Dosimetric comparison of biologically-guided radiotherapy and X-ray-guided stereotactic ablative radiotherapy for oligometastatic prostate cancer William T. Hrinivich¹, Ryan Phillips¹, Angela J. Da Silva², Noura Radwan¹, Michael A. Gorin³, NS HOPKINS Steven P. Rowe⁴, Kenneth J. Pienta³, Martin G. Pomper⁴, John Wong¹, Phuoc Tran¹, Ken Wang¹ ¹Dept. of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University, Baltimore MD, USA; ²RefleXion Medical, Inc., Hayward CA, USA; **RADIATION ONCOLOGY &** ³Dept. of Urology, Johns Hopkins University, Baltimore MD, USA; ⁴Dept. of Radiology, Johns Hopkins University, Baltimore MD, USA MOLECULAR RADIATION SCIENCES **Re-planning Workflow** Results Purpose Stereotactic ablative radiotherapy Identify 15 OM prostate Add BgRT-specific Fuse diagnostic PSMAoligometastatic (OM) (SABR) Of 0.85 structures (BFZ) to cancer patients with

can prostate cancer improve tracking clinical outcomes [1], but soft-tissue lesions small during challenging with treatment IS current techniques.

PSMA-PET/CT currently provides



unparalleled sensitivity and specificity to metastatic prostate cancer [2], with an example in Fig. 1a).

A linear accelerator capable of biologically-guided radiotherapy (BgRT) is being developed to make use of PET emissions for tumor tracking during treatment, shown in Fig. 1b).



Figure 1a)¹⁸F-DCFPyL PSMA-PET fused with a CT sim. b) BgRT linear accelerator design for PET-guided radiotherapy (reproduced from RefleXion Medical Inc.).

The purpose of this study is to produce ¹⁸F-DCFPyL **PSMA-PET-based BgRT plans in a cohort of OM** prostate cancer patients using a novel plan optimizer, and compare resultant plans to clinical SABR plans.

Methods

15 OM prostate cancer patients imaged with ¹⁸F-DCFPyL PSMA-PET/CT and treated with SABR as part of our phase II randomized trial of SABR for hormone-sensitive OM prostate cancer [3] were re-planned using a research treatment planning system (TPS) designed for the BgRT tumor tracking approach outlined in Fig. 2.

Compare clinical SABR and BgRT plans in terms of:				
a) maximum PTV dose	e) mean OAR dose vs. max. PTV dose			
b) mean dose to two most proximal OARs	of BgRT relative to clinical SABR			
c) Paddick conformity index [4]	f) correlation of max. PTV dose with			
d) Paddick gradient index [5]	max. PET activity			

Figure 4 Flow chart indicating the steps in the BgRT re-planning workflow

Example Plans



Table 1 Mean±standard deviation dose metrics for each planning approach.

8	PTV D _{max}	Conformity	Gradient	OAR D _{mean}
	(% of Rx)	Index	Index	(% of Rx)
Clinical SABR	128±11	0.74±0.08	4.47±0.63	11±8
Research BgRT	150±13	0.72±0.08	5.40±0.83	10±8



120-

0

Figure 6a-d) Box plots of metrics. Center lines dose indicate median values and indicate inter-quartile boxes P-values are from range. Summary t-tests. paired statistics are provided in Table

6e) Scatter plot of mean OAR dose versus maximum PTV dose for BgRT relative to clinical SABR with Pearson correlation coefficient, solid line of best fit, and dashed blue identity line (slope = 1).



Figure 2 Schematic of the proposed BgRT tumor tracking technique. The system reconstructs a partial PET image with every 180° of gantry rotation (500 ms). The BFZ mask is applied to prevent treatment outside the target, the PET signal is converted to fluence, and the beam is delivered with an average of 400 ms latency.

A **biological firing zone (BFZ)** structure was added to each CT to prevent the treatment of non-specific PET uptake outside of the target, as shown in Fig. 3. The re-planning Clinical SABR workflow is shown in Fig. 4.

a) Conventional Target Volumes b) BgRT Target Volumes

r = 0.59, *p* = 0.02 6f) Scatter plot of max. PTV dose versus max. PTV activity with corresponding Pearson correlation coefficients. 150 max PTV activity (kBq/ml)

Conclusions

- BgRT plans resulted in significantly higher maximum PTV doses while decreasing mean dose to OARs.

- The majority of points below the identity line (dashed, slope = 1) in Fig. 6e) indicate that BgRT improved the ratio of PTV-to-OAR dose for most patients.

- A statistically significant correlation between PTV D_{max} maximum PSMA-PET activity indicates the and dependence of the BgRT optimizer on the underlying PET data, which is necessary for PSMA-PET based biological guidance.



Dose Dose (Gy) (Gy) 70 70 35 35

Figure 3 BgRT uses PET emissions to track internal tumor motion, eliminating the need for an internal target volume (ITV). BgRT requires a biological firing zone (BFZ), which acts as a mask to prevent the treatment of non-specific uptake Figure 5 Example fused PSMA-PET/CT sim images, clinical SABR dose distribution, research BgRT dose distribution, and cumulative DVH curves outside of the target. In this study, the clinical PTV was also used for BgRT planning and the BFZ was produced by for two patients. In the DVH curves, solid lines correspond to clinical SABR and dotted lines correspond to research BgRT. Note that the spatial expanding the clinical PTV by 4 mm isotropically. distribution of the BgRT dose does not match the spatial distribution of the PET activity.

-The BgRT plans provided similar target coverage to the clinical SABR plans, making use of PET-avid regions as fiducials to track and treat the entire PTV.

References

[1] Ost et al. J Clin Oncol 2018; 36(5):446-454 [2] Eiber et al. *J Nucl Med* 2015; 56(5):668-674 [3] Radwan et al. *BMC Cancer* 2017; 17(1):453-462 [4] Paddick. *J Neurosurg* 2000; 93:219-222 [5] Paddick & Lippitz. *J Neurosurg* 2006; 105:194-205