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Changes in Tumor Size Following Systemic Therapy for Oligometastatic Prostate Cancer

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Abstract

Objective: The oligometastatic concept suggests that selected patients may benefit from aggressive multimodality treatment approaches that combine systemic therapy with local ablative modalities such as surgery or radiation therapy (RT). However, the degree of tumor response following systemic therapy and its potential impact on local treatment planning remain insufficiently characterized in oligometastatic prostate cancer. In this study, we sought to evaluate tumor size changes after systemic therapy in patients with oligometastatic prostate cancer and to assess the potential implications of these changes for radiotherapy planning and adaptive treatment strategies.

Materials and methods: Patients with oligometastatic prostate cancer who had available radiologic imaging both before and after systemic therapy were included in the analysis. Tumor measurements were derived from imaging studies obtained prior to the initiation of systemic treatment and after completion of therapy. Changes in tumor size were evaluated for both the primary prostatic tumor and metastatic lesions using standardized radiologic assessment criteria. Comparative analyses were subsequently performed to assess variations in tumor dimensions following systemic therapy using paired statistical methodology.

Results: Patients with oligometastatic prostate cancer were included in the analysis, and all individuals completed the planned course of systemic therapy. Comparative evaluation of pre- and post-treatment imaging demonstrated a measurable reduction in tumor burden in most patients following systemic therapy with reductions observed in both primary and metastatic lesions. These treatment-related anatomical changes appeared clinically relevant for subsequent RT planning, particularly with respect to target volume delineation and the potential application of adaptive radiotherapy approaches.

Conclusion: Systemic therapy appears to result in meaningful tumor size reduction in patients with oligometastatic prostate cancer. These findings may have important implications for RT planning and support the integration of adaptive and individualized radiotherapy strategies within multimodality treatment paradigms. Further prospective studies are needed to optimize treatment sequencing, refine adaptive RT approaches, and improve oncologic outcomes in this evolving patient population with limited metastatic disease.

Keywords: Oligometastatic Prostate Cancer, Systemic Treatment, Tumor Size Changes Adaptive Radiotherapy, Treatment Planning

Abbreviations: STSs: Soft Tissue Sarcomas; SBRT: Stereotactic Body Radiotherapy; OARs: Organs at Risk; MRI: Magnetic Resonance Imaging; GTVs: Gross tumor volumes; PTVs: Planning Target Volumes; STSs: Soft Tissue Sarcomas; CT: Computed Tomography; IGRT: Image-Guided Radiotherapy; ART: Adaptive Radiotherapy; GTVs: Gross Tumor Volumes; CTV: Clinical Target Volume; PTV: Planning Target Volume; CBCT: Cone-Beam CT; DVH: Dose-Volume Histogram

Introduction

Prostate cancer remains one of the most frequently diagnosed malignancies among men worldwide and continues to represent a major cause of cancer-related morbidity and mortality [1,2]. Despite substantial advances in screening, imaging, systemic therapies, and local treatment modalities, disease progression and metastatic dissemination continue to pose significant clinical challenges [2,3]. While many patients are initially diagnosed with localized diseases amenable to curative treatment, a considerable proportion ultimately develop metastatic involvement either at presentation or during disease evolution [2,4].

Importantly, metastatic prostate cancer is increasingly recognized as a biologically and clinically heterogeneous entity rather than a single uniform disease state [3,5]. Within this heterogeneous spectrum, oligometastatic prostate cancer has emerged as a distinct clinical condition characterized by a limited metastatic burden, most commonly involving osseous structures and regional or distant lymph nodes [5,6]. The oligometastatic paradigm proposes that selected patients with a restricted number of metastatic lesions may harbor a disease biology that is intermediate between localized and widely disseminated metastatic disease [5,7].

This concept has generated substantial interest because it raises the possibility that aggressive multimodality treatment approaches may improve disease control and potentially delay progression in carefully selected patients [6-8]. In this context, treatment strategies integrating systemic therapy with local ablative interventions such as surgery or radiation therapy (RT) have gained increasing attention [6,8]. Systemic therapy remains a fundamental component of management because it targets both visible disease and occult micro metastatic tumor deposits that may not yet be radiologically detectable [4,9]. In addition to controlling systemic disease, systemic treatment may also reduce tumor burden, improve symptom control, and potentially enhance the feasibility and effectiveness of subsequent local therapies [8,9].

However, despite the growing adoption of multimodality treatment paradigms, the magnitude and pattern of tumor response following systemic therapy remain insufficiently characterized in patients with oligometastatic prostate cancer [8,9]. A more comprehensive understanding of tumor regression after systemic treatment may carry important implications for radiotherapy planning and treatment adaptation.

Reductions in tumor size may influence target delineation, treatment volumes, dose distribution, and normal tissue sparing. Furthermore, anatomical and volumetric changes occurring during treatment may alter the spatial relationship between tumor targets and adjacent organs at risk, thereby affecting the therapeutic ratio [10,11].

RT has undergone remarkable technological evolution over recent decades. Contemporary techniques including image-guided radiotherapy (IGRT), intensity-modulated radiotherapy (IMRT), stereotactic body radiotherapy (SBRT), and adaptive radiotherapy (ART) enable highly conformal dose delivery with improved precision and reduced irradiation of surrounding healthy tissues [10-12]. These advances are particularly relevant in oligometastatic prostate cancer, where accurate localization and treatment of limited metastatic lesions are critical for maximizing local control while minimizing treatment-related toxicity [6,10].

Adaptive radiotherapy approaches offer the potential to account for anatomical and tumor-related changes occurring while treatment, thereby allowing more individualized and dynamic treatment delivery [11,12]. Given these considerations, evaluation of tumor size alterations following systemic therapy may provide clinically meaningful information for treatment planning and optimization. Therefore, in the present study, we aimed to assess tumor size changes after systemic therapy in patients with oligometastatic prostate cancer and to explore the potential implications of these changes for RT planning and adaptive treatment strategies.

Materials and Methods

This retrospective study was conducted at the Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences, a tertiary referral institution providing oncologic care for patients from Turkey and international centers. Institutional clinical records and imaging data were retrospectively reviewed to identify eligible patients diagnosed with oligometastatic prostate cancer who underwent systemic therapy and had available radiologic imaging both before and after treatment. The study was designed as a retrospective observational analysis aimed at evaluating treatment-related radiologic tumor response and its potential implications for subsequent radiotherapy planning.

Oligometastatic disease was defined as the presence of a limited number of metastatic lesions considered potentially amenable to local therapeutic intervention according to contemporary oligometastatic disease definitions and institutional multidisciplinary consensus criteria. Patients were included if adequate diagnostic imaging studies were available for comparative assessment of tumor burden prior to initiation of systemic therapy and following completion of treatment. Patients without sufficient imaging data or incomplete treatment information were excluded from analysis.

The primary study endpoint was radiologic change in tumor size following systemic therapy, assessed in both primary and metastatic lesions. Secondary exploration endpoints included evaluation of the potential impact of observed tumor regression on radiotherapy target delineation and adaptive treatment planning considerations. All patients underwent multidisciplinary evaluation before treatment planning. Clinical management decisions were discussed within a tumor board consisting of urologists, medical oncologists, nuclear medicine physicians, diagnostic radiologists, and radiation oncologists. Systemic treatment approaches were selected according to institutional treatment protocols, disease characteristics, performance status, and multidisciplinary consensus recommendations.

Diagnostic imaging modalities utilized for disease evaluation included computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography/computed tomography (PET/CT), and bone scintigraphy when clinically indicated. Baseline imaging studies obtained before initiation of systemic therapy were compared with post-treatment imaging

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performed after completion of therapy. Tumor measurements were obtained for both the primary prostate lesion and metastatic sites. Changes in tumor dimensions were evaluated using standardized radiologic assessment principles based on lesion size measurements obtained from available imaging studies and were interpreted in accordance with routine institutional radiologic reporting standards.

Comparative analyses were performed to document alterations in tumor burden following systemic therapy. Attention was directed toward evaluating reductions in lesion size that could potentially influence subsequent radiotherapy target delineation and treatment planning considerations. Observed anatomical changes were qualitatively assessed with respect to their potential relevance for target volume reduction, organ-at-risk sparing, and the feasibility of adaptive radiotherapy implementation. Clinical, radiologic, and treatment-related data were collected and reviewed retrospectively.

To minimize observer-related bias, imaging findings were reviewed in conjunction with multidisciplinary clinical documentation and radiologic reports. Descriptive analyses were performed to assess tumor response patterns after systemic therapy in patients with oligometastatic prostate cancer because of the exploration nature of the study and the limited cohort. Given the exploratory nature of the study and limited cohort size, analyses were primarily descriptive. Tumor response patterns were evaluated using comparative radiologic assessment, with emphasis on clinically relevant changes that could influence subsequent radiotherapy planning.

Results

This retrospective analysis included patients with oligometastatic prostate cancer who underwent systemic therapy and had available radiologic imaging before and after treatment. All patients completed the planned systemic treatment regimen according to institutional protocols and multidisciplinary treatment recommendations. Comparative evaluation of imaging studies demonstrated measurable reductions in tumor burden following systemic therapy in most patients. Both primary prostatic lesions and metastatic sites exhibited decreases in tumor dimensions after treatment.

Although the magnitude of radiologic response varied between individuals, a consistent overall trend toward tumor regression was observed across the cohort. Tumor regression was observed across different metastatic locations, including nodal and osseous sites when evaluable by imaging. Assessment of pre-treatment and post-treatment imaging revealed that systemic therapy resulted in notable changes in tumor geometry and lesion size. In some cases, reductions in tumor volume appeared sufficiently pronounced to potentially alter radiotherapy target delineation and clinical treatment planning strategies. In several patients, reductions in tumor volume appeared substantial enough to potentially influence local treatment planning considerations, including target volume definition and radiation treatment field design.

The observed tumor size reductions suggest that systemic therapy may improve the feasibility of highly conformal local treatment approaches by decreasing tumor burden prior to RT. Furthermore, anatomical changes following systemic treatment highlighted the potential relevance of adaptive radiotherapy strategies designed to account for interval tumor regression and treatment-related anatomical modifications. Given the descriptive nature of the analysis, results were not stratified by specific systemic treatment regimens or metastatic burden subgroups; however, both primary and metastatic disease sites demonstrated a generally concordant pattern of response.

Although the magnitude of response varied among patients, the overall pattern suggested a favorable treatment-related reduction in measurable disease burden. Notably, both primary prostatic lesions and metastatic deposits demonstrated regression, supporting the systemic effectiveness of initial therapy prior to local treatment intensification. Overall, the findings demonstrated that systemic therapy was associated with measurable radiologic tumor response in patients with oligometastatic prostate cancer, affecting both primary and metastatic disease sites.

Discussion

Prostate cancer continues to represent a substantial global health challenge and remains among the leading causes of cancer-related morbidity and mortality in men worldwide [1,2]. Although metastatic prostate cancer has traditionally been associated with unfavorable clinical outcomes, increasing evidence suggests that metastatic disease encompasses a broad spectrum of biologically diverse clinical states [3,5]. Within this spectrum, oligometastatic prostate cancer has emerged as a potentially distinct disease entity characterized by limited metastatic dissemination, frequently involving bone and lymph node sites [5,6].

The oligometastatic paradigm has challenged the traditional binary distinction between localized and widely metastatic disease [5,7]. Rather than representing uniformly disseminated systemic disease, oligometastatic prostate cancer may reflect an intermediate biological state in which selected patients could derive benefit from aggressive local and systemic treatment approaches [6-8]. Consequently, multimodality management strategies combining systemic therapy with surgery or radiotherapy have gained increasing interest in recent years [6,8].

Systemic therapy constitutes a central component of treatment because it addresses both clinically detectable disease and occult microscopic metastatic deposits [4,9]. In addition to systemic disease control, treatment-induced tumor regression may improve the feasibility and precision of local consolidative therapies [8,13]. In this context, radiologic tumor regression observed in the present study supports the concept that systemic therapy may not only provide systemic disease control but also actively modify the

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spatial and volumetric characteristics of disease burden, thereby influencing subsequent local treatment strategies. Nevertheless, despite increasing integration of multimodality treatment strategies, the extent of tumor response after systemic therapy and its potential implications for radiotherapy planning remain incompletely understood [8,13].

The present study demonstrated that systemic therapy was associated with measurable reductions in tumor size in patients with oligometastatic prostate cancer. Tumor regression was observed in both primary prostate lesions and metastatic sites, suggesting that systemic treatment may substantially alter disease burden prior to local therapy consideration [13,14]. These observations may have important implications for radiotherapy planning and treatment adaptation [10,11]. Importantly, this finding is consistent with the biological rationale of metastatic hormone-sensitive prostate cancer management, where early systemic intensification has been shown to improve disease control in randomized trials such as CHAARTED and LATITUDE, as well as combination approaches evaluated in PEACE-1 [15-17].

Reduction in tumor volume following systemic therapy may facilitate the application of highly conformal radiotherapy techniques by decreasing target size and potentially improving sparing of adjacent organs at risk [10-12]. Smaller target volumes may permit improved dose conformity and more favorable dose distributions while reducing unnecessary irradiation of surrounding normal tissues [10,18]. This consideration is particularly relevant in pelvic RT, where critical structures such as the rectum, bladder, bowel, and femoral heads may be susceptible to treatment-related toxicity [18,19]. Modern RT technologies including IGRT, IMRT, SBRT, and ART are particularly well suited to capitalize on treatment-related anatomical changes [10-12].

Image guidance improves target localization accuracy, while IMRT and SBRT allow highly conformal dose delivery to complex target volumes [10,11]. ART strategies may further optimize treatment by incorporating interval imaging to account for tumor regression, anatomical shifts, and changes in organ motion during treatment [11,12,20]. Notably, response-adapted radiotherapy concepts are increasingly supported by emerging clinical evidence such as the ORIOLE and STOMP trials, which highlight the potential benefit of metastasis-directed therapy in carefully selected oligometastatic patients [13,14]. Such approaches may enhance the therapeutic ratio through individualized adaptation of treatment plans over time [20].

The findings of the present study also underscore the importance of multidisciplinary evaluation and treatment sequencing. While systemic therapy may improve local treatment feasibility through tumor reduction, excessive delay in definitive local therapy could potentially compromise disease control in selected patients [8,21]. Accordingly, individualized decision-making based on multidisciplinary assessment remains essential to optimize treatment timing and sequencing [21]. From a clinical standpoint, this raises an important therapeutic sequencing question: whether systemic therapy should be used solely as disease control or also as a “neoadjuvant debulking strategy” to optimize radiotherapy planning in oligometastatic disease.

The present findings should also be interpreted in the context of emerging evidence supporting treatment intensification in metastatic hormone-sensitive prostate cancer, including the PEACE-1 and CHAARTED trials, which demonstrated improved oncologic outcomes with earlier multimodality intervention. Several limitations should be considered when interpreting the results of this study. The retrospective design and limited patient cohort may restrict the generalizability of the findings. Additionally, heterogeneity in imaging modalities and systemic treatment approaches may influence assessment of tumor response.

Long-term oncologic outcomes including local control, progression-free survival, and overall survival were not specifically evaluated in the present analysis. Future prospective investigations involving larger patient populations are warranted to better define the relationship between tumor regression, radiotherapy adaptation, and clinical outcomes in oligometastatic prostate cancer [6,8,20]. Furthermore, the absence of volumetric contouring and standardized response quantification limits precise correlation between radiologic regression and dosimetric planning impact, which should be addressed in future prospective imaging-guided studies. The absence of standardized volumetric contouring and centralized radiologic review represents an additional limitation that may have introduced measurement variability.

In conclusion, systemic therapy appears to result in meaningful tumor size reduction in patients with oligometastatic prostate cancer. These findings may have important implications for RT planning and support the integration of adaptive and individualized radiotherapy strategies within multimodality treatment paradigms [11,12,20]. Further prospective studies are needed to optimize treatment sequencing, refine adaptive RT approaches, and improve oncologic outcomes in this evolving patient population [6,21].

This study should be regarded as hypothesis-generating and may provide a rationale for prospective trials investigating response-adapted radiotherapy strategies in oligometastatic prostate cancer.

Conflicts of Interest

There are no conflicts of interest and no acknowledgement.

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