Original Article

Incidence of Suboptimal Applicator Placement and the Resulting Dosimetric Impact in Image-Based Intracavitary Brachytherapy

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Abstract

Aim: With the advent of computed tomography (CT)-based brachytherapy, it is possible to view the appropriate placement of the applicator within the uterine canal and detect uterine perforation. In this study, the incidence of suboptimal placement of the intracavitary applicator and the resulting dosimetric impact were analyzed and compared with a similar set of ideal applicator placement. **Materials and Methods:** CT datasets of 282 (141 patients) high dose rate brachytherapy insertions between January and April 2016 were analyzed. The target volumes and organs at risk (OAR) were contoured as per the Groupe Européen de Curiethérapie European Society of Therapeutic Radiation Oncology guidelines. The position of the applicator in the uterine cavity was analyzed for each application. **Results:** The suboptimal insertion rate was 11.7%. There were 26 perforations and 7 subserosal insertions. The most common site of perforation was through the posterior wall of the uterus (42.4%). Fundus perforation and anterior wall perforation were seen in 24.2% and 12.1% of patients, respectively. The average dose to 90% of the target volume (D90 to high-risk clinical target volume) was the highest (9.15 Gy) with fundal perforation. Average dose to 2 cc (D2cc) bladder was highest for fundus perforation (7.65 Gy). The average dose received by 2 cc of rectum (D2cc) was highest (4.49 Gy) with posterior wall perforation. The average D2cc of the sigmoid was highest with anterior perforation (3.18 Gy). **Conclusion:** In order to achieve better local control and to decrease doses to OAR, it is important to perform a technically accurate applicator placement. A cost-effective, real-time image guidance modality like ultrasound is recommended for all insertions to ensure optimal applicator insertion.

Keywords: Computed tomography planning, intracavitary brachytherapy, suboptimal applicator placement

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Introduction

Brachytherapy has a pivotal role in the management of locally advanced cervical cancers.[1] The ultimate outcome of locally advanced cervical cancers is determined by the total dose of radiation delivered by the combination of external beam radiotherapy and brachytherapy.[2-4] Brachytherapy procedure is performed by inserting a tandem into the uterus through the cervical os under sedation or anesthesia. Suboptimal placement of the applicator can result in uterine perforation, inadequate dose to the target and excess dose to adjacent normal tissues.

Conventionally, orthogonal radiographs were performed after the brachytherapy procedure. Hence, suboptimal placement of the applicator or uterine perforation could not be assessed. Conventionally, an intracavitary application was considered to be ideal and technically accurate if the tandem is in the midline and midway between the ovoids on an anteroposterior radiograph and when the tandem bisected the ovoids on the lateral radiograph.[5] With the advent of computed tomography (CT)-based brachytherapy, it is possible to view the appropriate placement of the applicator within the uterine canal and detect uterine perforation.

In this study, the incidence of suboptimal placement of the intracavitary applicator and the resulting dosimetric impact were analyzed and compared with a similar set of ideal

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applicator placement in subsequent intracavitary insertions for the same patient.

Materials and Methods

CT datasets of 282 (141 patients) high dose rate (HDR) brachytherapy insertions between January and April 2016 were analyzed. Patients were taken up for brachytherapy after an external beam radiotherapy dose of 50 Gy along with weekly cisplatin 40 mg/m^2.

Intracavitary application procedure

All the procedures were done under general anesthesia in the operating room. A Foley catheter was used to drain the bladder in all patients. Foley bulb was filled with 7 ml of iodinated contrast and normal saline to locate the bladder neck. Adequate bowel preparation was done in all patients before the procedure. A CT/magnetic resonance (MR) compatible tandem ovoid applicator or a metallic tandem ring applicator was used for the insertion. After sounding the uterine cavity, the CT/MR compatible central tandem was inserted into the uterine canal after serial dilatations without any radiological guidance. The appropriate size of ovoids was inserted into the vaginal fornices and the applicator was secured in position. Anterior and posterior vaginal gauze packing was done. For the tandem ring applicators, central tandem was inserted after sounding the uterine cavity. Serial dilatations were not done as the central tandem had a thin stem. The ring applicator was secured in position and anterior vaginal gauze packing was done. A rectal retractor was used to displace the rectum posteriorly in tandem ring applicators.

Simulation

Three-millimeter slice CT images were obtained using a CT simulator (Somatom, Siemens, Erlangen, Germany). CT images were acquired with the patient in supine position. The position of the central tandem, presence of perforation, and subserosal insertion of the tandem were assessed on the CT images and the CT images were exported to the Oncentra treatment planning system (Oncentra, Elekta, Veenendaal, The Netherlands).

Contouring and planning

The high-risk clinical target volume (HRCTV) and organs at risk (OAR) (bladder, rectum, and sigmoid) were contoured by the radiation oncologists as per the Groupe Européen de Curiethérapie European Society of Therapeutic Radiation Oncology (GEC ESTRO) guidelines.[6,7] The outer bladder wall was contoured from the dome to the urethra. The outer rectal wall was contoured from the level of ischial tuberosities to the rectosigmoid junction. The sigmoid was contoured from the rectosigmoid junction to the level where the sigmoid crosses anteriorly at pubic symphysis. The entire cervix was contoured as the CTV and modified to include adjacent areas of involvement as per the clinical findings at the time of brachytherapy.

Treatment planning was done using Oncentra Masterplan (version 4.3). Catheter reconstruction was done manually for every insertion. The tip of the tandem was not loaded for patients with uterine perforation. Otherwise, a standard loading pattern was followed. Point A and Point B doses were defined and dose was normalized to Point A. A dose of 8 Gy was prescribed to Point A. Dose–volume histograms were generated and dose to 0.1 cc, 1 cc, and 2 cc of the bladder, rectum, and sigmoid were recorded. CTV parameters such as D100, 98, 90, 50, and V100 (dose received by 100%, 98%, 90%, and 50% of the CTV and volume receiving 100% of the prescribed dose, respectively) were recorded. Manual optimization was done if necessary to achieve GEC ESTRO recommended dose constraints to OAR. HDR brachytherapy was delivered using ^{192}Ir (Oncentra, Elekta, Veenendaal, The Netherlands).

The CT datasets were analyzed for the position of the uterus, position of the tandem inside the uterus, the presence of perforation, and subserosal insertion of the tandem. For applications with misplacement of applicator, a standard planning was done and the dose to CTV and OAR were analyzed. Plan was approved only when there was an acceptable CTV coverage (total EQD2 D90 >85 Gy) and the constraints to OAR were met. The subsequent applications of brachytherapy for patients with misplacement of applicator in the first fraction were also analyzed and the dosimetric data were recorded. Sagittal CT image of an intracavitary application showing acute anteversion of the uterus and posterior wall insertion of central tandem is shown in Figure 1.

Statistical analysis

Logistic regression analysis was used to analyze the correlation between suboptimal placement and age of the patient, stage of the disease, type of applicator, and the position of the uterus. Student *t*-test was used to analyze the dosimetric differences between optimal and suboptimal applicator insertion.

Results

Patient characteristics

Between January and April 2016, a total of 282 image-guided intracavitary insertions were performed out of which 33 insertions were found to be suboptimal. The suboptimal insertion

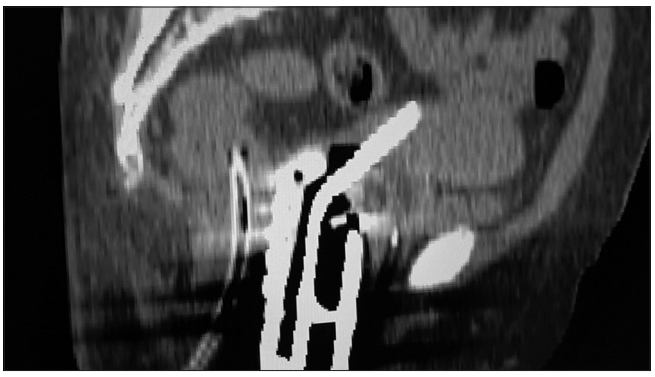

Figure 1: Computed tomography image of an intracavitary application showing anteversion of the uterus and posterior wall insertion of the central tandem

rate was 11.7%. The median age of patients with suboptimal applicator insertion was 60 years [range 38–68 years]. Nearly 60.6% of patients had Stage IIIB disease, 30.3% had Stage IIB, and 3.03% had Stage IB2, IIA2, and IVA, respectively. 72.7% of patients with suboptimal placement had tandem ovoid applicator *in situ*. Tandem ring applicator was used in the remaining 27.3%.

Uterus position was found to be anteverted (87.8%) in majority of patients with an inappropriate applicator placement. Uterine perforation was found in 26 insertions and subserosal insertion was found in 7 applications. The most common site of perforation was through the posterior wall of the uterus. Fundus perforation was seen in 24.2%. Anterior wall perforation was seen in 12.1% of patients. Patient details and suboptimal insertion characteristics are tabulated in Table 1.

For patients with perforation, the tip of the tandem outside the uterus was not loaded and the planned dose was delivered. All patients were managed conservatively, and there were no major complications in any of the patients. Logistic regression analysis showed only age to be a significant predictor of suboptimal applicator placement (P = 0.003) and not the stage (P = 0.178) or the uterus position (P = 0.715).

Dosimetry of applications with suboptimal placement

The dose–volume parameters of the 33 applications with inappropriate applicator placement are summarized in Table 2.

Dose to the target and organs at risk for various types of misplacement

Dose to clinical target volume

The average dose to 90% of the target volume (D90 to CTV) was the highest (9.48 Gy) with fundus perforation compared to other types of inappropriate applicator placement (anterior wall perforation – 9.15 Gy, posterior wall perforation – 8.08 Gy, and subserosal perforation – 6.8 Gy).

However, the average volume receiving 100% of prescribed dose (V100) was the highest (93.48%) with anterior wall perforation. V100 was 81.9%, 79.6%, and 81% for fundus perforation, posterior wall perforation, and subserosal insertion, respectively.

Dose to organs at risk

Since with anterior perforation, tandem is close to the bladder, the average dose received by 2 cc of bladder (D2cc) was highest with anterior wall perforation (8.1 Gy). Average D2cc bladder for fundus perforation, posterior wall perforation, and subserosal insertion were 7.65 Gy, 7.55 Gy, and 7.51 Gy, respectively.

Similarly, the average dose received by 2 cc of rectum (D2cc) was highest (4.49 Gy) with posterior wall perforation. Average D2cc of the rectum for anterior wall, fundus perforation, and subserosal insertion were 4.4 Gy, 4.48 Gy, and 3.5 Gy, respectively.

The average D2cc of sigmoid was highest with anterior perforation (3.18 Gy).

Table 1: Patient characteristics and suboptimal insertion characteristics (n=33 insertions)

Variables	*n* (%)
Age (years)	
Range	38-68
Median	60
Stage	
IB2	1 (3.03)
IIA2	1 (3.03)
IIB	10 (30.3)
IIIB	20 (60.6)
IVA	1 (3.03)
Uterus position	
Anteverted	29 (87.8)
Retroverted	4 (12.2)
Type of applicator	
Tandem ovoid	24 (72.7)
Tandem ring	9 (27.3)
Type of misplacement	
Anterior wall	4 (12.1)
Fundus	8 (24.2)
Posterior wall	14 (42.4)
Subserosal	7 (21.3)

Table 2: Average dose-volume parameters for 33 applications with inappropriate placements

Dose volume parameters	Mean±SD
CTV volume (cc)	21.7±10.2
Bladder volume (cc)	51.8±20.6
Rectal volume (cc)	32.9±10.5
Sigmoid volume (cc)	12±6.3
V100 CTV (%)	85.1±16.6
D90 CTV (Gy)	8±2.4
D0.1cc bladder (Gy)	11.2±2.9
D1cc bladder (Gy)	8.6±1.9
D2cc bladder (Gy)	7.6±1.6
D0.1cc rectum (Gy)	5.8±1.2
D 1cc rectum (Gy)	4.7±0.9
D2cc rectum (Gy)	4.2±0.8
D0.1cc sigmoid (Gy)	3.9±1.5
D1cc sigmoid (Gy)	3.1±1.1
D2cc sigmoid (Gy)	2.7±0.9

SD: Standard deviation, CTV: Clinical target volume

Average D2cc of sigmoid for fundus perforation, posterior wall perforation, and subserosal insertion were 3.06 Gy, 2.52 Gy, and 2.56 Gy, respectively. The results are displayed in the Figure 2.

Comparison of dosimetry between optimal and suboptimal insertions

Out of the 33 suboptimal insertions, we identified 10 applications which had optimal insertion during the subsequent fraction. The difference in dose delivered to CTV and bladder, rectum, and sigmoid were analyzed between the optimal and suboptimal insertions. The average dose received by Point A,

Point B, CTV, bladder, rectum, and sigmoid for optimal and suboptimal insertions are tabulated in Table 3.

Of all the dosimetric parameters analyzed between the optimal and suboptimal insertions, the doses delivered to right Point B and V100 (volume receiving 100% of prescribed dose) was found to be statistically significant. There was no significant difference between the doses delivered to the bladder, rectum, and sigmoid.

Discussion

An essential component in the management of cervical carcinoma is intracavitary brachytherapy. Proper applicator placement aids in adequate dose delivery to the target and thereby results in superior clinical outcomes.[8,9] Suboptimal applicator placement can result in inadequate doses to target

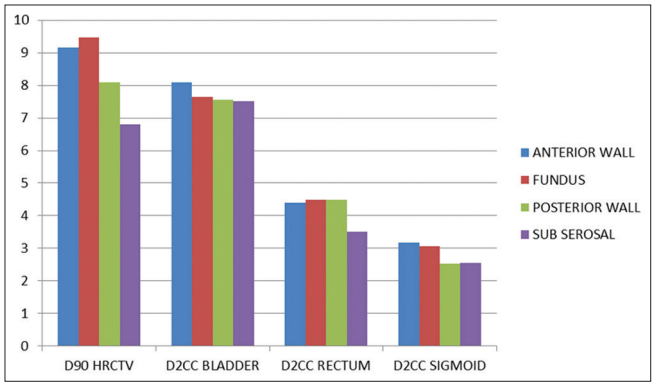

Figure 2: Chart showing the average dose to target and organs at risk in suboptimal applicator placement

Table 3: Average dose to clinical target volume and organs-at-risk for optimal and suboptimal insertion

Parameters	Suboptimal insertion (average±SD)	Optimal insertion (average±SD)	*P*
Right point A	7.8±0.6	7.8±0.8	0.43
Left point A	7.9±0.7	7.7±0.8	0.50
Right point B	1.9±0.1	2.2±0.4	0.04
Left point B	1.9±0.2	2.1±0.4	0.09
D100 CTV	4.4±1.7	5.5±1.3	0.66
D98 CTV	5.6±2	6.9±1.3	0.32
D90 CTV	7.4±2.4	8.5±1.2	0.07
D50 CTV	15.2±4.5	13.9±1.9	0.10
V100 CTV	83.1±12.8	95.3±4.1	0.00
D0.1cc bladder	11±3.7	10±4.2	0.88
D1cc bladder	8.1±2.0	7.9±2.5	0.64
D2cc bladder	7.1±1.5	7.1±2	0.37
D0.1cc rectum	5.4±1.4	5.7±1.5	0.51
D1cc rectum	4.6±1.2	4.5±1.2	0.60
D2cc rectum	4.2±1.1	3.9±1	0.80
D0.1cc sigmoid	4.2±1.5	3.8±1	0.62
D1cc sigmoid	3.3±1.1	3.8±1.3	0.34
D2cc sigmoid	2.8±0.9	2.6±1	0.33

SD: Standard deviation, CTV: Clinical target volume

and a uterine perforation of tandem can result in enhanced dose delivery to adjacent bowel and can cause significant gastrointestinal toxicity.[10] Frequency of uterine perforation during intracavitary brachytherapy has been reported earlier in literature.

The most common sites of perforation reported in the literature are the posterior wall of the uterus and the fundus.[11-14] Advanced stage, old age, and extreme positions of the uterus can result in uterine perforation.[11,12,14,15] In our study, uterus position was found to be anteverted in 87.8% of suboptimal insertions. Retroverted uterus was found only in 12.2% of the applications. Granai *et al*. reported[15] perforations in 50 consecutive patients by performing a postoperative B-mode ultrasound to evaluate the position of the tandem. A 10% incidence of perforation was reported by Davidson *et al*.[16] with 35 insertions in 21 patients. Matsuyama *et al*.[17] reported a 10% perforation rate.

Barnes *et al*.[12] reported a uterine perforation rate of 13.7% using CT with 124 consecutive insertions. A 3% uterine perforation rate was reported among 428 image-guided brachytherapy applications by Segedin *et al*.[13] A 1.4% incidence of uterine perforation was reported in 356 ultrasound-guided applicator placements by Schaner *et al*.[18] A large series reported by Jhingran and Eifel[11] found 113 perforations in 7662 insertions. Using intraoperative and postoperative ultrasound, Rotmensch *et al*. found 6 perforations in 20 insertions.[19]

A 6% incidence of uterine perforation, 8.6% incidence of subserosal insertion, and 4.8% incidence of both subserosal insertion and uterine perforation were found among 231 brachytherapy insertions by Bahadur *et al*.[20] In 18 patients with retroverted uterus, Mayr *et al*.[21] used ultrasound guidance to insert the tandem and antevert the uterus. It has been demonstrated in several studies[18,19,21] that an intraoperative ultrasound-guided applicator placement diminishes the risk of uterine perforation several folds.

The uterine perforation rate in the present series was found to 9.2%. The suboptimal insertion rate was found to be 11.7% which includes both uterine perforation (9.2%) and subserosal insertion (2.5%). The dosimetric impact of suboptimal applicator placement was addressed by Bahadur *et al*.[20] They found an increase in the rectal and bladder D2cc dose up to 70.3% and 43.8%, respectively, for the suboptimal insertion of the central tandem. In the present series, the HRCTV receiving 100% of the prescribed dose (V 100) was the least with posterior wall perforation of the uterus. The average dose received by 2 cc of the bladder was the highest with anterior wall perforation of the central tandem.

It is evident from our dosimetric data that the suboptimal insertions do not lead to any significant variations in the dose to the target and OAR (except V100 to CTV) [Table 3] when compared to optimal insertions in subsequent fractions. This may be due to patient geometry or minor deviations from

optimal insertion. However, the data analyzed is too small to arrive at a meaningful conclusion.

To achieve good local control and to minimize toxicity, optimal applicator placement is very essential in intracavitary brachytherapy. Narrow cervical os, extreme anteversion, or retroversion of the uterus can result in suboptimal applicator placement and uterine perforation. With the advent of image-based brachytherapy, more perforation rates are being identified in intracavitary brachytherapy. Hence, it becomes essential to use intraoperative, cost-effective, image guidance modality like ultrasound for all insertions to confirm optimal tandem placement. In a survey conducted among American Brachytherapy Society members,[22] 56% of physicians used ultrasound guidance to aid applicator insertion during intracavitary brachytherapy.

Conclusion

The incidence of suboptimal insertion and uterine perforation of the central tandem in intracavitary brachytherapy reported in the present study is similar to that reported in the literature. In certain situations, suboptimal placement of the tandem can have serious detrimental effect on the final outcome. In order to achieve better local control and to decrease doses to OAR, it is important to perform a technically accurate applicator placement. A cost-effective, real-time image guidance modality like ultrasound should be used for all insertions to ensure optimal applicator insertion.

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Conflicts of interest

There are no conflicts of interest.

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