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A comparative analysis of tumor control and normal tissue complication probability in consequential Radiotherapy plans of Carcinoma cervix using 6 MV X-ray and Cobalt -60 gamma rays

KEYWORDS TCP, NTCP, DVH

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ABSTRACT 20 cases of carcinoma cervix were planned on treatment planning system and optimal plan was obtained with the help of dose volume histogram (DVH) which was further utilized for evaluating the plan radiobiologically. The tumor control probability (TCP) and normal tissue complication probability (NTCP) was calculated with the help of BIOPLAN for the total dosage planned including brachytherapy. NTCP for rectum and bladder was obtained using Lyman-Kutcher-Burman (LKB) and relative seriality model. TCP was evaluated both by BIOPLAN and Brenner's formula. It was found that Gamma photon of Co-60 could also provide equivalent consequential plan comparable to 6 MV x-rays. Since visual inspection of dose distribution in of DVH or on CT slices can only form the basis to select the optimal treatment plan, it is imperative for objective treatment plan evaluation to deduce the outcome in terms of radiobiological parameters.

Introduction

The recent development in Radiobiology, Dosimetry and computational techniques have provided new tool to choose the best possible consequential radiotherapy plans. A clear definition of radiobiological end points may be formulated in terms of Tumor control probability (TCP) and Normal Tissue Complication Probability (NTCP). This study has been performed to evaluate the TCP and NTCP for radiobiological effectiveness in combination of external radiotherapy using high energy X-ray beams or cobalt-60 and Ir-192 gamma radiation for high dose rate (HDR) brachytherapy in Carcinoma cervix. Various workers have published their data (ref) on suitability of TCP and NTCP for obtaining suitable radiobiological plan. However, these studies have many lacunas. This study attempts to obtain a single denominator for selecting the most suitable radiobiologically effective plan amongst the rival plans in radiotherapy of carcinoma cervix and compare it with DVH based plans. The standard protocol as detailed in **ICRU-50[1], ICRU-62[2] and ICRU-83[3]** has been utilized for tumor delineation and definition of dose constraints. The TCP and NTCP have been evaluated using the program proposed by **Sanchez-Nieto** and **Nahum. A [4]** to obtain the best radiotherapy treatment plan.

Material and Methods:

External Beam Radiotherapy

All the patients included in study were subjected to CT simulation and 3mm slices were obtained with appropriate immobilizations. The CT images were transferred to treatment planning system using DICOM 3.0 protocol target volumes such as Gross tumor volume, clinical target volume, planning target volume irradiation volume, and OAR's (rectum and bladder bowel loops . sigmoid colon) were contoured. After contouring the patients data was transferred to treatment planning system which had the beam library of specific LINAC with multileaf collimator (MLC). Various combinations of beam portals depending upon clinical needs were utilized both for cobalt -60 treatment unit and 6MV X ray Linear accelerators.

Brachytherapy

CT supported brachytherapy was performed with due target volume delineations in every sitting. The prescription and planning for Intracavitory application was done according to ICRU-38. The critical organs such as Bladder, Rectum , sigmoid colon and bowel loops were marked as organs at risk. Optimal plans were generated using **Task Group-43[8]** protocol of American Association of Physicists in Medicine (AAPM). The plan having minimal dose to critical structures and isodose shape near to the ideal pears shape was selected for the treatment.

Brachytherapy using Micro-selectron High dose rate (mHDR) with Iridium192 (Half-life 73.8 Days) radioactive source (average energy of 0.36 MeV) was performed in complete accordance with **ICRU 38**[7] recommendations. EQD_2 (Dose equivalent for 2 Gray per fraction dose with external Radiotherapy) was calculated for all patient. This was added to the dose delivered with external Radiotherapy. The calculation of TCP and NTCP was performed assuming this as the total dose.

Radiobiological Evaluation of Treatment plans:

Accurate determination of dose-response relations by available clinical data depends on the accuracy of the derived clinical information. BIOPLAN (Biological evaluation of PLANs) developed by Sanchez-Nieto et al [4] as PC-based friendly software has been utilized in this study. This allows treatment plan evaluation from the (more objective) point of view of the biological response of the irradiated tissues. BIOPLAN provides flexibility in the use of models and parameters. It utilizes Dose Volume Histograms (DVH) and can accept a number of different formats (including DVH files from commercial treatment planning systems). BIOPLAN provides a variety of tools such as Tumor Control Probability (TCP) Normal Tissue Complication Probability (NTCP) calculations (using either the Lyman-Kutcher-Burman or the relative seriality models), Equivalent Uniform Dose (EUD)[5], individualized dose prescription and parametric sensitivity analysis of the TCP/NTCP.

Brenner TCP Model [6] demonstrated dependence of TCP and NTCP on the size of the irradiated volume, the density of clonogenic cells and the dose received, together with the and parameters of the linear-quadratic model of cell kill. According to this model if a volume V of clonogenic tumor cells with uniform density, is irradiated to a uniform dose D the number of clonogenic cells surviving the irradiation can be written as:

$N_s = V\exp\{-(D+GD^2)\}$ where, G is a quantity (1) and depends on the fractionation schemes allowing for incomplete repair, and the half time for sub-lethal damage repair. The predicted TCP is written as:

Volume - 7 | Issue - 3 | March - 2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

$TCP(V,D) = \exp(-N_s)$

For our case the equation derives to

$TCP(V,D) = \exp\{-V \exp(-1.2D)\}$

An excel program has been generated for easy execution of the formulae. The value of constants and are taken as 107 cell/cc and 0.297/ Gy respectively. The TCP calculated with both the modalities i.e. gamma photon of Co-60 and 6 MV X rays of linear accelerator along with the TCP calculated with the theoretical formula of Brenner et al for all sites are tabulated in tables 1 for different organs. The resulting 2 Gy per fraction equivalent DVH is then used as the input DVH in the NTCP Module of BIOPLAN. The same procedures have been repeated for all organs at risk encountered in a course of radiotherapy. The NTCP calculated with both the modalities i.e. gamma photon of Co-60 and 6 MV X rays of linear accelerator are tabulated in table 2.

Table 1

Tumor Control Probability (%)- Ca Cervix			
Gamma Photon of Co-60 and Gamma Photon of Ir-192	**X-Ray photon of Linear Accelerator and Gamma Photon of Ir-192**	**Variation (%) w.r.t. Gamma Photon of Co-60 and Gamma Photon of Ir-192**	**Brenner's formula**
68.3	69.3	1.5	99.2
55.4	71.8	29.6	99.8
36.8	38.7	5.2	100.0
74.4	77.2	3.8	99.9
76.0	86.7	14.1	100.0
24.1	27.0	12.0	99.4
91.7	93.8	2.3	98.8
67.8	79.8	17.7	98.2
75.8	89.2	17.8	97.6
80.0	84.0	5.0	97.0
84.4	86.7	2.8	96.4
88.7	94.5	6.5	95.8
93.0	95.6	2.8	95.2
85.6	81.8	4.5	100.3
96.5	81.5	15.6	100.4
86.7	80.6	7.0	100.4
48.5	89.5	84.5	100.5
90.0	91.1	1.2	100.6
78.3	92.7	18.3	100.6
Average 73.8	**Average 79.5**	**Average 13.3**	**Average 99.0**

Table 2

Normal tissue Complication Probability(%)-Ca Cervix					
Rectum			**Bladder**		
Gamma Photon of Co-60 and Gamma Photon of Ir-192	**X-Ray photon of Linear Accelerator and Gamma Photon of Ir-192**	**Variation (%) w.r.t. Gamma photon of Co-60 and Gamma Photon of Ir-192**	**Gamma Photon of Co-60 and Gamma Photon of Ir-192**	**X-Ray photon of Linear Accelerator and Gamma Photon of Ir-192**	**Variation (%) w.r.t. Gamma photon of Co-60 and Gamma Photon of Ir-192**
20.8	14.1	32.2	0.0	0	0.0
0.0	0.0	0.0	4.3	3.3	23.3
0.0	0.0	0.0	0.0	0.0	0.0
0.6	0.0	100.0	0.0	0.0	0.0
0.7	1.4	106.1	0.0	0.0	0.0
0.8	1.5	94.9	0.0	0.0	0.0
0.3	0.0	100.0	0.0	0.0	0.0
0.4	2.2	464.1	0.0	0.0	0.0
0.5	0.0	100.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.4	0.3	23.3
1.0	1.8	73.3	1.0	1	0.0
0.8	1.6	86.1	0.1	0.1	6.5
0.9	1.7	79.1	0.0	0	0.0
0.0	0.0	0.0	0.0	0.0	0.0
1.1	1.9	68.4	0.1	0.3	117.5
1.2	2.0	64.2	0.0	0.2	0.0
1.3	2.1	60.7	4.0	1.0	75.0
Average 1.6	**Average 1.9**	**Average 16.9**	**Average 0.5**	**Average 0.3**	**Average 38.0**

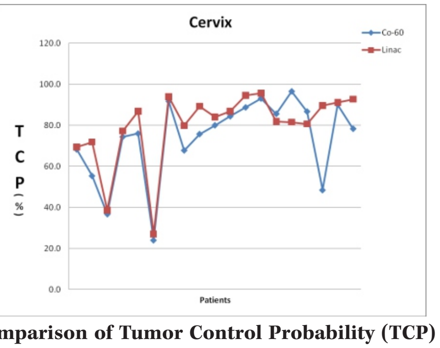

Fig 1: Comparison of Tumor Control Probability (TCP) for Ca Cervix

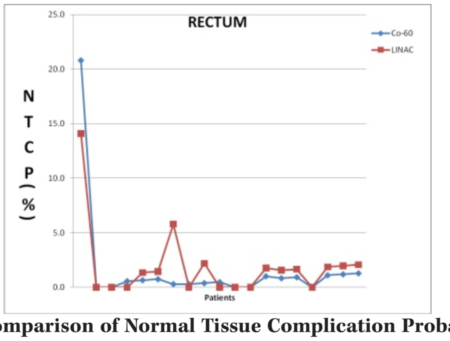

Fig 2: Comparison of Normal Tissue Complication Probability (NTCP) of Rectum

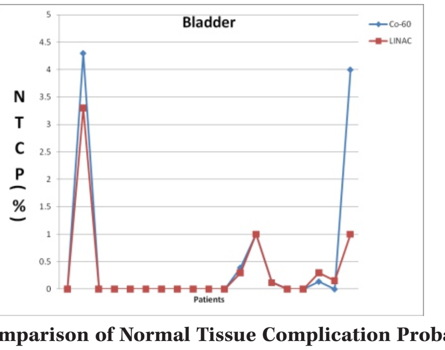

Fig 3: Comparison of Normal Tissue Complication Probability (NTCP) of Bladder

Results:

The minimum and maximum tumor control probability (TCP) for gamma photon of Co-60 is 24.1% and 96.5 % respectively and the corresponding values calculated with Brenner's formula are 99.4% and 100.4% **(table 1 and figure 1)**. The TCP for 6 MV X rays of linear accelerator, the minimum and maximum TCP is 27.0% and 95.6 % respectively and corresponding values calculated with Brenner's formula are 99.4 and 95.2%. The average TCP for gamma photon of Co-60, X rays of Linac and that calculated by Brenner's formula is 73.8%, 79.5% and 99.0% respectively. From **Table 2** and its graphical representation in **figure 2 and figure 3,** it is found that the minimum and maximum Normal Tissue complication Probability for rectum with gamma photon of Co-60 is 0.0 and 20.8% respectively. The minimum and maximum NTCP with LINAC is 0.0 and 14.1 %

Volume - 7 | Issue - 3 | March - 2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

respectively. For Bladder the minimum and maximum NTCP with gamma photon Co-60 is found to be 0.0% and 4.3% respectively. The minimum and maximum values with LINAC are 0.0 and 3.3 % respectively. The average NTCP for Rectum with gamma photon of Co-60 and X-ray photon of Linac is 1.6 and 1.9% respectively. The average NTCP for Bladder with gamma photon of Co-60 and X-ray photon of Linac is 0.5 and 0.3% respectively.

Conclusion:

The results analyzed for the cases of Carcinoma cervix, shows that the patient treated with Co-60 and LINAC have an average TCP of 73.8% and 79.5% respectively when BIOPLAN is utilized for calculating TCP. The average NTCP for Rectum with gamma photon of Co-60 and X-ray photon of Linac is 1.6 and 1.9% respectively. The average NTCP for Bladder with gamma photon of Co-60 and X-ray photon of Linac is 0.5 and 0.3% respectively. Hence there is 0.3 % more chance of rectum complication with Linac whereas the complication for bladder reduces by 0.2 %. it can be concluded that Gamma photon of Co-60 can also provide a tumor cure comparable to high energy Linacs, if treatment plan evaluation is measured in terms of radiobiological parameters. TCP and NTCP has emerged better indicators than physical parameters such as Dose Volume Histogram (DVH) etc. This study advocate the quantification of treatment outcome in terms of radiobiological parameters TCP and NTCP because the visual inspection of radiation dose distribution either in terms of DVH or on CT slices can only form the basis to select the optimal treatment plan has its own limitations.

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