Explore the Feasibility of a Brachytherapy Alternative in the Form of Radiobiologically Optimized Stereotactic Body Radiotherapy for Locally Advanced Cervical Cancer

Pin Johnson, Mahsa Dehghanpour, EdD, Paul Mobit, PhD, and William N. Duggar, PhD

School of Health Professions, The University of Texas MD Anderson Cancer Center & Department of Radiation Oncology, The University of Mississippi Medical Center

INTRODUCTION

The standard treatment for locally advanced cervical cancer (LACC) is external beam radiotherapy (EBRT) followed by image-guided adaptive interstitial/intracavity brachytherapy (BT) boost.[1]

The quality of BT implant relies heavily on clinicians' techniques, and the geometry of the applicators relative to the target. Patients with bulky tumors, and unfavorable anatomy may not be suitable candidates for BT in addition to the compliance issues due to the relatively invasive procedure.[2] Furthermore, BT accessibility is limited in many developing countries due to inadequate funding and training.[3]

Tumor control probability (TCP) and normal tissue complication probability (NTCP) have been used to assess dose-effects in various cancers. The purpose of this research is to explore the feasibility of radiobiologically optimized SBRT boost as an alternative techniques for BT in the treatment of LACC utilizing TCP and NTCP model in RayStation[4]. Moreover, the biological optimization and evaluation of treatment planning may improve clinical decision making in balancing tumor control and harm to organs at risk (OARs).

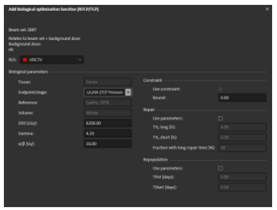

Fig. 1 Biological optimization parameters for HRCTV

METHODS

DICOM images and DICOM-RT files of one fraction of the entire BT course were transferred to RayStation. Then, the EBRT plan was copied to the BT planning Computed Tomography via scripting or replanning. TCPs of high-risk clinical target volume (HRCTV) and NTCPs of bladder, rectum and sigmoid of the composite plan of previous treatment were calculated, which were used as the biological constraints to generate SBRT plan with the background dose of the EBRT plan. The parameter for the HRCTV biological objective was illustrated in **Fig. 1**. The target and the prescription were the same in both plans. The minimum weighted planning target volume with 2 mm margin was used as a physical objective illustrated in **Fig. 2**.

EQD2 of the HRCTV D90 and EQD2 of the OARs D2cc, in addition to TCPs and NTCPs of both SBRT and Brachytherapy were evaluated to compare both techniques dosimetrically.

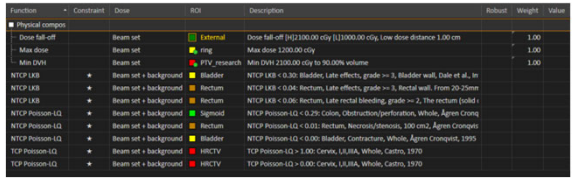

Fig. 2 Example of physical and biological objectives

RESULTS

A total of 10 patients were included in the analysis. See patient characteristics in **Table 1**. There was no statistically significant difference in TCPs between both techniques, while SBRT plan shows significances in NTCPs of late rectal bleeding, and sigmoid obstruction and perforation demonstrated in **Table 2**. Dosimetrically, SBRT plans increased an average EQD2 of D90 of the HRCTV volume by 821.56 cGy while reducing the dose to OARs. Notably, the mean EQD2 to D2cc rectum was reduced by 284.83 cGy, as demonstrated in **Table 3**. The DVH comparison is shown in **Fig. 3**.

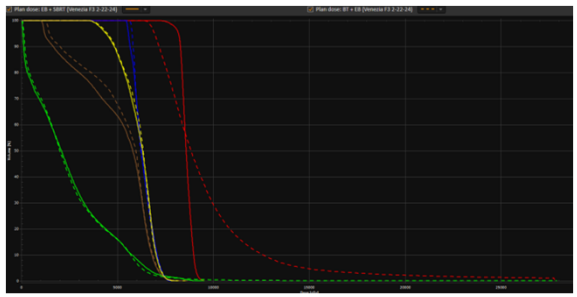

Fig. 3 Composite DVH comparison between SBRT (solid line) and BT (Dotted line) in large tumor

Table 1

Patient characteristics

Characteristic		No.	alpha/ beta ratio
Age	Mean	49	
	Range	32-58	
HRCTV (cc)	Mean	52	10
	Range	33-98	
Stage			
I-II		4	
III-IV		6	
External			3

Table 2

Mean, mean difference, and p-values for biological HRCTV TCP and OARs NTCP comparisons between brachytherapy and SBRT boost in composite of initial EBRT

Biological Objective	Subjects	Mean	Mean Difference	p-value
HRCTV TCP	BT	0.893	0.036	0.179
	SBRT	0.929		
Bladder NTCP/Late effects, grade>=3	BT	0.606	-0.073	0.060
	SBRT	0.533		
Bladder NTCP/Contracture	BT	0.184	-0.006	0.313
	SBRT	0.178		
Rectum NTCP/Late effects, grade >= 3	BT	0.112	-0.038	0.098
	SBRT	0.074		
Rectum NTCP/Late rectal bleeding, grade >= 2	BT	0.055	-0.008	**0.011**
	SBRT	0.047		
Rectum NTCP/Necrosis/stenosis	BT	0.038	-0.007	0.066
	SBRT	0.031		
Sigmoid NTCP/Obstruction /perforation	BT	0.581	-0.067	**0.019**
	SBRT	0.514		

Table 3

Mean, mean difference, and p-values comparison for EDQ2 of HRCTV D90, and OARs D2cc between brachytherapy and SBRT boost in composite of initial EBRT.

Physical Objective	Subjects	Mean (cGy)	Mean Difference (cGy)	p-value
HRCTV D90 EQD2	BT	8556.83	821.56	**0.023**
	SBRT	9378.39		
Bladder D2cc EQD2	BT	9032.96	-407.70	0.073
	SBRT	8625.25		
Rectum D2cc EQD2	BT	6746.41	-284.83	**0.025**
	SBRT	6461.58		
Sigmoid D2cc EQD2	BT	6857.22	-279.28	0.148
	SBRT	6577.94		

CONCLUSIONS

Radiobiologically optimized SBRT is a feasible technique that can achieve similar TCPs as BT and provide improvement in NTCPs of OARs while delivering extra dose to large or irregular tumors and minimizing the toxicity in rectum and sigmoid (**Fig. 4**). However, the data is not sufficient to demonstrate the superiority of SBRT plan regarding clinical outcomes. BT remains the recommended boost in the treatment of LACC.

Fig. 4 Composite isodose line comparison between SBRT (top) and BT (bottom) in large/irregular tumor.

References

1) Pötter, R. et al. The EMBRACE II study: The outcome and prospect of two decades of evolution within the GEC-ESTRO GYN working group and the EMBRACE studies. Clinical and Translational Radiation Oncology 9, 48-60; 2018.
2) Lazzari R. et al. Intensity modulated radiation therapy boost in locally-advanced cervical cancer in the absence of brachytherapy. International Journal Gynecological Cancer 30 (5), 607-612; 2020.
3) Grover, S. et al. The unique issues with brachytherapy in low- and middle-income countries. Seminars in Radiation Oncology 27 (2), 136-142; 2017.
4) RaySearch Laboratories. Biological Optimization and Evaluation in RayStation.