ORIGINAL ARTICLE

Comparison of Doses in Organs at Risk of Conventional and Three-Dimensional Treatment Planning in Hybrid Brachytherapy

Mohd Ramli FA[a], Abdullah R[a,b], Mohd Zahri AA[c], Chen SC[a,b]*

[a]Medical Radiation Programme, School of Health Sciences, Health Campus, Universiti Sains Malaysia, Kelantan, Malaysia.
[b]Hospital USM, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia.
[c]Advanced Medical and Dental Institute, Universiti Sains Malaysia, Bertam, Pulau Pinang, Malaysia.

ABSTRACT

INTRODUCTION: This retrospective study aims to evaluate the doses of organs at risk (OARs) calculated by conventional two-dimensional (2-D) and three-dimensional (3-D) treatment planning techniques in hybrid high dose rate (HDR) brachytherapy for cervical cancer. **MATERIALS AND METHODS:** Data of five patients treated with combination of intracavitary and interstitial brachytherapy were used. For each implant, computed tomography (CT) images were obtained, and the clinical target volume and OARs were contoured on CT images. In 3-D planning, the volumes of OARs were derived from dose -volume histogram (DVH) on a dose volume of 2 cc for bladder, rectum, and sigmoid. The OARs defined in replanning for 2-D treatment were the ICRU-38 bladder (bICRU) and rectum (rICRU) points. Paired T-tests were used to analyse the radiation doses of bladder and rectum obtained from both techniques. **RESULTS:** The mean point doses evaluated via bICRU) and rICRU were 89.34 GyEQD2 and 75.92 GyEQD2, respectively. Meanwhile, the mean volumetric doses of D_{2cc} for bladder and rectum were 80.50 GyEQD2 and 69.08 GyEQD2, respectively. There is a significant difference in mean doses of ICRU point and D_{2cc} volume for bladder ($p<0.05$). However, there is no significant difference in mean doses of ICRU point and D_{2cc} for rectum ($p>0.05$). Overall, ICRU point doses overestimated volumetric D_{2cc} doses with a mean dose ratio of 1.110 for bladder and 1.099 for rectum respectively. **CONCLUSION:** The bICRU in 2-D planning could not represent the bladder 2 cc used in 3-D planning, thus resulting in different total dose; whereas rICRU of 2-D planning was discovered to be similar with rectum 2 cc of 3-D planning and deemed reliable in total dose estimation

Keywords
conventional 2-dimensional, 3-dimensional, hybrid high dose rate brachytherapy, bladder, rectum

Corresponding Author
Chen Suk Chiang
Medical Radiation Programme, School of Health Sciences, Health Campus, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia.
Email: chensc@usm.my

Received: 3rd June 2021; Accepted: 2nd March 2022

Doi: https://doi.org/10.31436/imjm.v21i3

INTRODUCTION

Cervical cancer is the fourth most frequently diagnosed cancer in female and fourth leading cause of cancer death in women worldwide, with an estimated 570,000 new cases and 311,000 deaths in 2018 from Global Cancer Incidence, Mortality and Prevalence (GLOBOCAN).[1]

The Malaysian National Cancer Registry Report (2007–2011) reported that breast cancer (32.1%), colorectal (10.7%), cervix (7.7%), ovary (6.1%), and lung cancer (5.6%) were the five most common cancers among women.[2] In the newer version of Malaysian National Cancer Registry Report by Azizah et al. (2019), cancer of cervix uteri (6.2%) remained as the third most common cancer among Malaysian women from 2012 to 2016.[3]

In addition to external beam radiation, brachytherapy is often used as a primary treatment for cervical cancer. It can be classified into two categories: interstitial and intracavitary.[4] Traditionally, the two-dimensional (2-D) treatment planning is based on 2-D orthogonal X-ray imaging. The dose is prescribed to point A as the target based on the Manchester method[5], where the bladder and

rectum doses are quantified using the bladder and rectal reference points identified in Report No. 38 by the International Commission on Radiation Units and Measurement (ICRU).[6]

Presently, the three-dimensional (3-D) method uses dose-volume histogram (DVH) to evaluate the radiation doses calculated for organs. DVH provides the radiation dosage information in 3-D dose distribution. This histogram typically demonstrates the dosage of the total volume on the ordinate axis and the dose on the abscissa as a percentage.[7] The dose monitoring guidelines for 3-D image-based brachytherapy were issued by the Groupe Européen de Curiethérapie-European Society of Therapeutic Radiation Oncology (GEC-ESTRO) group. On consecutive CT slices, the target and organs at risk are contoured.[8]

Several types of applicators have been used in the treatment of cervical cancer. One example of the applicator used is the Vienna applicator. It allows for the combined interstitial and intracavitary technique brachytherapy or hybrid brachytherapy (HBT). When the applicator is placed within the patient body, the ring serves as a template for insertion of interstitial needles. The needles are inserted into the section of the tumour that receives inadequate doses via intracavitary brachytherapy. Because the short distance between the ring and the target allowed for greater control of needle positioning, an effective and reproducible insertion is achieved by using tandem and ring applicators with interstitial applicators,. [9]

MATERIALS AND METHODS

SELECTION OF PATIENT'S DATA

In this retrospective study, the dataset used consisted of 3 plans for each five selected patients (three fractions per patient) undergoing external beam radiation therapy (EBRT) accompanied by CT-guided hybrid HDR brachytherapy using Vienna applicator at the Advanced Medical and Dental Institute, Universiti Sains Malaysia (USM), from 2016 to 2019. For all five patients, the dose prescribed for 3-D planning was ranged 6–9.5 Gy per fraction for a total of three fractions, which received external beam radiotherapy (EBRT) of 1.8 Gy with 25 fractions to the whole pelvis before brachytherapy.[10] Patients with a history of hysterectomy, applied brachytherapy treatment other than the three fractions, and the use of only 2-D treatment planning were excluded from this study. This study had been approved by the Human Research Ethics Committee of USM (JEPeM-USM) effective 5 March 2019 for a duration of 1 year.

3-D TREATMENT PLANNING

The 3-D treatment planning used DVH in the calculation model of the Oncentra TPS (Nucletron B.V., Veenendaal, The Netherlands), which then optimised the organ and target radiation doses. The dose ranged from 6–9.5 Gy per fraction had been prescribed for each patient at the target volume. Clinical target volume (CTV), volume of the bladder, rectum, and sigmoid colon were delineated on CT images. [13] For OARs, according to GEC-ESTRO guidelines, the hot spot dose was recorded in 2 cm^3 (D_{2cc}) [8] and dosed to 90% to a target (D_{90}). Therefore, for all individual fractions, the dose was recorded for the irradiated 2 cc volume of rectum and bladder. Radiation doses at 2 cc bladder (bD_{2cc}) and 2 cc rectum (rD_{2cc}) volumes were then analysed and compared with point doses of bladder (bICRU) and rectal (rICRU) in 2D planning. The rectum and bladder dosage must be less than 80% of the recommended cervical dose, according to American Brachytherapy Society (ABS) recommendations. [7, 14] For each HDR brachytherapy plan, the conformal index (CI) was calculated using formula from the previous study, as shown in Equation 1.[15]

$$CI = CTV_{target}/V_{total} \quad (1)$$

where, CTV_{target} is part of the high-risk clinical target volume (HR-CTV) receiving at least the prescribed dose. V_{total} is defined as the total volume receiving at least the prescribed dose.

2-D TREATMENT PLANNING

The conventional 2-D treatment planning was carried out as recalculation using Oncentra TPS (Nucletron B.V.,

Veenendaal, The Netherlands) based on specific points on the patient's CT images. At point A, all five patients were given a dose of 6 to 9.5 Gy per fraction. Point A has been specified for the ring applicator at 2 cm perpendicular from the intrauterine tandem and 2.4 cm from the vaginal source plane. By using the ICRU 38 recommendation guidelines, reference points were introduced in the treatment plan to calculate ICRU bladder and rectal reference doses. [11] The lateral view of the ICRU rectal point was 0.50 cm from the posterior vaginal outline, while the ICRU bladder point was in the same view at 0.15 cm from the outer bladder wall. [12] In order to obtain the average value, two additional rectal and bladder points were also inserted at the slice above and below the source slice.

DOSIMETRIC ANALYSIS

The organ doses and mean doses for OARs (bladder and rectum) were calculated and evaluated with the dose limits recommended by ABS in total equi-effective dose (EQD2) for 3-D or 2-D treatment planning techniques. Sigmoid is only available in 3-D planning, hence, it is excluded from dosimetric comparison in this study. An EQD2 is used to determine the physical dose and number of fractions for brachytherapy and EBRT for target, OARs, and dose points. EQD2 is a total dose equivalent in a fraction of 2 Gy, calculated using the Excel spreadsheet of EQD2 recommended by ABS. The total EQD2 was determined using the linear quadratic method consisting of four steps: i) total EBRT EQD2; ii) brachytherapy EQD2 for each fraction; iii) total brachytherapy EQD2; and iv) accumulated total EBRT + brachytherapy EQD2.

Tumour or early-responsive tissue has the property of 10 Gy of irradiated tissue (α/β). In the case of late-responsive healthy tissues or OARs (rectum and bladder), the property of irradiated tissue (α/β) is 3 Gy. In adopting ABS recommended spreadsheet, the EQD2 formula is shown in Equation 2.

$$EQD2 = D \{d + (\alpha/\beta)/2\ Gy + (\alpha/\beta)\} \quad (2)$$

where, D is total dose, d is dose per fraction, and (α/β) is property of the irradiated tissue. In cervical cancer, the dose limit for bladder is 90 Gy EQD2; whereas for rectum or sigmoid, it is 75 Gy EQD2.

Paired T-test was used as a parametric test to compare the mean organ doses (EQD2) of two OARs obtained from 2 -D and 3-D treatment plans. A p value of less than 0.05 indicated the difference of mean organ dose is significant.

RESULTS

The doses to OARs as ICRU bladder and rectum points were recorded for 2-D treatment planning. The 2-D evaluations consisted of two approaches, which were ICRU bladder and rectum doses in Gy EQD2 and total doses for ICRU bladder and rectum in Gy. In this study, to fulfil the purpose for direct comparison with 3-D treatment planning, only organ doses in Gy EQD2 as tabulated in Table 1 will be evaluated. Table 1 shows the comparison of total doses calculated for bladder and rectum between ICRU point doses in 2-D planning and D_{2cc} volumetric doses in 3-D planning.

Table 1: Comparison of bladder and rectum total doses by using EQD2 and conformity index (CI) for 5 patients

EBRT + BT	Bladder Dose (Gy EQD2) *Dose limit: ≤ 90 Gy EQD2		Rectum Dose (Gy EQD2) *Dose limit: ≤ 75 Gy EQD2		Conformity Index (CI)
	bICRU	bladder D_{2cc}	rICRU	rectum D_{2cc}	
Patient 1	86.00	69.10	55.80	69.00	0.94
Patient 2	96.90	91.80	87.20	65.10	0.94
Patient 3	81.60	72.50	65.70	65.60	0.97
Patient 4	82.70	76.00	80.90	67.90	0.97
Patient 5	99.50	93.10	90.00	77.80	0.90
Maximum Dose	99.50	93.10	90.00	77.80	0.97
Minimum Dose	81.60	69.10	55.80	65.10	0.90
Mean Dose (SD)	89.34 (8.30)	80.50 (11.19)	75.92 (14.66)	69.08 (5.13)	0.94
Mean Dose Ratio (ICRU Point Dose/ Volumetric D_{2cc} Dose)	1.110		1.099		-

In 3-D treatment planning, dose assessment is based on D_{2cc} doses for OARs of bladder and rectum. Table 1 portrays the total doses (in Gy EQD2) bladder D_{2cc}, with dose constraints at 90 Gy EQD2 as a reference dose. Patient 2 and patient 5 received bladder doses that had exceeded the dose constraints, but the overall mean

bladder dosage for all patients was within the dose limits. The dose limit for rectum was 75 Gy EQD2. As shown in Table 1, rectum dose of patient no. 5 had exceeded the limit with 77.80 Gy EQD2. Overall, the mean total doses of rectum were still below the dose limits for all patients.

For recalculation in 2-D planning, again patient 2 and patient 5 who received the bladder dose that had exceeded the limit, but the overall mean bladder dose for these patients was still within the limit, with a value of 89.34 Gy EQD2, as tabulated in Table 1. For rectum, the doses of three out of five patients (patient 2, patient 4 and patient 5) exceeded the limit and thus, the mean of total rectum doses for the five patients reached 75.92 (14.66-) Gy EQD2.

In this study, the mean dose ratio (ICRU point dose/ volumetric D_{2cc} dose) was 1.110 and 1.099 for bladder and rectum respectively. Table 1 also shows each individual patient's conformity index (CI) for three fractions. The maximum and minimum values for CI are 0.97 and 0.90, respectively; and for all cases, the mean CI is 0.94. In this study, lower values of CI could indicate more organ doses exceeded dose limits. Overall, the mean ICRU point doses of bladder and rectum were found higher than the mean D_{2cc} dose, which acts as the mean volumetric doses of these two OARs.

Paired T-test was used as a parametric test to compare the mean organ doses of 2-D and 3-D treatment planning. There was a significant difference between 2-D and 3-D treatment planning for the bladder, but there was no significant difference for the rectum, as the p-value for the bladder was less than 0.05 ($p = 0.014$) and the p-value for the rectum was more than 0.05 ($p = 0.326$). Summary of doses to bladder and rectum are tabulated in Table 2 and Table 3 respectively.

Table 2: Summary of doses to bladder calculated based on bladder D_{2cc} and bICRU

Variables	Mean (SD)		t statistics (df)	p-value
	bladder D_{2cc}	bICRU		
Organ dose based on D_{2cc} volume of bladder and bICRU point	80.50 (11.19)	89.34 (8.30)	- 4.178 (4)	0.014

Table 3: Summary of doses to rectum calculated based on rectum D_{2cc} and rICRU

Variables	Mean (SD)		t statistics (df)	p-value
	rectum D_{2cc}	rICRU		
Organ dose based on D_{2cc} volume of rectum and rICRU point	69.08 (5.13)	(14.66)	- 1.120 (4)	0.326

DISCUSSION

In the 3-D treatment planning, Table 1 indicated two (40%) out of five patients had received a calculated bladder dose surpassing the ABS recommendation. This is because the size of the bladder is constantly changing during the filling while the remaining volume can also change during treatment. In this study, all patients had undergone three fractions of the brachytherapy to complete the treatment. However, the mean bladder dose for D_{2cc} was still below dose limit. One (20%) out of five patients had exceeded the rectum dose limit for D_{2cc}, but the mean rectum dose for all patients remained below the dose limit; the same result was also obtained by Tan *et al.* (2010) and Wibowo and Haris (2017).[7, 14] The rectum had a high dose due to the separation of rectum that was extremely close to the applicator, thus receiving higher dose. According to a report by Zhang *et al.* (2014), the nearer the separation between the organs and the source in the applicator, the greater the dose of radiation obtained by the organs. [17] Among the two OARs, the bladder had a higher rate (40%) of patients with total dose surpassing the recommended value, compared to the rectum (20%) in 3-D treatment planning.

In 2-D recalculation, the bladder and rectum ICRU points do not represent the entire volume of the organs. The total doses of ICRU bladder and rectum points in Gy EQD2 based on Table 1 showed that two (40%) and three (60%) patients have had their bladder and rectum doses exceeded the limit respectively. A possible explanation from a previous study is that in some cases, the ICRU points may lie outside the bladder and rectum. [16] The abovementioned finding could be attributable to the use of an interstitial catheter in place of the ring and tandem applicator or referred to as Vienna applicator. The locations of ICRU points (bladder and rectum) may be

too close to the interstitial catheters from which the sources come, leading to increased dose of the organs. However, the mean bladder dose of five patients is within the dose limit. Meanwhile, the mean rectum dose exceeded dose limit with a value of 75.92 Gy EQD2.

This study found that the D_{2cc} volumetric doses could be overestimated by ICRU reference points for bladder and rectum. There was a statistically significant difference in total dose to the bladder when using bICRU and D_{2cc} ($p = 0.014$; $p < 0.05$) (Table 2). The mean dose ratio (bICRU point dose/volumetric bladder D_{2cc} dose) obtained is 1.110 (Table 1). Previous studies by Tan *et al.* (2010) and Chottaweesak *et al.* (2014) concluded that dose of bICRU was statistically significantly lower than bladder D_{2cc}. [12, 14] In this study, the dose of bICRU was found higher but did not accurately represent the dose to 2cc volume of bladder, considering it was not a reliable parameter to be used as a criterion in 3-D treatment planning. This is most probably because when the bladder was filled with urine, it was able to affect the radiation dose because it expanded and pushed the applicator away from the surrounding organs. Thus, the radiation dose of bladder volume changed when the bladder is empty.[7]

Results in Table 3 revealed that ICRU and D_{2cc} doses of rectum were not significantly different ($p = 0.326$; $p > 0.05$). The mean dose ratio (rICRU point dose/volumetric rectum D_{2cc} dose) is 1.099 (Table 1). The findings showed a similar pattern, according to Kirisits *et al.* (2006) and Koom *et al.* (2007), where rICRU overestimated rectum D_{2cc}, but the difference was not significant.[18,19] The variation of rectal doses may be affected by some factors such as the technique used to define ICRU rectum and accuracy of organ contour. Therefore, rICRU can be used to calculate the total rectum dose and interpreted as D_{2cc} in 3-D treatment planning.

A hybrid intracavitary-interstitial applicator was utilised for this work, and previous reports have also shown that this approach allows for an improvement in target coverage, treatment volume, and total dose without increasing the dose of organs at risk. [11, 18, 20, 21] Therefore, the conformity index (CI) for all patients has a CI approach value of 1, as demonstrated in Table 1. The results of this study showed the target volume has an ideal dose coverage or high uniformity of radiation dose. However, this study revealed that when the CI values were slightly lower, more organ doses could exceed the dose limits. In this study, a safety risk was revealed when two patients exceeded the dose limits of bladder when bladder dose was calculated using bICRU and D_{2cc} bladder, while three patients exceeded rectum dose limit when rectum dose was calculated using rICRU. If 3-D planning is not in place, 2-D treatment planning may overestimate OAR doses in hybrid HDR brachytherapy, necessitating further care.

CONCLUSION

This study aimed to evaluate doses to organs at risk between two-dimensional and three-dimensional treatment planning in hybrid HDR brachytherapy of cervical cancer. The results of this study indicated that the ICRU reference point doses for bladder (bICRU) and rectum (rICRU) had overestimated D_{2cc} volume doses with a mean dose ratio (bICRU dose/volumetric bladder D_{2cc} dose) of 1.110 for bladder and (rICRU dose/ volumetric rectum D_{2cc} dose) of 1.099 for rectum. For bladder, the finding is statistically significant ($p < 0.05$); while for rectum, there is no statistical significance ($p > 0.05$) when comparing both above mentioned treatment planning techniques. In conclusion, bICRU cannot be used to represent a 2 cc bladder in 3-D treatment planning dosage calculations. In 3-D treatment planning for hybrid HDR brachytherapy, instead of utilising the 2 cc rectum, rICRU can be used to compute the total rectum dosage. This study also found that 2-D treatment planning may overestimate OAR doses in hybrid HDR brachytherapy, demanding further care based on individual patient OAR dosage evaluation.

ACKNOWLEDGEMENT

This work is supported by Bridging Incentive Grant (Grant no. 304.PPSK.6316461) from Universiti Sains Malaysia (USM). The authors thank the Director of Advanced Medical and Dental Institute (AMDI), Universiti Sains Malaysia, Kepala Batas, Pulau Pinang, Malaysia, for granting permission to use patients' medical

data and assets belonging to the institute during the process of conducting this research.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre, LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA-Cancer J Clin 2018; 68:394-424. Available at: https://doi.org/10.3322/caac.21492
2. Azizah AM, Hashimah B, Nirmal K, et al. Malaysia National Cancer Registry Report 2012-2016. Putrajaya: National Cancer Institute, Ministry of Health Malaysia; 2019 June. Report no: MOH/P/IKN/05.19(AR). Available at: http://nci.moh.gov.my/index.php/ms/main-menu-2/laporan
3. Suntharalingam N, Podgorsak EB, Tölli H. Brachytherapy: physical and clinical aspects. In: Podgorsak EB, Radiation Oncology Physics: A Handbook for Teachers and Students. Vienna: International Atomic Energy Agency, 2005: 451-484.
4. Derks K, Steenhuijsen JL, van den Berg HA, Houterman S, Cnossen J, van Haaren P, De Jaeger K. Impact of brachytherapy technique (2D versus 3D) on outcome following radiotherapy of cervical cancer. J Contemp Brachyther 2018; 10:17-25. Available at: https://doi.org/10.5114/jcb.2018.73955
5. Rangarajan R, Subramanian S, Gopalakrishnan K. Comparison between DVH-based doses and ICRU point-based doses to the rectum and the bladder using CT-based high-dose rate brachytherapy to the cervix. Med Dosim 2018; 43:276-283. Available at: https://doi.org/10.1016/j.meddos.2017.10.005
6. Wibowo RA, Haris B. Dose evaluation of organs at risk (OAR) cervical cancer using dose-volume histogram (DVH) on brachytherapy. *J Phys: Conf* Ser 2017; 853. Available at: doi: 10.1088/1742-6596/853/1/012013
7. Pötter R, Haie-Meder C, Van Limbergen E, Barillot I, De Brabandere M, Dimopoulos J, Dumas I, Erickson B, Lang S, Nulens A. Recommendations from gynaecological (GYN) GEC ESTRO working group (II): concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy—3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. Radiother Oncol 2006; 78:67-77. Available at: https://doi.org/10.1016/j.radonc.2005.11.014
8. Viswanathan AN, Beriwal S, Jennifer F, Demanes DJ, Gaffney D, Hansen J, Jones E, Kirisits C, Thomadsen B, Erickson B. American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part II: high-dose-rate brachytherapy. Brachytherapy 2012; 11:47-52. Available at: doi: 10.1016/j.brachy.2011.07.002
9. Han DY, Webster MJ, Scanderbeg DJ, et Al. irection modulated brachytherapy high-dose-rate treatment of cervical cancer. I: Theoretical design. Int J Radiat Oncol Biol Phys 2014; 89:666-673. Available at: https://doi.org/10.1016/j.ijrobp.2014.02.039
10. Yaparpalvi R, Mutyala S, Gorla GR, Butler J, Mah D, Garg MK, Kalnicki S. Point vs. volumetric bladder and rectal doses in combined intracavitary-interstitial high-dose-rate brachytherapy: correlation and comparison with published Vienna applicator data. Brachytherapy 2008; 7: 336-342. Available at: https://doi.org/10.1016/j.brachy.2008.05.005
11. Chottaweesak P, Shotelersuk K, Amornvichet N, Khorprasert C, Oonsiri P. Comparison of bladder and rectal doses between conventional 2D and 3D brachytherapy treatment planning in cervical cancer. Biomed Imaging Interv J 2014; 10:1-7. Available at: doi: 10.2349/biij.10.1.e2
12. Gao M, Albuquerque K, Chi A, Rusu I. 3D CT-based volumetric dose assessment of 2D plans using GEC-ESTRO guidelines for cervical cancer brachytherapy. Brachytherapy 2010; 9:55-60. Available at: https://doi.org/10.1016/j.brachy.2009.05.004
13. Tan YI, Choo BA, Lee KM. 2D to 3D evaluation of organs at risk doses in intracavitary brachytherapy for cervical cancer. J Contemp Brachyther 2010; 2:37-43. Available at: doi: 10.5114/jcb.2010.13721
14. Liu Z, Liang H, Wang X, Yang H, Deng Y, Luo T, Yang C, Lu M, Fu Q, Zhu X. Comparison of graphical optimization or IPSA for improving brachytheraphy plans associated with inadequate target coverage for cervical cancer. Sci Rep 2017;

7:16423. Available at: doi: 10.1038/s41598-017-16756-w
15. Patil V, Patel F, Chakraborty S, Oinam A, Sharma S. Can point doses predict volumetric dose to rectum and bladder: a CT-based planning study in high dose rate intracavitary brachytherapy of cervical carcinoma? Br J Radiol 2011; 84:441-448. Available at: doi: 10.1259/bjr/33758793
16. Zhang W, Bhatia SK, Sun W, Modrick JM, Kim Y. Bladder and rectum dose estimations on digitized radiographs for vaginal brachytherapy after hysterectomy. J Appl Clin Med Phys 2014; 15:240-246. Available at: doi: 10.1120/jacmp.v15i6.5033
17. Kirisits C, Lang S, Dimopoulos J, Berger D, Georg D, Pötter R. The Vienna applicator for combined intracavitary and interstitial brachytherapy of cervical cancer: design, application, treatment planning, and dosimetric results. Int J of Radiat Oncol 2006; 65:624-630. Available at: https://doi.org/10.1016/j.ijrobp.2006.01.036
18. Koom WS, Sohn DK, Kim JY, Kim JW, Shin KH, Yoon SM, Kim DY, Yoon M, Shin D, Park, SY. Computed tomography-based high-dose-rate intracavitary brachytherapy for uterine cervical cancer: preliminary demonstration of correlation between dose–volume parameters and rectal mucosal changes observed by flexible sigmoidoscopy. Int J of Radiat Oncol 2007; 68:1446-1454. Available at: https://doi.org/10.1016/j.ijrobp.2007.02.009
19. Dimopoulos JC, Kirisits C, Petric P, Georg P, Lang S, Berger D, Pötter R. The Vienna applicator for combined intracavitary and interstitial brachytherapy of cervical cancer: clinical feasibility and preliminary results. Int J of Radiat Oncol 2006; 66:83-90. Available at: https://doi.org/10.1016/j.ijrobp.2006.04.041
20. Walter F, Maihöfer C, Schüttrumpf L, Well J, Burges A, Ertl-Wagner B, Mahner S, Belka C, Gallwas J, Corradini S. Combined intracavitary and interstitial brachytherapy of cervical cancer using the novel hybrid applicator Venezia: clinical feasibility and initial results. Brachytherapy 2018; 17:775-781. Available at: doi: 10.1016/j.brachy.2018.05.009