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Research Article

A Feasibility Study on the Role of Ultrasound Imaging of Bladder Volume as a Method to Improve Concordance of Bladder Filling Status on Treatment with Simulation

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ABSTRACT

Purpose: Accurate positioning of the prostate is of paramount importance to ensure optimal target coverage and normal tissue sparing in stereotactic ablative body radiation when large doses per fraction are delivered with tight margins around the prostate. Bladder and rectal filling play an important part in controlling the accuracy of a patient's setup and therefore the overall toxicities and outcomes. The aim of this study was to establish the value of characterizing patients' bladder filling kinetics at the time of simulation with ultrasound scans so that a predictive model can be used to ensure that a bladder volume at treatment would match at simulation.

Methods: A prospective trial was conducted in unfavorable risk prostate cancer patients to evaluate the utility of ultrasound bladder monitoring. Thirty patients ($n = 30$) were enrolled in this study. Patients were required to void before simulation and then were given 500 mL of fluids to drink. Ultrasound measurements of the bladder were documented at 15-minute intervals for up to four measurements before simulation. On treatment, bladder volumes were measured at a single time point; typically, half an hour after the patient voided and consumed 500 mL of fluids. The kinetic model was then used to predict the optimal time to set up the patient for treatment such that the bladder volume at treatment would match the volume at simulation. Every patient had a cone beam computed tomography scan before each fraction to ensure accurate patient positioning before dose delivery. Bladder volumes at treatment were measured and compared with those at simulation on the cone beam computed tomography data sets using MIMVISTA software.

Results: Of 30 patients, 26 were analyzed. The comparison of the bladder contours at treatment compared to simulation yielded a DICE coefficient (similarity) of 0.76 ± 0.11. The largest variation in bladder size was seen in the anterior-posterior direction.

Conclusions: This study demonstrated that ultrasound monitoring of the bladder status was a valuable tool in ensuring reproducible bladder filling on treatment. The bladder kinetic model indicated the general time required to achieve optimal bladder filling was 60 minutes after voiding and drinking 500 mL of water.

RÉSUMÉ

But : Le positionnement précis de la prostate est d'une importance primordiale pour assurer une couverture optimale de la cible et la protection des tissus normaux en radiothérapie stéréotaxique d'ablation (SABR) lorsque des doses élevées par fraction sont administrées avec des marges serrées autour de la prostate. Le remplissage de la vessie et du rectum joue un rôle important pour contrôler la précision du positionnement du patient et donc la toxicité et les résultats globaux. Le but de cette étude était d'établir par échographie la valeur de la caractérisation de la cinétique de remplissage de la vessie du patient au moment de la simulation, de façon à pouvoir utiliser un modèle prédictif pour faire en sorte que le volume de la

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vessie au moment du traitement corresponde au volume à la simulation.

Méthodologie : Un essai prospectif a été réalisé chez des patients ayant un cancer de la prostate à risque défavorable afin d'évaluer l'utilité de la surveillance échographique de la vessie. Trente patients (n = 30) ont participé à cette étude. Les patients devaient vider leur vessie avant la simulation et devaient ensuite boire 500 mL de liquides. Les mesures par échographie de la vessie ont été documentées à des intervalles de 15 minutes, avec un maximum de quatre mesures avant la simulation. Pendant le traitement, le volume de la vessie a été mesuré à un seul moment: habituellement, une demi-heure après que le patient ait vidé sa vessie et bu 500 mL de liquides. Le modèle cinétique a ensuite été utilisé pour prédire le moment optimal pour préparer le patient pour le traitement, afin que le volume de la vessie corresponde à son volume lors de la simulation. Chacun des patients a subi un examen de tomodensitométrie à faisceau conique (CBCT) avant chaque fraction afin d'assurer un positionnement précis du patient avant l'administration de la dose. Le volume de la vessie au moment du traitement a été mesuré et comparé à celui au moment de la simulation sur les ensembles de données de CBCT à l'aide du logiciel MIMVISTATM.

Résultats : Vingt-six des trente patients ont été analysés. La comparaison du contour de la vessie au moment du traitement par rapport à la simulation a produit un coefficient de Dice (similitude) de 0.76 ± 0.11. La plus forte variation dans la taille de la vessie a été constatée en direction antéropostérieure.

Conclusions : Cette étude a démontré que la surveillance échographique de l'état de la vessie était un outil valide pour assurer la reproductibilité du remplissage de la vessie lors du traitement. Le modèle cinétique de la vessie indique que le temps général requis pour obtenir un remplissage optimal de la vessie se situait à 60 minutes après que le patient ait vidé sa vessie et bu 500 mL d'eau.

Keywords: Bladder volume; image guided radiotherapy (IGRT); prostate cancer; stereotactic body radiotherapy (SBRT); ultrasound

Introduction

Prostate cancer is the most common cancer and the third leading cause of death from cancer in men in Canada. It is estimated that 21,300 men (21% of all new cancer cases) will be diagnosed with prostate cancer in 2017 [1]. Evidence has emerged that prostate cancer has a low α/β ratio in the range of 1–3 Gy [2]. Based on 5969 patients treated with a range of 1.8–6.7 Gy per fraction, Miralbell et al calculated the α/β ratio to be 1.4 Gy. It was suggested that the α/β ratio might be higher in high-risk tumors, but this was not statistically significant (0.6, 1.7, and 1.6 for low-, intermediate-, and high-risk prostate cancers, respectively; $P = .13$). In addition, this study found that the α/β ratio was unchanged by the use of androgen deprivation therapy [3]. Thus, it is hypothesized that prostate cancer has greater sensitivity to large fraction sizes and high dose per fraction radiotherapy theoretically allows for biological dose escalation with fewer visits and no additional toxicity.

Several randomized trials have studied dose-escalated radiotherapy and have reported increased gastrointestinal (GI) toxicities [4–8]. Al-Mamgani et al [4] conducted a phase III multicenter, randomized trial comparing 78 Gy in 39 fractions against 68 Gy in 34 fractions. They demonstrated that the incidence of late grade 2 or greater GI toxicity was 35% versus 25%, respectively. Studies demonstrate that the radiotherapeutic treatment of prostate cancer is ideally suited to hypofractionated dose regimens [9]. Stereotactic ablative body radiation (SABR) is emerging as a cost-effective method to deliver hypofractionated prostate radiotherapy [10,11]. SABR is most readily practiced by leveraging modern linear accelerator infrastructure that is image-guided radiotherapy capable. Even in the context of SABR, dose and margins are critical predictors of late toxicity. Our group found that 5 Gy more dose and a 1 mm greater margin increased late GI [12] and genitourinary toxicities [13]. Therefore, tight margins are required so that organs at risk are spared and rectal and bladder toxicities are minimized [14].

The setup of patients is of critical importance for target localization to maintain small margins. Reproducibility of patient setup from simulation is often limited by external changes and, more importantly, the relative arrangement of internal anatomy on treatment. Variances in organs at risk and prostate position are in large part due to rectal and bladder filling. Previous studies have evaluated the effect of bladder and rectal changes on prostate movement [15]. Mangar et al [16] conducted a computed tomography (CT) study assessing the impact of bladder and rectal changes on prostate movement over a 35-minute interval during simulation in the same radiotherapy planning position. Despite adhering to the drinking protocol, there were considerable intrapatient variations in initial bladder volume (46–485 mL) and rate of bladder fill (0.9–12.4 mL min^{-1}). This study also found a small positive correlation ($r = 0.43$, $P = .03$) between the superior and inferior prostate movement perhaps suggesting that as the bladder fills, the prostate is displaced inferiorly with little change at the bladder neck. Chen et al [17] studied the dosimetric impact of differences in bladder versus rectal filling during prostate cancer radiotherapy. They demonstrated that variances in rectal filling had a smaller impact compared with the bladder, later recommending that bladder status be monitored before treatment delivery. Moreover, Pinkawa et al evaluated 30 patients' prostate position variability and dose-volume histograms with full and empty bladder status [18]. Patients were planned with comfortably full bladders, which had a distinct advantage over empty bladders in terms of sparing a large proportion of bladder doses close to the prescription and pushing some bowel away from the higher dose regions.

Other studies have shown greater variability among bladder volumes when full than empty [18–20]. Tsai et al (2009) used daily cone beam computed tomography (CBCT) to assess