

Using the Computed Tomography in Comparison to the Orthogonal Radiography Based Treatment Planning in High dose Rate (HDR) Brachytherapy in Cervical Uteri Cancer Patients; A Single Institution Feasibility Study

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ABSTRACT

Introduction: Brachytherapy is an integral part in the treatment of cervical uteri cancer patients. Orthogonal treatment planning is the standard mode of calculation based on reference points. Introduction of the innovative 3-D computer based treatment planning allows accurate calculation based on volumetric information as regards the target volume and organs at risk (OAR). Also provide dose volume histogram (DVH) for proper estimation of the dose in relation to the volume.

Aim: To correlate and compare the information obtained from the two approaches for high dose rate brachytherapy of cervical uteri cancer; the orthogonal conventional method and the computerized tomography (CT) three dimensions (3D) based calculation method in relation to the target and organ at risk (OAR).

Methods: From 6 patients of cervical uteri cancer, 21 applications with orthogonal planning using the Brachy Vision treatment planning system version 7.3.10 were performed. In 10 applications; comparison between orthogonal and CT based planning was done. In orthogonal planning; the dose to point A, rectum and bladder were defined according to the American Brachytherapy Society (ABS) recommendation. From the CT based planning the target volume and dose volume histogram (DVH) were calculated for the clinical target volume (CTV), rectum and bladder. From these two sets, information was obtained and compared and mean values were derived.

Results: For dose prescription at point A, an average of 63.5% of CTV received the prescribed dose. The mean ICRU dose to the bladder point is 2.9 Gy \pm 1.2 SD (Standard Deviation) and 17% of the bladder volume derived from CT was encompassed by 2.9 Gy isodose line. The mean ICRU dose at the rectum point is 3.4 Gy \pm 1.2 SD and 21%

of the rectum volume from CT was encompassed by 3.4 Gy isodose line. The maximum dose to the rectum and the bladder derived from the CT and compared to the maximal dose at ICRU is 1.7 and 2.8 times higher than the orthogonal reference points; with the corresponding *p* value of (*p*=0.53 and *p*=0.005) for the rectum and the bladder respectively.

Conclusions: CT based treatment planning for HDR brachytherapy of cervical uteri cancer is reliable and more accurate in definition and calculation of the dose to the target as well as the critical organs. It allows dose calculation based on the actual volume rather than points or bony landmarks.

Key Words: Cervical uteri cancer – Brachytherapy – CT based planning HDR – 3-D treatment planning.

INTRODUCTION

The curative potential of radiation therapy in the management of cervical uteri cancer is greatly enhanced by the use of brachytherapy [1-4]. Success of brachytherapy requires delivery of a high radiation dose directly to the tumor while sparing, to some degree, the surrounding normal tissues.

Cervical uteri cancer has traditionally been treated with low-dose rate (LDR) brachytherapy. High dose rate brachytherapy (HDR) was developed to overcome the potential disadvantage of LDR; including radiation exposure to medical staff, prolonged treatment time, mandatory hospitalization and applicator movement [5-7]. The primary disadvantage of HDR is the potential late toxicity of large dose per fraction; as with external beam radiation therapy (EBRT), which also delivered at high dose rates.

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These radiobiological disadvantages can be overcome through adequate fractionation and better delineation of organs at risk. Additionally, in HDR brachytherapy complications might be minimized more effectively than in LDR, because of low possibility of normal tissue displacement (the bladder anteriorly and the rectum posteriorly in short treatment time and with the use of retraction devices in some applications [8,9].

Several studies (including randomized, non randomized, prospective trials, with a survey of published data and meta analysis) have compared LDR with HDR brachytherapy in the management of cervical cancer. In summary, both modalities have comparable local control, survival, and morbidity [10-22]. Some even showed lower rectal morbidity with the use of HDR [14,17,18].

Modern approach in the treatment planning of cervical uteri cancer is based on series of transverse computed tomography (CT) sections and on three dimensional (3-D) dose computations. This allows evaluating dose distributions in different volumes as regards the gross tumor volume (GTV), clinical target volume (CTV) and organs at risk.

When these techniques are not available, dose calculation was based on orthogonal radiographs which provide the position of the applicator relative to bony structures, this allow dose calculation at defined fixed points; point A and B representatives to the tumor and pelvic side wall respectively and other reference points considered representative for the organs at risk (bladder and rectum) [23].

In order to correlate information obtained with these two approaches, we compared the two treatment planning methods (radiographs and CT planning methods) in a feasibility study including 6 patients, with 21 applications, for whom 10 applications were compared.

MATERIAL AND METHODS

Between December 2004 and May 2005, 21 applications of HDR remote afterloading using Ir¹⁹² were done for 6 patients of cervical uteri cancer following external beam radiotherapy (EBRT) at Radiation Oncology unit of King Abdul Aziz University Hospital (KAUH); Jeddah; Kingdom of Saudi Arabia; with individualized treatment dose and schedules. For these, CT was

done in 10 applications. Patients were treated based on the orthogonal calculation, and another calculation was performed based on the CT information, and both methods data were compared.

Patient selection:

This feasibility study included 6 patients; 4 were stage IIB, one stage IB, and one stage IIIA. Four patients had squamous cell carcinoma, one patient with adenocarcinoma, and one patient reported as poorly differentiated carcinoma.

All patients undergone examination under anesthesia (EUA) with cystoscopy and proctoscopy and CT or MRI of the abdomen and pelvis before the start of EBRT. EUA was repeated in selected patients before brachytherapy. CT or MRI was repeated before brachytherapy to assess the response and to help for insertion of the applicator.

Treatment scheme:

Treatment consists of combination of external beam therapy and high dose rate (HDR) brachytherapy; External beam therapy was delivered at a dose of 45 Gy with daily dose of 1.8 Gy over 5 weeks, 5 fractions/week, using a linear accelerator of 18 MV, applying the four fields "Box technique" with no midline shielding. Three patients received concomitant chemotherapy with EBRT in the form of weekly Cisplatin 40 mg/m².

All patients received brachytherapy after the end of the EBRT. HDR brachytherapy with Ir¹⁹² source was performed in 3-4 fractions, one fraction per week, depending on the department load and the anesthesia schedule; using dose range between 6-7 Gy per fraction for most of the patients.

External beam radiotherapy (EBRT) technique:

All of the patients received pelvic irradiation, with 4 fields (Box technique); Anterior-Posterior (AP), Posterior-Anterior (PA), and 2 lateral fields.

The upper border of the AP and the PA field was at the interspaces of lumbar vertebrae 4-5; with the lower border 3 cm below the gross tumor, usually at the level of the obturator foramen. The lateral borders were 1.5 cm from the lateral pelvic brim. For the lateral fields, the upper and lower borders were the same as the AP, PA fields, while the anterior border was at the tip of the symphysis pubis and the poste-

rior border is 2 cm behind the posterior extension of the tumor.

Brachytherapy technique:

Fractionated afterloading HDR brachytherapy was performed, using the Fletcher Suit Delclos applicator (FSD) or Henschke applicator, as soon as finishing the EBRT using the uterine tandem of 20 to 50 mm length with 2 medium or large sized ovoids according to the anatomical variations.

Packing was done anterior and posterior to the applicator to displace the bladder and the rectum. Foleys' catheter was inserted into the bladder and the balloon was inflated with diluted 7 cc of iodinated contrast, and pulled downwards so that it lies at the trigone (neck) of the bladder. Rectal catheter for insertion of diluted barium into the rectum with rectal marker also was inserted.

Two orthogonal films; one anterior-posterior (Fig. 2) and one lateral (Fig. 3) were taken for determination of the prescribing, bladder and rectum points. The dose was prescribed to point A (point H) using the American Brachytherapy Society (ABS) recommendation for HDR for cervical uteri cancer (Fig. 1) [24].

The standard locations for specifying rectal and bladder doses followed the International Commission for Radiation Units (ICRU) in report 38 [23]. In this report; the bladder point in the anterior film lies in the center of the catheter balloon, while in the lateral film it lies on the most posterior surface of the balloon. The point selected corresponds to the maximum dose on the surface of this balloon; this point may not be the posterior aspect of the bladder as it may be situated either to one side or significantly superior or inferior to the vaginal applicator.

The rectal point is defined on the lateral film as 0.5 cm posterior to the posterior vaginal wall, or the nearest rectal point to the vaginal ovoids and this point is reflected in the anterior film guided by the rectal marker. Alternatively, the anterior rectal wall may be visualized by injecting a diluted solution of contrast (50% barium: 50% saline) with some air contrast in the rectum.

The patients were treated based on the orthogonal film calculation. Starting with digitization of films using the Vedar system, the position of the applicator (the tandem and

ovoids), rectal and bladder reference points as well as A and B points were digitized in the anterior-posterior film and verified in the lateral films; to ensure the same position in relation to the anatomy of the patients. Computerized planning was then done with determination of the dwell time and position of the source using the Brachy Vision V 7.3.10 planning system, with source strength (activity) ranged from 4.4 to 6.8 Ci (mean value of 5.7 Ci). Normalization of the dose was done to point A and the relative dose to the bladder and rectum reference points and point B were then calculated.

CT based planning brachytherapy technique:

At the time of calculation for orthogonal films, CT scanning was done for the patients (10 out of 21 applications) with 0.25-0.5 cm interspaces. Data from CT were read into the planning system via a line connection. The 3-D data set and the dose grid of the position of the applicator is identified; using the same dwell position of the source used in the orthogonal film.

Point A was identified to be more accurately close to point A in the orthogonal film. In the CT images; the CTV, bladder and rectum were contoured; delineation of the GTV was performed based on the CT information at the time of the brachytherapy and supported by the clinical findings. The macroscopic tumor was delineated as appropriate as possible.

We added safety margin (usually one cm in the 3 dimensions) to create the CTV. Additional margin was added to CTV to create the PTV. In principal, the cervix, which could be defined on the CT, was included. If the parametrium structures had also to be included, the depth and the width of infiltration were estimated. If the images showed a normal configuration of the corpus uteri only the central part of the corpus was enclosed, and if there was an involvement of the fornices or proximal vagina, these were included.

Delineation of rectum and bladder was done along the outer contour. The rectum was contoured from about 2 cm below the lowest point of the ovoids up to the recto-sigmoid junction. The whole bladder was contoured. Anatomical dose volume histogram was calculated for the CTV, bladder and rectum. These data were compared with data derived from the orthogonal films (Figs. 6,7,8).

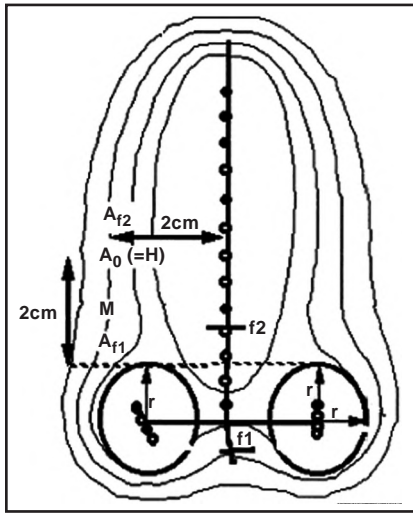


Fig. (1): An illustration relevant for intracavitary dosimetry for a tandem and ovoids application.

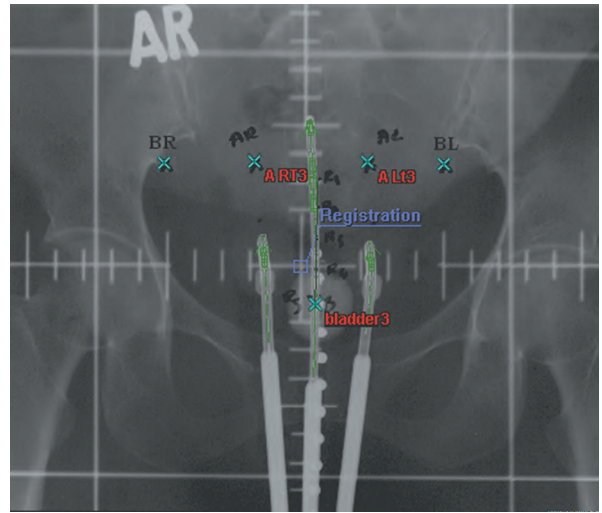


Fig. (2): Antero-posterior (AP) orthogonal film.

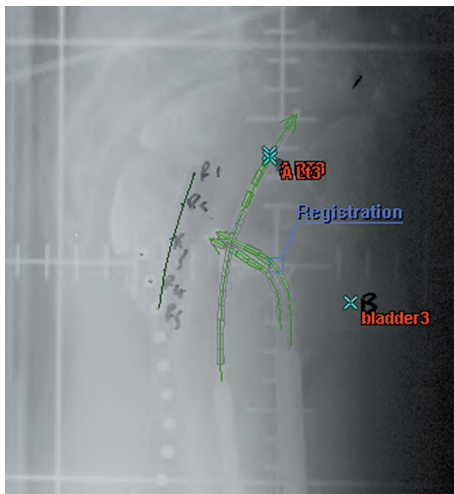


Fig. (3): Lateral orthogonal film.

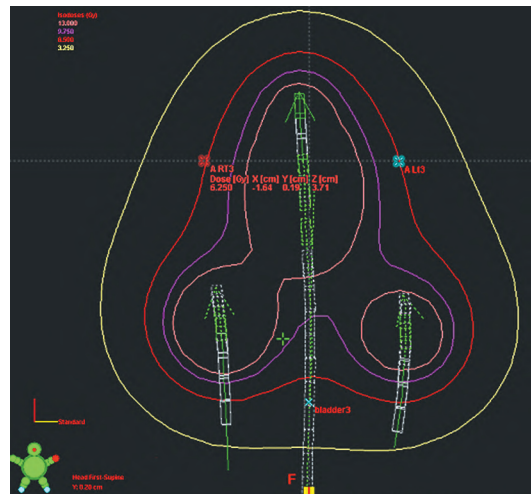


Fig. (4): Isodose distribution on AP view.

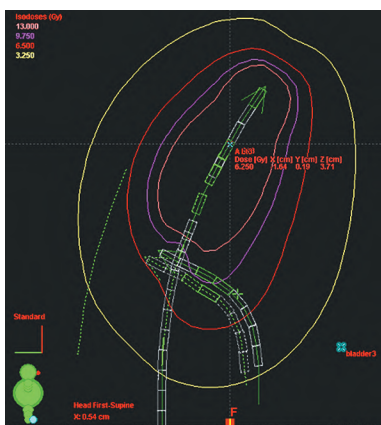


Fig. (5): Isodose distribution on lateral view.

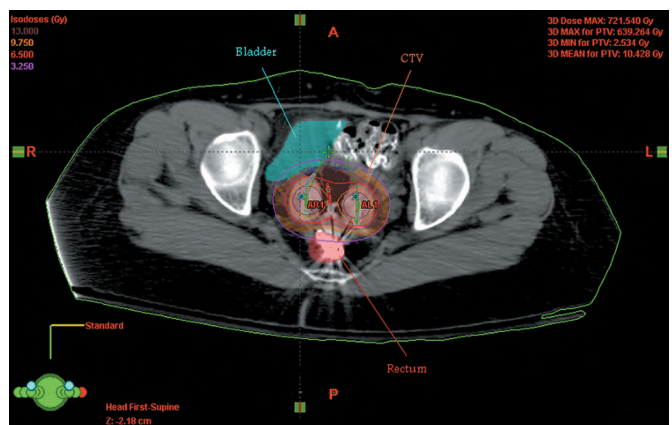


Fig. (6): Transverse CT cut showing target volume, bladder, rectum and isodose distribution.

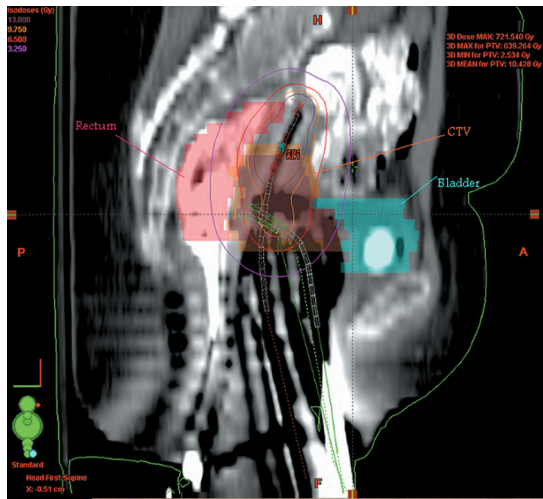


Fig. (7): Longitudinal CT cut showing target volume, bladder, rectum and isodose distribution.

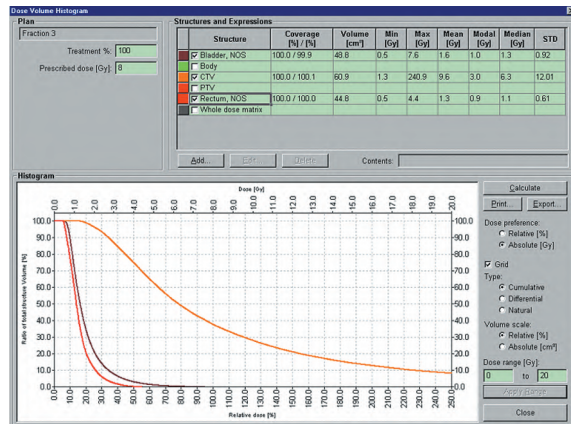


Fig. (8): Dose Volume Histogram (DVH) for target volume, bladder and rectum.

Statistical methods:

We used the SPSS software computer program to calculate the mean \pm standard deviation (SD) for the calculated parameters. Wilcoxon Signed Ranks Test was used to compare the maximum orthogonal dose versus CT based dose to the rectum and the bladder with p -value ≤ 0.05 is considered significant.

RESULTS

Radiography based treatment planning:

The mean dose to point A was $6.6\text{Gy} \pm 0.6$ SD; ranged between 6 to 8 Gy, the dose to point B ranged between 20 to 25% of the dose to point A. The mean dose to bladder and rectum points according to the ICRU definition were $2.9\text{Gy} \pm 1.2$ SD and $3.4\text{Gy} \pm 1.2$ SD respectively

with a range of 1.2-4.3 Gy for the bladder, and 1.5-5.7 Gy for the rectum.

CT based treatment planning:

The mean absolute volume of CTV for the 10 applications was $85\text{cm}^3 \pm 22.2$ SD (ranged from 60.9 to 132 cm^3). The mean percentage volume was $63.5\% \pm 15.1$ (ranged from 38 to 84%) that received the prescribed dose to point A; in another words 63.5% of the CTV received the prescribed dose to point A.

The mean dose to bladder point from the orthogonal film, which was $2.9\text{Gy} \pm 1.2$ SD, corresponded to the 21% of bladder volume in CT (mean volume is $20\text{cc} \pm 12.7$; with range between 4.7-42 cc; correlate to $67\text{cm}^3 \pm 34$; range between 26-139 cm^3). While the mean dose to the rectum point in orthogonal film ($3.4\text{Gy} \pm 1.2$) was corresponded to 17% of the volume of the rectum in CT (with a mean of 17 ± 17 cc; range between 3-58 cc and correlate to $59\text{cm}^3 \pm 31$ range between 26.5-108 cm^3) (Table 2).

From the above data it is estimated that; the 3.4 and 2.9 Gy isodose lines from orthogonal calculation corresponded to the 17% and 21% of rectum and bladder volume in CT; respectively.

By comparing the maximum dose to bladder and rectum derived from ICRU which is $3.4\text{Gy} \pm 1.3$ for the bladder and $4.3\text{Gy} \pm 2.4$ for the rectum, with that of the CT based calculation: $9.5\text{Gy} \pm 6.1$ and $7.3\text{Gy} \pm 3.8$ for the bladder and rectum; respectively; the ratio is 2.8 and 1.7 times higher than orthogonal reference points for the bladder and rectum, respectively, the difference was significant for the bladder with p : 0.005 while border line significant for the rectum with p : 0.053 for rectum (Table 3).

The relation between percentage of the CT volume (25, 50, 75, 100%) of the CTV, rectum and bladder with the mean dose in Gy prescribed to point A and corresponding percentage of that dose to these volumes revealed that: with the mean prescribed dose to point A which is $6.6\text{Gy} \pm 0.6$, an average of about 25-30% of the CTV not received this dose. While about 25% of the rectal and bladder volume received 40% of the dose to point A, and 13-15% of the volume of the rectum and the bladder received 100% of the dose to point A (Table 4).

Table (1): Volume and percentage of CTV received the prescribed dose (PD) to point A.

Patient no. & dose (Gy)	Mean absolute volume of CTV (cm ³)	Mean percentage volume of CTV (%) which received the PD
1 (7Gy)	81.3	55
2 (6Gy)	68.7	75
3 (6.5Gy)	104.4	63
4 (7Gy)	103.25	63
5 (8Gy)	66.9	50
6 (6Gy)	81.9	75
Mean±SD	85±22.2	63.5±15.1

Table (2): The mean dose to the ICRU rectum and bladder points from orthogonal planning and its correlation to their CT volume.

Patient no. & dose (Gy)	Mean bladder dose (Gy)	Bladder CT volume (cc)	Mean rectal dose (Gy)	Rectum CT volume (cc)
1 (7Gy)	1.2	26.81	3.6	4.9
2 (6Gy)	4.2	6.61	1.7	38.2
3 (6.5Gy)	2.4	58.12	3.8	22.6
4 (7Gy)	3.6	3.5	4	3.4
5 (8Gy)	2.9	17.11	2.5	5.7
6 (6Gy)	2.8	38.6	4.8	17
Mean±SD	2.9±1.2	20±12.7	3.4±1.2	17±17

Table (3): The max. dose to the bladder and rectum (CT) and its correlation with ICRU.

Patient no. & dose (Gy)	CT bladder max dose (Gy)	Orth. max. dose (Gy)	CT rectum max dose (Gy)	Orth. max. dose (Gy)
1 (7Gy)	3.5	1.1	6.9	6.5
2 (6Gy)	16	4.2	5	2.1
3 (6.5Gy)	11	2.3	11	5.31
4 (7Gy)	5.3	4.3	5.3	3.83
5 (8Gy)	10.1	3.2	3.1	4.31
6 (6Gy)	7.8	5.7	11.1	3.6
Mean±SD	9.5±6.1	3.4±1.3	7.3±3.8	4.27±2.4
Ratio	2.8		1.7	
p value	0.005		0.053	

Table (4): Relation of CTV, rectum and bladder CT volume and the mean dose (Gy) with its standard deviation (SD), with corresponding percentage of this dose in relation to point A mean prescribed dose.

CT volume	Mean dose in Gy and its standard deviation (% of the mean prescribed dose to point A)		
	CTV	Rectum	Bladder
25%	12.3±2.3 (186)	2.6±0.74 (39)	2.7±0.93 (40)
50%	8±1.2 (121)	2±0.54 (30)	2.04±0.76 (28)
75%	5.6±0.88 (85)	1.5±0.44 (23)	1.6±0.63 (24)
100%	2±0.55 (30)	0.86±0.35 (13)	1±0.44 (15)

DISCUSSION

With radiography, the calculation of dose distribution is based on visualization of the applicator relative to bony structures. Reference volume, doses at point A and B and doses to other points like the ICRU 38 reference points can be derived [24]. This method does not allow the evaluation as to what extent the treated volume encompasses the CTV. In contrast, CT-based planning allows the delineation in each slice, the CTV and organs at risk and from these; the dose-volume relations can be calculated [25]. Modern treatment planning in brachytherapy allows combining (a) dose-volume histogram calculation based on CT sections (b) point dose calculation based on orthogonal radiography [26,27].

In this study, data from both methods were compared and correlated. In addition, we attempted to apply the concept of CTV definition, as recommended in ICRU 50 report for external beam therapy to the brachytherapy treatment [28].

The ICRU 38 [24] was developed for dose and volume specification and for reporting intracavitary therapy in gynecological malignancies. Volumes like targets, treatment, references and irradiated volume were already defined. The use of ICRU 38 in clinical practice is part of a common quality assurance program and contributes teaching consensus between different centers [29]. ICRU reference points are used in only a few groups who calculated and reported the dose to these points [30,31,32].

Our data showed that the ICRU reference point dose to the bladder and rectum were 2.9 Gy±1.2 SD and 3.4 Gy±1.2 SD; respectively. This dose corresponds to 21% (20cc) and 17% (17cc) of the bladder and rectum volume calculated from CT. This was less than that reported by Fellner et al. [25] in a similar study using HDR with corresponding mean dose to the rectum and bladder at the ICRU reference point of 4.3 and 5.8 Gy; respectively; with related volume of the rectum and bladder that received this dose were 12% (9cc) and 8% (16cc); respectively. Other investigators using LDR reported similar data [30-31]. About 50% of the rectal and bladder volume in our study received dose below the corresponding doses calculated at the ICRU point from the orthogonal film.

This agreed with the data reported by others [25,33,34].

The maximum dose to the organs at risk was calculated from dose volume histograms. Based on 3D calculations, the maximum dose compared to the ICRU point was found to be 2.8 and 1.7 times higher than the orthogonal reference points for the bladder and rectum respectively; (p : 0.005 and p : 0.053). The results reported by Fellner et al. [25], showed that the maximum dose to the rectum is 1.5 times higher than ICRU reference point while the maximum dose to the bladder is 1.4 times higher than its corresponding ICRU point calculation.

Deshpande et al. [35] investigated points other than the ICRU rectum reference points to estimate the maximum dose in 182 application. It was concluded that several points along the rectal wall should be considered. Hunter et al. [36] found that the ratio of maximum bladder dose (calculated from CT images) to the ICRU reference dose (calculated with radiographs) varied from 1.01 to 3.59 times. Barillot et al. [37] found that the maximum dose in bladder (calculated from ultrasonography) were on average 2.7 times higher than dose at ICRU reference points (calculated with radiographs). Schoeppel et al. [34] found a ratio on average of 2.3 for the bladder and 1.3 for the rectum, which is more or less fit to our results.

According to the literature, it is evident that the ICRU reference points [23] underestimate dose in the maximum dose in the rectum and bladder. However, the published data vary within a broad range. These differences could be due to the fact that several methods (radiography, ultrasound, CT) were used and that the individual patient's anatomy varies significantly. In our study a complete 3-D assessment of organs was included whereas most of the publications deal with points. The present study demonstrates that for dose estimation; the 3-D assessment of the organ should be considered, not only points.

The mean dose calculated at point A is 6.6 Gy \pm 0.6 SD with about 63.5% of the CTV volume derived from CT covered by this isodose line. This means that using the ICRU reference point (Point A) for calculation may under dose the target volume. Similar data reported by Fellner et al. [25] with an average 83% of the CT derived CTV covered by the prescribed isodose line.

Conclusion:

The aim of this study was to evaluate and correlate two different methods of calculations, the point dose based on orthogonal radiographs and the volume methods based on sectional images. For valid and reliable dose estimation in CTV and in organs at risk, a 3-D imaging based treatment planning seems to be superior compared to treatment planning based on points in radiographs; special attention was paid to organs at risk (rectum and bladder) [23] and the encompassed volumes by these doses were calculated in order to translate accepted reference points into volumes. Also the maximum doses in these organs were calculated. It is obvious that 3-D imaging based treatment planning is more comprehensive and more adequate for volume assessment of critical organs. As the dose to the OAR is significantly higher with volume calculation based on CT imaging relative to ICRU points. This makes its use, as substitute to the orthogonal film calculation, more logic. Also, in further studies these dose volume relations have to be correlated with data of clinical outcome, side effects and tumor control.

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