Comparison of normal tissue toxicity and target coverage robustness of two simultaneous integrated boost planning techniques for cervical cancer with positive lymph nodes

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INTRODUCTION

- Cervical cancer is a global concern, with lymph node (LN) involvement indicating worsening prognosis. This study compares the dosimetric impact and robustness of two simultaneous integrated boost (SIB) techniques, a homogenous plan (HO-P) technique following MD Anderson's uniform target dose approach and a heterogeneous plan (HE-P) technique following the EMBRACE protocol, on normal tissue (NT) and target coverage in LN-positive cervical cancer patients.

HYPOTHESIS

- We hypothesize that the Homogeneous plans will perform best in reducing NT toxicity and achieving optimal target coverage and OAR sparing compared to the Heterogenous plans and Robust-optimized plans. When comparing the two SIB plans, we expect the Homogeneous plans to show improved robustness after RayStation analysis, largely due to their consistent dose distribution, which lessens the effect of positioning uncertainties.

METHODS AND MATERIALS

- Twenty patients initially planned with sequential boosts were replanned using the two SIB methods. The targets include the uterus, cervical tumor, and lymphatic chain (CTV4500), which are within PTV4500 (CTV4500 + 7 mm), and PET/biopsy-positive lymph nodes (GTV5750), which are within PTV5750 (GTV5750 + 7 mm). These targets received 4500 cGy and 5750 cGy, respectively.
- Plans were evaluated for coverage of the targets, NT toxicity (sigmoid, rectum, and bladder), and low dose spillage with robust evaluations in RayStation assessing target coverage within 5mm-isocentric shifts. Robust optimization planning (RO-P) techniques in RayStation were also tested on five patients to assess setup uncertainties while attempting to maintain target coverage without increasing NT toxicity. The RO-P plans were then compared to the HO- P and HE-P results in terms of coverage, NT sparing, and robustness.

ROI/POI	Clinical goal	Passed	Current scenario	Worst scenario	Nominal result
CTV4500	At least 4500 cGy dose at 99.99 % volume	71 %	4513 cGy	4453 cGy	4519 cGy
GTV5750	At least 5750 cGy dose at 99.99 % volume	64 %	5799 cGy	5617 cGy	5858 cGy
ROI/POI	Clinical goal	Passed	Current scenario	Worst scenario	Nominal result
CTV4500	At least 4500 cGy dose at 98.00 % volume	43 %	4499 cGy	4452 cGy	4502 cGy
GTV5750	At least 5750 cGy dose at 98.00 % volume	93 %	5822 cGy	5749 cGy	5835 cGy
ROI/POI	Clinical goal	Passed	Current scenario	Worst scenario	Nominal result
GTV5750	At least 5750 cGy dose at 99.99 % volume	0 %	5578 cGy	5487 cGy	5995 cGy
CTV4500	At least 4500 cGy dose at 99.99 % volume	43 %	4493 cGy	4471 cGy	4582 cGy

Figure 4. (From top to bottom) Robust evaluation passing rates for HO-P, HE-P, and RO-P in a selected example patient.

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RESULTS

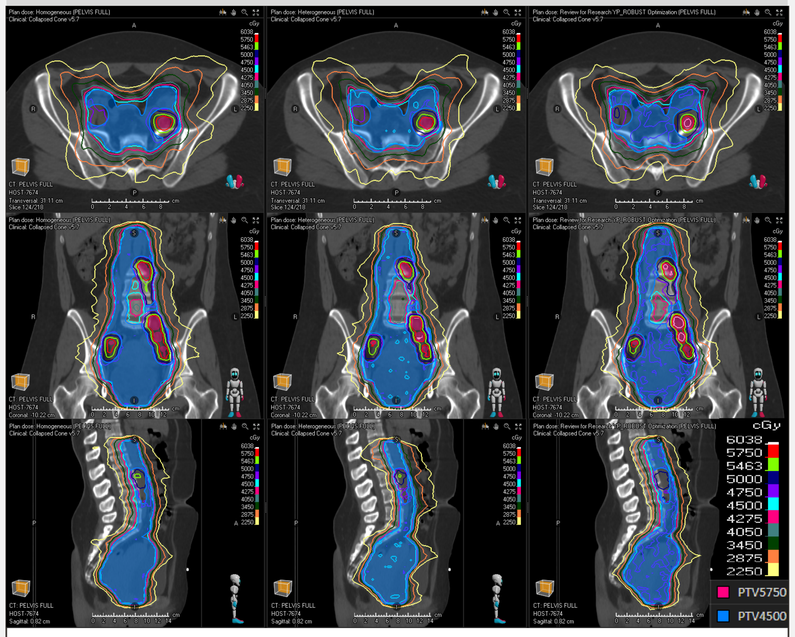

Figure 1. (From left to right) Dose distribution comparison of HO-P, HE-P, and RO-P. (From top to bottom) Axial, Coronal, and Sagittal views for an example patient.

- HE-P better spared the rectum and sigmoid, whereas RO-P showed better sparing of the bladder likely due to limited sample size. HE-P also offered more effective low-dose-level (V22.5 Gy and V13.5 Gy) sparing.

Target or OAR	Volume or DVH metric	HO-P (D100% CTV & GTV, D95% PTV)	HE-P (D98% CTV & GTV, D95%/95 PTV)	RO-P 5 patients (D100% CTV & GTV, D95% PTV)
Target	CTV4500 (cGy)	4516	4510	4528
	PTV4500 (cGy)	4566	4475	4390
	GTV5750 (cGy)	5878	5850	5949
	PTV5750 (cGy)	5854	5707	5629
Rectum	Dmax (cGy)	4867	4865	5062
	V30 (%)	89	87	81
	V40 (%)	83	80	73
Bladder	Dmax (cGy)	5280	5227	5147
	V30 Gy (%)	82	80	79
	V40 Gy (%)	72	68	69
Sigmoid	Dmax (cGy)	5341	5301	5350
	V30 Gy (%)	98	97	99
	V40 Gy (%)	93	91	97
Normal Tissue	V13.5 Gy (cc)	14442	13592	13789
	V22.5 Gy (cc)	6617	5871	6031

Table 1. Optimization algorithm average comparison for target coverage, dose received by OARs, and normal tissue dose across HO-P, HE-P, and RO-P.

- Robustness testing with 14 scenarios of 5 mm-isocentric shifts (280 robust scenarios evaluated per technique) demonstrated that the HO-P robust scenarios achieved 57% CTV4500 and 29% GTV5750 pass rates, as seen in Table 2. The HE-P robust scenarios had target passing rates of 50% CTV4500 and74% GTV5750. RO-P scenarios achieved low CTV4500 and GTV5750 pass rates

		HO-P	HE-P	RO-P (5 patients)
CTV4500	Pass Rate (%)	57±31	50±25	11±18
	Nominal (cGy)	4530±26	4510±19	4577±64
	Worst Case (cGy)	4412±101	4476±25	4061±460
GTV5750	Pass Rate (%)	29±31	74±34	1±3
	Nominal (cGy)	5884±66	5850±79	5978±71
	Worst Case (cGy)	5528±178	5704±105	5245±149

Table 2. Robust evaluation average ± standard deviation for HO-P, HE-P, and RO-P comparing pass rate, worst case scenarios, and nominal dose across all 280 robust scenarios.

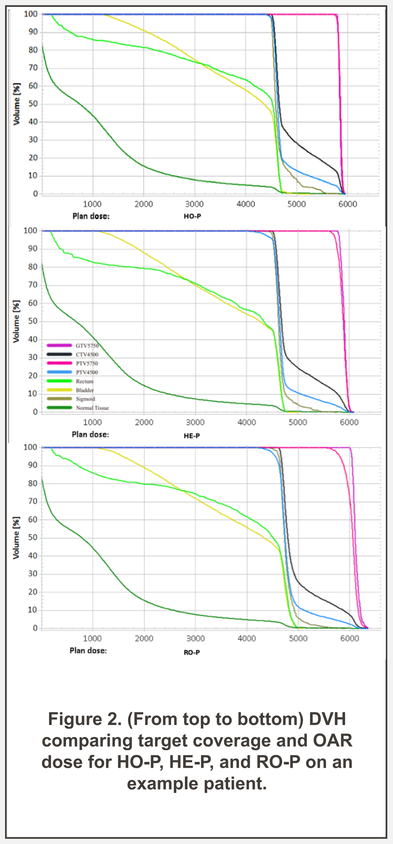

Figure 2. (From top to bottom) DVH comparing target coverage and OAR dose for HO-P, HE-P, and RO-P on an example patient.

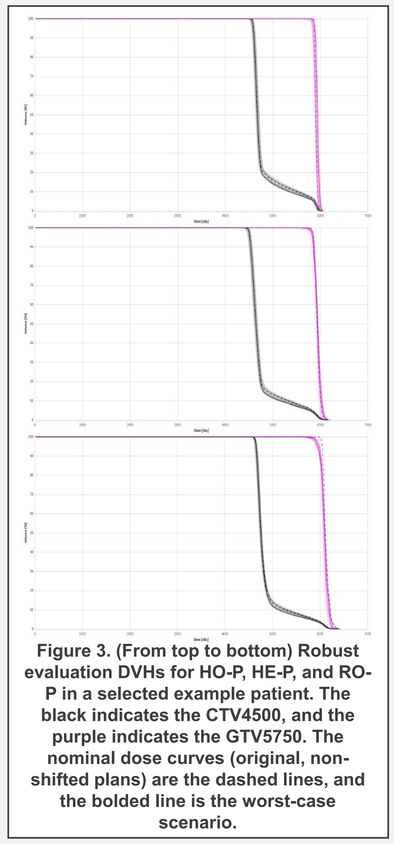

Figure 3. (From top to bottom) Robust evaluation DVHs for HO-P, HE-P, and RO-P in a selected example patient. The black indicates the CTV4500, and the purple indicates the GTV5750. The nominal dose curves (original, non-shifted plans) are the dashed lines, and the bolded line is the worst-case scenario.

LIMITATIONS

- This study had some limitations that may have influenced the findings. The small sample size of only 20 patients, with just 5 undergoing robust optimization, may have skewed the results and analysis. The D100% for CTV4500 and GTV5750 was evaluated for HO-P and RO-P, while the D98% for these targets was evaluated for HE-P. These differences in dose evaluation could have influenced the results to be more favorable to HE-P.

CONCLUSION

- In conclusion, the study demonstrated that the HO-P, HE-P, and RO-P techniques all achieved clinically acceptable target coverage. RO-P provided the highest coverage to the GTV5750 and CTV4500, while HO-P provided superior PTV coverage. HE-P was the most effective at sparing OARs, particularly the rectum and sigmoid, and it showed better low dose sparing compared to other techniques. HO-P also demonstrated the highest robustness for maintaining consistent CTV4500 coverage across shifts, while HE-P showed superior robustness for GTV5750 coverage. Although all three techniques provided adequate target coverage, each demonstrated unique strengths in terms of OAR sparing and plan robustness. Overall, the HE-P plans had only slightly less passing rates for the CTV coverage, while far exceeding the other techniques for GTV coverage, as well as having a higher (i.e. closer to prescription) worst-case scenario dose for both CTV and GTV. This indicates HE-P techniques could be a good compromise between coverage, OAR sparing, and robustness.