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Body mass index, dose to organs at risk during vaginal brachytherapy, and the role of three-dimensional CT-based treatment planning

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Abstract

PURPOSE—To assess the effect of body mass index (BMI) on dose to organs at risk (OARs) during high-dose-rate vaginal brachytherapy and evaluate the role of three-dimensional dose evaluation during treatment planning.

METHODS AND MATERIALS—Three-dimensional dosimetric data for rectum, bladder, sigmoid colon, and small bowel for 125 high-dose-rate vaginal brachytherapy fractions were analyzed. Dose–volume histograms were generated for $D_{0.1\text{ cc}}$ and $D_{2\text{ cc}}$ of each OAR. Contributing factors including the use of urinary catheter and cylinder size were also recorded. As different dose fractionations were used, the OAR doses were tabulated as a percent dose prescribed to 0.5 cm. All patients were treated to 4 cm of the vaginal length.

RESULTS—Median BMI in this cohort was 31.7 kg/m². The BMI values had a weak inverse correlation with $D_{0.1\text{ cc}}$ to sigmoid colon ($r_s = -0.18$, $p = 0.047$) and $D_{0.1\text{ cc}}$ to bladder ($r_s = -0.19$, $p = 0.038$). There was a strong inverse correlation of $D_{2\text{ cc}}$ and increasing BMI ($r_s = -0.64$, $p = 0.003$). The median $D_{2\text{ cc}}$ was 25.1% for BMI higher than 31 and 61.9% for BMI of 31 or lower. For $D_{0.1\text{ cc}}$, there was also a strong inverse correlation with increasing BMI ($r_s = -0.57$, $p < 0.001$). Median $D_{1\text{ cc}}$ was 33.5% for BMI >31 and 84.4% for BMI ≤ 31. On multivariate analysis higher BMI remained a significant predictor of lower small bowel $D_{2\text{ cc}}$ ($p < 0.001$) and $D_{0.1\text{ cc}}$ ($p < 0.001$).

CONCLUSIONS—Women with a lower BMI receive higher doses to the bladder and small bowel compared with those with a higher BMI. Three-dimensional dose evaluation should be considered in patients with low BMI, particularly when combined with external beam radiation.

Keywords

Vaginal brachytherapy; High-dose rate; Three-dimensional planning; Body mass index; Dosimetry

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Introduction

The primary treatment for endometrial cancer is total hysterectomy with bilateral salpingo-oophorectomy. Indications for postoperative radiation have been elucidated by a number of randomized trials (1–3). Vaginal brachytherapy (VBT) either with or without pelvic external beam radiation therapy (EBRT) is often used as adjuvant treatment after surgery. The Gynecologic Oncology Group trial, GOG-99, demonstrated that the primary site of pelvic recurrence for patients with endometrial cancer is at the vaginal cuff (2). The Postoperative Radiation Therapy in Endometrial Carcinoma trial, PORTEC-2, randomized patients after surgery to adjuvant radiation with either pelvic EBRT or VBT and demonstrated no difference in vaginal cuff recurrences or overall survival between the two modalities (4). The results of these studies have translated into increasing utilization of high-dose-rate (HDR) VBT, evidenced in a survey published by the American Brachytherapy Society (5).

Obesity has been identified as a risk factor for endometrial cancer and shown to be prognostic of treatment outcome (6, 7). It has been our observation that patients with lower body mass index (BMI) have less abdominal adipose tissue and tend to have greater amounts of small bowel in the low pelvis. A study published by Patil *et al.* (8) demonstrated that men with lower BMI received higher doses to the rectal wall during permanent prostate brachytherapy. However, to our knowledge, there is no comparable study assessing doses delivered to organs at risk (OARs) during VBT in relation to BMI. The goals of this study were to (1) assess the dose delivered to OAR during VBT and (2) ascertain whether individual anthropometrics affect these doses.

Methods and materials

A total of 30 consecutive women treated postoperatively with VBT using three-dimensional (3D) CT-based planning, either as a part of adjuvant treatment after surgical staging or in combination with EBRT for a vaginal recurrence, were identified. A total of 127 insertions were assessed with a CT scan obtained with each fraction. All patients were treated from a standard library of plans using a single-channel cylinder to deliver the prescription dose to a depth of 5.0 mm from the cylinder surface to the proximal 4 cm of the vagina. For the apex, a reference point was placed 5.0 mm from the applicator dome. Owing to anisotropy, the dose at the apex is 5–10% low. The 4-cm treatment length was chosen as a standard length owing to the general agreement that 3–5 cm is acceptable, and is generally less than half of the vaginal length. Exceptions are made in cases where there is concern for distal vaginal involvement. The applicator is secured in place with the pelvic girdle on each fraction, which results in a stable position in most women. Adequate applicator position is defined by good approximation of the applicator dome to the apex without air gaps. No constraints to OARs were used to modify plans.

With each insertion, OARs, including the rectum, bladder, sigmoid colon, and small bowel were contoured. All organs were contoured by outlining the whole organ. For small bowel, this included individual loops of bowel as captured at the time of CT simulation. It has previously been shown that when assessing the dose delivered to small volumes ($<5\text{ cm}^3$), external organ contours provide an accurate surrogate for organ walls (9). The dose–volume

histograms were assessed for each fraction and data were collected for the $D_{0.1 \text{ cc}}$ (minimum dose within the 0.1 cm³ volume receiving the highest dose) and $D_{2 \text{ cc}}$ (minimum dose within the 2 cm³ volume receiving the highest dose) of each OAR were collected. To account for different fraction sizes, all doses were tabulated as a percent of the prescription dose. Individual anthropometric data were collected and BMI was calculated using the standard formula: mass (kg)/height (m²). With each insertion, other factors that may have affected individual dosimetry, such as cylinder size and use of a Foley catheter, were recorded.

Statistics

International Business Machines Corporation Statistical Package for the Social Sciences version 20 (New York, NY) was used to calculate correlations between BMI and all dosimetric endpoints collected, using Spearman's method. All tests were two tailed. Correlations between use of a urinary catheter, cylinder size, and dosimetric endpoints were also assessed. Regression analysis was used to determine the effect size and statistical significance of the correlation between BMI and dosimetric endpoints controlling for urinary catheter use and cylinder size.

Results

The median BMI for the patient cohort was 31.7 (interquartile range: 27.6–38.4). No patients were underweight. The most common fractionation scheme was 25 Gy delivered in 5-Gy fractions ($n = 20$). Pelvic EBRT was used in addition to VBT for 11 patients. The stump sizes used, measured as a diameter, were 3.5 cm ($n = 8$), 3 cm ($n = 103$), and 2.6 cm ($n = 16$). A urinary catheter was present in a total of 40 insertions. All doses are reported as a percentage of prescription dose.

For the rectum, there was no significant correlation of BMI and $D_{2 \text{ cc}}$ ($p = 0.76$), although there was a trend toward an inverse correlation between BMI and $D_{0.1 \text{ cc}}$ ($p = 0.128$; Table 1). Of note, dose to small volumes of rectum was higher than for other OARs, with a median $D_{0.1 \text{ cc}}$ of 113.2%. For the sigmoid colon, there was no significant correlation of BMI and $D_{2 \text{ cc}}$ ($p = 0.251$). There was a weak, but significant, inverse correlation between BMI and $D_{0.1 \text{ cc}}$ ($p = 0.047$). Similarly for bladder, $D_{2 \text{ cc}}$ had no correlation with BMI ($p = 0.186$) and a weak, but significant inverse correlation for $D_{0.1 \text{ cc}}$ ($p = 0.038$).

For small bowel, the median $D_{2 \text{ cc}}$ and $D_{0.1 \text{ cc}}$ of the small bowel were 44.0% and 56.4%, respectively for all patients. There was a strong inverse correlation of $D_{2 \text{ cc}}$ and increasing BMI, with a correlation coefficient for BMI of -0.64 ($p = 0.003$). The median dose was 25.1% for BMI higher than 31 and 61.9% for BMI of 31 or lower (Fig. 1). For $D_{0.1 \text{ cc}}$, there was also a strong inverse correlation with increasing BMI, reflected by a correlation coefficient of -0.57 ($p < 0.001$). Median dose was 33.5% for BMI higher than 31 and 84.4% for BMI of 31 or lower (Fig. 2). Larger stump size was also inversely correlated with small bowel doses, with correlation coefficients of -0.27 ($p = 0.003$) for $D_{2 \text{ cc}}$ and -0.31 ($p > 0.001$) for $D_{0.1 \text{ cc}}$.

A multivariate analysis was performed of factors known to influence small bowel dose, including use of a urinary catheter, and for stump size. Increasing BMI remained

significantly associated with a lesser small bowel $D_{2\text{ cc}}$ ($p < 0.0001$) and $D_{0.1\text{ cc}}$ ($p < 0.0001$). The relationship between increasing stump size and increased small bowel dose remained significant for $D_{0.1\text{ cc}}$ ($p = 0.004$), although of only borderline significance with $D_{2\text{ cc}}$, ($p = 0.068$). The use of a Foley catheter was associated with a trend toward higher $D_{0.1\text{ cc}}$, although this did not reach statistical significance (Table 2).

Discussion

The VBT is commonly used as adjuvant treatment for endometrial cancer following surgical staging. Several factors have been identified that increase the risk of locoregional recurrence following surgery (10–12). A number of randomized trials have clarified the role of adjuvant radiotherapy in reducing the risk of locoregional failure (1–4). The PORTEC-2 study established the noninferiority of VBT compared with pelvic EBRT (4). Several single institution series have demonstrated high rates of locoregional control with VBT alone (13–20). Furthermore, VBT alone is associated with very low rates of toxicity. One representative study by Barney *et al.* (21) reported no greater than Grade 1 acute toxicities and only 1 of 24 patients developing a late toxicity greater than Grade 1 (one Grade 3 gastrointestinal toxicity).

Treatment planning for VBT is traditionally based on guidelines established by the International Commission on Radiation Units and Measurements (22). Dose delivered to OARs, such as the bladder and rectum, are limited to 2D point doses. With the increasing availability of CT imaging, there has been a renewed interest in understanding volumetric dose to OARs, including the bladder, rectum, and small bowel. In patients with endometrial cancer who have undergone total hysterectomy, the absence of the uterus allows for small bowel to fall into the lower pelvis. Therefore, dose to the small bowel becomes of particular importance.

There is a limited amount of literature investigating the role of 3D treatment planning during VBT. Two studies in which CT imaging was obtained at the time of insertion have demonstrated that bladder filling can reduce the dose delivered to the small bowel (23, 24). A retrospective study by Holloway *et al.* (25) sought to define the role of 3D treatment planning in the determination of dose to the bladder, rectum, and sigmoid colon with each fraction. Retrospective analysis of 38 patients (125 fractions) revealed a minimal interfraction variance of the $D_{2\text{ cc}}$ for the bladder and rectum (6–8%). There was, however, a substantial degree of variance for the sigmoid colon (20.3%). It was proposed that this interfraction variance reflected the relative mobility of the sigmoid colon. The authors concluded that there was no evidence to support recording the doses to OARs with each fraction. A second study, published by Kim *et al.* (26) similarly sought to define the role of 3D treatment planning. The authors generated both a 2D library-based plan and a 3D CT-based plan for 84 consecutive patients. The 3D plans defined a clinical target volume by expanding the upper 2.5 cm of the cylinder by 5 mm in all directions and editing to exclude any bladder and rectum. The dose was prescribed to provide a D_{90} (dose to 90% of clinical target volume) of 100% or greater. Plans were analyzed based on their coverage of the tissue within 5 mm of the upper 3 cm of the cylinder. Although both 2D and 3D plans provided adequate coverage of more than 100%, it was found that there were significantly lower

$D_{0.1\text{ cc}}$, $D_{1\text{ cc}}$, and $D_{2\text{ cc}}$ to the bladder and rectum with 3D-based planning. Unlike the conclusions of Holloway *et al.* (25), it was concluded that 3D planning of the first fraction may play a role for a subset of patients who benefit from individualized planning by reducing the dose to OARs.

By identifying a group of patients who may be at risk of receiving significant dose to small volumes of OARs, our data add further credence to the use of 3D-based treatment planning. Our study demonstrates a weak but statistically significant inverse correlation between BMI and $D_{0.1\text{ cc}}$ to the sigmoid colon and $D_{0.1\text{ cc}}$ to the bladder. The strongest correlation was found for both $D_{2\text{ cc}}$ and $D_{0.1\text{ cc}}$ to the small bowel. It has been our experience that women with low BMIs tend to have less abdominal adipose tissue and more frequently have loops of small bowel in close proximity to the vaginal apex, subjecting the normal tissue to higher doses. Figure 3 illustrates two cases from our series. Representative sagittal CT images are depicted of a woman with a BMI of 45 and another with a BMI of 24. Isodose lines are overlaid and dose–volume histograms are shown for each case. The dosimetric differences between the two cases are apparent.

There are inherent limitations to our study. Although we have controlled for the use of a Foley catheter at the time of treatment, we have not accounted for individual bladder filling. The use of a Foley catheter is not a perfect surrogate, and it is possible that individual variation in bladder filling may affect dosimetry. Additionally, although we did capture anthropomorphic data, we have not accounted for variation in anatomy among patients. These variations can in turn result in differential positioning of the applicator in relation to surrounding organs.

The small bowel dose constraints during VBT have not been clearly delineated. Furthermore, the clinical relevance of our observations is yet to be determined; and to draw meaningful conclusions, a larger number of patients will be needed. Dose to small bowel during VBT monotherapy may not prove to be of clinical significance. However, in the instance of VBT used as a boost to pelvic EBRT, as in recurrent or high-risk disease, the dose to small bowel during VBT may become more important. Future work will be directed toward further exploring the relationship of dose and small bowel toxicity, particularly when VBT is combined with EBRT, and it is our current practice to sum the doses to the OARs when VBT is used as a boost, when the small bowel dose may exceed 55 Gy.

Conclusion

In conclusion, small bowel dose was significantly higher in women with low BMI, with minor trends observed in the bladder, sigmoid colon, and rectum. Consideration of 3D dose evaluation should be given in these patients, particularly when combined with EBRT.

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Fig. 1.

Box plot of small bowel dose and BMI class. The line represents the median, the box the interquartile range, and the whiskers represent range. D_{2cc} is the minimum dose to the 2 cm^3 of bowel receiving the highest dose. BMI = body mass index.

Fig. 2.

Box plot of small bowel dose and BMI class. The line represents the median, the box the interquartile range, and the whiskers represent range. $D_{0.1 \text{ cc}}$ is the minimum dose to the 0.1 cm^3 of bowel receiving the highest dose. BMI = body mass index.

Fig. 3. Sagittal planning CT images and corresponding dose-volume histograms in a woman with BMI 45 (*left*) and BMI 20 (*right*). Note: the bowel presence much more inferiorly in the woman with low BMI, and in close proximity to the applicator and dose cloud. BMI = body mass index.

Table 1

Body mass index (BMI) and dosimetric correlations

Organ at risk	Parameter	Correlation	p-Value	Median dose (IQR), %	Median dose (IQR), % (BMI > 31)	Median dose (IQR), % (BMI < 31)
Rectum	D_{2cc}	-0.28	0.76	88.9 (79.2–95.0)	88.9 (80.0–93.6)	89.0 (77.4–96.7)
	$D_{0.1cc}$	-0.14	0.128	113.2 (105.4–119.)	113.2 (105.6–116.2)	113.5 (105.3–120.1)
Sigmoid colon	D_{2cc}	-0.10	0.251	48.2 (30.8–60.95)	47.3 (34.1–56.1)	50.4 (27.2–63.7)
	$D_{0.1cc}$	-0.18	0.047	71.9 (45.9–89.6)	67.9 (44.4–76.1)	79.1 (50.4–97.5)
Bladder	D_{2cc}	-0.25	0.186	86.3 (77.9–91.4)	82.8 (75.3–88.5)	89.4 (84.1–92.5)
	$D_{0.1cc}$	-0.19	0.038	106.9 (97.6–112.4)	103.35 (91.8–109.5)	109.1 (103.3–113.4)
Small bowel	D_{2cc}	-0.64	0.003	44 (20.1–68.4)	25.1 (15–41.6)	61.9 (45.5–79.3)
	$D_{0.1cc}$	-0.57	<0.001	56.4 (28.0–97.0)	33.5 (21.5–57.5)	84.4 (50.7–113.7)

IQR = interquartile range.

Table 2Multivariate analysis^a

Independent variable	<i>p</i> -Value
Small bowel $D_{2\text{ cc}}$	
BMI	<0.0001
Stump size	0.068
Small bowel $D_{0.1\text{ cc}}$	
BMI	<0.0001
Stump size	0.004
Urinary catheter	0.10

BMI = body mass index.

^aRegression analysis controlled for effect of BMI, use of Foley catheter, and stump size.