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Toxicity outcome in patients treated with modulated arc radiotherapy for localized prostate cancer

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ABSTRACT

Aim: This study evaluates the acute toxicity outcome in patients treated with RapidArc for localized prostate cancer.

Background: Modern technologies allow the delivery of high doses to the prostate while lowering the dose to the neighbouring organs at risk. Whether this dosimetric advantage translates into clinical benefit is not well known.

Materials and methods: Between December 2009 and May 2012, 45 patients with primary prostate adenocarcinoma were treated using RapidArc. All patients received 1.8 Gy per fraction, the median dose to the prostate gland, seminal vesicles, pelvic lymph nodes and surgical bed was 80 Gy (range, 77.4–81 Gy), 50.4 Gy, 50.4 Gy and 77.4 Gy (range, 75.6–79.2 Gy), respectively.

Results: The time between the last session and the last treatment follow up was a median of 10 months (range, 3–24 months). The incidence of grade 3 acute gastrointestinal (GI) and genitourinary (GU) toxicity was 2.2% and 15.5%, respectively. Grade 2 acute GI and GU toxicity occurred in 30% and 27% of patients, respectively. No grade 4 acute GI and GU toxicity were observed. Older patients (>median) or patients with V60 higher than 35% had significantly higher rates of grade ≥2 acute GI toxicity compared with the younger ones.

Conclusions: RapidArc in the treatment of localized prostate cancer is tolerated well with no Grade >3 GI and GU toxicities. Older patients or patients with higher V60 had significantly higher rates of grade ≥2 acute GI toxicity. Further research is necessary to assess definitive late toxicity and tumour control outcome.

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1. Background

Prostate Cancer is one of the most frequent tumours in men around the world. In the United States of America, prostate cancer is the number one non coetaneous cancer in men, and it is the second most common in Europe.[1] The American Cancer Society estimates that in 2013 there will be 238,590 new cases diagnosed of prostate cancer in the United States and 29,720 men will die for it.[2]

External beam radiotherapy (EBRT) is a standard treatment modality for localized and locally advanced prostate cancer.[3,4] The practice of primary EBRT for prostate cancer has changed dramatically over the past years. Modern technologies allow the delivery of high doses to the prostate while lowering the dose to the neighbouring organs at risk.[5,6] Escalation of the radiation dose beyond 70 Gy has improved biochemical control in low, intermediate and high risk patients, but the rates of rectal toxicity also increased. Volumetric modulated arc therapy using RapidArc is a novel modality of radiotherapy delivery that allows the radiation dose to be delivered during gantry rotation. This technology improves dose conformity while significantly shortening treatment time; it delivers treatments two to eight times faster than other treatments. It has been made possible by a treatment planning algorithm that simultaneously changes three parameters during treatment: rotation speed of the gantry, shape of the treatment aperture using the movement of multileaf collimator leaves in both directions and delivery dose rate.[7]

However, even with IMRT, up to 50% of the patients treated with doses >70 Gy experience bladder of bowel symptoms during treatment.[8] Clinical variables such as any pretreatment symptoms, androgen suppression, and prior transurethral resection of the prostate appeared to be important prognostic factors for radiation induced acute genitourinary (GU) and gastrointestinal (GI) toxicity.[5] The use of modern radiation technology is needed to avoid excessive toxicity technology is needed to avoid excessive toxicity with higher doses, as has been shown in randomized trials.[9]

2. Aim

The purpose of this study was to evaluate the acute toxicity outcome in patients treated with RapidArc for localized prostate cancer, with the hypothesis that using RapidArc it is possible to reach local control by giving a standard dose to the target volume without increasing the risk of injury or toxicity in the organs at risk in patients with localized disease.

3. Materials and methods

3.1. *Selection criteria*

Between December 2009 and May 2012, 45 patients were treated for primary prostate cancer. Inclusion criteria were primary diagnosis of adenocarcinoma of the prostate (T1c-T4)[10] and no prior history of radiotherapy. All patients were stratified by risk groups, based upon the current National Comprehensive Centre Network prognostic risk groupings, which include the low risk, intermediate risk and high risk.[11] Pretreatment evaluation consisted of documented history and physical examination, including performance status, digital rectal examination and serum prostate specific antigen (PSA) values performed. Base line patient characteristics are shown in Table 1.

3.2. *Treatment*

All patients were treated using a Clinac iX, equipped with Millenium Multileaf Colimator (MLC120), On Board Imager, and RapidArc capabilities. Patients were immobilized in the supine position with the same immobilization device combifix and instructions were given regarding daily preparation, full bladder (instructed to drink a glass of water 30 min before treatment). The planning target volume (PTV) was defined by 5–10 mm margin from the prostate or surgical bed.

All the treatment plans consisted in two complete arcs, with 177 control points each. Optimization for the PTV, bladder, rectum femoral heads, penile bulb and bowels was done using Eclipse V8.6 (Varian Medical Systems) optimizator and the Analytical Anisotropic Algorithm (AAA) for dose calculation. Dose constraints used in the plan prescription are shown in Table 2. All treatment plans were verified by quality assurance process before treating the patient, using the gamma analysis criteria (DD = 3%, DTA = 2 mm, (<1) 94%). The average dose volume histograms for the PTV, bladder and rectum can been seen in Figs. 1–2.

Table 1 – Patient characteristics.

Characteristic	No. of patients (%)
Age (years)	
Median (range)	67 (43–81)
Gleason	
<7	2 (4)
7	21 (47)
>7	12 (48)
T stage	
T1	10 (22)
T2	16 (36)
T3	18 (40)
T4	1 (2)
PSA (ng/ml)	
<10	27 (60)
10–19	9 (20)
>20	9 (20)
Risk	
Low	2 (4)
Intermediate	11 (24)
High	32 (72)
Androgen deprivation	
No	12 (48)
Yes	33 (52)
Radiation dose (Gy)	
Median (range)	80 (77.4–81)
PLNs irradiation	
No	3 (7)
Yes	42 (93)
Prostate planning tumour volume (cc)	
Median (range)	95 (27–245)