4-20-2017

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

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

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

Scott E. Jordan MD[1], Ida Micaily MD[2], Enrique Hernandez MD[3], J. Stuart Ferriss MD[4], Curtis T. Miyamoto MD FACR[3], Shidong Li PhD[5], and Bizhan Micaily MD[3]

[1]Temple Health Fox Chase Cancer Center, Dept. of Gynecologic Oncology, [2]Abington Jefferson Health Dept. of Internal Medicine, [3]Lewis Katz School of Medicine at Temple University, [4]Dell Medical School, University of Texas at Austin, [5]Temple University Hospital

INTRODUCTION

In patients with multiple medical comorbidities which preclude surgical therapy for early stage endometrioid typ e endometrial cancer, radiotherapy is considered to be the only curative treatment.[1] With the advent of iridium-192 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 target tissues, with lower doses reaching surrounding structures, such as bladder and bowel.[2]

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 T1a or T1b endometrioid 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 myometrial depth. In 2016, a protocol was initiated where gross tumor volume (GTV) was defined as the width of the endometrial stripe as demonstrated by MRI. Clinical target volume (CTV) was defined as the entire uterine corpus, cervix, and proximal 4-5 cm of vaginal wall, excluding fibroids. Goal cumulative dose to 90 percent of the tissue volume (D_{90}) in equivalent 2 Gy fractions (EDQ_2, α/ß=10) was 80-90 Gy for GTV and 60 Gy for CTV.

The decision to give external beam radiotherapy (EBRT) prior to brachytherapy was made on the basis of MRI-demonstrated myometrial invasion, indicating increased risk of occult pelvic nodal 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 fibroids.

To estimate the delivered doses given to the GTV and CTV in the patients who were dosed by the older protocol, isodose distributions were mapped onto the original treatment plans. GTV and CTV doses were calculated for each fraction of HDR brachytherapy. Equivalent dosage in 2 Gy fractions was calculated for each volume. Total dose to $2cm^3$ of bowel and bladder were also calculated using equivalent dose in 2 Gy fractions (α/ß= 3). Average follow-up time and survival were also calculated.

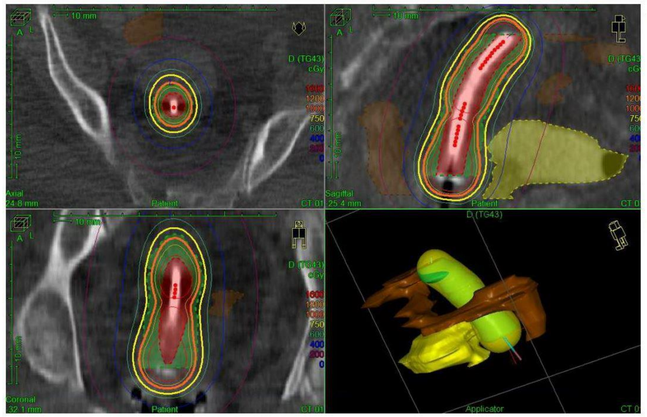

Figure 1: Sample CT-guided dose distribution plan with (clockwise from top left) transverse image, sagittal reconstruction, coronal reconstruction, and 3-D reconstruction. GTV is marked in red, CTV in light green, bowel in brown, and bladder in yellow. Isodose lines are also shown—Red=160%, Orange=120%, and Yellow=100%. The transparent 100% isodose cloud encompassed most of CTV in 3D display.

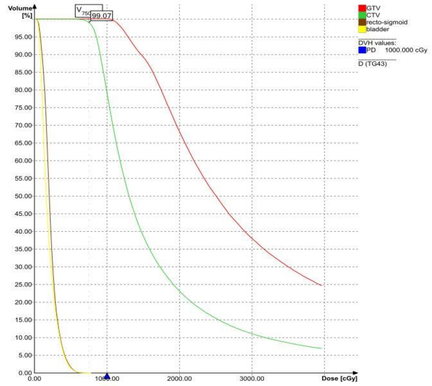

Figure 2: Dose volume histogram for the treatment plan in figure 1 to demonstrate 99% GTV coverage and 80% CTV coverage with the prescription dose of 1000 cGy while having relative low dose to the bladder and bowel (including rectum and sigmoid as well as small bowel labeled as recto-sigmoid)

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 96.0 Gy (70.5-177.1**) in equivalent dose in 2 Gy fractions (EDQ2, α/ß=10**). Mean cumulative D90 EDQ2 to CTV was 51.6 Gy (18.6-74)**.

Average follow-up was 29 months. Four patients died from concurrent disease(s) at an average of 2.83 years after completion of treatment. **Except for one (6.6%) patient who recurred at 9 months following completion of treatment, all patients remained disease-free for the remainder of follow-up**. Side effects were minimal, and included grade 1-2 diarrhea and dysuria most commonly.

Treatment	Avg D_{90} EDQ_2 GTV	Avg D_{90} EDQ_2 CTV	D_{2cc} EDQ_2 Bowel	D_{2cc} EDQ_2 Bladder
HDR ICBT	90.8 (73.8-121)	41.0 (18.6-66.6)	42.3 (31.1-52.3)	44.4 (34.7-53.6)
HDR ICBT + EBRT	100.5 (70.5-177.1)	60.9 (48.1-74)	68.0 (60.3-75.0)	63.1 (53.7-70.9)
All patients	96.0	51.6		

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.

CONCLUSIONS

Comorbid conditions are common in patients with low-grade, endometrioid type endometrial cancer. Most often, a combination of morbid obesity, diabetes, severe COPD, prior history of DVT with or without pulmonary embolism, and cardiac disease, which increase surgical risks, are also likely causes of premature death. In the event of inoperability due to the severity of these comorbid conditions, an unexpected late recurrence of endometrial cancer previously treated with radiotherapy is unlikely to be a significant driver of premature mortality when compared to the patient's other medical problems.

The Society recommends that the D90 for GTV should be at least 80 Gy, and that the D_{90} for CTV be at least 48 Gy with intracavitary brachytherapy alone and at least 65 Gy when combined with EBRT.[2] Our data demonstrate that at 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 those studies included patients with higher grade disease and histologic subtypes other than endometrioid, and many used applicators other than tandem and ovoid.[3-6] The dosimetry techniques used in this cohort demonstrate that lower radiotherapy doses to the CTV may provide similar efficacy to the ABS recommended minimum doses. The use of a single tandem in combination with EBRT allows greater flexibility in dose distribution without requiring the use of multiple applicators or dose delivery under general anesthesia. For patients unable to undergo surgical management of early-stage endometrioid endometrial cancer due to medical contraindications, treatment with intracavitary HDR brachytherapy is an excellent option for local disease control.

ACKNOWLEDGEMENTS

The authors wish to acknowledge David Serratorre, MMP and Karen Houck, MD for their assistance.

REFERENCES

1. Dankulchai P, Petsuksiri J, Chansilpa Y, Hoskin PJ. Image-guided high-dose-rate brachytherapy in inoperable endometrial cancer. Br J Radiol. 2014;87:20140018.
2. Schwarz JK, Beriwal S, Esthappan J, Erickson B, Feltmate C, Fyles A, et al. Consensus statement for brachytherapy for the treatment of medically inoperable endometrial cancer. Brachytherapy. 2015 ;14:587–99.
3. Acharya S, Esthappan J, Badiyan S, DeWees TA, Tanderup K, Schwarz JK, et al. Medically inoperable endometrial cancer in patients with a high body mass index (BMI): Patterns of failure after 3-D image-based high dose rate (HDR) brachytherapy. Radiother Oncol. 2016;118:167–72.
4. Coon D, Beriwal S, Heron DE, Kelley JL, Edwards RP, Sukumvanich P, et al. High-dose-rate Rotte "Y" applicator brachytherapy for definitive treatment of medically inoperable endometrial cancer: 10-year results. Int J Radiat Oncol Biol Phys. 2008;71:779–83.
5. Gill BS, Kim H, Houser C, Olsen A, Kelley J, Edwards RP, et al. Image-based three-dimensional conformal brachytherapy for medically inoperable endometrial carcinoma. Brachytherapy. 2014;13:542–7.
6. Weitmann HD, Pötter R, Waldhäusl C, Nechvile E, Kirisits C, Knocke TH. Pilot study in the treatment of endometrial carcinoma with 3D image-based high-dose-rate brachytherapy using modified Heyman packing: clinical experience and dose-volume histogram analysis. Int J Radiat Oncol Biol Phys. 2005;62:468–78.

CONTACT INFORMATION

Scott E Jordan. Fellow, Advanced Pelvic Surgery and Minimally Invasive Gynecology. Fox Chase Cancer Center, Philadelphia, PA. scottejordan@gmail.com. 727-709-3671