

Body mass index versus bladder and rectal doses using 2D planning for patients with carcinoma of the cervix undergoing HDR brachytherapy

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Original Article

Abstract

Purpose: To assess bladder and rectum doses in relation to body mass index of patients undergoing high dose rate brachytherapy for the treatment of carcinoma of the cervix. **Methods:** The cohort consists of fifty subjects with carcinoma of the uterine cervix presented with grade II and III. Patient's height and weight was measured before the insertion of applicator in situ. Body mass index (BMI) of the patient was calculated in accordance to World Health Organization definition (weight in Kg/ height in m²). Adequacy of position and orientation of the applicator was confirmed with the help of orthogonal X-ray images and the same were transferred to the treatment planning system (TPS) to generate treatment plan. Prescription doses were optimized to Point A and to reference lines placed at 0.5 cm apart from the surface of ovoids. The following dose reference points were identified on orthogonal x-ray images for analysis using the rectal marker and Foleys bulb inflated with radio opaque dye Rectal points at the level of femoral heads (RL) and pubis symphysis (RLP), Anorectum Junction (AR Jn) point and Rectosigmoid (RS) point and Bladder point (BL). Pearson regression analysis was used to analyze data from TPS. **Results:** The mean BMI was 22.7 kg/m² and average age was 49.9 years. Analysis showed that RL point dose and BMI were inversely correlated with a coefficient -0.45 ($p = 0.001$). The trend continued along the rectal tube in cranio-caudal direction, as RLP and AR Jn points showed inversion co-efficiency with increase in BMI, -0.48 ($p < 0.01$) and -0.51 ($p < 0.01$) respectively. Bladder point showed weak positive correlation to BMI, 0.12 ($p = 0.38$). **Conclusion:** Significant rectal dose reduction is observed with increase in BMI. Bladder dose did not show statistically significant correlation with BMI. Based on the findings, BMI constitutes a confounding factor in the treatment of carcinoma of cervix.

Keywords: Body Mass Index; Rectum; Bladder and Cervical Cancer

1. Introduction

Carcinoma of the cervix is radiosensitive and radiation is used in all stages and where surgery is not possible. Intracavitary brachytherapy (ICBT) along with external beam radiotherapy (EBRT) forms an essential component in the management. It provides high therapeutic index by delivering a high dose to the primary cervical lesion and lower doses to adjacent

organs, resulting in increased local control and survival without increase in toxicity.¹⁻⁴ Body mass index (BMI), a measure of body weight in relation to height, is related to numerous morbidities. These include diabetes, high blood pressure, hyperlipidemia and psychiatric wellness. BMI is also linked to cancers of the colon and the breast.⁵⁻⁶ Authors reported that link between cancer

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risk and BMI is likely to involve sex and growth hormones and effects of nutrition.⁷⁻⁸

Brachytherapy is an advanced cancer treatment modality, which uses radioactive seeds or sources placed in or near the tumor itself, giving a high radiation dose to the tumor while reducing exposure to organs at risk. ICBT procedure involves placing the applicator in the uterus in situ to deliver radiation to cervix. Bladder, rectum and bowels are organs at risk (OAR), radiation doses to which should be considered. The accurate calculation of dose to organ at risk is a crucial objective in treatment planning. This is particularly true in the case of high dose rate (HDR) brachytherapy.⁹

Several studies evaluated radiation induced toxicities to OARs i.e., bladder, rectum and bowel using dosimetric parameters.¹⁰⁻¹² Nora *et al.*¹³ studied effects of BMI on complications and survival outcomes in patients undergoing curative chemoradiotherapy for cervical carcinoma. Jihoon *et al.*¹⁴ studied dependence of rectal doses on BMI of the patient underwent ICBT with the application of tandem and ring applicator. Brachytherapy sources exhibit steep dose fall off with distance and this phenomenon is utilized to deliver high dose to tumor while sparing surrounding normal tissues.

If rectum and bladder distance increases from the applicator in situ due to deposition of fat i.e., the case of higher BMI, there is a reduction in dose to bladder and rectum. The purpose of the present work is to analyze relation between BMI and bladder and rectal doses in the patients who underwent ICBT for treatment of carcinoma of the cervix with tandem and ovoid applicator. This study adds to the literature the effect of BMI as a confounding factor in the treatment of carcinoma of cervix and would be of help for further investigations.

2. Methods and Materials

The sample consists of fifty patients with carcinoma of the uterine cervix of grade II and grade III with age ranging from 26 years to 70 years. All patients were recruited with the approval of hospital ethics committee. Standard Henschke applicator set (Mick Radio-Nuclear Instruments, Inc., NY, USA) with different tandem lengths and ovoid diameters was used depending on the patients' anatomy. Tandem lengths of 5 cm to 6 cm and ovoid diameters from 2 cm to 3 cm were employed. Height and weight of the patient was recorded prior to the insertion of applicator and BMI was calculated using World Health Organization definition i.e., weight in Kg/height in m². Patients were imaged on acuity physical simulator (Varian, Palo Alto, CA, USA). Orthogonal X-ray images were obtained to confirm the adequacy of position of applicator in anteroposterior and lateral

directions at gantry angles 0° and 270° respectively. The same were transferred to the Brachyvision treatment planning system (TPS) Version 7.3 (Varian Medical Systems, Palo Alto, CA, USA) via Aria network (Varian Medical Systems, Palo Alto, CA, USA) for planning.

Treatment regime for the treatment of cervical cancer consists of concurrent weekly cisplatin chemotherapy of 40 mg/m² in 5 cycles and external beam radiation therapy of 50 Gy combined with 3 sessions of HDR Brachytherapy with dose per fraction ranging from 6 Gy to 7 Gy. First fraction of HDR Brachytherapy starts after a dose of 30 Gy delivered by external beam radiation therapy.

Prescribed dose is optimized to Point A and to the reference lines placed at 0.5 cm apart from the surface of ovoids. The following dose reference points were identified on orthogonal x-ray images for analysis: point A, bladder point (BL), rectal points (RL, RLP), anorectal junction (AR Jn) point and rectosigmoid (RS) points.

International Commission on Radiation Units and Measurements (ICRU 38) recommendations were followed to identify bladder point. In addition two more points were digitized at the superior and inferior surface of the Foley bulb and named as BLS and BLI (Figure 1). Rectal tube with dummy marker wire was used to locate the modified rectal point. It was identified at a point on the rectal marker wire in lateral view at the level of (a line joining) the centers of the right and left femoral heads in antero-posterior view. Two additional points were marked at 1 cm on either side of the modified rectal point in cranio-caudal direction. RLP point was located on rectal tube at the inferior portion of pubic symphysis. An AR Jn point mimics the anorectal junction is marked on the rectal tube at the intersection of a line connecting pelvic ischial tuberosity. RS point was marked at the anterior surface of S1-S2 junction in lateral view and at the same level on the midline in anteroposterior view. Regression analysis was carried out to find out relation between BMI and dose at defined reference points.

3. Results

Data of doses at defined reference points from TPS was analyzed and following results were observed. Patients were classified as per the definition of BMI given by WHO. Out of fifty patients 2 were morbidly obese, 5 were obese, 7 were overweight, 27 were normal and 9 were under weight. The mean BMI was 22.7 kg/m² with a range from 13.1 kg/m² to 35.7 kg/m². The average age was 49.7 years and range from 26 to 70 years. The mean dose to bladder point was 6.36 Gy with a range from 3.9 Gy to 7.9 Gy.

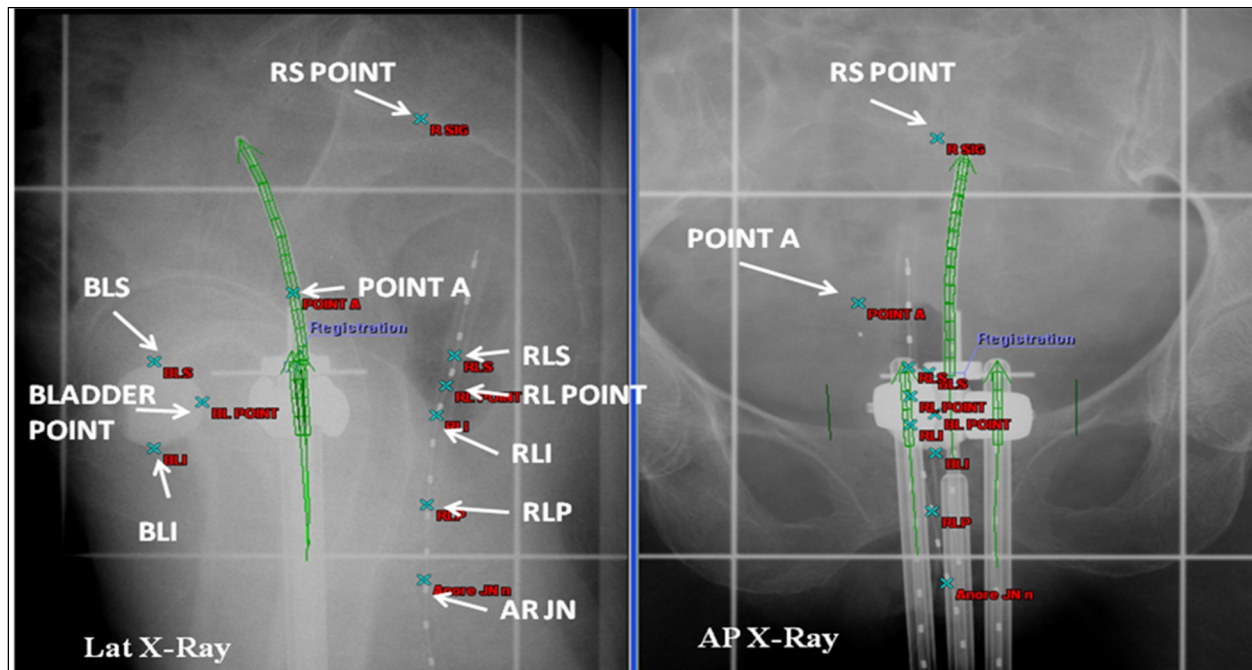


Figure 1: Orthogonal X-ray radiographs.

Table 1: Correlation coefficients and dose characteristics.

	Dose in cGy			95% CI		p-value	CC
	Mean	Range	SD	lower	Upper		
Bladder Point	636	394.2–787.2	92.9	609.3	662.7	0.38	0.13
Rectal Point	512.8	314.4–702	110.9	481.0	544.7	0.001	-0.45
RLP	242.8	100.3–435.4	81.6	219.4	266.3	<0.001	-0.48
AR Jn	121.2	60.2–211.1	32.2	112.0	130.4	<0.001	-0.51
RS Point	202.6	76.8–397.5	80.2	179.6	225.7	0.34	0.13

SD = standard deviation; CI= confidence interval; CC= Correlation coefficient

RLP: Rectal point at the level of Pubis Symphysis, AR Jn: Anorectal Junction, RS Point: Recto Sigmoid Point.

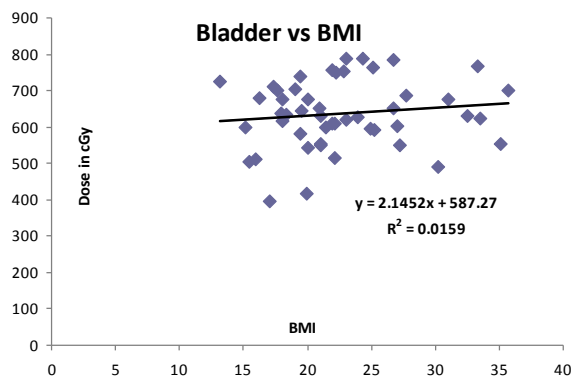


Figure 2: Regression plot of BMI vs Dose to ICRU Bladder point.

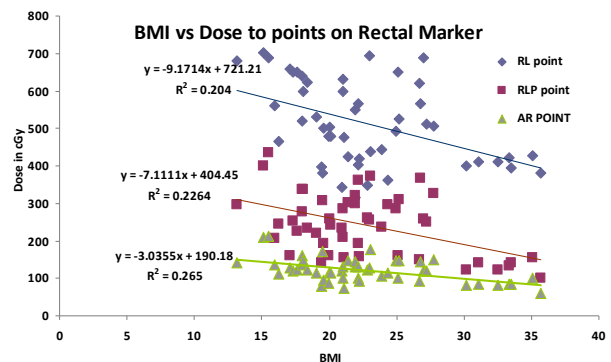


Figure 3: Regression plot of BMI vs Dose to points on Rectal marker.

Pearson regression analysis was used to study correlation of BMI and dose to different points i.e., Bladder point, rectal points, RS point and AR point. Bladder point showed weak positive correlation, 0.13 (Table 1) to BMI (Figure 2). Analysis showed that RL point dose and BMI were inversely correlated with a coefficient -0.45 ($p = 0.001$) (Figure 3). The trend continued along the rectal tube in craniocaudal direction as RLP point and AR In point negatively correlated, -0.48 with -0.51 (Table 1) respectively with BMI. No correlation was observed between RS point and BMI with coefficient 0.13 ($p = 0.34$).

4. Discussion

The aim of radiotherapy is to deliver high dose to tumor while sparing surrounding normal tissue by not exceeding the tolerance doses. Brachytherapy sources are characterized by steep dose gradients¹⁵⁻¹⁶ which results in sparing normal tissues. HDR brachytherapy involves delivery of higher radiation doses over a short period of time and carries risk of acute and late complications particularly to rectum and bladder as any other radiation technique. There are many factors that contribute to acute and late complications like dose per fraction, total dose, treatment time and patient characteristics. Potential factors that may affect treatment complications are co-morbidities, pelvic surgical history, tobacco and anticoagulation medication.

In this study doses to OARS are categorized based on the BMI of the patients. Treatment plans were generated to deliver prescribed dose to point A (and reference lines to ovoids without checking for violation of dose to organ at risk). Treatment planning is carried out on 2D planar images and the dosimetry of various dose reference points related OARs is studied. This study is carried out to correlate and establish the dosimetric results from earlier studies. Jihoon *et al.*¹⁴ studied extensively the impact of BMI on rectal complications in the case of treatment of locally advanced carcinoma of the cervix. The study found that there was a negative correlation between dose to 2 cc rectum and increase in BMI.

Authors did not find any association of BMI and acute or late morbidity of rectum even when controlling for confounders such as age, smoking, hypertension, anticoagulants and diabetes. The same is observed in our study, different rectal points RLS, RLI and RLP with correlation coefficients -0.34 ($p = 0.150$), -0.48 ($p = 0.001$) and - 0.47 ($p = 0.001$) respectively, showing reduction in dose with increase in BMI. In contrast to this Kizer *et al.*¹⁷ showed patients with higher BMI to have lower rectal toxicities (compared to lower BMI) undergoing chemoradiation treatment. In another study Boyle *et al.*¹⁸ studied body mass index and dose to organ at risk during vaginal cuff brachytherapy with vaginal cylinders and concluded that women with higher BMI

received lower bladder and small bowel dose compared to patients with lower BMI. However, we did not find statistical significance in correlation of BMI and bladder dose. This may be due to applicator type used and surrounding tissue. In addition to the dose to bladder at ICRU Bladder point we have studied dose at two other dose points (Figure 1) BLS and BLI, located at superior and inferior ends of the Foleys bulb. Doses at these two points no way correlated to BMI of the patient, correlation coefficients were 0.1 ($p = 0.4$) and -0.08 ($p = 0.5$) respectively. Gastrointestinal dose parameters studied in earlier studies^{14,18} showed weak or no correlation with BMI, which is in concurrence with our study with RS Point showing weak positive correlation to BMI, i.e., 0.13 ($p = 0.34$).

5. Conclusion

This study concludes that dose along the rectum decreases with increase in BMI. We did not find statistical significance in correlation of BMI and bladder dose. Rectosigmoid point showed weak positive correlation. This study is in strong coherence with the current literature.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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