

**Quality of treatment plans and accuracy of in-vivo portal dosimetry in
hybrid intensity-modulated radiation therapy and volumetric
modulated arc therapy for prostate cancer**

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Running head: Hybrid IMRT and VMAT

Keywords: IMRT, VMAT, prostate, treatment planning, portal dosimetry

Abstract

Background and purpose Delivering selected parts of volumetric modulated arc therapy (VMAT) plans using step-and-shoot intensity modulated radiotherapy (IMRT) beams has the potential to increase plan quality by allowing specific aperture positioning. This study investigates the quality of treatment plans and the accuracy of in-vivo portal dosimetry in such a hybrid approach for the case of prostate radiotherapy.

Material and methods Conformal and limited-modulation VMAT plans were produced, together with five hybrid IMRT / VMAT plans, in which 0%, 25%, 50%, 75% or 100% of the segments were sequenced for IMRT, while the remainder were sequenced for VMAT. Integrated portal images were predicted for the plans. The plans were then delivered as a single hybrid beam using an Elekta Synergy accelerator with Agility head to a water-equivalent phantom and treatment time, isocentric dose and portal images were measured.

Results Increasing the IMRT percentage improves dose uniformity to the planning target volume ($p < 0.01$ for 50% IMRT or more), substantially reduces the volume of rectum irradiated to 65 Gy ($p = 0.02$ for 25% IMRT) and increases the monitor units ($p < 0.001$). Delivery time also increases substantially. All plans show accurate delivery of dose and reliable prediction of portal images.

Conclusions Hybrid IMRT / VMAT can be efficiently planned and delivered as a single beam sequence. Beyond 25% IMRT, the delivery time becomes unacceptably long, with increased risk of intrafraction motion, but 25% IMRT is an attractive compromise. Integrated portal images can be used to perform in-vivo dosimetry for this technique.

Introduction

It has been recognised very early in the development of volumetric modulated arc therapy (VMAT) that there might be a role for a mixture of intensity-modulated arc therapy (IMRT) and VMAT beams in a hybrid approach [1]. This has been investigated by Robar and Thomas [2], who find that target dose homogeneity is improved with hybrid therapy compared to either a dynamic conformal arc or five-field IMRT separately, and that in prostate radiotherapy, rectal dose is equivalent with hybrid therapy compared to IMRT, but lower than with a dynamic conformal arc. In their solution, a 340° arc is used, with an additional equispaced five-field IMRT beam arrangement superimposed. The same type of approach, using IMRT beams in conjunction with a conformal arc, is shown by Martin et al. [3] to be promising for treatment of oesophagus, while Chan et al. [4] find that two partial RapidArc beams, in conjunction with two IMRT beams accounting for around 50% of the total dose, are beneficial compared to conformal beams and RapidArc for treatment of non-small cell lung cancer.

Probably the most sophisticated study is that of Matuszak et al. [5], who begin with a conformal arc and successively introduce IMRT beams, thereby obtaining a significant improvement of the plan quality in several clinical examples. Selection of beam orientations at which to use IMRT beams is on the basis of a gradient measure, which reflects edges in the intensity maps.

All of these methods begin with a relatively simple conformal arc and add intensity-modulated beams at specific gantry angles. The effect of this is that plan quality tends to improve with increased percentage of IMRT as the IMRT component adds additional degrees of freedom. However, if the starting point is a fully modulated VMAT arc, it is not so clear whether the hybrid approach is beneficial. Comparing a VMAT plan with an IMRT plan consisting of the same number of segments, the differences are firstly that the IMRT plan is more discrete in gantry angle, and secondly that the segments in the IMRT plan are delivered at specific locations in the beam's eye view which may be separate from one another, with no radiation being delivered between these

locations. This latter feature of IMRT may provide a small benefit in plan quality which might be exploited in hybrid IMRT and VMAT delivery. The present study aims to quantify this potential benefit.

A further aim of this study is to evaluate the performance of in-vivo portal dosimetry for hybrid IMRT and VMAT delivery. In-vivo portal dosimetry may be of the forward projection type, in which integrated images are predicted during treatment planning and then compared with the images obtained during treatment [6, 7], or it may be of the back projection type, where measured images are back-projected to planes or volumes within the patient to provide a dose distribution which can be compared with the planned dose [8, 9]. The latter approach is undoubtedly the more sophisticated, as it provides a three-dimensional dose distribution in the patient using gantry-resolved images. However, the former approach is also a valuable indicator that the correct dose has been delivered to the patient. The forward projection method has recently been implemented at this centre for VMAT delivery [10] and it is further evaluated in this study to examine its performance in the context of hybrid delivery. The back projection method is beyond the scope of this study.

Materials and Methods

Patients

Five consecutive prostate patients were retrospectively studied. For their treatment, all of the patients were supine, with a full bladder and empty rectum. Treatment plans were based on CT scans with 2.5 mm slice spacing. Two clinical target volumes (CTVs) were delineated, the first, CTVp, consisting of the prostate alone, and the second, CTVpsv, consisting of the prostate plus seminal vesicles. Median CTVp volume was 49.6 cm³ (range 20.6 cm³ – 107.8 cm³) and median CTVpsv volume was 55.9 cm³ (range 25.8 cm³ – 114.2 cm³). Three planning target volumes (PTVs) were produced from these volumes: PTV74 consisted of CTVp plus 5 mm in all directions except posteriorly, where the margin was 0 mm and the rectum was excluded; PTV71 consisted of

PTV74 plus a further 5 mm in all directions, and PTV60 consisted of CTVpsv plus 10 mm in all directions. The PTVs were arranged so that the outer, larger volumes excluded the smaller, inner volumes. Rectum, bladder, femoral heads (not including the necks) and penile bulb were also contoured. A mean dose of 74 Gy in 37 fractions was prescribed to PTV74, while 71 Gy and 60 Gy concomitantly in 37 fractions were prescribed to PTV71 and PTV60 respectively.

Treatment plans

Treatment plans were created using the AutoBeam in-house inverse planning system (v5.6) [11, 12] using the objectives given in Supplementary Table 1. All plans used the 6 MV flattened beam of a Synergy accelerator (Elekta AB, Stockholm, Sweden) with Agility MLC [13], and consisted of a single coplanar anticlockwise gantry rotation from gantry angle 110° to gantry angle 250°, in accord with previously determined class solutions for prostate radiotherapy [14, 15], but also as a practical means of avoiding couch bars where present. Collimator was fixed at 2° throughout, so as to spread out any interleaf leakage.

All plans consisted of 111 segments, nominally corresponding to a 2° spacing (although this was adjusted in the case of the hybrid plans; see below). The inverse planning process consisted of the now classical three-stage method: fluence optimisation, sequencing and further optimisation of the deliverable treatment plan [11, 12], with hybridisation taking place as part of the sequencing step. During fluence optimisation, the gantry angles were grouped into segment groups of 20° width separated 22° apart and a fluence map was produced using the iterative least squares method at the central gantry angle of each group. Each group was then sequenced into deliverable segments using a double close-in method which successively closed the MLC in on one peak of the fluence map, opened out again, and then repeated the process on a further peak of the fluence map. During sequencing, a chosen percentage of the control point groups were selected for IMRT delivery, while the remainder defaulted to VMAT delivery. Selection was on the basis of the complexity of each fluence map, with the most complex groups being identified for IMRT delivery. Complexity was

defined according to the following measure:

$$\text{Complexity } c = \frac{\sqrt{\frac{1}{N} \sum_i (f_i - f_{mean})^2}}{f_{95}} \quad (1)$$

Where f_i was the intensity at each pixel in the fluence map, f_{mean} was the mean fluence of the map, and f_{95} was the 95th percentile of the fluence map, representing the maximum fluence with any outlying high-intensity pixels removed.

The segments were then further optimised in terms of MLC leaf positions and segment weights, again using iterative least squares using previously described methods [12]. However, during this process, IMRT segments were required to satisfy IMRT constraints while the remaining VMAT segments were required to meet dynamic delivery constraints. The IMRT constraints were a minimum of 3 monitor units per segment, while the VMAT delivery constraints were that the gantry should not reduce speed below 3°/s, the collimator should not move faster than 80 mm/s, the MLC leaves should not move more than 30 mm/s, the dose rate should not reduce below 45 MU/min and also should not change between segments by a factor of more than 4. All segments, regardless of whether delivered by IMRT or VMAT, were required to have a minimum dimension of 15 mm, so as to allow accurate dose calculation. During this process, dose was calculated using a fast convolution method incorporating tissue inhomogeneities [16].

Based on these concepts, seven plans were constructed for each patient: the first of these, CO, was a conformal VMAT plan with 111 control points, but with all apertures conforming to the envelope of the PTVs, plus a penumbra margin of 5 mm laterally and 6 mm in the superior-inferior direction. Optimisation of this plan was limited to the segment weights. The second plan, LM, was a VMAT plan with limited modulation: two out of three control point groups were conformal, but every third control point group was sequenced according to the sequencing method described above [12] and then its MLC leaf positions and segment weights optimised for VMAT. The remaining

five plans, designated HY0 to HY100, were hybrid plans with 0%, 25%, 50%, 75% and 100% IMRT segments, with HY0 (0% IMRT) corresponding to normal, fully-modulated VMAT delivery and HY100 (100% IMRT) corresponding to a 10-beam IMRT plan with beams located every 22° (Figure 1).

For all plans, the quality was assessed using the root-mean-square dose variation from the prescribed dose in the PTVs, irradiated volumes of rectum, bladder and femoral heads, and mean dose to the penile bulb. The dose statistics were evaluated against the dose constraints for the CHHiP trial [17-19], which were principally that 99% of each PTV should receive >95% dose, rectum $V_{50\text{Gy}} < 60\%$, rectum $V_{65\text{Gy}} < 30\%$, bladder $V_{50\text{Gy}} < 50\%$, bladder $V_{60\text{Gy}} < 25\%$, femoral heads $V_{50\text{Gy}} < 50\%$. The dose statistics shown in Supplementary Table 1 were also weighted according to importance factor and negated in the case of objectives requiring maximisation, and the sum of these weighted statistics was used as a quality index, a lower value indicating better plan quality. The total monitor units were recorded for each treatment plan. Data were demonstrated by quantile-quantile plots to be normally distributed and compared to the HY0 (normal VMAT) case using two-tailed paired Student t-tests.

Delivery and verification

In-vivo portal imaging was simulated in a phantom scenario by means of forward image prediction [10]. Following inverse planning, each plan was recalculated with the isocentre located centrally in a homogeneous water phantom of width 300 mm, length 300 mm and height 200 mm. The mean dose at the centre of the phantom in a volume representing a 0.6 cm³ Farmer ionisation chamber (Saint Gobain Crystals and Detectors, Reading UK) was calculated. This volume was contained within a region of PTV74 receiving a homogeneous dose. The planned doses due to all segments of the hybrid plans were then forward projected from the isocentre plane to the plane of the portal imager and summed to give a single total predicted image for the treatment.

The hybrid treatment plans were then delivered to a water equivalent phantom (Solid Water,

Radiation Measurements, Inc., Madison, WI), using a Synergy accelerator. The total time for delivery of each plan was recorded and the dose at the centre of the phantom was also recorded. The integrated portal image for each plan was also measured using an iViewGT portal imager (Elekta AB). The imaging panel was observed to reduce in output by 4% when recording a 100 x 100 mm field delivered by 100 segments of 3 MU each, compared to a single delivery of 300 MU, with the accelerator output measured by an ionisation chamber as a reference [20, 21]. The measured images were therefore increased by 1% for every 25% of IMRT to account for the low monitor units per segment encountered in the IMRT components of the arcs. All images were also increased by 3% to account for couch absorption, which was not included in the prediction model. The measured portal images were compared with the predicted images using OmniPro I^mRT (IBA, Schwarzenbrück, Germany), using a global gamma index for 3% and 3 mm and a dose threshold of 10%. Both the mean gamma index and percentage of measurements with gamma index less than unity were recorded.

Results

Mean dose-volume histograms for the seven types of treatment plan are shown in Figure 2 and the corresponding statistics are given in Table 1. The conformal VMAT plan CO is not able to provide the required doses to the three PTVs due to its conformal nature, and the rectal and bladder doses are also very high, but this plan is included for purposes of comparison as the baseline against which the other techniques can be measured.

The limited modulation VMAT plan LM provides good coverage of the PTVs but again irradiates a slightly large volume of rectum and bladder, the rectal dose constraints used in the CHHiP trial [17-19] being met but the bladder $V_{60\text{Gy}}$ being excessively high.

The hybrid IMRT and VMAT plans all provide good differentiation of the PTV dose levels and adequate sparing of the rectum and bladder. However, raising the IMRT component improves PTV dose uniformity ($p < 0.01$ for 50% or more), reduces the volume of rectum irradiated to 50 Gy

($p < 0.05$ except for 75% IMRT), reduces the volume of rectum irradiated to 65 Gy ($p < 0.05$ for 25% IMRT and 50% IMRT) and increases the monitor units ($p < 0.001$).

The distribution of IMRT segment groups is predominantly anterior (Supplementary Figure 1), indicating that the IMRT group selection method is choosing gantry angles at which the fluence distribution is higher laterally and lower in the central area, where the rectum passes through the beam's eye view. Use of IMRT in such a situation means that the beam can be switched off while the aperture passes from one side of the rectum to the other, which improves the rectal sparing. However, this improvement in plan quality is obtained at the expense of a short treatment time, as the delivery time increases considerably with increased percentage of IMRT (Table 1).

All types of plan can be delivered reliably, with measured isocentric doses within 3% of the planned dose (Table 1). Agreement between measured and predicted portal images is closest for CO and LM due to the simple nature of the segments, but the agreement of the hybrid plans is also good. Sample images are shown in Figure 3 and the full results are given in Table 1.

Discussion

These results confirm that adding modulation to selected parts of a conformal VMAT arc can improve the plan quality. The conformal VMAT arc (CO) is very simple and in this study is unable to differentiate between the dose levels required for the different PTVs. However, introducing modulated sections of arc improves the plan quality considerably (LM), without impacting very much on the overall treatment time. However, a fully modulated VMAT arc (HY0) provides considerably superior plan quality to either of these options. The more important question is therefore: how much improvement can be achieved by use of IMRT for some of the sections of VMAT arc? This study shows that plan quality definitely improves by the use of IMRT for some of the sections, with maximum benefit achieved with 100% IMRT. However, this increases the treatment time, which in turn increases the likelihood of intrafraction motion [22-25], so it is likely that there is a trade-off between improved plan quality due to increased IMRT and degrading

dosimetry due to long treatment time. Several authors have evaluated the relationship between intrafraction motion and treatment dosimetry [26, 27], but the impact of treatment time on this relationship is not very clear, so a pragmatic compromise is recommended, such as 25% IMRT. Time available for treatment of the patient is also an important factor which varies from centre to centre.

These results are similar to those of Robar and Thomas [2], who find that target dose homogeneity is improved with hybrid therapy compared to either a dynamic conformal arc or five-field IMRT separately, and that rectal dose is equivalent with hybrid therapy compared to IMRT, but lower than with a dynamic conformal arc. The results are also broadly in agreement with those of Matuszak et al [5], who begin with a conformal arc and successively introduce IMRT beams, thereby obtaining a significant improvement of the plan quality in their prostate phantom case.

The reduction in irradiated volume of rectum at the 65 Gy level seen in the hybrid plans is likely to result in a small reduction in the probability of grade 2 rectal toxicity [28-30]. This is achieved without significant detriment to any of the other dose statistics. Meanwhile, the improvement in PTV homogeneity seen with the hybrid plans contributes to accurate dose delivery, particularly in the presence of any interfraction motion. It is likely to be the improved PTV coverage which gives rise to the small and statistically insignificant increase in mean dose to the penile bulb.

In-vivo portal dosimetry also functions reliably for hybrid IMRT and VMAT treatment plans. The results show that the forward prediction method is able to conveniently predict the expected integrated images to within 3% and 3 mm, which is acceptable for clinical use and considerably better than the 5% and 5 mm agreement recommended by ICRU 83 for pre-treatment verification [31]. This is important, because the introduction of a new technique in a modern setting requires corresponding quality measures to be similarly included [32]. For prostate, in-vivo portal dosimetry is in widespread clinical use for treatment verification [9], increasingly as the sole dosimetric measure [33], so demonstration of accurate performance of in-vivo portal dosimetry for hybrid

IMRT and VMAT is essential. Further work is needed to implement back projection in-vivo portal dosimetry for hybrid delivery and to investigate the differences between the forward and back projection methods.

Conclusion

Hybrid IMRT / VMAT can be efficiently planned and delivered as a single beam sequence, giving improved target dose homogeneity and rectal sparing. Beyond 25% IMRT, the delivery time becomes unacceptably long, with increased possibility of intrafraction motion, but 25% IMRT is an attractive compromise. Integrated portal images can be used to perform accurate in-vivo dosimetry for this technique.

Conflict of interest statement

This work was carried out using a research linear accelerator shared with Elekta AB. JLB is the recipient of a research grant from Elekta and ACT is the recipient of a travel grant from Elekta.

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Tables

Table 1. Mean (± 1 SD) statistics for the seven types of treatment plan.

	PERCENTAGE IMRT IN HYBRID PLAN						
	CO	LM	HY0	HY25	HY50	HY75	HY100
PTV74 RMS* (%)	4.6 \pm 0.7	1.4 \pm 0.1	2.1 \pm 0.3	2.0 \pm 0.2	1.8 \pm 0.3	1.4 \pm 0.2	1.2 \pm 0.1
PTV71 minimum dose (Gy)	64.0 \pm 3.2	63.6 \pm 1.6	64.4 \pm 2.2	64.9 \pm 2.1	65.0 \pm 2.1	65.2 \pm 1.9	65.1 \pm 1.8
PTV60 minimum dose (Gy)	60.2 \pm 3.2	56.8 \pm 1.6	55.6 \pm 1.6	55.8 \pm 1.8	55.9 \pm 1.9	56.1 \pm 1.8	56.5 \pm 2.0
Rectum V30Gy (%)	81.1 \pm 9.0	77.6 \pm 9.1	76.9 \pm 9.5	76.2 \pm 10.2	78.3 \pm 9.8	77.3 \pm 9.7	74.7 \pm 10.0
Rectum V50Gy (%)	55.9 \pm 9.8	51.9 \pm 9.6	43.8 \pm 9.3	41.8 \pm 8.2	41.3 \pm 8.2	40.5 \pm 7.9	39.5 \pm 8.0
Rectum V65Gy (%)	21.2 \pm 7.6	17.2 \pm 5.9	15.2 \pm 5.1	13.6 \pm 4.3	13.4 \pm 4.0	13.3 \pm 4.0	13.2 \pm 3.9
Bladder V50Gy (%)	39.5 \pm 11.9	33.7 \pm 10.8	31.5 \pm 9.4	32.6 \pm 9.6	33.8 \pm 10.5	32.9 \pm 10.2	32.0 \pm 10.3
Bladder V60Gy (%)	32.0 \pm 9.5	26.1 \pm 8.8	23.6 \pm 7.8	23.8 \pm 7.7	24.0 \pm 7.7	23.9 \pm 7.5	23.8 \pm 7.5
Femoral heads V50Gy (%)	0.0 \pm 0.0	0.3 \pm 0.7	0.0 \pm 0.0	0.1 \pm 0.1	0.0 \pm 0.0	0.0 \pm 0.0	0.0 \pm 0.0
Penile bulb mean dose (Gy)	57.4 \pm 12.7	57.4 \pm 12.6	55.6 \pm 12.7	56.8 \pm 12.7	57.2 \pm 13.1	57.3 \pm 13.3	57.3 \pm 13.4
Quality index	8.6 \pm 0.7	8.0 \pm 0.8	7.6 \pm 0.7	7.4 \pm 0.7	7.4 \pm 0.6	7.3 \pm 0.6	7.1 \pm 0.6
Total monitor units	314 \pm 11	347 \pm 9	341 \pm 10	376 \pm 11	388 \pm 14	400 \pm 12	406 \pm 11
Delivery time (s)	44 \pm 2	56 \pm 2	75 \pm 4	202 \pm 10	277 \pm 17	379 \pm 26	439 \pm 36
Measured dose vs plan (%)	0.4 \pm 0.6	0.3 \pm 1.3	0.9 \pm 1.3	1.1 \pm 1.3	1.2 \pm 1.6	0.4 \pm 0.9	0.0 \pm 1.0
Mean gamma	0.35 \pm 0.06	0.34 \pm 0.07	0.33 \pm 0.08	0.39 \pm 0.09	0.39 \pm 0.09	0.44 \pm 0.18	0.48 \pm 0.14
Gamma < 1 (%)	99.1 \pm 1.7	98.8 \pm 2.2	98.7 \pm 1.3	95.6 \pm 4.8	97.1 \pm 3.8	93.1 \pm 10.5	93.3 \pm 9.3

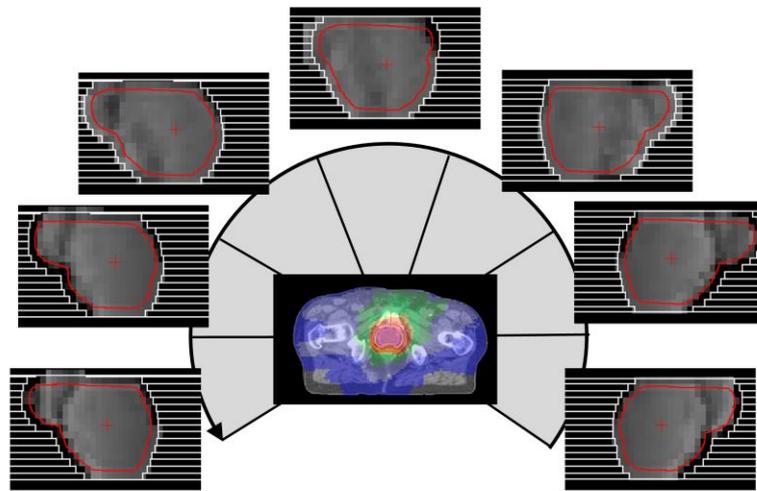
*RMS: root mean square dose variation.

Figure captions

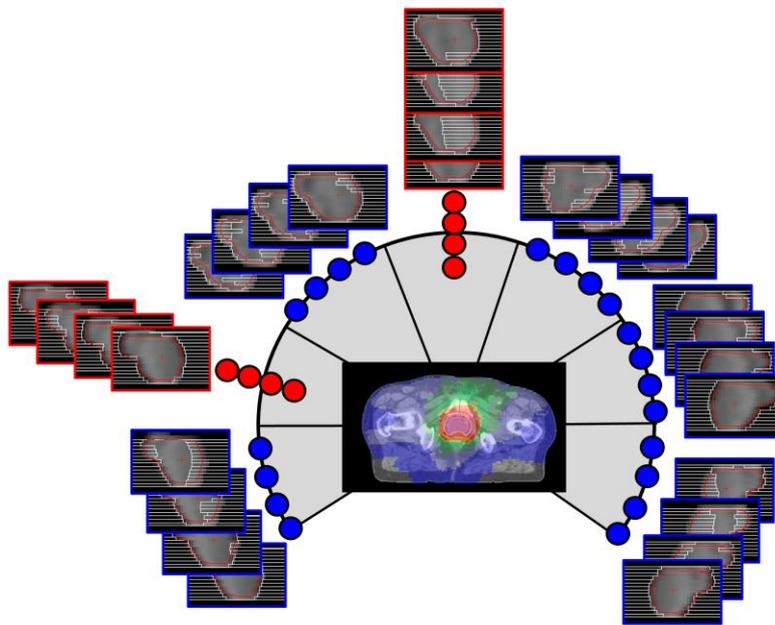
Figure 1. Schematic diagram showing the concept of hybrid IMRT and VMAT optimisation and delivery. (a) The arc is divided into segment groups and fluence is optimised for each group. (b) The segment groups are further optimised for either VMAT delivery (blue) or IMRT delivery (red). VMAT segments are distributed over the gantry range of each segment group, while IMRT segments are all positioned at the central gantry angle of each segment group. The whole sequence is delivered as a single beam.

Figure 2. Mean dose-volume histograms for the seven different types of treatment plan. The insets to the histograms for PTV74, PTV71 and PTV60 show the transaxial, sagittal and coronal dose distributions, respectively, for HY25.

Figure 3. Typical portal imaging results for HY25. (a) predicted image, (b) measured image, and (c) gamma distribution for 3% and 3 mm.



(a)



(b)

Figure 1

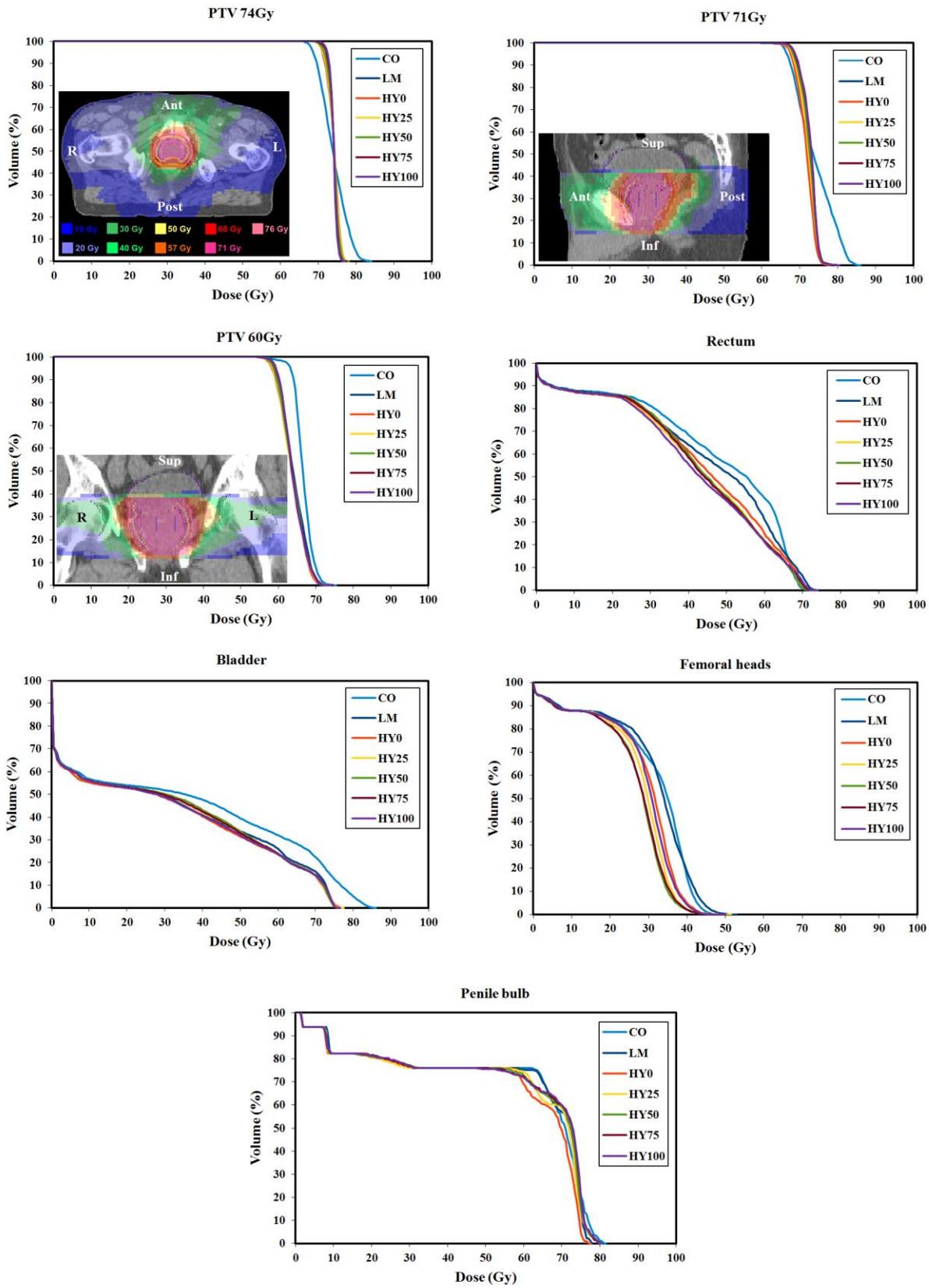
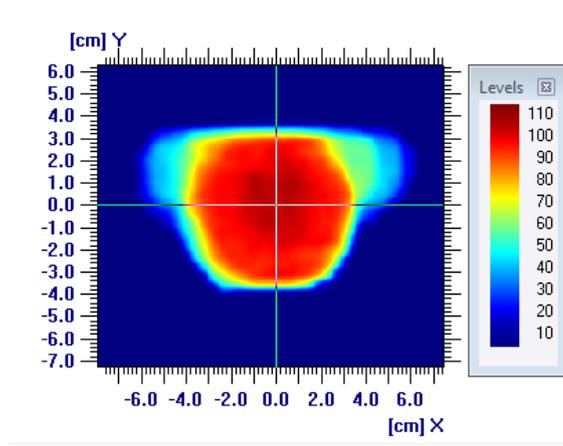
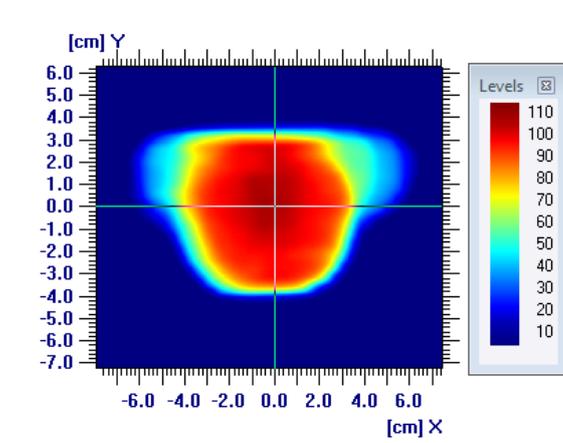


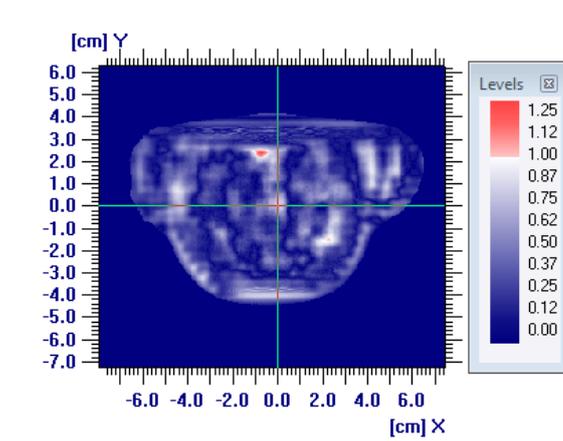
Figure 2



(a)



(b)



(c)

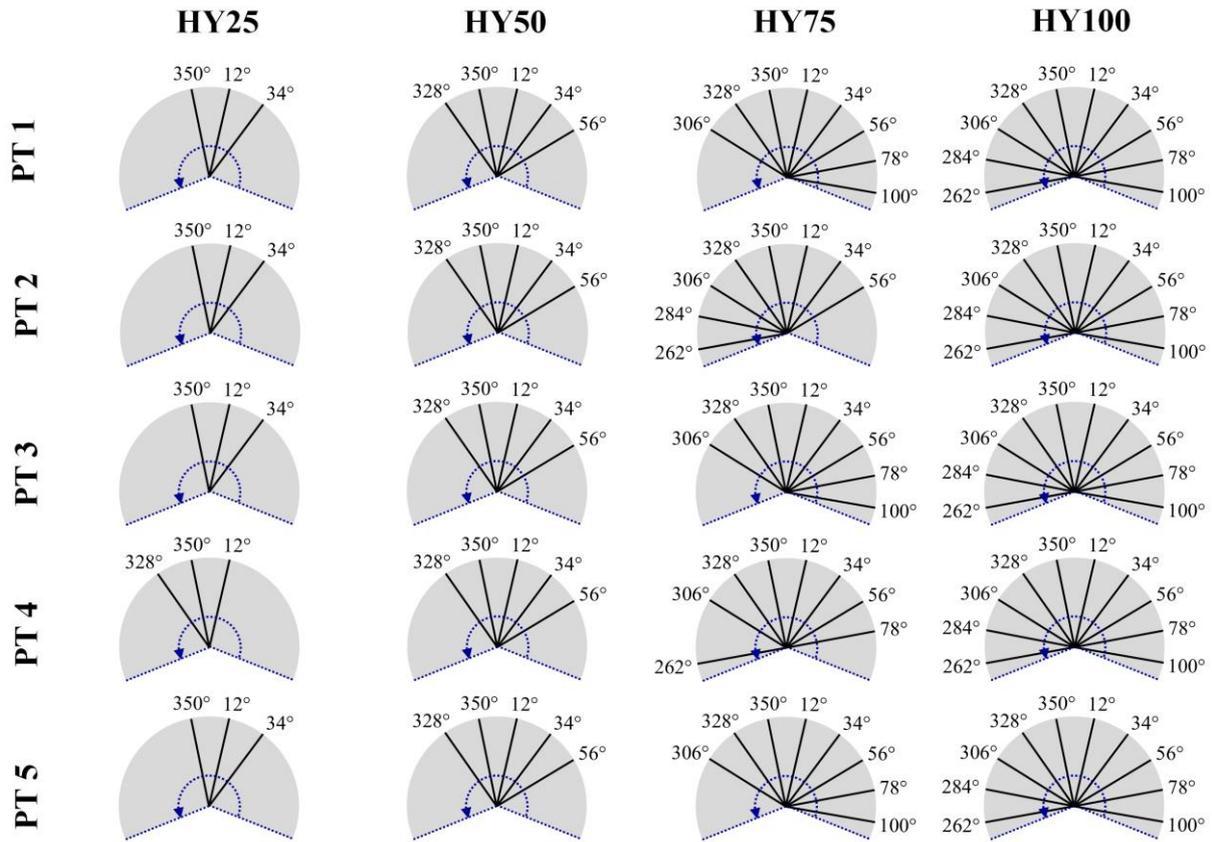
Figure 3

Supplementary material

Supplementary Table 1. Inverse planning objectives.

ACTION	VOLUME	STATISTIC	IMPORTANCE
Minimise	PTV74	RMS* dose around 74 Gy	with weight 20
Minimise	PTV71	RMS* dose around 74 Gy	with weight 20
Minimise	PTV60	RMS* dose around 62 Gy	with weight 20
Maximise	PTV71	minimum dose	with weight 20
Maximise	PTV60	minimum dose	with weight 20
Minimise	Rectum	vol irradiated to 30 Gy	with weight 40
Minimise	Rectum	vol irradiated to 50 Gy	with weight 40
Minimise	Rectum	vol irradiated to 65 Gy	with weight 40
Minimise	Bladder	vol irradiated to 50 Gy	with weight 4
Minimise	Bladder	vol irradiated to 60 Gy	with weight 4
Minimise	Femoral heads	vol irradiated to 50 Gy	with weight 1
Minimise	Penile bulb	mean dose	with weight 1

*RMS: root mean square dose variation.



Supplementary Figure 1. Distribution of IMRT segment groups among the hybrid plans in the five patients.