The Use of Accelerated Fractionation Methods for Irradiation of Prostate Cancer: VMAT-SIB and IMRT-SIB

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Abstract:

The use of the latest technology in radiation therapy for prostate cancer treatment by (VMAT-SIB and IMRT-SIB) methods is conducted with using 3D in treatment planning. The purpose of this study is to calculation done the total radiation doses by linear quadratic model (LQ). Mainly, the study objective is to a comparative analysis of methods of irradiation of prostate cancer. Use highly radiation doses for prostate cancer treatment while keeping normal cells (rectum, bladder, left femur, right femur, and bones) safe from highly radiation doses. The study of seven prostate cancer patients was conducted. The first patient had done prostate cancer treatment in two sessions by VMAT-SIB and IMRT-SIB methods and use a 9-field sliding window IMRT technique. The second patient had done prostate cancer treatment in three sessions by VMAT-SIB and IMRT-SIB methods and use a 4-field sliding window IMRT technique. Calculation of radiation doses was carried out for four patients. We done radiation treatment planning work to the patient with prostate cancer by 3D technique and using (VMAT-SIB and IMRT-SIB) methods. Total radiation doses (48.000GY). Calculate was done total radiation doses (minimum dose, maximum dose, mean dose, and other doses) for each normal tissues are (rectum, bladder, left femur, right femur, and bones) in stage the prostate cancer prostate treatment. The VMAT-SIB and IMRT-SIB) methods are more effective treatment, increased higher total radiation doses, shorter total treatment time, and at the same time had low side effects on normal tissues.

Keywords: Radiation Therapy, VMAT-SIB, IMRT-SIB, LQ.

1. Introduction

Radiation therapy uses high-energy radiation for DNA damage in cancer cells. Since high levels of radiation work to destroy and prevent cancer cells from developing and dividing. Radiation therapy is using radiation to kill or infects cancer cells so that they cannot multiply. In advanced stages, radiation therapy can be used as primary cancer therapy. Radiation treatment is the only therapy used for treating cancer cells, and occasionally in combination with surgery or chemotherapy, or other treatments. The beam is used to destroy cancer cells, reduce, and cut the size of the tumor Known radiation therapy to reduce tumor size to facilitate its removal. Or after ablation surgeries as an added treatment to eliminate any tumor cells that may remain in the body. (Beyzadeoglu et al., 2010).

Prostate cancer occurs when abnormal cells form in the prostate, and it is a type of cancer that develops in a special part of the body, in the prostate glands. These cells can continue to reproduce uncontrollably and sometimes spread outside the prostate; to the near parts like in the bladder, rectum, and femoral head. Also, it can spread to outside prostate parts like in the bone, chest, and other areas. Prostate is a small nut-shaped gland in the men to produce semen that nourishes and transports sperm. Generally, prostate cancer is a slow-growing disease. However, the disease is highly spread rapidly and may be fatal. The rate of disease discovery differs around the world, asit is less in South and East Asia than in "Europe" and "The United States" in particular. Prostate cancer is most common in men over the age of fifty. Globally, prostate cancer is considered the sixth type of cancer. It is the secondcause of death in (the United States of America). One of the more common cancer types found in males is prostate cancer (Thomas Jr, 2014).

Radiation therapy aims to control and destroy cancer and DNA damage of the cancer cells. Also, it aims to ensure that the tumor receives all radiation doses while protecting healthy tissues. Treatment planning includes identifying the tumor size to be treated, then designing the appropriate radiation fields to treat a particular tumor size (Robert and Donna, 2009). Three-dimensional treatment planning in which patient data obtained from CT scan, MRI, PET, others to help determine the target size and the location of the tumor. The packages are designed using complex mathematical algorithms, for example, pencil beam, convolution/superposition method, or others. As the major improvements are made in dose-calculation methods, revolutionary software developments have occurred this allows planning of complex treatments in radiation therapy such as three-dimensional (3-D), Image-guided radiation therapy (IGRT), intensity modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), simultaneous integrated boost (SIB), (SIB-IMRT or SIB-VMAT), and others. One of the most powerful treatment planning algorithms, which allows the scheme to determine the desired beam dose distribution for the tumor and to preserve normal tissue from the beam. Inverse planning is to provide a therapeutic radiation dose to the target while preserving the normal tissues, which can now be achieved with a high degree of development. However, despite the major improvements that have been made using (3-D) imaging methods that more allow anatomy to be correctly identified. Use inverse planning techniques to improve the radiation dose where the target size is determined, the members at risk are identified and the dose values in the surrounding normal tissues are reduced. Where the IMRT or VAMT is usually using inverse planning. It leads to the distribution of the required radiation dose for the tumor. Which to try to maximize the beam dose to the target size and reduce the beam dose to the normal tissues (Xia et al., 2018).

2. Material and Methods

Using VMAT-SIB and IMRT-SIB methods for prostate cancer treatment.

2.1 VMAT-SIB and IMRT-SIB methods

Current Radiation therapy for treatment cancer strikes small targets of using high radiation doses to target the tumor and tries to reduce side effects on normal tissues. However, in the past, using high radiation doses affect normal tissues because the equations used to establish the dose and treatment plan in the past didn't perform with large radiation doses well. New Radiation treatment administered at lower and higher radiation doses than in the past, which required a long sequence of low-dose treatments. To enhance our ability to irradiate small, targeted areas targeting tumors. Developed new approaches to preserve patient stability by using higher radiation doses on target of the tumor with normal tissues are less vulnerable to doses. Now that radiation therapy has evolved to provide a general equation that applies to both low and high radiation dose therapy for the efficacy of existing cancer radiation therapies. Radiation doses when included in the treatment plan for the cancer patient.

Several methods of different strategies (SIB-IMRT or SIB-VMAT) for dosage prescribing and treatment planning techniques tried to achieve better tumor control and better sparing for organs at risk (OARs). Variable strength of multiple radiations is used by IMRT techniques resulting in substantially improved to target volume with improved sparing of normal tissues and organs at risk (OARs). IMRT also can generate Inhomogeneous distributions of the doses, allowing various doses for each fraction that distributed simultaneously to different areas within a target volume. Simultaneous integrated boost (SIB) delivery is the main reason for the improved results of IMRT. VMAT lets simultaneous variation for three different parameters over treatment, speed of rotation gantry, dose rate, and treatment aperture form the movement of MLC leaves. This Results in further improving the control on target volume and avoid (OAR) (Rapole et al., 2018; Beyzadeoglu et al., 2010; Frometa-Castillo et al., 2020).

Use linear Quadratic Model (LQ) to calculation total radiation doses. The number of radiation doses required to kill cancer cells was determined by the equation of the linear-quadratic model. The linear-quadratic model leads to an overestimation of the quantitative effects of high radiation doses in targeting the tumor and with low side effects on healthy tissues. One of the most important methods in radiation biology and physics is the linear-quadratic model because it offers a clear relationship between cell survival and the delivered radiation doses.

3. Results and Discussions:

The treatment of prostate cancer in this study was conducted by radiation therapy. The treatment plan for treatment patient by using the IMRT-SIB and VMAT-SIB methods. The Study would demonstrate how to use radiation doses to have a higher effect on prostate cancer while having a lower effect on healthy tissues than higher radiation doses, as shown below.

Case 1: treating a patient with prostate cancer by radiation therapy. The treatment plan for the patient by external beam planning with the SIB method. The IMRT-SIB, VMAT-SIB methods use in prostate cancer treatment. Use total radiation doses for patient treatment with prostate cancer which is (48.000GY), the number of fractions is (24), and the dose per fraction is (2.000GY), While keeping on normal tissues (rectum, bladder, left femur, right femur, and bones) than higher radiation doses and as shown in cases:

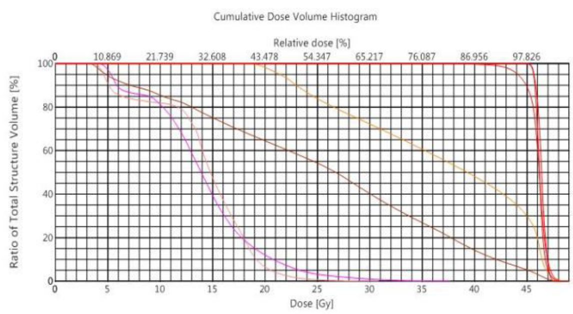
Case 1A: Treatment of the patient in the first session

The treatment of the patient in the first session is conducted by high radiation doses. Using high radiation doses for prostate cancer treatment while the effect is low on normal tissues near the tumor location. As explained below:

- Radiation doses for rectum is performed with a total volume (62.5cm), the minimum dose is (3.3GY), the maximum dose is (48.9GY), the mean dose is (25.5CGY), std Dev is (12.4GY).
- Radiation doses for left femur is performed with a total volume (80.9cm), the minimum dose is (3.5GY), the maximum dose is (30.8GY), the mean dose is (14.1CGY), std Dev is (4.9GY).
- Radiation doses for bladder is performed with a total volume (91.8cm), the minimum dose is (18.6GY), the maximum dose is (48.8GY), the mean dose is (36.9CGY), std Dev is (9.0GY).

Note, high radiation doses are used to target the tumor (GTV), (CTV), and (PTV) as shown in the red color in the histogram (from 100 volumes to 50 doses).

The effect of low radiation doses used on normal tissues (rectum, bladder, left femur, right femur, and bones), as shown in the histogram. As shown in figure 1:



DVH	Structure	Structure Status	Coverage [%/%]	Volume	Min Dose	Max Dose	Mean Dose	Modal Dose	Median Dose	Std Dev
	Rectum	Approved	100.0 / 100.0	62.5 cm³	3.3 Gy	48.9 Gy	25.5 Gy	4.0 Gy	26.7 Gy	12.4 Gy
	Femur_left	Approved	100.0 / 100.0	80.9 cm³	3.5 Gy	30.8 Gy	14.1 Gy	13.7 Gy	14.8 Gy	4.9 Gy
	Bladder	Approved	100.0 / 100.0	91.8 cm³	18.6 Gy	48.4 Gy	36.9 Gy	46.1 Gy	39.3 Gy	9.0 Gy

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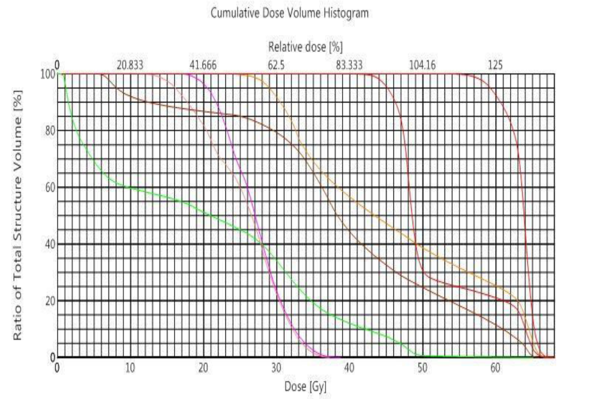
Figure 1. Treatment histogram for the tumor

Case 1B: Treatment of the patient in the second session.

Treatment of prostate cancer by high radiation doses. The session time is 30 minutes. Using high radiation doses on prostate cancer while keeping normal tissues near the tumor safe as explained in radiation doses below:

- Radiation doses for rectum is performed with a total volume (62.5cm^2), the minimum dose is (5.4GY), the maximum dose is (65.9GY), the mean dose is (39.0GY).
- Radiation doses for left femur is performed with a total volume (80.9cm), the minimum dose is (11.6GY), the maximum dose is (37.2GY), the mean dose is (25.6CGY).
- Radiation doses for bladder is performed with a total volume (91.8cm), the minimum dose is (23.2GY), the maximum dose is (67.8GY), the mean dose is (45.9GY).
- Radiation doses for right femur is performed with a total volume (107.5cm), the minimum dose is (16.7GY), the maximum dose is (38.7GY), the mean dose is (27.0GY).
- Radiation doses for PTV_ALL are performed with a total volume (1232.1cm), the minimum dose is (37.4GY), the maximum dose is (68.0GY), the mean dose is (51.7GY).
- Radiation doses for PTV are is performed with a total volume (280.0cm), the minimum dose is (51.8GY), the maximum dose is (68.0GY), the mean dose is (63.4GY).
- Radiation doses for bones is performed with a total volume (1049.6cm), the minimum dose is (0.3GY), the maximum dose is (65.1GY), the mean dose is (20.1GY).

Note that radiation doses used in the treatment of prostate cancer, use high radiation doses for prostate cancer treatment. Much higher radiation doses are used to target the tumor (GTV), (CTV), and (PTV) as shown in the red color in the histogram (from 100 volumes to 70 doses). While the effect is lower on the normal tissues (rectum, bladder, left femur,



DVH	Structure	Structure Status	Coverage [%/%]	Volume	Min Dose	Max Dose	Mean Dose	Modal Dose	Median Dose	Std Dev
—	Rectum	Approved	100.0/ 100.0	62.5 cm³	5.4 Gy	65.9 Gy	39.0 Gy	37.6 Gy	38.3 Gy	15.4 Gy
—	Femur_left	Approved	100.0/ 100.0	80.9 cm³	11.6 Gy	37.2 Gy	25.6 Gy	27.9 Gy	26.5 Gy	5.4 Gy

right femur, and bones) than high radiation doses as shown in the figure 2:

(A)

(B)

Figure 2. A-B Treatment histogram for the prostate cancer

A 9-field sliding window IMRT technique is used in the treatment of prostate cancer. It is more effective, target tumor more directly, and had fewer side effects on normal tissues. As shown in figure 3:

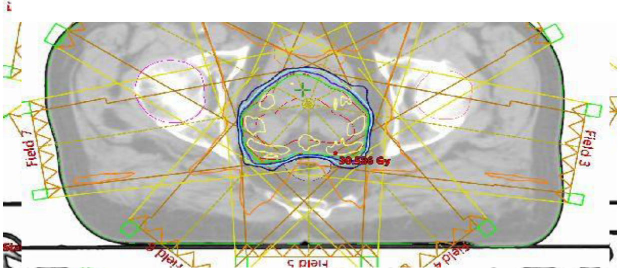
(A)

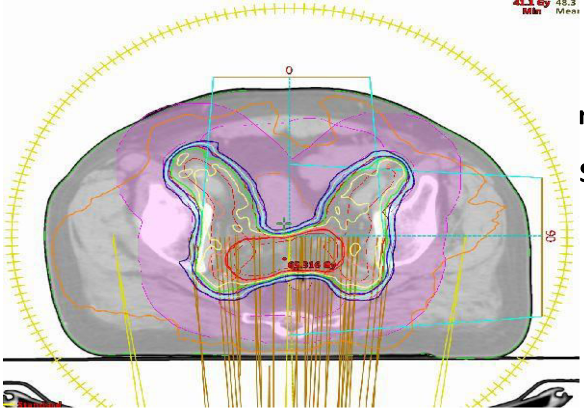
(B)

DVH	Structure	Structure Status	Coverage [%/%]	Volume	Min Dose	Max Dose	Mean Dose	Modal Dose	Median Dose	Std Dev
—	Bladder	Approved	100.0/ 100.0	91.8 cm³	23.2 Gy	67.8 Gy	45.9 Gy	64.9 Gy	43.4 Gy	13.1 Gy
—	Femur_right	Approved	100.0/ 100.0	107.5 cm³	16.7 Gy	38.7 Gy	27.0 Gy	27.1 Gy	27.0 Gy	4.1 Gy
—	PTV_ALL	Approved	100.0/ 100.0	1232.1 cm³	37.4 Gy	68.0 Gy	51.7 Gy	48.1 Gy	48.5 Gy	6.7 Gy
—	PTV	Approved	100.0/ 100.0	280.0 cm³	51.8 Gy	68.0 Gy	63.4 Gy	64.0 Gy	63.9 Gy	1.9 Gy
—	Bones	Approved	100.0/ 100.0	1049.6 cm³	0.3 Gy	65.1 Gy	20.1 Gy	1.3 Gy	21.0 Gy	15.8 Gy

Plan prescription

Plan Sum	Plan Sum Course	Plan Weight	Plan	Plan Course	Prescription dose	Dose per Fraction	Number of Fractions	Total Dose at Primary Ref. Point	Prescribed Percentage	Normalization Mode	Normalization Value
-	-	-	Tb arc boost+	C1	48.000 Gy	2.000 Gy	24	48.000 Gy	100.0 %	No plan normalization	100.0 %





(C)

Figure 3. A-B-C Prostate cancer treatment by IMRT method

Note that IMRT-SIB, SIB-VMAT methods use high radiation doses. Total radiation doses are (47.711GY), (30,586GY) with a 9-field sliding window IMRT technique are used in prostate cancer treatment. Using high radiation doses on the target of the tumor for (GTV), (CTV), and (PTV) while avoiding the effect of high radiation doses on normal tissues (OAR). These techniques are more effective treatment, radiation doses to different targets at different high radiation dose levels in the first treatment session to target the tumor, low effect on normal tissues from high radiation doses.

Case 2: The treatment of a patient with prostate cancer by radiation therapy. The treatment plan of the patient conducted by external beam planning with the SIB method. The IMRT-SIB, VMAT-SIB methods used in prostate cancer treatment in three sessions:

- the first session on October, 2020
- the second session on November, 2020
- the three session on December, 2020

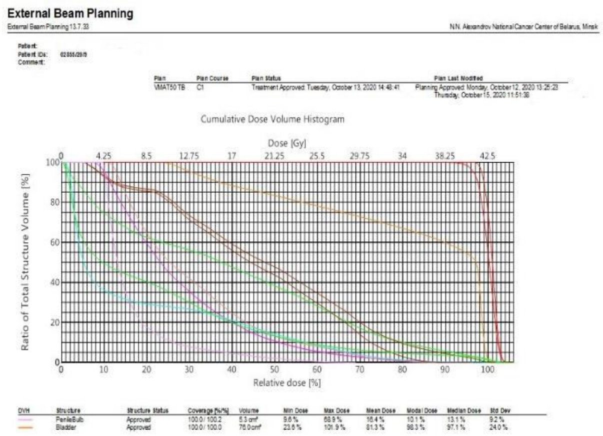
Using total radiation doses for patient treatment with prostate cancer is (48.000%), while keeping on normal tissues (rectum, bladder, left femur, right femur, and bones) safe from high radiation doses, as shown in cases below:

Case 2A: Treatment of the patient in the first session

The patient treatment in three session is performed by high radiation doses as shown in radiation doses:

- Radiation doses for penile bulb is performed with a total volume (5.3cm2), the minimum dose is (9.6%), the maximum dose is (68.9%), the mean dose is (16.4%).
- Radiation doses for rectum is performed with a total volume (76.0cm2), the minimum dose is (23.6%), the maximum dose is (101.9%), the mean dose is (91.3%).

Note, using higher radiation doses to target the tumor for (GTV), (CTV), and (PTV) as shown in the red color in the histogram (from 100 volumes to 160 doses). At the same time there

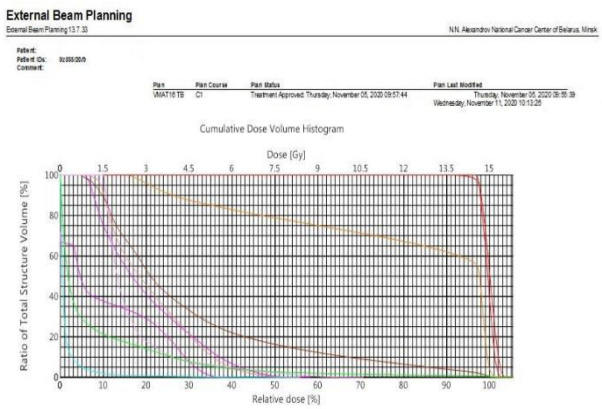


is a low effect on normal tissues from high radiation doses as shown in the histogram. As shown in figure 4:

Figure 4. Histogram for prostate cancer treatment in the first session

Case 2B: Treatment of the patient in the second session

The patient treatment in the second session is performed with high radiation doses. Using high radiation doses to target the tumor for (GTV), (CTV), and (PTV) as shown in the red color in the histogram (from 100 volumes to 110 doses) while the effect is low on normal



tissues near the tumor location. As shown in the histogram and figure 5:

Figure 5. Histogram for prostate cancer treatment in the second session

Case 2C: Treatment of the patient in the three session

Treatment of prostate cancer by high radiation doses. The session time is 10 minutes. Using high radiation doses on prostate cancer while keeping normal tissues near the tumor safe as shown in radiation doses:

- Radiation doses for rectum is performed with a total volume (117.0cm2), the minimum dose is (6.6%), the maximum dose is (144.3%), the mean dose is (67.0%), std Dev is (27.1%).
- Radiation doses for (PTV_ekv50) is performed with a total volume (845.7 cm2), the minimum dose is (79.6%), the maximum dose is (150.8%), the mean dose is (110.3%), std Dev is (16.9%).
- Radiation doses for (PTV_bk_test) is performed with a total volume (196.9 cm2), the minimum dose is (113.7%), the maximum dose is (150.8%), the mean dose is (139.1%), std Dev is (4.6%).

Note, using higher radiation doses to target the tumor for (GTV), (CTV), and (PTV) as shown in the red color in the histogram (from 100 volumes to 160 doses). At the same time there is a low effect on normal tissues as shown in the histogram. As shown in figure 6:

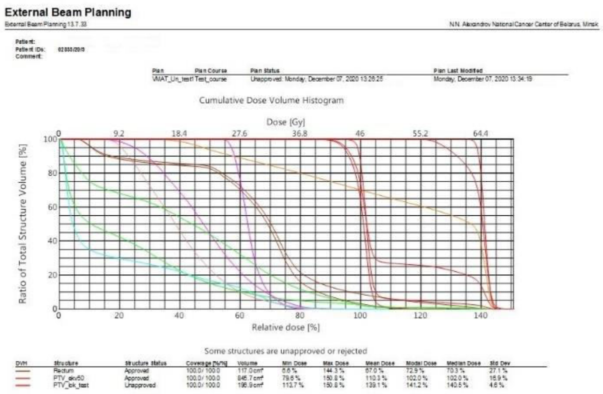
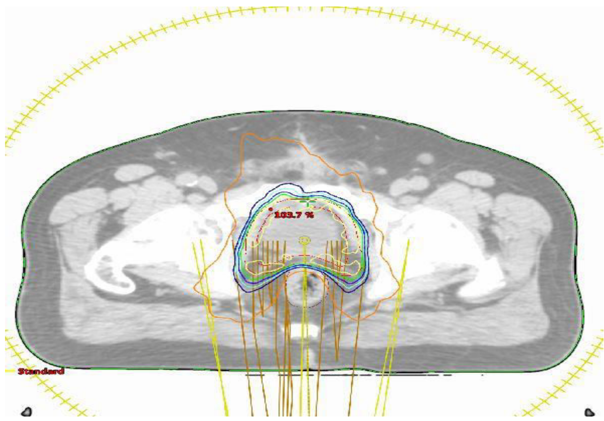


Figure 6. Histogram for prostate cancer treatment in the three session

4-field sliding window IMRT technique used in the treatment of prostate cancer. It is more effective, target tumor more directly, and had fewer side effects on normal tissues. Note in the figures below that IMRT-SIB, SIB-VMAT methods use high radiation doses. Total radiation doses are (47.711GY), (30,586GY) with a 4-field sliding window IMRT technique used in prostate cancer treatment. Using high radiation doses to target the tumor for (GTV), (CTV), and (PTV) while avoiding normal tissues for (OAR) from the effect of high radiation doses. As shown in figure 7:

(A)



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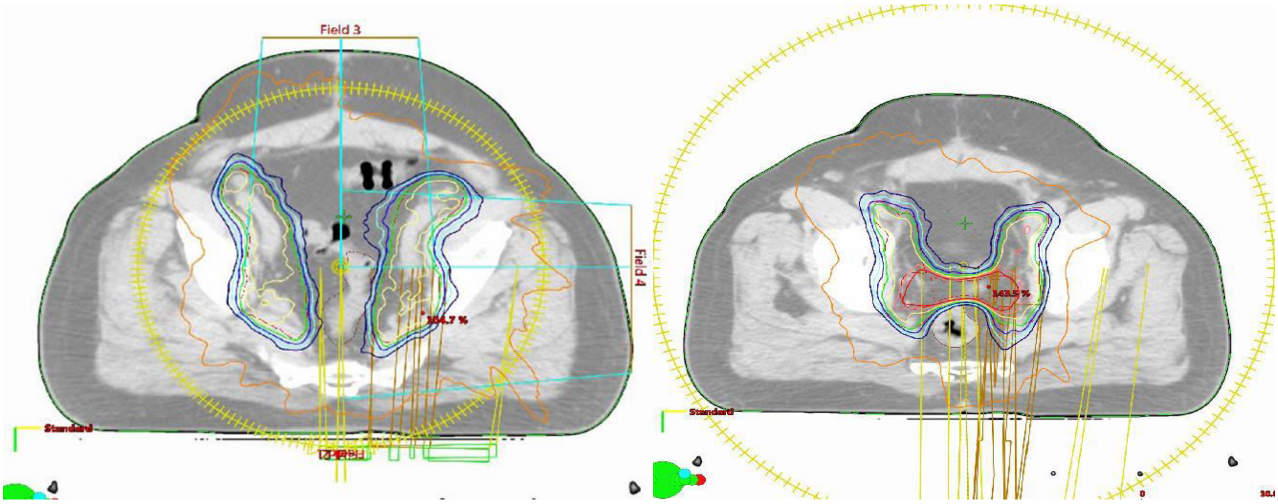

(B) (C)

Figure 7. A-B-C Prostate cancer treatment

Radiation doses calculation. Calculation of radiation doses was carried out for four patients:

1) Critical organs count to 2 Gr:

$$EQD_2 = D\frac{d + \alpha/\beta}{2 + \alpha/\beta}$$

In order to find the equivalent for 2 Gr at a dose of 65 Gr for Loc, set the Total Dose = 56 Gr.

$$EQD_2 = 56\frac{3{,}25+3}{2+3} = 64{,}96 \text{ Gr}$$

2) Swerve Boost and PTV loc:

№	Bladder		Rectum		Femur.right		Femur.left	
	Plansum 50%	Boost 50%	Plansum 50%	Boost 50%	Plansum max	Boost max	Plansum max	Boost max
1	60	50,6	40,89	49,6	50,1	45,1	43,6	43,4
2	74,2	76,5	24,7	39,3	45	52,5	44	48,5
3	28,7	43,4	27	46,4	40,2	35	39	44,1
4	73,9	77,2	40,3	47,5	48,6	49	47,3	45,9

Table 1. Calculation for Boost and PTV loc

3) HI it is uniformity of dose distribution within the target.

HI was calculated:

$$HI = \frac{D_5}{D_{95}}$$

Where D_5 = minimum dose in 5% of the Planning Target Volume (PTV), indicating the "maximum dose", and D_{95} = minimum dose in 95% of the PTV, indicating the "minimum dose". The lower (closer to one) the index, the better is the dose homogeneity.

CI is the shape of the volume area as close as possible to the tumor.

CI was calculation

$$CI = \frac{V_{95\%}}{V_{PTV}}$$

	1	2	3	4
HI	1,08	1,15	1,08	1,08
CI	0,95	0,98	0,95	0,95

Table 2. Calculation for HI and CI

4)

$$t= \frac{the\ sum\ of\ monitor\ units\ for\ all\ fractions}{dose\ rate}$$

	t,min			
№	1	2	3	4
PTV all	3,8	3,9	3,2	2,66
loc	2,3	2,88	2,5	2,09
Boost	2,5	4,3	0,8	4,3

Table 3. Calculation for t,min

Case 7: we done radiation treatment planning work for patient with prostate cancer by 3D and use IMRT, VMAT, SIB methods for use a high radiation doses for DNA damage on prostate cancer with a low radiation dose on normal tissue as shown in figure 8 below:

Figure 8. Treatment planning 3D

The red color is prostate cancer is GTV

The yellow color is CTV

The gray color is PTV

Colors are OAR is bladder and rectum and head femur

The patient has taken an image by computerized tomography Scan. The treatment planning for the patient using 3D with SIB-IMRT or SIB-VMAT methods. Radiation dose distribution is based on isodose. Use highly radiation dose to target tumor while avoiding normal tissue from radiation. Use SIB-IMRT or SIB-VMAT methods to shortening the time for treatment, radiation dose more on the tumor. We calculate the equivalent dose load by the equation $BED = \text{nd}\frac{1+\text{d}}{\alpha/\beta}$.The SIB-IMRT or SIB-VMAT methods use highly radiation doses for prostate cancer treatment. Total radiation doses and radiation doses exposure to normal tissues were calculated effectively by Linear Quadratic Model (LQ).

4. Conclusion:

Proving this study that the IMRT-SIB, VMAT-SIB methods are used in the treatment of prostate cancer in two cases:

1. IMRT-SIB, VMAT-SIB methods are more effective, increase total doses, minimize total treatment time in prostate cancer treatment.
2. High radiation doses used in prostate cancer treatment have a low effect on normal tissues by using IMRT-SIB, VMAT-SIB methods.

Using the SIB method in the treatment plan for prostate cancer treatment. For more total radiation dose distribution performed to increase tumor control without endangering neighboring organs by increasing the dose for each portion of the tumor itself with lower effect on healthy cells from high radiation therapy.

More radiation dose distribution could use the IMRT-SIB, VMAT-SIB methods in treatment planning, which increase high radiation doses for each part of the tumor with a lower effective on healthy cells.

Recommendations

We recommend using the methods SIB-IMRT with SIB-VMAT in the treatment planning for prostate cancer because: Safely raises the total administered dose. Shorten the total treatment time which results in improved treatment of tumor. At the same time, keep the side effects low on normal tissues.

Abbreviations

RT	Radiation therapy
RTP	Radiation treatment planning
VMAT	Volumetric modulated arc therapy
IMRT	Intensity modulated radiation therapy
SIB	Simultaneous integrated boost
LQ	Linear quadratic model

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