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Image-Guided High-Dose Rate Intracavitary Brachytherapy in the Treatment of Medically Inoperable Early-Stage Endometrioid Type Endometrial Adenocarcinoma

Scott E. Jordan, MD  
*Temple Health Fox Chase Cancer Center*

Ida Micaily, MD  
*Abington Jefferson Health*

Enrique Hernandez, MD  
*Temple University*

J. Stuart Ferriss, MD  
*University of Texas*

Curtis T. Miyamoto, MD, FACR  
*Temple University*

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Authors
Scott E. Jordan, MD; Ida Micaily, MD; Enrique Hernandez, MD; J. Stuart Ferriss, MD; Curtis T. Miyamoto, MD, FACR; Shidong Li, PhD; and Bizhan Micaily, MD
In patients with multiple medical comorbidities which preclude surgical therapy for early stage endometrial type endometrial cancer, treatment options include radiation therapy, chemotherapy, or a combination of multiple modalities. In the setting of medically inoperable disease, patients are often treated with radiation therapy as definitive treatment, where combination of external beam radiation therapy (EBRT) followed by intracavitary brachytherapy is the most common approach. In the first 25 years of this procedure, there was an emphasis on delivering high radiotherapy doses to the clinical target volume (CTV) encompassed most of the tumor volume in order to decrease the risk of local recurrence. However, with the advent of linear accelerator-based high dose rate (HDR) brachytherapy, radioactive sources can be delivered to the target volume while sparing surrounding healthy tissue, with lower doses reaching surrounding structures, thus allowing greater flexibility in dose distribution without requiring the use of multiple applicators or multiple fractions of treatment. In this cohort, we determined that lower radiotherapy doses to the CTV and GTV may provide similar efficacy when compared with the previously recommended doses. Our findings are consistent with other case series in the literature, though those studies included patients with higher grade disease and histologic subtypes other than endometrioid, and many used applications other than tandem and ovoid. The dosimetry techniques used in this cohort demonstrate that lower radiobiologic doses to the CTV may provide similar efficacy compared with the ABB recommended minimum doses. The use of a single tandem in combination with HDR better preserves bladder function without requiring the use of multiple applicators or fraction delivery under general anesthesia. For patients unable to undergo surgical management of metastatic/recurrent endometrial cancer due to medical contraindications, treatment with HDR brachytherapy is an excellent option for local disease control.

All American Joint Committee on Cancer (AJCC) stage Ia or Ib endometrial type endometrial cancer with medical comorbidities precluding surgical management treated at Temple University Hospital since 2010 were reviewed. Exclusion criteria were any evidence of nodal or cervical disease, or histologic types other than endometrioid. All treatment planning utilized CT imaging following placement of HDR applicators (tandem with ring or tandem with ovoids). Prior to 2016, a high-risk clinical target volume was defined by the radiation oncologist as approximately 2 cm depth. In 2016, a protocol was initiated where gross tumor volume (GTV) was defined as the entire myometrial invasion, indicating increased risk of occult pelvic nodal disease, or when it was marked in red, CTV in yellow, isodose lines are also shown—Red: 100%; Orange: 70%; Yellow: 40%. The contours encompassed most of the CTV in 3D display.

RESULTS

Eight patients received external beam radiation therapy (EBRT) followed by HDR brachytherapy. Seven patients underwent intracavitary HDR brachytherapy alone. In all patients, mean cumulative dose to 90% (D90) of GTV was 90.9 Gy (96.5-171.1) in equivalent dose in 2 Gy fractions (EQD2; α/β=10). Mean D90 to CTV was 51.6 Gy (45.7-57).

Average follow-up was 29 months. Four patients died from recurrent disease at an average of 2.83 years after completion of treatment. For those who remained disease-free for the remainder of follow-up. Side effects were minimal, and included grade 2-3 diarrhea and dysuria most commonly.

Table 1: Average D90 EDQ2 to GTV and CTV, as well as D2cc EDQ2 to bladder and bowel in HDR ICBT alone and in combination with EBRT. Units: Gy. Ranges shown in parentheses.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Avg D90 EDQ2 GTV</th>
<th>Avg D90 EQD2 CTV</th>
<th>D2cc EDQ2 Bowel</th>
<th>D2cc EDQ2 Bladder</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDR ICBT</td>
<td>90.8 (73.8-121)</td>
<td>41.0 (18.6-66.6)</td>
<td>42.3 (31.5-52.3)</td>
<td>44.4 (37.5-53.6)</td>
</tr>
<tr>
<td>HDR ICBT + EBRT</td>
<td>100.5 (70.5-177.1)</td>
<td>60.9 (48.1-74)</td>
<td>68.0 (60.3-75.0)</td>
<td>63.1 (53.7-70.9)</td>
</tr>
</tbody>
</table>

All patients 96.0 51.6

Figure 1: Sample CT- guided dose distribution plan with isodose from top left: Intracavitary image, axial reconstruction, coronal reconstruction, and 3-D reconstruction. GTV in red, CTV in yellow, isodose lines are also shown—Red: 100%; Orange: 70%; Yellow: 40%. The contours encompassed most of the CTV in 3D display.

Figure 2: Dose volume histogram for the treatment plan in Figure 1 to demonstrate 99% GTV coverage and 80% CTV coverage with the prescription dose of 100 Gy while having relative low dose to the bladder and bowel (including rectum and sigmoid as well as small bowel labeled as recto-sigmoid).

CONCLUSIONS

Comorbid conditions are common in patients with low grade, endometrial type endometrial cancer. HDR brachytherapy is a combination of multiple modalities, with lower overall mortality, diabetes, severe COPD, prior history of DVT or PE, without or with pulmonary embolism, and cardiac disease, which increase surgical risk, are also likely causes of premature death. In the event of inoperability or comorbid conditions, or if an occult pelvic nodal disease is suspected, an unexpected late recurrence of endometrial cancer in patients with treatment with HDR is unlikely to be a significant drive of premature mortality when compared to their other medical problems.

The Society recommends that the D90 of GTV should be at least 80 Gy, and that the D2 cc for GTV should be at least 65 Gy when combined with EBRT. Our data demonstrate that a dose lower than recommended [many of our patients were treated prior to these recommendations], treatment still has a high level of success.

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REFERENCES


