Iran. J. Radiat. Res., 2009; 6 (4): 189-194

"Maximum dose" points in cervical and endometrial cancer medium dose rate brachytherapy

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Background: Best dose distribution in target volume and control of Organ at Risk (OAR) dose are the two main goals in brachytherapy. ***Materials and Methods:*** In this study *in vivo* dosimetry in 4 rectal points was performed by Transillumination Dosimeter (TLD) s and the measured doses were compared in different patients. One point was reported to have the maximum dose in each patient and the very dose was considered as rectal dose according to ICRU-38 prescription; however, the next higher dose was also considered the same as the highest point when the difference was not more than 10% of the highest value. ***Results:*** In more than 50% of the cases the 1st and 2nd highest points were in the same range with less than 10% variation. There were 3 points in approximately equal dose in 7% of cases. ***Conclusion:*** These findings are challenging with the ICRU-38 recommendations reporting the existence of a sole maximum rectal dose. So it seems wise to consider an isodose plate of maximum doses instead of one point only. **Iran. J. Radiat. Res., 2009; 6 (4): 189-194**

Keywords: *RBrachytherapy, cervical & endometrial cancer, points of "maximum dose", dosimetry.*

INTRODUCTION

Radiation therapy (RT), through a combination of external beam radiotherapy (EBR) and intracavitary brachytherapy, is the standard treatment of most stages of cervix and endometrial cancer. Brachytherapy delivers a high radiation dose directly to the tumor while sparing the adjacent normal tissues.(1)

Assessment of local tumor control, as well as the incidence of late sequelae caused by treatment are important factors in the analysis of the outcome of RT. Theses sequelae consist of rectal (proctitis and fistulae) and urinary tract complications. Urinary tract sequelae are frequently reported in 8–12% of all the cases. As for the rectal complications, it should be noted that the incidence of severe proctitis in cancer of the cervix is stated to be dose dependent; as reported in less than 4% of the cases using the dosage of 80 Gy; 7 to 8% for 80–95 Gy, and 13% for 95 Gy.(2)

The combination of intra secom (IS) implantation and high dose radiotherapy (HDR) brachytherapy permits the delivery of a high dosage of radiation to the tumor and relatively less dosage to the adjacent normal tissues; which is potential for improved local tumor control and reduction of treatment morbidity.(3)

Many studies have shown the combination of total doses to the paracentral point in the range of 75–95 Gy can be delivered relatively safe, leading to cure rates as high as 90–50% for patients with stage IB-IIIB disease.(4)

As a result, best dose distribution in target volume (target volume in cervical & endometrial cancers consists of endometer, cervix, parameters and their lymphatics) and dose control in normal nearby organs such as bladder and rectum are the 2 main goals of intra - cavitary brachTherapy (ICBT) (5).

The international commission on radiation units and measurements (ICRU) has tried to improve the uniformity of the concepts, definitions, dose specification and

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dose determination in radiation therapy for the past decades.[6]

ICRU in its 38th quota has recommended the usage of R1 through R4 as dosimetric rectal points for brachytherapy [7]. This report was prepared more than 15 years ago, and during the subsequent years, many important changes took place in the field of brachytherapy. These changes include dramatic progress in imaging, more powerful and accurate 3-D treatment planning, availability of better and safer therapy equipment, and the development of high dose rate (HDR) and pulse dose rate (PDR) stepping source brachytherapy [6].

According to ICRU Report 38, R1 is considered as a point at the exact 0.5 centimeter on behalf of the last visible posterior wall of the vagina (figure 1), R2 point is considered 1 centimeter below the R1 point and R3 point is 1 centimeter above the very point in axial direction. R4 is located 1 centimeter below the R2 point. It seems such sequences may be useful not only to obtain rectal doses but to reveal the maximum dose points in the rectum (quality control for dose distributions). The rectal reference point is considered to be the point with maximum dose. Points R2 to R4 are necessary for quality control during the therapy. [5, 7]

During the recent years, reporting the dose distributed to specific points of critical organs has been recommended. [6]

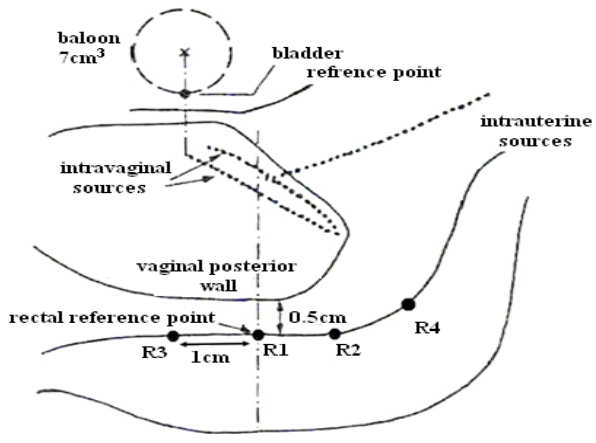

Figure 1. Rectal reference point according to ICRU-38 suggestion

Several groups have proposed modifications of this classic method by using an isodose reference volume and computation of a dose–volume histogram (DVH) or the minimal dose received by the tumor. [8]

Deshpande and colleges in their study in 1997 in India planned an *in vivo* rectal dosimetry by using TLD in 4 rectal points. According to their conclusion, there was at least one other point rather than the main point of maximum dose in more than half of the patients in which its calculated *in vivo* dose was in the range of 90% of the point of maximum dose (10% of variation was considered clinically negligible) [9].

In May 1998, The GEC-ESTRO (Groupe EuropeÂen de CurietheÂrapie) devoted a full day of its annual meeting to the discussion of ICRU Report 38 [10] and, in particular the question of the needs for a revision was raised [10-12]. Besides, it can be seen that ICRU 38 is not integrated to its full extent into recording in clinical practice and reporting in literature for uterovaginal brachytherapy [6].

According to the ICRU reference to doses bladder point often do not correlate well with bladder complications, although the ICRU bladder point is easily reproducible. Indeed, some authors found a correlation between incidence and severity [9,10], however the majority did not [6,12,13,15].

In addition, several dosimetric studies have demonstrated the maximal dose to the bladder to be underestimated using the ICRU bladder point [9, 10]. The maximum dose is usually reported to be located 2±3 cm more cranially and laterally at the levels of the ovoids [6, 12, 13, 15].

The exact positions of the rectal ICRU points are not determined, because the location of the posterior vaginal wall is not clear when using specific application techniques. Some centers even describe rectal points lying within a rectal catheter (filled with contrast for visualization), which does not correspond with the ICRU rectal point definition [16].

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Dosimetric studies have found a good correlation between the distributed dose to the ICRU rectal reference point and calculated maximal doses of the rectal mucosa. But it has also been shown that the maximal dose of the rectal mucosa may be found 1±2 cm more cranially or caudally than the ICRU reference point, depending on the geometry and loading of the source trains, and the dwell positions and times. [17]

With more advanced imaging techniques more information will become available with regard to dose±volume relationship, which will enable the prediction and if possible prevention of morbidity due to rectal complications. [6]

In most cases reporting the absorbed doses at certain reference dose points in the bladder and the rectum according to the ICRU report 38 recommendations can not be positioned against the organ's wall where the dose is anticipated to be the highest. So, the evaluation based on the calculated dose at these selected points may lead to suboptimal clinical decisions, adversely affecting the treatment outcome. [2]

The aim of the present study was to reevaluate the ICRU-38 suggestions by considering in-vivo rectal doses and using TLD dosimetry.

MATERIALS AND METHODS

In this study, 4 pairs of TLDs (TLD100 R Show/England) were used, in four points of the rectum of 33 patients. *In vivo* dosimetry was performed according to ICRU -38 suggestions and analyzed according to 10% difference from the maximum point dose value.

Dosimetry

The cubic TLD-100 chips (0.9×3×3 millimeters) were used in this study. All TLD-100 chips were exposed to Co-60 radiation machine synchronously and their ECC (Equivalent Consistency Coeffient) was calculated. All TLDs were then irradiated with doses differing from 1 to 20 Gray in the batches of 3, by a calibrated Co-60 machine. The average readings against given doses was plotted in each series, the calibration curve was also obtained.

In order to calculate the correction factor, six groups of TLD's in batches of 3 were exposed to 1.5-10 Gy with ^{137}Cs X-ray beam. The dose given to the patients and the values measured by TLD were plotted. The data were fitted in a linear equation.

Then, every two TLDs were packed in a plastic coverage. Each four pairs of TLDs were placed with 1cm distance from each other in a plastic cover; a tiny marker indicated the minimal absorption and/or distribution effect of each pack. These packs were used in rectal applicators covered with a condom sheet. After insertion of vaginal applicators; rectal applicator was fixed and then the orthogonal X-ray images were carried out. One of the four points (R_1 to R_4) on the marker was made to coincide with the reference point (defined by ICRU-38). Rectal applicators were adjusted wherever required. Two TLDs were considered for background in each insertion (figures 2 and 3).

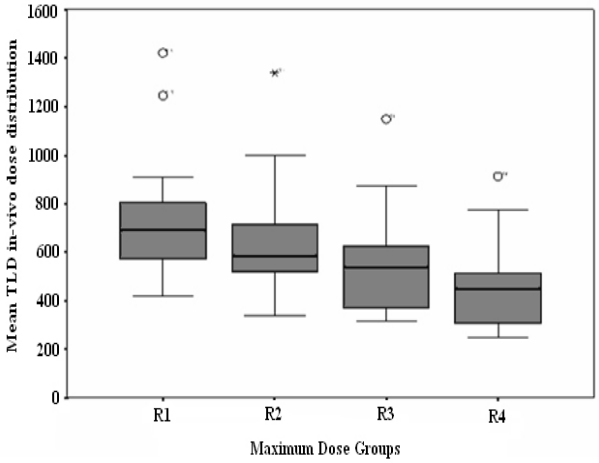

Figure 2: Mean TLD In-vivo dose distribution in maximum dose groups.

The treatment was done for each patient using individual planning schedules by low dose rate (LDR) / medium dose rate (MDR) remote after loading selectron

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machine containing small ^{137}Cs sources. The treatment duration varied from 4 to 7 hours; as a result, all TLDs remained in rectum during the treatment period in order to receive their doses. TLD reader revealed raw values of doses in micro columbe (μc). These values were then interpreted to doses in Centi Gray by using calibration curve as well as correction factor. The point average doses from two TLDs were considered as the point dose.

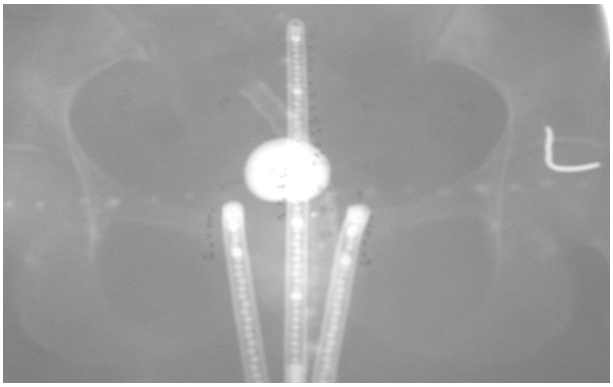

Figure 3. A view of applicator and TLD inserted in a patient before irradiation and dosimetry.

The point doses were evaluated in all 33 patients with cervix or endometrial cancers with different stages of I to III, point doses evaluated in two ways: Treatment planning and *in vivo* dosimetry by TLD measurement.

At first we compared the above two doses with each other and with considering the *in vivo* dose as the standard and the maximum dose points were calculated.

To analyze the *in vivo* calculated doses in any patient, the point doses ranked from the maximum to minimum and coded as 1-4. Meanwhile, all code 1 points were compared with the other 3 code groups separately. Comparing these four groups was achieved in three methods: Evaluating the average and percentage of dose difference between the maximum dose points (code 1) and the others separately and finally considering mean TLD doses and their changes.

SPSS v11.5 software was used to analyse the data. Paired sample *t–test* and χ^2 were the statistical tests used to determine the chance for error (P value) in comparisons with numeric and categorical variables, and two categorical variables, respectively.

RESULTS

All 33 patients aged between 33 to73 years (mean=50.3, SD=10.8). 29 patients (87.9%) had cervix cancer and 4 (12.1%) had endometrial cancer. 16 (%48.5) patients had undergone surgical treatment (total abdominal hysterectomy + oophorectomy) and 17 (51.5%) patients had not undergone any previous pelvic surgery. The application used included tandem/ovoid applicator in 15 patients (45.4%), ovoid applicators in 14 patients (42.4%), cylinder applicator in 2 patients (6%) and tandem/cylinder applications in 2 (6%) other patients.

External Radiation dose (before starting brachytherapy) differed from 50 Gy in 25 fraction (11 patients, 33%), to 60 Gy in 30 fraction (12 patients, 36.3%) and 50.4 Gy in 28 fraction (5 patients, 15.2%); the altered mean dose/rate was 224.3 cGy/hours (*SD=23.2*).

The mean planning rectal dose was 654cGy (*SD=245*) (55.5% of A point calculated dose) with the maximum dose and the minimum of 1384 cGy (115%) and 355 cGy (22%), respectively. The mean TLD (in-vivo) dose in every points was equal to 579cGy (SD=214). The background dose did not influenced the results.

The second dose points were in the range of ± 90% dose of the maximum *in vivo* dose in 17 patients (51.5%) (confidence interval (CI) = 34-68 %). The third and fourth points were in the same range in 4 patients (7.3%, CI95% = 1-23%), and in one case (1.8%, CI 95% = 0-9%), respectively.

Mean maximum point doses (code 1) was 705 (SD=217.4) (CI 95% = 628-782 cGy). Mean point doses for the second group (code 2) was 627 cGy (SD= 204) (CI =555 – 699 cGy) , for the third group (code 3) was 542 cGy (SD= 186) (CI= 467-542 cGy), and finally for the fourth group (code 4) was 445

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cGy (SD = 157.5) (CI = 389 – 501 cGy).

The coefficient of variation for these four measurements for code 1 to 4 was about 30.8%, 32.5%, 34.3% and 35.4%, respectively. Mean dose difference between the first and the second group was 77.7 cGy which was not statistically significant (P-value >0.445) (CI 95% = -56.5 – 212). Mean dose difference between the first maximum points (code 1) and the third group (code 3) was 163 cGy with a statistically significant difference from zero. (P-value < 0.01)(CI 95% = 29-297). The mean difference between the maximum dose group and the fourth group (code 4) was also significant, and equal to 260 cGy (P- value < 0.001) (CI 95% = 125-394) (table 1).

In 9 of the 15 patients using tandem/ ovoid applicators (60%, CI 95% = 35-83%) and only 5 cases of 14 those using Ovoid applicators (36%, CI 95% = 11-61%) the second ranked dose points was classified in the same clinical equivalent dose (± 10% difference). The cylinder and tandem/ cylinder applicator were not evaluated because of the lack of the cases.

DISCUSSION

According to this study there was another point in 90% range of the maximum dose point of 51.5 % of the cases. In addition there is a third dose point in the range of the maximum dose points of 7.3% of cases.

The mean difference between the first and the second dose points was about 77.7 cGy which was not statistically significant.

It may be concluded that there were two maximum dose points in more than a half of the 33 evaluated patients, and 3 maximum dose points in about 7% of patients.

The conclusion was against in the ICRU –38 suggestions referring to the existence of a sole maximum dose point in the rectum. It should be noted that the points between the two maximum doses have never been assessed, so the presence of another maximum dose points would be possible, and should be considered.

The study concluded by Deshpande *et al.* in Ta Ta – Memorial hospital, India in 1997, supports this conclusion. According to their study, R2 was the maximum dose point in 113 points of 182 applications. R4, R1 and R3 were reported to be in the range of 90% of the maximum dose point (R2) in 86 patients (76%) in 25 (22.1%) cases in 2 (1.7%) of the cases, respectively [9].

In a study based on dosimetery on 20 patients, five times for each patient the researchers have emphasized the discrepancies in the site of maximum expected dose point (R1). They analyzed the measurement in 3 dimensional pattern and realized variations in the maximum dose point. [18]

In another study for *in vivo* dosimetry for gynaecological brachytherapy, the researchers showed the differences between ICRU calculated dose point and measured doses and found that in some range there is no considerable difference (less than 10%) from the maximum dose point. [19]

The reasons for the presence of more than one maximum dose point can not be revealed in the current study, and other investigations should be done, while the following hints should be considered:

1) The probability of the second maximum point dose in tandem/ovoid applicators is

Table 1. The mean difference of 1st max dose to the other points.

1st max dose	Mean Difference (cGy)	CI 95%	P value (Testing the difference from zero)
2nd max dose	77.7	-56.5 - 212	>0.445
3rd max dose	163	29 - 297	<0.01
4th max dose	260	125 - 394	<0.001

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more than the ovoid ones. The reason is not clear, however the number of sources (16-20 vs.8-10) in one hand, and the dose distribution center mismatch in tandem/ovoid applicators (vs. ovoid) with ICRU suggestions and the longer dose distribution ways in tandem/ovoid considered as important factors.

2) Although, more than one extra clinical maximum dose point was confirmed in at least 50% of the patients of this study, an extended study with more patients and using more reliable *in vivo* dosimetric methods such as real time "DIODE" applications should be carried out. It should be mentioned that for intracavitary brach therapy treatments, an extra checkpoint by *in vivo* dosimetry is needed; whereas, the dose measurement for the other rectal points except the suggested point in gynecologic cancers is recommended.

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