HIGH DOSE-RATE BRACHYTHERAPY IN THE RADICAL TREATMENT OF CERVICAL CANCER. AN ANALYSIS OF DOSE EFFECTIVENESS AND INCIDENCE OF LATE RADIATION COMPLICATIONS

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ABSTRACT

Worldwide, uterine cervical cancer is one of the most frequently occurring cancers in women, with more than 80% of these cases occurring in developing countries. The South African screening policy and screening program, implemented in 2001, attempt to reduce this incidence of cervical cancer in South Africa. It is essential to treat these women with the best modalities available. This retrospective study focused specifically on the curative potential of radiotherapy administered to patients at the Oncology Department, Bloemfontein, since a new modality of high dose-rate intracavitary brachytherapy was implemented in 1994. Late radiation complications were also investigated.

Keywords: cervical cancer; radiotherapy; high-dose-rate brachytherapy; biologically effective dose; late radiation complications

1. INTRODUCTION

Radiotherapy plays an important role in the treatment of uterine cervical cancer, and a combination of external beam radiotherapy (EBRT) and high dose-rate (HDR)-intracavitary brachytherapy (ICBT) is the accepted mode of treatment.[1] Although a large number of fractionation schedules are used worldwide in treating cervical cancer, the optimal schedule has yet to be decided. Petereit and Pearcey[2] analyzed the fractionation schedules reported in 24 published articles and came to the conclusion that there was no optimal fractionation schedule available. They suggested that reasonable fractionation schedules should be based on single institutional experience with accurate reporting. A need exists, however, to deliver biologically effective doses of irradiation to ensure the highest probability of tumor control in the pelvis, with minimal late rectal complications. Organs at risk are the radiosensitive organs in or near the target volume. Careful monitoring of the biological doses for both the rectum and bladder is an important factor for minimizing late sequelae.[3] The sites of radiation-related complications most frequently noted in uterine cervical cancer radiotherapy are (a) rectum, most commonly the anterior rectal wall; (b) bladder, most commonly the posterior bladder wall; (c) vaginal vault; (d) sigmoid colon; (e) small bowel; (f) abdomen; (g) ureters; (h) skin; and (i) bone and hip.

In April 1994, the Oncology Department, Universitas Annex, Bloemfontein, implemented a high dose-rate brachytherapy treatment system, an ^{192}Ir Nucletron Microselectron afterloading source, using the ring applicator. The International Atomic Energy Agency (IAEA) has published recommendations specifically for implementing HDR ^{192}Ir brachytherapy in developing countries.[4] The IAEA recommendations and those of the American Brachytherapy Society,[5] based on the Patterns of Care studies,[6] were used as guidelines to develop a HDR-ICBT treatment protocol for patients with uterine cervical cancer (FIGO stages I-III) at the Oncology Department, Universitas Annex.

The initial staging system of uterine cervical cancer proposed in 1929 by a subcommittee of the League of Nations was revised in 1937 and 1950. These functions were taken over by the International Federation of Gynecologists and Obstetricians (FIGO) in collaboration with the World Health Organization (WHO) and the International Union Against Cancer.[7] It is imperative that the gynecologist and the radiation oncologist jointly stage the tumor in every patient with bimanual pelvic and rectal examination. In FIGO stage I, the cervical cancer is confined to the uterus; in stage II, the cancer invades beyond the uterus, but not the pelvic wall or the lower third of the vagina; and in stage III, the cervical cancer extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or nonfunctional kidney. Tumor staging also depends on whether the regional lymph nodes are involved and whether the presence of distant metastases can be assessed.[8]

The advent of HDR brachytherapy in the department brought a convenient treatment option for patients with uterine cervical cancer, permitting treatment of 10 to 15 patients weekly. The advantages of HDR brachytherapy include individualized dosimetry, outpatient treatment, a reduction in hospitalization costs, and elimination of radiation exposure of medical personnel.

The aim of the current study was to calculate the biologically effective dose (BED) for the fractionation schedule implemented at the Oncology Department since 1994, and to determine whether the fractionation schedule delivered BEDs that led to local tumor control without severe late radiation complications. Analysis of the treatment schedule, regarding the calculated BED, would indicate whether the total dose given to the planned tumor volume (PTV) by means of EBRT and the gross tumor volume (GTV) by means of HDR-ICBT, had led to local tumor control with negligible late toxicity to organs at risk, such as the rectum and bladder. To achieve tumor control with HDR brachytherapy, attention to the dose/fraction schedule and the normal tissue doses is mandatory. In general, the α/β values for tumor and early-responding tissues are approximately 10 (Gy_{10}) and for late-responding tissues 3-5 ($Gy_{3\text{-}5}$). The values derived are not actual doses, but biologically effective ones that take into consideration dose-rate and impact of fraction size.[8] The cumulative BEDs, calculated for the combination of EBRT and HDR-ICBT, to the tumor Gy_{10} and the rectum Gy_3 for cervical cancer patients would enable the Oncology Department to compare BED values for the first time with those of

other institutions in South Africa and worldwide.

2. METHODS AND MATERIALS

2.1. Patient selection

Patients (n=696) diagnosed with FIGO stages I-III cervical cancer, who had completed their radiotherapy treatment (EBRT and HDR-ICBT) at the Oncology Department, were eligible to be included in this retrospective study. The treatment and follow-up details were analyzed and the patients were included if they were treated at the Department for FIGO stages I-III cervical cancer, received only radiotherapy (EBRT and HDR ICBT) as treatment modality, and had at least a two-year follow-up record for analysis of late radiation complications. Of the 696 patients, 348 patients did not receive their follow-up examinations in the Free State, 196 had follow-up periods of less than two years, and 58 did not have complete dosimetric data. Consequently, the data of 94 patients were included in the study. The patient information was entered into a data sheet designed for the study, and was pilot-tested on ten patient files. The study was approved by the Ethics Committee of the Faculty of Health Sciences, University of the Free State, Bloemfontein (ETOVS NR 31/06).

2.2. Radiotherapy

Radiotherapy consisted of EBRT followed by HDR-ICBT. The EBRT was given over a six-week period, while the 4-6 fractions of HDR-ICBT were interdigitated (once weekly) into the EBRT treatment schedule. The overall duration of treatment ranged from 32 to 60 days (mean 41 days). Most of the patients (60%) received their EBRT treatment via the 6-MV photon beam accelerator (ELEKTA SL 75/6), whereas 37.2% of patients received 8-MV and 3.2% of patients were treated via 15-MV photon beam. The technique used was by four-field-box with anterior, posterior and two lateral planned fields with classic limits. The standard prescribed doses of EBRT to the whole pelvis was 50 Gy, consisting of 25 fractions of 2 Gy/fraction. The HDR brachytherapy was administered to all patients by utilizing a ^{192}Ir Nucletron Microselectron afterloading unit. A medical physicist at the Oncology Department planned the HDR-ICBT treatment using the computerized planning program PLATO SYSTEM 3.3.1, version 2 (Nucletron International BV, The Netherlands). The standard prescribed dose for each HDR-ICBT treatment was 2 Gy/fraction to the highest rectum dose point. The mean dose per fraction to point A for the 94 patients was 3.66 Gy (range 2.55 - 6.68 Gy; SD 1.03), and the mean value of the total dose administered to these patients during HDR-ICBT was 18 Gy.

The dose to point A differed for each patient due to different rectum positions during each HDR-ICBT treatment. Therefore, the dose to clinical point A (2 cm lateral and 2 cm superior of the cervical os) would vary as a function of the highest rectum dose point for each fraction given. The position of the rectum relative to the ring applicator was defined by an oncologist on the lateral

radiograph, and the dose distribution was normalized with respect to the maximum rectal dose. The rectal reference point according to the guidelines in the International Commission on Radiation Units and Measurements (ICRU) Report 38,[9] was therefore not used. The lateral X-ray film, which verified the placement of the ring applicator with regard to the barium-outlined rectum, was used by the physicist to portray the rectum dose points in a 2D-projection. Dosimetric planning of HDR-ICBT was performed in each application for all patients by a standard plan template, which was based on the definition of the Manchester System of point A. Standard plans were developed for each of the ring applicator sets (45° or 60° degree sets) in use, and source dwell times and positions were adjusted to suit the dose distribution required for each individual patient. Pear-shaped distributions were required, therefore manual optimization was done. Consequently, no planned optimization was done and the prescribed dose was computed to point A. However, in some cases, the ^{192}Ir dwell positions were altered from the standard plan template. These adjustments were necessary because of a dose escalation to the rectum caused by its position with regard to the central applicator. Figure 1 shows the standard calculated isodose distribution.

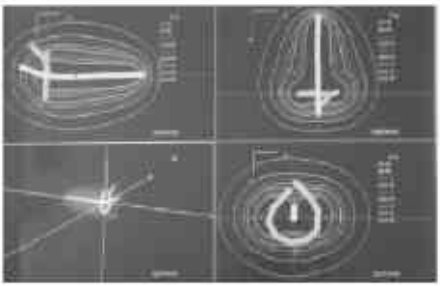

Figure 1. Standard calculated isodose distribution based on the Manchester System. (Permission to use above figure has been duly granted.)

2.3. Biologically effective dose calculation

The dose effectiveness of the fractionation schedule was analyzed retrospectively by calculating the cumulative/total BED of the combination of EBRT and HDR-ICBT for FIGO stages I-III cervical cancer patients (Total BED = BEDEBRT + BEDHDR-ICBT). The linear quadratic model (LQ model), originally applied to fractionated radiotherapy by Fowler and Stern in 1960, was refined and expanded by Barendson in 1982 and Dale in 1985, and its use has been reviewed by Fowler.[10] The basic equation defines the amount of radiation damage, E, resulting from n high dose-rate fractions of size d each as:

$$E = n(\alpha d + \beta d^2) \quad (1)$$

$$BED = \frac{E}{\alpha} = nd\left(1 + \frac{d}{\alpha/\beta}\right) \quad (2)$$

The LQ model was used to calculate the biologically effective doses for all patients who met the inclusion criteria for this retrospective study. It is a mathematically simple way to quantify biological responses to different fractionation schedules.[11] Calculations of the BED of the fractionation schedule were done by the Department of Biostatistics, University of the Free State. On the basis of the LQ model, the cumulative BED to the tumor and the rectum, generated from the contribution of EBRT and HDR-ICBT, was calculated for all patients. The BED was calculated to the tumor ($\alpha/\beta = 10$) and the rectum ($\alpha/\beta = 3$) for both EBRT and HDR-ICBT. The cumulative BED to the tumor for each patient was the sum of the total EBRT midline dose (50 Gy) and the total point A dose of HDR-ICBT. The cumulative BED to the rectum for each patient was the sum of the EBRT dose, determined by dose-volume histograms, and a dose of 2 Gy/fraction prescribed to the highest rectum dose point for HDR-ICBT.

2.4. Patient follow-up and scoring criteria for late radiation complications

The patients were followed-up by radiation oncologists by means of a clinical examination one month after radiotherapy had been completed. Thereafter, the patients were followed-up every three months for the first year and every four months for the second and third year. Follow-up procedures included a clinical (pelvic) examination and cervical Papanicolaou smears. When central and/or parametrial recurrence was suspected by pelvic examination and/or Papanicolaou smears, a biopsy was taken for confirmation. A chest radiograph was taken annually. Other imaging studies such as computer tomography, ultrasonography and bone scintigraphy, were not routinely performed.

The retrospective scoring of the late radiation complications was done by using the information notes of the radiation oncologists taken during the patients' follow-up examinations. Late radiation complications were scored according to the Radiation Therapy Oncology Group (RTOG)/European Organization for Research and Treatment of Cancer (EORTC).[12]

2.5. Statistical analysis

Results were summarized by frequencies and percentages (categorical variables) and means, standard deviations, median, minimum and maximum (numerical variables). The software used was SAS 9.1.3 Service Pack 3. Survival analysis was used to determine the probability of recurrence, late complications and metastases at various time points. The cumulative BED

values of the combination of EBRT and HDR-ICBT were investigated using the log-rank test based on survival analysis. The data collected for this retrospective study was processed by the Department of Biostatistics, University of the Free State, Bloemfontein.

3. RESULTS

3.1. Patient demographics

The mean age of the 94 patients was 55 years (range 26 -76 years; SD 9.5). HIV tests revealed that 87 (92.6%) patients were HIV-negative and seven (7.5%) HIV-positive. All patients were staged according to the FIGO staging for uterine cervical cancer. The FIGO staging for the 94 patients is given in Table 1. Median follow-up time for the 94 patients was 40 months (3.3 years), with a range of 24-93 months (7.8 years).

Table 1. FIGO staging of all patients (n=94) and patients with late radiation complications (n=15)**.**

FIGO stage	Total patients (n=94)		Late radiation complications (n=15)	
	Frequency	Percentage	Frequency	Percentage
Stage Ib	1	1.05	0	0
Stage Ib1	2	2.13	0	0
Stage IIb	3	3.19	1	6.67
Stage IIb1	12	12.77	3	20.00
Stage IIb2	27	28.72	4	26.66
Stage IIIb1	43	45.74	6	40.00
Stage IIIb2	6	6.38	1	6.67

3.2. Treatment results

Dose effectiveness-tumor recurrence

Survival was 100% for all FIGO stages I-III. At the time of the analysis, 83 patients (88.3%) had no tumor recurrence. The FIGO staging results of the eleven patients with tumor recurrence showed that two patients (18%) were stage IIIb2; four patients (36%) were stage IIb2, and five patients (45%) were stage IIIb1. Histology results of patients' biopsies showed that three of the seven patients (43%) with adenocarcinoma, and only eight of the eighty-seven patients with squamous carcinoma (9.2%), presented with tumor recurrence (p=0.03). Six of the 11 patients had local infiltration, of which five

were bladder and one rectum infiltration. Seven patients (7.5%) developed metastases, and of these, six also presented with tumor recurrence. The most common site of metastases was the para-aortic lymph nodes, followed by bone infiltration, lungs, liver and brain. Only one of the seven HIV-positive patients developed tumor recurrence (CD_4 count = 480 x 10^6 cells/L). The probability of tumor recurrence and late radiation complications at various time points (using survival analysis) is shown in Table 2.

Table 2. Probability of tumour recurrence and late radiation complications (n=94).

Time span	Tumour recurrence probability	Late radiation complication probability
6 months	0.01	0.05
1 year	0.03	0.07
2 years	0.09	0.11
3 years	0.09	0.16
4 years	0.13	0.19

3.3. Late radiation complications

Of the 94 patients in this study, 15 (16%) had RTOG/EORTC grade IV late rectal/bladder complications. The FIGO staging of the 15 patients who presented with late radiation complications, is illustrated in Table 1. Most patients had stages IIb2 (26.7%) and IIIb1 (40.0%) uterine cervical cancer. Late radiation complications occurred at a median time interval of 12.4 months (range 131 months) after completion of radiotherapy treatment. Of the 15 patients who presented with late radiation complications, 10 had bladder and five had rectum complications. Two of the 15 patients were HIV-positive (CD_4 counts of 550 x 10^6 cells/L and 480 x 10^6 cells/L, respectively). The crude incidence (grading) of first late bladder radiation complications (RTOG/EORTC scoring of these organs) was as follows: six patients with grade I, three with grade II, and one with grade III. The RTOG/EORTC grading for first late rectum complications were: grade I for three patients, grade II for one patient, and grade III for one patient. The median time for rectal complication development was six months (range 110 months). Late rectal complications varied from blood-streaked stool and rectal bleeding to proctitis. Bladder complications were teleangiectasia, intermittent macroscopic hematuria and severe frequency and dysuria.

Three of the 15 patients with late radiation complications also presented with a second late radiation complication. These patients first presented with late radiation complications of the rectum, followed by second late radiation

complications of the bladder (n=2) and rectum (n=1). Of the three patients who presented with a second late radiation complication, one patient presented with a grade II rectum complication (increased stool frequency and bleeding), and the other two had grade III bladder complications (severe frequency and dysuria). Only one of the three patients with a second late radiation complication developed a third late radiation complication of the rectum (proctitis) and the bladder (cystitis). The patient received palliative treatment (medication). All of these patients were treated medically according to the symptoms.

4. CUMULATIVE BED TO THE TUMOR AND RECTUM

The cumulative BED to the tumor of EBRT and HDR-ICBT for the 94 patients had a mean value of 87.59 Gy_{10}, while the cumulative BED to the rectum had a mean of 106.20 Gy_3 (Table 3). The median BED_{10} varied from 88.85 Gy_{10} for non-bulky stage I/II disease to 86.36 Gy_{10} for stage IIIb patients. Median cumulative BED_{10} for the 11 patients with tumor recurrence, was 86.03 Gy_{10}, and 87.62 Gy_{10} for the 83 patients with no tumor recurrence. The median cumulative BED_{10} values did not differ significantly (p=0.68). The median cumulative BED for the rectum Gy_3 of the 15 patients with late radiation complications was 106.62 Gy_3, and 105.90Gy_3 in the remaining 79 patients. The difference between doses was not statistically significant (p=0.17).

Table 3. Cumulative BED values for EBRT and HDR-ICBT (n=94).

	Tumour Gy_{10}	Rectum Gy_3
Mean BED	87.59	106.20
Standard deviation	4.36	3.55
Median BED	87.27	106.26
Minimum BED	72.98	93.71
Maximum BED	101.18	113.86

The BED_{10} results obtained after analysis of the fractionation schedule for dose effectiveness are summarized and compared to those of other fractionation schedules[13] in Table 4.

Table 4. BED_{10} values the Department of Oncotherapy, Bloemfontein (1998 - 2003) and HDR fractionation schedules for recently published studies. (10)

	Whole-pelvis dose	HDR FX	BED Gy_{10}
Dept. of Oncotherapy, Bloemfontein (1998-2003)	50 Gy 25 Fx	Mean of 4 Gy x 4- 6 Fx	87
Wong	40 Gy 20 Fx	7 Gy x 3	86
		6 Gy x 4	88
Sood et al.	45 Gy 25 Fx	9 Gy x 2	89
Fornigno et al	45 Gy 25 Fx	6 Gy x 4	92
Pearcey (National Cancer Institute of Canada trial)	45 Gy 25 Fx	8 Gy x 3	96
Gynecologic Oncology Group standard	45 Gy 25 Fx	6 Gy x 5	101
American Brachytherapy Society recommendations	45 Gy 25 Fx	5.3-7.5 Gy x 5-8 Fx	98-109

5. DISCUSSION

5.1. Dose effectiveness

The main objective of this retrospective study was to analyze the dose effectiveness of the fractionation schedule implemented since 1994 at the Oncology Department, Bloemfontein, by calculating the BED for the combination of EBRT and HDR-ICBT to the tumor Gy_{10} and the rectum Gy_3, using the linear quadratic model. Despite some radiation oncologists who have questioned the actual predictive role of the cumulative BED, which is derived by adding up the BEDs of EBRT and HDR-ICBT, our BED levels of fractionation scheme compared favourably with those of HDR brachytherapy fractionation schedules in published studies (Table 4).[13] The BED levels of fractionation scheme in a more recent study done by Chen et al.,[3] have also shown that their BED levels of fractionation were similar to those recommended by the ABS.[3] Standardization of HDR-ICBT on an international level will assist institutions in terms of comparing toxicities and outcomes in patients with cervical cancer, and will also allow for the exchange of information and uniformity in a multi-institutional randomized clinical trial that permits HDR-ICBT.[14]

The median BED_{10} for the 94 patients was 87.27 Gy_{10} to the tumor. Although the BED_{10} value in this study was approximately 10-15 Gy_{10} less than in other studies done in a pre-chemotherapy era,[2,1517] the 3.3-year local control rate of 88.3% for all FIGO stages and a 100% overall survival, compared well with reported studies (Table 4). No statistically significant differences were observed in the BED_{10} values (p=0.68) of patients with local tumor recurrence (median 86.03 Gy_{10}), compared to those with no recurrence (median 87.62 Gy_{10}). Consequently, BED_{10} values could not be correlated with local tumor control.

Although the patients in the present study received EBRT and HDR-ICBT as treatment modality in a pre-chemotherapy era, the American Brachytherapy Society recommends the addition of cisplatinum-based chemotherapy during pelvic EBRT. Five prospective randomized trials have demonstrated a 10-15% increase in local control and survival without increase in complications when concurrent chemotherapy was added to radiation therapy.[5] A more recent study published by Patel et al.[18] on optimizing of HDR-ICBT schedules by treating patients with only two fractions of 9 Gy/fraction, has proven to be safe and effective with good local control, survival and manageable normal tissue toxicity. Thus, HDR schedule of higher dose per fraction with fewer treatment sessions reduces treatment burden, overall treatment time, and results in potential cost savings in a resource-limited country such as India.[18]

5.2. Late radiation complications

The Brazilian Experience, as reported by Ferrigno et al.,[19] is one of the most concise HDR brachytherapy papers written to date as the authors provided adequate fractionation details, calculated and correlated BED to the tumor and late responding tissues, and prospectively studied their patients. One hundred and thirty-eight patients were treated with 45 Gy EBRT and four HDR-ICBT treatments of 6 Gy prescribed to point A. Patients treated with cumulative BED at rectum points above 110 Gy_3 had a higher, although not statistically significant, five-year actuarial rate of complications. Sood et al.[17] reported on 49 patients with cervical cancer treated with a combination of 45 Gy (1.8 Gy/fraction) of EBRT and 2 HDR-ICBT treatments of 9-9.5 Gy prescribed to point A. The median BED_3 at the rectal point in their study was 95.5 Gy_3 (range 79.9-110.2 Gy_3). These authors suggested that the low rate of rectal complications in the study could be attributed to the low BED_3 at the rectal point, although the point A doses were achieved as prescribed.[17] Patel et al.[18] have recently published their results on a prospective clinical study of 104 patients (Stages IIB and IIIB) treated with HDR-ICBT, comparing 9 Gy per fraction in two fractions (Arm A) with 6.8 Gy per fraction in three fractions (ARM B). Grades II and III late rectal toxicities were observed in six and three patients respectively in Arm A and two patients and one patient respectively in Arm B. The three-year actuarial risk of developing grade III or IV late rectal toxicity was 4.5% for Arm A and 2.78% for Arm B (p=0.5463). The median total rectal BED received by the patients in Arm A from EBRT and HDR-ICBT, was 115.3 Gy_3, and in Arm B it was 108.51 Gy_3.[18]

In the current retrospective study, the fractionation schedule did not include the ICRU Report 38[9] rectal reference point, but the maximal rectal dose to the anterior rectal mucosa identified by contrast medium. The standard prescribed protocol at the Oncology Department in Bloemfontein was 2 Gy/fraction, normalized to the highest rectum dose point to achieve a minimum total dose of 15 Gy to point A. The dose to point A therefore varied from patient to patient, and fraction to fraction. Point A is a geometric point in relation to the cervical os and uterine axis, and the rectal doses can be

significantly different depending on the geometry of the implant, size of applicators, amount of packing, source of activity and optimization with HDR-ICBT. The median dose per fraction to point A was 3.66 Gy/fraction and the median total dose was 18 Gy.

The median BED_3 at the rectal point in this retrospective study was 106.2 Gy_3 (range 93.7-113.9 Gy). Patients who developed late radiation complications received a median of 106.62 Gy_3, while those who did not develop complications received a median of 105.89 Gy_3. These BED_3 values did not differ significantly (p=0.17), and therefore BED_3 values could not be correlated with late radiation complications. The incidence and severity of late radiation complications were retrospectively analyzed and graded according to the RTOG/EORTC scoring scheme. Severe late rectal and bladder complications were uncommon in this study. One patient presented with grade IV complications (proctitis and cystitis), while 10 patients presented with late radiation complications of the bladder (grade I-III). This was, however, expected as the HDR-ICBT treatment did not include bladder shielding. Toita et al.[20] suggested that cumulative BED_3 at the rectal point should be kept below 100-120 Gy_3 to prevent late rectal complications. At the local Oncology Department, the cumulative BED_3 at the rectal point (106.2 Gy_3) was within these limits and as a result, only 16% of the 94 patients presented with late radiation complications.

The BED_3 and BED_{10} values calculated for the fractionation schedule of this study were adequate. The available data indicated that it was not necessary to adapt the prescribed treatment protocol for patients diagnosed with stages I-III uterine cervical cancer. The study had a three-year follow-up period, but according to Petereit et al.,[13] longer follow-up results would be required to determine if lower BED_{10} values compromise pelvic control rates. Therefore, five-year follow-up results to determine whether or not BED_{10} values in this study compromised pelvic control rates, are proposed. Although the median BED_{10} of 87.27 Gy_{10} to the tumor was effective (88.3% tumor control) with a low incidence of late radiation complications (16%), there is, however, room to increase the prescribed dose to the rectum from 2 Gy/fraction to 2.5 Gy/fraction. The current fractionation schedule places a lot of emphasis on the rectum dose, while the dose delivered to the bladder has not been calculated. Considering that the bladder was affected in 10 of the 15 patients who presented with late radiation complications, it may be necessary to take the total dose to the bladder of this schedule into account.

Recently, the benefits of image-guided three-dimensional intracavitary radiotherapy(3D-ICR) in reducing the late complication rates have been reported for cervical cancer.[21] Evidence supports the use of 3D planning with computed tomography or magnetic resonance imaging (MRI) over conventional two-dimensional planning with fluoroscopic imaging, as there is improved anatomical delineation of structures and more accurate assessment

of volumetric doses.[22] Guidelines have been published by the Brachytherapy Group of the European Society for Therapeutic Radiology and Oncology (GEC ESTRO) and the American Society of Brachytherapy.[21]

6. CONCLUSION

The findings obtained by this retrospective study suggest that 50 Gy EBRT to the whole pelvis combined with HDR-ICBT with a median total dose of 18 Gy to point A, administered in 4-6 fractions, is an effective and safe fractionation schedule in the treatment of FIGO stages I-III uterine cervical cancer patients, if undertaken in a mean treatment period of 41 days. Although this schedule appears to be both safe and effective, it is only a preliminary step to establishing windows of opportunity for BED_{10} to tumors and BED_3 to rectal tissues.

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