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Evaluation of Organ at Risk (OAR) Doses based on 2D Treatment Planning in Intracavitary Brachytherapy of Cervical Cancer

(Penilaian Dos Organ Berisiko berdasarkan Perancangan Rawatan 2 Dimensi Brakiterapi Intrarongga bagi Kanser Servik)

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ABSTRACT

Conventional two-dimensional (2D) treatment planning of intracavitary brachytherapy is still a common practice at the radiotherapy center. The purpose of this study was to evaluate the organ at risk (OAR) doses estimated based on International Commission on Radiation Units and Measurements (ICRU) reference-point in patients with cervical cancer treated with high-dose-rate (HDR) intracavitary brachytherapy (ICBT). Between January 2010 and April 2014, 21 cervical cancer patients were treated with 42 fractions of brachytherapy using tandem and ovoids and underwent post-implant two-dimensional (2D) radiograph scans. HDR brachytherapy was delivered to a dose of 18 Gy in two fractions. Using the Oncentra brachytherapy treatment planning system (BTSP) software version 4.1 (Nucletron, Netherlands), the bladder and rectum points were retrospectively reconstructed based on 42 orthogonal radiographs datasets. The ICRU bladder and rectum point doses were recorded. As for results, the mean percentage dose of rectum and bladder for selected patients treated with intracavitary brachytherapy treatment (ICBT) were 47.27 and 75.59%, respectively. Combinations of ovoid's size, length of tandem and anatomy variation between each patient were factors that affected the dose to the OAR. Therefore, the ICRU reference points can still be used with the 2D brachytherapy treatment planning in evaluating the OAR doses.

Keywords: International Commission on Radiation Units and Measurements (ICRU) reference points; intracavitary brachytherapy treatment (ICBT); organ at risk (OAR) doses; two-dimensional (2D) treatment planning

ABSTRAK

Perancangan konvensional dua dimensi (2D) rawatan brakiterapi intrarongga masih merupakan amalan biasa di sesetengah pusat radioterapi. Tujuan kajian retrospektif ini dijalankan adalah untuk menilai dos pada organ berisiko (OAR) berdasarkan syor oleh Suruhanjaya Antarabangsa mengenai Unit Sinaran dan Pengukuran (ICRU) pada pesakit dengan kanser serviks dirawat dengan dos berkadar tinggi (HDR) brakiterapi intrarongga (ICBT). Antara Januari 2010 dan April 2014, 21 pesakit kanser serviks telah dirawat dengan 42 pecahan brakiterapi menggunakan tandem dan ovoid serta menjalani imbasan dua dimensi (2D) radiografi pasca-implan. Dos rawatan HDR brakiterapi yang digunakan adalah sebanyak 18 Gy dalam dua fraksi. Menggunakan perancangan rawatan brakiterapi Oncentra perisian 4.1 (Nucletron, Netherlands), titik pundi kencing dan rektum telah ditandakan semula pada 42 radiografi ortogonal dalam kajian retrospektif ini. Hasil kajian menunjukkan peratusan dos purata rektum dan pundi kencing bagi pesakit dipilih dirawat dengan ICBT masing-masing 47.27 dan 75.59%. Kombinasi saiz ovoid, panjang tandem dan anatomi yang berbeza antara pesakit merupakan beberapa faktor yang memberi kesan dos terhadap OAR. Oleh itu, titik rujukan ICRU dalam 2D perancangan rawatan brakiterapi masih boleh digunakan untuk menganggar dos OAR.

Kata kunci: Dos pada organ berisiko (OAR); mata rujukan Suruhanjaya Antarabangsa mengenai Unit Sinaran dan Pengukuran (ICRU); perancangan rawatan dua dimensi (2D); rawatan brakiterapi intrarongga (ICBT)

INTRODUCTION

According to the National Cancer Registry Report (2002), cervix uteri cancer is the second most common form of cancer that strikes Malaysian women. Furthermore, it is the fourth most common cause of death among Malaysian women. It is uncommon before the age of 30 years old; the risk of developing it increases with age, with a peak incidence at ages 60 to 69 years old and declining thereafter. In 2006, there were 19 radiotherapy and oncology centers

in this country comprising 5 public hospitals and 14 private centers (Lim 2006). These centers provided radiotherapy treatment facilities that consist of 25 linear accelerators, 7 cobalt-60 teletherapy machines, 15 brachytherapy units, 11 simulators and 4 computed tomography (CT) simulation units to the whole nation.

Brachytherapy treatment is delivered after cervical cancer patient completed external beam radiotherapy treatment (EBRT) to enhance the dose to the tumour

while sparing the surrounding healthy tissue. In some cancer center that do not have computed tomography (CT) simulator, orthogonal radiographs are taken using conventional simulator and planned with two-dimensional (2D) treatment planning, which is a common practice for intracavitary brachytherapy treatment. For ICBT, the dose was prescribed to point A. Point A as recommended by Manchester system was originally defined as 2 cm superior to the lateral vaginal fornix and 2 cm lateral to the cervical canal (Khan 2010). The duration of the treatment is based on the dose rate calculated at point A, although the dose at the other points is taken into consideration in evaluating a treatment plan. With the availability of the treatment-planning computers, most users of the Manchester system examine the isodose distributions in the frontal and sagittal planes in addition to obtaining dose at point A and at the same time dose to OAR such as bladder and rectum.

Meanwhile, the most frequent clinical complications of the treatments result from a high dose delivered to portions of the rectum and bladder that are in close proximity to the irradiation area. Applicator placement in intracavitary brachytherapy is very important in order to keep the dose received by these critical organs as low as possible. Therefore the dose received by these two organs must be evaluated in order to avoid complications. Bladder and rectum point doses can be estimated using recommendation by ICRU report No. 38 (1985) reference points for 2D planning. The simplicity and cost-effectiveness of radiograph-based 2D planning has ensured its continued applicability for dose reporting in brachytherapy (Patil et al. 2011). Thus, the purpose of this study was to evaluate organ at risk (OAR) doses estimated based on International Commission on Radiation Units and Measurements (ICRU) reference-point in patients with cervical cancer treated with high-dose-rate (HDR) intracavitary brachytherapy (ICBT).

MATERIALS AND METHODS

This is a retrospective study of 21 cervical cancer patients who underwent radical radiotherapy treatment in Hospital Universiti Sains Malaysia (Hospital USM). Twenty one cancer patients (age, 41-71 years old) with the International Federation of Gynecology and Obstetrics (FIGO) stage of IIB to IVA treated between January 2010 and April 2014 were selected in this study. All patients underwent external beam radiotherapy followed by. All selected patients were treated with a standard treatment for cervical cancer consists of external beam radiotherapy (EBRT) and followed with digital orthogonal radiographs based HDR intracavitary brachytherapy. Either anterior-posterior (AP) parallel opposed or four-field box beams (depend on the patient's body separation) was used for EBRT in treating cervical area. 45 Gy were prescribed to the midplane of the patient's body and delivered in 20 to 25 fractions of EBRT in 4 or 5 weeks. After the EBRT treatment, these patients underwent 2 fractions of HDR brachytherapy treatment once a week. 9 Gy was prescribed for each fraction of the treatment. The

dose was prescribed at point A as recommended by the Manchester system. Two types of applicator combinations commonly used for intracavitary brachytherapy are Fletcher-Williamson applicator set (consist of a tandem and a pair of ovoid) and a ring applicator set (consist of a ring and a tandem applicators) as illustrated in Figures 1 and 2. Fletcher-suit type of applicators (Nucletron, Netherlands) is a pair of ovoids and the diameters of 15, 20 and 25 mm are commonly used. Meanwhile, Williamson type of applicator (Nucletron, Netherlands) is a tandem applicator with 3 different angles of 15, 30 and 45°. For the ring applicator set, 2 diameter sizes that are commonly used which are 2.6 and 3.2 cm and combined with 45° angle of a tandem applicator. The Ir-192 source was used as a radiation source for high-dose-rate (HDR) brachytherapy microSelectron remote afterloader treatment unit (Nucletron, Netherlands).

INTRACAVITARY BRACHYTHERAPY

Each application was performed under spinal anaesthesia in the lithotomy position. Foley balloon was inserted to the patient's body and filled with 7 cc of potassium iodide (KI) diluted in normal saline. Then, it was pulled down to be seated on the bladder trigone. Rectal probe is also inserted to the patient's body and placed in the rectum. The selections of the applicator set applied to patient were chosen according to the suitability of patient's anatomical structures. Packing procedure was conducted during insertion of applicators to avoid any shifts or changes in the geometry of the applicators position and at the same time prevent the relocation of rectum and bladder. The OAR markers and applicators were checked to position the probe at the right place before patients moved to the simulation room.

For simulation procedures, x-ray markers or dummies were inserted through the applicator's cavity. The markers are function to visualize the image of each applicator on the radiographs and source loading positions in treatment planning. Anterior-posterior (AP) and lateral view (orthogonal radiographs) of the patients were taken using Simulix digital simulator (Nucletron, Netherlands). The radiographs taken should clearly visualize the bony structures of pelvic region, dummies inside each applicator and OAR markers. The radiographs were stored in the simulator workstation. In this study, orthogonal radiographs of selected patients were exported to the treatment planning system workstation in digital imaging and communications in medicine (DICOM) files through local area network (LAN).

Based on the radiograph images of dummy inside each applicators, the source positions, OAR reference points and each applicators were then retrospectively reconstructed using Oncentra Brachytherapy Treatment Planning System (BTPS) Software Version 4.1 (Nucletron, Netherlands). Sources positions through the applicator were planned accordingly to cover the targeted area. 9 Gy was prescribed to point A and then the calculation algorithm calculated the



FIGURE 1. Fletcher-Williamson applicator set



FIGURE 2. Ring applicator set

dose (Figure 3). The ICRU bladder and rectum point doses were recorded. The mean percentage of OAR doses were calculated using the following formula:

As example for mean percentage of bladder dose (Rb) for both fractions of ICBT, where $f1$ was first fraction and $f2$ was second fraction.

$$Rb = \frac{[(b1f1+b2f1+b3f1)/3]+[(b1f2+b1f2+b3f2)/3]}{2}. \quad (1)$$

The same formula was applied for calculating the mean percentage dose for rectum. As a standard department practice, the dose to bladder and rectum should not exceed 80 and 60% of dose to point A, respectively, in order to keep the dose to the both organs less than their tolerance dose (less than 60 Gy for bladder and less than 50 Gy for rectum) (Figure 4).

RESULTS AND DISCUSSION

Figure 5 shows the comparison of bladder doses for each fraction of ICBT for 21 selected patients. 52.4% exceeded

80% of dose to point A for the first fraction (11 out of 21 plans) and reduced to 27.6% (6 out of 21 plans) for the second fraction. Figure 6 shows the comparison of rectum doses for each fraction of ICBT for 21 selected patients. 19.0% (4 out of 21 plans) exceeded 60% of dose to point A for the first fraction and reduced to 14.3 % for the second fraction. Table 1 shows that 6 out of 21 plans (28.6%) exceeded the standard department practice for bladder for both fractions and only 4 plans (19%) exceeded the standard department practice for rectum dose for both fractions. Generally, the dose to the OAR for either bladder or rectum of fraction 1 was higher compared with fraction 2. As applicator is a rigid device, it was a challenge in order to repack to adjust the insertion after the patients went out from the operation theater as all procedures were performed under conscious sedation. Then for the next fraction of treatment, the oncologist was aware and made some adjustment for the insertion procedure to reduce dose to OAR.

There are several factors that affected doses to OAR in brachytherapy treatment. Dose to the rectum and bladder depends upon the patient's anatomy, disease extent, applicator design, technical details of the insertion and

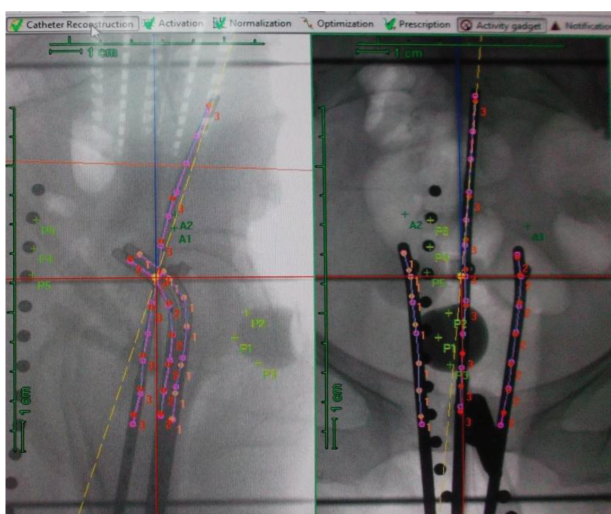


FIGURE 3. Reconstructions of applicators and identification of OARs points and point A

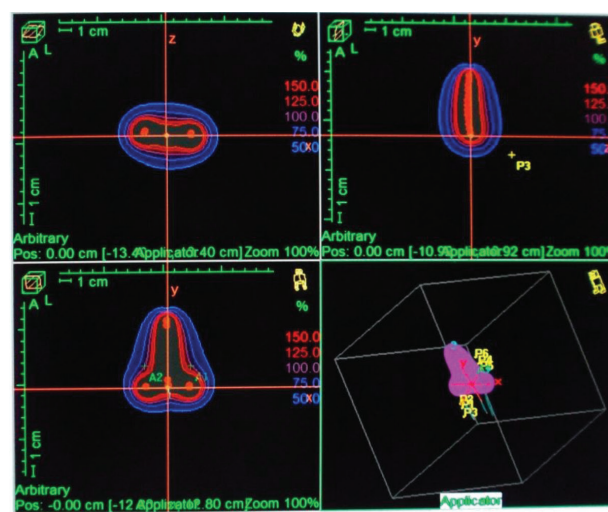


FIGURE 4. Dose distribution calculated by Oncentra brachytherapy treatment planning software

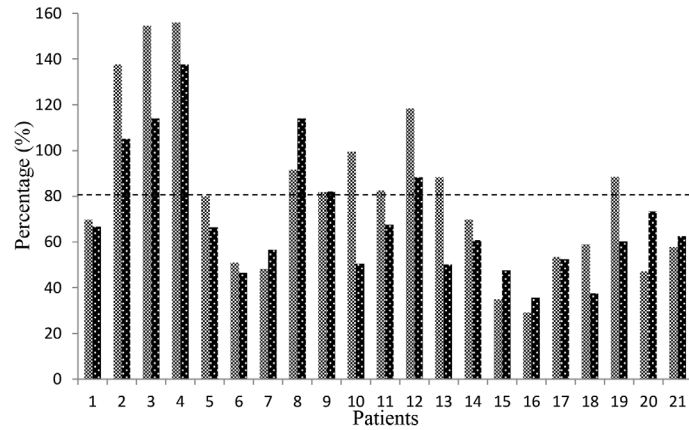


FIGURE 5. Percentage of bladder dose to point A for each patient of ICBT; (▨): Fraction 1 and (■): Fraction 2; patient 1-17 used Fletcher-Williamson, patient 18-19 used ring and patient 20-21 used Fletcher-Williamson (fraction 1) and ring applicators (fraction 2)

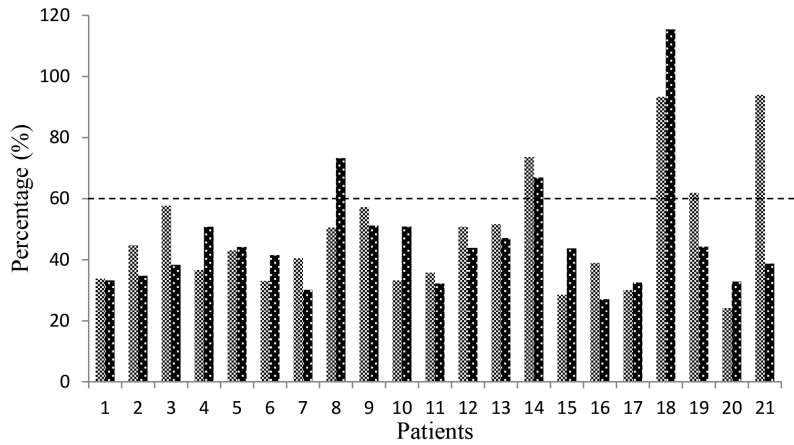


FIGURE 6. Percentage of rectum dose to point A for each patient of ICBT; (▨): Fraction 1 and (■): Fraction 2; patient 1-17 used Fletcher-Williamson, patient 18-19 used ring and patient 20-21 used Fletcher-Williamson (fraction 1) and ring applicators (fraction 2)

TABLE 1. Number of patients with the total OARs exceeding standard department practice

	Bladder	Rectum
Number of patients ($n = 21$)	6/21	4/21
Percentage (%)	28.6	19.0

*Bladder doses < 80% of dose for point A * Rectum doses < 60% of dose for point A

accuracy in reconstruction procedures. Since there are anatomy variations between each patient, it will affect the dose of bladder and rectum (Hunter et al. 2001). This is because to the distance between cervix to rectum or cervix to bladder depends on the individual's anatomy and it is different for each patient. The distance between the posterior bladder wall and the active sources is also an important factor affecting the bladder dose in brachytherapy, which is different for each individual patient. Bladder distention may change this distance due to the increase of bladder volume. The bladder distention

is also different in each individual patient, whether the patients are advised to empty the bladder before insertion procedures are carried out to minimize the bladder volume. Besides, an applicator is also one of the contributors to the variation in doses to OARs. An applicator is a rigid device and made of stainless steel. It is inserted into the patients' vaginal and uterine cavities, with sufficient packing around the applicator. The applicator set consists of combination of a pair of ovoid and a tandem. The size of ovoid and the length of tandem applied for ICBT are the major factors that affect the dose to the organ at risks. The size of

ovoid represents the diameter of the ovoid and the dose is more uniform as the diameter of the ovoid increases. More scattered photons that attenuated within the ovoid materials lost its energy to reach point A (prescription point). Thus, only primary photons are distributed to the prescription point and at the same time less dose to the bladder and rectum. Most of the patients treated in this study have ovoid's size of 1.5 cm diameter (13 out of 21) and the number of patients surpassed 80 and 60% of the prescribed dose at point A for bladder and rectum, respectively, were 6 out of 21 for bladder and only 1 out of 21 for rectum. It shows that ovoid with smaller size is unable to filter scattered photon and gives higher dose to OARs. The lengths of tandem varied among the patients. The shortest was 3 cm while the longest length 6 cm. This was decided by the doctor based on the disease or stage of cancer. Most of the patients in this study were treated with tandem length ≤ 5 cm (14 out of 21) and the number of patients surpassed 80 and 60% of the prescribed dose at point A for bladder and rectum, respectively, were 5 out of 21 for bladder and 3 out of 21 for rectum. This shows that shorter tandems have a tendency to increase the doses of rectum and bladder.

Other than that, the technical details during the insertion of the applicator affect the variation of doses to OARs. The insertion of an applicator depends on the doctor's skills and experiences in handling the procedures. Inadequate packing may cause higher dose to OAR and it challenges the oncologist to place the applicator with adequate packing for each insertion and each individual patient. As all procedures were performed under conscious sedation, sufficient packing was difficult, as well as the patient's movement during the procedures. A gauze pack serves two purposes; it pushes the rectum and bladder away from the applicator and produces enough immobilization to the applicator *in situ*. Gauze packing is one of the factors affecting the dose to rectum and bladder (Garipagaoglu et al. 2006). Patient's movements also greatly affect the variation doses to bladder and rectum. Not only the

movements happened during the insertion procedures in the operation theater, but it could also happen while the patient was transferred to the couch for simulation procedures. Patient's movements in any intracavitary brachytherapy procedure can displace the applicators, especially the tandem. Anterior shifts are correlated with high bladder dose differences. Immobilization of the patient's hips and legs, as well as stabilization of applicators, would reduce these shifts (Pham et al. 1998).

The variations in OAR doses may also be the consequence of some factors such as the technique used to define prescription points (point A), the accuracy of rectum and bladder points' position, the image quality of orthogonal radiographs and accuracy of applicator reconstruction in 2D planning. It is difficult to mark the rectum and bladder points in AP radiograph and identify the rectum points because the image of rectum marker could be superimposed with bladder marker and dummies inside the applicators. The rectum position can be easily identified in lateral radiograph. In contrast, the bladder points are easily identified in AP radiograph and in some cases, it is difficult in lateral radiograph because the bladder image was cut off by field size collimation. In order to improve image quality, collimation of field size area must be sufficient. Then, it improved the orthogonal radiograph contrast for better visualization of smaller object images especially the dummies inside the applicators. The accuracy of reconstruction in 2D planning depends highly on the image of dummies identified in orthogonal radiographs. This is because the reconstructions of applicators based on the identification of dummies and the accuracy could be analyzed with reconstruction shift between AP and lateral radiographs. It would be difficult to identify the dummies in AP radiographs when its images were superimposed with images of bladder and rectum markers. In some cases, it was impossible to obtain clarity due to overlap of ovoid in lateral radiograph. The dummies inside the applicator were difficult to identify in lateral radiograph because of the thickness of pelvis's tissues.

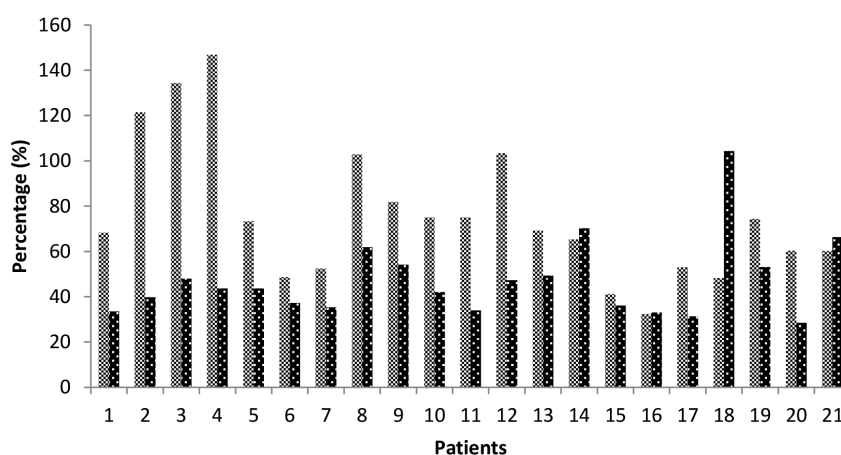


FIGURE 7. Mean percentages of bladder and rectum doses to point A for each patient of ICBT; (. . .): Bladder and (x x x): Rectum

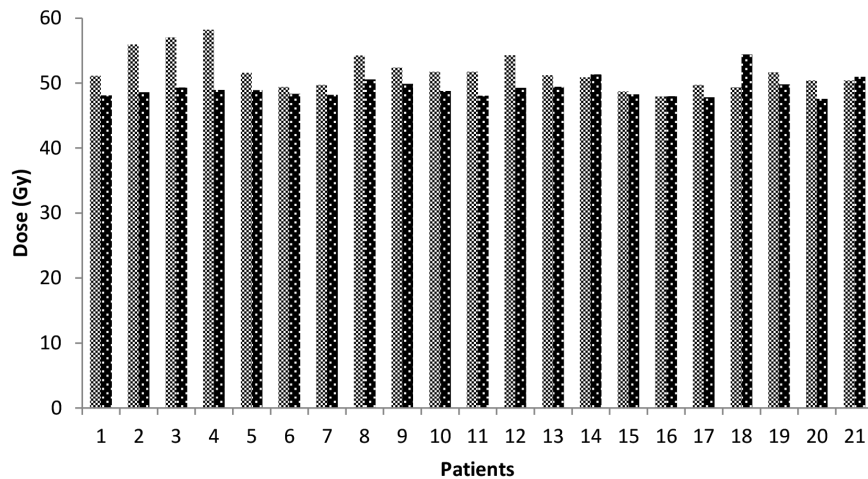


FIGURE 8. Bladder and rectum doses for each patient of both EBRT and ICBT treatments; (▨): Bladder and (■): Rectum

Figure 7 shows the mean percentages of bladder and rectum doses to point A for each patient of ICBT. The mean percentages of rectum and bladder doses of ICBT for 21 selected patients were 47.27 and 75.59%, respectively. Figure 8 shows the total dose to bladder and rectum, respectively, received by each individual patient from the external beam radiotherapy and brachytherapy treatments. For EBRT, all these 21 patients had received the dose of 45 Gy. The irradiation field included the pelvic area, therefore 45 Gy of dose also tended to receive by bladder and rectum. The results showed that the dose to bladder was still below the tolerance dose which is 60 Gy for each patient after receiving external beam radiotherapy and brachytherapy treatments. Besides, the dose tolerance for rectum should be less than 50 Gy and only 4 patients received the dose over the tolerance dose. The mean rectum and bladder total doses received by 21 selected patients from ICBT and EBRT were 49.26 and 51.8 Gy, respectively.

CONCLUSION

In this retrospective study, the results showed that the mean percentages of rectum and bladder doses of ICBT for 21 selected patients were 47.27 and 75.59%, respectively. We had observed that the doses to OAR differed between different applicator sets applied for ICBT. The dose to bladder and rectum were also various compared to the first fraction and the second fraction of treatment. The combinations of ovoid's size, the length of tandem and the anatomy variations between each patient were contributing factors that affects the dose to the OAR. In this study, the doses to OARs were below the tolerance dose of each OAR after receiving HDR intracavitary brachytherapy treatment. Thus, it is important to keep the dose to these organs as low as possible with guidance from reference document to avoid the late complication due to radiation side-effect. Therefore, the ICRU reference points can still be used the

2D brachytherapy treatment planning in evaluating the OAR doses.

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