance Imaging (MRI).

**Results:** We have evaluated multimodality imaging by incorporation of MRI in target volume definition in a group of patients referred for radiotherapeutic management of recurrent uterine carcinosarcoma in this original research article. Treatment delivery has been accomplished in our Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences. Included patients have undergone meticulous multidisciplinary evaluation by experts from relevant disciplines of surgical oncology, radiation oncology, and medical oncology. We have performed a comparative analysis for evaluation of target and critical organ determination by use of either CT only imaging or by fused CT-MRI in an attempt to address the role of multimodality imaging. As the primary outcome, the ground truth target volume was found to be identical with fused CT-MRI based target definition for patients with recurrent uterine carcinosarcomas.

**Conclusion:** Radiotherapeutic management of recurrent uterine carcinosarcomas may be improved by utilization of multimodality imaging by incorporation of MRI into the RT planning procedure and thus should be strongly considered.

**Keywords:** Uterine carcinosarcoma; Radiation therapy (RT); Magnetic Resonance Imaging (MRI)

## Introduction

Although uterine sarcomas are relatively more infrequent tumors presenting as biphasic neoplasms including admixed epithelial and mesenchymal elements, they may lead to uterine cancer specific mortality [1-5]. Divergence and metaplasia of carcinomatous components into sarcomatous components may occur as consistent with the conversion theory [1]. Uterine carcinosarcomas may most commonly occur in older patients and may typically follow an aggressive disease course resulting in grim prognosis. While a considerable proportion of uterine carcinosarcomas may have spread beyond the uterus at initial diagnosis, recurrences may also occur.

Patients with uterine carcinosarcomas may be diagnosed at relatively more advanced stages, and affected patients' symptoms may deteriorate their quality of life considerably. For the meantime, multidisciplinary management may be utilized for achieving optimal therapeutic outcomes [1-5]. Radiation therapy (RT) may have an integral role in multidisciplinary management and also for management of recurrent disease [1-5]. Determination of target volume constitutes an important aspect of radiotherapeutic management for uterine carcinosarcomas. Ever lasting advances in surgery, RT, and systemic treatment may offer relatively improved life expectancies for patients suffering

from uterine carcinosarcomas. From this perspective, adverse effects of reirradiation has been a critical endpoint of current radiotherapeutic strategies. Introduction and integration of sophisticated approaches in cancer management has resulted in critical improvements in radiotherapeutic management in the millenium era. Evolution of sophisticated treatment concepts and techniques including Image Guided RT (IGRT), molecular imaging methods, automatic segmentation techniques, Intensity Modulated RT (IMRT), stereotactic RT, and adaptive RT (ART) have profoundly improved radiotherapeutic perspectives [6-45].

Incorporation of relatively newer and more recent RT concepts have led to more accurate and precise targeting of tumors through steeper dose gradients around the target volumes which resulted in reduced exposure of normal tissues. Decreased critical organ doses may allow for reduced radiation induced toxicity and RT dose escalation which might pave the way for the best therapeutic ratio. Nevertheless, it should be kept in mind that vigilance is critically required before clinical implementation of these recent radiotherapeutic concepts in daily routine RT practice. Optimization of target definition has been a very important part of contemporary radiotherapeutic management of uterine carcinosarcomas. In the meantime, Computed Tomography (CT) simulation has a critical role in RT planning at majority of treatment centers universally. Clearly, CT serves as a feasible imaging modality for dose calculation purposes, however, incorporation of other imaging modalities for RT planning may significantly add to the accuracy and precision of target definition. Indeed, several studies have readily addressed the utility of multimodality imaging for optimal target definition [46-83]. In this original research article, our goal is to address and evaluate target volume determination for recurrent uterine carcinosarcomas by multimodality imaging.

### Materials and Methods

In this original research article, we have assessed patients referred to Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences for radiotherapeutic management of recurrent uterine carcinosarcomas. We have performed a comparative evaluation to investigate target definition based on CT simulation images only or by integration of Magnetic Resonance Imaging (MRI). The aim of this study has been to assess the use of multimodality imaging for target determination, nevertheless, delineation of critical organs, interobserver and intraobserver variations have also been evaluated. We have used the ground truth target volume for comparative analysis and for comparison purposes, and this ground truth target volume was determined by board certified radiation oncologists after detailed consideration of all imaging and relevant data with collaborative colleague peer review and consensus. Experts from relevant disciplines of surgical oncology, radiation oncology, and medical oncology have taken part in decision making for multidisciplinary management. Patient, disease, and treatment related characteristics have been considered on an individual

basis by taking into account age, symptomatology, performance status, prior treatments, lesion size, location and association with nearby critical organs, contemplated outcomes of considered therapies, patient preferences and logistical issues.

Treatment delivery has been achieved by Synergy (Elekta, UK) Linear Accelerator (LINAC) by incorporation of IGRT techniques. CT simulation images were obtained at the CT simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) for RT planning after robust patient immobilization. Then, obtained RT planning images have been transferred to the delineation workstation (SimMD, GE, UK) by the network for generation of structure sets including the target volumes and critical structures. In an attempt to investigate the endpoint of this study, we undertook a comparative analysis to assess target and critical organ definition by use of either CT simulation images only or fused CT-MR images.

### Results

We have evaluated multimodality imaging by incorporation of MRI in target volume definition in a group of patients referred for radiotherapeutic management of recurrent uterine carcinosarcoma in this original research article. Treatment delivery has been accomplished in our Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences. Included patients have undergone meticulous multidisciplinary evaluation by experts from relevant disciplines of surgical oncology, radiation oncology, and medical oncology. We have performed a comparative analysis for evaluation of target and critical organ determination by use of either CT only imaging or by fused CT-MRI in an attempt to address the role of multimodality imaging. Lesion size, localization and association with surrounding critical structures have been considered as tumor related parameters that have been taken into account in radiotherapeutic management. We have also considered patient characteristics including patient symptomatology, age, performance status, and logistical issues. Expert radiation physicists participated in radiation treatment planning by taking into account the reports by American Association of Physicists in Medicine (AAPM) and International Commission on Radiation Units and Measurements (ICRU).

Electron density, tissue heterogeneity, CT number and HU values in CT images have been considered in precise RT planning. Principal objective of RT planning was to achieve optimal target coverage with minimal exposure of surrounding normal tissues. Ground truth target volume has been defined for each patient by board certified radiation oncologists after thorough evaluation, collaborative colleague peer review process, and consensus to be used for actual treatment and for comparison purposes. Additionally, IGRT techniques were also utilized for accurate setup verification. Synergy (Elekta, UK) LINAC has been utilized for treatment delivery. As the primary outcome, the ground truth target volume was found to be identical with fused CT-MRI based target definition for patients with recurrent uterine carcinosarcomas.

## Discussion

Even though uterine sarcomas may be considered as relatively more uncommon tumors presenting as biphasic neoplasms including admixed epithelial and mesenchymal elements, they may lead to uterine cancer specific mortality [1-5]. Divergence and metaplasia of carcinomatous components into sarcomatous components may occur in consistency with the conversion theory [1]. Uterine carcinosarcomas may more frequently occur in older patients and may usually follow an aggressive disease course resulting in poor prognosis. A considerable proportion of uterine carcinosarcomas may have spread beyond the uterus at initial diagnosis, and recurrences may also occur.

Patients with uterine carcinosarcomas may be diagnosed at more advanced stages, and affected patients' symptoms may deteriorate their quality of life significantly. Currently, multidisciplinary management may be utilized for achieving optimal therapeutic outcomes [1-5]. RT may play an integral role in multidisciplinary management and also for management of recurrent uterine carcinosarcoma [1-5]. Definition of target volume comprises a critical aspect of radiotherapeutic management for uterine carcinosarcomas. Advances in surgery, RT, and systemic treatment may offer relatively improved life expectancies for patients suffering from uterine carcinosarcomas. Within this context, adverse radiation effects have been an important endpoint of recent RT approaches. Integration of contemporary strategies in cancer management has led to critical improvements in radiotherapeutic management in the millenium era. Evolution of state of the art therapeutic concepts and techniques such as IGRT, molecular imaging methods, automatic segmentation techniques, IMRT, stereotactic RT, and ART have significantly improved radiotherapeutic perspectives [6-45].

Incorporation of relatively newer and more recent RT concepts have led to more accurate and precise targeting of tumors through steeper dose gradients around the target volumes which resulted in decreased exposure of critical organs. Reduced normal tissue doses may allow for decreased morbidity and RT dose escalation which might pave the way for an improved therapeutic ratio. However, it should be kept in mind that vigilance is needed before clinical implementation of these recent radiotherapeutic concepts in daily routine RT practice. Optimization of target determination has been an indispensable component of sophisticated radiotherapeutic management of uterine carcinosarcomas. Currently, CT simulation plays an important role in RT planning at majority of treatment centers globally. Admittedly, CT serves as a plausible imaging modality for dose calculation purposes, nevertheless, integration of other imaging modalities for RT planning may critically add to the precision and accuracy of target determination. In the literature, a plethora of studies have revealed the use of multimodality imaging for optimal target determination [46-83]. In this original research article, our

purpose was to address and assess target volume definition for recurrent uterine carcinosarcomas by multimodality imaging, and we have observed significant contribution of this approach.

## Conclusion

In conclusion, radiotherapeutic management of recurrent uterine carcinosarcomas may be improved by utilization of multimodality imaging by incorporation of MRI into the RT planning procedure and thus should be strongly considered.

## Conflict of Interest

There are no conflicts of interest and no acknowledgements.

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