

Original Article

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Single catheter 3D volume-based hybrid inverse planning optimisation in IVBT can improve organ sparing*

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Abstract

Purpose: To analyse the dosimetric benefit of the hybrid inverse planning optimisation (HIPO) planning method over the graphical optimisation (GrO) planning method for 3D volume-based intravaginal brachytherapy (IVBT) in a mono-centre patient cohort.

Material and methods: Twenty-five patients surgically staged with endometrial cancer were considered for the study. All the patients had received adjuvant IVBT for three fractions with one-time computed tomography image-based planning. The data on the patient, tumour, plan, and treatment characteristics were retrieved from the database. All the plans were re-optimised with GrO and HIPO techniques for this comparison study. The different dosimetric parameters were compared between the two methods, and the collected data were tabulated and shown graphically. The statistical evaluation was performed with IBM SPSS version 26, and Origin Pro 8.5 was employed for plots.

Results: HIPO plans show similar target coverage in terms of $D_{90(\%)}$, $V_{95(\%)}$ and conformity index with no significant statistical difference from the GrO plans with an acceptable increase in homogeneity index ($0.087 \pm 0.062\%$). It succeeds in achieving a statistically significant reduction of dose to organs at risk such as D0.1 cc, D1.0 cc and D2.0 cc for the bladder (11.59%, 4.8% and 3.99%), rectum (41.33%, 16.9% and 16.05%) and sigmoid (20.97%, 13.53% and 11.21%), respectively, in comparison with GrO optimisation.

Conclusion: Considering the dosimetric outcome of 3D-based IVBT, it is suggested to adopt inverse optimisation techniques like HIPO over GrO to achieve higher quality treatment plan in terms of adequate target dose and lesser dose to OARs.

Introduction

Endometrial cancer is the sixth most common malignant disorder worldwide.¹ The incidence is increasing due to high rates of obesity, physical inactivity, and also an increased ageing population.² The mortality rate is higher in low socio-economic countries due to a lack of evidence-based care.^{3,4} The management essentially includes surgical staging followed by adjuvant treatment in the form of radiotherapy and/or chemotherapy. Adjuvant radiotherapy is delivered through external beam radiation therapy (EBRT) and intravaginal brachytherapy (IVBT). IVBT is almost integral to adjuvant management of all stages of endometrial cancer.⁵ The selection of applicators, such as cylinders or ovoids for IVBT, usually depends on the shape of the vagina and the extent of the lesion.⁶

In general, single catheter-based IVBT is delivered mostly with 2D planning methods such as plain-film radiograph-derived plans or library plans.^{6,7} It can also be performed by three-dimensional (3D) imaging (CT- and MRI-based) forward planning, that is, point normalisation, manual dwell time optimisation and graphically optimised (GrO) plans. In the modern brachytherapy system, inverse planning options such as hybrid inverse planning optimisation (HIPO) and inverse planning simulated annealing (IPSA) are available in the treatment planning system (TPS) software to improve the plan quality.

The conventional 2D planning methods are disadvantageous: first, due to consideration of ICRU-defined points for the bladder and rectum which may not represent the actual 3D volume,⁸ and second, in post-hysterectomy status, small bowel loops and the sigmoid colon tend to migrate to the pelvis and lie in close proximity to these organs which can be neglected completely.⁹

Although there is some positivity with 3D imaging-based forward planning to surpass the first problem of conventional planning methods (2D),¹⁰ to address the second problem, GrO method requires a lot of iteration leading to a time-consuming process and depends on the expertise of the planner as well.¹¹

3D imaging (CT and MRI) for target delineation has strengthened the foundation for the study of inverse planning optimisation in the last two decades in brachytherapy.¹² It has been proven that HIPO could generate smoother dwell time distribution which may result in more clinically desirable dose distribution in comparison with the IPSA method for cervical brachytherapy planning.¹³ Here, our prime objective is to investigate the efficacy of the HIPO relative to forward planning with GrO for single catheter-3D-based IVBT.

Material and Methods

Twenty-five patients of endometrial cancer who underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy were included in this retrospective study. Endometrioid adenocarcinoma was the most common histopathology (72%), and the majority were early-stage tumours (64%). Twenty patients had received EBRT with or without chemotherapy before IVBT, and five patients received only IVBT as per the PORTEC-2 (post-operative radiation therapy for endometrial cancer-2) trial. At the time of treatment, cylindrical vaginal applicators having a diameter ranging from 2.5 cm to 3.5 cm were used depending on the anatomical flexibility of the vaginal cavity. The treatment length for each patient was specified according to the stage and grade. The patients in this study were treated with a treatment length in the range of 4 cm to 7 cm. The detailed characteristics of the patients included in this study are given in Table 1. Computed tomography scans of all the patients were taken, with a slice thickness of 2.5 mm, and the axial images, along with the reconstructed images, were obtained and used for treatment planning. The CT-based plan with point normalisation was performed for the first fraction only and presumed similar applicator positioning with the same dosimetric parameters for the remaining fractions.

To perform the re-optimisation, the previous CT data of all the patients were used from the Oncentra brachytherapy TPS version 4.6.0. The American Association of Physicists in Medicine Task Group-43 dose calculation algorithm was employed for 3D re-optimisation for every patient by different optimisation techniques, that is, GrO and HIPO. For both GrO and HIPO planning, the volume of interest for the target, as well as organs at risk, was contoured. To perform optimisation in both the cases, clinical target volume (CTV) was created for all the patients by creating a 0.5 cm strip around the vaginal cylinder as per the required treatment length. The detailed delineation of the target volume is shown in Figure 1.

Graphical optimisation (GrO)

Vaginal brachytherapy treatment by point prescription with GrO is one of the most practised 3D image-based planning methods. In this study, all the plans were previously optimised by point-based prescription, where axis points were created at a distance of 0.5 cm from the surface of the cylindrical applicator. A dose prescription of 6 Gy in three fractions or 7 Gy in three fractions was prescribed to the axis points throughout the desired treatment length. To meet the requirement of target coverage and limit the dose to organs at risk, as recommended by ICRU 89¹⁴ was performed by GrO

Table 1. The characteristics of the patients included in this study and the patient's age, histopathology, stage, active treatment length, cylinder size, and fractionation schedule

Number of patients		25
Age	<50	3
	50–60	9
	>60	13
Histopathology	Endometrioid adenocarcinoma	18
	Papillary serous carcinoma	5
	Squamous cell carcinoma	2
Stage	I	13
	II	3
	III	7
	IV	2
Active length (cm)	4	4
	5	12
	6	6
	7	3
Cylinder size (cm)	2.5	2
	3	10
	3.5	13
Dose per fraction (Gy)	6	11
	7	14
Number of fractions		3

method, that is, by dragging the isodose line locally with the help of a computer mouse. For adequate dose coverage to the target volume, we tried to optimise at least 95% of the prescription dose (PD) to 95% of the CTV and at the same time kept the normal tissue dose to as low as practically possible.

HIPO optimisation

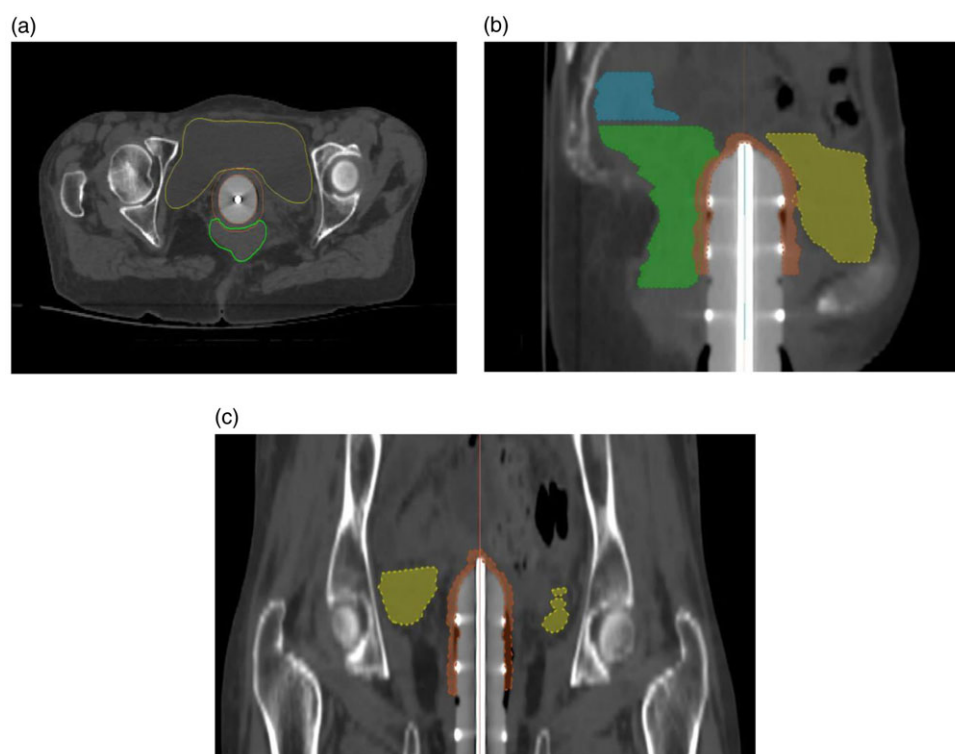
HIPO is one of the widespread inverse optimisation methods to create quality-improved brachytherapy plans for intracavitary as well as interstitial brachytherapy. The features of HIPO planning techniques are available in Oncentra brachytherapy V4.3 onwards. In this method, along with the definition of volume of interest, there is a requirement of the objective function for the target and dose constraints for the normal structures. The HIPO optimisation window provides the user to designate different target volumes, specify target objectives and apply the constraints to organs at risk. Amongst the dose–volume constraints, there is an option to set priority levels for the different contoured regions of interest.

The HIPO inverse optimisation was performed for each case as per the desired objective function for target and dose constraints for normal tissues. The parameters explaining the target objective and normal tissue constraints are in Table 2.

For HIPO optimisation, the highest priority is given to the target volume, followed by the normal structure. During the inverse planning, the target volume was prioritised to be covered by the PD while restricting the maximum dose up to 200% of the PD.

Table 2. The dose–volume constraints for the target and organs at risk

Volume of interest	Min. dose (%)	Min. weight	Max. dose (%)	Max. weight	Priority
CTV (target)	100	100	200	10	1
Rectum	–	–	70	70	2
Bladder	–	–	75	65	3
Sigmoid	–	–	65	65	4
Normal tissue	–	–	150	10	–

**Figure 1.** (a) The axial CT section containing the target volume (CTV in sandy brown), bladder (in yellow) and rectum (in green). (b) & (c) The sagittal and coronal section of the same volume of interests in solid colours

According to the sensitivity of different normal structures and considering the total EQD2 for the rectum as 75 Gy, bladder 90 Gy and sigmoid 75 Gy, the priority levels and weights were considered in this study.¹⁴ Selection of priority and weights can be altered as per the application geometry. In this study, for most of the cases, adjacent structures such as the bladder, rectum and sometimes sigmoid were seen near the tip of the applicator. In this situation, the GrO method cannot control the high dose spread to normal tissue as it is a trial-and-error, manual planning method, while HIPO can control more efficiently.

Dosimetric evaluation

The dosimetric parameters for GrO and HIPO optimisation were computed as follows: $D_{90\%}$ (dose received by 90% target volume), $V_{95\%}$ (volume receiving 95% of PD), conformity index (CI), homogeneity index (HI) and overdose index (ODI) for CTV from the planning system. To account for the high dose inside the target volume, $V_{150\%}$ (volume receiving 150% of the PD) was evaluated. The HI and CI were assessed by the following formulas: $HI = (V_{100\%} - V_{150\%}) / V_{100\%}$ and $CI = \text{volume receiving the 95\% of PD} / \text{target volume (CTV)}$, respectively. For the calculation of ODI, the following formula was considered: $ODI = V_{200\%} / V_{100\%}$.

Normal tissue tolerance doses were evaluated in terms of D0.1 cc, D1.0 cc and D2.0 cc for the bladder, rectum and sigmoid, respectively.¹⁴

Results

All the dosimetric parameters for CTV and the doses to normal structures were evaluated for both optimisations.

Statistical analysis and plots

The paired sample *t*-test was conducted using the statistical package IBM SPSS version 26, and Origin Pro 8.5 was used to make the graphical representation of those data. In this analysis, it is found that there is no significant difference between the target coverage (for $D_{90\%}$, p -value = 0.258) for both optimisations (Table 3). Optimisation with the HIPO showed a significant reduction in the doses to the bladder, rectum and sigmoid colon (Table 4). All values obtained from the cumulative dose–volume histogram were recorded with mean difference between two methods for quantitative analysis.

From the analysis, it is found that in HIPO optimisation, to cover the target and at the same time to restrict the high-dose

Table 3. The DVH parameters for the target volume, $D_{90(\%)}$ = dose received by 90% of the CTV, $V_{95(\%)}$ = volume covered by 95% of prescribed dose, $V_{150(\%)}$ = volume receiving 150% of the prescribed dose, CI = conformity index, HI = homogeneity index and ODI = over dose index

CTV parameters	GrO	HIPO	Mean difference (GrO-HIPO)	p-Value
$D_{90(\%)}$	96.96 ± 2.071	96.60 ± 2.38	0.35 ± 1.550	0.258
$V_{95(\%)}$	92.51 ± 2.071	92.35 ± 3.302	0.17 ± 2.686	0.751
$V_{150(\%)}$	13.89 ± 6.312	6.54 ± 2.950	7.36 ± 5.123	0.001
CI	0.925 ± 0.027	0.924 ± 0.033	0.0017 ± 0.026	0.751
HI	0.83 ± 0.076	0.92 ± 0.034	-0.087 ± 0.062	0.001
ODI	0.05 ± 0.026	0.003 ± 0.004	0.050 ± 0.024	0.001

Table 4. The dose volume parameters for normal structures such as the bladder, rectum, and sigmoid in terms of $D_{0.1\text{ cc}}$, $D_{1.0\text{ cc}}$, and $D_{2.0\text{ cc}}$, respectively, where $D_{0.1\text{ cc}}$ is the dose received by 0.1 cc volume of the normal structure, $D_{1.0\text{ cc}}$ for 1.0 cc volume and $D_{2.0\text{ cc}}$ for 2.0 cc volume

Normal structures	DVH parameters	GrO	HIPO	Mean difference (GrO-HIPO)	p-Value
Bladder	$D_{0.1\text{ cc}} (\%)$	99.80 ± 26.458	88.21 ± 17.575	11.59 ± 23.246	0.02
	$D_{1\text{ cc}} (\%)$	79.46 ± 15.442	74.63 ± 14.309	4.82 ± 6.712	0.001
	$D_{2.0\text{ cc}} (\%)$	72.98 ± 14.047	68.99 ± 13.239	3.99 ± 5.360	0.001
Rectum	$D_{0.1\text{ cc}} (\%)$	151.90 ± 42.660	110.56 ± 12.826	41.33 ± 35.170	0.001
	$D_{1\text{ cc}} (\%)$	113.67 ± 23.065	96.76 ± 11.356	16.91 ± 16.758	0.001
	$D_{2.0\text{ cc}} (\%)$	101.59 ± 17.989	85.54 ± 20.260	16.05 ± 23.895	0.003
Sigmoid	$D_{0.1\text{ cc}} (\%)$	60.21 ± 30.200	39.24 ± 23.224	20.97 ± 21.661	0.001
	$D_{1\text{ cc}} (\%)$	45.43 ± 26.794	31.90 ± 18.077	13.53 ± 11.799	0.001
	$D_{2.0\text{ cc}} (\%)$	39.64 ± 23.014	28.43 ± 15.385	11.21 ± 9.443	0.001

volume ($V_{150\%}$) the difference between $V_{100\%}$ and $V_{150\%}$ increases; for this reason the HI index is higher than the GrO method, and it is desired in brachytherapy.

The isodose line covering the target volume with the dose to normal organs in both methods is compared and shown in Figure 2. This section contains information regarding the volume covered by 100% isodose line in white colour and 50% isodose line in blue colour. In both optimisations, the prescription isodose line encroached the target volume, but in GrO optimisation process at the tip of the applicator along with the target volume, the isodose line (white line) covered more than 0.5 cm distance, and there is a more spreading of dose to the rectum. While in the case of HIPO, no such scenario was observed. So only the target volume is covered with the desired dose, and the dose to normal structures is restricted.

Discussion

The 2D library plan can be inferior in terms of an overestimation or underestimation of the target coverage alongside its inability to assess the OAR doses for IVBT. 2D plan considers ICRU points for bladder and rectum which may not correlate with the actual 3D volume. 2D plan has no allowance to account for this alteration, but 3D imaging-based forward planning method does overcome these above issues finely. However, the altered anatomy of pelvis post-hysterectomy allows bowel loops into the target volume, which results higher dose to bowel. This problem can be solved by HIPO instead of GrO. In some clinical situations like recurrent cases and also for young patients who are sexually

active, the use of the most advanced treatment method which can lead to a better OAR sparing with no compromise to target dose is necessary. In order to achieve such a plan with as low as reasonable dose to OARs with optimised coverage, a lot of iterations are needed for GrO-based plan, leading to a time-consuming process as mentioned in Jemema et al.¹⁵ It too depends on the expertise of the planner as well.

Fu et al. showed that HIPO generates plans with smoother dwell time distribution which are closer to clinically preferable distribution in comparison with IPSA for cervical brachytherapy.¹³ Another method provided by Bahadur et al. for vaginal HDR brachytherapy showed that the use of a multichannel vaginal applicator with inverse planning is advantageous over a single-channel cylinder.¹² However, in practical scenarios, the use of a multichannel vaginal applicator for every patient is not suitable due to patient discomfort. For such cases, inverse planning method could be a better choice of the treatment optimisation method.

Here in our study, we obtained these findings regarding target coverage. $D_{90\%}$ was 96.96 ± 2.071% and 96.60 ± 2.686%, and $V_{95\%}$ was 92.51 ± 2.071% and 92.35 ± 3.302% for GrO and HIPO plan, respectively, with *p*-values of 0.258 and 0.751, respectively, which were not significant. For OARs, HIPO plans achieved lesser dose as compared to GrO with mean differences of: bladder $D_{0.1\text{ cc}} = 11.59 ± 23.24\%$, $D_{1\text{ cc}} = 4.82 ± 6.712\%$, and $D_{2\text{ cc}} = 3.99 ± 5.36\%$, rectum $D_{0.1\text{ cc}} = 41.33 ± 35.170\%$, $D_{1\text{ cc}} = 16.05 ± 23.895\%$, and $D_{2\text{ cc}} = 41.33 ± 35.170\%$, and sigmoid $D_{0.1\text{ cc}} = 20.97 ± 21.661\%$, $D_{1\text{ cc}} = 13.53 ± 11.799\%$, and $D_{2\text{ cc}} = 11.21 ± 9.443\%$ (all with significant *p*-values). It was also seen that there is a slight increase of HI for HIPO over GrO with a mean difference of

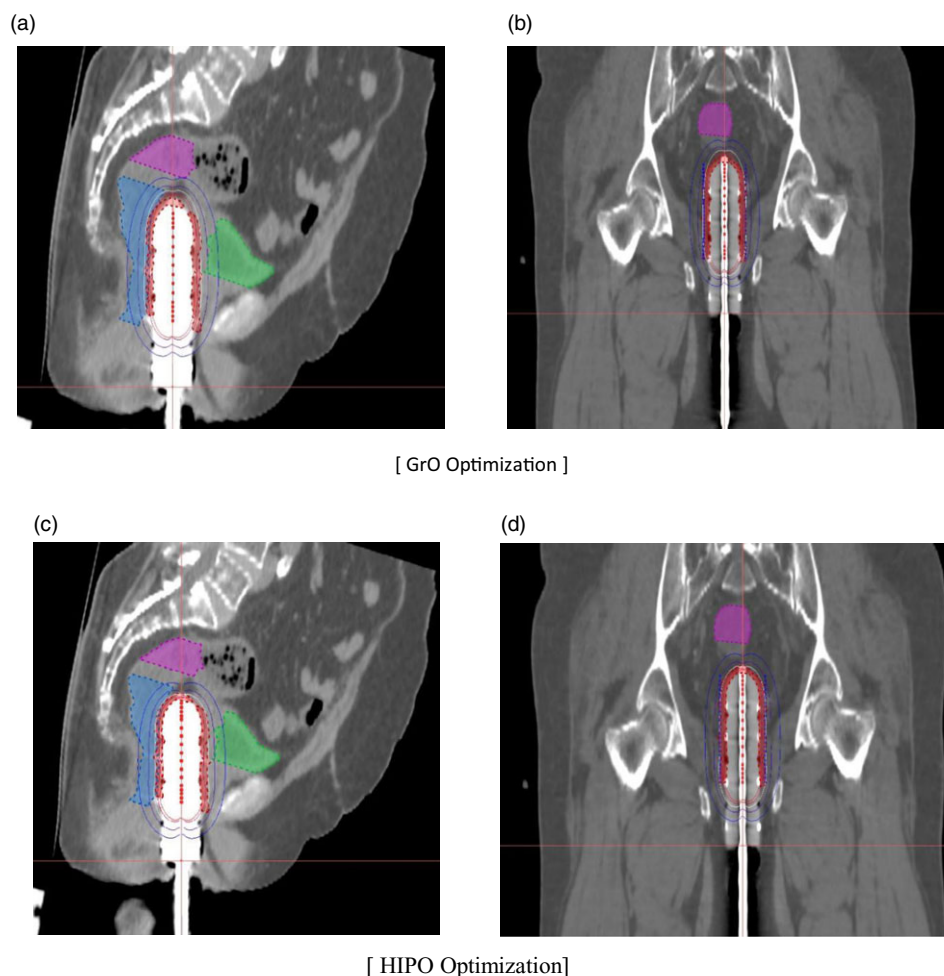


Figure 2. The isodose distribution for GrO as well as HIPO optimisation: (a) sagittal section showing dose distribution (100% in white colour and 50% in blue colour) for GrO optimisation; (b) coronal section for GrO optimisation; (c) the sagittal CT dose distribution for HIPO optimisation and (d) the coronal section for HIPO optimisation

$0.087 \pm 0.062\%$, which shows a better dose gradient as far as brachytherapy is concerned.^{16–18} Also, ODI was found to be lower in the HIPO, and it may be prudent to say that a decreased ODI may translate into a decreased dose to OARs which may result in lower toxicities.

As far as IVBT is concerned, repeated planning for each fraction using the same applicator and geometry may not affect the dosimetry. In this study, we have considered all the previous geometry for re-optimisation and data analysis. In addition to it, Holloway et al. have shown that repeated planning for each fraction does not make much significant difference in dosimetry.¹⁹

Conclusion

3D inverse planning is a simple and fast technique with better dose-sparing of normal tissues without compromising the target coverage. HIPO as a planning tool can be helpful to all levels of planners to make optimum treatment planning, unlike GrO, where better planning skills are required to control normal tissue toxicity.

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