Stereotactic Body Radiation Therapy, Intensity Modulated Radiation Therapy, and Brachytherapy Boost Modalities in Invasive Cervical Cancer – A Study of the National Cancer Data Base

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OBJECTIVES
Recent studies have shown the increased use of IMRT and SBRT boost for cervical cancer to be associated with increased risk of mortality, raising concerns about alternatives over brachytherapy. Tumor BED achieved by SBRT may be more similar to the tumor BED achieved by brachytherapy. Our objective was to determine if stereotactic body radiotherapy (SBRT), intensity-modulated radiation therapy (IMRT), and brachytherapy boost techniques have comparable overall survival in treating cervical cancer when adjusted for known prognostic factors in a large national database.

METHODS
We used the National Cancer Database to identify women with invasive cervical cancer who were treated with definitive radiation for cervical cancer between 2004 and 2013 as per Figure 1. A BED was computed for those patients in the SBRT and IMRT cohorts. Independent t-test and chi square tests were used to compare the 3 groups of patients; those who received brachytherapy, SBRT, or IMRT boost. Cox proportional hazard models were used to determine correlates of survival. A logistic regression model was built to identify factors associated with the receipt of SBRT and IMRT and to develop the propensity score. Patients were matched based on propensity score against patients who received brachytherapy. 1:3 variable ratio balanced nearest neighbor method matching without replacement was used for SBRT, and 1:1 was used for IMRT. Due to the small sample size of SBRT patients 1:3 matching was selected for SBRT patients in an attempt to decrease variance and increase the precision of matching. Cases were matched based on age, comorbidity index, histology, FIGO stage, nodal status, and presence of metastasis. Outcomes of the matched samples were compared using a Cox proportional hazard model.

RESULTS
A total of 14,394 (90.5%) patients received brachytherapy, 42 (0.8%) received SBRT, and 1468 (9.2%) received IMRT. Median follow-up was 24.8 months, 22.2 months, and 37.0 months for the SBRT, IMRT, and brachytherapy boost cohort respectively. Patients with SBRT boost had higher comorbidity (p=0.004), positive nodal disease (p=0.022), and a trend towards an advancing FIGO stage disease (p=0.068) and presence of metastasis (p=0.125). Patients with IMRT boost had a higher comorbidity index (p=0.002), advancing FIGO stage disease (<0.001), positive para-aortic nodes (p<0.001), positive nodal disease (p<0.001), and presence of metastatic disease (<0.001). When compared with patients treated with IMRT boost, patients treated with SBRT boost were older (p= 0.002), lower comorbidity index (p=0.016), lower FIGO stage (p = 0.026), smaller tumor size (p=0.001), and longer duration of radiation treatment (p=0.007).

A multivariable binary logistic regression model identified the following factors associated with the use of SBRT: advancing age, higher income status, Asian ethnicity, and FIGO Stage III cervical cancer. Additionally, we identified the following factors associated with the use of IMRT: advancing age, treatment at an academic/research program, treatment at an integrated network cancer program, private insurance, lower income status, FIGO Stage III, IVA, and IVB cervical cancer, positive nodal status, metastatic disease, and not receiving chemotherapy as part of the first course of treatment. Analysis of tumor BED demonstrated a significant difference in tumor BED between patients treated with SBRT (median 76.2 Gy) and IMRT (64.2 Gy).

Patients that are treated with SBRT boost initially appear to have poorer overall survival than brachytherapy patients on univariate analysis, but multivariable Cox regression analysis and propensity matching showed that there was no significant difference in overall survival after adjusting for key prognostic factors. IMRT, however, remained statistically inferior to brachytherapy, even after controlling for the confounders with multivariate Cox and propensity score matching.

CONCLUSIONS
We found that poor prognostic factors were associated with receipt of non-brachytherapy alternatives including advanced age, nodal involvement, larger tumor size, and presence of metastasis, indicating that patients with these poor prognostic factors are more likely to be selected to receive non-brachytherapy treatment. In a propensity matched analysis, those who received SBRT boost had equal OS when compared with brachytherapy, but those who received IMRT boost had worse OS when compared with brachytherapy. Brachytherapy is currently the preferred treatment modality, but for patients who are unable to receive brachytherapy for medical or psychological indications, SBRT boost may pose as a viable alternative with comparable BED and overall survival. Prospective studies are needed to validate the use of SBRT in selected patients who are not candidates for brachytherapy.

REFERENCES