Technical Note

A Pilot Study on the Comparison between Planning Target Volume-based Intensity-Modulated Proton Therapy Plans and Robustly Optimized Intensity-Modulated Proton Therapy Plans

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Abstract

The objective of this work is to compare the planning target volume (PTV)-based intensity-modulated proton therapy (IMPT) plans with robustly optimized IMPT plans using the robust optimization tools available in Pinnacle Treatment Planning System. We performed the study in five cases of different anatomic sites (brain, head and neck, lung, pancreas, and prostate). Pinnacle IMPT nonclinical version was used for IMPT planning. Two types of IMPT plans were created for each case. One is PTV-based conventionally optimized IMPT plan and the other is robustly optimized plan considering setup uncertainties. For the PTV-based plans, margins were on top of clinical target volume (CTV) to account for the setup errors, whereas in the robustly optimized plan, the setup errors were directly incorporated into the optimization process. The plan evaluation included target (CTV) coverage and dose uniformity. Our interest was to see how the target coverage and dose uniformity were perturbed on imposing setup errors in +X, −X, +Y, −Y, +Z, and −Z directions for both PTV-based and robust optimization (RO)-based plans. On the average, RO-based IMPT plans have shown a good consistency of target coverage and dose uniformity for all six setup errors scenarios as compared to PTV-based plans. In addition, RO-based plans have a better target coverage and dose uniformity under uncertainty conditions as compared to the PTV-based plans. The study demonstrates the superiority of robustly optimized IMPT plans over the PTV-based IMPT plans in terms of dose distribution under the uncertainty conditions.

Keywords: Intensity-modulated proton therapy, proton therapy, robust optimization, setup uncertainties

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Introduction

Intensity-modulated proton therapy (IMPT) offers an advantage over intensity-modulated radiation therapy (IMRT) in which the dose modulation is possible along the direction of the beam in addition to the lateral direction of the beam. Because of this unique advantage, one can achieve a very good sparing of healthy tissue while delivering the prescribed dose to target volume. However, unlike IMRT, the dose distribution obtained from IMPT is hugely impacted by the range and setup uncertainties.[1] In photon therapy, the planning target volume (PTV) can account for setup uncertainty.[2] This approach works in photon therapy because photon dose distribution is not significantly perturbed by changes in patient geometry. However, in IMPT, the dose distribution is highly sensitive to the changes in the patient geometry and hence the applicability of the concept of PTV in IMPT is limited.[3] To eliminate the drawbacks in the PTV-based approach, robust optimization (RO) approach was proposed.[4-6] Essentially, RO makes the IMPT plans less sensitive to uncertainties as compared to PTV-based plans.

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The purpose of this work is to demonstrate the superiority of robustly optimized plans over PTV-based plans in terms of organs-at-risk (OARs) sparing, target dose coverage, and dose uniformity. It is to be noted that recently a similar kind of study was presented for head-and-neck and prostate cases.[7] In our study, we have extended the RO approach for five different anatomic sites (brain, head and neck, lung, pancreas, and prostate).

Materials and Methods

Robust optimization

RO is a technique for optimizing an IMPT by taking into account range and setup errors. In RO, the setup uncertainty is modeled by simulating a set of independent uncertainty cases that mimic whole-body movement of the patient in six directions (three pair of positive and negative coordinates). For setup error, the RO minimizes a total objective value (RO OBV), which includes a clinical objective component (Nominal Plan OBV) and a patient setup error component (Setup Error OBV). Equation 1 provides an example of such an objective function considering only the setup errors.

$$\text{RO (Setup error) OBV} = \text{Nominal Plan OBV} + \text{Setup Error OBV} \quad (1)$$

where Set up error OBV = (+X error OBV) + (−X error OBV) + (+Y error OBV) + (−Y error OBV) + (+Z error OBV) + (−Z error OBV). Each objective value represents a respective uncertainty scenario. For example, +X error OBV is the objective value obtained from the dose statistics when the patient is shifted in a positive X direction by a factor specified by the user.

Study methodology

We performed the study in five cases of different anatomic sites (brain, head and neck, lung, pancreas, and prostate). Pinnacle IMPT nonclinical version was used for IMPT Planning. IBA spot scanning machine was modeled and used for generating IMPT plans, which has energy ranging from 70 MeV to 226 MeV. Pinnacle uses a pencil beam algorithm for IMPT dose computation. Two types of IMPT plans were created for each case. One is PTV-based conventionally optimized IMPT plan and the other is robustly optimized plan considering setup uncertainties. For the PTV-based plans, margins were created on top of clinical target volume (CTV) to account for the setup errors, whereas in the robustly optimized plan, the setup errors were directly incorporated into the optimization process. We restricted this study to setup errors and deliberately did not include range error in order to make an effective comparison between PTV approach and RO approach.

Table 2: Setup errors applied for the clinical cases in the study

Clinical case	X (±) (in cm)	Y (±) (in cm)	Z (±) (in cm)
Brain	0.5	0.5	0.5
Head and Neck	0.6	0.6	0.6
Lung	0.6	0.6	0.6
Pancreas	0.5	0.5	0.5
Prostate	0.5	0.3	0.5

Table 1: Details about the planning parameters used in the study

Anatomic site	No. of Beams	Beam angles used (in Degree)	Prescribed dose (D95) in cGy	Target details with volume in cm^3	OARs used for optimization++
Brain	4	100* 245* 280* 325*	5000	PTV (85.52 cm^3) CTV (50.44 cm^3)	Brainstem, Lens (R), Optic Chiasm, Optic Nerves (R/L), Cochlea (R/L)
H&N**	3	180 60* 300 *	7000 6300 5600	PTV70 (78.39 cm^3) PTV63 (269.21 cm^3) PTV 56 (592.045 cm^3) CTV70 (27.70 cm^3) CTV 63 (142.17 cm^3) CTV 56 (175.97 cm^3)	Spinal cord, Brain stem, Parotids (L/R), Larynx, Cochlea (L/R), Submandibular glands (L/R), Lips, Post Neck.
Thorax (Lung)	2	245 * 170 *	6600	PTV (179.05 cm^3) CTV (77.76 cm^3)	Spinal Cord, Lung (R/L), Bronchial tree.
Pancreas	3	40 * 130 * 310 *	5000	PTV (398.373 cm^3) CTV (296.885 cm^3)	Spinal Cord, Kidney (R/L), Liver, Small bowel, Stomach.
Prostate**	2	90 270	6600 5400	PTV66 (107.21 cm^3) PTV54 (622.93 cm^3) CTV66 (51.43 cm^3) CTV54 (326.03 cm^3)	Bladder, Rectum, Bowel Large, Femoral head (R/L), Small bowel

(*) Indicates that beams are used with Range shifters. (**) Indicates that more than one Targets are used in optimization. (++) OAR constraints used are based on RTOG guidelines

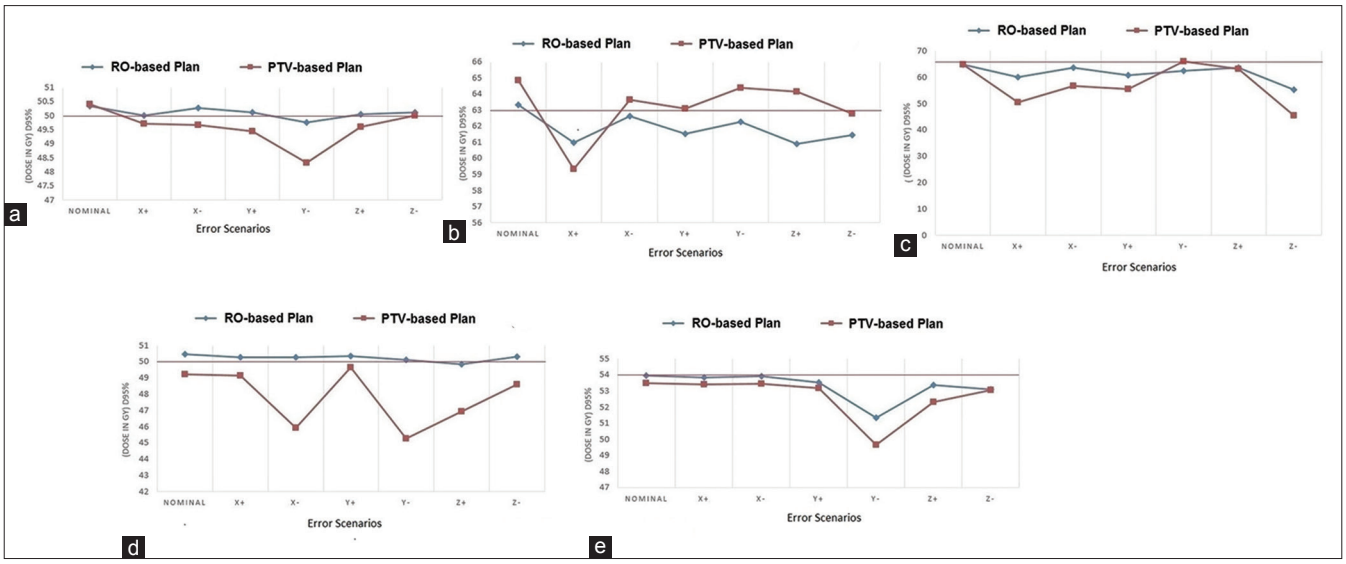

Figure 1: The comparison of target coverage between planning target volume-based plans and robust optimization-based plans under setup uncertainty conditions for brain case (a), head and neck case (b), lung case (c), pancreas case (d), and prostate case (e). The horizontal line in the graph indicates the prescribed dose to target (d95%)

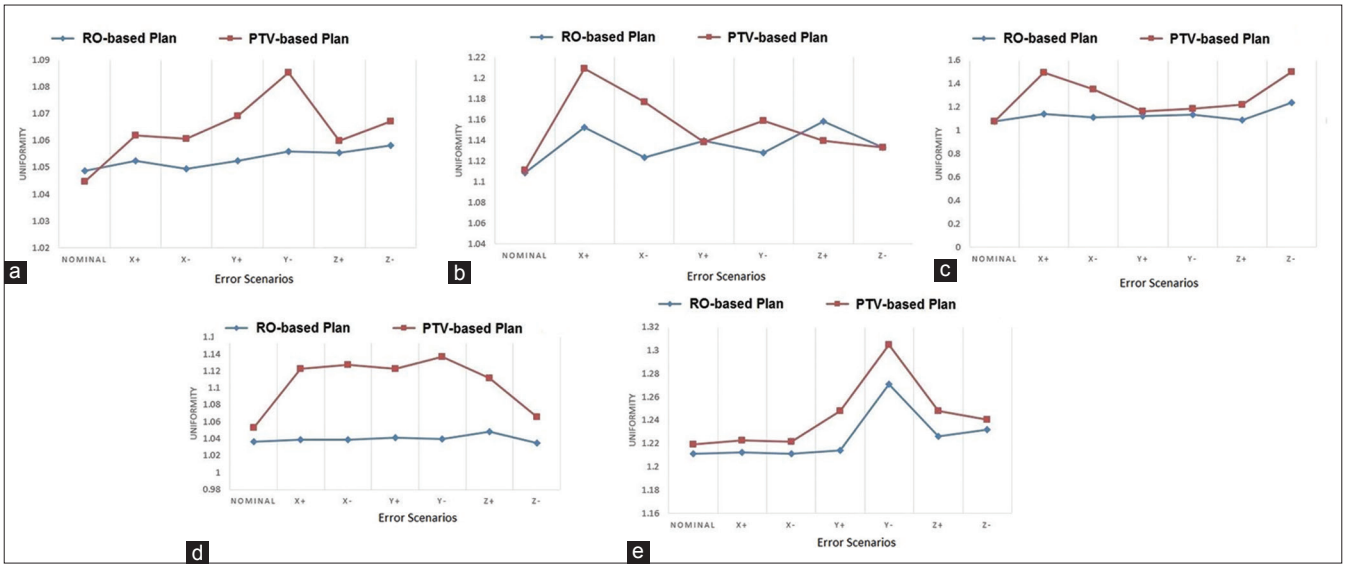

Figure 2: The comparison of target dose uniformity between planning target volume-based plans and robust optimization-based plans under setup uncertainty conditions for brain case (a), head and neck case (b), lung case (c), pancreas case (d), and prostate case (e)

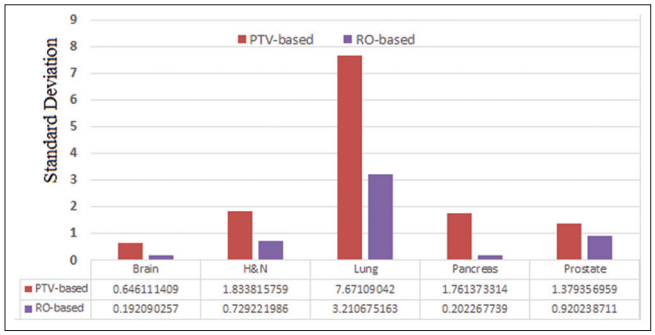

Figure 3: The comparison of the standard deviation of target coverage (CTV) under the imposed setup errors in +X, −X, +Y, −Y, +Z, and −Z directions for both planning target volume-based and robust optimization-based plans

Using the robustness analysis tools available in Pinnacle Treatment Planning System, we simulated the setup error scenarios in +X, −X, +Y, −Y, +Z, and −Z directions after generating the nominal plans from PTV-based approach and RO approach for an effective comparison. Table 1 provides details about the planning parameters and Table 2 gives the setup errors applied for each case. The plan evaluation included target (CTV) coverage measured by the parameter D95% and dose uniformity measured by the ratio D5%/D95% for both set of plans. Our interest was to see how the target coverage and dose uniformity is perturbed on imposing the setup errors in +X, −X, +Y, −Y, +Z, and −Z directions for both PTV-based and RO-based plans. The

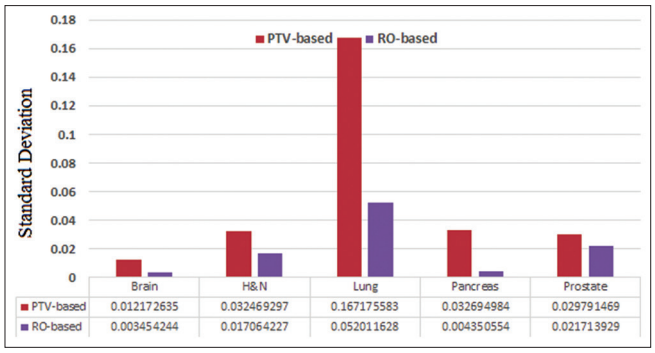

Figure 4: The comparison of the standard deviation of dose uniformity under the imposed setup errors in +X, −X, +Y, −Y, +Z, and −Z directions for both planning target volume-based and robust optimization-based plans

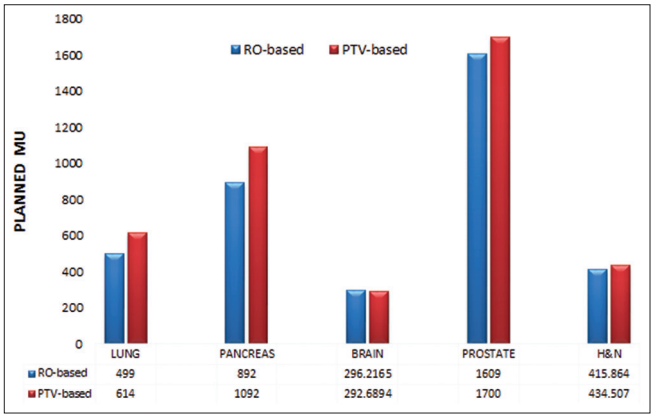

Figure 5: The comparison of total monitor units between planning target volume-based plans and robust optimization-based plans

total MUs resulting from PTV-based and RO-based plans were also compared for all five cases.

Results

Figure 1a-e shows the comparison of target coverage between PTV-based plans and RO-based plans under setup uncertainty conditions for brain case (a), head and neck case (b), lung case (c), pancreas case (d), and prostate case (e). Figure 2a-e shows the comparison of target dose uniformity between PTV-based plans and RO-based plans under setup uncertainty conditions for brain case (a), head and neck case (b), lung case (c), pancreas case (d), and prostate case (e). Figure 3 shows the comparison of the standard deviation of target coverage (CTV) under the imposed setup errors in +X, −X, +Y, −Y, +Z, and −Z directions for both PTV-based and RO-based plans. Figure 4 shows the comparison of the standard deviation of dose uniformity under the imposed setup errors in +X, −X, +Y, −Y, +Z, and −Z directions for both PTV-based and RO-based plans. Figure 5 shows the comparison of total MU between PTV-based plans and RO-based plans. Figures 6a-e show the dose–volume histogram (DVH) comparison of target coverage between PTV-based plans and RO-based plans under setup uncertainty conditions for brain case (a), head and neck case (b), lung case (c), pancreas case (d), and prostate case (e). Figures 7a-e show the dose distribution comparison of target coverage between PTV-based plans and RO-based plans under setup uncertainty conditions for brain case (a), head and neck case (b), lung case (c), pancreas case (d), and prostate case (e).

Discussion

PTV-based planning is a proven method for IMRT. However, when it comes to IMPT, the PTV-based approach fails due to the presence of high-dose gradients and the susceptibility of proton dose distribution to the changes in the patient geometry. Figure 1 shows how the target coverage fluctuates around the prescribed dose value when imposing the setup errors in +X, −X, +Y, −Y, +Z, and −Z directions. Similarly, Figure 2 shows how dose uniformity fluctuates on imposing the errors. It is evident from these figures that the fluctuation of target coverage and dose uniformity is significantly lower in RO-based plans as compared to PTV-based plans. This is also evident from Figures 3 and 4, which quantitatively measure the fluctuations in terms of standard deviation for target coverage and dose uniformity. Figure 6 shows how the DVH CTV is impacted on imposing the setup error in Y direction (+Y and −Y) considering the DVH curve obtained for the nominal plan as benchmark. It is evident from the DVHs that by introducing RO in the optimization, the susceptibility of the plan for setup uncertainties has been significantly reduced as compared to PTV-based approach. The mean standard deviation of target coverage for PTV-based and RO-based plans was 2.65 and 1.05, respectively, considering all five anatomic sites; similarly, the mean standard deviations of dose uniformity for PTV-based and RO-based plans were 0.055 and 0.02, respectively. This feature is seen in all anatomic sites, which indicates that RO is very useful across different anatomic sites. However, the impact of setup errors on target coverage and dose uniformity is huge in lung case as indicated in Figures 3 and 4 possibly due to the presence of more heterogeneities in the path of the beams. Hence, we recommend RO approach for the anatomic sites involving more heterogeneities. It is also evident from the results that, as compared to PTV-based planning, RO leads to a better target coverage and dose uniformity under the imposed uncertainty conditions. As mentioned before, we restricted this study to setup errors and deliberately did not include range errors so that a direct correspondence can be established between the PTV margin applied in PTV approach and setup errors imposed in RO approach. Moreover, this restriction allows an effective comparison between PTV-based and RO-based planning approaches. Since the error scenarios are directly included in RO for optimization, RO is inherently time-consuming as compared to PTV-based optimization. Typically, PTV-based IMPT optimization takes about 15–20 min, whereas RO-based

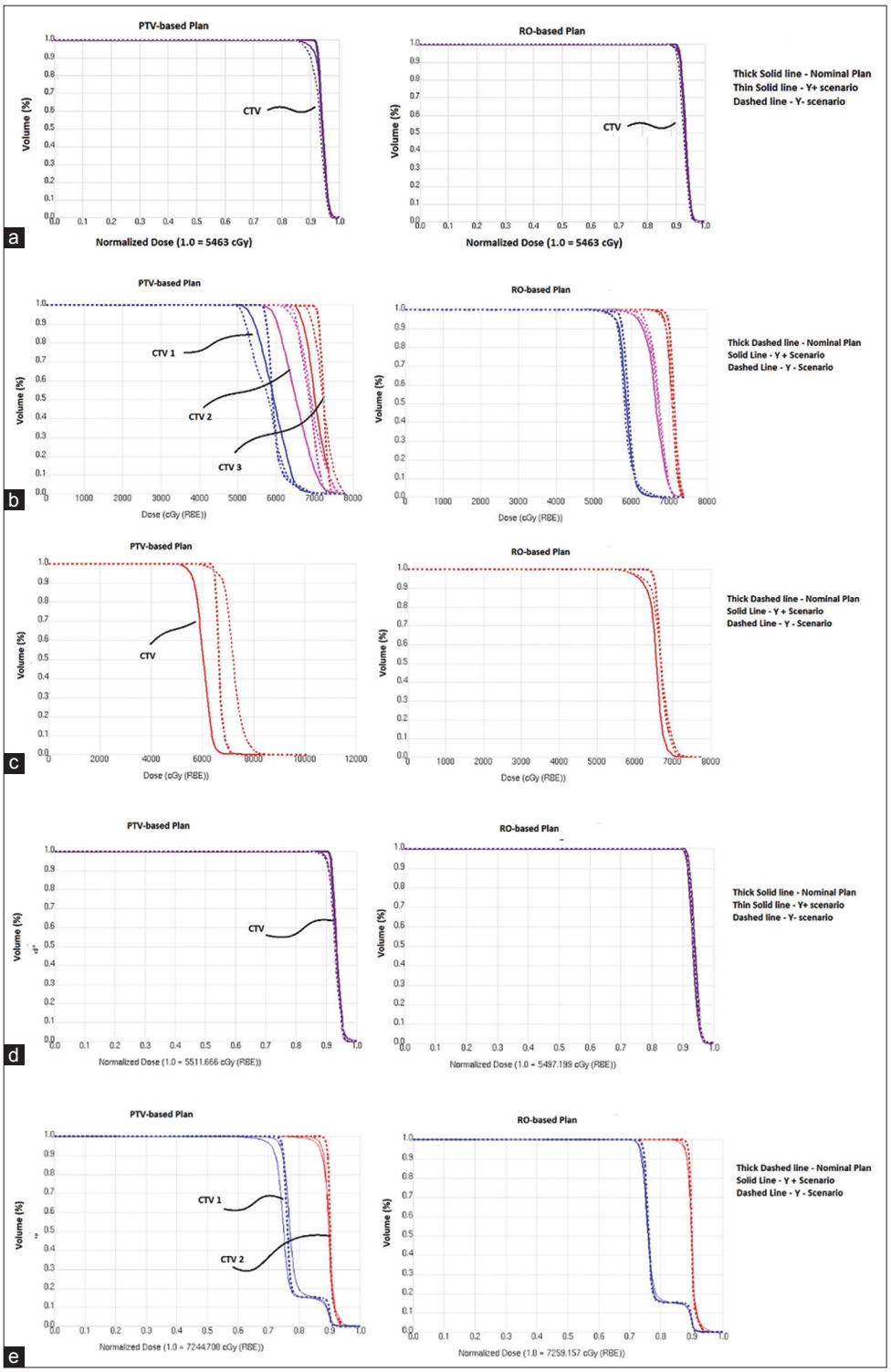

Figure 6: The dose–volume histogram comparison of target coverage between planning target volume-based plans and robust optimization-based plans under setup uncertainty conditions for brain case (a), head and neck case (b), lung case (c), pancreas case (d), and prostate case (e)

IMPT optimization takes about 30–40 min covering all setup errors (+X–X, +Y–Y, and +Z–Z). However, the dosimetric benefits resulting from RO radically outweighs the extra time spent in the optimization

Conclusion

Overall, the results obtained from the study clearly demonstrate the superiority of robustly optimized IMPT plans over the

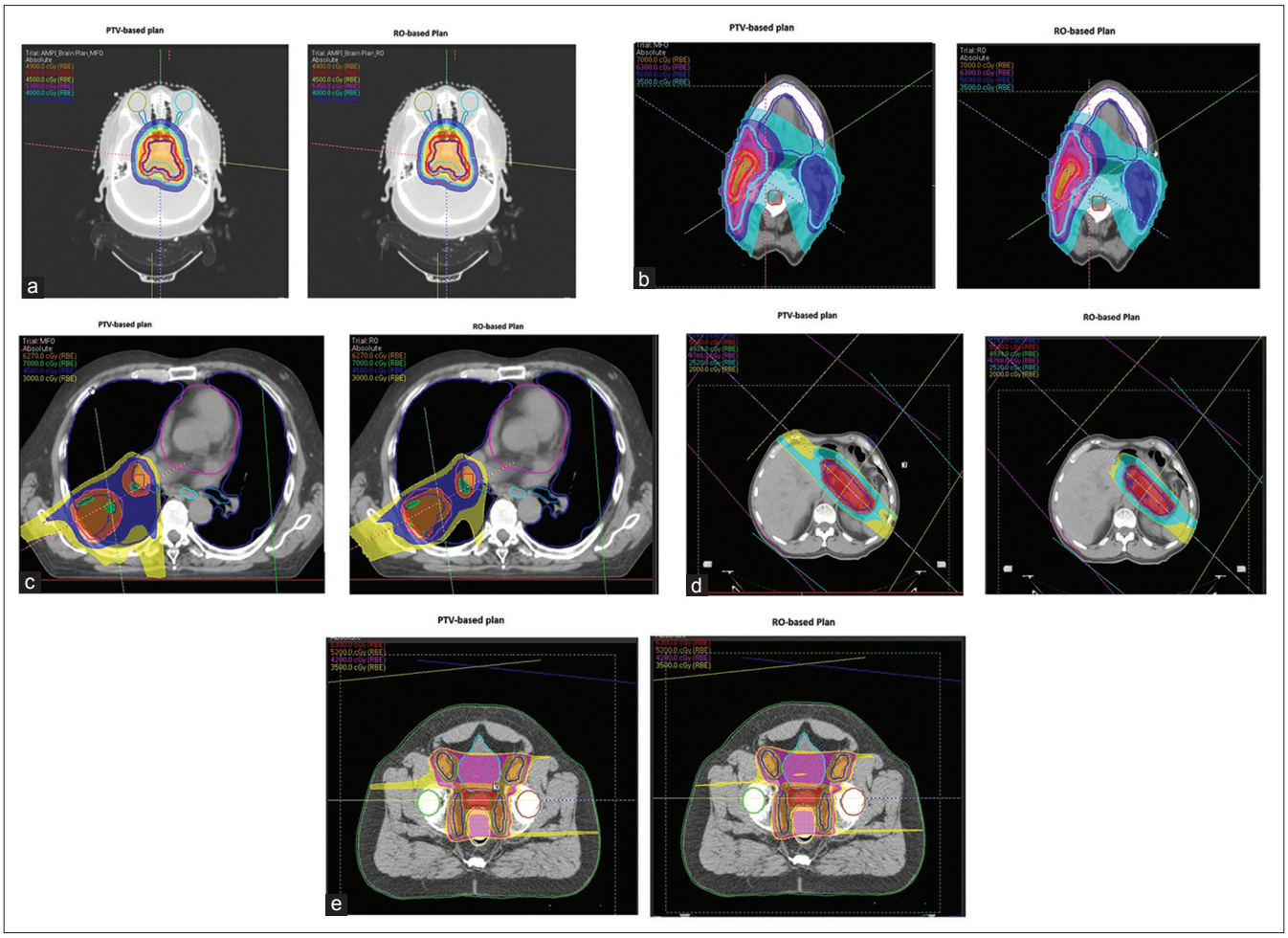

Figure 7: The dose distribution comparison of target coverage between planning target volume-based plans and robust optimization-based plans under setup uncertainty conditions for brain case (a), head and neck case (b), lung case (c), pancreas case (d), and prostate case (e)

PTV-based IMPT plans in terms of dose distribution under the uncertainty conditions.

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Conflicts of interest

There are no conflicts of interest.

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