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Dosimetric Validation of Physical and Biological Indexes from the Dose-Volume Histogram for Evaluation of 3D-CRT and IMRT Techniques with VMAT Treatment Plan Techniques in Cervical Tumors from In-House Developed Software

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ABSTRACT

Introduction:This study aims to investigate the Normal Tissue Complication Probability (NTCP) and Tumor Control Probability (TCP) of cervical cancer from Niemierko radiobiological model and compared with Lyman-Kutcher-Butcher (LKB) model's effective volume parameter in three different planning techniques such as 3-Dimensional Conformal Radiation Therapy (3D-CRT), Intensity Modulated Radiotherapy (IMRT) and Volumetric Arc Therapy (VMAT).

Material and Methods:Twenty patients were selected with Grade II and Grade III and the treatment plan was initially generated for 3D-CRT, IMRT and VMAT. The physical dose from each voxel in radiotherapy treatment planning was extracted through a dose volume histogram (DVH) text file from in-built software developed using python program. Software was developed by freely available python integration with an integrated Oracle database to store the outcome results with user-friendly graphical user interface for editing the radiological parameter values and viewing the DVH graph. The dosimetricconformalities parameters such as homogeneity index (HI) and conformity index (CI) along with radiobiological parameters such as TCP, NTCP and effective volume (V_{eff}) were compared with three different planning techniques.

Results:The IMRT and VMAT dose delivery techniques improve the efficiency of the treatment of cervical cancer with good coverage of target volume as well as low irradiation of Organ at Risk (OARs) compared with 3D-CRT.

Conclusion: There is no significant difference in effective volume for IMRT and VMAT, which proportionally increases with the advanced planning techniques, causes insignificant complication probability to normal tissues. Other conformalities parameters were showing good agreement for all the three techniques.

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Introduction

Empirical data indicates that augmenting the dosage of the tumour enhances its control, particularly in cases of prostate cancer [1,2]. The advances in external beam radiation therapy (EBRT), such as IMRT and VMAT, enable substantial doses to be delivered to the target with minimal exposures to important structures [3]. While the VMAT system is a rotational IMRT that enables the simultaneous adjustment of gantry rotation speed, dose rate, and multi-leaf collimator field aperture, the IMRT is an advanced type of 3-dimensional conformal radiation treatment that integrates intensity-modulated radiation beams with other radiation therapy techniques. Recently, VMAT is now widely acknowledged as the preferred method for treating cervical cancer.

Since 2008, the volumetric arc treatment (VMAT) has seen an enormous rise in clinical application. The effectiveness and quality of the plan have been clearly shown in the application of VMAT for cervical cancer. The VMAT's advantage is its quick treatment delivery, which increases treatment precision due to intra-fractional motions. The previous research has demonstrated that, when compared to IMRT and 3D

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conformal radiation, VMAT yields a dose distribution that is both closer to and more accurate. [4-6].

Minimal toxicity and complications should be accomplished through the OARs near the cervix, such as the bladder, femur, and rectum, in order to produce optimal therapeutic outcomes. In several studies, a statically significant reduction in chronic complications regarding gastrointestinal and haematological toxicities with VMAT has been reported [7-8].

The goal of radiation therapy is to deliver an adequate therapeutic dose to the planning target volume (PTV) while minimizing the risks of normal tissue complications [9]. Different radiotherapy treatment planning approaches can be employed in radiation therapy to minimise the complications to normal tissue, with two decades of experience, biological models in radiation therapy attempt to overcome the aforementioned problems. Several mathematical models are available for evaluating NTCP and TCP [10, 11]. These models get inputs in the form of dose distributions, or DVHs, along with a set of parameters that describe how different tissues will respond to photon therapy [12-16].

Currently, nevertheless, the active planning system only seldom makes use of TCP and NTCP models. Despite the existence of numerous software tools for radiobiological evaluation [17–19], very few of these may be used by the vendor to create a radiation treatment planning system directly. In the TPS radiobiological tools are not found and are sometimes incorrectly implemented with huge licensee cost.

In this context, the present study aimed to develop in-house software named Radiobiological Dose evaluation Software (RDS) offering functionalities of clinical relevance via a user-friendly graphical application tool like resizing, saving the graph and editing the biological model parameters to generate biological evaluation parameters such as Niemierko Model of TCP, NTCP and effective volume of OAR and physical parameters such as CI, HI and mean dose of the OAR. This programme will be helpful in evaluating radiation treatment planning since it takes into account target coverage for tumour control and normal tissue dose to minimise the likelihood of complications. This will increase treatment efficiency and improve patient quality of life.

Materials and Methods

Commercial language

MATLAB encompasses the entire package, including the IDE (Integrated development environment), and is a widely used numerical computing environment and programming language. Due to the product's commercial nature, it will be difficult for users to afford the new version that is released every six months with improved features. It's also impossible for third parties to develop or expand MATLAB research tools due to its proprietary nature and non-compatible portability.

The Python programming language is being used as a tool for the basic research on DVH analysis and biological plan evaluation to get around these challenges and make the programme more user-friendly.

Highlights of Python

Compared to MATLAB, Python has a number of advantages over licencing costs, easy source viewing and modification, ease of reading and programming, ability to translate concepts into code, large standard libraries, robust data types, cross-platform compatibility, and freely defined classes and functions.

Choice of programming language

All the additional MATLAB functionality is available in Python through the NumPy, SciPy, and Matplotlib packages, which are all open source. Developing biological modelling software does not require the use of Simulink, which is one example that Python does not address. The comparisons of MATLAB and Python are shown in Table 1.

It is highly appealing for quick application development because of its high-level built-in data structures, dynamic typing, and dynamic binding. A robust N-dimensional array object, NumPy arrays are composed of rows and columns. They can be initialised from nested Python lists by storing the dose of voxels produced by DVH and carrying out NumPy operations.

Graphical user interface

Matplotlib is a Python plotting package that works with NumPy, the language's extension for numerical mathematics. Using general-purpose Graphical User Interfaces (GUI) toolkits such as Tkinter, PyQt5, Kivy, wxPython, Libavg, and PySimpleGUI, among others, it offers an object-oriented application programming interface (API) for embedding plots into applications.

Table 1. Basic Comparison between MATLAB and Python

S. No.	MATLAB	PYTHON
1.	MATLAB is a closed-source software program and a proprietary commercial product	PYTHON is an open-source, high-level, general-purpose programming language, totally free
2.	MATLAB has an integrating development environment	PYTHON has no default development environment
3.	MATLAB does not have a host of libraries	PYTHON has libraries such as Numpy, SciPy, and Matplotlib
4.	MATLAB restrictions on portability	PYTHON is very portable/easily shared
5.	MATLAB allows matrix manipulations	PYTHON is best suited for web programming
6.	MATLAB plot functions were not so faster	PYTHON plot functions were comparably faster

Although there are many GUI frameworks for Python, only Tkinter is included in the standard library and offers a number of advantages. Tkinter was developed to provide contemporary developers with a standardised interface to the Tk GUI toolkit via Python bindings; the majority of the visual components, such as widgets, provide varying degrees of customisation. Linux, Mac OS, and Windows can all run its cross-platform code. It is regarded as the de-facto Python GUI framework since visual elements are produced using native operating system elements, making it easier to use and lighter than competing frameworks. This makes it an attractive option for developing GUI apps in Python, particularly for projects where creating something quickly that is both functional and cross-platform is more important than giving it a current polish.

Python uses PyCharm, an integrated development environment (IDE) made by JetBrains, a firm well-known for producing excellent software development tools. PyCharm comes in two versions, the community edition is a lightweight, free open-source version, while the professional version is ideal for scientific and Python programming.

Oracle and Data structures

The programme uses Oracle Database 19c Standard Edition 2 Release 19.0.0.0.0 - Production version. The output of the Python software is stored in a table from the Oracle database, which is available for free download.

Patient selection

All research techniques were carried out in accordance with the applicable laws and guidelines. A retrospective random selection process was used to choose twenty patients from our hospital who underwent cervical VMAT. The patients' average weight was 70 kg (49-85 kg), and their average age ranged from 58 to 80 years old. Before planning, computed tomography (CT) simulation was performed with twenty-five patients with grade II cervical cancer in a customized immobilization ORFIT branded mask from the POCL Medical system. The CT simulation was performed from Positron emission tomography (PET-CT) GE Health Care Discovery IQ (3mm with flat table top). All patients were asked to drink 1 litre of water before the start of the one-hour simulation, to ensure that bladder was filled and CT was performed using the GE Discovery PET-CT scanner (GE Health care). The patients were scanned according to diagnostic protocol and data were exported to Eclipse Treatment planning system (ETPS) version 15.6.1, the contour of target and OAR was generated according to Radiation Oncology Group (RTOG) protocol 0126

Radiotherapy Treatment Planning

PET imaging was used to distinguish the clinical target volume (CTV) on the planned CT from the cervix volume. Microscopic subclinical disease and large tumours were included in CTV. On the axial CT scans in the TPS (Varian Medical Systems, Palo Alto, CA), the OARs, including the rectum, bladder, and femoral heads, were distinguished together with the CTV, which included the prostate and proximal seminal vesicles, from the CTV, the PTV was produced by uniformly expanding it by 5 mm in every direction.

The OARs were defined as the rectum, bladder, and femoral head. Varian ClinaciX (Varian Medical Systems, Palo Alto, CA) with a prescription dose of 50 Gy in 25 fractions was used to set up the planning parameters for treatment plans using the Varian standard scale in the TPS (version 15.06). The 3D-CRT plan with two anterior 6 MV and two posterior 15 MV static fields were used as shown in Figure1.The seven dynamic fields with 6 MV were created for IMRT plan as shown in Figure 2 and the two full arc techniques using 6MV beam created for VMAT plan as shown in Figure 3 were optimized with the Eclipse “Analytical Anisotropic Algorithm”(AAA). The front-end page of in-house developed PYTHON software screen shot for biological modelling are shown in Figure 4.

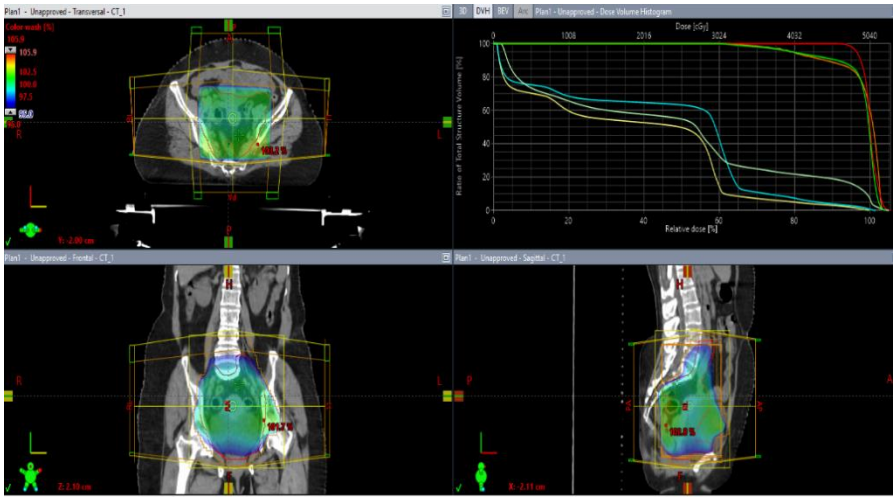


Figure 1. Beam geometry, dose distribution, and dose-volume histogram of 3D-CRT

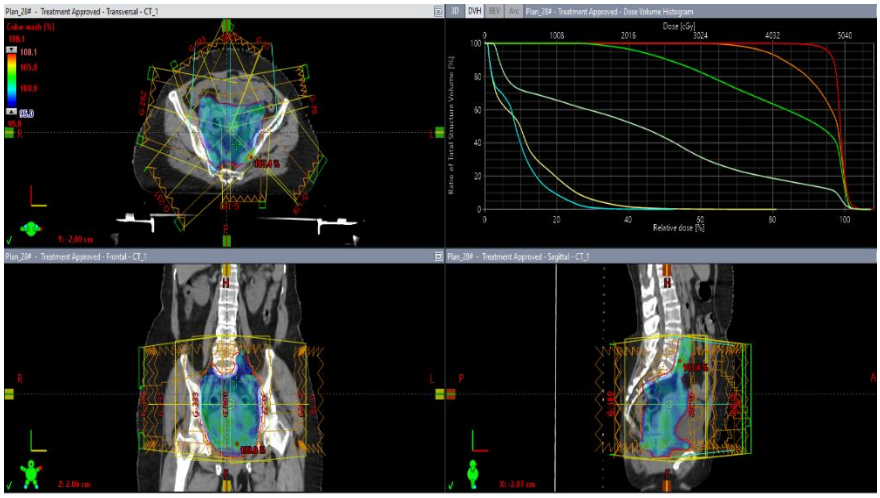


Figure 2. Beam geometry, dose distribution, and dose-volume histogram of IMRT

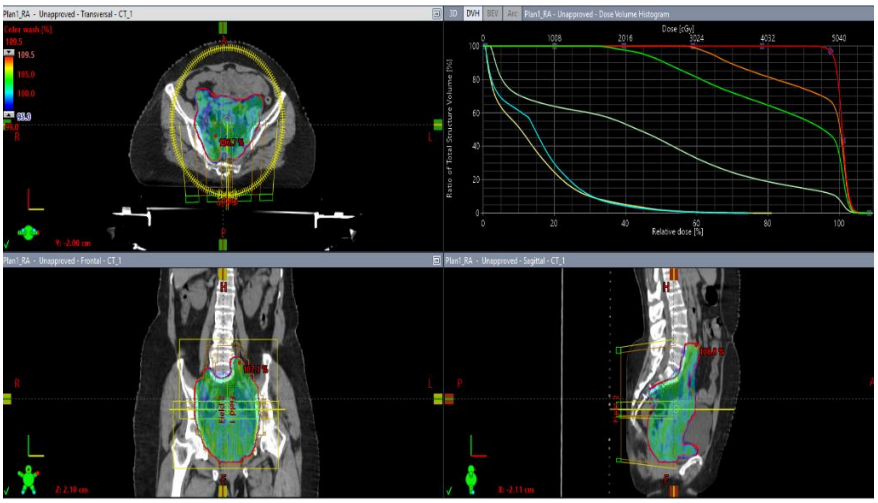


Figure 3. Beam geometry, dose distribution, and dose-volume histogram of VMAT

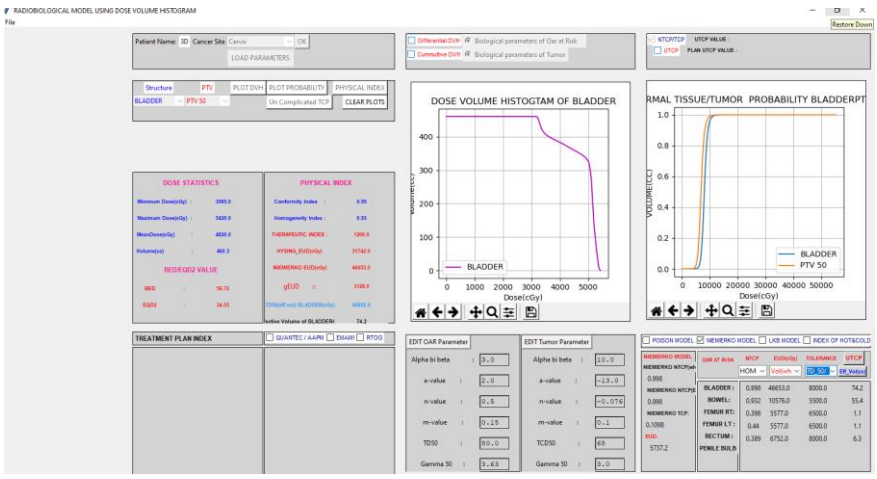


Figure 4. Function page of in-house developed python-based biological model plan evaluation software.

Physical index and evaluation

The conformity level of 3D-CRT, IMRT and VMAT planning can be assessed by the CI which is proposed by the RTOG in 1993[20] and described in the ICRU and Measurements Report 62 [21]. To calculate the physical dose the DVHs from the plan were exported from the Eclipse TPS system as a text file, the dosimetric parameters such as mean, maximum, minimum doses and volume for the PTV were analyzed. V_{95} of PTV was used as a measure of the target coverage in this study. The target dose of each VMAT, IMRT and 3D-CRT plan, HI, and CI were calculated.

The Homogeneity Index (HI) were calculated using the equations

$$HI = \frac{D_{95}}{D_5} \quad (1)$$

Where D_5 and D_{95}represent the dose to 5% and 95 % volume for the PTV respectively

Correspondingly, the Conformity Index (CI) was calculated using the equation

$$CI = \frac{V_{RI}}{TV} \quad (2)$$

Where V_{RI} is the volume of the reference isodose on the body and TV is the physical volume of PTV. The CI refers to the degree of dose conformity, and it is ideal for the CI to remain close to 1.

Radiobiological modelling

The cumulative DVHs of computed treatment plans were exported in text format from the Eclipse for use in the evaluation of radiobiological model response, for radiobiological analysis, in-house developed application were employed.To determine the Niemierko's equivalent uniform dose (EUD)-based NTCP and TCP values, we used a Python-based programme. The EUD [22] is described by Niemierko's phenomenological model as

$$gEUD = [\Sigma(V_i D_i)^a]^{1/a} \quad (3)$$

In equation (3), The volume effect specific to the target tumour or normal structure is described by the unit-less tissue-specific parameter "a.", and the i^{th} partial volume receiving dose Di in Gy is represented by the unitless vi. The total of all partial volumes vi will equal 1 because the relative volume of the entire structure of interest corresponds to 1.

Okunieff's paper [23] provided the parameter for TCD50 and $_{\gamma}50$. Additionally, the 2Gy biologically equivalent physical dose was described as follows:

$$EQD = D\frac{\left(\frac{\alpha}{\beta}+\frac{D}{nf}\right)}{\left(\frac{\alpha}{\beta}+2\right)} \quad (4)$$

Where nf and df = D/nf represent the treatment course's number of fractions and dose per fraction, respectively. The tissue-specific Linear Quadratic (LQ) parameter of the exposed organ is denoted by α/β [24].

The EUD-based TCP of TCP Niemierko [25] is described as:

$$TCP = \frac{1}{1+\left(\frac{TCD50}{EUD}\right)4_{\gamma 50}} \quad (5)$$

Where γ50 is a unitless model parameter unique to the tumour of interest that characterises the slope of the dose-response curve, and TCD50 is the 50% efficiency dose when exposed uniformly.

The definition of NTCP Niemierko's EUD-based NTCP [26] is:

$$NTCP = \frac{1}{1+\left(\frac{TD50}{EUD}\right)4_{\gamma 50}} \quad (6)$$

where TD50 is the tolerance dosage for a 50% complication rate at a given time interval (e.g., 5 years in the normal tissue tolerance data by Emami et al.) after the target organ has received a homogenous radiation dose. A unitless model parameter, the γ50 characterises the slope of the dose-response curve and is unique to the normal structure of interest. Table 2 contains a tabulation of all the parameters required to calculate NTCP and TCP.

Radiotherapy Treatment Planning

Four filed (anterior-posterior and left and right lateral field) were used for 3D-CRT planning, seven field used for IMRT planning and two full arcs were used for VMAT Planning. The prescribed dose for PTV is 50Gy dose prescription in 25 fractions and coverage should not be less than 95% of the dose delivered to 95% of the volume as per RTOG guidelines in dose constrain were reported for PTV and OARs volumes.

Effective Volume method

For an in-homogeneously irradiated OAR, Kutcher and Burman created a volume reduction technique for the Lyman Model. The resulting model is commonly known as the Lyman Kutcher Burman (LKB) model. According to the LKB model, there is a partial effective volume (v_{eff}) for every irradiated fractional sub volume (v_i) that is irradiated to dose d_i and reference dose d ref. The volume that, if it were the only volume exposed to radiation and it were exposed to dose d_{reff}, would produce the same NTCP in the Lyman model as if volume v_i were the only volume exposed and it had been exposed to dose d_i [27].

$$V_{eff} = v_i\left(\frac{d_i}{d_{ref}}\right)^{1/n} \quad (7)$$

Where 'n' is a parameter relating to the radiation response of the organ (n = 0, 1 for parallel and serial organs, respectively), and d_i is the dose applied to the volume fraction v.). The equivalent uniform irradiation of a fraction V_{eff} of the organ treated at the reference dose (d_{ref}) results by converting the inhomogeneous dose of radiation.

Table 2. Parameters used to calculate Niemierko's EUD-based TCP and NTCP

Tissue	End points	Volume type	a value	γ50 value	TD50 (Gy)	TCD50 (Gy)	α/β (Gy)
Cervix		Tumor	-10	3		67.5	10
Bladder	Bladder conjuncture / volume loss	Normal	2	4	80		3
Bowel	Obstruction/ perforation	Normal	6	4	55		3
Femur head	Marked limitation of joint function	Normal	4	2.65	65		6
Rectum	severe proctitis / necrosis/stenosis/fistula	Normal	8.33	4	80		3.9

Results

Physical dosimetry analysis

The Python program developed indigenously used for biological evaluations and comparison of treatment plan. The dose-volume text file is exported from TPS is manually imported to the python software program, which calculates dose statistics such as minimum, mean and maximum dose, TCP, NTCP, EUD, effective volume (V_{eff}), CI, and HI and finally uncomplicated tumor control probability (UTCP) as discussed in software development sub title.

The OAR and PTV of the DVH graph are generated from the in-house developed software precisely equivalent to the Eclipse TPS which can be edited with an inbuilt tool such as zoom, pan, forward, backward, save and reset features available in python matplotlib packages are shown in Figure 5. The output from the software is analyzed using the Statistical Packages for the Social Sciences version 20.0 software (SPSS) and Microsoft Soft Excel and graphs is plotted using Matplotlib interactive graphical visualizations in Python like zoom, pan, update

Mean dose

The treatment plans for 25 patients were generated with 3D-CRT, IMRT, and VMAT techniques and physical dose statistics are tabulated in Table 3. The differences in dose values of PTVs and OARs between 3D-CRT, IMRT and VMAT are significant.

It is vivid in Figure 6 that the mean dose of the femur head in IMRT and VMAT is distinguishably different from the 3D-CRT planning and the mean dose of femur head is relatively lesser than other OARs such as bladder, bowel,and rectum, *p*-value of OAR for IMRT and VMAT is greater than 0.05 considered statistically not significant between the planning techniques as shown in Table 4.

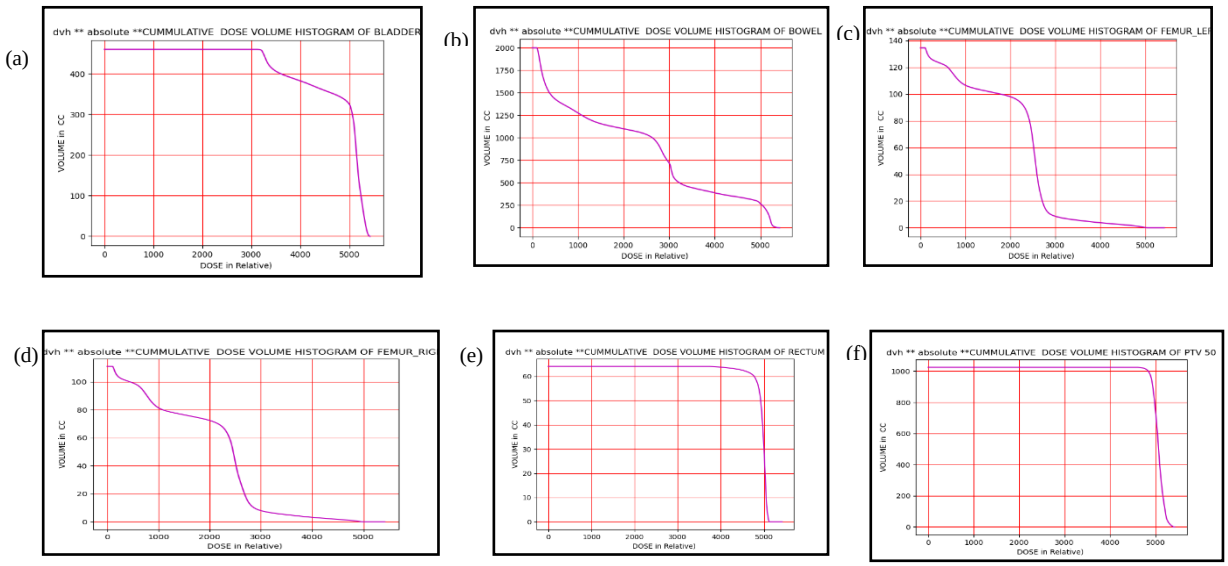


Figure 5. In -house developed biological model evaluation software generated dose volume histogram of organ at risk such as (a) Bladder (b) Bowel; (c) Femur Head left; (d) Femur Head right; (e) Rectum; (f) PTV.

Table 3. Comparison of mean doses of OAR for all three techniques

OAR	3D-CRT		IMRT		VMAT	
	Mean(cGy)	SD	Mean(cGy)	SD	Mean(cGy)	SD
Femur Head	23167.77	12.71	1149.27	11.15	1087.98	11.22
Rectum	4835.70	15.30	4496.56	12.91	4681.05	13.13
Bladder	4807.40	11.92	3972.23	11.76	4116.60	12.91
Bowel	2183.26	12.18	1818.21	12.39	1864.30	10.78

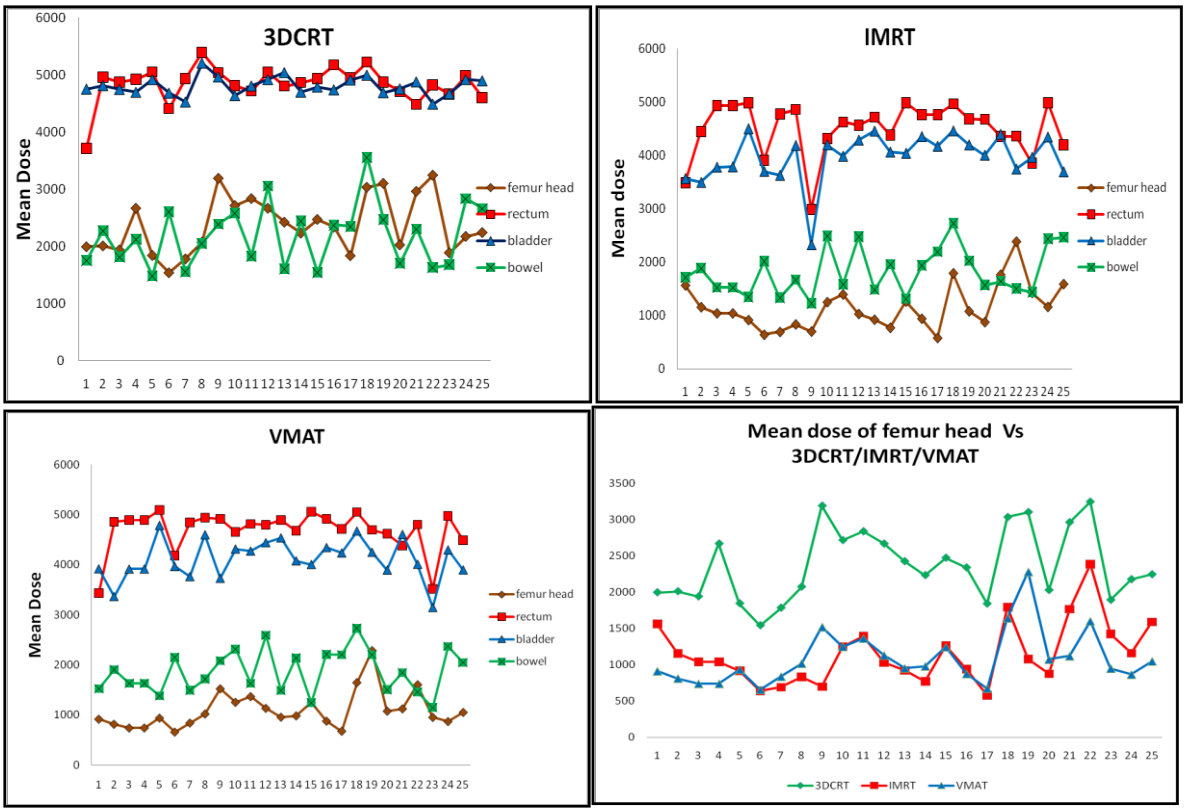


Figure 6. Comparison of the mean dose of OAR for three planning techniques 3D-CRT,IMRT and VMAT

Table 4. Comparison of physical mean dose of OAR with IMRT and VMAT

The organ at risk (OAR)	IMRT(mean dose cGy)	VMAT(mean dose c Gy)	p-value (two-tail)
Femur head	1132.09	1095.29	0.67
Bladder	3989.07	4124.9	0.07
Rectum	4538.85	4733.02	0.02
Bowel	1822.48	1878.44	0.24

Table 5. Comparison of effective volume (V_{eff}) of OAR for all three techniques

OAR	3D-CRT	IMRT	VMAT
	Mean effective Volume(cc)	Mean effective Volume(cc)	Mean effective Volume(cc)
Femur Head	1.78	0.42	0.63
Rectum	4.20	3.64	3.65
Bladder	64.8	48.78	49.25
Bowel	42.80	28.80	26.61

Table 6. Comparison of Effective Volume (Veff) of OAR with IMRT and VMAT

The organ at risk (OAR)	IMRT(mean effective volume cc)	VMAT(mean effective volume cc)	p-value (two-tail)
Femur head	0.43	0.36	0.23
Bladder	50.43	50.92	0.57
Rectum	3.65	3.7	0.86
Bowel	29.67	27.41	0.04

Table 7. Comparison between HI and CI of OAR for all three planning techniques

PTV	3D-CRT		IMRT		VMAT		*p*-value
	Index	SD	Index	SD	Index	SD	
Homogeneity	0.90	0.005	0.97	0.004	0.96	0.005	1.2E-10
Conformity	0.96	0.007	0.98	0.005	0.99	0.006	0.002678

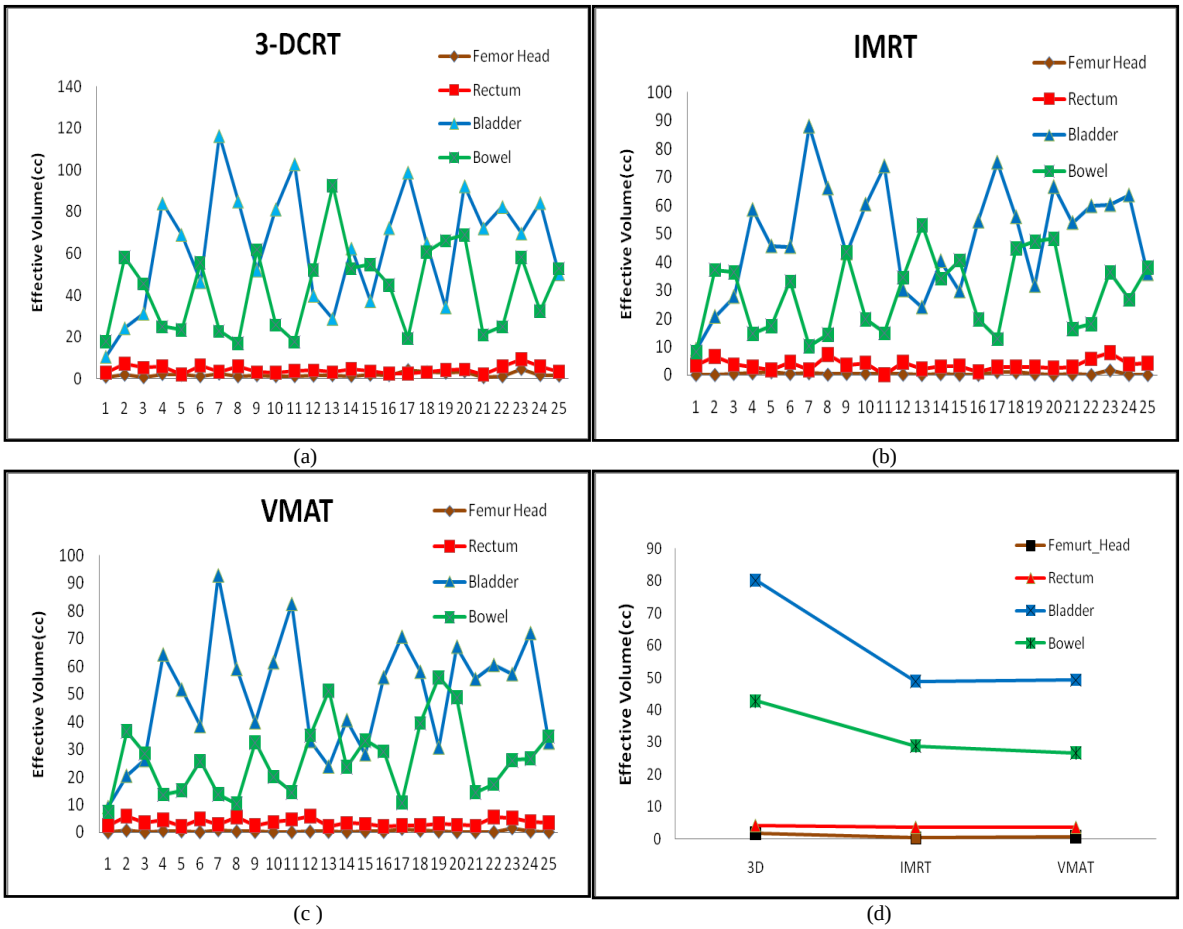


Figure 7. Comparison of effective volume (v_{eff}) with (a)3D-CRT; (b) IMRT; (c) VMAT; (d) OARs with 3D-CRT/IMRT/VMAT

Effective volume

The effective volume of organ at risk was calculated from the Lyman volume reduction algorithm for a homogeneously irradiated normal tissue by Kutcher and Burman (1989) called the LKB model. The effective volume V_{eff} was calculated for three different planning techniques from equation (7) and the data were tabulated for their mean as shown in Table 5.

It is establish that the effective volume of IMRT and VMAT are significantly same and comparatively less than 3D-CRT techniques, the p-value of OAR for IMRT and VMAT is greater than 0.05 shows there is no statistically significant difference between the planning techniques as tabulated in Table 6. The effective volumes of the femur head are comparatively lower than the other OARs such as the bladder, rectum and bowel in all three planning techniques such as 3D-CRT, IMRT and VMAT, as shown in Figure 7 (a, b & c). The mean effective volumes of the OARs versus all three planning techniques are shown in Figure 7d. The more the high-end planning techniques, the less effective volume involved with the normal tissue, which contributes to the complication probability.

Physical Index

Equation (2) provides the relationship that is used to calculate the conformity index (CI) between the target (TV) and the reference dose volume (VRI). The best confirmation is indicated if the CI equals 1. When the conformity index (CI) is higher than 1, it indicates that there are health concerns and that the irradiation volume exceeds the target volume. The target volume is partially irradiated if the CI is less than 1. The ranges of CI values have been established in accordance with RTOG guidelines to assess the quality of conformation. A minor breach occurs when an index falls between 0.9 and 1, or between 2 and 2.5, but if the CI is between 1 and 2, the treatment is following the plan and protocol violation is deemed serious if the index value is less than 0.9 or more than 2.5.

The HI takes into the homogeneity of the dose distribution within the target. There are many formulas, the following given in the equation (1), where D_5 and D_{95} represent the dose to 5% and 95 % volume for the PTV respectively. The HI of VMAT and IMRT planning techniques is significantly better same in than 3D-CRT and CI has no significant difference between the three planning techniques as shown in Figure 8 (box plots A and B, scattered plots C and D).

The CI and HI between IMRT and VMAT are shown in the Table 7 and the two-tailed *p*-value for CI and HI ($p < 0.05$) are statistically significant between the both planning techniques.

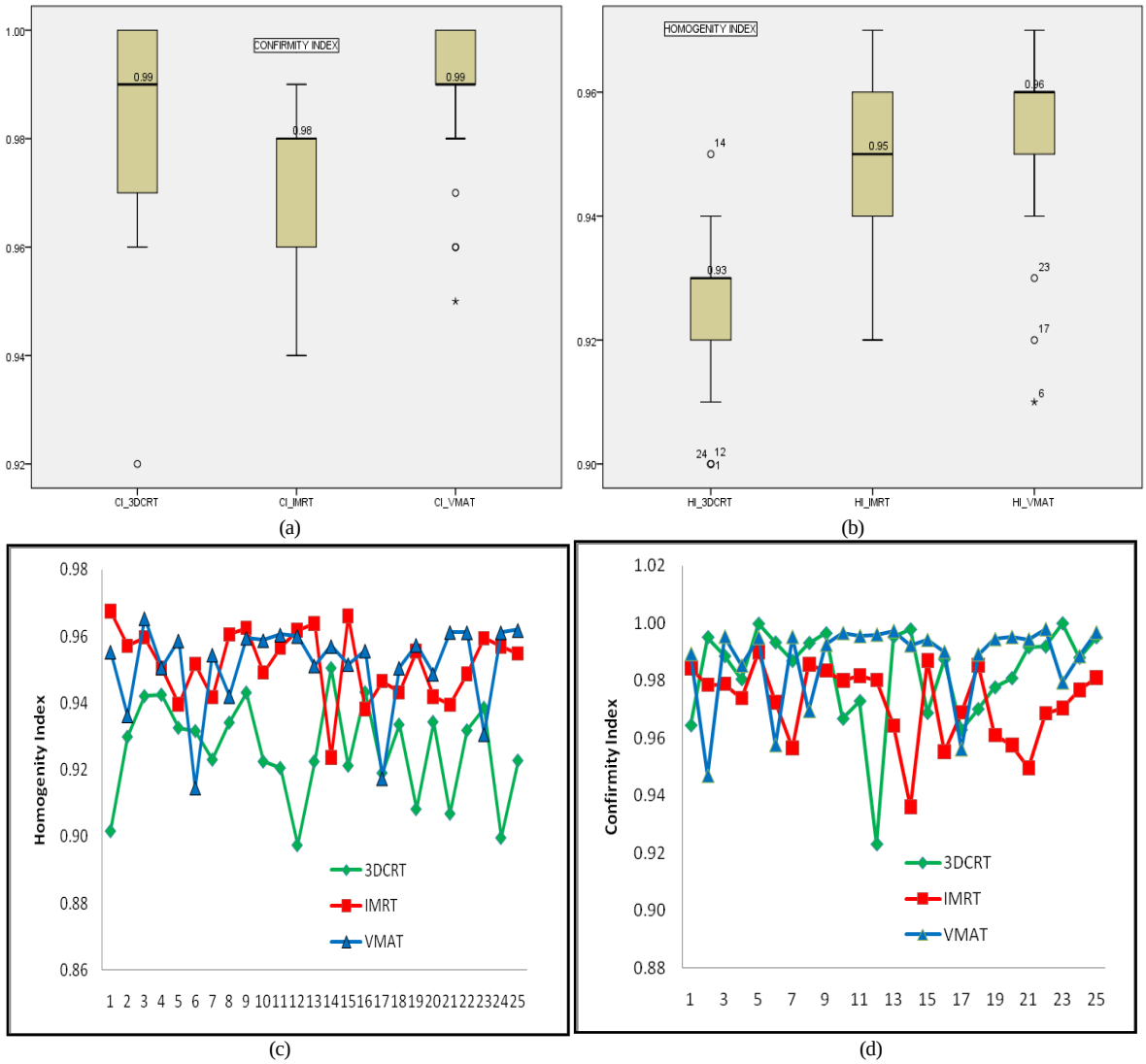


Figure 8. (a) Homogeneity Index- box plot; (b) Conformity Index- box plot; (c) Homogeneity Index –scatter plot; (d) Conformity Index – scatter plot.

It is clear that physical indexes are significantly same in all three planning techniques, which also plays major role in ranking of TCP.

Biological Dosimetry analysis

Tumor Control Probability

The tumor control probability (TCP) remains the same in all three planning techniques as shown in Figure 9. It is to establish that there negligible differences in CI and HI between IMRT and VMAT planning techniques, directly concurrent to the TCP. The Niemierko models of TCP remain the same in all three different treatment modality such as 3D-CRT, IMRT, and VMAT for all the patients.

The one-way ANOVA statistical analysis carried out for TCP between the three planning techniques was found (p-value < 0.05) to be statistically significant, and damage to the tumor from all three planning techniques is considerably same as tabulated in Table 8. Since the tumor control probabilities for all three different planning techniques were found statistically significant, closely concurrent with the CI of the target volume.

Normal tissue Complication Probability (NTCP)

The NTCP for all three planning techniques is displayed in Figure 10. It is clear that the NTCP for IMRT and VMAT are significantly same when compared to 3D-CRT. The femur head shows the drastic reduction of NTCP from 3D-CRT to IMRT and VMAT when compared to other normal tissue structures due to the effective volume of normal structure involved in all three planning techniques and is tabulated in Table 9.

The femur head NTCP is comparatively lower than other normal tissues and the complication probability remains the same for IMRT and VMAT planning techniques since the small values of the "n" for the normal tissues or organs means a high dependence of NTCP with volumes.

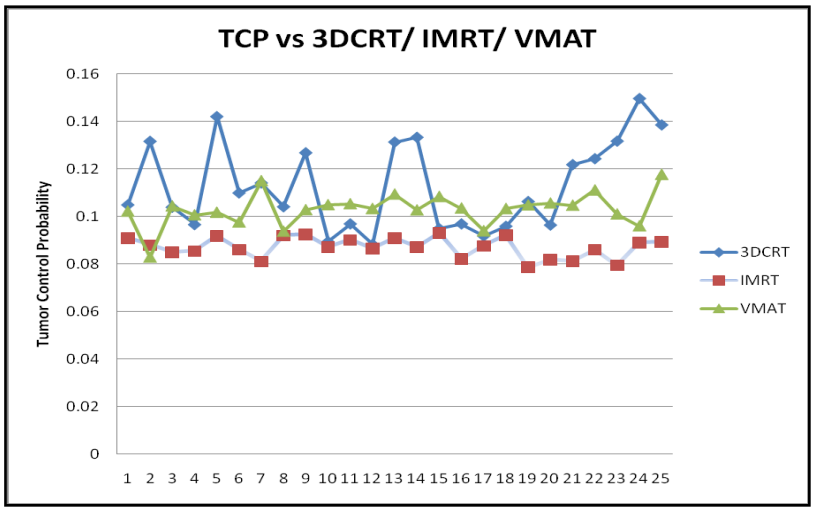


Figure 9. Comparison of Tumor Control Probability for all three planning techniques

Table 8. Comparison of TCP of PTV for all three techniques

	3D-CRT		IMRT		VMAT		*p*-value
	TCP	SD	TCP	SD	TCP	SD	
PTV	*0.10*	0.007	*0.09*	0.001	*0.10*	0.003	1.96E-09

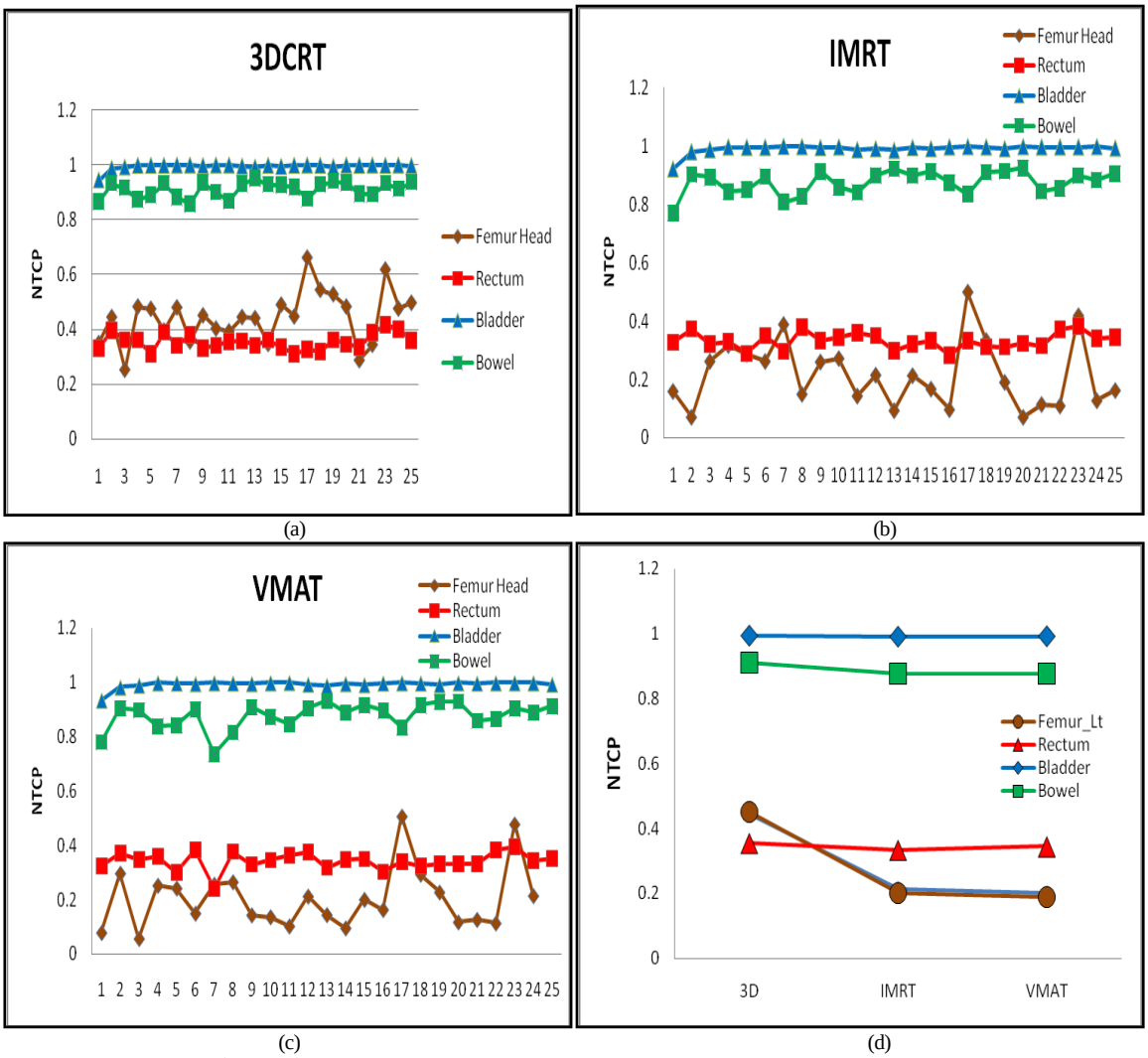


Figure. 10. Comparison of NTCP for all the three planning techniques

Table 9. Comparison of NTCP of OARs for three planning techniques

Patients	Femur Head			Rectum			Bladder			Bowel		
	3D	IMRT	VMAT	3D	IMRT	VMAT	3D	IMRT	VMAT	3D	IMRT	VMAT
1.	0.349	0.131	0.046	0.331	0.327	0.323	0.944	0.923	0.933	0.865	0.77	0.781
2.	0.468	0.082	0.306	0.394	0.373	0.372	0.987	0.981	0.982	0.932	0.903	0.905
3.	0.287	0.256	0.072	0.361	0.32	0.349	0.991	0.988	0.989	0.916	0.893	0.898
4.	0.474	0.317	0.28	0.36	0.328	0.36	0.998	0.997	0.998	0.873	0.844	0.839
5.	0.422	0.287	0.132	0.309	0.288	0.3	0.998	0.996	0.997	0.89	0.851	0.843
6.	0.44	0.303	0.24	0.389	0.349	0.382	0.998	0.996	0.995	0.932	0.896	0.899
7.	0.515	0.311	0.25	0.34	0.296	0.242	0.999	0.999	0.998	0.882	0.809	0.736
8.	0.371	0.14	0.2	0.379	0.378	0.377	0.999	0.998	0.997	0.856	0.828	0.816
9.	0.444	0.259	0.163	0.331	0.331	0.33	0.997	0.995	0.995	0.935	0.912	0.909
10.	0.415	0.302	0.142	0.34	0.344	0.346	0.999	0.997	0.998	0.899	0.859	0.872
11.	0.365	0.091	0.053	0.354	0.359	0.363	0.999	0.988	0.999	0.867	0.842	0.845
12.	0.426	0.174	0.193	0.357	0.349	0.376	0.995	0.991	0.993	0.931	0.9	0.905
13.	0.453	0.114	0.152	0.34	0.297	0.318	0.991	0.986	0.988	0.952	0.923	0.932
14.	0.406	0.222	0.114	0.36	0.32	0.349	0.998	0.995	0.995	0.928	0.899	0.889
15.	0.456	0.133	0.211	0.335	0.333	0.35	0.994	0.991	0.991	0.927	0.912	0.915
16.	0.485	0.159	0.178	0.31	0.281	0.303	0.998	0.997	0.997	0.918	0.875	0.895
17.	0.618	0.396	0.443	0.326	0.332	0.341	0.999	0.998	0.998	0.876	0.836	0.835
18.	0.488	0.188	0.146	0.319	0.311	0.324	0.998	0.997	0.997	0.928	0.911	0.916
19.	0.546	0.203	0.222	0.361	0.31	0.331	0.993	0.991	0.991	0.94	0.915	0.928
20.	0.562	0.031	0.117	0.344	0.323	0.332	0.999	0.998	0.998	0.934	0.925	0.929
21.	0.328	0.164	0.149	0.335	0.314	0.331	0.998	0.997	0.997	0.894	0.846	0.859
22.	0.38	0.109	0.099	0.387	0.37	0.382	0.999	0.997	0.998	0.892	0.856	0.865
23.	0.625	0.439	0.466	0.416	0.383	0.395	0.998	0.997	0.998	0.933	0.899	0.903
24.	0.469	0.098	0.2	0.398	0.34	0.345	0.999	0.998	0.998	0.913	0.884	0.889
25.	0.441	0.099	0.136	0.359	0.343	0.352	0.997	0.993	0.993	0.937	0.905	0.912

Table 10. Comparison of NTCP of OAR with IMRTand VMAT

The organ at risk (OAR)	IMRT (mean NTCP)	VMAT (mean NTCP)	p-value (two-tail)
Femur head	0.20	0.19	0.58
Bladder	0.99	0.99	0.10
Rectum	0.33	0.34	0.0
Bowel	0.88	0.88	0.89

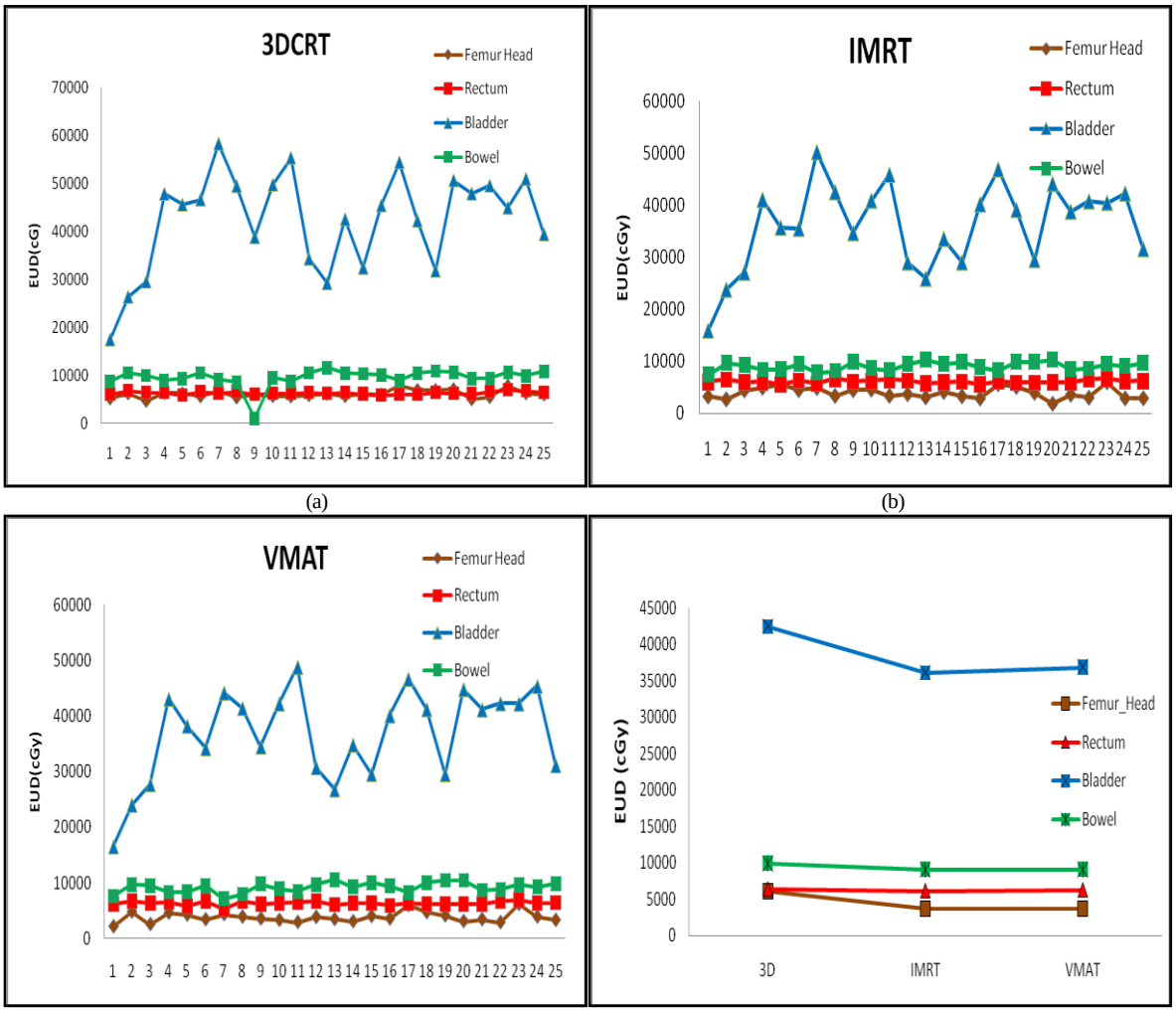
Table 11. Comparison of EUD of normal tissues of OAR and all three planning techniques

OAR	3D-CRT	IMRT	VMAT
	EUD (cGy)	EUD (cGy)	EUD (cGy)
Femur Head	6075.35	3672.15	3696.25
Rectum	6375.40	6151.00	6265.88
Bladder	42441.76	36131.96	36850.28
Bowel	9951.20	9095.16	9164.28

The femur head and rectum responded to lower NTCP than other OARs due to the tissue-specific parameters for the femur head and rectum being 0.25 and 0.12, respectively, and also due to less effective volume involved. When the effective volume decreases, the NTCP decreases and vice versa in all three different planning techniques such as 3D-CRT, IMRT and VMAT. The *p*-value NTCP of OAR for IMRT and VMAT is greater than 0.05; considered there is no statistically significant difference between the planning techniques as shown in Table 10. The "n" values are responsible for the Niemierko NTCP; the values should then be adjusted further to achieve a better fit with the available clinical dose-response data by editing the radiobiological parameter option available in the in-house developed software.

Equivalent Uniform Dose

The EUD for the femur head for IMRT and VMAT are lower as compared to 3D-CRT and within the tolerance limit of TD50, so the normal tissue complication probability of the femur head is comparably less than the other OAR such as bladder and bowel, as shown in Table 11.



(a) (b) (c) (d)

Figure 11. Comparison of EUD for all three planning techniques

Table 12. Comparison of EUD of organ at risk with IMRT and VMAT

Organ at risk (OAR)	TD_{50}(Gy)	IMRT(mean EUD)	VMAT(mean EUD)	p-value (two-tail)
Femur head	65	3900.20	3866.83	0.85
Bladder	80	36976.17	37698.5	0.07
Rectum	80	6153.00	6274.54	0.00
Bowel	55	9164.08	9231.20	0.20

To obtain a better TCP using a biological model, the text file of the dose-volume histogram is converted to EUD using the in-house software. The EUD should be close to the prescription dose and the homogeneity dose distribution on the PTV should be very high. The high EUD may produce a considerable "hotspot" in the target or normal tissue, necessary to constrain the hotspot to the gross tumor volume or clinical target volume to avoid over irradiation to OARThe expression for EUD computed in the present study given by Niemierko given in equation (3), it is observed the EUD of normal tissue are identical in both IMRT and VMAT; reduction of EUD dose is noticed in femur head when compared to other OAR in all three planning techniques as shown in Figure 11. The EUD value calculated from IMRT and VMAT planning techniques is tabulated and compared with dose tolerance (TD50) in Table 12. The p-value of OAR was greater than 0.05, showing no statistically significant difference between the planning techniques. The EUD of the femur head is comparably very much less than the TD50, which may conclude the femur head in all above planning techniques is completely spared, while the EUD of 3D-CRT is 6086 cGy which is close to a TD50 of complication, completely not spared.

Discussion

In pelvic radiotherapy such as cervix cancer the NTCP values for femoral heads, bladder, rectum, and bowel depend significantly on the choice of the radiobiological parameters and have confirmed the

meaningful difference in 3D-CRT, IMRT and VMAT plans. However, the normal tissue complication in IMRT and VMAT planning techniques was found almost the same and there is no statistically significant difference between the two advanced planning techniques. The sparing of OAR is relatively proportional to the effective volume involved in the advanced planning technique such as IMRT and VMAT.

The two-tailed paired t-test was performed (*p*-value>0.05) to determine the statistical significance and found there was no statistically significant difference in the mean NTCP for both IMRT and VMAT. The difference of mean effective volume (veff) of OAR in both planning techniques are statistically non-significant for both IMRT and VMAT, as a two-tailed *t*-test *p*-value greater than 0.05. It is also observed that there was no statistically significant difference in EUD of OAR for both IMRT and VMAT planning techniques.The effective volume is proportional to both mean dose and EUD, acts as both qualitative and quantitative indicator of radiobiological model for the complication of normal tissue homogeneous irradiated. To conclude the sparing of OAR in IMRT and VMAT, has no statistical significant difference between the planning techniques except the femur head, spared significantly (*p- value* < 0.05) in the advanced planning techniques when compared to that of 3D-CRT[28].

The performance evaluation for estimation of Physical and Biological parameters were showing good agreement for all the three techniques for inhouse developed Python based program and Eclipse treatment planning system outcomes. The graphical user interface allows the user to use the DVH in a well friendly manner to swipe the curves and data from one point to other and simultaneously analysing the indexes for different treatment plans.

The in-house developed named RDS (Radiobiological dose evaluation system) was developed by using PYTHON for calculating and evaluating the following radiobiological outcomes from DVH.

a. Physical dose (Minimum, Mean, Max dose) and Volume calculation
b. DVH of OAR and PTV
c. Probability function of NTCP/TCP and UTCP
d. Radiobiological parameter values for OAR and PTV
e. Niemierko model for NTCP/TCP
f. Lyman/LKB for NTCP/TCP
g. LKB effective volume calculation
h. Poison model for TCP
i. EUD calculation
j. Physical plan evaluation from RTOG/Emami/AAPM protocol
k. BED/EQD2 calculation
l. Hot/Cold spot display for the treatment plan
m. Retrieves NTCP/TCP biological parameters from oracle database table
n. Stores the NTCP/TCP to the oracle database table
o. Emami TD_{50}/TCD_{50} protocol on display based on treatment site

The RDS programme provides the aforementioned features in a versatile environment. It is an efficient and affordable DVH analysis module. Another helpful tool, CERR (Washington University, St. Louis), was created more specifically for plan viewing and image analysis than for the computing needs of DVH data analytics. RDS software system was developed as an alternative tool built for customisable DVH data statistics computational functionality due to the computational limits in CERR and other comparable tools, as well as the time-consuming and error-prone procedure of data extraction. RDS only accepts text files and numerous structures in a single DVH file, which is not possible with BIOPLAN, in contrast to SABRE software, which only accepts DICOM as inputs.It helps in managing numerous patient data analyses for research on radiation therapy.

Conclusion

The radiobiological index plays a vital role in the radiotherapy treatment planning optimization, it is uncertain that the established model parameters may influence the treatment outcomes and patient safety, a thorough understanding of models is mandatory before analysing the biological-based treatment plan, it is inevitable to improve models and should obtain more robust clinical related biological parameters, the choice of radiobiological parameter setting could over or under estimate NTCP and TCP.The in-house developed python based program introduces effective volume calculation more precisely for organ at risk in all three planning techniques which effectively improves NTCP and makes a promising evaluation tool for optimal treatment plan selection by the oncologist or physicist in contrast with other existing biological plan evaluation software by supplementary features like option for editing the radiobiological parameters of NTCP and TCP to Oracle database at research level is an another feather in a cap of this indigenously developed software from Python.

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