Volume 15, No 4 | International Journal of Radiation Research, October 2017

Study of dosimetric and spatial variations due to applicator positioning during inter-fraction high-dose rate brachytherapy in the treatment of carcinoma of the cervix: A three dimensional dosimetric analysis

M.K. Goyal[1, 2], D.V. Rai[2], J. Manjhi[2], J.L. Barker[1], B.H. Heintz[1], K.L. Shide[1], T.S. Kehwar[3*]

[1]Department of Radiation Oncology, Texas Oncology, Fort Worth, Texas, USA
[2]Shobhit University, Meerut, UP, India
[3]Department of Radiation Oncology, Merci Fitzgerald Hospital, Darby, PA 19023, USA

► ***Original article***

Corresponding authors:
Dr. T.S. Kehwar,
Fax: *+1 610 2375051*
E-mail: *drkehwar@gmail.com*

Revised: Sept. 2016
Accepted: Nov. 2016

Int. J. Radiat. Res., October 2017; 15(4): 377-382

DOI: 10.18869/acadpub.ijrr.15.4.377

ABSTRACT

Background: This study evaluates dosimetric and spatial variations in inter–fraction applicator positioning in high dose rate (HDR) brachytherapy. ***Materials and Methods***: This study includes 25 retrospective patients of carcinoma of the cervix. Each patient received 5 fractions of HDR intracavitary brachytherapy. High Risk-Clinical Target Volume (HR-CTV) were drawn on CT images. First implant was considered as a reference, and all subsequent CT data sets were rigidly registered on first implant's CT data set. Another point A, called point Aabs, was defined on first plan and all subsequent plans. Registration properties were recorded for all 125 plans that include X, Y, Z DICOM offset, rotational, translational values and normalized D90 (ND90) doses were also recorded. ***Results:*** The mean angle of rotation on X, Y and Z axis are 0.63 ± 1.85 deg, -0.86 ± 1.30 deg, -1.14 ± 2.44 deg, respectively. While mean translational motion on X, Y and Z axes are –2.77 ± 10.32 mm, -6.12 ± 9.71 mm and 14.62 ± 23.83 mm, respectively. Mean ND90, and mean HR-CTV were found to be 1.18 ± 0.26 and 26.91 ± 17.70 cc, respectively. ***Conclusion:*** Results of the study reveals that translational motion is higher than the rotational motions, and inter – fraction applicator variation does not produce any significant change in Point A doses. The change in volume coverage is observed only due to applicator motion. HR-CTV coverage decreases with increasing HR-CTV volume. Hence, dose prescription should be based on 3D HR-CTV volume.

Keywords: *Brachytherapy, GEC-ESTRO Guidelines.*

INTRODUCTION

The combination of external beam radiation and intracavitary brachytherapy is the standard of care for the radical treatment of locally advanced cervix carcinoma. The additional dose delivered by intracavitary brachytherapy (ICBT) after external beam radiation therapy (EBRT) to the whole pelvis is critical in curing Ca-cervix patients [1, 2].

The rapid dose fall-off allows a very high dose to the central pelvis, while relatively sparing bladder, rectum, sigmoid and small bowel [3]. Studies recommend completing the treatment with EBRT and BT within 8 weeks, as prolonged treatment duration leads to a decrease in local control and survival of approximately 1% per day [4-8] due to tumor cell proliferation.

ICBT dose is delivered in multiple fractions (typically 4-5 treatment) using suitable ICBT applicator. Tandem and ovoids/ring are the most commonly used ICBT applicators for treating cervical cancer.

Multiple HDR ICBT fractions are required for

[DOI: 10.18869/acadpub.ijrr.15.4.377]

treatment and so multiple applicator insertions/ implantations are needed. To obtain the best possible dose distribution to the cervix and organs at risk (OAR), applicator placement must be optimal[4]. Applicator position reproducibility is critically important during inter-fraction HDR ICBT applications.

This study was designed to retrospectively evaluate the dosimetric and spatial variation due to applicator positioning during inter-fraction ICBT delivery.

MATERIALS AND METHODS

A retrospective analysis was performed on the treatment plans of 25 consecutive patients with pathologically-proven locally-advanced (FIGO stage IB or higher) squamous cell carcinoma or adenocarcinoma of the uterine cervix treated between January 2009 and January 2013. A total of 125 treatments plans were analyzed.

This study was approved via expedited review by the department research committee and by the practice/academic review boards, and used deidentified retrospective data for study analysis.

All patients received whole pelvis EBRT dose of 45Gy in 25 fractions, 5 fractions per week over a period of 5 weeks with concurrent cisplatin-based chemotherapy. Patients also received 5 fractions of intracavitary high-dose-rate BT. ICBT implants were done twice a week keeping the complete EBRT and BT treatment duration 8 weeks or less to achieve the optimum local control [4-8].

CT/MR compatible Titanium Fletcher-style tandem and ovoid or tandem and ring applicators were used for intracavitary brachytherapy (ICBT) implants. Radiation oncology department has three T&O applicator sets with reference numbers (AL 13030000 for all, Lot/Batch Numbers 11171803, 10419, and 20408) and one tandem and ring applicator set (Reference Serial Number AL13017000). One of those applicator set was used for ICBT implant. These applicators were supplied by Varian Medical Systems, Inc (Palo Alto, California, USA) and were manufactured with Titanium CT/MR compatible material.

Tandem sizes vary as 2, 4, 6 and 8cm with angles of 15, 30, 45 and 60-degrees. Ovoid sizes included mini, small, medium and large with the buildup diameter of 1.6, 2.0, 2.5 or 3cm, respectively. Ring angles included 30, 45 and 60 degrees. Ring applicators had options of two buildup caps of 5 mm or 7.5 mm anterior-posteriorly with 5 mm build up laterally.

The first ICBT implant was performed with general anesthesia in the hospital operating room by the radiation oncologist. A Smit sleeve, supplied by Varian Medical Systems, Inc (Palo Alto, California, USA) was implanted during first ICBT procedure to facilitate subsequent outpatient treatment. Anterior and posterior vaginal packing was used during each implant to displace bladder anteriorly and rectum posteriorly to further minimize doses to adjacent non target tissues.

All patients underwent pelvic CT scan following ICBT implant using helical mode of CT scanner with slice thickness of 3.0 mm. A Foley catheter with the balloon insufflated with 7cc of radio-opaque contrast material was used for bladder determination of an ICRU bladder point. CT images were acquired such that the scan would include at least 3-4 cm margin superior to the proximal tandem position and to include the entire implant inferiorly, and were exported to Eclipse Brachyvision Treatment Planning System (TPS) for planning.

Treatment planning was performed using a volumetric CT dataset obtained for each brachytherapy fraction imported into a Brachyvision treatment planning system, supplied by Varian Medical Systems, Inc (Palo Alto, CA, USA). Applicators were defined in TPS and evaluated using 3D display tools. All 125 plans were clinically generated per conventional, point A based technique using ICRU-38 guidelines. Initially, sources were loaded using institutional protocol and then later modified using graphical dose shaper or with iterative/manual adjustment of individual HDR source dwell positions to optimize the prescription dose. Radiation dose was prescribed to point A. Dose to point A was in the

[DOI: 10.18869/acadpub.ijrr.15.4.377]

range of 4.0-6.0Gy per fraction. Treatment was administered using an Ir-192 remote afterloader (VariSource, Varian Medical Systems, Palo Alto, CA, USA).

For the purposes of this study, High-Risk Clinical Target Volumes (HR-CTVs) were contoured by the attending physician involved in the original case. Organs at risk (OAR), i.e. rectum and bladder, were also contoured for all treatment plans. Preset pelvis window/leveling CT parameters were used to maintain consistent contouring conditions for all treatment plans. The entire bladder wall and rectum were manually contoured, with the bladder wall including the balloon with contrast and the rectum contoured from anorectum to rectosigmoid junction. The sigmoid colon was contoured from the rectosigmoid junction to about 2 cm above the tip of the central tandem. Care was taken to insure that the sigmoid was contoured adjacent to or above the uterus near the implanted brachytherapy applicator, when applicable. OAR contours were contoured by single physicist to avoid any user variation. Contours were reviewed by attending physician for accuracy and modified as necessary.

Data Collection and Statistical Analysis

First ICBT CT data set was considered as the primary CT1 data set and an optimum plan was initially generated using Manchester System. Since this is a retrospective study so the existing plan already had point A, ICRU bladder and rectum reference points. HR-CTV, OARs and new points, like point A_{abs} were added. HR-CTV volume, ND90, point A and point A_{abs} data was recorded for all the plans.

CT1 (ICBT TX#1) data set was registered on the CT2, CT3, CT4 and CT5 (ICBT Tx #2-5) data sets. Eclipse TPS registration module was used to register the CT data sets. Optimum rigid registration was performed, which involved manually aligning the 2 data sets based on bony anatomy and then using automatic registration tool available in the program. Initial image fusion was analyzed and fine tuning was performed using manual methods to achieve the best image fusion. Spatial, translation and rotational registration coordinates were recorded for all registered CT data sets.

Points and structures were transferred onto fused data sets between the registered data sets. In all cases, the first plan dose points, i.e. point A, etc., were transferred to rest of the 4 plans and recorded the doses to the respective points keeping the dose point locations same as it was on first plan. This had provided difference in point A doses in subsequent implants, considering first plan as a primary reference plan. Recorded data includes; point A doses: plan1 through plan 5, point A_{Δ} variation plan1= plan2-plan1, plan3-plan1, plan4-plan1, plan5-plan1 and point A_{abs} doses.

RESULTS

Translational and rotational motion between plans was recorded for all 25 patients. The mean angle of rotation in X, Y and Z axis was found as 0.63 ± 1.85 deg, -0.86 ± 1.30 deg and -1.14 ± 2.44 deg, respectively. The mean translational motion between the plans in X, Y and Z axis were found as -2.77 ± 10.32 mm, -6.12 ± 9.71 mm and 14.62 ± 23.83 mm, respectively.

Figures 1-3 show the average rotational variation in X, Y and Z direction and Figs. 4-6 shows the average translational variation in X, Y and Z direction.

Figure 7 illustrates the point A dose difference when plan1 point A dose was compared on subsequent implants using fused image data set. Average point A dose varies from 0.13% to 19.21% with an average dose variation of 3.69% and standard deviation of 0.08.

Data shows that in 60% of cases (15 out of 25 patients), the point A dose difference was less than 5%, while in 12% of plans it was between 5% - <10% and in next 12% were between 10% - <15%. Only 4 (16%) plans have point A dose difference between 15% - 20%.

Figure 8 shows the point A_{abs} dose difference when plan1 point A_{abs} dose was compared on subsequent implants using fused image data set. Average point A_{abs} dose was found to vary from 0.10% to 19.19% with an average dose variation of 1.65% ± 0.08%.

[DOI: 10.18869/acadpub.ijrr.15.4.377]

Similar trend had been seen in dose variation with respect to point A_{abs} doses that 60% of cases (15 out of 25 patients), the point A_{abs} dose difference was less than 5%. 16% of patients have the point A_{abs} dose difference between 5% - <10% and other 16% were observed between 10% - <15%. Only 2 (8%) patients have point A_{abs} dose difference between 15% - 20%.

Figure 9 & 10 show relationship between HR-CTV verses ND90 (D90 normalized to Rx dose), and HR-CTV verses V100 (volume covering 100% dose) for 25 patients. The mean values of HR-CTV, ND90 and V100 with standard deviation, were found to be 26.91 ± 17.70 cc, 1.18 ± 0.26 and 85.55 ± 20.34 cc, respectively.

The mean of point A doses of each patient has compared with that of other patients using the method of the analysis of variance (ANOVA). The mean of all 5 plans of each patient do not have statistically significant difference (p=0.225). On the other hand, the difference between mean doses of all 25 patients (125 plans) at point A_{abs} (p=0.011), mean doses of point A registered (p=0.005) and mean doses of point A_{abs} registered (p=0.0032) respectively, were statistically different.

The comparison between the doses of the point A and Point A_{abs}, defined using ICRU-38, ABS 2011 and computed by registering on plan of first implant, were statistically different (p <0.05).

The mean HR-CTV of each patient were fitted with normalized D90 (ND90) and % Isodose Line (IDL) data using the method of least square fit. The ND90 data fits better with exponential function and negative correlation with HR-CTV while 100% Isodose Line (IDL) have positive correlation with HR-CTV, as seen in figures 11 and 12, respectively.

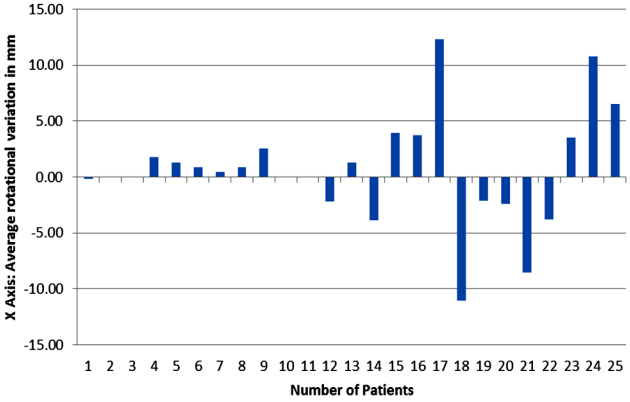

Figure 1. Average rotational variation in X axis

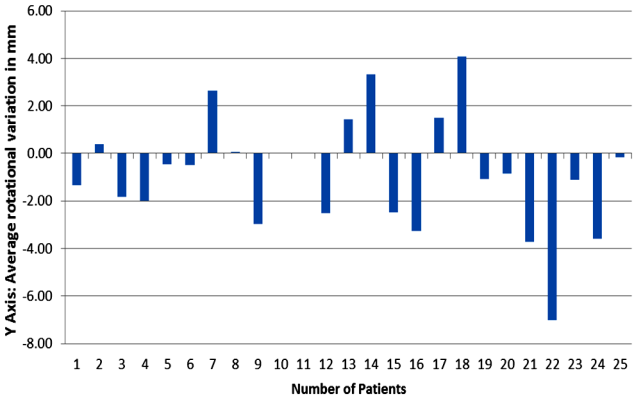

Figure 2. Average rotational variation in Y axis

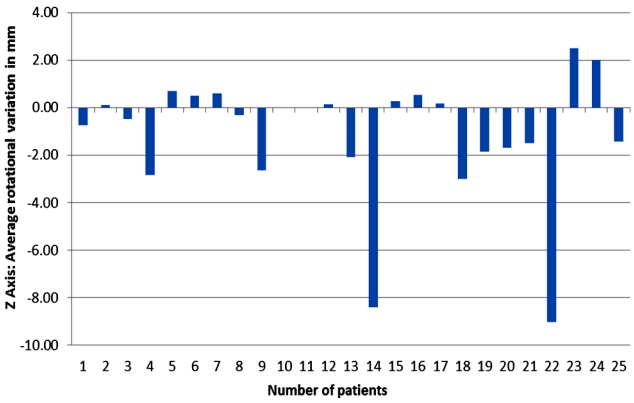

Figure 3. Average rotational variation in Z axis.

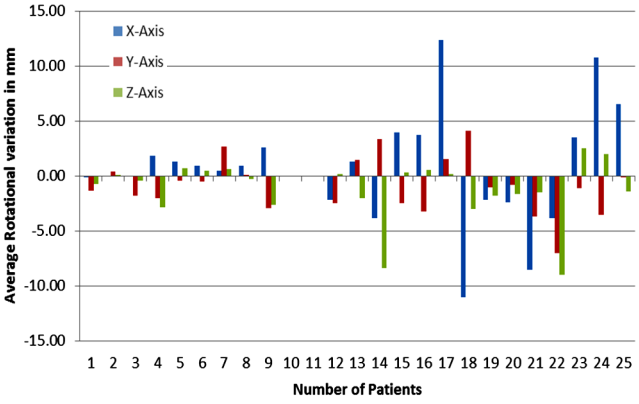

Figure 4. Average rotational variation in all axes (X, Y and Z).

[DOI: 10.18869/acadpub.ijrr.15.4.377]

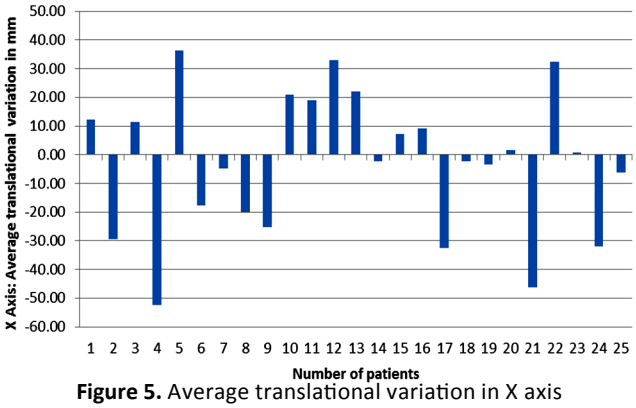

Figure 5. Average translational variation in X axis

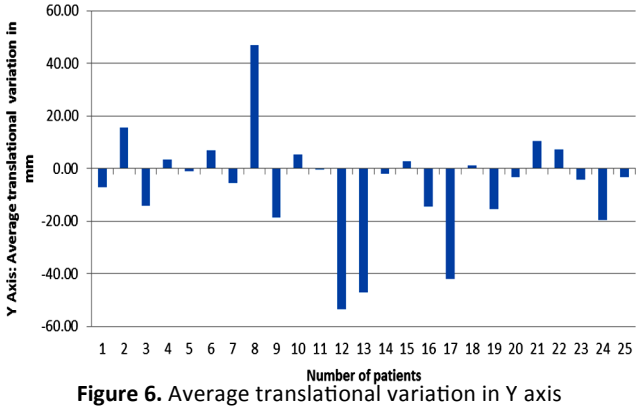

Figure 6. Average translational variation in Y axis

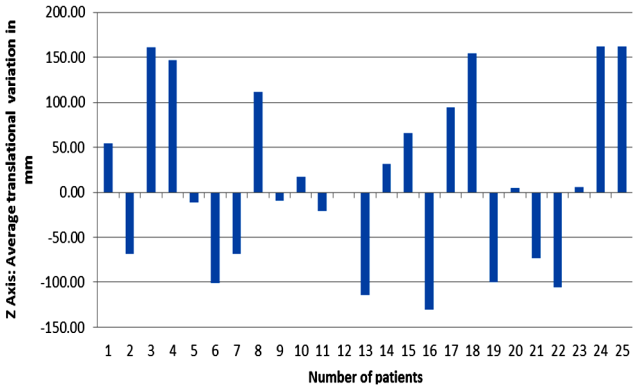

Figure 7. Average translational variation in Z axis

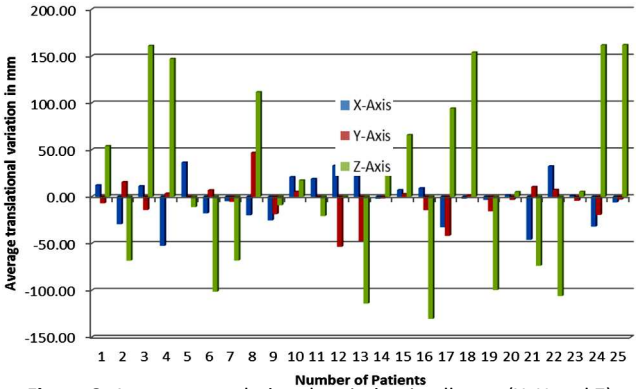

Figure 8. Average translational variation in all axes (X, Y and Z)

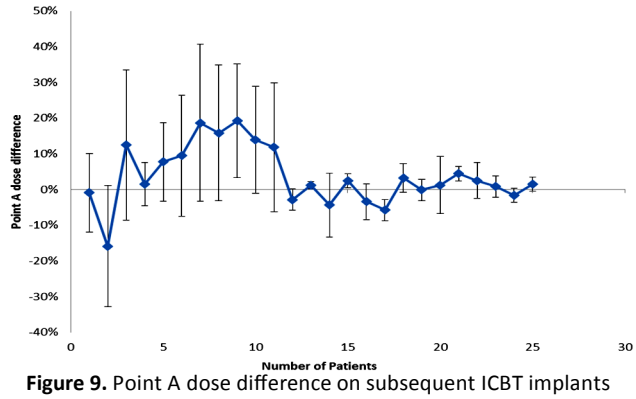

Figure 9. Point A dose difference on subsequent ICBT implants

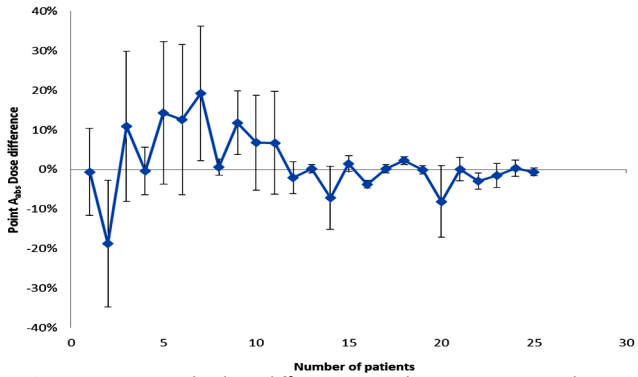

Figure 10. Point Aabs dose difference on subsequent ICBT implants

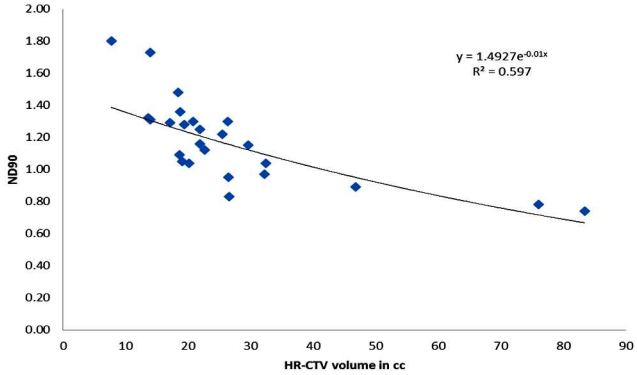

Figure 11. ND90 variation with HR-CTV volume

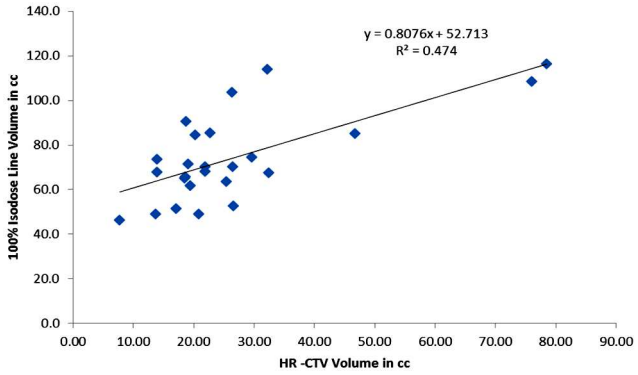

Figure 12. V100 volume variation with HR-CTV volume

[DOI: 10.18869/acadpub.ijrr.15.4.377]

DISCUSSION

Spatial and rotational variation of the applicator during HDR ICBT is quite common. Cause of such variations includes patient movement, applicator geometry during implant, organ movement and tumor regression during inter-fraction treatment.

Many of the authors have studied such variation in past utilizing orthogonal radiographs. Ebruli et *al.*[9] evaluated 8 patients to study applicator positional variability in HDR ICBT for tandem and ring applicators. Their results show standard deviation in application variability in the magnitude of 0.39 mm in mediolateral (x), 2.86 mm anteroposterior (y) and 3.83 mm in craniocaudal (z) direction.

Bahena *et al.* [10] evaluated 18 HDR tandem and ring patients to study interfraction geometric variation of the applicator and its impact on treatment. Their results show translational variation of the applicator for all cases 5.9 mm in right lateral direction (x), 7.7 mm in anterior-posterior direction (y) and 6.5 mm in superior-inferior direction (z) all with 1 standard deviation. The rotational variation was 3.4 degrees, 4.6 degrees and 6.0 degrees in patient's coronal, transverse and sagittal planes.

Datta *et al.* [11] evaluated 80 orthogonal radiographs from 20 consecutives patients of carcinoma cervix and concluded a significance differences (P<0.001) between insertions.

In conclusion, results of the study reveals that translational motion is higher than the rotational motions, and inter – fraction applicator variation does not produce any significant change in Point A doses. The change in volume coverage is observed only due to applicator motion. The positive correlation between 100% Isodose Line (IDL) and HR-CTV does not provide any valuable information because 100% Isodose Line (IDL) is the function of ovoid separation and the length of the intrauterine tube (central tandem). While negative correlation between ND90 and HR-CTV reveals that point A is a fixed geometric point, therefore, HR-CTV coverage decreases with increasing HR-CTV volume. Hence, dose prescription should be based on 3D HR-CTV volume.

***Conflicts of interest*:** *Declared none.*

REFERENCES

1. Klopp AH and Eifel PJ (2011) Chemoradiotherapy for cervical cancer in 2010. *Curr Oncol Rep,* ***13:*** *77-85*.
2. Monk B, Tewari K, Koh W (2007 Multimodality therapy for locally advanced cervical carcinoma: State of the art and future directions. *J Clin Oncol,*) ***25:*** *2952-65*.
3. Haie-Meder C, Potter R, Van Limbergen E, Briot E, De Brabandere M, Dimopoulos J, Dumas I, Hellebust TP, Kirisits C, Lang S, Muschitz S, Nevinson J, Nulens A, Petrow P, Wachlter-Gerstner N (2005) 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. *Radiotherapy and Oncology,* ***74:*** *235-245*.
4. Viswanathan AN and Thomadsen B (2012) American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part I: General principles. *Brachytherapy,* ***11:*** *33-46*.
5. Girinsky T, Rey A, Roche B, Haie C, Gerbaulet A, Randrianarivello H, Chassagne D (1993) Overall treatment time in advanced cervical carcinomas: A critical parameter in treatment outcome. *Int J Radiat Oncol Biol Phys,* ***27:*** *1051-1056*.
6. Perez CA, Grigsby PW, Castro-Vita H, Lockett MA (1995) Carcinoma of the uterine cervix. I. Impact of prolongation of overall treatment time and timing of brachytherapy on outcome of radiation therapy. *Int J Radiat Oncol Biol Phys,* ***32:*** *1275-1288*.
7. Petereit DG, Sarkaria JN, Chappell R, Fowler JF, Hartmann TJ, Kinsella TJ, Stitt JA, Thomadsen BR, Buchler DA (1995) The adverse effect of treatment prolongation in cervical carcinoma. *Int J Radiat Oncol Biol Phys,* ***32:*** *1301-1307*.
8. Lanciano RM, Pajak TF, Martz K, Hanks GE (1993) The influence of treatment time on outcome for squamous cell cancer of the uterine cervix treated with radiation: A patterns-of-care study. *Int J Radiat Oncol Biol Phys,* ***25:*** *391-397*.
9. Ebruli C, Demiral AN, Çetingöz R, Eyiler F, Kinay M *(*2007) The variability of applicator position among high dose rate intracavitary brachytherapy applications in cervical cancer patients treated with ring & tandem applicators. *Tumori,* ***93:*** *432–438*.
10. Bahena JH, Martinez A, Yan D, Mele E, Edmunson G, Brown D, Hardy M, Brabbins D, Gustafson G (1998) Spatial reproducibility of the ring and tandem high-dose rate cervix applicator. *Int J Radiat Oncol Biol Phys,* ***41:*** *13–19*.
11. Datta NR, Kumar S, Das KJ, Pandey CM, Halder S, Ayyagari S (2001) Variations of intracavitary applicator geometry during multiple HDR brachytherapy insertions in carcinoma cervix and its influence on reporting as per ICRU report 38. *Radiotherapy and Oncology,* **60:** *15–24*.

[DOI: 10.18869/acadpub.ijrr.15.4.377]