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

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INTRODUCTION

In patients with multiple medical comorbidities which preclude surgical therapy for early stage endometrial type endometrial cancer, survival is often not a goal of the treatment and the primary endpoints are often complete remission or low rate of recurrence. With the advent of iod-125 high dose rate (HDR) brachytherapy, as well as more sophisticated three dimensional computed tomography (CT) and magnetic resonance imaging (MRI), HDR intracavitary brachytherapy dosimetry has become much more precise, allowing higher doses to be used for large tumors, with lower doses reaching surrounding structures, such as bladder and bowel.

AIM

To report the experience with high dose rate, image guided intracavitary brachytherapy in the treatment of medically inoperable, early stage endometrial cancer.

METHODS

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 included any evidence of nodal or cervical disease, or histologic types other than endometrial. 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 two-thirds of myometrial depth. In 2016, a protocol was initiated where gross tumor volume (GTV) was defined as the width of the endometrial stripe as measured on MRI, rectal involvement (T3), palpable abdominal tumor mass (T4a), or distant metastasis (T4b). In 2017, a protocol was initiated where GTV was defined as the width of the endometrial stripe as measured on MRI, depth of invasion (T1c), palpable abdominal tumor mass (T4a), or distant metastasis (T4b). In all patients, mean cumulative dose to 90% (D90) of GTV was 90.6 Gy (79.5-117.1 Gy) in equivalent 2 Gy fractions (EDQ=0.516). Mean cumulative dose to 2 cc of bowel (D2cc) was 90.2 Gy (80.9-100.6 Gy) for GTV and 80 Gy for CTV. The decision to use external beam radiation therapy (EBRT) prior to brachytherapy was made on the basis of MRI-demonstrated myometrial invasion, involving more than 10% of the myometrium, in absence of gross pelvic node disease, or when it was thought that intracavitary brachytherapy alone would not deliver a sufficient dose to the entire CTV, most often in the setting of volume.

To determine the delivered doses given to the CTV and GTV in the patients who were done by the other protocol, dosimetric values were mapped onto the original treatment plans. CTV and GTV doses were recalculated for each fraction of HDR brachytherapy. Equivalent dose in 2 Gy fractions was calculated for each volume. Total dose to 90% of GTV and bladder were also calculated using equivalent dose in 2 Gy fractions (α/β=3). Average follow-up time and survival were also calculated.

RESULTS

Eight patients received external beam radiation therapy (EBRT) followed by intracavitary HDR brachytherapy. Seven patients underwent intracavitary HDR brachytherapy alone. In all patients, mean cumulative dose to 90% (D90) of GTV was 90.6 Gy (79.5-117.1 Gy) in equivalent 2 Gy fractions (EDQ=0.516). Mean cumulative dose to 90% of CTV was 51.6 Gy (50.6-52.9 Gy). Average follow-up was 29 months. Four patients died from comorbid diseases at an average of 2.83 years after completion of treatment. Except for one (8.6%) patient who recurred at 9 months following treatment, all patients remained disease-free for the remainder of follow-up. Side effects were minimal, and included grade 2-3 urinary and gastrointestinal toxicity most commonly.

CONCLUSIONS

Comorbid conditions are common in patients with low grade, endometrial type endometrial cancer, with a combination of morbid obesity, diabetes, severe COPD, prior history of DVT with or without pulmonary embolism, and cardiac disease, which increase surgical risk, are also likely causes of premature death. In the event of incomplete response to the initial treatment, the incidence of contralateral endometrioid cancer, and in particular endometrioid carcinoma, has been found to be much lower in patients with specific comorbid conditions.

The Society recommends that the D90 of GTV should be at least 80 Gy and the D90 for CTV at least 48 Gy with intracavitary brachytherapy alone and 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 likelihood of success. Our findings are consistent with other case series in the literature, though these studies included patients with higher grade disease and histologic subtypes other than endometrioid, and many used applicators other than tandem and ovoid.12-17 The dosimetry techniques used in this cohort demonstrate that lower radiation doses to the CTV may provide similar efficacy to the ABS-recommended minimum doses. The use of a single tandem in combination with EBRT shows greater flexibility in dose distribution without requiring the use of multiple applicators for dose delivery under general anesthesia. For patients unable to undergo surgical management of local disease, brachytherapy alone or in combination with vaginal HDR brachytherapy is an excellent option for local disease control.

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REFERENCES


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 EDQ2 CTV</th>
<th>D2cc EDQ2 Bowel</th>
<th>D2cc EDQ2 Bladder</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDR ICBT</td>
<td>90.8 (73.8-112.1)</td>
<td>41.0 (18.6-66.6)</td>
<td>42.3 (31.1-52.3)</td>
<td>44.4 (37.9-53.6)</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 (63.0-75.0)</td>
<td>63.1 (53.7-70.9)</td>
</tr>
</tbody>
</table>

All patients 96.0 51.6

Contact Information: Scott E. Jordan, Fellowship, Advanced Pelvic Surgery and Minimally Invasive Gynecology. Fox Chase Cancer Center, Philadelphia, PA. scott.jordan@foxchase.org.