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# Assessment of Changes in Tumor Size After Induction Systemic Therapy for Locally Advanced Cervical Squamous Cell Carcinoma Running title: Tumor size changes in cervical carcinoma

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**Abstract**

**Objective:** Cervical squamous cell carcinoma remains to be a major public health concern with its critical incidence around the globe. Admittedly, both the disease itself and the therapies utilized for management of cervical squamous cell carcinoma may deteriorate quality of life. Surgery, radiation therapy (RT), and systemic agents may be utilized for optimal treatment of cervical squamous cell carcinoma. In this study, we evaluated tumor size changes after neoadjuvant systemic treatment in patients with cervical squamous cell carcinoma.

**Materials and methods:** Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences serves as a tertiary cancer center for patients from Turkey and abroad. In this study, we aimed at assessing tumor size changes after neoadjuvant systemic treatment for patients with cervical squamous cell carcinoma. For this purpose, cerviwassquamous cell carcinoma patients with available imaging data as part of initial workup were studied.

**Results:** Tumor size changes after neoadjuvant systemic treatment were documented for comparative assessment. As the main outcome of the current study, we have found a mean decrease of 24% in tumor size after neoadjuvant systemic treatment for patients with cervical squamous cell carcinoma.

Conclusion: In this study, we have documented tumor size changes after neoadjuvant systemic treatment comparative evaluation. And as the main result of our study, we found a mean decrease of 24% in tumor size after neoadjuvant systemic treatment for patients with cervical squamous cell carcinoma. Our results may have implications for implementation of adaptive RT strategies despite the need for further supporting evidence.

**Keywords:** Cervical squamous cell carcinoma; Radiation therapy (RT); Neoadjuvant chemotherapy; Radiation oncology; Automatic segmentation techniques

**Abbreviations:** RT: Radiation Therapy; IGRT: Image Guided RT; IMRT: Intensity Modulated RT; ART: Adaptive RT; LINAC: Linear Accelerator; AAPM: Association of Physicists in Medicine; ICRU: International Commission on Radiation Units

## Introduction

Cervical squamous cell carcinoma remains to be a major public health concern with its critical incidence around the globe [1,2]. Admittedly, both the disease itself and the therapies utilized for management of cervical squamous cell carcinoma may deteriorate quality of life. Surgery, radiation therapy (RT), and systemic agents may be utilized for optimal treatment of cervical squamous cell carcinoma. Many forms of irradiation may be used, and sophisticated technologies including intensity modulation and adaptive RT techniques may improve radiotherapeutic results. Clearly, the use of higher effective doses may lead to better local control outcomes, nevertheless, toxicity profile of radiation delivery should also be considered to maintain patients' quality of life. Recent years have witnessed unprecedented advances in technology which clearly contributed to improved treatment results with RT. Molecular imaging methods, automatic segmentation techniques, Image Guided RT (IGRT), Intensity Modulated RT (IMRT), stereotactic RT, and adaptive RT (ART) were introduced for improved efficacy [3-40].

As a matter of fact, optimal treatment outcomes might solely be achieved by close collaboration among related disciplines for cancer management. Tumor boards improve collaboration among surgical oncologists, radiation oncologists, medical oncologists, imaging and other relevant specialists to discuss patients, tumor, and treatment characteristics. This helps determine the individualized treatment approach for optimal patient management. Neoadjuvant systemic therapy may be suggested for management of cervical squamous cell carcinoma [41-49]. The rationale behind neoadjuvant systemic treatment may include reduction of disease burden prior to administration of subsequent treatments. Also, neoadjuvant systemic treatment may prevent systemic spread. Nevertheless, there may also be controversies regarding neoadjuvant systemic treatments such as the risk of delayed local treatments such as RT or surgery. However, selected groups of patients with cervical squamous cell carcinoma may benefit from neoadjuvant systemic treatment [41-49]. In this study, we evaluated tumor size changes after neoadjuvant systemic treatment in patients with cervical squamous cell carcinoma.

## Materials and methods

Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences serves as a tertiary cancer center for patients from Turkey and abroad. A plethora of benign and malignant tumors are irradiated here by using modernized equipment and sophisticated technology including IGRT, IMRT, ART, stereotactic RT, automatic segmentation techniques, and molecular imaging methods [3-40]. In this study, we aimed at assessing tumor size changes after neoadjuvant systemic treatment for patients with cervical squamous cell carcinoma. For this purpose, cervical squamous cell carcinoma patients with available imaging data as part of initial workup were studied. All included patients received upfront neoadjuvant systemic treatment and then were referred for RT at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences. We executed a comparative analysis for tumor sizes at diagnostic CT scans of the patients and at CT-simulation for radiation treatment planning after neoadjuvant systemic treatment. CT simulations were performed at CT-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) available at our tertiary cancer center. Tumor size changes after neoadjuvant systemic treatment were documented for comparative assessment. Linear Accelerator (LINAC) furnished with state-of-the-art IGRT techniques was utilized for RT. Following rigid patient immobilization, planning CT images have been acquired at the CT simulator for radiation treatment planning. Thereafter, acquired RT planning images have been transferred to the contouring workstation through the network. Target volumes and critical structures have been delineated on these images and structure sets have been generated. All patients have been tirradiated by use of contemporary RT techniques at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences.

## Results

This original research article has been designed to investigate tumor size changes following neoadjuvant systemic treatment for patients with cervical squamous cell carcinoma. Irradiation procedures have been performed at our Radiation Oncology Department of Gulhane Medical Faculty at University of Health Sciences, Ankara. Prior to irradiation, all included patients have been individually evaluated by a multidisciplinary team of experts from surgical oncology, medical oncology, and radiation oncology. Cervical squamous cell carcinoma patients with available imaging data as part of initial workup have been included. Selected patients have initially received upfront neoadjuvant systemic treatment and were afterwards referred for RT at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences. We performed a comparative analysis for tumor sizes at diagnostic CT scan of the patients and at CT-simulation for radiation treatment planning after neoadjuvant systemic treatment. CT simulations of the patients have been performed at CT-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) available at our tertiary cancer center. Tumor size changes after neoadjuvant systemic treatment were documented for comparative assessment.

As the main outcome of the current study, we have found a mean decrease of 24% in tumor size after neoadjuvant systemic treatment for patients with cervical squamous cell carcinoma. Optimal RT planning procedure includes consideration of lesion sizes, localization and association with surrounding critical organs. Radiation physicists took part 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 procedure included consideration of electron density, tissue heterogeneity, CT number and HU values in CT images. The primary objective of RT planning has been to achieve optimal encompassing of treatment volumes along with minimized exposure of surrounding critical organs. All patients have been irradiated by using contemporary RT techniques at the Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences.

## Discussion

Cervical squamous cell carcinoma remains to be a major public health concern with its critical incidence around the


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globe [1,2]. Admittedly, both the disease itself and the therapies utilized for management of cervical squamous cell carcinoma may deteriorate quality of life. Surgery, radiation therapy (RT), and systemic agents may be utilized for optimal treatment of cervical squamous cell carcinoma. Many forms of irradiation may be used, and sophisticated technologies including intensity modulation and adaptive RT techniques may improve radiotherapeutic results. Clearly, the use of higher effective doses may lead to better local control outcomes, nevertheless, toxicity profile of radiation delivery should also be considered to maintain patients' quality of life. Significant advances have taken place in technology in the millenium era which clearly contributed to improved treatment results. Molecular imaging methods, automatic segmentation techniques, IGRT, IMRT, stereotactic RT, and ART have been introduced for optimal irradiation [3-40]. As a matter of fact, improved treatment outcomes may solely be acquired through close collaboration among the disciplines. Tumor boards may contribute to bringing together surgical oncologists, radiation oncologists, medical oncologists, imaging and other relevant specialists to discuss about patient, tumor, and treatment characteristics to select the optimal management strategy for the individual patient. Neoadjuvant systemic therapy may play a role in management of cervical squamous cell carcinoma [41-49]. The rationale behind neoadjuvant systemic treatment may include decreasing the disease burden and thus facilitating administration of subsequent therapies. Also, neoadjuvant systemic treatment may prevent early widespread dissemination.

Nevertheless, there may also be controversies regarding neoadjuvant systemic treatments including the risk of delayed local treatments such as RT or surgery. With this in mind, selected patients with cervical squamous cell carcinoma may benefit from neoadjuvant systemic treatment anyway. In the current study, we have evaluated tumor size changes after neoadjuvant systemic treatment in patients with cervical squamous cell carcinoma. Patients with available imaging data as part of initial workup have been included. All included patients have received upfront neoadjuvant systemic treatment and were then referred for RT at Department of Radiation Oncology at Gulhane Medical Faculty, University of Health Sciences. We have performed a comparative analysis for tumor sizes at diagnostic CT scan of the patients and at CT-simulation for radiation treatment planning following neoadjuvant systemic treatment. CT simulations of the patients were done at CT-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) available at our tertiary cancer center.

Tumor size changes after neoadjuvant systemic treatment have been documented for comparative assessment. As the primary outcome of our study, we have found a mean decrease of 24% in tumor size following neoadjuvant systemic treatment for patients with cervical squamous cell carcinoma. From the standpoint of radiation oncology, optimal target definition and critical organ sparing may be considered among the critical components of optimal irradiation. While definition of larger treatment volumes may result in excessive RT toxicity, definition of smaller treatment volumes may subsequently lead to treatment failures. Adaptive RT approaches and multimodality imaging-based target definition have been suggested for achieving improved outcomes [50-96]. In this study, we have documented tumor size changes after neoadjuvant systemic treatment comparative evaluation. And as the main result of our study, we found a mean decrease of 24% in tumor size after neoadjuvant systemic treatment for patients with cervical squamous cell carcinoma. Our results may have implications for implementation of adaptive RT strategies despite the need for further supporting evidence.

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