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Quantitative Research Article

Daily Rectal Dose-volume Histogram Variation in Prostate Intensity-modulated Radiation Therapy: Is It Clinically Significant in the Era of Image Guidance?

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ABSTRACT

Aim: Because of the steep dose gradient associated with dose-escalated intensity-modulated radiation therapy, interfraction motion and variation in rectal volume may result in the rectum receiving a larger dose than predicted at treatment planning. This study aims to quantify the variation in daily rectal dose-volume histograms (DVHs) from the treatment plan and to discuss the potential clinical significance of this variation.

Materials and Methods: Daily cone beam computed tomography scans of nine patients treated with definitive prostate intensity-modulated radiation therapy were collected. The daily dose distribution to the rectum was calculated retrospectively. The variation between the planned and on-treatment rectal DVHs was determined using Friedman tests with post hoc analysis and Wilcoxon matched-pairs tests. The on-treatment DVHs were compared with dose-volume constraints (DVCs) to assess the potential clinical significance of this variation using Wilcoxon signed-rank tests.

Results: Significant variation ($P < .05$) was observed between the planned and on-treatment DVHs. The DVCs for the volume receiving 50 Gy (V50), V60, and V65 were adhered to. The mean V70 and V75 values were above the DVC; however, this variation was not statistically significant.

Conclusion: The initial treatment plan does not accurately represent the dose received by the rectum on treatment. Investigation into the most effective rectal protocol is recommended to reduce the likelihood of these variations occurring on a daily basis.

Keywords: Rectal DVH; rectal variation; prostate; IMRT

RÉSUMÉ

But : En raison du gradient de dose élevé associé à la radiothérapie conformationnelle avec modulation d'intensité (RCMI) avec augmentation de la dose, le mouvement interfractionnel et la variation du volume du rectum peuvent faire en sorte que le rectum reçoive une dose plus élevée que prévu lors de la planification du traitement. Cette étude vise à quantifier la variation des histogrammes dose-volume rectal (HDV) par rapport au plan de traitement et à discuter de l'importance clinique potentielle de cette variation.

Matériel et méthodologie : Les scans quotidiens de tomographie volumétrique à faisceau conique (TVFC) de neuf patients traités par RCMI de la prostate ont été recueillis. La distribution de dose quotidienne au rectum a été calculée de façon rétrospective. La variation entre le HDV de planification et le HDV de traitement a été déterminée en utilisant le test de Friedman avec analyse post-hoc et le test de Wilcoxon sur échantillons appariés. Les HDV de traitement ont été comparés aux contraintes dose-volume(CDV) afin d'évaluer l'importance de cette variation, en utilisant le test de Wilcoxon (signed rank).

Résultats : Une variation importante ($p<0,05$) a été observée entre les HDV de planification et de traitement. Les CDV pour le volume recevant 50 Gy (V50), V60 et V65 ont été respectés. Les valeurs moyennes de V70 et V75 étaient supérieures au CDV; cependant, la variation n'était pas statistiquement significative.

Conclusion : Le plan de traitement initial ne représente pas avec précision la dose reçue par le rectum durant le traitement. Il est recommandé de procéder à des études afin de déterminer le protocole le plus efficace pour le rectum afin de réduire la probabilité que ces variations surviennent sur une base quotidienne.

Introduction

Dose-escalated intensity-modulated radiation therapy (IMRT) is a well-established treatment method for prostate cancer with proven biochemical control and impressive

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clinical outcomes [1–4]. Assuming there is minimal interfraction variation in patient set-up and internal anatomy from the planning computed tomography (CT) scan, the initial planned dose-volume histogram (DVH) is an important predictor for acute and late toxicities. Nonetheless set-up errors, interfraction motion and variation in rectal volume may result in on-treatment doses not being accurately predicted in the initial treatment plan [5–13].

Hatton et al [14] measured whether the planned DVH was an accurate estimate of the dose distribution on treatment. They concluded there was a tendency to underestimate the dose to the rectum as 65% of all on-treatment plans were higher than the planned DVH. Similar studies also found that the planned DVH was an inaccurate predictor of on-treatment rectal doses [12, 15, 16]. Pawloski et al found that rectal volumes varied up to 50% contributing to the variation in rectal dose [15]. McParland et al [12] calculated the variation in DVH from the plan for prostate IMRT and again, large variations between rectal volume at CT and during treatment delivery were recorded. Despite this, dose-volume constraints (DVCs) were rarely exceeded, hence the authors concluded rectal toxicity may not be of clinical concern.

The primary aim of this study was to determine whether the planned rectal DVH is an accurate representation of the on-treatment DVHs. Unlike previous research that did not make use of daily images or instead used megavoltage CT [12, 14–16], this study makes use of daily cone beam computed tomography scans (CBCTs) to obtain a more accurate representation of the dose delivered to the rectum throughout a course of dose-escalated IMRT.

In addition, this study aimed to determine whether there was a violation of DVCs as a result of variation in rectal size during treatment. It is often assumed in clinical practice that as the patient's treatment is planned according to the DVCs, the rectum will remain within the DVCs throughout treatment. The normal tissue complication probability models predict that the DVCs used in this study should limit the risk of Grade $\geq$2 late rectal toxicity to $<$15% and Grade $\geq$3 late rectal toxicity to $<$10% [17].

Ultimately, this study evaluates whether the planned DVH is a good reflection of on-treatment rectal doses and gives an insight into the implication of dose-escalated prostate IMRT on the risk of rectal toxicity.

Materials and Methods

Participant Population

After institutional ethical approval, irrevocably anonymized data for patients with intermediate-risk prostate cancer were included in this retrospective dosimetry study. As part of their treatment, each patient had a planning CT as well as kilo voltage CBCTs taken daily. As these imaging data were irrevocably anonymized, specific patient characteristics were unknown to the research team. Patients were excluded if they had undergone surgery along with radiation therapy, if they had a hip prosthesis as it would reduce the quality of the CBCT scans due to artifact, or if they had a prostate-rectum hydrogel spacer as it results in latent immobilization properties of the rectum [18]. A convenience sample of 18 consecutive intermediate-risk patients was chosen from an available database. Of these, nine met the inclusion criteria for this study. As the CT data were irrevocably anonymized for this retrospective study, specific patient characteristics were unknown to the research team.

Planning

All patients were simulated supine with a comfortably full bladder and an empty rectum. Patients were advised to adhere to a low-residue diet to reduce gas production. Rectal diameter at the time of simulation was $\leq$3.5 cm as per hospital protocol. The target consisted of the prostate and proximal seminal vesicles. The prostate (CTVp) and proximal first centimetre of seminal vesicles (CTVsv) were contoured by the radiation oncologist. The CTVp was expanded anisotropically by 0.7 cm and 0.5 cm posteriorly. The CTVsv had a uniform expansion of 0.8 cm. These volumes were then combined to create the planning target volume. Organs at risk (OARs) were contoured according to contouring guidelines [19].

A 6-MV seven-field IMRT plan was created for each patient using the Eclipse treatment planning system (v8.6.1.2) with a prescription of 80 Gy in 40 fractions to the target mean. The anisotropic analytical algorithm was used with a 2.5 $\times$ 2.5 grid for dose calculations. OAR DVCs were based on literature recommendations [17, 19, 20]. For the rectum that is, the volume receiving 50 Gy (V50) must be $<$50%, V60 $<$ 35%, V65 $<$ 25%, V70 $<$ 20%, and V75 $<$ 15%.

For each patient, the daily CBCTs were fused with the original planning CT scan. These images were matched to provide the best fit to the prostate CTV contour using both automatic and manual registration tools. To ensure interobserver agreement, the match result was approved by both members of the research team. Each patient's daily rectal volumes were then contoured based on the CBCT image, again in line with guidelines [17, 19]. Specifically, the rectum was contoured as a whole organ from the rectosigmoid junction down to the level of the ischial tuberosities inferiorly. In an attempt to reduce interobserver variability, each rectum was delineated by the same radiation therapist experienced in CBCT contouring. Daily rectal DVHs were generated based on the original plan and the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) DVCs were recorded for each fraction's DVH [17].

Data Analysis

The null hypothesis was that with rectal preparation protocols, there is minimal variation in rectal on-treatment DVHs from the planned DVH. A separate Friedman test with post hoc analysis was carried out for each rectal DVC point to test this. Dunn's multiple comparison tests were used for post hoc analysis.