IOSR Journal of Applied Physics (IOSR-JAP)
e-ISSN: 2278-4861.Volume 17, Issue 3 Ser. 2 (May. – June. 2025), PP 40-54
www.iosrjournals.org

Biological and Dosimetric Outcomes of Volumetric Modulated Arc Therapy (VMAT), Intensity Modulated Radiotherapy (IMRT) versus 3D Conformal Radiotherapy in Prostate Cancer

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Abstract
Radiotherapy is a cornerstone in the management of localized prostate cancer, with evolving technologies offering enhanced precision in dose delivery. Advanced techniques such as Intensity-Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) promise superior target conformity and organ-at-risk (OAR) sparing compared to conventional Three-Dimensional Conformal Radiotherapy (3DCRT). However, comparative evaluations integrating both dosimetric and radiobiological metrics remain limited. This study compares the dosimetric and radiobiological parameters of 3DCRT, IMRT, and VMAT using Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) models. Based on 16 patients with low-risk prostate cancer, results indicate that VMAT and IMRT achieve significantly improved PTV coverage and better OAR sparing without compromising tumor control. Radiobiological modeling confirmed the safety and effectiveness of all three modalities, with VMAT showing slight superiority in both TCP and NTCP trends.
Keywords: *Prostate Cancer, Radiotherapy Planning, Tumor Control Probability (TCP), Normal Tissue Complication Probability (NTCP)*
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Date of Submission: 12-06-2025 Date of Acceptance: 24-06-2025

I. Introduction:

Radiation therapy plays a pivotal role in the management of prostate cancer, with the primary objective of delivering an optimal therapeutic dose to the tumor while minimizing radiation exposure to surrounding normal tissues. Clinical evidence suggests that escalating tumor doses within safe thresholds can enhance tumor control rates, particularly in prostate cancer treatment, where precision is crucial for achieving favorable clinical outcomes [1,2].

Technological advancements in external beam radiation therapy (EBRT) have led to the development of sophisticated techniques, including Three-Dimensional Conformal Radiotherapy (3DCRT), Intensity-Modulated Radiation Therapy (IMRT), and Volumetric Modulated Arc Therapy (VMAT), each offering distinct dosimetric advantages [3-5]. IMRT and VMAT, in particular, have revolutionized treatment delivery by enabling dynamic modulation of beam intensity, multi-leaf collimator positioning, and gantry rotation speed, thereby achieving improved dose conformity and sparing of adjacent organs-at-risk (OARs) [3].

In parallel with advancements in treatment planning, radiobiological modeling has gained increasing attention in the evaluation of radiation therapy efficacy. Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) are essential metrics for assessing treatment plan quality and predicting clinical outcomes. However, many NTCP models do not fully account for fractionation effects, potentially limiting their accuracy in evaluating toxicity risks [6,7]. This study seeks to address this gap by applying advanced radiobiological models, including the Lyman-Kutcher-Burman (LKB) model and Poisson-based TCP models, in the assessment of 3DCRT, IMRT, and VMAT treatment plans. Furthermore, variations in dose per fraction and radiobiological parameters will be explored to refine the predictive accuracy of these models in prostate cancer radiotherapy.

II. Material And Methods

2.1 Study Design: This retrospective study evaluates the dosimetric and radiobiological differences between **Three-Dimensional Conformal Radiotherapy (3DCRT), Intensity-Modulated Radiotherapy (IMRT), and Volumetric Modulated Arc Therapy (VMAT)** in the treatment of **prostate cancer.** The study was conducted following approval from the, ensuring compliance with ethical research guidelines.
2.2 Patient Cohort: 16 male patients diagnosed with low-risk prostate cancer were retrospectively selected from international medical center

- Inclusion criteria:
  - Histologically confirmed low-risk prostate cancer
  - CT-based simulation scans available for treatment planning
  - Age range: 45–80 years
- Exclusion criteria:
  - History of previous pelvic radiation therapy
  - Concurrent chemotherapy during radiotherapy

2.3 Treatment Planning: For each patient, three distinct treatment plans were created using the Eclipse Treatment Planning System (TPS, Version 15.6, Varian Medical Systems, USA):

- **VMAT:** Two full arcs with dynamic multi-leaf collimation, optimizing beam modulation during gantry rotation.
- **IMRT:** Seven static beams with optimized beam intensity modulation to improve dose conformity and homogeneity.
- **3D-CRT:** Five fixed beams positioned to achieve adequate tumor coverage while reducing normal tissue dose.

Beam Configuration and Dosimetry: All plans were generated using a 15 MV photon beam delivered via a Truebeam Linear Accelerator (Varian Medical Systems, USA). Dose calculations were performed using the Anisotropic Analytical Algorithm (AAA), with plan normalization ensuring 95% of the Planning Target Volume (PTV) received the prescribed dose of 76 Gy in 38 fractions.

2.4 Dosimetric Analysis: Dosimetric parameters were extracted from Dose-Volume Histograms (DVHs) for both the target volume and organs at risk (OARs). Evaluated parameters included:

- **PTV Coverage**: D95%, V95, Dmin, and Dmax
- **Organ-at-Risk (OAR)** Constraints (Based on Quantitative Analyses of Normal Tissue Effects in the Clinic [QUANTEC]):
  - **Rectum:** V50 < 50%, V65 < 17.5%, V80 < 15%
  - **Bladder:** V65 < 50%, V75 < 25%, V80 < 15%
  - **Femoral Heads:** Dmax < 60 Gy

The dose volume constraints for the target and critical organs for the inverse planning are given in Table 1.

Table 1: Dose-volume constraints recommendations for target volume and organs at risk in prostate cancer radiotherapy

Volume	Constrains
Target Volume (PTV)	Dmin>90% The minimum dose for PTV must be higher than 90% of the prescribed dose V95>95 The volume receiving at least 95% of the prescribed dose must be higher than 90 % of the total volume
Bladder	V65<50% V70<35% V75<25% V80<15%
Rectum	V50<50% V40<35% V65<17.5% V80<15%
Femoral Head	Dmax=60 Gy V50<10% V40<45%
Bowel	Large Dmax = 55Gy Small Dmax=55 Gy V45< 195 cc V30< 300 cc

III. Radiobiological modeling

The evaluation of radiobiological effects in this study was conducted using **Tumor Control Probability (TCP)** and **Normal Tissue Complication Probability (NTCP) models**, which estimate the likelihood of tumor eradication and normal tissue toxicity, respectively. The following models were applied:

- **Lyman-Kutcher-Burman (LKB) Model for NTCP:** This model accounts for tissue-specific parameters and dose-volume effects in organs at risk (OARs), predicting the probability of normal tissue complications.
- **Poisson-Based TCP Model:** This model evaluates TCP based on differential dose-volume histograms (dDVHs) and accounts for variations in α/β ratios specific to prostate cancer.

Calculation of NTCP and TCP:

Dose-Volume Histograms (DVHs) extracted from each plan were analyzed using Biosuite software to derive Equivalent Uniform Dose (EUD), NTCP, and TCP values. The LKB model was applied to OARs to estimate NTCP, incorporating variable α/β ratios to assess fractionation sensitivity. The Poisson-based TCP model, in conjunction with the Linear Quadratic (LQ) model, was used to determine TCP for prostate cancer treatment plans.

The EUD for a given dose distribution was calculated using the equation:

$$EUD = (\sum_{i=1}^{N} v_{i} D_{i}^{a})^{\frac{1}{a}}$$

where N represents the number of elements in the differential DVH (dDVH), v_i is the fractional organ volume receiving dose D_i, and a (-10) is a tissue-specific parameter describing the volume effect.

For TCP estimation, the Poisson statistics approach was used. The model assumes that cell survival following radiation exposure in independent tumor sub volumes follows a Poisson distribution, and TCP is determined by:

$$TCP=e^{-KS}$$

where K is the tumor clonogenic cell number, and S is the average survival fraction, expressed as:

$$S = \Sigma i N\ v(Di)$$

For this study, TCP was calculated for α/β ratios of 10, 3, and 1.2, considering tumor heterogeneity. Other assumptions included $\alpha = 0.301\ Gy^{-1}$, αspread = 0.114, a homogeneous clonogenic cell density of 10^7 cells/cm³, a repopulation constant of 0, and a repopulation delay of 45 days. Two TCP estimations were used:

- TCPP (Poisson-based TCP estimation)
- TCPE (TCP derived from EUD calculations)

The biological parameters (M slope, N volume effect, and TD50) used for NTCP calculations were derived from established clinical data and are listed in Table 2.

Table 2: Biological parameters, n, m, and TD50 used for the NTCP calculation

Organ	M slope	N volume effect	TD50 (cGy)	Endpoint
Bladder	0.11	0.5	80	Contracture
Rectum	0.27	0.085	97.7	Stricture-Bleeding
Femoral head	0.12	0.25	65	Necrosis
Bowel	0.16	0.15	55	Obstruction-Perforation

IV. Treatment Planning Techniques

This study evaluates the dosimetric and radiobiological impacts of Three-Dimensional Conformal Radiotherapy (3DCRT), Intensity-Modulated Radiotherapy (IMRT), and Volumetric Modulated Arc Therapy (VMAT) in the treatment of prostate cancer. Each technique employs distinct methodologies to optimize tumor dose coverage while minimizing radiation exposure to surrounding organs at risk (OARs).Treatment plans were generated using the Eclipse Treatment Planning System (TPS, Version 15.6, Varian Medical Systems, USA). A 15-MV photon beam was used for all plans, delivered via a Truebeam Linear Accelerator (Varian Medical Systems, Palo Alto, CA, USA). The beam was shaped using a high-definition multi-leaf collimator (MLC) with 120 leaves to ensure precise target coverage. Dose calculations were performed using the Anisotropic Analytical Algorithm (AAA) with a dose rate of 400 MU/min. Each plan was normalized to ensure that 95% of the Planning Target Volume (PTV) received the prescribed dose of 76 Gy in 38 fractions (8).

A. Three-Dimensional Conformal Radiotherapy (3DCRT)

3DCRT is an external beam radiotherapy technique that utilizes multiple static radiation beams to conform the dose distribution to the tumor shape while reducing exposure to adjacent healthy tissues. Beam shaping is achieved using collimators, ensuring precise targeting of the prostate. In this study, five fixed fields were used to deliver radiation from multiple angles, optimizing dose distribution and maintaining a balance between tumor coverage and normal tissue sparing. However, due to its static nature, 3DCRT provides less flexibility in modulating dose intensity compared to IMRT and VMAT, which may lead to increased radiation exposure to surrounding organs at risk (OARs).

B. Intensity-Modulated Radiation Therapy (IMRT)

IMRT is an advanced radiotherapy technique that allows for intensity modulation of individual radiation beams, enabling highly conformal dose distribution. Unlike 3DCRT, IMRT optimizes dose delivery by adjusting beam intensity at each angle, allowing for steep dose gradients that enhance target coverage while minimizing radiation exposure to normal tissues.

In this study, IMRT plans were created using seven static fields, with beam intensities optimized using inverse planning algorithms. The multi-leaf collimator (MLC) dynamically shapes the radiation beam to match the tumor contours, ensuring higher conformity and improved dose homogeneity compared to 3DCRT. This technique is particularly effective in reducing radiation dose to sensitive organs such as the rectum and bladder, thereby lowering the risk of toxicity.

C. Volumetric Modulated Arc Therapy (VMAT)

VMAT is a highly advanced form of IMRT that delivers radiation in a continuous arc around the patient, allowing for greater dose modulation and improved treatment efficiency. Unlike static-field IMRT, VMAT enables simultaneous variation of gantry speed, dose rate, and MLC position, further enhancing dose conformity.

In this study, VMAT plans were generated using two full arcs, where the collimator leaves continuously adjust during gantry rotation to optimize dose distribution. The dynamic nature of VMAT allows for reduced treatment time compared to IMRT while maintaining equivalent or superior dosimetric advantages. This approach enhances tumor coverage, improves dose homogeneity, and minimizes dose to adjacent normal tissues, making it a preferred technique in prostate cancer radiotherapy.

5. MATLAB-Based Radiobiological Analysis (PROGTCP)

To evaluate the radiobiological impact of each technique, a MATLAB-based program, PROGTCP, was utilized to analyze dose-volume histogram (DVH) data. The program calculates Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) using the input parameters:

- α/β ratio for the organ of interest
- Dose-response slope at 50% complication probability (M-Slope)
- Tolerance dose (TD50) for 50% complication risk

Once the necessary data were input, PROGTCP computed TCP and NTCP values, allowing for a comparative assessment of the three radiotherapy techniques. This software-based evaluation enabled a more comprehensive analysis of radiobiological effects, complementing the dosimetric assessment.

V. Result:

1-PTV Dosimetrics

Analysis of the planning target volume (PTV) dosimetric outcomes (Table 1) revealed significant differences among the three radiotherapy techniques. The mean **D95%** coverage of the PTV was highest with

VMAT (RA) at **99.51%**, followed closely by **IMRT (99.16%)**, while **3DCRT** had the lowest value at **97.69%**. Statistically significant differences were observed between 3DCRT and both IMRT (p = 0.003) and VMAT (p = 0.000), whereas the difference between IMRT and VMAT was not statistically significant (p = 0.481).

Regarding **D2%**, 3DCRT delivered the highest maximum dose (**7934.31 cGy**), followed by VMAT (**7793.56 cGy**) and IMRT (**7779.44 cGy**). Significant differences were found between 3DCRT and both IMRT and VMAT (p = 0.000), while the comparison between IMRT and VMAT remained nonsignificant (p = 0.854). Similarly, **D98%** values were highest with VMAT (**7436.97 cGy**), followed by IMRT (**7402.38 cGy**) and 3DCRT (**7271.25 cGy**), with statistically significant differences between 3DCRT and the other two techniques (p = 0.014 vs IMRT; p = 0.002 vs VMAT). For the **V105%**, values remained low across all techniques, with IMRT registering zero hotspots, 3DCRT showing a mean of **2.59 cc**, and VMAT showing a mean of **0.44 cc**. These differences were not statistically significant (p = 0.079). **PTV volumes** were consistent across all techniques, with no statistically significant differences (mean ≈ 159.79 cc). The **V100%** coverage also showed no significant difference among techniques (p = 0.883).

In terms of the **mean dose** to the PTV, 3DCRT delivered the highest dose (**7723.23 cGy**), compared to VMAT (**7685.18 cGy**) and IMRT (**7660.41 cGy**). A statistically significant difference was found between 3DCRT and IMRT (p = 0.034), but not between other pairwise comparisons. Additionally, the **maximum dose** to the PTV was highest with VMAT (**7976.66 cGy**), followed by 3DCRT (**7966.50 cGy**) and IMRT (**7881.68 cGy**). Significant differences were observed between IMRT and both 3DCRT (p = 0.047) and VMAT (p = 0.023), while the difference between 3DCRT and VMAT was not significant (p = 0.958). Finally, **homogeneity index** and **Paddick conformity index** values were equal across all techniques (HI = 1.000, CI = 0.9375 for IMRT and VMAT, and 1.000 for 3DCRT), indicating no statistically significant differences in dose homogeneity or conformity.

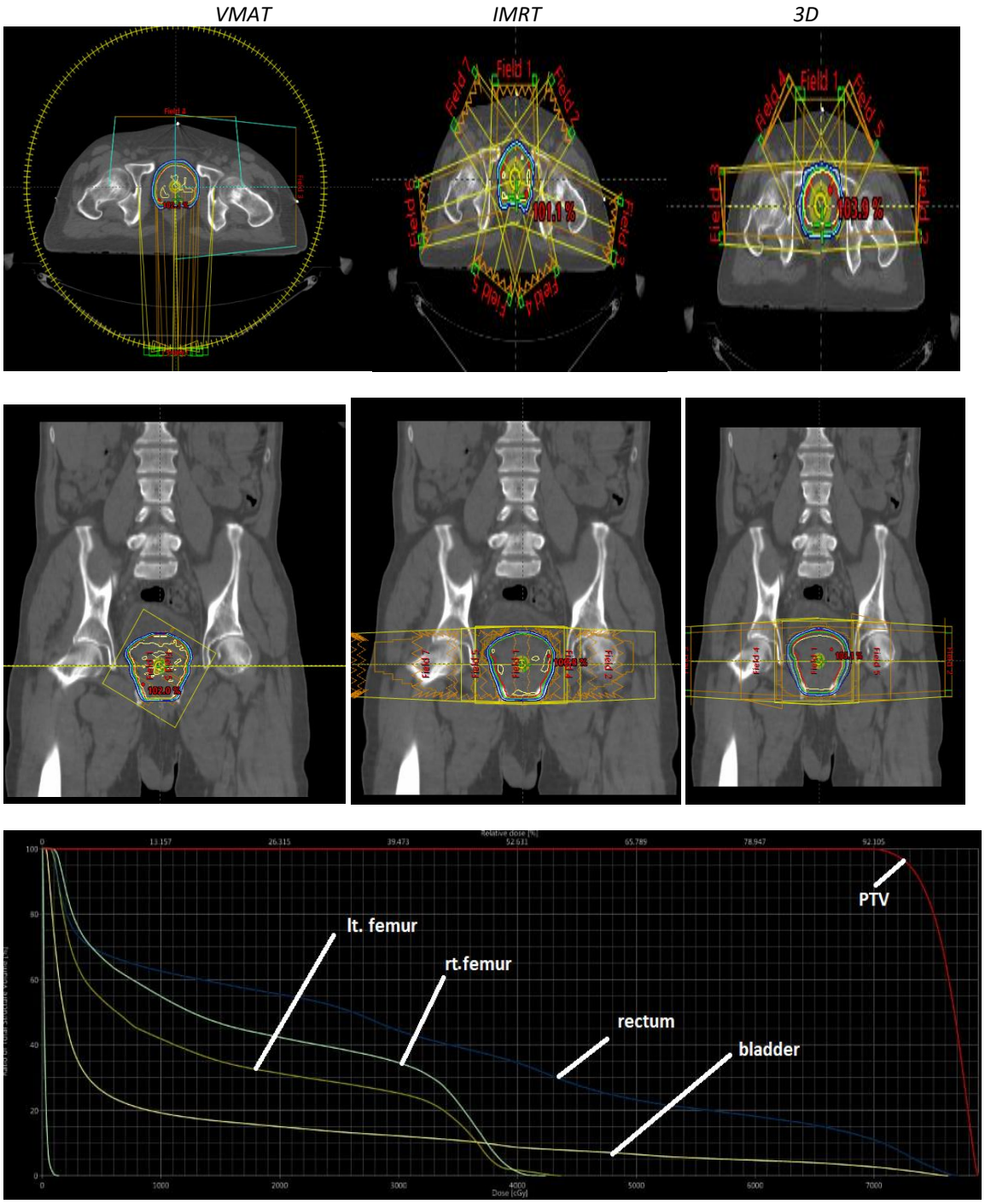
2-OAR Dosimetrics

Dosimetric analysis of organs at risk (OARs) (Table 2) revealed important differences among the three radiotherapy techniques. Regarding **rectal dose exposure**, 3DCRT resulted in a significantly higher volume receiving 50 Gy (**V50Gy = 36.90% ± 10.44**) compared to both IMRT (**26.25% ± 5.15**, p = 0.004) and VMAT (**26.81% ± 5.54**, p = 0.007), with no significant difference observed between IMRT and VMAT (p = 0.953). In contrast, no statistically significant differences were observed for the **bladder V65Gy (%)** among the three techniques (p = 0.356), although VMAT had the lowest mean value (**25.38% ± 7.69**) compared to IMRT (**29.87% ± 6.84**) and 3DCRT (**28.01% ± 11.21**).

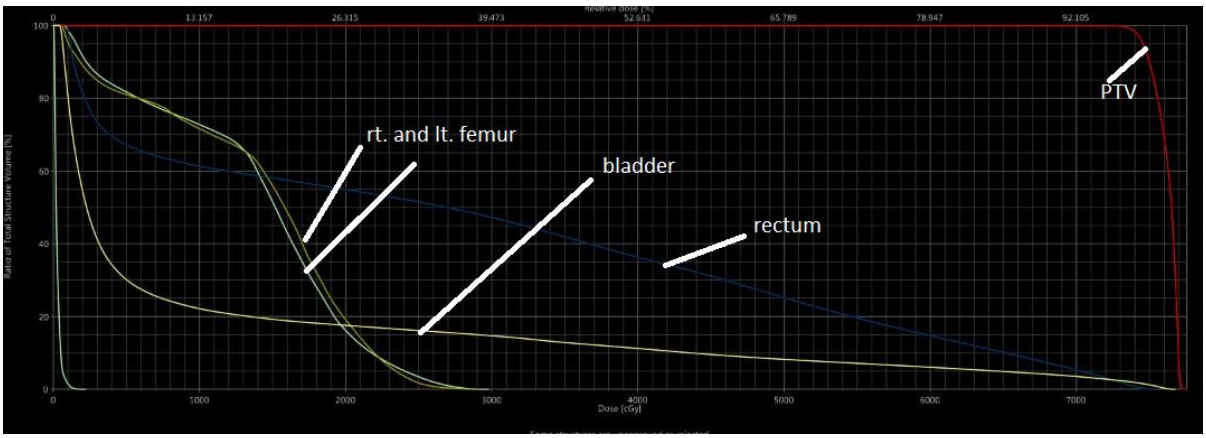
With respect to the **right femoral head**, 3DCRT delivered the highest mean dose (**2828.79 ± 405.85 cGy**), significantly greater than both IMRT (**1153.06 ± 484.10 cGy**, p = 0.000) and VMAT (**1482.69 ± 354.97 cGy**, p = 0.000). Similar patterns were observed for the maximum dose, with 3DCRT (**5194.31 ± 713.81 cGy**) again exceeding IMRT (**3166.38 ± 558.53 cGy**) and VMAT (**3553.19 ± 772.19 cGy**), both comparisons reaching statistical significance (p = 0.000). For the **left femoral head**, while the mean dose was highest with 3DCRT (**2718.81 ± 409.09 cGy**), only the difference between 3DCRT and VMAT was statistically significant (p = 0.000), with no significant difference noted between 3DCRT and IMRT or between IMRT and VMAT. The maximum dose to the left femoral head followed the same pattern: 3DCRT (**5247.00 ± 1036.58 cGy**) was significantly higher than both IMRT (**2976.14 ± 480.15 cGy**) and VMAT (**3376.53 ± 676.66 cGy**) with p-values < 0.001.

Regarding the **penile bulb**, 3DCRT again delivered the highest mean dose (**3952.13 ± 1411.35 cGy**), significantly more than both IMRT (**2817.44 ± 934.92 cGy**, p = 0.033) and VMAT (**2647.69 ± 1059.35 cGy**, p = 0.017). Lastly, no differences were observed across techniques in terms of **homogeneity index**, where all values were reported as 1.0000. Likewise, **Paddick conformity index** showed no statistically significant differences between techniques (p = 0.500), with IMRT and VMAT both yielding a value of **0.9375 ± 0.2500**, and 3DCRT scoring 1.0000.

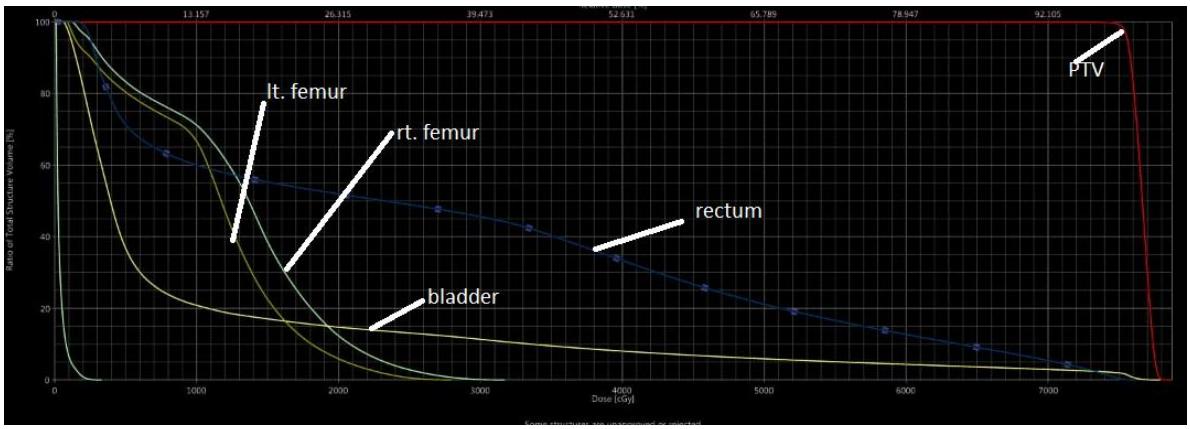
In Figure 1, the dose distribution and DVH comparison.



3D



IMRT



VMAT

3-TCP and NTCP

The **Tumor Control Probability (TCP)** values (Table 3) across all three planning techniques were uniformly high, reflecting effective tumor dose coverage. RA achieved the highest mean TCP (**99.74% ± 0.71**), followed by IMRT (**99.36% ± 0.88**) and 3DCRT (**99.10% ± 0.96**). Although the observed differences suggest a trend favoring advanced techniques, they did not reach statistical significance (overall ANOVA p = 0.121; 3D vs IMRT: p = 0.706; 3D vs RA: p = 0.103; IMRT vs RA: p = 0.398), indicating that all three modalities performed comparably in terms of tumor control.

With regard to the **Normal Tissue Complication Probability (NTCP)** (Table 3)**,** all observed values were extremely low, suggesting a negligible risk of complications across treatment plans. For the **rectum**, the NTCP values were lowest with VMAT (**0.25% ± 0.49**) and IMRT (**0.29% ± 0.52**), and slightly higher for 3DCRT (**0.68% ± 0.79**), though none of the comparisons yielded significant differences (p = 0.110). Similarly, **bladder NTCP** values were close to zero for all techniques (3DCRT: **0.03% ± 0.09**, IMRT: **0.03% ± 0.09**, RA: **0.01% ± 0.03**), and the differences were not statistically significant (p = 0.804).

Analysis of NTCP for the **femoral heads** further supported these findings. The left femur had uniformly negligible complication probabilities across all modalities (3DCRT: **0.00088**, IMRT: **0.00014**, RA: **0.00014**), with p-values ranging from 0.541 to 1.000. A similar pattern was observed for the **right femur** (mean NTCP: 3DCRT: **0.00124**, IMRT: **0.00009**, RA: **0.0000011**; p = 0.383), and for the **bowel bag**, where the NTCP values remained under **0.01%** across all plans.

Overall, while VMAT and IMRT demonstrated slight dosimetric advantages in OAR sparing, these did not translate into statistically significant differences in NTCP. The findings affirm the clinical equivalency of all three techniques in minimizing complications while achieving excellent tumor control, reinforcing the safety and efficacy of each modality when used appropriately in prostate cancer treatment

VI. Discussion:

This study aimed to investigate and compare the physical and radiobiological parameters associated with three modern external beam radiation therapy techniques—Three-Dimensional Conformal Radiotherapy (3DCRT), Intensity-Modulated Radiation Therapy (IMRT), and Volumetric Modulated Arc Therapy (VMAT/RA)—in the treatment of localized prostate cancer. The central research question addressed whether

there are significant differences among these modalities in terms of target coverage, organ-at-risk (OAR) sparing, and the estimated Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP).

The dosimetric evaluation revealed that both IMRT and VMAT techniques provided superior PTV coverage compared to 3DCRT. Specifically, the highest mean PTV D95% was observed with VMAT (99.51%), followed by IMRT (99.16%) and 3DCRT (97.69%), with statistically significant differences between 3DCRT and the advanced techniques ($p < 0.003$). Similar trends were noted in other PTV-related metrics, including D2%, D98%, and mean dose, indicating improved dose homogeneity and conformality with IMRT and VMAT. While PTV volumes and V100% values were statistically comparable across all modalities, maximum dose differences favored VMAT, which delivered the highest values with a statistically significant margin ($p = 0.017$), aligning with previous studies that highlight the precision of rotational arc therapies in achieving optimal target coverage [9,10].

Regarding OAR sparing, IMRT and VMAT demonstrated a clear advantage over 3DCRT. The rectal V50Gy was significantly lower with IMRT (26.25%) and VMAT (26.81%) compared to 3DCRT (36.90%) ($p < 0.007$), supporting existing evidence that advanced modulation techniques can reduce high-dose exposure to the rectum and subsequently lower the risk of late rectal toxicity [11]. Similarly, for femoral heads and penile bulb, 3DCRT plans consistently yielded the highest doses, with significant differences noted between 3DCRT and the other techniques ($p < 0.001$), reinforcing concerns about peripheral dose distribution in non-modulated plans [12].

Radiobiological modeling using the Poisson TCP model and the Lyman-Kutcher-Burman NTCP model indicated that all three techniques achieved excellent tumor control probabilities, with TCP values exceeding 99% across the board. VMAT recorded the highest TCP (99.74%) followed by IMRT (99.36%) and 3DCRT (99.10%), although these differences were not statistically significant ($p = 0.121$). NTCP values for rectum, bladder, and femoral heads remained consistently low (<1%) across all techniques, indicating minimal predicted normal tissue complications and no statistically significant differences between groups. These findings are consistent with recent literature reporting minimal differences in clinical TCP/NTCP outcomes when dose constraints are adequately respected, irrespective of planning modality [13–14].

The present study's findings align with a growing body of evidence supporting the superior dosimetric performance of intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) over conventional three-dimensional conformal radiation therapy (3DCRT) in the treatment of prostate cancer. Several clinical trials and dosimetric analyses have consistently demonstrated the advantages of IMRT and VMAT in achieving enhanced target conformity and improved organ-at-risk (OAR) sparing, which are critical in minimizing radiation-induced toxicity and enhancing therapeutic outcomes.

In terms of target volume coverage, this study found that both IMRT and VMAT achieved significantly higher PTV D95% and D98% values compared to 3DCRT, with VMAT recording the highest mean PTV D95% (99.51%). These findings are congruent with those reported by Wortel et al. (2016), who demonstrated improved target coverage and reduced rectal and bladder doses with IMRT compared to 3DCRT in two large prospective cohorts of prostate cancer patients [10]. Similarly, Viani et al. (2016) documented that IMRT provided superior dose conformity and homogeneity compared to 3DCRT, with lower toxicity rates and equivalent biochemical control, thereby reinforcing the clinical benefit of advanced modulation techniques [9].

OAR sparing observed in this study also supports previous dosimetric investigations. The significantly lower rectal V50Gy values achieved with IMRT and VMAT are consistent with reports by Sujenthiran et al. (2017), who used national population-based data to show reduced gastrointestinal toxicity with IMRT compared to 3DCRT [11]. Likewise, Michalski et al. (2010), in a multi-institutional trial under the Radiation Therapy Oncology Group (RTOG), confirmed the advantage of IMRT in limiting OAR doses without compromising disease control [15]. The reduction in maximum and mean doses to the femoral heads and penile bulb with VMAT and IMRT in this study also corroborates the work of Bi et al. (2022), who found that VMAT achieved improved dose gradients and steeper fall-off compared to 3DCRT in pelvic irradiation [16].

Regarding radiobiological metrics, the observed high tumor control probabilities (TCP >99%) for all three modalities affirm their clinical effectiveness. The absence of statistically significant differences in TCP values among 3DCRT, IMRT, and VMAT reflects findings from Dearnaley et al. (2016), who reported similar biochemical control outcomes among patients treated with these modalities when dose prescription and constraints were standardized [17]. Notably, the marginally higher mean TCP observed with VMAT in the current study echoes the results from Zhang et al. (2012), who demonstrated that VMAT can enhance tumor coverage and maintain biological effectiveness while reducing treatment time [18].

Furthermore, the NTCP values for rectum, bladder, and femoral heads remained uniformly low across all techniques in this study, indicating favorable toxicity profiles. These outcomes resonate with the evidence synthesized by Li et al. (2012) and the recommendations from QUANTEC and AAPM Report 166, which

support the use of radiobiological modeling tools such as Lyman-Kutcher-Burman (LKB) and Poisson models in clinical plan evaluation and comparison [13].

This study provides valuable insight into how dosimetric performance translates into radiobiological efficacy in prostate cancer treatment across three techniques: 3DCRT, IMRT, and VMAT. While conventional dosimetric endpoints—such as PTV coverage, homogeneity, and doses to organs at risk—remain the standard for treatment plan evaluation, they do not inherently convey biological impact. Therefore, the inclusion of radiobiological modeling, specifically Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP), adds essential clinical depth to plan assessment.

The TCP analysis revealed no statistically significant differences among the three modalities, with all techniques achieving exceptionally high tumor control probabilities above 99%. RA demonstrated the numerically highest TCP (99.74%), followed by IMRT (99.36%) and 3DCRT (99.10%). Although not statistically significant, this trend suggests a marginally enhanced tumoricidal potential of RA due to its superior dose conformity and target coverage [3,18]. These findings underscore the idea that, despite differences in plan quality metrics, all three modalities—when optimized—can achieve comparably robust tumor control outcomes in localized prostate cancer.

In contrast, the NTCP values for rectum, bladder, femoral heads, and bowel bag were remarkably low across all techniques, reaffirming the clinical acceptability of the evaluated plans. Notably, although rectal NTCP showed a slight numerical elevation with 3DCRT (mean = 0.68%) compared to IMRT and RA (both approximately 0.25%), this difference did not reach statistical significance ($p = 0.110$). These data align with prior studies which suggest that IMRT and VMAT more effectively spare rectal tissue compared to 3DCRT, particularly due to their enhanced modulation capabilities and steeper dose gradients [9-11].

The alignment between physical dose metrics and radiobiological indices in this study affirms the predictive utility of models like Lyman-Kutcher-Burman (LKB) and the Poisson TCP model when used in conjunction with detailed DVH analysis. For instance, the higher maximum and mean rectal doses observed in 3DCRT correspond with its relatively elevated NTCP for rectal toxicity. Conversely, IMRT and VMAT exhibited both lower mean rectal doses and lower NTCP values, reinforcing the consistency between dosimetric advantage and reduced biological risk. Overall, these findings suggest that although modern techniques such as IMRT and VMAT do not confer statistically significant benefits over 3DCRT in TCP and NTCP under the conditions studied, they do offer marginal improvements in conformity and organ sparing. These dosimetric improvements translate into potentially clinically meaningful radiobiological gains, especially in patients with borderline anatomical or dosimetric constraints. The findings support the growing consensus favoring advanced modulation techniques for optimized prostate cancer radiotherapy [16-17].

The evaluation of organ-at-risk (OAR) sparing is a critical determinant in prostate cancer radiotherapy, given the proximity of radiosensitive pelvic structures such as the rectum, bladder, femoral heads, and penile bulb to the treatment volume. This study demonstrated measurable dosimetric advantages of IMRT and VMAT over 3DCRT in reducing radiation exposure to these critical organs, though statistical significance varied among parameters. These results corroborate the theoretical and clinical premise that conformal and modulated techniques enhance the therapeutic ratio by improving dose conformity and steepening dose fall-off outside the target volume. Most notably, rectal sparing was significantly improved with IMRT and RA compared to 3DCRT. Rectal V50Gy was highest with 3DCRT (mean = 36.90%), while both IMRT (26.25%) and RA (26.81%) showed a statistically significant reduction ($p = 0.004$ and 0.007, respectively). This finding is clinically important, given the established correlation between intermediate rectal dose volumes (V50–V70Gy) and late rectal toxicity, such as proctitis and bleeding. Similarly, although bladder V65Gy values did not significantly differ among techniques, RA demonstrated a lower mean dose, suggesting a modest clinical advantage[10-15].

A particularly striking finding was the substantial dose reduction to the femoral heads in IMRT and RA compared to 3DCRT. The mean right femoral head dose dropped from 2828.79 cGy in 3DCRT to 1153.06 cGy in IMRT and 1482.69 cGy in RA, with statistically significant differences between 3DCRT and both modulated techniques ($p < 0.001$). This is of clinical relevance in minimizing the risk of avascular necrosis and maintaining patient mobility, particularly in elderly populations. Similarly, the left femoral head received significantly less radiation in RA than in 3DCRT ($p < 0.001$), despite IMRT showing greater variability.

Penile bulb dose, though less frequently emphasized, has been increasingly linked with sexual dysfunction following prostate radiotherapy. Here, 3DCRT resulted in the highest mean dose (3952.13 cGy), while IMRT (2817.44 cGy) and RA (2647.69 cGy) offered statistically significant reductions ($p = 0.033$ and 0.017, respectively). These findings reinforce the advantage of advanced techniques in preserving genitourinary function, an often underreported but impactful outcome on patient quality of life. Although the conformity and homogeneity indices did not significantly differ among techniques—likely due to the protocolized planning normalization criteria—the differences in OAR dosimetry suggest that IMRT and VMAT provide clinically

meaningful improvements in toxicity risk profiles. Previous clinical trials and large cohort studies have similarly reported decreased gastrointestinal and genitourinary toxicity rates with IMRT compared to 3DCRT [9,11,12].

Strengths:

The results of this study offer critical insight into the comparative effectiveness of 3DCRT, IMRT, and VMAT, with notable implications for clinical decision-making, technology adoption, and radiotherapy treatment planning in prostate cancer management. Although all three modalities achieved acceptable tumor coverage and organ-at-risk sparing, the findings clearly favor the use of advanced modulated techniques—particularly IMRT and VMAT—for optimizing the therapeutic ratio.

From a dosimetric standpoint, the significant reductions in rectal and femoral head doses with IMRT and VMAT, without compromising target coverage, suggest that these modalities are more effective in minimizing radiation-induced toxicity. In a setting where long-term quality of life is paramount, especially for patients with favorable-risk disease and long survival expectations, such improvements are not merely technical enhancements but clinically relevant priorities. These findings are consistent with previously published evidence demonstrating that modern techniques like IMRT are associated with lower rates of gastrointestinal and genitourinary toxicity compared to 3DCRT.

Furthermore, the non-significant differences observed in Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) across the three techniques underscore the principle that dosimetric advantages do not necessarily compromise tumor control. The equivalence in radiobiological outcomes suggests that selection of more advanced techniques can be safely made on the basis of toxicity reduction and resource availability rather than concerns about efficacy. These results support the rationale behind recent guideline recommendations that endorse IMRT or VMAT as the preferred techniques in prostate radiotherapy, particularly for cases requiring dose escalation or hypofractionation.

From a practical perspective, VMAT offers additional benefits such as shorter treatment delivery times and greater efficiency compared to fixed-beam IMRT, which can improve patient throughput and comfort. The logistical and operational advantages of VMAT may be particularly valuable in high-volume centers and resource-constrained settings, despite its higher initial cost and infrastructure requirements.

In comparison to studies from other Arab or regional contexts, there remains a paucity of published dosimetric or radiobiological data specific to prostate cancer treated with IMRT or VMAT. This underscores the value of the current research in filling a contextual gap and contributing locally relevant insights into practice optimization. The findings are thus important not only from a technical standpoint but also for informing evidence-based policy and resource allocation within regional radiotherapy centers.

Limitations:

Despite the valuable insights yielded by this comparative dosimetric and radiobiological analysis of 3DCRT, IMRT, and VMAT in prostate cancer, several limitations should be acknowledged:

1. **Use of Simulated Plans on Archived Data**:

This study was conducted retrospectively using archived CT datasets of previously treated patients rather than analyzing actual clinical outcomes. While this allows for controlled plan comparisons, it does not account for inter-patient anatomical variations during treatment or patient-specific responses, which limits the ability to generalize the findings to real-world clinical effectiveness.

2. **Small Sample Size and Single-Center Design**:

The analysis was limited to a modest number of anonymized cases from a single institution, which may reduce the statistical power of the results and the generalizability across diverse clinical settings with varying planning protocols, contouring practices, or equipment platforms.

3. **Exclusion of Clinical Outcomes**:

The study did not include follow-up data on actual tumor control rates, toxicity, or quality-of-life outcomes. Although Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) offer predictive insights, they remain model-based estimations and may not fully substitute for long-term clinical endpoints.

4. **Radiobiological Modeling Assumptions**:

The TCP and NTCP calculations were based on specific modeling parameters (e.g., α/β ratios, clonogen density, no repopulation correction) derived from literature rather than individualized to patient characteristics. As such, these predictions may not accurately reflect the full biological complexity of prostate tumors or the tolerance of normal tissues.

5. **Limited Organ-at-Risk (OAR) Assessment**:

While several key OARs were included (e.g., rectum, bladder, femoral heads), other potentially relevant structures such as the urethra, penile bulb in more detail, or bowel loops were not extensively assessed. This could underrepresent some aspects of late toxicity risk.

6. **Uniform PTV Definition and Margins**:
The planning target volume (PTV) margins were standardized across all techniques, which does not consider the possibility of tighter margins with advanced techniques like VMAT due to better conformity and image guidance. This may have underestimated the advantages of more modern approaches.
7. **Lack of Image-Guided Radiotherapy (IGRT) Considerations**:
The plans did not incorporate the influence of daily IGRT, which is particularly important for VMAT and IMRT techniques where smaller margins and higher conformity may increase sensitivity to setup variations or organ motion.
8. **No Cost-Effectiveness or Resource Utilization Analysis**:
Although the study highlights dosimetric and biological advantages of advanced techniques, it did not evaluate economic factors or planning and treatment time, which are important for healthcare decision-making, especially in resource-limited settings.

Future Research Directions
Building upon the findings of this study, several avenues for future research are warranted to further refine prostate cancer radiotherapy and validate the clinical utility of advanced planning techniques:
1. **Prospective Clinical Trials with Long-Term Outcomes**
While this study relied on radiobiological models and dosimetric comparisons, future prospective trials incorporating long-term clinical follow-up are essential. Such studies should assess actual tumor control, late toxicity, and quality-of-life outcomes to verify the predictive value of TCP/NTCP modeling in real-world settings.
2. **Patient-Specific Radiobiological Modeling**
Incorporating individualized radiobiological parameters—such as genomic radiosensitivity, α/β ratios, or organ-specific tolerance variability—may enhance the accuracy of TCP and NTCP predictions. Future studies should explore the integration of radiogenomic profiling with modeling algorithms to personalize treatment planning.
3. **Evaluation of Hypofractionation and Ultra-Hypofractionation**
With growing interest in moderate and extreme hypofractionation for prostate cancer, future research should compare these regimens using VMAT and IMRT while applying radiobiological models that account for fractionation sensitivity. This would help establish optimal schedules that maintain efficacy while improving patient convenience and resource efficiency.
4. **Integration of Image-Guided Radiotherapy (IGRT) and Adaptive Planning**
Further research should assess the impact of daily image guidance and adaptive radiotherapy on dosimetric precision, especially for techniques like VMAT. Studies should evaluate how margin reduction enabled by IGRT affects both tumor control and OAR toxicity using biologically-driven endpoints.
5. **Comparative Cost-Effectiveness Analyses**
Given the varying resource demands of 3DCRT, IMRT, and VMAT, future investigations should incorporate health economic evaluations. Cost-effectiveness analyses accounting for treatment duration, planning complexity, toxicity management, and patient-reported outcomes are necessary to guide rational adoption, particularly in low-resource settings.
6. **Application of Machine Learning in Radiobiological Prediction**
Emerging machine learning algorithms offer the potential to improve prediction of treatment response and toxicity by integrating large-scale clinical, dosimetric, and biological data. Future studies may leverage artificial intelligence to refine NTCP and TCP estimation beyond conventional models.
7. **Assessment of Sexual and Urinary Functional Outcomes**
More focused studies are needed to assess the impact of different techniques on genitourinary and sexual function—particularly relating to penile bulb and urethral dose distributions—which are not routinely captured in current toxicity metrics but significantly affect quality of life.

VII. Conclusion:

This study provides a comprehensive comparative analysis of three contemporary radiotherapy techniques—Three-Dimensional Conformal Radiotherapy (3DCRT), Intensity-Modulated Radiotherapy (IMRT), and Volumetric Modulated Arc Therapy (VMAT)—in the treatment of localized prostate cancer. Through the integration of physical dosimetric assessment and radiobiological modeling, including Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP), the findings reveal nuanced yet clinically significant distinctions among these modalities.

VMAT and IMRT demonstrated superior dosimetric performance over 3DCRT in terms of Planning Target Volume (PTV) coverage, dose homogeneity, and conformity. The advanced modulation capabilities of IMRT and the continuous arc delivery of VMAT yielded higher D95% and D98% values with reduced dose hotspots. Notably, these techniques provided statistically significant reductions in radiation exposure to critical

organs at risk (OARs), such as the rectum, femoral heads, and penile bulb, supporting a more favorable therapeutic ratio. These improvements are particularly pertinent given the long survival expectancy and quality-of-life considerations in prostate cancer management.

Radiobiological evaluation revealed uniformly high TCP values (>99%) across all techniques, affirming the efficacy of contemporary dose-escalated protocols in achieving optimal tumor control. Although the numerical advantage of VMAT in TCP did not reach statistical significance, its enhanced conformity and delivery efficiency suggest potential clinical value in high-precision contexts. NTCP values remained consistently low for rectum, bladder, and femoral heads across all modalities, indicating effective normal tissue sparing and minimal risk of late toxicity when standard dose constraints are respected.

Despite the absence of statistically significant differences in radiobiological outcomes, the alignment between improved dosimetry and predicted reductions in complication probabilities reinforces the clinical utility of IMRT and VMAT. These findings are consistent with international literature advocating the routine implementation of advanced techniques in prostate cancer radiotherapy.

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Table 1: PTV Dosimetric

		Mean	Std. Deviation	95% Confidence Interval for Mean		P value
				Lower Bound	Upper Bound	(One Way ANOVA)
	3D	97.6875	1.34058	96.9732	98.4018	All:0.000
	IMRT	99.1563	0.85086	98.7029	99.6096	3D vs IMRT:0.003

PTV D95% (%)	RA	99.5125	0.87550	99.0460	99.9790	3D vs RA:0.000 IMRT vs RA:0.481
PTV D2% (cGy)	3D	7934.3125	97.63109	7882.2886	7986.3364	All:0.000
	IMRT	7779.4375	73.29390	7740.3819	7818.4931	3D vs IMRT:0.000
	RA	7793.5625	75.86213	7753.1384	7833.9866	3D vs RA:0.000 IMRT vs RA:0.854
PTV D98% (cGy)	3D	7271.2500	139.26402	7197.0414	7345.4586	All:0.001
	IMRT	7402.3750	102.90894	7347.5387	7457.2113	3D vs IMRT:0.014
	RA	7436.9688	103.37321	7381.8851	7492.0524	3D vs RA:0.002 IMRT vs RA:0.614
PTV V105% (cc)	3D	2.5938	5.59958	-.3901	5.5776	All:0.079
	IMRT	.0000	.00000	.0000	.0000	3D vs IMRT:0.187
	RA	.4388	1.74967	-.4936	1.3711	3D vs RA:0.329 IMRT vs RA:0.586
PTV volume (cc)	3D	159.7938	49.68171	133.3202	186.2673	All:0.000
	IMRT	159.7938	49.68171	133.3202	186.2673	3D vs IMRT:1.000
	RA	159.7938	49.68171	133.3202	186.2673	3D vs RA: 1.000 IMRT vs RA: 1.000
PTV V100% (cc)	3D	126.8050	43.19374	103.7887	149.8213	All:0.883
	IMRT	124.7500	41.98433	102.3781	147.1219	3D vs IMRT:0.990
	RA	131.5725	33.24879	113.8555	149.2895	3D vs RA:0.935 IMRT vs RA:0.867
PTV mean dose (cGy)	3D	7723.2313	70.34668	7685.7461	7760.7164	All:0.041
	IMRT	7660.4063	64.07579	7626.2627	7694.5498	3D vs IMRT:0.034
	RA	7685.1813	70.27745	7647.7330	7722.6295	3D vs RA: 0.291 IMRT vs RA: 0.557
PTV max. dose (cGy)	3D	7966.5000	103.17170	7911.5237	8021.4763	All:0.017
	IMRT	7881.6750	88.34412	7834.5997	7928.7503	3D vs IMRT:0.047 3D vs RA: 0.958
	RA	7976.6625	102.76580	7921.9025	8031.4225	IMRT vs RA: 0.023

Table 2: OAR

		Mean	Std. Deviation	95% Confidence Interval for Mean		P value (One Way ANOVA)
				Lower Bound	Upper Bound	
Body V100% (cc)	3D	150.2344	50.55043	123.2980	177.1708	All:0.560 3D vs IMRT:0.633 3D vs RA:0.663 IMRT vs RA:0.984
	IMRT	134.5000	46.22553	109.8682	159.1318	
	RA	136.9563	34.14660	118.7608	155.1517	
Rectal V50Gy (%)	3D	36.8988	10.44012	31.3356	42.4619	All:0.000 3D vs IMRT:0.004 3D vs RA:0.007
	IMRT	26.2500	5.15429	23.5035	28.9965	

	RA	26.8125	5.54038	23.8602	29.7648	IMRT vs RA:0.953
BLADDER dose V65GY (%)	3D	28.0125	11.21439	22.0368	33.9882	All:0.356 3D vs IMRT:0.840 3D vs RA:0.721 IMRT vs RA:0.205
	IMRT	29.8688	6.84171	26.2231	33.5144	
	RA	25.3750	7.69307	21.2757	29.4743	
RT Femoral head mean dose(cGy)	3D	2828.7938	405.84976	2612.5317	3045.0558	All:0.000 3D vs IMRT:0.000
	IMRT	1153.0625	484.10240	895.1025	1411.0225	
	RA	1482.6875	354.96605	1293.5394	1671.8356	3D vs RA: 0.000 IMRT vs RA: 0.090
RT Femoral head max dose(cGy)	3D	5194.3125	713.81311	4813.9483	5574.6767	All:0.000 3D vs IMRT:0.000 3D vs RA:0.000 IMRT vs RA:0.253
	IMRT	3166.3750	558.53259	2868.7540	3463.9960	
	RA	3553.1875	772.18851	3141.7173	3964.6577	
LT Femoral head mean dose(cGy)	3D	2718.81250	409.088616	2500.82456	2936.80044	All:0.221 3D vs IMRT:0.666 3D vs RA: 0.000 IMRT vs RA: 0.837
	IMRT	1978.35625	3376.794658	178.98939	3777.72311	
	RA	1493.68750	367.947228	1297.62226	1689.75274	
LT Femoral head max dose(cGy)	3D	5247.00000	1036.579761	4694.64564	5799.35436	All:0.000 3D vs IMRT:0.000 3D vs RA:0.000 IMRT vs RA:0.163
	IMRT	2976.14375	480.146461	2720.29176	3231.99574	
	RA	3376.53333	676.662700	3001.81002	3751.25665	
Penile pulb dose (Mean)	3D	3952.1250	1411.34663	3200.0715	4704.1785	All:0.005 3D vs IMRT:0.033 3D vs RA:0.017 IMRT vs RA:0.881
	IMRT	2817.4375	934.92388	2319.2517	3315.6233	
	RA	2647.6875	1059.35431	2083.1974	3212.1776	
Homogeneity index	3D	1.0000	.00000	1.0000	1.0000	NA
	IMRT	1.0000	.00000	1.0000	1.0000	
	RA	1.0000	.00000	1.0000	1.0000	
Paddick Conformity index	3D	1.0000	.00000	1.0000	1.0000	All:0.500 3D vs IMRT:0.588 3D vs RA:0.588 IMRT vs RA:1.000
	IMRT	.9375	.25000	0.8043	1.0707	
	RA	.9375	.25000	0.8043	1.0707	

Table 3: Prostate: TCP, NTCP

Prostate		Mean	Std. Deviation	95% Confidence Interval for Mean		P value (One Way ANOVA)
				Lower Bound	Upper Bound	
TCP%	3D	99.10460036618748	0.956213953049074	98.59506991726640	99.61413081510857	All:0.121
	IMRT	99.36476285993750	0.883818401632161	98.89380927730845	99.83571644256655	3D vs IMRT:0.706
	RA	99.73760035993750	0.709237345985679	99.35967445523870	100.11552626463630	3D vs RA:0.103 IMRT vs RA:0.398
NTCP%: Rectum	3D	0.67789257468750	0.792754361769911	0.25546359365375	1.10032155572125	All:0.110
	IMRT	0.29132025525000	0.523122427863656	0.01256798996447	0.57007252053553	3D vs IMRT:0.252
	RA	0.25270618118750	0.490642769631455	0.00873889590329	0.51415125827829	3D vs RA:0.182 IMRT vs RA:0.975
NTCP%: Bladder	3D	0.02827545462500	0.093191706272988	0.02138290037137	0.07793380962137	All:0.804
	IMRT	0.02823258225000	0.093473909970938	0.02157614848231	0.07804131298231	3D vs IMRT:1.000
	RA	0.01226664081250	0.034625292609017	0.00618387523659	0.03071715686159	3D vs RA:0.798 IMRT vs RA:0.800
NTCP%: Lt. Femur	3D	0.00088214220625	0.002725038542084	0.00056992833429	0.00233421274679	All:0.337
	IMRT	0.00013554246875	0.000498060497237	0.00012985523637	0.00040094017387	3D vs IMRT:0.541
	RA	0.00013862863750	0.000552369057004	0.00015570805638	0.00043296533138	3D vs RA:0.546 IMRT vs RA:1.000
NTCP%: Rt Femur	3D	0.00124205650000	0.004838654286435	0.00133628036999	0.00382039336999	All:0.383
	IMRT	0.00008646481250	0.000281143783250	0.00006334613476	0.00023627575976	3D vs IMRT:0.616
	RA	0.00000112406250	0.000003118532507	5.3768617E-7	0.00000278581117	3D vs RA: 0.573 IMRT vs RA: 0.463
NTCP%: Bowel Bag	3D	0.00484993742500	0.008666865287513	0.00023169090538	0.00946818394462	All:0.633
	IMRT	0.00242780901875	0.006619298521304	0.00109936618754	0.00595498422504	3D vs IMRT:0.652
	RA	0.00303017828194	0.006820492678212	0.00060420572293	0.00666456228680	3D vs RA:0.788 IMRT vs RA:0.965