RADIATION DOSE COMPARISON BETWEEN THE TWO TECHNIQUES OF INTRACAVITARY BRACHYTHERAPY IN CERVICAL CANCER

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Abstract

Background and purpose:

Radiotherapy is effective in the treatment of locally advanced cervical cancer. However, the treatment is associated with significant morbidity of the urinary bladder and rectum. This study has been designed to ascertain the potential for dose reduction to bladder and rectal points by using intravaginal foley balloon catheters as a mechanism for structural displacement during tandem and ovoid in high-dose-rate intracavitary brachytherapy of the uterine cervix.

Materials and Methods:

Twenty four patients of cervical carcinoma stage IIB-IIIB, were received four times of 600 cGy high dose rate intracavitary brachytherapy(ICBT) treatment. Two times of ICBT with conventional gauze packing (control arm) were compared with two times of ICBT with two foley balloons placed intravaginally(study arm), one balloon was placed anterior and another balloon was placed posterior to the tandem, as close to the flange as patient geometry allowed. A series of 96 consecutive digitized treatment plans was assessed: 48 plans with control arm and 48 plans of study arm. Planning orthogonal X-rays were acquired and digitized. Dose reference points of bladder and rectum were calculated following ICRU No. 38 guideline, both with control and study arm. We compared the rectal dose and bladder dose between conventional gauze packing and foley balloon catheters

Results:

The Foleys balloon catheter significantly reduced the bladder point dose comparing with

conventional gauze packing from 77.87% to 69.83% (p=0.008). There was no difference in rectal point dose between the conventional gauze packing and the foley balloon catheter respectively (58.65% and 58.39%; p=0.561).

Conclusion:

A significant reduction in radiation dose to the bladder can be achieved by intravaginal insertion of the foley balloon catheters. This technique is simple, consistent and reproducible within an acceptable range. As such, further exploration of this technique is warranted.

INTRODUCTION

Radiation therapy is one of the standard treatment modality for treating a carcinoma of uterine cervix. A combination of external beam radiotherapy and intracavitary brachytherapy (ICBT) is the most common mode of radiation treatment(1,2). The major advantage of ICBT is that high radiation dose can build-up in tumor while sparing the adjacent normal tissue, such as the rectum and bladder(3).

The high dose rate (HDR) intracavitary brachytherapy has been use for over 40 year and the facility has increasingly become available throughout the world. HDR use is predicate on idea that shorter treatment time result in lesser patient discomfort and greater patient compliance secondary to being an outpatient treatment procedure. Studies have shown comparable clinical toxicity profile to low dose rate intracavitary brachytherapy, possibly some radiobiologic advantage and produced pelvic control and survival rates comparable to other LDR series (4,5). However there have been concern regarding the possibility of increasing risk of late complication. The large radiation dose produces variable degree of complication to surrounding structure. The most common site is rectum, bladder and small bowel. Overall normal tissue complication rate have been report to be around 10%(6). The five year actuarial incidence of rectal, bladder and small bowel late complication were 16%, 11% and 14% respectively. The complication increased in advance age (more than 70 years old), advance stage and high radiation dose (7-9). The rectal complications were 17% in the patient whose cumulative rectal biologic equivalent dose significant greater than 140 Gy and 8.6% in patient whose cumulative rectal biologic equivalent dose less than 140 Gy. The bladder complications were 19% and 12% in patient who have cumulative bladder biologic equivalent dose greater and less than 125 Gy respectively(10,11).

Several conventional methods have

been used in an attempt to reduce the bladder and rectal dose in ICBT. These include the vaginal gauze packing and/or using various kind of shielded applicator(12-15). We have experimented with low cost equipment to physically displace critical structures in HDR intracavitary brachytherapy by using foley balloon catheters. Because minor alteration in the applicator position geometry may produce a notable difference in dose received(16,17). We hypothesize that displacement of the bladder and rectum from radiotherapeutic source position secondary to properly placed intracavitary foley balloon catheter inflation can decrease the of bladder and rectal dose from of HDR intracavitary brachytherapy.

MATERIAL AND METHOD

Research design

Prospective study

Study population

This study has been taken at Division of Therapeutic Radiology and Oncology. Department of Radiology Faculty of medicine Chiangmai University from June 2006 to November 2007. New 24 cervical cancer patients were treated with external beam radiation therapy and high dose rate intracavitary brachytherapy.

Inclusion criteria

- Patients with FIGO stage Ib to IIIb cervical carcinoma.
- Treatment with high dose rate (Ir-192) intracavitary brachytherapy using the standard application, uterine tandem and vaginal ovoid.
- Performance status:ECOG score 0-2 and normal mental status.
- Age younger than 70 years old.

Exclusion criteria

- Cervical cancer patients with vaginal involvement.
- Previous history of intraabdominal surgery.
- Patient with urinary stenosis.

Sample size

Sample size was calculated from the data collected from our three pilot studies. The sample size was calculated by the following formula.

$$N = \frac{(Z_{\square} + Z_{\square})^2 \text{ (SD of difference)}^2}{\text{(Mean of difference)}^2}$$

	Bladder radiation dose			
	Insertion	Patient 1	Patient 2	Patient 3
The conventional packing	First	383.9	404.4	454.4
	Second	391	275.9	415.7
Packing by used of foley	First	361.5	456.1	500.8
catheter balloons	Second	456.1	353.5	500.3

$\square$= 0.05 $Z_{\square}$ = 1.96 $\square$= 0.2 $Z_{\square}$ = 0.84

SD of difference = 15.89

Mean of difference = 55.95

$$N = \frac{[(1.96+084)^2(15.89)]^2}{(55.95)}$$

N = 1 pair (2 patients)

Because the substantial difference in the calculated sample size was only 2 patients. We decided to examine 24 samples for evaluation of the standard difference.

Study procedure

The patients received conventional fraction of external beam radiotherapy with a dose ranging from 50 Gy. Midline block was done when radiation dose 40 Gy. The parametriam was boosted to 56 Gy when the parametriam was involved. HDR intracavitary brachytherapy with Fletcher applicator was given no later than the fourth to fifth week of the external beam radiotherapy. The treatments were interdigitated with the rest of external beam radiation therapy once or twice a week. All patients were received four times of 600 cGy HDR intracavitary brachytherapy treatment. In each time of HDR, an approximate size of tandem and ovoid applicator was inserted. After the applicator was inserted, we used the two packing techniques as following.

1. The conventional gauze packing. (control arm) (fig.1)



Figure 1 Anteroposterior and lateral orthogonal film of conventional gauze packing, with dose point, bladder point (▲) and rectal point (✦)

2. Packed by using of foley balloon catheters, with excess tip removed, were inserted anterior to the tandem, as near the flange as patient geometry permitted to the vaginal apex, posterior to the bladder. The same technique was used to place the second foley balloon catheter posterior to the applicator, between the ovoids, anterior to the rectum. After applicator and foley balloon catheters were properly positioned and secured, 5-10 mL of contrast media, as tolerated by the patient, was slowly injected into the foley balloon catheters. The vaginal cavity was packed with gauze in the conventional manner to secure the applicator. (Study arm;fig.2) The treatment schema was shown in fig.3

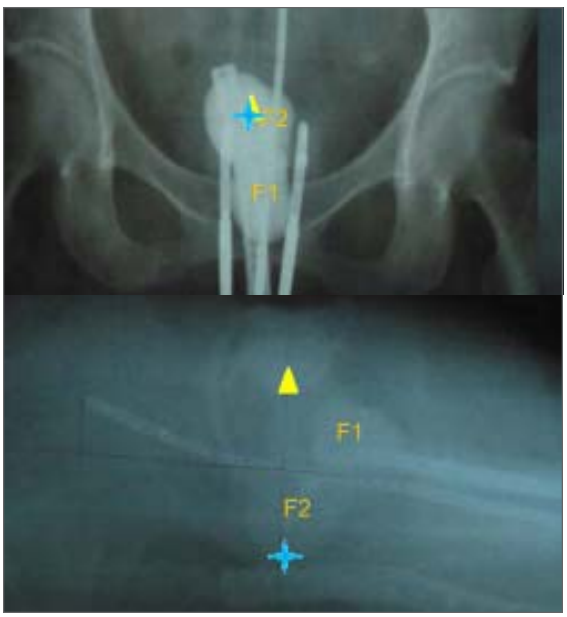


Figure 2 Anteroposterior and lateral orthogonal film with foley balloon catheters, with dose point, bladder point (▲) and rectal point (✛) and the anterior balloon catheter (F1) and posterior foley balloon catheter (F2)

After vaginal packing, orthogonal X-rays were taken in the two packing techniques to assessed position of the applicator and foley balloon catheters. Upon clinical determination, if excessive superior spatial positioning was present, the intravaginal foley balloon catheters would be deflated, retracted, and reinflated to achieve desired critical organ displacement.

Subsequently, the films were digitized, and isodose calculations were attained using Nucletron Plato[TM] Brachytherapy version 14.2.6 treatment planning software (Nucletron, Veenendaal, The Netherlands). Point A was specified as a 2 cm point superior the cervical os along the tandem and 2 cm perpendicular to the tandem, in the same plane as the mid-dwell position of the ovoids. Bladder and rectum points were assessed using the International Commission on Radiation Units and Measurements (ICRU)#38 system of point nomenclature(18). In the process of point dose calculation, the built-in bladder and rectal shields of the applicator were not considered. Relative weighting(dwelling time) dependent on size, active length, and number of dwell positions of the ovoids was optimized.

All bladder and rectal points, both with two packing techniques, were cumulatively assessed as groups designated bladder point dose with conventional gauze packing (BPgauze), bladder point dose packing with foley balloon catheters (BPfoley), rectal point

dose with conventional gauze packing (RPgauze), and rectal point dose packing with foley balloon catheters(RPfoley). Calculated dose was evaluated as both an absolute dose and percentage of prescribed dose to target Point A. Statistical analysis was performed with SPSS version 13 (SPSS, Inc., Chicago, IL). The dose percentile at predetermined points with conventional gauze packing and with foley balloon displacement were compared using pair t-test statistical analysis.

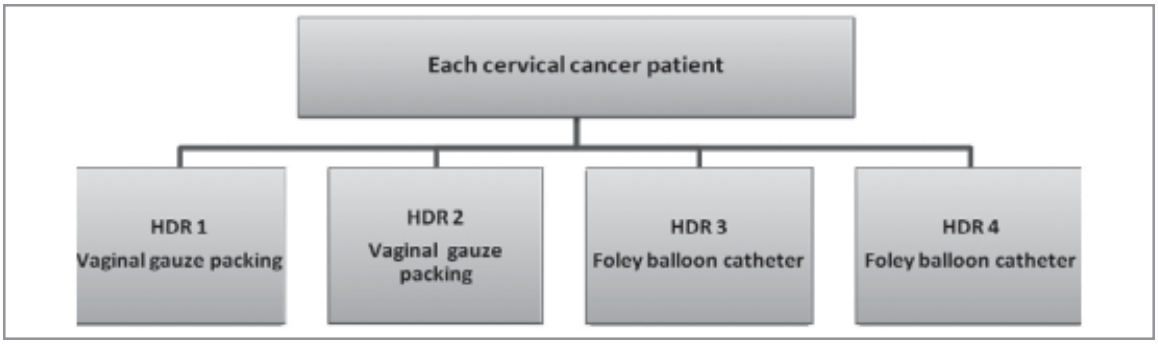


Figure 3 Treatment schema (HDR = high dose rate intracavitary brachytherapy)

RESULT

Twenty four patients with invasive carcinoma of uterine cervix were entered into the study between June 2007 to November 2007. The range (median value) or distribution for the characteristics were: The median age was 49 years old (age 28-70 years old), stage: IIb:15, IIIb:9.

There were ninety six experimental studies. The average bladder and rectal doses are the parameter for comparing between conventional gauze packing and with foley balloon catheter. The comparison of bladder dose in 2 techniques was shown in table 2 and 3. In bladder radiation dose, the mean of bladder point dose (BP) with conventional packing and with the foley balloon catheter were 461.50 cGy and 410.68 cGy(77.87% and 69.83% of prescribed dose to target point A). Which was statistical significant (p=0.008).

From the according data, Foley balloon catheters can reduce dose to the bladder in 18 patients from 24 patients. There had a lot of variation of reducing dose ranging from 0.80% to 46.7%. In six patients the bladder dose were increased. Totally the foley balloon catheters can reduce the bladder dose 8.04%, significantly ($p<0.08$) by pair t-test. This following figure 4 demonstrate the percentage of dose difference between using conventional packing versus foley balloon catheters(A) and percentage of dose reduction when used foley balloon catheters(B).

Table 2. Bladder point dose in 24 patients with conventional gauze packing and with foley balloon catheters

NO	Bladder point dose (cGy)						
	HDR 1	HDR 2	Mean	HDR 3	HDR 4	Mean	Difference
	BPgauze1	BPgauze2	BPgauze	BPfoley 1	BPfoley 2	BPfoley	
1	361.5	495.7	428.6	383.9	398.1	391.0	37.6
2	456.1	353.5	404.8	404.4	275.9	340.2	64.7
3	500.8	500.3	500.6	454.2	415.7	435.0	65.6
4	454.6	466.0	460.3	398.4	368.9	383.7	76.7
5	402.0	490.6	446.3	476.3	583.4	529.9	-83.6
6	252.3	355.5	303.9	236.9	258.9	247.9	56
7	393.5	504.4	449.0	472.8	460.9	466.9	-17.9
8	344.2	228.2	286.2	300.8	234.6	267.7	18.5
9	461.5	418.8	440.2	353.1	355.5	354.3	85.9
10	470.0	527.5	498.8	536.3	648.4	592.4	-93.6
11	408.1	609.9	509.0	207.0	272.2	239.6	269.4
12	499.6	395.8	447.7	344.1	443.0	393.6	54.2
13	287.7	258.8	273.3	391.7	346.5	369.1	-95.9
14	526.0	595.1	560.6	483.9	489.5	486.7	73.9
15	425.1	518.0	471.6	353.9	518.0	436.0	35.6
16	644.1	503.6	573.9	425.6	478.9	452.3	121.6
17	507.7	578.9	543.3	527.9	548.9	538.4	4.9
18	619.6	552.8	586.2	482.4	350.3	416.4	169.9
19	419.0	451.9	435.5	477.7	554.9	516.3	80.9
20	448.1	377.2	412.7	408.0	482.8	445.4	-32.8
21	958.1	657.4	807.8	602.2	690.1	646.2	161.6
22	333.9	263.3	298.6	214.0	289.8	251.9	46.7
23	447.1	443.2	445.2	293.9	303.6	298.8	146.4
24	649.4	610.7	630.1	649.4	444.2	546.8	83.3

Abbreviation BP : Bladder point dose, HDR: high dose rateintracavitary brachytherapy

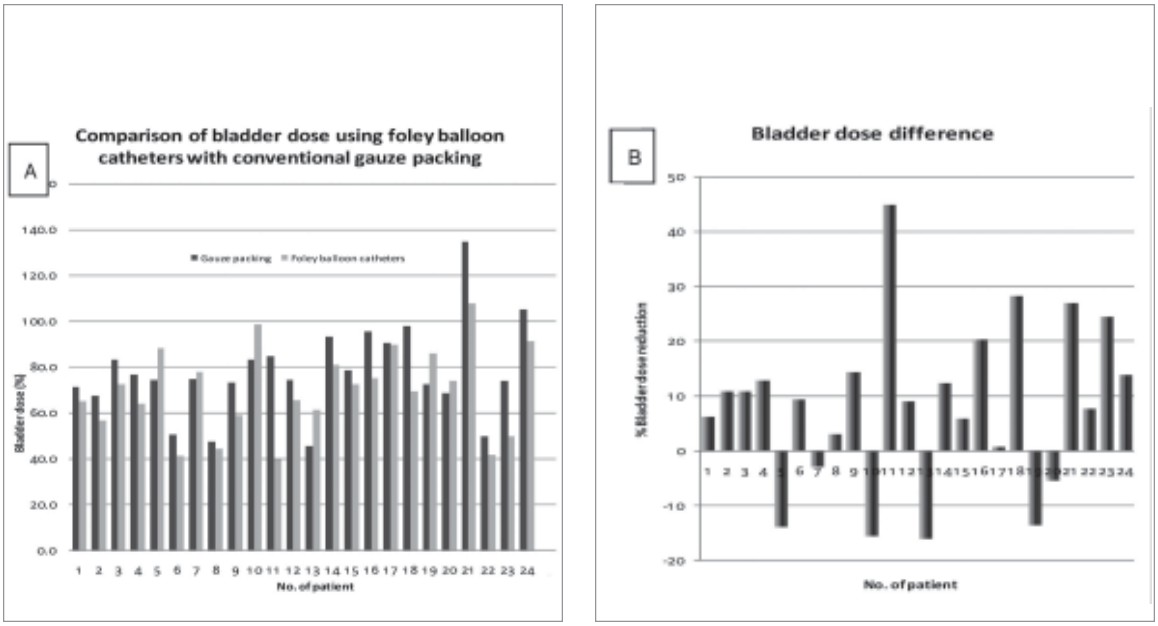


Figure 4 (A)Comparison of the percentage bladder point dose difference between using conventional packing versus foley balloon catheters (B) percentage of bladder dose reduction when used foley balloon catheters.

Table 3. Bladder point dose comparisons in all 96 insertions.

Bladder point dose	Mean(cGy)	Std. Diviation	Std error Mean	sig
Conventional gauze packing (control arm)	461.50	123.16	25.14	0.008
Foley balloon (study arm)	410.68	117.46	23.97	

However, the rectal dose was no significant changed. The mean rectal point dose(RP) with conventional gauze packing and with foley balloon catheter were 354.37 cGy and 349.17cGy (58.65% and 58.39% of prescribed dose to target Point A) (p=0.561). The comparison of rectal dose in 2 techniques was shown in table 4 and 5. This following figure 5 demonstrate the percentage of dose difference between using conventional packing versus foley balloon catheters and percentage of dose reduction when used foley balloon catheters.

Table 4. Rectal point dose in 24 patients with conventional gauze packing and with foley balloon catheters

NO	Rectal point dose (cGy)						
	HDR 1	HDR 2	Mean	HDR 3	HDR 4	Mean	Difference
	RPgauze1	RPgauze2	RPgauze	RPfoley 1	RPfoley 2	RPfoley	
1	370.4	286.8	328.6	375.3	346.9	361.1	-32.5
2	352.6	352.7	352.7	399.0	386.2	392.6	-40.0
3	336.9	249.3	293.1	353.1	438.7	395.9	-102.8
4	398.0	440.2	419.1	414.8	345.3	380.1	-39.1
5	295.6	259.9	277.8	242.7	229.0	235.9	41.9
6	247.9	266.4	257.2	288.6	267.7	278.2	-21.0
7	286.9	372.1	329.5	331.8	285.9	308.9	20.7
8	302.3	306.2	304.3	309.3	372.1	340.7	-36.5
9	372.1	361.5	366.8	357.3	384.0	370.7	-3.8
10	329.9	448.2	389.1	336.2	358.3	347.3	41.8
11	356.3	468.5	412.4	357.0	293.6	325.3	87.1
12	355.0	384.5	369.8	367.1	379.0	373.1	-3.3
13	259.8	256.8	258.3	365.3	325.3	345.3	-87.0
14	303.3	326.7	315.0	320.9	363.9	342.4	-27.4
15	361.5	385.7	373.6	403.4	385.7	394.6	-20.9
16	377.5	360.3	368.9	382.5	334.9	358.7	10.2
17	342.8	360.3	351.6	332.4	399.7	366.1	-14.5
18	422.1	420.6	421.4	360.4	416.4	388.4	33.0
19	378.4	437.6	408.0	417.0	286.2	351.6	56.4
20	319.4	326.6	323.0	354.1	316.3	335.2	-12.2
21	285.9	367.0	326.5	315.7	297.7	306.7	19.8
22	347.1	351.8	349.5	328.4	387.8	358.1	-8.6
23	389.9	467.5	428.7	367.4	352.8	360.1	68.6
24	423.7	421.3	422.5	423.7	362.1	392.9	29.6

Abbreviation RP : Rectal point dose, HDR : high dose rate brachytherapy

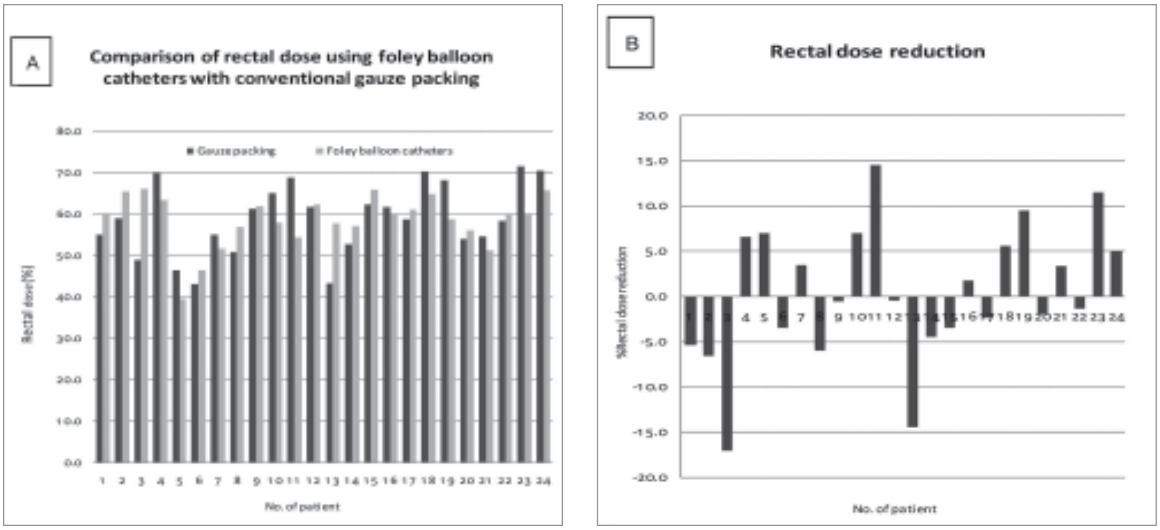


Figure 5 (A)Comparison of the percentage rectal point dose difference between using conventional packing versus foley balloon catheter (B) percentage of rectal dose reduction when used foley balloon catheters.

Table 5. Rectal point dose comparisons in all 96 insertion.

Rectal point dose	Mean(cGy)	Std. Diviation	Std error Mean	sig
Conventional gauze packing (control arm)	354.37	48.67	9.93	0.561
Foley balloon (study arm)	349.17	38.84	7.92	

There was no serious complication during and after foley balloon catheter insertion. Only few patients felt more pain during foley balloon catheter inflation.

DISCUSSION

The conventional gauze packing in HDR intracavitary brachytherapy treatment has been use worldwide for a long time. This packing is important because the copostats have a tendency to lie somewhat posteriorly. To prevent deviation of colpostat, packing is placed around the applicator. Moreover, The packing decrease the dose delivered to the bladder and rectum. From our study result, Foleys balloon catheter can significantly reduce dose to bladder compare with conventional gauze packing from 77.87% to 69.83% (p=0.008) but no difference in rectal dose (58.65% vs 58.39%) in conventional gauze packing and with foley balloon catheter respectively. We found that the bladder dose was reduced more than rectal dose by using foley balloon catheter. The result can describe as in the literature suggests, much of dose

delivered is dependent up on patient geometry and positional stability of the applicator(20-22) .In our study, when the patients were in supine position, the foley balloon catheter in the posterior to the applicator could be easily to displaced more than the anterior foley balloon catheter because inconsistency in the position of the posterior foley balloon catheter more than the foley balloon catheter in the anterior to applicator. Eng, et al reported the shielding effect of the foley balloon catheters placed anterior and posterior to the tandem as our study, but their study reported that reduction in calculated dose with inflation of intracavitary foley balloon catheter 16% and 17% for bladder and rectal point(12). Kamal, et al used three-dimension plan generated using CT image. They reported that the significant in radiation dose to the bladder base can achieved by inflating the foley balloon catheter at the anterior fornix region(13).

The issues of patient comfort, as well as usability within a wide range of patient geometry are not easily resolved, secondary to standardized device size specifications. In addition to customizable placement alteration of balloon inflation and positioning, using Foley balloon catheters to displace critical organs also allows better patient comfort and tolerance. It also shares the advantages of conventional vaginal packing.

However, the positional regard to balloon catheters placement must be evaluated with every treatment, as with any HDR treatment (24). For instance, if the balloons are placed in a fashion insufficient to displace critical structures, the device should be repositioned. Similarly, plan optimization (25-26) is recommended. The practical ease of this methodology also allows for removal or deflation of the Foley catheter balloon if planning software detects a possible increase in dose to critical tissues, so the patient can be assured of nontarget tissue dose minimization.

Several investigators have studied image-based three dimensional (3D) ICR planning using ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), and positron-emission tomography (PET) in cervical cancer. Although the studies had some different findings, the conventional point A plan, compared with the image-guided 3D plan, generally overestimated the minimal dose delivered to the target volume and underestimated the maximal doses to the rectum and bladder (27-30). However in this study used two dimensional treatment planning, the accuracy for evaluation dose at bladder and rectum may have some error. In order to obtain more accuracy, three dimensions ICBT planning with calculation of dose volume histograms of bladder and rectum are proposed.

CONCLUSION

The technique using intravaginal insertion of foley balloon catheters is effective to reduce dose to bladder in pelvic brachytherapy field. In summary, with the low cost, simple and save of implementation and the ability to significantly reduce unintended bladder dose, the used of foley balloon catheters make this procedural technique a viable option in HDR brachytherapy.

In the future research, three dimensions treatment planning with dose volume histograms calculation may be used to obtain more accurate information of bladder, rectum and other organ of interested. Furthermore, clinical aspect of acute and late complication should be explored in randomized controlled trial

REFERENCE

1. Bradley KA, Petereit DG. Radiation therapy for gynecologic malignancy. Hematol Oncol Clin North Am 2006;20(2):347-61.
2. Perez CA, Camel HM, Walz BJ et al, Radiation therapy alone treatment of carcinoma : A 20 year experience. Gynecol Onco 1986;23:127-40.
3. Kim RY. Radiotherapeutic management in carcinoma of the uterine cervix: GOG experience. Yonsei Med J 1992;33:97-103.
4. Orton CG. High dose rate brachytherapy may be radiobiologically superior to low dose rate due to slow repair of late responding normal tissue cell. Int J Radiat Oncol Biol Phys 2001;49:183-9.
5. Lorvidhaya V, Tonusin A, Changwiwit W, Chitapanarux I, et al. High-dose-rate afterloading brachytherapy in carcinoma of the cervix: an experience of 1992 patients. Int J Radiat Oncol Biol Phys 2000 Mar 15;46(5):1185-91.
6. Stryker JA, Bartholomew M, Velkley DE, Cunningham DE, et al. Bladder and rectal complications following radiotherapy for cervix cancer. Gynecol Oncol 1988 Jan;29(1):1-11.
7. Perez CA, Grigsby PW, Lockett MA, Chao KS, et al. Radiaiton therapy morbidity in carcinoma of uterine cervix dosimetric and clinical correlation. Int J Radiation Oncol Biol Phys 2000;47:955-61.
8. Clark BG, Souhami L, Roman TN, Chappell R, et al. The prediction of late rectal complications in patients treated with high dose rate brachytherapy for carcinoma of cervix. Int J Radiation Oncol Biol Phys 1997;38:989-93.
9. Chen SW, Liang JA, Yang SN, Liu RT, et al. The prediction of late rectal complication

following the treatment of uterine cervix cancer by high dose rate intracavitary brachytherapy. Int J Radiation Oncol Biol Phys 2000;47:955-61.
10. Ferrigno R, dos Santos Novaes PE, Pellizzon AC, Maia MA, et al. High dose rate brachytherapy in the treatment of uterine cervical cancer. Analysis of dose effectiveness and late complication. Int J Radiation Oncol Biol Phys 2001;50:1123-35.
11. Noda SE, Ohno T, Kato S, Ishii T, et al. Late rectal complications evaluated by computed tomography-based dose calculations in patients with cervical carcinoma undergoing high-dose-rate brachytherapy. Int J Radiat Oncol Biol Phys. 2007;69(1):118-24.
12. Eng T, Fuller D, Cavanaugh SX, Blough M, et al. Significant rectal and bladder dose reduction via utilization of Foley balloon catheters in high-dose-rate tandem and ovoid intracavitary brachytherapy of the uterine cervix. Int J Radiat Oncol Biol Phys. 2004;59(1):174-8.
13. Malaker K, Shukla V, D'Souza H, Weatherburn H. Minimizing urinary bladder radiation dose during brachytherapy for carcinoma of the cervix using balloon inflation technique: In regard to Malaker. Int J Radiat Oncol Biol Phys 2005;61:257-66.
14. Lee KC, Kim TH, Choi JH, Choi MS, et al. Use of the rectal retractor to reduce the rectal dose in high dose rate intracavitary brachytherapy for a carcinoma of the uterine cervix. Yonsei Med J 2004 Feb 29;45(1):113-22.
15. Bahena JH, Martinez A, Yan D, Mele E, et al. Spatial reproducibility of the ring and tandem high-dose rate cervix applicator. Int J Radiat Oncol Biol Phys 1998;41:13-9.
16. Rutten RR, Lawyer AA, Berner P. Dose variation due to differences in applicator placement used for intracavitary brachytherapy of cervical cancer. Med Dosim 1998;23(1):57-63.
17. Senkus-Konefka E, Kobierska A, Jassem J, Badzio A, et al. Patient-related factors determining geometry of intracavitary applicators and pelvic dose distribution during cervical cancer brachytherapy. Int J Radiat Oncol Biol Phys 1997;37: 531-6.
18. International Commission on Radiation Units and Measurements (ICRU). Dose and volume specification for reporting intracavitary therapy in gynaecology, ICRU report 38. Bethesda : ICRU ; 1985.
19. Pham HT, Chen Y, Rouby E, Lustig R, et al. Changes in high-dose-rate tandem and ovoid applicator positions during treatment in an unfixed brachytherapy system. Radiology 1998;206:525-31.
20. Osman A, Rupak K, Bhudatt R, Mostafa D, et al. Anatomic variation of prescription points and treatment volume with fractionated high-dose rate gynecological

brachytherapy. J Appl Clin Med Phys 2002;3:1-5.
21. Datta NR, Kumar S, Das KJ, Ayyagari S, et al. Variations of intracavitary applicator geometry during multiple HDR brachytherapy insertions in carcinoma cervix and its influence on reporting as per ICRU report 38. Radiother Oncol 2001;60:15-24.
22. Uno T, Itami J, Aruga M, Kotaka K, et al. High dose rate brachytherapy for carcinoma of the cervix: Risk factors for late rectal complications.Int J Radiat Oncol Biol Phys 1998;40:615-21.
23. Van Lancker M, Storme G, Ferrigno R, et al. Prediction of severe late complication in fractionated, high dose rate brachytherapy in the gynecologic applications. Int J Radiat Oncol Biol Phys 1991;20:1125-9.
24. Nag S, Chao C, Erickson B, Fowler J, et al. The American Brachytherapy Society recommendations for low-dose-rate brachytherapy for carcinoma of the cervix. Int J Radiat Oncol Biol Phys 2002;52:33-48.
25. Barillot I, Horiot JC, Maingon P, Truc G, et al. Impact on treatment outcome and late effects of customized treatment planning in cervix carcinomas: Baseline results to compare new strategies. Int J Radiat Oncol Biol Phys 2000;48:189-200.
26. Fellner C, Poetter R, Knocke TH, Wambersy A, et al. Comparison of radiography and computed tomography-based treatment plan in cervix cancer in brachytherapy with specific attention to some quality assurance aspects. Radiother Oncol 2001;58:53- 62.
27. Haie-Meder C, Poetter R, Van Limbergen E, Briot E,et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): Concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. Radiother Oncol 2005;74:235-45.
28. Malyapa RS, Mutic S, Low DA, Imran Zoberi et al. Physiologic FDG-PET three-dimensional brachytherapy treatment plan for cervical cancer. Int J Radiat Oncol Biol Phys 2002;54:1140 -6.
29. Mutic S, Grigsby PW, Low DA, Harms WB,et al. PET-guided three dimensional treatment planning of intracavitary gynecologic implants. Int J Radiat Oncol Biol Phys 2002;52: 1104 -10.
30. Pelloski CE, Palmer M, Chronowski GM, Jhingran A, et al. Comparison between CT-based volumetric calculations and ICRU reference-point estimates of radiation doses delivered to bladder and rectum during intracavitary radiotherapy for cervical cancer.Int J Radiat Oncol Biol Phys 2005;62:131-7.