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Bladder radiotherapy treatment: A retrospective comparison of 3-dimensional conformal radiotherapy, intensity-modulated radiation therapy, and volumetric-modulated arc therapy plans

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ABSTRACT

To examine tumor's and organ's response when different radiotherapy plan techniques are used. Ten patients with confirmed bladder tumors were first treated using 3-dimensional conformal radiotherapy (3DCRT) and subsequently the original plans were re-optimized using the intensity-modulated radiation treatment (IMRT) and volumetric-modulated arc therapy (VMAT)-techniques. Targets coverage in terms of conformity and homogeneity index, TCP, and organs' dose limits, including integral dose analysis were evaluated. In addition, MUs and treatment delivery times were compared. Better minimum target coverage (1.3%) was observed in VMAT plans when compared to 3DCRT and IMRT ones confirmed by a statistically significant conformity index (CI) results. Large differences were observed among techniques in integral dose results of the femoral heads. Even if no statistically significant differences were reported in rectum and tissue, a large amount of energy deposition was observed in 3DCRT plans. In any case, VMAT plans provided better organs and tissue sparing confirmed also by the normal tissue complication probability (NTCP) analysis as well as a better tumor control probability (TCP) result. Our analysis showed better overall results in planning using VMAT techniques. Furthermore, a total time reduction in treatment observed among techniques including gantry and collimator rotation could encourage using the more recent one, reducing target movements and patient discomfort.

Introduction

The 3-dimensional conformal radiotherapy (3DCRT) was considered the standard modality to treat patients with tumor before the advent of the intensity-modulated radiation treatment (IMRT) that has given better results in sparing organs at risks (OARs), reducing toxicity and improving at the same time the tumor control in many cancer treatments. Studies[1,2] have showed the IMRT superiority in prostate as well as in head and neck radiotherapy in terms of dose conformity, homogeneity, and sparing of critical structures. With the more recent advent of the volumetric-modulated arc therapy (VMAT), further comparisons among techniques are carried out to evaluate the best treatment quality to be offered to the patients in terms of treatment time, dose delivered to the tumor, and organs' biological response. Even if the 2 more recent techniques have in common, with respect to the 3DCRT, the ability to treat more than one dose level to the target volume at the same time, as for simultaneous integrated boost (SIB),[3-6] their main disadvantage to be factored in during the treatment is the increased number of monitor units (MUs) that can result in a higher organs at risk and body integral dose due to radiation leaking and scattering. As a consequence, a higher risk of developing secondary malignancies is observed. If the 3DCRT seems sometimes unable to spare dose to vital organs without reducing dose to the target volume, the IMRT achieves better results using modulated beams. Including a large number of beam directions from an arc trajectory and delivering dose dynamically during a single or multiple gantry rotation, VMAT is capable to deliver to the target similar or even better dose distribution compared to the fixed-fields IMRT technique. In addition, VMAT

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significantly reduces treatment time so as to lead to a better patient comfort and to avoid uncertainty due to motion that may result in a risk of geographical target miss.

To assess the degree to which the VMAT technique could provide for efficient and effective planning outcomes, the present study was undertaken to retrospectively compare the delivered 3DCRT bladder radiotherapy treatment plans[7] to the recalculated IMRT and constant dose rate (DR) VMAT ones. Target dose distribution, its coverage, conformity, and its homogeneity were analyzed; body and OARs integral doses were calculated. A radiobiological tumor and organs' response was evaluated in terms of tumor control probability (TCP) and normal tissue complication probability (NTCP) formulas based on the equivalent uniform dose (EUD) models.

Methods and Materials

Patient characteristics

Ten patients with localized bladder tumor were treated at the Royal Free Hospital Radiotherapy Department, London, from December 2012 to May 2014. Six patients (60%) were male and 4 (40%) female with a mean age of 78.7 years; T1, T2a, and T3 tumor stages were treated (Table 1). None of the patients had received prior radiotherapy, and all of them were free of distant metastases.

CT simulation scans were acquired using a dedicated Toshiba Aquilon CT scanner in noncontrast enhanced and at supine patient position. Before starting the images acquisition, patients were asked to empty their bladder.[8] Owing to the large geographical target variation, the same request was made before each radiotherapy fraction to improve tumor localization and to reproduce the best of the initial bladder CT geometry so as to reduce target and organs' over and under dosage. The Combifix (Combifix CIVICO) System was used as standard practice for the immobilization of all pelvic patients, and all CT images were acquired at 3 mm slice thickness. Marks were placed on the patient's skin and used for patient treatment setup. All set of scans were imported to be contoured in Pinnacle (V9.2 Philips) treatment planning system workstation via local area network. The clinical target volumes, planning target volumes (PTVs), and OARs volumes were contoured by radiation oncologists. The PTV volume was obtained from a uniform 1.5 to 2 cm expansion of the whole bladder clinical target volume; rectum and femoral heads were contoured as organs at risk.

Planning technique

Originally, the 3DCRT technique was used to treat all patients. Conformal plans were carried out using 6 and 10 MV photon energy fields. Four patients were treated prescribing 64 Gy in 32 fractions; 2 patients received 36 Gy in 6 fractions; 2 patients received 40.05 Gy in 15 fractions; 1 patient received 30 Gy in 10 fractions, and 1 patient received 66 Gy in 33 fractions. Retrospectively, all plans were recalculated using step-and-shoot IMRT and constant DR SmartArc VMAT techniques. Further, 6 and 10 MV beams at 35°, 105°, 180°, 255°, and 325° gantry angles with a fixed DR of 300 MU/min were used to perform IMRT plans. Optimizations were carried out using the Pinnacle direct machine parameter optimization algorithm; a mean number of 45 segments were obtained and no segments with less than 5 MUs were generated. VMAT plans were performed using a constant 300 MU/min DR single (clockwise) or multiple (one clockwise and one counter-clockwise) arcs modality, 4° control point spacing, and a start and stop gantry angle of 200° and 160°, respectively; the collimator was rotated at 45° to minimize the Multileaf Collimator (MLC) tongue and groove radiation effect. By setting a treatment time at 90 or 120 seconds, a total of 81 control points were obtained per treatment. The dose calculation grid was set for all 3 techniques to 0.25 cm in all directions, and the same adaptive convolve convolution algorithm was used to compute the beams/arcs dose.

Table 1
Patients and related tumor characteristics

Characteristics	Average (range)
Mean age at RT (y)	78.7 (64-87)
Sex	
Male	6 (60%)
Female	4 (40%)
Tumor stage	
T1	80%
T2a	10%
T3	10%
Mean PTV volume (ml)	510.02 (329.91-1015.92)
Mean rectum volume (ml)	80.80 (40.35-185.43)

Dose plan comparison

Plans were compared using the Dose-Volume Histograms (DVHs). No minimum target coverage of less than 95% of the prescribed dose to 98% of PTV was accepted, and no more than 5% of the target received more than 105% of prescribed dose. Rectum and right and left femoral heads were considered OARs. Rectum dose limits were evaluated using the following parameters: 30 Gy to no more than 80% of all organ volume ($V_{30} < 80\%$); 40 Gy to $<70\%$ of rectum volume ($V_{40} < 70\%$); 50 Gy to $<50\%$ of volume ($V_{50} < 50\ \%$); and 60 Gy to $<40\%$ of volume ($V_{60} < 40\%$). No more than a maximum dose limit of 55 Gy was accepted for femoral heads. Finally, irradiated rectum, femoral heads, and body-OARs volumes at dose levels of 10, 20, 30, 40, 50, and 60 Gy were calculated and compared for the 3 different plan modalities.

The target dose conformity was evaluated using the conformity index (CI) defined as follows:

$$\mathrm{CI} = \frac{V_{95\%}}{V_T}$$

where $V_{95\%}$ is the target volume that receives 95% of the prescription dose and VT is the target volume. A conformity index value close to 1 indicates a tight dose distribution around the PTV volume and better tissues sparing.

Plans homogeneity was calculated using the homogeneity index (HI) given as the ratio of the difference between the dose that covers 2% and 98% of the whole target volume and the median PTV dose ($D_{50\%}$).

$$\mathrm{HI} = \frac{D_{2\%} - D_{98\%}}{D_{50\%}}$$

HI values close to zero indicate more homogeneous dose within the target.

Tissue and organs were evaluated in terms of integral dose (ID) that describes the total energy deposited within the whole body/organ. It is considered as a physical quantity capable of representing the “physical aggression” and risk of complications due to radiation therapy. The ID was calculated as a product of body or organs' dose mean, their volume, and their mean density.

$$\mathrm{ID(J)} = D_{\mathrm{mean}}(\mathrm{Gy}) \cdot V\left(\mathrm{cm}^3\right) \cdot \rho(\mathrm{kg} \times \mathrm{cm}^{-3})$$

No ID threshold value is given for treatment, but it is a good practice to maintain it as lower as possible without compromising tumor coverage so as to reduce the risk of developing secondary malignancies.