Novel Hybrid Scattering- and Scanning-Beam Proton Therapy Approach

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Abstract

Purpose: To determine whether a hybrid intensity-modulated proton therapy (IMPT) and passive scattered proton therapy (PSPT) technique, termed HimpsPT, could be adopted as an alternative delivery method for patients demanding scanning beam proton therapy.

Patients and Methods: We identified 3 representative clinical cases—an oropharyngeal cancer, skull base chordoma, and stage III non–small-cell lung cancer—that had been treated with IMPT at our center. We retrospectively redesigned these cases using HimpsPT. The PSPT plans for all three cases were designed with the same prescriptions as those used in the IMPT plans. In this way, the whole treatment was delivered using alternating or sequential PSPT and IMPT.

Results: All HimpsPT plans met the clinical dose criteria and were of similar quality as the IMPT plans. In the skull base case, the mixed plan was more effective at sparing the brain stem because the sharp penumbra of the aperture in the PSPT plans was not present in the IMPT plans. The HimpsPT plans were more robust than the clinical IMPT plans generated without robust optimization.

Conclusion: The HimpsPT delivery technique can achieve a treatment-plan quality similar to that of IMPT, even in the most challenging clinical cases. In addition, at centers equipped with both scattering and scanning beam capabilities, the HimpsPT technique may allow more patients to benefit from scanning beam technology.

Keywords: intensity-modulated proton therapy; passive scattered proton therapy; hybrid, optimization

Introduction

In passive scattered proton therapy (PSPT), a narrow monoenergetic proton beam is spread uniformly over a large volume [1–3], after which apertures and compensators are used to conform the proton beam to the target [4–6]. In intensity-modulated proton therapy (IMPT), a narrow beam is scanned across the target volume using scanning magnets that deflect the beam perpendicular to the beam direction. The beam intensities and energies can be optimally changed in each scanned spot to conform proton dose to the target [4, 7, 8]. It has been demonstrated that in different disease sites, including the
head and neck (HN) [9–13], central nervous system (CNS) [14–18], and lungs [19, 20], both IMPT and PSPT are more effective at sparing normal tissue than intensity-modulated radiation therapy (IMRT). However, IMPT is usually considered more flexible than PSPT and can achieve better conformity, especially for targets with complicated shapes because of many degrees of freedoms offered by scanning spots [4]. Scanning beam proton therapy is in fact becoming the dominant delivery technique in proton therapy. Compared with PSPT, however, IMPT is generally considered less robust as well as more sensitive to setup and range uncertainties, inter- and intrafractional motion, and patient anatomy changes [21, 22].

In this study, we investigated a hybrid technique, known as HimpsPT, that is analogous to the hybrid 3-dimensional conformal and IMRT technique used in photon radiation therapy [23, 24]. The HimpsPT treatment plan consisted of PSPT and IMPT plans that were designed using the same prescriptions to allow treatment to be delivered by alternating or sequential PSPT and IMPT delivery. We suggest that the HimpsPT technique can be adopted as an alternative method for patients demanding IMPT techniques with a combination of the conformity of IMPT and the sharp lateral penumbra and robustness of PSPT. The HimpsPT approach facilitates control over the low dose distributions and robustness of the final plan by adjusting the weights of the IMPT and PSPT plans. In busy proton facilities, like our proton center, the gantry rooms with scanning beam capability are often overutilized, but gantry rooms with capability to deliver PSPT may not be fully utilized. The HimpsPT technique can balance the use of gantry rooms with IMPT capability and those with PSPT capability, thereby increasing clinical efficiency without compromising patient care.

In this study, 3 challenging cases were retrospectively investigated using our HimpsPT approach. The dose-volume histogram (DVH) parameters, along with the robustness of the PSPT, IMPT, and HimpsPT plans, were evaluated to assess treatment plan quality.

Patients and Methods

Patient Selection

At our proton therapy center, the 3 common disease sites and conditions treated using the scanning beam line are the HN, CNS, and lung cancer. In each case, target volumes may be of complex shape. We selected representative HN, CNS, and lung cancer cases that had been treated with IMPT. We intentionally selected particularly challenging cases with the rationale that if the HimpsPT technique can not only achieve similar dosimetric quality but also retain or further improve the robustness of IMPT in these examples, then most IMPT cases treated at our center could be treated using this technique.

The patient in the HN case was a 78-year-old man who was positive for human papilloma virus and had a history of T4 N0 squamous cell carcinoma of the base of the tongue. He had completed definitive concurrent chemotherapy and radiation therapy and was receiving weekly carboplatin and IMPT to a total dose of 70, 63, and 57 Gy relative biological effectiveness (RBE) for the primary target, high-risk lymph nodes, and additional at-risk nodal areas, respectively, in 33 fractions.

The patient in the CNS case was a 41-year-old man with a history of skull base chordoma (clival chordoma) who had undergone a transsphenoidal subtotal resection. He had a small amount of residual disease. His final dose of 70 Gy (RBE) using IMPT was determined by the achievable dose within the tolerance of the nearby structures. The dose to critical structures included the brainstem, temporal lobe, optic apparatus, cochlea, and trigeminal nerves.

The patient in the lung case was a 68-year-old man with stage IIIB non–small-cell lung cancer favoring adenocarcinoma of the left lower lobe. He underwent definitive treatment with concurrent chemoradiotherapy to a total dose of 70 Gy (RBE) in 35 fractions using proton beam therapy.

Treatment Planning

Treatment planning was carried out using the Eclipse (Varian, Palo Alto, California) treatment planning system (version 11.0). The multiple field optimization method was used to design the treatment plans to achieve the optimal balance of target irradiation and normal tissue sparing for the complicated cases selected in this study.

IMPT Plan Design

All IMPT plans were designed by our experienced medical dosimetrists and approved by the treating radiation oncologist. For the HN case, the IMPT plan used 3 beams, 2 of which were non-coplanar. At our center, these beam arrangements represent our beam angle class solution for complicated HN cancer plans. Figure 1A shows the 3 targets and beam directions in the
Figure 1. The beam arrangements for the intensity-modulated proton therapy plans and target structures in the 3 clinical cases: (A) head and neck with 3 beams (ARAPB, BLAPB, and CPAPB); the targets are CTV70 (orange), CTV63 (blue), and CTV57 (yellow); (B) central nervous system with 3 beams (ARPPB, BLAPB, and CSIPB); the targets are GTV (dark red), CTV (light pink), and PTV (light blue); the brain stem (light black) is also shown; (C) lung case with 4 beams (AASPB, BPIPB, CPAPB, and DPLPB); the targets are GTV (dark red), CTV (light pink), and PTV (light blue). The beams are named based on our center’s naming convention. For example, ARAPB means pencil beam A with right anterior direction.
transverse and sagittal computed tomography views. For the CNS case, the IMPT plan used 3 beams, including 1 non-coplanar beam. Figure 1B shows the targets and beam directions in the transverse and sagittal views. In the lung case, the IMPT plan used 4 beams, including 3 non-coplanar beams. Figure 1C shows the targets and beam directions in the transverse and sagittal views. Table 1 summarizes the beam parameters and target volumes of the 3 cases for the IMPT plans.

**PSPT Plan Design**

Since forward planning was used to design PSPT plans, it was difficult to achieve conformality without sacrificing target coverage (if the target was proximal to at least one critical structure) and to achieve conformal dose distribution to the target, as the IMPT plan does [19]. In our PSPT plan design for the current work we sought to (1) achieve similar normal tissue sparing to that of IMPT; (2) allow greater heterogeneity in the target, which could be improved by combining it with the IMPT plan; and (3) allow reduced conformality in direct comparison to the IMPT plan, which could later be improved upon by being combined with the IMPT plan. To achieve these goals, the PSPT plan had to be very carefully designed, including utilization of beam angles that may not commonly be employed.

In this study, in-house collision-avoidance software was used to help us select non-coplanar beam angles and minimize the air gap between the snout and the patient. For example, we used 4 beam angles for the PSPT plan in the CNS case, with 2 coplanar beams irradiating planning target volume (PTV) and two non-coplanar beams irradiating gross tumor volume (GTV) GTV70 only. Figure 2A through 2D show the beam-eye view of the 4 beams, with aperture shapes. Figure 2E and 2F show the 2 non-coplanar angles in the collision check software. Note that we used the aperture edge to create a sharp dose gradient between the PTV and brain stem.

For the HN case, the major challenge in the design of a good PSPT plan was distributing 3 relatively conformal dose levels to the 3 targets. The PSPT plan used 6 coplanar beams, including 3 beams irradiating the combined target for the clinical target volume (CTV; CTV70, CTV63, and CTV57) and 3 beams irradiating CTV70 only.

The lung case was particularly challenging. The IMPT plan already used 3 non-coplanar angles, assisted by our collision check software. The PSPT plan used the same angles. However, we used 2 beams to irradiate PTV at the right and the other 2 beams to irradiate PTV at the left. Figure 3A through 3D shows the beam-eye view of these 4 beams, with aperture shapes. Figure 3E and 3F shows the view of the 2 non-coplanar beams in our collision avoidance software. Table 2 summarizes the beam parameters and planning parameters used for the PSPT plan design for all 3 cases.

**HimpsPT Plan**

In this study, the IMPT plan and PSPT plan were equally weighted for the HimpsPT plan. Although the final HimpsPT plan achieved acceptable dose distribution, the distributions differed in the PSPT and IMPT delivery fractions. To minimize the biological effects of the HimpsPT plan, we suggest delivering the IMPT plan and PSPT plan alternately. In this way, patients get the dose shown in the cumulative DVH every 2 fractions. In our center’s practice, the ratio of IMPT and PSPT fractions is determined by the resource (schedule) and plan quality.
Robust Analysis

A worst-case dose was used to perform the robust analysis. For the given beam arrangement, we computed 9 different dose distributions: the nominal dose distribution (i.e., with no consideration of uncertainties) and the dose distributions that incorporated setup uncertainties (obtained by shifting the isocenter of the computed tomography images by ±3 mm (for the lung case) and ±2 mm for the HN and CNS cases along the anterior-posterior, left-right, and superior-inferior directions.

Table 2. Beam parameters of the passive scattered proton therapy plans for the HN, CNS, and lung cases.

| Case     | Beams | Gantry | Couch | Range (cm) | SOBP (cm) |
|----------|-------|--------|-------|------------|-----------|
| HN       | APA1A | 180    | 0     | 18.27      | 6         |
|          | BLA1A | 55     | 0     | 16.07      | 12        |
|          | CRA1A | 305    | 0     | 16.23      | 13        |
|          | DLR1A | 90     | 0     | 10.36      | 6         |
|          | ERL1A | 270    | 0     | 10.49      | 7         |
|          | FAP1A | 0      | 0     | 11.46      | 7         |
| CNS (BOS)| ARP1A | 260    | 0     | 12.19      | 7         |
|          | BLA1A | 85     | 0     | 12.44      | 7         |
|          | CAS1A | 70     | 290   | 15.97      | 5         |
|          | DRA1A | 75     | 270   | 16.77      | 5         |
| Lung     | AAS1A | 340    | 90    | 13.79      | 8         |
|          | BPI1A | 165    | 90    | 16.69      | 7         |
|          | CPA1A | 180    | 0     | 11.84      | 5         |
|          | DPL1A | 120    | 9     | 11.17      | 8         |

Abbreviations: SOBP, spread-out Bragg peak; HN, head and neck; CNS, central nervous system; BOS, base of skull.
yielding 6 dose distributions) and range uncertainty (obtained by scaling the relative stopping power ratios to water by $\pm 3.5\%$, yielding an additional 2 dose distributions). Notice that the shifts applied for the setup uncertainties represent the systematic setup uncertainties and are smaller than the PTV margins. The worst-case dose distribution is then represented by the minimum of the 9 doses in each voxel in the target and the maximum of the 9 doses in each voxel outside the target. This worst-case dose calculation approach was used to evaluate the treatment plans.

Plan Comparison

The PSPT, IMPT, and HimpsPT plans were evaluated using DVHs and dose distributions. We also compared the conformality index (CI) and heterogeneity index (HI).

$$CI = \frac{V_{D_p}}{TV},$$

where $V_{D_p}$ is the volume enclosed by the prescribed iso dose surface and TV is the target volume.

$$HI = \frac{D_1}{D_{99}},$$

where $D_1$ and $D_{99}$ are the doses encompassing 1% and 99% of the target volume, respectively.

Results

Comparisons of the IMPT, PSPT, and HimpsPT Plans

The top panel of Figure 4 shows a comparison of the DVHs of the IMPT, PSPT, and HimpsPT plans for the HN case. Three target volumes (CTV70, CTV63, and CTV57) were the most homogeneous and conformal in the IMPT plan and least homogeneous and conformal in the PSPT plan. As shown in Table 3, for the CTV70 target, the HI and CI for the HimpsPT plan were 1.11 and 1.28, respectively, compared with 1.06 and 1.23 in the IMPT plan and 1.17 and 1.41 in the PSPT plan. As shown in the bottom panel of Figure 4, the dose distributions of the 3 plans indicate that the HimpsPT plan improved the conformity and heterogeneity compared with the PSPT plan. The sparing of organs at risk was comparable in the 3 plans. For example, the IMPT plan spared the larynx slightly better than did the PSPT plan, but the PSPT plan spared the esophagus.

Figure 3. The beam-eye view of the beam arrangements and aperture shape of 4 beams: (A) AAS1A, (B) BPI1A, (C) CPA1A, and (D) DPL1A for the passive scattered proton therapy plan in the lung case. Light blue indicates the PTV. (E) AAS1A and (F) BPI1A are shown in our collision check software.
slightly better. The HimpsPT plan was the average of the PSPT and IMPT plans for these 2 organs. The mean parotid dose among the 3 plans was comparable.

The top panel of Figure 5 shows the DVHs of the IMPT, PSPT, and HimpsPT plans for the CNS case; the bottom panel shows the dose distributions for the 3 plans. In general, PSPT achieved the best organ sparing on the brain stem, hypothalamus, hippocampus, and temporal lobe but sacrificed GTV and CTV homogeneity. The IMPT plans achieved the best target homogeneity but had the poorest normal tissue sparing. As shown by the dose distribution, the PSPT plan achieved the sharpest dose gradient between GTV and the brainstem because of the sharp penumbra of the aperture edge. The dose gradient of the IMPT plan was the largest. The biggest challenge in the CNS case was the proximity of the brainstem to the target volume. At our center, the use of apertures has not been commissioned for scanning beam delivery. The spot size is relatively large for our machine, leading to a larger penumbra for IMPT delivery. As shown in Table 4, because of the sharp penumbra in the HimpsPT plan, the maximum dose to the brainstem was decreased from 56.4 Gy (RBE) in the IMPT plan to 51.5 Gy (RBE) in the HimpsPT plan while the target dose was not compromised (GTV D99 = 66.5 Gy (RBE) in the IMPT plan compared with 66.0 in the HimpsPT plan). The HimpsPT plan was the best balance of IMPT and PSPT techniques with optimal normal tissue sparing and homogenous target dose.

The top panel of Figure 6 shows the DVHs of the IMPT, PSPT, and HimpsPT plans for the lung case, and the bottom panel shows the dose distributions of the 3 plans. Table 5 compares important dosimetric data. A very important difference between the HimpsPT plan and the IMPT plan was the reduction in low-dose irradiation of the lung (lung V5 decreased from 55.4% to 50.5%). This reduction was again attributed to the sharp penumbra of the aperture in the PSPT plan and can also be seen in the dose distribution and DVH comparison among the 3 plans, shown in Figure 6: (1) dose distribution in the PSPT plan was not conformal; (2) the IMPT plan achieved better dose conformity, but the low dose to the lung was higher due to the large
### Table 3. Dosimetric indices of the nominal PSPT, IMPT, and hybrid HimpsPT plans for the HN cases and the corresponding values in the worst-case scenarios on the basis of a robust analysis. The differences in the dosimetric indices between the worst and nominal scenarios are also shown in the 3 plans.

| Regions of Interest | PSPT   | IMPT   | HimpsPT | PSPT   | IMPT   | HimpsPT | PSPT   | IMPT   | HimpsPT |
|---------------------|--------|--------|---------|--------|--------|---------|--------|--------|---------|
| CTV70 D1 (Gy)       | 79.9   | 74.7   | 76.9    | 80.6   | 78.2   | 78.2    | 0.7    | 3.5    | 1.3     |
| CTV70 D99 (Gy)      | 68.02  | 70.5   | 69.4    | 61.8   | 64.1   | 63.7    | 6.22   | 6.4    | 5.7     |
| CTV70 HI            | 1.17   | 1.06   | 1.11    | -      | -      | -       | -      | -      | -       |
| CTV70 CI            | 1.41   | 1.23   | 1.28    | -      | -      | -       | -      | -      | -       |
| CTV63 D1 (Gy)       | 79.60  | 74.80  | 76.80   | 80.40  | 77.90  | 78.10   | 0.8    | 3.2    | 1.3     |
| CTV63 D99 (Gy)      | 62.20  | 64.80  | 63.70   | 56.60  | 58.80  | 58.10   | 5.6    | 6      | 5.6     |
| CTV63 HI            | 1.28   | 1.15   | 1.21    | -      | -      | -       | -      | -      | -       |
| CTV57 D1 (Gy)       | 70.30  | 65.60  | 67.45   | 71.70  | 68.60  | 69.30   | 1.4    | 3      | 1.85    |
| CTV57 D99 (Gy)      | 53.30  | 58.00  | 56.30   | 48.10  | 52.6   | 51.40   | 5.2    | 5.4    | 4.9     |
| Brainstem Dmax (Gy) | 26.8   | 10.7   | 17.9    | 32.5   | 13.2   | 22.3    | 5.7    | 2.5    | 4.4     |
| Cord Dmax (Gy)      | 30.90  | 33.80  | 31.70   | 33.40  | 34.80  | 33.00   | 2.2    | 1      | 1.3     |
| Esophageus Dmax (Gy)| 36.00  | 47.20  | 41.60   | 42.90  | 56.10  | 48.90   | 6.9    | 8.9    | 7.3     |
| Left parotid mean (Gy)| 23.1  | 24.9   | 23.6    | 28.5   | 27.7   | 27.8    | 5.4    | 2.8    | 4.2     |
| Right parotid mean (Gy)| 21.4 | 21.2   | 21.7    | 28.5   | 24.8   | 26.4    | 7.1    | 3.6    | 4.7     |
| Brain mean (Gy)     | 1.66   | 1.25   | 1.45    | 2.06   | 1.58   | 1.81    | 0.4    | 0.33   | 0.36    |
| Oral cavity mean (Gy)| 10.2  | 9.9    | 10.1    | 13.2   | 12.4   | 12.7    | 3      | 2.5    | 2.6     |
| Larynx mean (Gy)    | 38.6   | 33.8   | 36.1    | 43.4   | 39.4   | 41.1    | 4.8    | 5.6    | 5       |

**Abbreviations:** PSPT, passive scattered proton therapy; IMPT, intensity-modulated proton therapy; HimpsPT, hybrid IMPT and PSPT technique; HN, head and neck; CTV, clinical target volume; Dmax, maximum dose.

### Table 4. Dosimetric indices of the nominal PSPT, IMPT, and hybrid HimpsPT plans for the CNS cases and the corresponding values in the worst-case scenarios on the basis of the robust analysis. The differences in the dosimetric indices between the worst and nominal scenarios are shown in the 3 plans.

| Regions of Interest | PSPT   | IMPT   | HimpsPT | PSPT   | IMPT   | HimpsPT | PSPT   | IMPT   | HimpsPT |
|---------------------|--------|--------|---------|--------|--------|---------|--------|--------|---------|
| GTV D1 (Gy)         | 82.5   | 76.53  | 78.98   | 83.2   | 77.2   | 79.55   | 0.7    | 0.67   | 0.57    |
| GTV D99 (Gy)        | 66.3   | 66.5   | 66      | 58.35  | 62.3   | 60.6    | 7.95   | 4.2    | 5.4     |
| GTV HI              | 1.24   | 1.15   | 1.20    | -      | -      | -       | -      | -      | -       |
| GTV CI              | 3.24   | 1.54   | 2.37    | -      | -      | -       | -      | -      | -       |
| CTV D1 (Gy)         | 82.20  | 76.20  | 78.77   | 83.00  | 76.90  | 79.32   | 0.8    | 0.7    | 0.55    |
| CTV D99 (Gy)        | 63.10  | 58.90  | 61.95   | 55.80  | 55.60  | 57.20   | 7.3    | 3.3    | 4.75    |
| CTV HI              | 1.30   | 1.29   | 1.27    | -      | -      | -       | -      | -      | -       |
| CTV CI              | 2.47   | 2.36   | 2.37    | -      | -      | -       | -      | -      | -       |
| Brainstem Dmax (Gy) | 48.52  | 56.4   | 51.5    | 55.9   | 60.4   | 58.1    | 7.38   | 4      | 6.6     |
| Pituitary gland Dmax (Gy)| 60.8 | 60.7   | 60.6    | 67     | 63.3   | 65.1    | 6.2    | 2.6    | 4.5     |
| Hypothalamus Dmax (Gy)| 38.4  | 42.8   | 40.3    | 41.3   | 45.5   | 43.4    | 2.9    | 2.7    | 3.1     |
| Right optic nerve Dmax (Gy)| 33.7 | 37.3   | 24.3    | 23.2   | 31.1   | 26.8    | 10.5   | 6.2    | 2.5     |
| Left optic nerve Dmax (Gy)| 23.3 | 28.9   | 26.2    | 25.2   | 31     | 27.4    | 1.9    | 2.1    | 1.2     |
| Optic chiasm Dmax (Gy)| 33.3  | 34.8   | 34      | 34.1   | 37.1   | 35.5    | 0.8    | 2.3    | 1.5     |
| Right hippocampus Dmax (Gy)| 22.4 | 35.1   | 29.6    | 26.7   | 39.5   | 33.1    | 4.3    | 4.4    | 3.5     |
| Left hippocampus Dmax (Gy)| 10.8 | 16.2   | 11.5    | 11.2   | 18.4   | 13.6    | 0.4    | 2.2    | 2.1     |
| Right temporal lobe mean (Gy)| 2.67 | 5.06   | 3.93    | 3.37   | 5.75   | 4.54    | 0.7    | 0.69   | 0.61    |
| Left temporal lobe mean (Gy)| 1.98 | 2.95   | 2.39    | 2.39   | 3.25   | 2.79    | 0.41   | 0.3    | 0.4     |
| Brain mean (Gy)     | 2.38   | 3.18   | 2.75    | 2.77   | 3.54   | 3.14    | 0.39   | 0.36   | 0.39    |

**Abbreviations:** PSPT, passive scattered proton therapy; IMPT, intensity-modulated proton therapy; HimpsPT, hybrid IMPT and PSPT technique; CNS, central nervous system; GTV, gross tumor volume; CTV, clinical target volume; Dmax, maximum dose.

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Figure 5. The dose-volume histograms (top panel) and dose distributions (bottom panel) of the 3 plans for the central nervous system case. The solid, dashed, and dotted lines denote intensity-modulated proton therapy, hybrid, and passive scattered proton therapy plans, respectively.

Table 5. The dosimetric indices of the nominal PSPT, IMPT, and hybrid HimpsPT plans for the lung cases and the corresponding values in the worst-case scenarios on the basis of a robust analysis. The differences in the dosimetric indices between the worst and nominal scenarios are shown in the 3 plans.

| Nominal | Worst scenario | Difference |
|---------|----------------|------------|
| PSPT    | IMPT           | HimpsPT    | PSPT    | IMPT           | HimpsPT    | PSPT    | IMPT           | HimpsPT    |
| CTV D1 (Gy) | 84.2 | 82 | 80.9 | 86.6 | 86.9 | 84.9 | 2.4 | 4.9 | 4 |
| CTV D99 (Gy) | 70.8 | 71.2 | 72.2 | 63.7 | 62.2 | 65.2 | 7.1 | 9 | 7 |
| PTV VPres (%) | 94.5 | 94.8 | 95.3 | - | - | - | - | - | - |
| Heterogeneity index | 1.19 | 1.15 | 1.12 | - | - | - | - | - | - |
| Conformality index | 1.29 | 1.17 | 1.18 | - | - | - | - | - | - |
| Lung V5 (%) | 46.6 | 55.5 | 50.5 | 52.7 | 60.6 | 55.6 | 6.1 | 5.1 | 5.1 |
| Lung V20 (%) | 36.3 | 36.6 | 36.7 | 42.3 | 41 | 41.7 | 5.5 | 4.4 | 5.5 |
| Lung V30 (%) | 32.4 | 30.1 | 31.6 | 37.3 | 34.2 | 36 | 4.9 | 4.1 | 4.4 |
| MLD (Gy) | 21.2 | 21.3 | 21.3 | 25.2 | 24.7 | 24.9 | 4 | 3.4 | 3.6 |
| Heart V40 (%) | 7.76 | 7.66 | 7.13 | 10.1 | 9.4 | 8.9 | 2.34 | 1.74 | 1.77 |
| MHD (Gy) | 7.48 | 8.74 | 8.11 | 9.3 | 10.4 | 9.76 | 1.82 | 1.66 | 1.65 |
| Esophagus V60 (%) | 11.1 | 15.4 | 12.2 | 17.5 | 20.2 | 18.6 | 6.4 | 4.8 | 6.4 |
| MED (Gy) | 19.3 | 22.4 | 20.4 | 22.6 | 25.5 | 23.9 | 3.3 | 3.1 | 3.5 |
| Cord Dmax (Gy) | 36.1 | 36.8 | 35.5 | 36.7 | 39.5 | 37.4 | 0.6 | 2.7 | 1.9 |

Abbreviations: PSPT, passive scattered proton therapy; IMPT, intensity-modulated proton therapy; HimpsPT, hybrid IMPT and PSPT technique; CTV, clinical target volume; PTV, planning target volume; MLD, mean lung dose; MHD, mean heart dose; MED, mean esophagus dose; Dmax, maximum dose.

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penumbra of the spots; and (3) the HimpsPT plan took advantage of both the PSPT plan and IMPT plan, resulting in balance between dose conformality and low dose sparing.

**HimpsPT Technique Improves Robustness of Treatment Plan**

Figures 7 and 8 show a comparison among the DVH band graphs for the HN case (Figure 7A), CNS case (Figure 7B), and lung case (Figure 8) between the IMPT and HimpsPT plans. The IMPT plans tended to have a wider DVH band than did the HimpsPT plans, indicating that the HimpsPT plan was more robust. For the HN case, there was a smaller difference in the dosimetric index between the worst-case and nominal HimpsPT plan, as shown in Table 2. For example, the differences in D99 for CTV70, CTV63, and CTV57 were 5.7 Gy (RBE), 5.6 Gy (RBE), and 4.9 Gy (RBE) , respectively, in the HimpsPT plan compared with 6.4 Gy (RBE), 6 Gy (RBE), and 5.4 Gy (RBE) in the IMPT plan. We conclude that the HimpsPT plan is more robust than the IMPT plan in terms of target coverage. The robustness of the normal tissue was also evaluated using the difference in the dosimetric indices between the worst-case and nominal plans. The difference was bigger for some structures (brainstem and left parotid) in the HimpsPT plan. However, for some other structures (larynx and esophagus), the difference was smaller in the HimpsPT plan. We conclude that for normal structures, the HimpsPT plan achieves better robustness than the IMPT plan in terms of target coverage but similar robustness in terms of OAR.

The robustness of the CNS plan was very interesting. As listed in Table 4, the differences between the D99 and D1 for GTV and CTV were smaller in the IMPT plan than in the PSPT plan. The differences in some other dosimetric indices, such as the maximum dose of the brainstem, pituitary gland, and right optic nerves in the PSPT plan, were also smaller in the IMPT plan than in the PSPT plan. The IMPT plan was actually more robust than the PSPT plan, mainly because the targets were smaller (for example, the GTV was only 4.06 cm³) in the CNS case and the major regions of interest were spared as a result of sharp...
aperture age in the PSPT plan. It may be preferable to treat patients with the HimpsPT plan, which achieves a balance between robustness, target conformality, and normal tissue sparing.

In the lung case, the difference in the D99 for CTV was 7 Gy (RBE) in the HimpsPT plan, which was smaller than the 9 Gy (RBE) found for the IMPT plan. The HimpsPT plan was more robust than the IMPT plan in terms of target coverage. The robustness of normal structures in the HimpsPT plan was comparable to that in the IMPT plan.

Discussion

Our results suggest that the HimpsPT delivery technique can achieve similar treatment plan quality to IMPT. This result may have significant implications for proton therapy facilities. Our center has 1 scanning beam gantry and 2 passive scattering beam gantries. Patients are treated from 4 AM to midnight in the scanning beam gantry, but the other gantries commonly finish treatments in the late afternoon. If the HimpsPT plan technique were adopted, the facility might operate during normal business hours while not compromising treatment quality; alternatively, it could treat more patients. Currently, we offer physicians the HimpsPT plan if the patients need to wait for more than 3 weeks to be scheduled for the scanning beam gantry. For some patients, we suggest the HimpsPT plan on the basis of a rigorous dosimetric comparison of the HimpsPT plan, PSPT plan, and IMPT plan. For example, for a recent patient with lung cancer who was undergoing re-irradiation, our clinicians requested an IMPT plan to limit the spinal cord dose to less than 10 Gy (RBE). After comparing the HimpsPT plan, IMPT plan, and PSPT plan (Figure 9), we recommended the HimpsPT plan because it took advantage of both the sharp penumbra of the aperture edge, allowing better cord sparing, and the more conformal dose distribution of the IMPT plan, allowing better skin sparing. We now routinely use HimpsPT technology in our clinic to benefit both patients’ care and proton facility operation. We also hope that the results of this study will be useful when selecting scanning or mixed scattering and scanning beam capabilities in future proton facility designs.

Hybrid photon therapy techniques have been reported in the literature [23–25]. Mayo et al [23, 24] reported a hybrid technique that combined 3-dimensional conformal radiotherapy (approximately two-thirds dose) and IMRT (approximately one-third dose) beams for lung and esophagus cancer, reducing the dose to the lungs while also reducing the potential magnitude of dose
deviations due to intrafraction motion and small field calculation accuracy. To our knowledge, our work is the first to report the use of a similar hybrid technique for use with proton therapy. Some of our findings are coincidentally similar to those found for the hybrid photon therapy technique. We also observed a reduced dose in the lung case. For both lung cancer and esophageal cancer, the interplay effect is the major motion uncertainty of the scanning beam technique [26, 27]. By combining the scanning beam with the scattering beam, this uncertainty will be reduced, as was observed with the photon therapy hybrid technique. More importantly, the demand for the hybrid technique is higher at busy proton centers equipped with both scattering and scanning beam lines since it allows improved clinical efficiency without compromising treatment quality.

In this study, the HimpsPT technique improved IMPT treatment efficiency on the basis of delivering half of the cumulative dose by PSPT and half by IMPT. Different IMPT and PSPT ratios could also be adopted. In practice, the ratio of IMPT and
PSPT fractions is determined by the resource (schedule) and plan quality. Since the total fractions are the same for both HimpsPT and IMPT techniques, the patient setup, imaging, and beam request time are similar between these 2 techniques. The HimpsPT approach needs more beam preparation time since the range modulator wheel, compensator, and aperture need to be manually mounted by therapists for PSPT fractions. The beam on time is reduced for HimpsPT technique since PSPT delivers much faster than pencil beam scanning. For a 3-field plan, beam on time for PSPT is $2.7 \pm 1.5$ minutes but $9.4 \pm 2.4$ minutes for the IMPT technique.

One of the indirect results from this study is that we were forced to improve PSPT plan quality when applying the hybrid technique. This is due to the fact that treatment plan design is still an art that varies among different planners. In this retrospective study, we demonstrated that an HimpsPT plan can reach the quality of an IMPT plan even for most difficult cases. We achieved this by designing a better PSPT plan. We found that the demanding hybrid plan improves the quality of PSPT plan since the planner has a good plan (IMPT plan) to compare with.

Although the robustness of the IMPT plan tends to be relatively worse than that of the PSPT plan, the improvement of IMPT plan on the conformity of the dose distribution cannot be matched by the PSPT plan, even in the worst-case scenarios. In the clinic decision process of our center, our clinicians often choose the IMPT plan because of the much improved conformality it offers. If the IMPT plan cannot be scheduled, the HimpsPT plan is used to take advantage of the much improved conformality by IMPT plan.

**Conclusion**

The HimpsPT delivery technique can achieve similar or better treatment plan quality than can IMPT, even for the most challenging clinical cases. The dosimetric advantages offered by IMPT are retained when using the HimpsPT technique. The HimpsPT technique may enable more patients to benefit from scanning beam technology in centers equipped with both scattering and scanning beam capabilities.

**ADDITIONAL INFORMATION AND DECLARATIONS**

**Conflicts of interest:** The authors have no conflicts of interest to disclose.

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