



# Quad Shot Radiotherapy Volume Determination in Head and Cancer Patients



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**Submission:** April 01, 2024; **Published:** May 02, 2024

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## Abstract

**Objective:** The dose determination of quad shot was evaluated in head and neck cancer radiotherapy.

**Materials and methods:** Head and neck area is the most commonly cancer site of unknown primary worldwide. Radiotherapy and or chemotherapy is a crucial treatment modality for patients with head and neck cancer. The development of different dose schemes in head and neck cancer patients undergoing radiotherapy has led to the exploration of various strategies. Primary goal of this study has been to evaluate pacemaker dose determination for breast cancer. We have carried out a comparative analysis of treatment volume determination by CT simulation images only or by integration of PET. While we primarily focused on evaluation of incorporated multimodality imaging for treatment volume determination, we also assessed critical organ contouring along with interobserver and intra observer variations. Ground truth target volume has been utilized for comparative analysis, and it was determined by board certified radiation oncologists after detailed evaluation of all imaging and relevant data with thorough colleague peer review and consensus.

**Results:** Ground truth target volume was used as the reference for comparative evaluation, and our results revealed that use of fused PET-CT based treatment volume determination was identical with ground truth target definition in our selected group in head and neck cancer patients.

**Conclusion:** This article aims to review the association between the use of quad shot radiotherapy in head and neck cancer patients, focusing on the materials and methods employed, results obtained, and the subsequent discussions surrounding the topic.

**Keywords:** Quad shot; Head and Neck Cancer; Radiotherapy; Surgical Oncology; Medical Oncology and Radiation Oncology

**Abbreviations:** IMRT: Intensity-Modulated Radiotherapy; SBRT: Stereotactic Body Radiation Therapy; LINAC: Linear Accelerator; AAPM: American Association of Physicists in Medicine; ICRU: International Commission on Radiation Units and Measurements; RT: Radiation Therapy

## Introduction

Quad Shot radiotherapy is a regimen designed for palliation in advanced head and neck cancer patients, characterized by delivering a higher fraction of radiation over a shorter period. The volume determination for Quad Shot radiotherapy is typically guided by the same principles as conventional radiotherapy, where a radiation oncologist delineates the target volumes on planning images, such as a computed tomography scan.

Despite advances in the treatment of head and neck cancer, 15 to 50 percent of patients will develop recurrent disease. Survivors also are at risk to develop second primary tumors, the incidence of which is estimated at 8 to 22 percent, with approximately one-third occurring in the head and neck. Therapeutic options are

limited for patients who present with locally recurrent disease or a second primary tumor in a previously irradiated field. Surgical salvage with a curative-intent resection is the preferred option for those with limited-volume disease. Reirradiation is an alternative for patients who are not candidates for surgical salvage.

Reirradiation with or without the addition of chemotherapy may hold promise for long-term survival for appropriately selected patients. Indications for reirradiation may include: Patients who undergo surgical salvage but are found to have high-risk features or who are medically suitable for curative-intent interventions but are not amenable to curative-intent resection and or who are not candidates for curative-intent interventions but may benefit from palliative treatment.

A thorough analysis of the initial treatment volumes and dose distributions relative to the location of the locoregional recurrence or second primary tumor should be made when reirradiation is considered. Determination of the dose received at the site of recurrence may demonstrate geographic tumor miss and is necessary for treatment planning since a geographic or marginal miss may not represent the same radioresistant disease as a true in-field recurrence, even with a disease-free interval of less than a year.

Reirradiation treatment volumes for patients treated with IMRT (typically with concurrent chemotherapy) are usually limited to a 1 to 2 cm margin around the gross tumor or the surgical site, with even smaller margins when tumors are near critical structures such as the skull base/brainstem, spinal cord, optic nerve, or optic chiasm. This approach was validated in a retrospective review of 66 re-irradiated patients, which demonstrated that 96 percent of locoregional recurrences following reirradiation occurred within the gross tumor volume and only 4 percent occurred in untreated regional sites. The cumulative dose to the spinal cord from all courses of treatment is usually limited to 50 Gy, with the reirradiation dose to the spinal cord restricted to 10 percent of the prescribed reirradiation dose. Treatment volumes for patients re-irradiated with stereotactic body radiation therapy (SBRT) are often limited to small deposits of gross disease and a <1 cm margin for patient setup uncertainty [1-15].

### Materials and Methods

Conventionally, such patients are prescribed a dose of 30 Gy/2 weeks/10 fractions for palliation of symptoms. Squamous cell carcinoma of the head and neck region constitute approximately 20% of the total cancer patient population treated different centers worldwide, and about 40% of these patients are treated with only palliative intent. However, recent trials have suggested alternative hypo-fractionated schedules for palliation where the overall treatment duration is further reduced.

Primary goal of this study has been to evaluate treatment volume determination for head and neck cancer based on PET and CT fusion. We have carried out a comparative analysis of treatment volume determination by CT simulation images only or by integration of PET. While we primarily focused on evaluation of incorporated multimodality imaging for treatment volume determination, we also assessed critical organ contouring along with interobserver and intra observer variations. Decision making procedure for individualized patient management has involved multidisciplinary input from experts on surgical oncology, radiation oncology, medical oncology. Patient, disease, and treatment related factors were all considered. Patient age, previous treatments, symptomatology, lesion size, performance status, lesion localization and association with normal tissues, contemplated outcomes of alternative treatment alternatives, patient preferences and logistical issues have also been taken

into account. A Linear Accelerator (LINAC) furnished with sophisticated IGRT techniques has been utilized for RT. Following robust patient immobilization, planning CT images were obtained at CT simulator for radiation treatment planning. Then, acquired RT planning images have been transferred to the delineation workstation via the network.

The process includes defining the gross tumor volume, which contains the visible tumor, and the clinical target volume, which includes the GTV plus a margin to cover any microscopic disease spread. Additionally, a margin is added to the CTV to create the planning target volume, which accounts for patient movement and variations in treatment setup and delivery. Treatment volumes and normal tissues have been outlined on these images and structure sets have been generated. Either CT simulation images only or fused CT-MR images have been used for assessment and comparative data analysis.

### Results

The results from several studies have demonstrated that quad shot radiotherapy administered concurrently or sequentially with chemotherapy can decrease the pain in head and neck cancer patients. We designated this original research article to assess the utility of multimodality imaging with incorporation of PET-CT fusion for treatment volume determination in a selected group of patients with head and neck cancer. Irradiation of patients was performed at our Radiation Oncology Department of Gulhane Medical Faculty at University of Health Sciences, Ankara. Before irradiation, patients were individually evaluated by multidisciplinary collaboration of surgical oncology, medical oncology and radiation oncology disciplines. We executed a comparative analysis based on either CT only imaging or by fused PET-CT to evaluate the use of this sophisticated strategy. Optimal RT planning procedure included consideration of lesion sizes, localization, and association with nearby critical structures. Radiation physicists were included in RT planning process with consideration of reports by American Association of Physicists in Medicine (AAPM) and International Commission on Radiation Units and Measurements (ICRU). Precise RT planning process included consideration of electron density, tissue heterogeneity, CT number and HU values in CT images. Primary objective of RT planning has been to achieve optimal coverage of treatment volumes along with minimized exposure of surrounding critical structures. Truth target volume was used as the reference for comparative evaluation, and our results revealed that use of fused PET-CT based treatment volume determination was identical with ground truth target definition in our selected group of patients with head and neck cancer.

### Discussion

The Quad Shot regimen specifically involves delivering four fractions on two consecutive days, for a total of four cycles, which can repeat every 4 weeks. Each fraction is generally a higher

dose than in standard fractionation, targeting a rapid palliative response while still trying to minimize side effects. Because this method is palliative, the volumes may be somewhat smaller and focused compared to those used in curative treatments, with the aim of alleviating symptoms and maintaining the quality of life. However, the exact delineation of volumes would depend on individual patient anatomy, the extent of the disease, and the clinical judgment of the treating radiation oncologist.

Corry et al described the 'Quad Shot' radiation dose schedule was 14 Gy/2 days/ 4 fractions as by. The patients were treated in Cobalt60 teletherapy units and the gross tumor volume (including the primary tumor and involved nodes) with 2 cm margin was irradiated. Two fractions of radiation were given every day with a minimum 6-hour gap between the two fractions. The Biologically Equivalent Dose for one Quad Shot was 18.9 Gy10 and 30.38 Gy3 for tumor and late reacting tissues (LQED2 15.75 Gy10 and 18.19 Gy3), respectively. Patients were reviewed 3 weeks later for response and toxicities.

IMRT is being used to deliver a radical radiation dose to the primary tumor and high-risk nodal volumes only (PTV1), with a simultaneous integrated boost to the gross nodal disease to a higher dose with or without a sequential boost to the primary tumor (PTV2). This will help determine the feasibility of a complex dose-dense IMRT regimen, along with gathering early evidence of high rates of loco-regional control in poor prognosis head and neck cancer sub-sites with acceptable toxicity. This is a rare and difficult to treat cancer which has a high probability of being cured with radiation alone, or in combination with surgery [16-35].

The use of intensity-modulated radiotherapy (IMRT) is widespread in the treatment of head and neck cancers. It has been shown to consistently achieve a higher degree of target conformity and normal tissue sparing. Given these potential gains, the aims of this study were to investigate the feasibility of a new form of high-precision radiation treatment, dynamic IMRT, and to determine the potential gains in target coverage and normal tissue sparing achievable compared with conventional IMRT. Carcinomas of the head and neck account for 5% of all tumors. Radiation alone, or in combination with surgery or chemotherapy, has been the accepted method of treatment for many years. This is based on the results of randomized trials which have shown equivalent survival rates and organ preservation with radiation compared to surgery, along with the improvement in loco-regional control and quality of life compared to palliative care. Step and shoot IMRT has been shown to facilitate the delivery of altered fractionation regimes compared with 3D conformal radiotherapy and has thus been widely adopted as the method of choice for definitive or adjuvant radiation treatment of head and neck cancers in many centers. An optimal radiation therapy regimen in terms of fractionation and dose has yet to be determined, although altered fractionation regimes have shown promise in terms of improving loco-regional

control and survival at the expense of increased acute and late toxicities [36-65].

Although data are limited, palliative irradiation is an option for patients whose tumor is significantly impacting quality of life and who are not candidates for an aggressive course of reirradiation. In general, tumor shrinkage with palliative reirradiation is expected to be greater than the response to chemotherapy. Lower doses and larger fraction sizes are delivered to patients receiving palliative reirradiation. The lower dose should result in a lower risk of acute toxicity, and the increased risk of late complications with larger fraction sizes is generally not relevant.

The "Quad Shot" approach to palliative radiation therapy (RT) delivers short, cyclical courses to maximize clinical response and minimize toxicity. Each cycle consists of twice-daily hypofractionated RT administered over two days in four-week intervals for a total of two or more cycles depending on treatment response. This approach allows mucosal stem cells to repopulate before the next cycle. While the best data regarding the Quad Shot approach come from an uncontrolled perspective trial in patients without prior RT exposure, this approach is offered to the patients with prior RT exposure who are not candidates for more aggressive treatment, as the limited observational data in the setting of reirradiation are promising.

In two retrospective studies including a total of 101 patients with incurable recurrent or metastatic head and neck cancer treated with the Quad Shot approach, responses were seen in 70 percent, and there was a low rate of grade  $\geq 3$  toxicities [66-99]. As a conclusion, detailed protocols for Quad Shot radiotherapy volume determination might not be universally standardized and therefore should be individualized based on the patient's specific clinical scenario and the treating institution's guidelines.

### Conflict of Interest

No.

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DOI: [10.19080/CTOIJ.2024.25.556197](https://doi.org/10.19080/CTOIJ.2024.25.556197)

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