

Review Article

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Dosimetric and Clinical Outcomes of Volumetric Modulated Arc Therapy for Prostate Cancer

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ABSTRACT

Objectives: To evaluate the dosimetric aspects through dose coverage and tolerance as well as the clinical outcomes of radiation therapy for prostate cancer by a technique of Volumetric Modulated Arc Therapy (VMAT).

Methodology: This is a retrospective study of 71 patients treated for prostate cancer consecutively at the International Cancer Center of Dakar (CICD) from July 2020 to December 2023. All patients received radiation therapy in intensity modulation by VMAT technique. The diagnostic data, treatment information including dosimetric and results were collected and analyzed.

Results: The average age was 68.9 ± 6.1 years. The circumstance of discovery was fortuitous by PSA assay in 42.3% and symptomatic in 57.7% of cases. The median initial PSA level was 20 ng/ml (3.7–662). Adenocarcinoma was the histological type in all patients. Pelvic node involvement was found in 12.6% of patients and 5.6% were metastatic. For localized forms, high risk was predominant (49.3%). First-line radiotherapy was performed in 94.4% of cases. The average doses of the D95% and Dmax of the high-risk forecast target volume were 70.69 ± 5.2 Gy and 77.06 ± 5.88 Gy, respectively. All dose constraints have been met on the target volumes and organs at risk. No Grade 3 acute toxicity was observed. With a median follow-up of 20.67 months, the overall survival (OS) and biochemical relapse-free survival (BFS) rates at 2 years were 98.6% and 92.9%, respectively.

Conclusion: Radiotherapy occupies a prominent place in the treatment of prostate cancer. New techniques by intensity modulation allow better oncological results and improve the tolerance of treatments.

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Introduction

Prostate cancer is the most common cancer in men over 50 [1]. Its management is multidisciplinary, combining regional therapies such as surgery and radiotherapy with systemic treatments such as hormone therapy, chemotherapy and other targeted therapies [2]. Radiotherapy is essential at all stages of the disease. Two types of radiotherapy are used in the treatment of prostate cancer: external radiation therapy and brachytherapy. External radiation therapy is carried out using different techniques such as three-dimensional conformal radiotherapy (RC3D), and those with intensity modulation including volumetric arc therapy (VMAT). The modulated volumetric arc therapy is a new form of radiation therapy administration that allows for delivering the radiation dose in a single 360° rotation of the gantry giving a better dose coverage gradient compared to other intensity modulation techniques at fixed fields [3]. The objective of this study was to evaluate the dosimetric aspects through dose coverage and tolerance as well as the oncological outcomes of radiation therapy for prostate cancer by a technique of intensity modulation in volumetric arc therapy

Methodology

It was a retrospective study of 71 prostate cancer cases treated consecutively at the International Cancer Center of Dakar (CICD) from July 2020 to December 2023. Patients were included considering the following criteria:

- Histologically confirmed prostate cancer
- Patient treated with VMAT radiotherapy
- Patient with a complete medical record containing patient information (age, lifestyle, personal and family history of prostate cancer), diagnosis (consultation delay, discovery circumstance, clinical examination data, PSA, histology, imaging data, extension assessment and classification), treatment (strategies, means, acute and chronic toxicities) and evolution (overall survival, biochemical recurrence-free survival)

We excluded patients with a history of pelvic radiation, and those lost to follow-up.

We used the WHO classification to assess the general condition of patients. The disease was classified according to the TNM 2010 and the d'Amico system for localized stages. Overall survival was defined as the time elapsed between the date of initial diagnosis (biopsy) and the date of death or news. The biochemical recurrence-free survival according to the criteria of phoenix [4].

The data was entered into Epi Info from the medical records and analyzed on Microsoft Excel 2016. For the quantitative variables, we appreciated the minimum data, the maximum, the average and the standard deviation. For all qualitative variables, the calculation of frequency and percentage was carried out. The probabilities of overall survival and biochemical relapse-free survival were estimated with the Kaplan Meier survival curve.

Ethical Considerations

The data collection was carried out with due regard for the confidentiality of the information.

Results

Seventy-one patients with a mean age was 68.9 ± 6.1 years were collected. The median age was 70 years with extremes of 52 and 84 years. A family history of prostate cancer was found in 9 patients (12.6%). Ten patients were diabetic (14.1%) and 24 cases were hypertensive (33.8%). The circumstance of discovery was fortuitous by PSA assay in 42.3% and symptomatic in 57.7% of cases. The symptoms were dominated by lower urinary tract disorders (69%), 37% of which consisted of both dysuria and pollakiuria. The median of the initial PSA level was 20 ng/ml (3.7–662) and 37 patients (52.1%) had a PSA > 20 ng/ml at diagnosis. Twenty-two patients (31%) underwent a prostatic ultrasound showing a median prostatic volume of 58.52cc with extremes of 26 and 145cc. Sixty-seven patients (94.4%) had pelvic magnetic resonance imaging (MRI) before the biopsy. Adenocarcinoma was the histological type in all patients. The main diagnostic aspects are summarized in Table I.

Basic Characteristics of the Population (N=71)	
Variable	Value n(%)
Symptoms at Diagnosis	
Lower urinary tract disorders	49 (69%)
Erectile disorders	17 (22%)
Bone pain	5 (7%)
Acute urine retention	2 (2%)
General State (WHO)	
WHO 1	39 (54,9%)
WHO 2	29 (40,8%)
WHO 3	3 (4,2%)
ISUP Group	
ISUP 1	25 (35,2%)
ISUP 2	18 (25,4%)
ISUP 3	16 (22,4%)
ISUP 4	7 (9,9%)
ISUP 5	5 (7%)
Extension Report	
Pelvic MRI	67 (94,4%)
pelvic CT	6 (8,5%)
Thoraco-abdomino-pelvic CT	67 (94,4%)

Bone scan	28 (39,4%)
Spinal MRI	12 (16,9%)
PET-TDM with choline	4 (5,6%)
TNM Classification	
T1	7 (7,7%)
T2	40 (56,3%)
Q3	23 (32,3%)
T4	1 (1,4%)
N+	9 (12,6%)
M+	4 (5,6%)
Classification by Stage	
Localized	61 (85,9%)
Advanced (T4/N+)	10 (14%)
Metastatic (M+)	4 (5,6%)
Amico Classification of Localized Forms	
Low Risk	2 (1,2%)
Intermediate risk favorable	17 (28%)
Intermediate Risk unfavorable	12 (20%)
High Risk	30 (49%)

Sixty-seven patients (94.4%) received a curative treatment and 5.6% a palliative treatment. Two patients underwent a curative radical prostatectomy type surgery associated with a flushing in one case. Transurethral prostate resection and adenectomy were performed in 2 patients. Hormone therapy based on LHRH analogues and peripheral anti-androgens was prescribed in 94.4% of cases. It was short-term (6 months) in 47.8% of patients and long-term in 52.2% of cases. The average duration of the theoretical indication for long-term hormone therapy was 15.19 ± 9.7 months and the average duration of actual intake was 11 ± 6.5 months.

All patients received VMAT radiotherapy. It was curative intent in all patients, including 5.6% of oligo-metastatic cases after hormone therapy. Radiation therapy was adjuvant in two patients. The dose of 76 Gy in 38 fractions was most used in 59 cases (83.1%) followed by the dose of 20Gy in 20 fractions in 9 patients (12.7%). Two patients had received a dose of 74Gy in 37 fractions and one patient had a dose of 70Gy in 35 fractions. Forty patients (56.3%) received prophylactic lymph node irradiation and 68 patients (95.8%) benefited from seminal vesicle irradiation by delimiting a specific volume associated with prostatic irradiation.

All constraints were respected at the level of target volumes and organs at risk, only 2 patients had a prostate PTV dose higher than 107%, corresponding to doses of 108 and 109% respectively of high-risk PTV. The main dosimetric data on volumes of interest are grouped in table 2.

No Grade 3 acute toxicity was observed. The most common acute toxicities were genitourinary in 50 patients (76.9%) (grade 1: 67.7%; grade 2: 9.2%) and digestive (30.8%) of which only 7.7% were grade 2. Eight cases of chronic toxicities were noted, all grade 1 including 6 cystitis and 2 rectites.

Interest volumes	Objective	Average	SD	Median	Minimum	Maximum
PTVHR 95%	D95% PTV HR	70,69 (Gy)	5,2	72,68 (Gy)	55,40	74,14
PTVHR107%	D max	77,06 (Gy)	5,86	79,30 (Gy)	61,25	82,8
Bladder	V60 (Gy)	14,75 (%)	9,73	13,00 (%)	1	47
	V70 (Gy)	8,07 (%)	6,62	7,00 (%)	0	31
Rectum	V55 (Gy)	14,54 (%)	6,12	14,00 (%)	1	28
	V65 (Gy)	7,86 (%)	5,01	8,00 (%)	0	21
Bowel	V40 (Gy)	10,21 (%)	8,44	10 (%)	0	24

The median follow-up was 20.67 months with extremes between 4.3 and 115.3 months. The median post-radiation PSA value was 0.05ng/ml (0.002-31.9) and 0.13ng/ml (0.02-13.0) at 12 and 24 months, respectively. With this median follow-up, one death was observed, five biochemical relapses including two metastatic ones. Complete remission was noted in 65 patients. The mean duration of overall survival was 113.7 ± 1.6 months. Overall survival (OS) and biochemical relapse-free survival (BFS) at 2 years were 98.6% and 92.9%, respectively (figure 1).

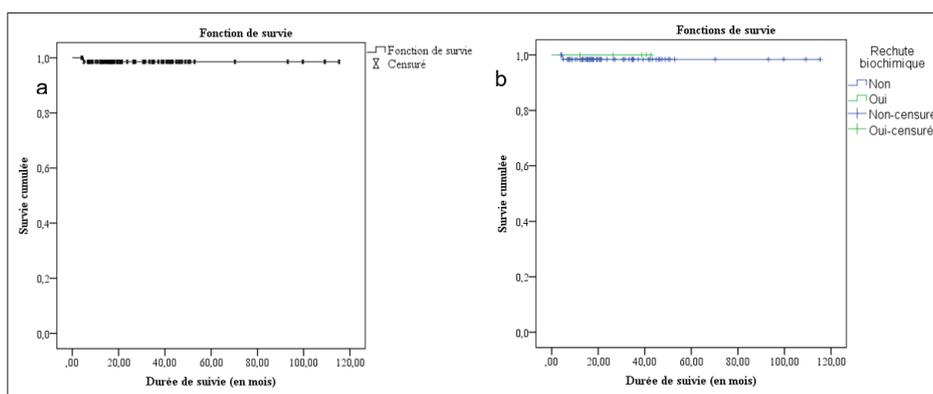


Figure 1: Survival Curves
 a) Overall Survival (OS)
 b) Biochemical Relapse-Free Survival (SSR)

In multivariate statistical analysis, only a V40Gy of the rectum greater than 30% was associated with acute grade 2 digestive toxicity ($p= 0.022$). No other diagnostic or therapeutic data were associated with acute toxicity of the treatment or survival rates.

Discussion

The therapeutic indications for prostate cancer have changed significantly over the past decade. The multiplicity of therapeutic strategies underscores the challenges inherent in managing this condition and emphasizes the necessity of multidisciplinary discussions prior to any therapeutic decision-making [5]. Prostatectomy is indicated for local control of localized prostate cancer. It is routinely indicated in low-risk tumours. It is possible in intermediate-risk tumours and can be proposed in high-risk tumours with the possibility of an associated multimodal treatment [6].

In a study on radical prostatectomy surgery with discharging in high-risk prostate cancers conducted in Dakar and published in 2018, Sine et al. had regained a 5-year recurrence-free survival of 70% and a 6-year specific survival of around 90% [7]. Radical prostatectomy is an alternative to hormonal-radiotherapy in patients with a long life expectancy and with a tumor at high risk of local progression but low metastatic risk.

Metastatic cancers have gained consensus regarding the choice of hormone therapy as a reference treatment since it has shown a moderate but significant increase in overall survival. It also has indications in localized prostate cancers at intermediate and high risk associated with radiotherapy [6]. In this latter indication,

the duration of hormone therapy varies from 6 months for intermediate adverse risks to 18 to 36 months for high risks [8-10]. Chemotherapy showed an increase in overall survival in patients with prostate cancer resistant to conventional hormone therapy or with significant metastatic volume [11,12]. The results of the phase III PEACE1 study showed the interest in a triplet by combining classic androgen suppression, next-generation hormone therapy, and chemotherapy in de novo metastatic and hormone-sensitive patients [13,14].

Radiotherapy is a locoregional treatment essential for the management of prostate cancer at all stages of the disease. It is indicated as curative in the localized and oligo-metastatic stages [6]. Radiotherapy techniques have evolved from regional irradiation to a more adapted volume of radiotherapy allowing dose escalations on target volumes and better sparing of organs at risk. This dose escalation is associated in several studies with better biochemical control [15,16]. The comparison of radiobiological models between three-dimensional conformal radiation therapy (RC3D) and other modalities of intensity modulation radiation therapy (IMRT) shows that the latter are more suitable for reducing the vesical dose, rectal and digestive while offering more possibilities for dose escalation [17]. In a cohort study comparing RC3D and IMRT, showed a difference in late grade 2 gastrointestinal (10% vs 24%, $p=0.0001$) and genitourinary toxicity (13.1% vs 15.4%, $p=0.85$) with no observed difference in overall survival, without progression and without metastases between the two arms [18]. The IMRT initially developed by the implementation of stationary beams, gradually towards the use of treatment arches under the name of volumetric modulated

arc therapy (VMAT) have shown the feasibility of arc therapy between 76 and 78 Gy in classical fractionation in 45 patients [19]. Regarding the acute toxicity, no patient had grade 2-3 rectal toxicity; (12%) of the patients had grade 2 dysuria and 44% of the cases retained full or partial erectile function. In our series of 71 patients, no grade 3 acute toxicity was also observed and that of grade 2 was low: genitourinary (9.2%); gastrointestinal (7.7%) despite that 12.7% of patients had a hypofractionated treatment and 56.3% of cases had prophylactic lymph node irradiation. It therefore appears that the toxicities reported in the literature by the series with VMAT are lower than those using RC3D and classical IMRT [19,20].

The oncological results show that the dose escalation allowed by these innovative intensity modulation techniques improves survival without biochemical relapse and not the overall survival [15,21]. However, a benefit in overall survival can be expected in the near future because in the study, the authors showed that a PSA value of 0.2ng/ml for 4 to 5 years post-irradiation was associated with 98% relapse-free survival at 10-15 years [22].

Conclusion

Radiotherapy plays a central role in the management of prostate cancer. The new techniques by intensity modulation, in particular VMAT, allow for better oncological results through the improvement of acute and chronic toxicities and greater biochemical control thanks to dose escalation. We reported the preliminary experience of the international cancer center in Dakar whose analysis shows dosimetric values respecting published constraints, low acute toxicity and good biochemical control.

Conflicts of Interest

The authors declare no conflict of interest.

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