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**Research Paper**

# Hypofractionated Radiotherapy Versus Conventional Radiotherapy in Prostate Cancer Using VMAT Technique in Terms of Dosimetry; A Comparative Study

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**ABSTRACT:**

**BACKGROUND:**

Prostate cancer (PC) is the second most frequent malignancy in men beyond lung cancer. Modern radiation therapy techniques employ over 3D conformal radiotherapy has been widely used now a day.

**OBJECTIVE:**

The study aimed to compare between hypofractionated radiotherapy with conventional radiotherapy in prostate cancer using VMAT technique and to investigate the dose delivered to organs at risk in prostate cancer treated with conventional and hypofractionated VMAT techniques.

**PATIENTS AND METHOD:**

A prospective clinical and dosimetric study in radiotherapy, medical physics, and dosimetry. Forty patients diagnosed with proven PC will be treat with the VMAT technique. Two prescribed dose methods used for each patient, the first method is the conventional fractionation as VMAT-SEQ with a prescribed dose of 78 Gy delivered in 39 sessions (2 Gy per session), and the second method is the hypofractionated dose as VMAT-SIB with a prescribed dose of 60 Gy in 20 sessions (3 Gy per session).

**RESULTS:**

Forty patients with PC, the mean age (±SD) was 60.45 years (±8.77). The mean dose of rectum in sequential group was greater than SIB group with no significant difference ($p=0.055$). Regarding doses distribution at V80, V60 of rectum, the mean of sequential group was much lower than SIB group with a high significant difference ($p<0.0001$), while at V40 of rectum, the mean of sequential group was greater than SIB group with a high significant difference ($p<0.0001$). Regarding dose distribution at V45 of bowel, the mean of sequential group was greater than SIB group with a high significant difference ($p<0.0001$).

**CONCLUSION:**

The SIB deliver lower doses to rectum, bladder, head of femurs, bowel and penile bulb than sequential planning. Hypofractionated achieve better PTV coverage, improved the dosimetry and decline the dose delivery time for targets. SIB Hypofractionated RT produce better coverage to the targets and better protection of OARs.

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## INTRODUCTION:

In 2020, prostate cancer (PC) was the second most common cancer in men, after lung cancer. It caused 375,304 deaths (3.8% of all cancer fatalities) and there were 1,414,259 new cases (7.3% of all new cancer cases) globally [(1)]. About 80 percentage rise in incidence of PC has been predicted by the year 2040 [(2)]. The incidence of PC is lower in Asian countries [(2)], compared with the North American countries [(3)]. The age-standardized incidence rate in Asia is 19.7/100,000, compared with 98.27/ 100,000 in the USA [(3)].

The diagnosis of PC is conventionally based on an elevated prostate-specific antigen (PSA) level or trans-rectal ultrasonography–guided needle biopsy of the prostate [(4-6)].

There are established risk factors for PC which include age, ethnicity and family history. The risk of PC typically increases after 55 years of age and peaks at age 70–74 years [(7)]. African

Americans are about 60% more prone to PC than Caucasians [8, 9], and first-degree relative is affected more [10].

Treatment options for managing prostate cancer include radical prostatectomy, radiation, brachytherapy, and androgen deprivation therapy (ADT) [11, 12]. External-beam radiotherapy is often used among low or intermediate risk patients; it is also used as an adjuvant treatment for high risk patients following prostatectomy [13-15].

Contemporary radiation therapy methods employ modulated Intensity Modulated Radiation Therapy (IMRT), Volumetric Modulated Arc Therapy (VMAT), or Proton Therapy beams instead of 3D conformal radiotherapy (3DCRT), which has been extensively researched. Recent surveys and evaluations have suggested a transition from 3DCRT to VMAT, particularly when paired with different dose fractionation methods such as hypofractionation, Stereotactic Body Radiation Therapy (SBRT), and Simultaneous Integrated Boost (SIB) [16].

The study aimed to compare between hypofractionated radiotherapy with conventional radiotherapy in prostate cancer using VMAT technique and to investigate the dose delivered to organs at risk in prostate cancer treated with conventional and hypofractionated VMAT techniques.

## PATIENTS AND METHODS:

### Study design and setting

A prospective clinical and dosimetric study in radiotherapy, medical physics, and dosimetry performed at Baghdad Radiotherapy and Nuclear Medicine Center, Baghdad Medical City complex in period between May 2022 and December 2023.

### Data collection

Forty patients diagnosed with proven prostatic cancer are treated with the VMAT included in the study. Patient files, planning records, dose volume histogram (DVH) data, and physic room records. These were included: age, rectum mean dose (SEQ), rectum V80<3 (SEQ), rectum V70<20 (SEQ), rectum V60<40 (SEQ), rectum V40<60 (SEQ), bladder mean dose (SEQ), bladder v70<20 (SEQ), HOF L mean dose (SEQ), HOF L v50<5 (SEQ), HOF L v45<10 (SEQ), HOF R mean dose (SEQ), HOF Rv50<5 (SEQ), HOF R v45<10 (SEQ), bowl mean dose (SEQ), bowl v45<195 cc (SEQ), bowl max< 5050 cGy (SEQ), penile pulb mean (50-52 Gy) (SEQ), rectum mean dose (simulated integrated boost (SIB)), rectum V60<15 (SIB), rectum V56<25 (SIB), rectum V52<35 (SIB), rectum V48<50 (sib), Bladder mean dose (SIB), bladder v60<25 (SIB), bladder v56<35 (sib), bladder v52<50 (SIB), HOF L mean dose (SIB), HOF L max<45 (SIB), HOF R mean dose (SIB), HOF R max<45 (SIB), small bowl mean dose (SIB), small bowl v45<200 cc (SIB), and penile pulb mean (50-52 Gy) (SIB).

### Inclusion criteria

1. Biopsy prostatic adenocarcinoma.
2. High-risk prostate cancer.
3. No hormonal treatment.
4. No pelvic RT.

### Exclusion criteria

1. Metastatic PC.
2. T1 and T2.
3. Uncomfortable and un-welling.
4. Loss of follow-up.
5. Low and intermediate risk.
6. Missing reports of patients, radiotherapy planning, physics, and dosimetry.

### Treatment protocols

Two prescribed dose methods used for each patient, the first method is the conventional fractionation as VMAT-SEQ with a prescribed dose of 78 Gy delivered in 39 sessions (2 Gy per session), and the second method is the hypofractionated dose as VMAT-SIB with a prescribed dose of 60 Gy in 20 sessions (3 Gy per session). Volumetric-modulated arc therapy (VMAT) planning technique is used to deliver the two prescribed dose methods.

### Follow-up

Two, four to six months beyond the radiotherapy course.

### Tools

These included CT pore scanner (85 cm) (Philips ® 16 series), Linear Accelerator [**Infinity™** and **Synergy®**]; 2013 (core beam CT) [Elekta], Monaco® Electa HP version 5, XiO® Electa system version 5, (Figures 1-4).

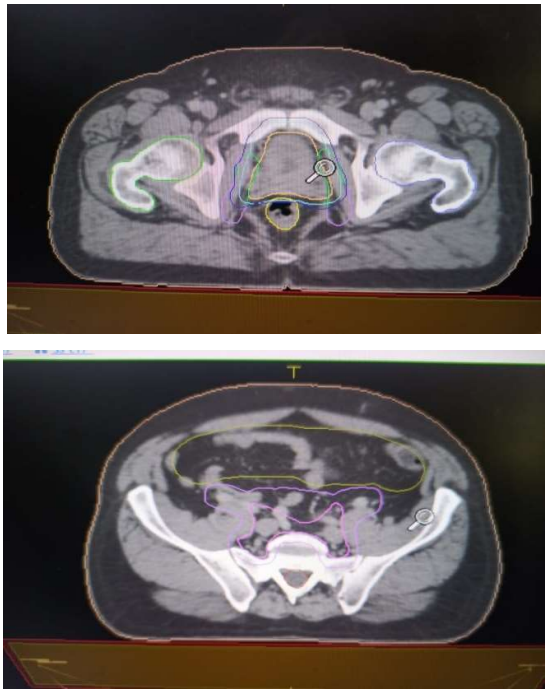
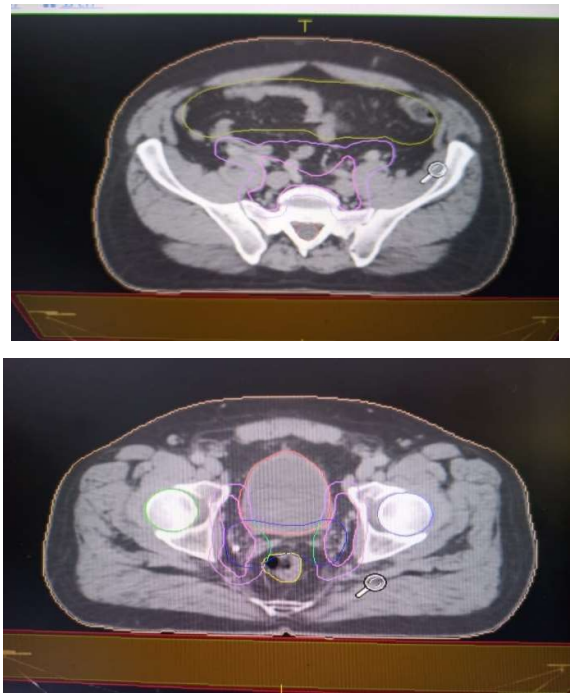


**Figure 1: Photograph of Monaco® Electa HP version 5 (Planning Room) showed GTV, CTV, and PTV of prostate (right), CTV and PTV of LN (left).**



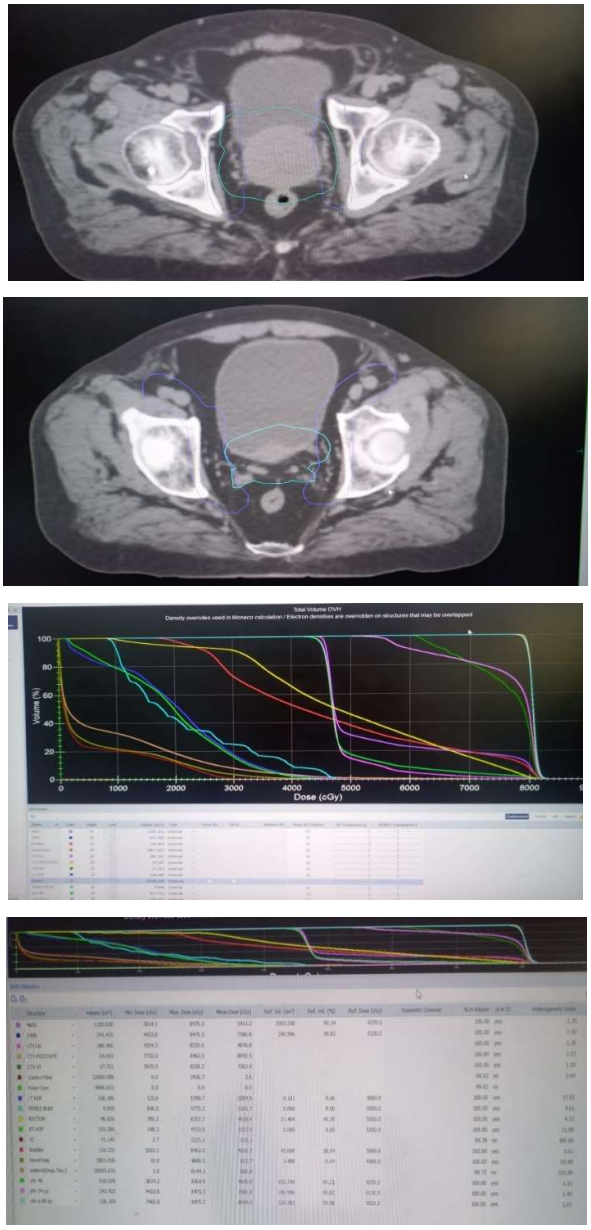



**Figure 2: Photograph of XiO® system version 5 (Physics Room) of VMAT-SEQ of prostate.**

**Radiotherapy planning volumes**

A commonly accepted approach is to establish a clinical target volume (CTV) that encompasses the entire prostate gland and any potential extension beyond its outer covering, including either the base of the seminal vesicles or the complete seminal vesicles. The Roach formulas are used to determine the likelihood of the seminal vesicles being affected, and the target volume is selected based on this information. Prostate outlining starts on the mid gland slice along the fat plane between the prostate and pelvic floor muscles and along Denovilliers' fascia posteriorly. The basal portion of the seminal vesicles is encompassed within the clinical target volume (CTV) for all individuals. The term "this" denotes a distinct anatomical component positioned around 1-2 cm from the base of the prostate. This anatomical feature is referred to as the central seminal vesicles, which frequently extends into the bladder at the same level as the middle lobe of the prostate. With a three-dimensional margin surrounding the central

transverse section (CTV), the PTV is defined. This margin includes an internal margin that considers physiological differences in the form, position, and size of the prostate, as well as a set-up margin that compensates for uncertainties in patient position and set-up during the planning and treatment process. The organs at risk (OAR) in this context include the rectum, bladder, nerves of the prostatic plexus located near the penile bulb, small bowel, and femoral heads. The rectum is demarcated from the lower extent of the ischial tuberosities and extends at least 1 cm below the planning target volume (PTV) to the recto-sigmoid junction above the PTV, resulting in a length of roughly 12 cm. It is crucial to take into account the small bowel when treating pelvic nodes.

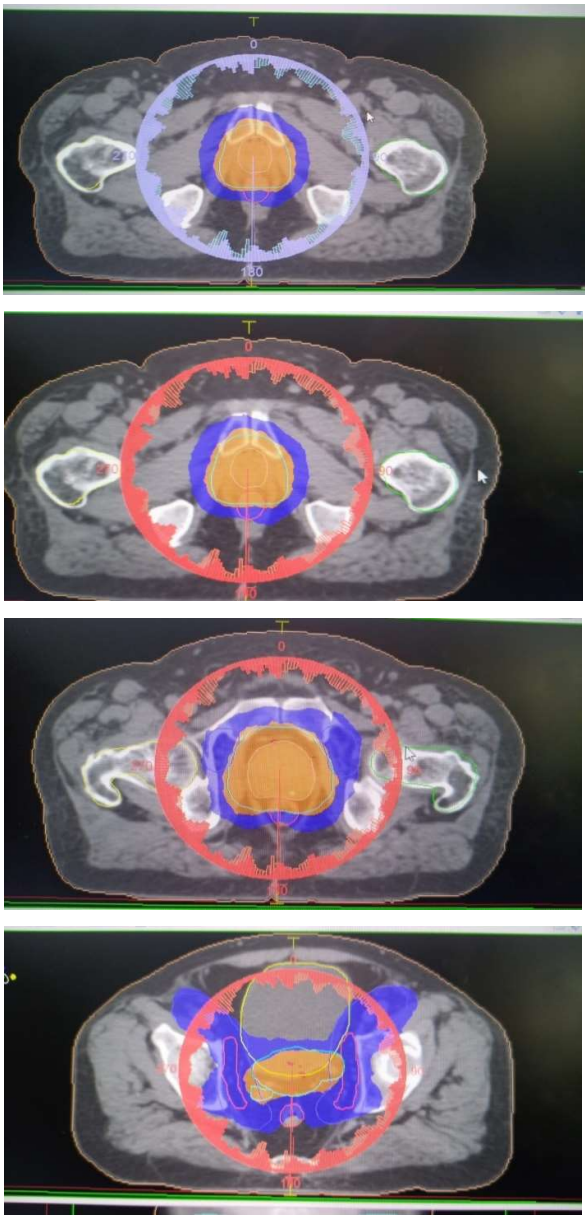


**Figure 3: Photograph of XiO® system version 5 (Physics Room) of VMAT-SIB of prostate.**

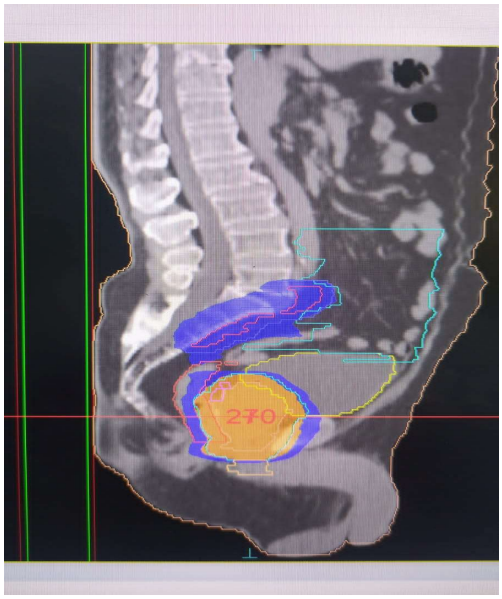



**Figure 4: Photograph of XiO® system version 5 (Physics Room) of VMAT-SIB of prostate.**

**Ethics**

This work was approved by Iraqi Board of Medical Specialization for Clinical Radiation oncology. All patients or their parent's signature the written inform consent for enrolling in this study.

**Statistics**

The statistical analysis was performed using SPSS v24 (IBM Inc., Chicago, IL, USA). Descriptive statistics represented as numbers, and percentages. Mean, median, range, min, max, and SD for categorical data calculated. T-test unpaired analysis was used to compared between groups. A *P*-value of $< 0.05$ was considered significant.

## RESULTS:

**Baseline demographic and clinical characters**

Forty patients with PC, the mean age (±SD) was 60.45 years (±8.77) and the median was (58 years). In relation to prostate stages, stage I accounted for 57.5% whereas stage II-III reported in 42.5%. The gleason score (2-6) was most common presented (15, 37.5%) followed by (7) in (13, 32.5%) and (8-10) in (12, 30.0%). The PSA less than 10 ng/mL was found in 40.0% of cases while it was more than100 ng/mL in 22.5% of patients. The low risk group patient consisted from 27.5% while high risk group were 45.0%. About 55.0% of cases received ADT and 72.5% of cases recorded with comorbidity. (Table 1)

**Table 1: The baseline demographic and clinical characteristics of patients.**

| Variables | | No. / mean±SD | % |
|---|---|---|---|
| Age (years) | | 60.45±8.77 | - |
| Tumor stage | I | 23 | 57.5 |
| | II-III | 17 | 42.5 |
| GS | 2-6 | 15 | 37.5 |
| | 7 | 13 | 32.5 |
| | 8-10 | 12 | 30.0 |
| PSA (ng/mL) | <10 | 16 | 40.0 |
| | ≥10-100 | 15 | 37.5 |
| | >100 | 9 | 22.5 |
| Risk group | Low | 11 | 27.5 |
| | Intermediate | 11 | 27.5 |
| | High | 18 | 45.0 |
| ADT | | 22 | 55.0 |
| Comorbidity | | 29 | 72.5 |

**Rectum dosimetry**

Table (2) showed the doses to rectum in both techniques used. The dose of rectum in sequential group was greater than SIB group (4640.28±530.04 cG >4449.35±652.52 cG), (p=0.055). Regarding dose distribution at V80 of rectum, the mean of sequential group was much lower than SIB group (3.74±1.14 G < 11.79±11.49 G), (p<0.0001). Regarding dose distribution at V70 of rectum, the mean of sequential group was lower than SIB group (11.17±8.47 G < 21.99±15.45 G), (p=0.399). Regarding dose distribution at V60 of rectum, the mean of sequential group was lower than SIB group (22.41±10.22 G < 31.81±15.9 G), (p<0.0001). Regarding dose distribution at V40 of rectum, the mean of sequential group was greater than SIB group (59.9±15.29 G > 40.97±17.06G), (p<0.0001).

**Table 2: Dosimetric parameters for VMAT plans (SEQ and SIB) for rectum doses.**

| **Dosimetric parameters for VMAT plans (SEQ and SIB) for rectum mean dose** | | |
|---|---|---|
| **Parameter** | **SEQ** | **SIB** |
| Mean | 4640.28±530.04 | 4449.35±652.52 |
| Median | 4734.00 | 4638 |
| Minimum | 3782 | 2737 |
| Maximum | 5500 | 5369 |
| 95% CI | **-4.38- -386.23** | |
| **t-test** | **1.977** | |
| **P value** | **0.055** | |
| **Dosimetric parameters for VMAT plans (SEQ and SIB) for rectum V80<30** | | |
| **Parameter** | **SEQ** | **SIB (V60<15)** |
| Mean | 3.74±1.14 | 11.79±11.49 |
| Median | 0.05 | 10.4 |
| Minimum | 0 | 0.2 |
| Maximum | 17 | 54 |
| 95% CI | **-13.84- - -6.86-** | |
| **t-test** | **-5.996-** | |
| **P value** | **<0.0001** | |
| **Dosimetric parameters for VMAT plans (SEQ and SIB) for rectum V70 < 20** | | |
| **Parameter** | **SEQ** | **SIB (V56<25)** |
| Mean | 11.17±8.47 | 21.99±15.45 |
| Median | 9.7 | 21.24 |
| Minimum | 0.1 | 0 |
| Maximum | 33 | 66 |
| 95% CI | **-8.66- - 3.52** | |
| **t-test** | **-0.853-** | |
| **P value** | **0.399** | |
| **Dosimetric parameters for VMAT plans (SEQ and SIB) for rectum V60 < 40** | | |
| **Parameter** | **SEQ** | **SIB (V52<35)** |
| Mean | 22.41±10.22 | 31.81±15.9 |
| Median | 23.3 | 31 |
| Minimum | 7.6 | 2.75 |
| Maximum | 45 | 72 |
| 95% CI | **-13.53- - -5.26-** | |
| **t-test** | **-4.596-** | |
| **P value** | **<0.0001** | |
| **Dosimetric parameters for VMAT plans (SEQ and SIB) for rectum V40 < 60** | | |
| **Parameter** | **SEQ** | **SIB (V48<50)** |
| Mean | 59.9±15.29 | 40.97±17.06 |
| Median | 62 | 40 |
| Minimum | 28.7 | 5.58 |
| Maximum | 94.3 | 76 |
| 95% CI | **12.75 -25.11** | |
| **t-test** | **6.195** | |
| **P value** | **<0.0001** | |

**Bladder dosimetry**

Table (3) showed the dose delivered to the bladder in both techniques used. The mean dose of bladder in sequential group was greater than SIB group (4743.18±641.21 cG > 4157.3±659.86 cG), (p<0.0001). Regarding doses distribution at V70 of bladder, the mean of sequential group seems the same as SIB group at V60/25 (17.94±8.92 G > 17.19±14.58 G), however it was low at (V56/35= 24.98±18.1 G and V52/50= 30.32±19.79 G), respectively, (p=0.005).

**Table 3: Dosimetric parameters for VMAT plans (SEQ and SIB) for bladder doses.**

| **Dosimetric parameters for VMAT plans (SEQ and SIB) for bladder mean dose** | | |
|---|---|---|
| **Parameter** | **SEQ** | **SIB** |
| Mean | 4743.18±641.21 | 4157.3±659.86 |
| Median | 4656 | 3918 |
| Minimum | 3530 | 3394 |
| Maximum | 6001 | 5734 |
| 95% CI | **2357.57 - 3252.12** | |
| **t-test** | **12.684** | |
| **P value** | **<0.0001** | |
| **Dosimetric parameters for VMAT plans (SEQ and SIB) for bladder V70 < 20** | | |
| **Parameter** | **SEQ** | **SIB** |
| Mean | 17.94±8.92 | V60/25= 17.19±14.58<br>V56/35= 24.98±18.1<br>V52/50= 30.32±19.79 |
| Median | 17.85 | V60/25= 14.4<br>V56/35= 20.7<br>V52/50= 25 |
| Minimum | 0.8 | V60/25= 3.3<br>V56/35= 6.8<br>V52/50= 8.9 |
| Maximum | 33.5 | V60/25= 64<br>V56/35= 78<br>V52/50= 83 |
| 95% CI | **-11.78- - -2.3-** | |
| **t-test** | **-3.008-** | |
| **P value** | **0.005** | |

**Head of femur dosimetry**

Table (4) showed the mean doses delivered to the left and right femurs in both techniques used. The mean dose of left femur in sequential group was greater than SIB group (1853.88±411.96 cG > 1521.81±499.5 cG) with a high significant difference (p<0.0001). The mean dose of right femur in sequential group was greater than SIB group (1893.78±617.51 cG > 1755.45±476.6 cG), (p=0.022). Regarding doses distribution at V50 and V45 of left head of femur, the mean of sequential group seems lower than SIB group (< 4094.95±258.9 cG), (p<0.0001). Furthermore, the doses distribution at V50 and V45 of right head of femur, the mean of sequential group seems greater than SIB group (>4196.55±326.62 cG), (p<0.0001).

**Table 4: Dosimetric parameters for VMAT plans (SEQ and SIB) for left and right femur heads doses.**

| **Left femur** | | |
|---|---|---|
| **Parameter** | **SEQ** | **SIB** |
| Mean | 1853.88±411.96 | 1521.81±499.5 |
| Median | 1849 | 1585 |
| Minimum | 1230 | 14.18 |
| Maximum | 2705 | 2424 |
| 95% CI | **173.39 - 490.73** | |
| **t-test** | **4.233** | |
| **P value** | **<0.0001** | |
| **Right femur** | | |
| **Parameter** | **SEQ** | **SIB** |
| Mean | 1893.78±617.51 | 1755.45±476.6 |
| Median | 1851 | 1630 |
| Minimum | 1138 | 957 |
| Maximum | 4054 | 2755 |
| 95% CI | **21.37- 255.27** | |
| **t-test** | **2.392** | |
| **P value** | **0.022** | |
| **Dosimetric parameters for VMAT plans (SEQ and SIB) for left femur head V50 and V45** | | |
| **Parameter** | **SEQ** | **SIB** |
| Mean | V50=0.03±0.09<br>V45= 0.44±0.3 | Max =<br>4094.95±258.9 |
| Median | V50= 0<br>V45= 0.1 | 4081 |
| Minimum | V50= 0<br>V45= 0 | 3329 |
| Maximum | V50= 0.4<br>V45= 1.5 | 4588 |
| 95% CI | **-4177.71- - -4012.12-** | |
| **t-test** | **-100.043-** | |
| **P value** | **<0.0001** | |
| **Dosimetric parameters for VMAT plans (SEQ and SIB) for right femur head V50 and V45** | | |
| **Parameter** | **SEQ** | **SIB** |
| Mean | V50=0.15±0.06<br>V45= 0.67±0.42 | Max =<br>4196.55±326.62 |
| Median | V50= 0<br>V45= 0.1 | 40814090 |
| Minimum | V50= 0<br>V45= 0 | 3755 |
| Maximum | V50= 0.7<br>V45= 2.6 | 5293 |
| 95% CI | **-4300.93- - -4092.04-** | |
| **t-test** | **-81.267-** | |
| **P value** | **<0.0001** | |

**Bowel dosimetry**

Table (5) showed the mean doses delivered to the bowel in both techniques used in this study. The mean dose of sequential group was smaller than SIB group (1762.18 ± 1216.51 cG < 1938.33±1459.95 cG).

Regarding dose distribution at V45 of bowel, the mean of sequential group was greater than SIB group with a high significant difference ($p<0.0001$).

**Table 5: Dosimetric parameters for VMAT plans (SEQ and SIB) for bowel doses.**

| Dosimetric parameters for VMAT plans (SEQ and SIB) for bowel mean dose | | |
|---|---|---|
| **Parameter** | **SEQ** | **SIB** |
| Mean | 1762.18±1216.51 | 1938.33±1459.95 |
| Median | 1548 | 1522 |
| Minimum | 220 | 189 |
| Maximum | 6049 | 6172 |
| 95% CI | **-668.4- - 316.1** | |
| **t-test** | **-0.724-** | |
| **P value** | **0.474** | |
| **Dosimetric parameters for VMAT plans (SEQ and SIB) for bowel volumes** | | |
| **Parameter** | **SEQ** | **SIB (V45& 200 cc)** |
| Mean | V45= 63.04±51.16<br>Max (50)= 5497.25 | 276.25±1111.44 |
| Median | V45= 60.8<br>Max (50)= 5046 | 21.75 |
| Minimum | V45= 0.3<br>Max (50)= 4660 | 0 |
| Maximum | V45= 209<br>Max (50)= 7700 | 5059 |
| 95% CI | **23.05-51.36** | |
| **t-test** | **5.318** | |
| **P value** | **<0.0001** | |

**Penile bulb dosimetry**

Table (6) showed the mean dose delivered to the penile bulb in both techniques used in this study. The mean dose of sequential group was larger than SIB group (3245.5±1940.71 cG > 2362.28±1418.21 cG), ($p<0.0001$).

**Table 6: Dosimetric parameters for VMAT plans (SEQ and SIB) for penile bulb.**

| **Parameter** | **SEQ** | **SIB** |
|---|---|---|
| Mean | 3245.5±1940.71 | 2362.28±1418.21 |
| Median | 3255 | 2148 |
| Minimum | 299 | 239 |
| Maximum | 7717 | 6163 |
| 95% CI | **509.92-1256.52** | |
| **t-test** | **4.786** | |
| **P value** | **<0.0001** | |

## DISCUSSION:

This study is a clinical and dosimetric investigation of 40 individuals who have been diagnosed with confirmed prostate cancer at the Baghdad Radiotherapy and Nuclear Medicine Center, located in the Baghdad Medical City complex. The mean age of patients was 60.45 years (±8.77). The stage I accounted for 57.5% whereas stage II-III reported 42.5%. The GS (2-6) was most common presented (15, 37.5%) followed by (7) in (13, 32.5%) and (8-10) in (12, 30.0%). The PSA less than 10 ng/mL was found in 40.0% of cases. The low risk group patient consisted from 27.5% while high risk group were 45.0%. About 55.0% of cases received ADT and 72.5% of cases recorded with comorbidity. Dislike with Faria et al. [17] studied 105 cases were classified as high-risk PC which were clinical stage T3N0M0, PSA> 20 ng/mL, or GS of 8-10, and were never exposed to any ADT or RT.

Faria et al. [17] treated all cases with combined androgen deprivation therapy (ADT) and HypoRT. The protocol used in our study is identical to PTV60 (60 Gy/20 fractions of 3 Gy) and PTV44 (44 Gy/20 fractions of 2.2 Gy per fraction). Each field was administered treatment once daily, with a frequency of 5 treatments per week for a period of 4 weeks. The dose volume limitations for the organ at risk (OAR) were adjusted to a daily fraction of 3 Gy using the linear quadratic formula, as follows: for the rectum V60 G < 15%; V56 G < 25%; V52 G <

35%; V48 G < 50%; for bladder V60 G < 25%; V56 G < 35%; V52 G < 50%; for penile bulb (mean dose) < 42 G; for femoral heads (maximum dose) < 45 G; for bowel V45 G < 200 cm3; D5 cm3 < 60 G.

The curative HypoRT usage has become an attractive therapeutic option in the treatment of localized PC. The recent evidence-based guidelines from ASTRO, ASCO, and AUA have declared that HypoRT can be provided as an option for patients who choose EBRT as their treatment [18].

When the HypoRT was utilized in situations involving high-risk prostate cancer, the randomized prospective studies conducted by Arcangelli et al [19], using the HYPRO trial to compare hypofractionated radiotherapy with conventionally fractionated radiotherapy for localized prostate cancer [20], In the CHHIP trial (21), a comparison was made between big conventional and hypofractionated high-dose IMRT for PC. It was found that 12% of the participants were placed in the high-risk group.

Karklelyte and co-authors [22] The study documented the trial of an individual who conducted research on 221 cases of high-risk prostate cancer. The participants were randomly assigned to undergo either hypofractionated treatment (63 G delivered in 20 fractions) or conventionally fractionated treatment (76 G delivered in 38 fractions), in addition to androgen deprivation therapy (ADT). Retweet. The LN irradiation was given (44 G / 20 fractions and 46 G / 23 fractions, respectively). They observed a non-significant disparity in toxicity between both groups.

The British CHHIP and the Canadian Prostate Fractionated Irradiation Trial (PROFIT) trials both administered a dosage of 60 G over 20 portions [21, 23], while in the Radiation Therapy Oncology Group 0415, the dose was 70 G / 28 fractions [24]. These studies have shown conclusive data to confirm HypoRT as a viable method for predominantly low- and intermediate-risk prostate cancer.

In the present study, the mean dose delivered to the rectum in sequential group was greater than SIB group with no significant difference (p=0.055). However, the doses distribution at V80, V70, V60 of rectum are lower in the sequential group than SIB group with a high significant difference (p<0.0001). Whereas dose distribution at V40 of rectum is greater in the sequential group than SIB group with a high significant difference (p<0.0001). Also, the mean dose delivered to the bladder in the sequential group was greater than SIB group with a high significant difference (p<0.0001). Besides, the doses distribution at V70 of bladder is the same of both groups, however it was low at (V56/35= 24.98±18.1 G and V52/50= 30.32±19.79 G), respectively with a significant difference (p=0.005). The mean doses delivered to the left and right femurs in both techniques are greater in sequential group than SIB group (p<0.0001 and p=0.022). The mean dose of sequential group was smaller than SIB group with no significant difference (p=0.474). The mean dose of sequential group was larger than SIB group with a high significant difference (p<0.0001). An agreement with Faria and co-authors [17] who reported low gastrointestinal or GU toxicity were 7% and 9%. These supported by Quon et al. [25] in their study including cases with high-risk PC who received 67.5 G to the prostate and 45 G to the LN delivered in 25 fractions with IMRT.

Musunuru et al. [26] conducted a phase I/II trial called the SATURN trial, which investigated the use of severe hypofractionation in the treatment of high-risk prostate cancer, including regional lymph node irradiation. Their favorable toxicity assessment indicates that in the future, the use of extreme hypofractionation/stereotactic body radiation therapy (EBRT) may become a regular practice in the treatment of prostate cancer (PC).

Researchers in China, led by Zhong and colleagues [27], conducted a study between 2016 and 2018 where they treated 92 patients using two different radiation therapy techniques: hypo fractionated IG-VMAT (HFRT) with a dose of 70 G/2.5 G delivered in 28 fractions for 46 patients, and conventionally fractionated IG-VMAT (CFRT) with a dose of 80 G/2 G delivered in 40 fractions for the other 46 patients. The researchers discovered that the occurrence of grade 2 and more severe late gastrointestinal/genitourinary toxicity was minimal in both groups, and no patient experienced grade 3–5 toxicities.

Several randomized controlled trials have compared mild hypofractionated radiotherapy (HFRT) with conventionally fractionated radiotherapy (CFRT) for prostate cancer (PC) and have shown that the two treatments have similar effectiveness and side effects [20, 21, 28-30].

The CHHiP experiment is currently the largest randomized trial conducted thus far [21], The HYPRO trial is a study comparing hypofractionated radiotherapy to conventionally fractionated radiotherapy for patients with prostate cancer [20], the RTOG-0415 trial [30], and the Prostate Fractionated Irradiation Trial (PROFIT) [23]. The RTOG-0415 trial conducted a randomized study including over a thousand

individuals diagnosed with low-risk prostate cancer. Intensity-modulated radiation therapy (IMRT), commonly used in the form of volumetric modulated arc therapy (VMAT), effectively provides precise targeting of the tumor, accurate dose distribution, preservation of healthy tissues, and decreased treatment duration [27]. This phenomenon can be elucidated by the radiobiological rationale that a low rate of cell division in prostate cancer is indicated by an α/β ratio of 1.5, which is like that of nearby organs at risk (OAR) that are limited by toxic effects. This suggests that hypofractionated radiation treatments will offer equivalent disease control without increasing the occurrence of harmful side effects [27].

Faria et al. [17] concluded that the HypoRT modalities of 60 G to the prostate and 44 Gy to the pelvic LN, is safe and effective, with low rates of acute and late toxicity and high rate of tumor control which shorten treatment duration and is convenient for patients and the health system While Zhong et al. [27] It was determined that the toxic effects of radiation therapy (RT) are favorable when using both hypofractionated (70 G/2.5 G/ 28F) and conventionally fractionated (80 G/2 G/) treatment schedules IG-VMAT. The healthcare system and the patient can both benefit from the use of HFRT, as it can reduce costs and save time. These benefits are especially significant in countries with limited resources, such as Iraq.

Takakusagi et al. [31], in Japan, treated 10 cases with cFF-VMAT. Was noted a non-statistically significant differences were seen in the DVH values for the target volume, as well as in all parameters for the bladder and rectum, between both groups. The mean values of monitor units (MU) were 686±52 and 784±80 in cFF-VMAT and FFF-VMAT, respectively ($p < 0.001$) and the mean beam-on time (BOT) was 97.0±6.6 sec and 72.9±1.4 sec for cFF-VMAT and FFF-VMAT, respectively ($p < 0.001$). Finally, they concluded that the MU was significantly higher, and the BOT was significantly shorter than those in cFF-VMAT.

Previously, similar findings are seen in a study of Kim et al. [32]. They treated 58 patients aged 71.5±1.82 years (range, 56-83 years), 3 (5.2%), 32 (55.2%) and 23 (39.6%) They belonged to the low, intermediate, and high-risk categories, respectively. The incidence of Acute grade 1 and 2 GU-toxicities was 8.6% and 5.2%, respectively. Similarly, the occurrence of mild (grade 1) and moderate (grade 2) genitourinary (GU) toxicities was 63.8% and 24.1%, respectively. There was no acute toxicities ≥ grade 3 occurred. The grade 2 late GI toxicity was 8.6% and ≥ grade 3 toxicity was not reported. Grade 2 late GU toxicity was at 13.8% and no ≥ grade 3 toxicity. Dosimetric data are median value of mean PTV dose was 72.3 Gy with median value of V95% resulting in 98.9%. Among OARs, the median value of mean rectal dose was 3530 cG, median rectal V40, V50, V60 and V70 G was 38.8%, 25.2%, 14.5% and 1.8%, respectively. The median value of the mean bladder dosage was 3220 cG. The median bladder V40, V50, V60, and V70 G were 36.9%, 25.7%, 15.9%, and 6.7%, respectively. There was no statistical connection between acute GI/GU toxicities and dosimetric parameters.

Recent investigations have demonstrated that hypofractionated radiation schedules yield comparable positive results to dose increased conventionally fractionated radiation therapy [32].

Dearnaley D et al. presented a randomized trial comparing conventional (74G/ 37f) and two hypofractionated (60 G /20f and 57 G /19f) RT in localized PC [33]. The 5 years DFS was 88.3% in the 74 G group, 90.6% in the 60 G group and 85.9% in the 57 G group. The estimated cumulative incidence of grade ≥ 2 GI and GU toxicities were 13.7% and 9.1% in the 74 G group, 11.9% and 11.7% in the 60 G group, 11.3% and 6.6% in the 57 G group, respectively. Late toxicities were similar between all groups [21]. Catton CN et al. [23] and Hoffman et al. [28] supported these results.

Recently, VMAT is a widely used RT technique for PC [32]. VMAT employs a multitude of beam orientations along an arc trajectory and administers doses dynamically while the gantry rotates, in contrast to IMRT [25]. VMAT has been demonstrated to be equivalent or superior to IMRT in terms of target coverage and preservation of adjacent normal tissue in prostate cancer radiation therapy [27].

Zhang et al. [34] assessed the effectiveness of VMAT plans in comparison to regular IMRT plans for the treatment of PC. The use of VMAT led to enhanced sparing of the rectum, resulting in a decrease of 1.5% in the chance of complications in normal tissue. Mellon et al. [35] conducted a comparison between VMAT and step-and-shoot IMRT. VMAT significantly decreased the average time the beam was turned on ($P=0.03$). There was no statistically significant variation in PTV volumes between the VMAT and step-and-shoot IMRT groups. However, VMAT exhibited more uniform dose distributions, as shown by a P-value of 0.003.

Kim and co-authors [32] concluded VMAT-IGRT is better for localized PC showed favorable

outcomes without grade ≥3 toxicity. They highlighted the potential issue of this treatment to contribute to the reduction of the clinical and economy burden.

Soni et al. [36] administered hypofractionated and conventional fractionated radiation therapy (RT) treatments using VMAT to the prostate and seminal vesicles in a total of 168 subjects. The hypofractionated group demonstrated a statistically significant improvement in biochemical control compared to the conventional group, without any statistically significant occurrence of late radiation toxicities. In Italy, the hypofractionated arm showed a 10-year freedom from biochemical failure rate of 72% and a 10-year overall survival rate of 75%. In comparison, the conventional arm had a 10-year freedom from biochemical failure rate of 65% and a 10-year overall survival rate of 64%. These results align with several published studies [19, 29].

In 2023, Fathy et al. conducted a study (37) to evaluate the effects of different widths of the multi-leaf collimator (MLC) on the quality of treatment plans for prostate cancer (PC). They also investigated the influence of the MLC energy mode on three types of MLCs: Agility flattening filter (AFF), MLC Agility-free flattening filter (AFFF), and MLCi2. The study utilized two techniques, namely intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT). According to their findings, the width of MLCs is a significant factor in determining the quality of SIB plans.

With the help of new radiotherapy modalities, MLC design has the potential to enhance plan dosimetric parameters and overcome obstacles in the process of developing appropriate treatment plans for PC. The decreased width of MLCs always produced greater PTV coverage, increased the dosimetric parameters, and reduced the time of dose delivery. This was owing to better target coverage and better protection of OARs. This was the case for both IMRT and VMAT procedures [37].

## CONCLUSION:

Old age, high risk group, comorbid, and PSA more than 10 ng/mL are characteristic features of PC in Iraq. The SIB deliver lower doses to rectum, bladder, head of femurs, bowel and penile bulb than sequential planning. Hypofractionated achieve better PTV coverage, improved the dosimetry and decline the dose delivery time for targets. SIB Hypofractionated RT produce better coverage to the targets and better protection of OARs.

## Recommendations:

Longer follow up requirement for large cohort study about PC. Additional studies are required to determine the biochemical, disease free and overall improvements. Dosimetric studies to calculated the conformity index and homogeneity index of SIB Hypofractionated RT.

**Disclosure**

**None**

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