Original article

A study on the variation of bladder and rectal doses with respiration in intracavitary brachytherapy for cervix cancer

Ramachandran Prabhakar, PhD, Pandjatcharam Jagadesan, MD, Kunhi P Haresh, MD, Singh Karuna, MD, Pramod Kumar Julka, MD, Prof., Goura Kishor Rath, MD, Prof.

Department of Radiation Oncology, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India

Abstract

Purpose: In cervical intracavitary brachytherapy, it is mandatory to evaluate if the doses to bladder and rectum are within tolerance limits. In this study, an effort has been made to evaluate the effect of respiration on the doses to bladder and rectum in patients undergoing brachytherapy.

Material and methods: Fifteen patients with cervix cancer treated with concurrent chemoradiation followed by intracavitary brachytherapy were included in this study. At the time of brachytherapy, all patients underwent 4D computed tomography (CT) imaging. Five out of fifteen patients were scanned with empty bladder while the rest had full bladder during sectional imaging. Four sets of pelvic CT image datasets with applicators in place were acquired at equal interval in a complete respiratory cycle. Treatment plans were generated for all the CT datasets on a Plato™ Sunrise planning system. A dose of 7 Gy was prescribed to Point A. Doses to ICRU (Report No.38) bladder (IBRP) and rectal (IRRP) reference points were calculated in all the CT datasets.

Results: The mean of maximum dose to IBRP at four different respiratory phases for full and empty bladder were 53.38 ± 19.20%, 55.75 ± 16.71%, 56.13 ± 17.70%, 57.50 ± 17.48% and 60.93 ± 15.18%, 60.29 ± 16.28%, 60.86 ± 15.90%, 60.82 ± 15.42% of the prescribed dose respectively. Similarly, maximum dose to IRRP for full and empty bladder were 55.50 ± 18.66%, 57.38 ± 14.81%, 58.00 ± 14.97%, 58.38 ± 17.28% and 71.96 ± 6.90%, 71.58 ± 7.52%, 68.92 ± 6.21%, 71.45 ± 7.16% respectively.

Conclusions: Our study shows that respiration affects the dose distribution to the bladder and rectum in intracavitary brachytherapy of cervix cancer. It is advisable to reduce the critical organ dose to account for the dose variation introduced by respiratory motion.

J Contemp Brachyther 2010; 2, 1: 24-27

Key words: brachytherapy, cervix cancer, bladder, rectum, respiration.

Purpose

Cervix cancer is one of the leading causes of cancer morbidity among women worldwide and it is the second most common cancer among women in developing countries [1]. Except for early stage, cancer cervix is usually treated with radiotherapy which consists of external beam radiotherapy followed by intracavitary brachytherapy. Bladder and rectum are the main organs at risk in the treatment of cervical intracavitary brachytherapy whose doses are ensured not to exceed the limits of tolerance. Several authors have shown that the dose distribution is affected by the geometry of the intracavitary applicators, age of patient [2], disease stage [2], length [2] and angulation of the tandem, size of the ovoids and tandem [2, 3], volume of bladder and rectum. Similarly dwell position of source [4], vaginal packing [5], balloon inflation technique [6, 7] and proximity of the applicator to the bladder and rectum do affect the dose to organs at risk. It is a well known fact that the abdominal and pelvic organs move during respiration and can therefore lead to changes in the dose to organs at risk. Although there are many studies related to critical organ dose variation with respect to the factors as stated above, there is no study which evaluates the possible dose alteration induced by respiration in intracavitary brachytherapy. In this study, an effort has been made to evaluate the effect of respiration on the doses to bladder and rectum for patients undergoing cervical intracavitary brachytherapy.

Material and methods

Fifteen cervix cancer patients of FIGO stage IIb-IIIb were included in this study. They were treated with external beam radiotherapy and concurrent chemotherapy followed

Address for correspondence: Ramachandran V Prabhakar, PhD, Department of Radiation Oncology, Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India, phone 91-9953935790, ✉ e-mail: prabhakar_smr@hotmail.com

Received: 27.12.09
Accepted: 16.03.10
Published: 28.03.10

by intracavitary brachytherapy. External beam radiotherapy was delivered to pelvis to a total dose of 50 Gy in two phases, 40 Gy in 22 fractions by four field box technique in first phase and 10 Gy in 5 fractions with midline shield in the second phase. Subsequently all of them were treated with high dose rate intracavitary brachytherapy to a total dose of 21 Gy delivered in three equal fractions at an interval of 1 week. During the procedure, a Foley catheter was inserted into the bladder and its balloon was filled with 7 cc of radio-opaque fluid (Omnipaque™). The insertion of intracavitary applicators was performed under general anaesthesia and in each application an intrauterine tandem was place inside the uterine cavity and the ovoids in the vagina at the level of fornices. Five patients were kept on continuous bladder drainage while the rest had their Foley's tube clamped to allow formation of full bladder. All the patients were scanned with Philips™ Brilliance Big Bore 16 slice CT scanner following intracavitary applicator insertion. The movement of the patient's chest was monitored using bellows during the scanning procedure. The respiratory bellows (Philips Medical Systems™, Cleveland, OH) was tied around the chest at thoraco-abdominal junction. As the belt gets stretched with every respiratory effort, the pressure transducer produces disturbance in electrical voltage which is displayed in the monitor as waveforms corresponding to different phases of respiration. Four sets of CT image datasets each of 3 mm slice thicknesses with applicator in place were acquired at different phases of a respiratory cycle. These CT datasets were transferred to the Plato™ treatment planning system. The brachytherapy applicators were reconstructed from the CT image datasets and treatment plans were generated for all the four CT datasets on the planning system. In each treatment session, a dose of 7 Gy was prescribed to point A. Doses to ICRU 38 bladder (IBRP) and rectal (IRRP) reference points were evaluated in all the four CT datasets [8]. Besides, another point was taken at the center of the foley's balloon chosen to represent the mean dose to the bladder (B_{mean}). Repeated mea-sures analysis was used to compare the differences in IBRP, IRRP and mean bladder dose in all the four respiratory phases.

Results

Figure 1A shows the topogram of a patient with intracavitary applicator and 1B displays the respiratory waveform displayed on the Philips 4D CT console. Table 1 shows the mean, range and median of the maximum dose to IBRP in all the four different respiratory states for full and empty bladder. Similarly, Table 2 shows the mean, range and median doses of the mean doses to the bladder for full and empty bladder. The maximum dose to the ICRU 38 rectal reference point in the four different respiratory phases is displayed in Table 3. The maximum observed variation in doses to IBRP for full and empty bladder among the four respiratory phases was 15% and 3% respectively. Similarly the maximum observed variation in doses to IRRP for full and empty bladder among the four respiratory phases was 12% and 8% respectively. The mean variation between the doses to full bladder at different phases of respiration is 4% whereas it is less than 1% with empty bladder. The dose to ICRU rectal reference point is within 3% for both full and empty bladder. No statistical significance was observed between different respiratory phases with IBRP, IRRP and B_{mean} for full and empty bladder condition.

Discussion

The doses to bladder and rectum are the major determining factor for late complications in intracavitary brachytherapy. There are several studies illustrating the

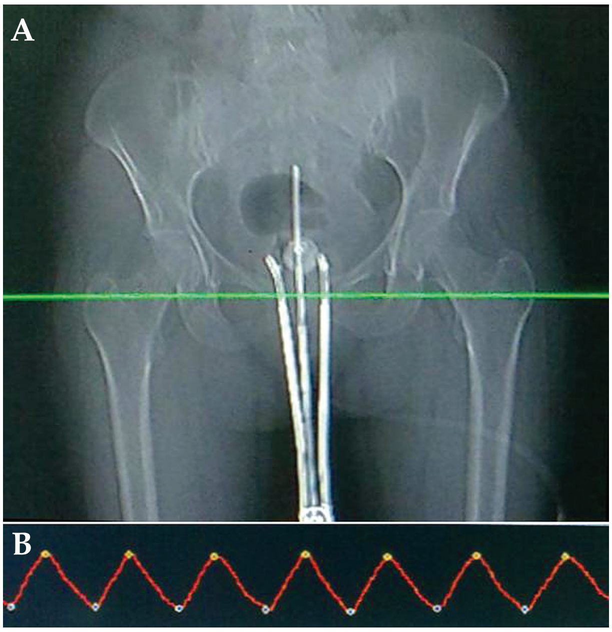

Fig. 1. A) Topogram of a patient with applicator, B) Respiratory waveform displayed on Philips 4D CT console

Table 1. Dose to ICRU bladder reference point (IBRP)

Max Bladder Dose	Mean ± StDev (%)		Range (%)		Median (%)	
	Full Bladder	Empty Bladder	Full Bladder	Empty Bladder	Full Bladder	Empty Bladder
Phase I (%)	53.38 ± 19.20	60.93 ± 15.18	24.00-78.00	34.38-72.15	51.5	67.19
Phase II (%)	55.75 ± 16.71	60.29 ± 16.28	24.00-74.00	32.67-74.76	59.5	65.43
Phase III (%)	56.13 ± 17.70	60.86 ± 15.90	24.00-73.00	33.2-71.36	58	67.5
Phase IV (%)	57.50 ± 17.48	60.82 ± 15.42	24.00-75.00	34.45-72.3	62.5	67.81

Table 2. Mean dose to bladder (B_{mean})

Mean Bladder Dose	Mean ± StDev (%)		Range (%)		Median (%)	
	Full Bladder	Empty Bladder	Full Bladder	Empty Bladder	Full Bladder	Empty Bladder
Phase I (%)	33.50 ± 12.84	37.52 ± 10.88	16.00-56.00	19.80-38.89	30.76	38.89
Phase II (%)	34.14 ± 11.10	37.90 ± 11.64	15.00-52.00	19.05-38.36	32.71	38.36
Phase III (%)	35.16 ± 12.39	37.56 ± 11.24	15.00-52.00	20.05-39.07	31.63	39.07
Phase IV (%)	35.36 ± 11.31	37.52 ± 11.26	15.00-51.00	19.07-39.85	35.5	39.85

Table 3. Dose to ICRU rectal reference point (IRRP)

Ractum Max Dose	Mean ± StDev (%)		Range (%)		Median (%)	
	Full Bladder	Empty Bladder	Full Bladder	Empty Bladder	Full Bladder	Empty Bladder
Phase I (%)	55.50 ± 18.66	71.96 ± 6.90	33.00-78.00	60.54-77.60	58.50	73.03
Phase II (%)	57.38 ± 14.81	71.58 ± 7.52	36.00-75.00	58.36-76.18	60.50	74.21
Phase III (%)	58.00 ± 14.97	68.92 ± 6.21	37.00-79.00	59.40-74.96	59.00	71.76
Phase IV (%)	58.38 ± 17.28	71.45 ± 7.16	34.00-81.00	59.73-77.24	59.00	74.88

different ways of reducing the dose to these organs at risk. Jain et al have demonstrated that proper vaginal packing and patient anatomy can minimize the dose to the bladder and rectum [5]. Haie-Meder *et al.* have shown that the bladder and rectal doses can be reduced by adjusting the dwell positions and relative dwell times of source positions [4]. Studies have also shown that inflating the balloon of a foley catheter significantly reduces the dose to rectum and bladder [6, 7]. Studies concerning organ motion in intracavitary brachytherapy are very scarce in literature. Taylor *et al.* quantified the displacement of points identified on the anterior uterine body, posterior cervix and upper vagina [9]. They found that rectal filling may affect cervical position, while bladder filling has more impact on uterine body position, highlighting the need for specific instructions on bladder and rectal filling for treatment. Chan *et al.* studied the internal movement of tumour, cervix, and uterus using serial cinematic magnetic resonance imaging scans and point-of-interest analysis [10]. The intra-scan motion was much smaller. Both inter- and intra-scan motion was greatest at the fundus of the uterus, less along the canal, and least at the cervical os. The isotropic internal target margins required to encompass 90% of the interscan motion were 4 cm at the fundus and 1.5 cm at the os. In contrast, smaller margins of 1 cm and 0.45 cm, respectively, were adequate to encompass the intrascan motion alone.

Currently 4D CT is being used extensively in imaging organs with evident internal movement. In many institutions, sectional imaging is replacing conventional 2D simulation in brachytherapy treatment planning. MRI guided 3D optimization significantly improved the target coverage while retaining the constraints to organs at risk [11-14]. In this study, we have used the 4D CT datasets to analyze the bladder and rectal dose at different respiratory phases. We noted that there is a difference between the doses to rectum and bladder at different phases of respiration. To the best of our knowledge, this is a unique study addressing the issue of organ motion with respiration in brachytherapy of cervix cancer.

In our practice, the intracavitary treatment plan based on point A prescription is finalized when the rectal and bladder doses are below the limits of tolerance. ICRU points are preferably chosen for treatment evaluation than the 3D volume DVH parameters to avoid the possible dosimetric errors introduced by organ contours in the latter method. In our study, the variation of dose distribution in bladder is more with full bladder than when it is empty. Filling status of bladder also affects the rectal dose variation.

An important observation from our study is that the dose to IBRP for those patients with full bladder was less as compared to those with empty bladder. This may be due to the fact that when the bladder is full, the foley's balloon falls farther from the applicator. The individual IBRP dose variation was of the order of 15% as compared to 3% for full and empty bladder respectively. This indicates that the foley's balloon get displaced with respiration when the bladder is distended but remain restricted in position in an empty bladder. The individual dose to IRRP for different respiratory phases with full bladder is 12% as compared to 8% with empty bladder condition.

Hence, the radiation oncologist could be advised to consider a possible variation in the doses to the bladder and rectum while planning intracavitary brachytherapy. This study has been performed according to ICRU bladder and rectal reference points. One of the limitations of this study is that the study has been performed with CT based brachytherapy whereas GEC-ESTRO recommends MRI based brachytherapy that enables accurate delineation of bladder and rectal volumes.

Conclusions

Our study shows that respiration affects the bladder and rectal doses in cervix cancer brachytherapy. The dose to IRRP was found to be affected with both full and empty bladder whereas the dose to IBRP was found to be affected more with full bladder than with empty bladder. Even though the mean variation in dose to bladder and rectum was within 4%, large individual dose difference was observed in some patients. Hence it is advisable to reduce the critical organ dose to account for the dose variation introduced by respiratory motion.

References

1. Shanta V, Krishnamurthi S, Gajalakshmi CK et al. Epidemiology of cancer of the cervix: global and national perspective. *J Indian Med Assoc* 2000; 98: 49-52.
2. Senkus-Konefka E, Kobierska A, Jassem J 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: 531-536.
3. Senkus-Konefka E, Kobierska A, Jassem J et al. Influence of brachytherapy applicators geometry on dose distribution in cervical cancer. *Strahlenther Onkol* 1997; 173: 323-329.
4. Haie-Meder C, Mazeron R, Verezesan O et al. Three-dimensional brachytherapy optimization techniques in the treatment of patients with cervix cancer. *Cancer Radiother* 2009; 13: 520-524.
5. Jain VS, Sarje MB, Singh KK et al. High-dose-rate-intracavitary brachytherapy applications and the difference in the bladder and rectum doses: a study from rural centre of Maharashatra, India. *J Cancer Res Ther* 2007; 3: 116-120.
6. Malaker K, Shukla V, D'Souza H et al. Minimizing urinary bladder radiation dose during brachytherapy for carcinoma of the cervix using balloon inflation technique. *Int J Radiat Oncol Biol Phys* 2005; 61: 257-266.
7. Eng TY, Fuller CD, Cavanaugh SX 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: 174-178.
8. ICRU Report 38. Dose and Volume Specification for Reporting Intracavitary Therapy in Gynecology. Bethesda: International commissioning on Radiation units and Measurements. 1985.
9. Taylor A, Powell ME. An assessment of interfractional uterine and cervical motion: implications for radiotherapy target volume definition in gynaecological cancer. *Radiother Oncol* 2008; 88: 250-257.
10. Chan P, Dinniwell R, Haider MA et al. Inter- and intrafractional tumor and organ movement in patients with cervical cancer undergoing radiotherapy: a cinematic-MRI point-of-interest study. *Int J Radiat Oncol Biol Phys* 2008; 70: 1507-1515.
11. De Brabandere M, Mousa AG, Nulens A et al. Potential of dose optimisation in MRI-based PDR brachytherapy of cervix carcinoma. *Radiother Oncol* 2008; 88: 217-226.
12. Kirisits C, Pötter R, Lang S et al. Dose and volume parameters for MRI-based treatment planning in intracavitary brachytherapy for cervical cancer. *Int J Radiat Oncol Biol Phys* 2005; 62: 901-911.
13. Lindegaard JC, Tanderup K, Nielsen SK et al. MRI-guided 3D optimization significantly improves DVH parameters of pulsed-dose-rate brachytherapy in locally advanced cervical cancer. *Int J Radiat Oncol Biol Phys* 2008; 71: 756-764.
14. Tanderup K, Nielsen SK, Nyvang GB et al. From point A to the sculpted pear: MR image guidance significantly improves tumour dose and sparing of organs at risk in brachytherapy of cervical cancer. *Radiother Oncol* 2010; 94: 173-180.