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

Bojarajan Perumal1,2, Harikrishna Ett Sundaresan2, Ranganathan Vaitheeswaran3
1Philips Radiation Oncology Systems, Philips India Ltd, 2ICAP Clinical Applications, Philips India Ltd,Bangalore, Karnataka, 3Department of Medical Physics, Bharathiar University, Coimbatore, India

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.[4,5] Essentially, RO makes the IMPT plans less sensitive to uncertainties as compared to PTV-based plans.

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Address for correspondence: Mr. Bojarajan Perumal, Philips Radiation Oncology Systems, Philips India Limited, Manyatha Tech Park, Nagavara, Bengaluru - 560 045, Karnataka, India. E-mail: bojarajan.perumal@philips.com

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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.

\[
\text{RO (Setup error) OBV} = \text{Nominal Plan OBV} + \text{Setup Error OBV}
\]

where \(\text{Set up error OBV} = (+X \text{ error OBV}) + (-X \text{ error OBV}) + (+Y \text{ error OBV}) + (-Y \text{ error OBV}) + (+Z \text{ error OBV}) + (-Z \text{ error OBV})\). Each objective value represents a respective uncertainty scenario. For example, \(+X \text{ error OBV}\) 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 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 cm³ | OARs used for optimization++ |
|---------------|--------------|-----------------------------|-----------------------------|----------------------------------|-------------------------------|
| Brain         | 4            | 100* 245* 280* 325*         | 5000                        | PTV (85.52 cm³)                  | Brainstem, Lens (R), Optic Chiasm, Optic Nerves (R/L), Cochlea (R/L) |
| H&N**         | 3            | 180 60* 300 *              | 7000                        | PTV70 (78.39 cm³)                | 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 cm³)                | Spinal Cord, Lung (R/L), Bronchial tree. |
| Pancreas      | 3            | 40 * 130 * 310 *         | 5000                        | PTV (398.373 cm³)               | Spinal Cord, Kidney (R/L), Liver, Small bowel, Stomach. |
| Prostate**    | 2            | 90 270 *                 | 6600                        | PTV66 (107.21 cm³)              | 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.
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.
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 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 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 planning target volume-based and robust optimization-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 planning target volume-based and robust optimization-based plans. Figure 5 shows the comparison of total MU between planning target volume-based plans and robust optimization-based plans.

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

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Nil.

**Conflicts of interest**
There are no conflicts of interest.

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