Dosimetric Evaluation of VMAT Grid Therapy for Bulky Tumors Using Generalized Equivalent Uniform Dose (gEUD) and Normal Tissue Objective (NTO) Optimization

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Innovation/Impact:

Treating radioresistant and bulky tumors (≥6 cm) is challenging due to their inherent resistance to standard therapies and their large size. Grid spatially fractionated radiation therapy (GridRT) offers promising solutions to these issues. This approach delivers radiation in a grid-like pattern, creating high-dose peaks surrounded by low-dose valleys. This pattern enables the destruction of significant portions of the tumor while sparing healthy tissue and may induce additional immune response. Various approaches are available for the creation of the grid. VMAT GridRT utilizes modulated arcs to create this dose pattern and is especially useful for tumors that are surrounded by sensitive critical structures. It is widely accessible and can be readily implemented. However, optimization for this unique geometry is challenging and time-consuming. Previous studies have utilized traditional physical dose-volume objectives (D-V) which require significant planner input, especially for >5 small sphere grid targets. To simplify, the generalized equivalent uniform dose (gEUD) optimization is effective. This is the first study to compare physical D-V based and biological gEUD based objectives and investigate the impact of built-in Normal Tissue Objective (NTO_{manual}) on optimization efficiency, dosimetric quality and plan complexity.

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INTRODUCTION

Spatially fractionated radiation therapy, specifically grid radiation therapy (GridRT),is a treatment option for bulky tumors. This approach delivers radiation in a grid-like pattern, creating high-dose peaks surrounded by low-dose valleys. This pattern enables the destruction of significant portions of the tumor while sparing healthy tissue and may induce additional immune response. Various approaches are available for the creation of the grid. VMAT GridRT utilizes modulated arcs to create the grid of spherical targets within the tumor. It is widely accessible and can be readily implemented. However, optimization for this unique geometry is challenging and time-consuming. This study evaluates optimization parameters to determine the ideal strategy for VMAT GridRT planning.

METHODS AND MATERIALS

In this retrospective planning study, a cohort of 10 patients was studied. Mean GTV volume was 509.6 ± 281.3cm^3.Plans utilized 5-15 spheres of 1.5 cm diameter. Spheres were placed with the previous studies. A prescription of $V_{50\%}$ = 20Gy to each sphere in a single fraction was used. 2 distinct VMAT GridRT plans using 6MV-FFF with 2 full arcs were designed and optimized. One plan was optimized with physical dose-volume objectives (D-V) without normal tissue objectives (NTO),and the other plan was optimized with generalized equivalent uniform dose (gEUD) and manually built-in NTO ($gEUD+NTO_{manual}$) in Eclipse™ (V16.1).A comprehensive comparative evaluation was performed to assess dosimetric quality. Metrics evaluated included the D_{mean} and dose gradient($D_{10\%Rx}/D_{90\%Rx}$) for the GTV and all sphere targets(z_Sphere all),and Dmax for all inner, middle and outer rings (z_IC, z_MC and z_OC) and normal tissues(body-spheres).The peak-to-edge dose ratio (PEDR) and peak-to-valley dose ratio (PVDR) were evaluated. Differences were assessed for statistical significance($p<0.05$) by use of Student's t-test.

Table 1: Objective list

	Dose-Volume(D-V)		$gEUD+NTO_{manual}$	
Structures	Objectives	Weights	Objectives	Weights
Each Sphere	D_{mean}=Rx	100	target gEUD=Rx	100
	D_{50}=Rx	100		
	D_{100} =125Rx	80		
Inner Control (z_IC)	D_{max}=98Rx	60	D_{max}=98Rx	60
	$D_{1\%}$=95Rx	50		
Middle Control (z_MC)	D_{max}=50Rx	60	D_{max}=50Rx	60
	$D_{1\%}$=48Rx	50		
Outer Control (z_OC)	D_{max}=30Rx	60	D_{max}=30Rx	60
	$D_{1\%}$=20Rx	50		
Body-spheres	$D_{1\%}$=15Rx	60		
Total Objectives # for 5 spheres	**22**		**8**	
NTO	N/A		Manual	140

RESULTS

Average dosimetric results across all cases evaluated are summarized in Table 2. No significant dosimetric difference in Dmean and dose gradient was seen for the GTV or z_Sphere all. However, gEUD+NTOmanual plans provided more consistent and conformal dose for each sphere target. gEUD+NTOmanual plans showed significantly lower Dmax in all rings and the body-spheres volume compared to D-V. The PVDR and PEDR did not change significantly (p~0.2).Optimization time was approximately 5min for gEUD+NTOmanual optimizations and increased to at least 10min for D-V to achieve similar target Dmean. GTV and z_Sphere all showed D_{mean} values that were similar on average between optimization techniques. The dose gradient ($D_{10\%Rx}/D_{90\%Rx}$) showed improvement for on average for the z_Sphere all structure for gEUD optimization. The 0.5 cm (z_IC), 1cm (z_MC) and 3cm (z_OC) ring structures and normal tissue (body-spheres) showed improved Dmax values with gEUD optimization. The peak-to-edge dose ratio (PEDR) is defined as $\frac{D_{grid}}{D_{valley}}$ and the peak-to-valley dose ratio (PVDR) is defined as $\frac{D_{grid}}{D_{edge}}$ where the valley is defined the GTV minus the grid targets and the edge is defined the 2-mm ring around the GTV. These parameters were not significantly affected.

Table 2: Result summary.

Objectives/Dose Matrix	GTV		z_Sphere all		z_IC	z_MC	z_OC	body-spheres	PVDR	PEDR
	D_{mean}(Gy)	$D_{10\%Rx}/D_{90\%Rx}$	D_{mean}(Gy)	$D_{10\%Rx}/D_{90\%Rx}$	D_{max}(Gy)	D_{max}(Gy)	D_{max}(Gy)	D_{max}(Gy)	D_{sphere}/D_{Vally}	D_{sphere}/D_{edge}
Dose-Volume (D-V)	5.8±1.5	4.1±0.6	20.1±0.1	1.5±0.1	21.7±1.9	13.9±0.2	10.6±0.1	14.0±0.2	4.1±0.9	5.6±1.7
$gEUD+NTO_{manual}$	5.1±2.8	4.5±1.4	20.2±0.1	1.3±0.0	19.5±0.7	11.8±0.1	0.9±0.1	11.8±0.1	3.9±0.9	5.0±1.4
p-vaule	0.248	0.317	0.163	0.0001	0.033	0.004	0.0001	0.004	0.198	0.130

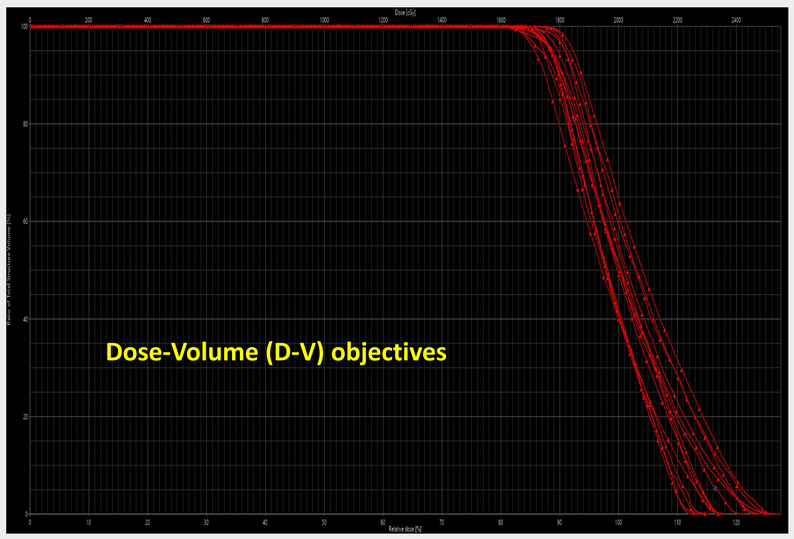

Figure 1 :The example of each sphere DVH (this case has 14 spheres) Left: gEUD + NTO_{manual} plans; Right: D-V plans

CONCLUSIONS

VMAT GridRT for bulky tumors is an emerging treatment technique with challenging planning requirements. Utilization of a single gEUD objective per sphere combined with NTO, can simplify optimization setup and reduce optimization time while preserving and/or improving plan quality compared to traditional physical optimization methods.

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