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Proton energy optimization and reduction for intensity-modulated proton therapy

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Abstract

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Intensity-modulated proton therapy (IMPT) is commonly delivered via the spot-scanning technique. To “scan” the target volume, the proton beam is controlled by varying its energy to penetrate the patient’s body at different depths. Although scanning the proton beamlets or spots with the same energy can be as fast as 10–20 m/s, changing from one proton energy to another requires approximately two additional seconds. The total IMPT delivery time thus depends mainly on the number of proton energies used in a treatment. Current treatment planning systems typically use all proton energies that are required for the proton beam to penetrate in a range from the distal edge to the proximal edge of the target. The optimal selection of proton energies has not been well studied. In this study, we sought to determine the feasibility of optimizing and reducing the number of proton energies in IMPT planning. We proposed an iterative mixed-integer programming optimization method to select a subset of all available proton energies while satisfying dosimetric criteria. We applied our proposed method to six patient datasets: four cases of prostate cancer, one case of lung cancer, and one case of mesothelioma. The numbers of energies were reduced by 14.3%–18.9% for the prostate cancer cases, 11.0% for the lung cancer cases, and 26.5% for the mesothelioma case. The results indicate that the number of proton energies used in conventionally designed IMPT plans can be reduced without degrading dosimetric performance. The IMPT delivery efficiency could be improved by energy layer optimization leading to increased throughput for a busy proton center in which a delivery system with slow energy switch is employed.

1. Introduction

The delivery of intensity-modulated proton therapy (IMPT) is commonly achieved via the spot-scanning technique, also called pencil beam scanning, whereby the tumor target is actively scanned by placing Bragg peaks of protons throughout the three-dimensional volume (Gillin *et al.*, 2010; Smith *et al.*, 2009). The lateral beam position (X and Y) is controlled by two scanning magnets, and the depth (Z) scanning is controlled by varying the energy of protons extracted from the accelerator. The treatment volume is virtually discretized into a number of energy layers, and the depth of each layer is determined by an energy level of protons. All layers are scanned sequentially from the furthest to the nearest in the beam’s penetration depth (i.e., from the highest to the lowest energy). In each energy layer, uniformly allocated scanning spots are irradiated one by one either discretely (i.e., with the beam on only when stopping at each scanning spot) or continuously (i.e., with the beam on all the time). The scanning nozzle available at The University of Texas MD Anderson Cancer Center delivers the IMPT discretely spot-by-spot and layer-by-layer (Zhu *et al.*, 2010). Although the speed of spot scanning within the same energy layer is very fast, the time required to change from one proton energy to another requires approximately two additional seconds per change because both deceleration and acceleration of protons are required. Therefore, using fewer energy layers may effectively reduce treatment delivery time.

In the IMPT planning based on using commercial system (Eclipse, Varian Medical Systems, Palo Alto, CA), all proton energies with ranges covering the target volume longitudinally in each beam angle are included in optimization and used in delivery. However, the need to employ all available proton energies to achieve the desired IMPT dose distributions has not

been well studied. If reducing the number of proton energies is possible, the IMPT delivery time may be effectively reduced.

In IMPT planning with multi-field optimization, the intensities of scanning spots from all energy layers in all beam angles are simultaneously and independently optimized. Although highly complex dose distributions can be achieved via multi-field optimization, the optimal treatment plans are often degenerate (Albertini *et al.*, 2010). In other words, various, and sometimes vastly different, solutions of spot intensities can meet the planning criteria by ensuring a sufficient dose is delivered to the target while maximally sparing the surrounding health tissues. Thus, we hypothesized that treatment plans with a subset of all available proton energies could deliver the desired dose distributions without degrading the plan quality compared with treatment plans that employ all available energies.

In addition to determining whether the use of all proton energies in IMPT is indispensable, this study also provides an optimization approach to automatically determining the most efficient energy selections while optimizing the IMPT plan. The results of this study will improve our understanding of the impact of energy selection on IMPT plan quality.

2. Methods

2.1. Mixed-integer programming model for optimal energy selection

Since a binary variable is essentially needed for selecting proton energies, we consider a mixed-integer programming (MIP) model to formulate the energy selection problem in IMPT planning. Suppose that A , L , and S , respectively, are a given set of beam angles, energy levels, and scanning spots available for designing a treatment plan. The continuous decision variable is the scanning spot intensity $\mathbf{x} = (x_{a,l,s})$ of beam angle a at scanning spot s with energy l , where $a \in A$, $l \in L$ and $s \in S$. The integer variable is the binary energy selector $\mathbf{y} = (y_{a,l})$, $y_{a,l} \in \{0, 1\}$, where its value of 1 indicates energy l from beam angle a is selected, and 0 indicates not selected. Let $d_{v,a,l,s}$ denote the dose influence from the scanning spot (a, l, s) to voxel v , where $v \in V$, and V is the set of all voxels in the treatment volume, including the target, organs at risks, and healthy tissue. Thus, the total dose received by a voxel v , D_v or $D(\mathbf{x}, \mathbf{y})$, is

$$D_v = D(\mathbf{x}, \mathbf{y}) = \sum_{a \in A} \sum_{l \in L} \sum_{s \in S} x_{a,l,s} \cdot y_{a,l} \cdot d_{v,a,l,s}. \quad (1)$$

Note that the multiplication of variables $\mathbf{x}$ and $\mathbf{y}$ in (1) would introduce additional complexity to the optimization model. It can be equivalently simplified to two constraints by reformulating as follows,

$$D_v = D(\mathbf{x}) = \sum_{a \in A} \sum_{l \in L} \sum_{s \in S} x_{a,l,s} \cdot d_{v,a,l,s}, \quad (2)$$

$$0 \leq x_{a,l,s} \leq C_{a,l,s} \cdot y_{a,l}, \quad (3)$$

where $C_{a,l,s}$ is a large enough positive value to ensure that $x_{a,l,s} = 0$, if $y_{a,l} = 0$, and $x_{a,l,s} = C_{a,l,s}$, if $y_{a,l} = 1$. In addition, the lower and upper dose limits of structure V_i are assigned by the constraints:

$$LB_{v \in V_i} \leq D_{v \in V_i} \leq UB_{v \in V_i}, \quad (4)$$

where V_i represents the sets of voxels in structure i , i.e., $V = \cup_i V_i$; and $0 \leq LB_{v \in V_i} \leq UB_{v \in V_i} < \infty$.

The composite cost function to be minimized for optimizing IMPT scanning spot intensity and energies, $F(\mathbf{x}, \mathbf{y})$, is defined as

$$\min F(\mathbf{x}, \mathbf{y}) = \alpha f(D(\mathbf{x})) + \beta \|\mathbf{y}\|_1, \quad (5)$$

where $f(D(\mathbf{x}))$ is a cost function to capture dosimetric measures and $\|\mathbf{y}\|_1$, i.e., $\sum_{a \in A} \sum_{l \in L} y_{a,l}$, is the total number of energies used in the optimized plan; α and β are weighting factors for these two objectives. The techniques to formulate $f(D(\mathbf{x}))$ in the literature can be generalized as a function of the p -norm of the dose deviation vector between the calculated dose D_v and the prescription dose $\bar{D}_v$:

$$f(D(\mathbf{x})) = \|D_v - \bar{D}_v\|_p. \quad (6)$$

When $p = 2$, the cost function $f(D(\mathbf{x}))$ becomes quadratic (Lomax, 1999; Liu *et al.*, 2012; Albertini *et al.*, 2010); when $p = 1$, $f(D(\mathbf{x}))$ is linear (Cao *et al.*, 2013; Romeijn *et al.*, 2003; Lim and Cao, 2012). We used a linear cost function in this study as follows,

$$f(D(\mathbf{x})) = \sum_i w_{V_i} \frac{\|D_{v \in V_i} - \bar{D}_{v \in V_i}\|_1}{|V_i|}, \quad (7)$$

where w_{V_i} indicates the importance factor of structure V_i based on the treatment planner's preference. The normalization factor is the cardinality of V_i , i.e., $|V_i|$. Therefore, the MIP model (2)–(5) is formed for optimizing spot intensities and energies simultaneously in IMPT planning.

2.2. MIP-based iterative method for energy reduction

Although the problem of optimizing spot intensities while reducing proton energies can be conveniently modeled as described in Section 2.1, the MIP model (2)–(5) remains challenging to solve. There are two practical difficulties. First, it is non-trivial to find appropriate weighting factors (α and β) in the composite cost function (5). A relatively larger value of α would prevent the model from finding a minimal number of energies, whereas a relatively larger value of β would otherwise diminish the impact of dosimetric measures among different incident plans. Second, the MIP model itself is computationally difficult to solve owing to its combinatorial nature. The solution time would be impractical

if the model is applied to typical clinical datasets. Therefore, we propose a hybrid solution approach by solving a relaxed MIP model iteratively to obtain local optima to the problem.

The relaxed MIP model is defined by reducing the composite cost function (5) for minimization to the dose-based cost function only, e.g.,

$$\min F(\mathbf{x}) = f(D(\mathbf{x})), \quad (8)$$

and introducing an upper bound constraint for the total number of energies, i.e.,

$$\sum_{a \in A} \sum_{l \in L} y_{a,l} \leq N, \quad (9)$$

where N is a positive integer, and it is not greater than the number of all available energies N , i.e., $N \leq N$. Thus, the difficulty of choosing optimization priorities between the plan quality and the number of energies can be avoided by this reformulation. The relaxed MIP is then formed by (2)–(4), (8), and (9). Specifically, this relaxed model is devised to obtain an optimal selection of N energies out of N candidates from all beam angles and optimal spot intensities based on the selected energies. In order to find a reduced number of energies, the relaxed MIP can be solved iteratively with a decreasing N until the plan degradation is observed. In other words, a reduction of energy/energies can be imposed by solving the relaxed MIP in each iteration, and the iterations continue until plan is degraded beyond an accepted level. Note that we used $\Delta = 1$ in this study, i.e., reducing one energy at one time. We limited this to one so the computational complexity for solving a single MIP can be minimized. The flow chart of the proposed proton energy reduction (PER) method is shown in Figure 1.

The performance of an energy selection is evaluated by its resulting dose-based cost function, which is consistent as those used in conventional IMPT planning. It is assumed that the initial set of proton energies available always supports a treatment plan of acceptable quality. The terminating criterion for the PER method is the violation of the plan quality degradation specified by a threshold value θ . Suppose the cost function value obtained from the initial energy selection L_0 is $F(L_0)$. In any PER iteration i , the optimized energy selection L_i obtained from MIP is accepted only if the following condition is satisfied:

$$\frac{F(L_i) - F(L_0)}{F(L_0)} \leq \theta. \quad (10)$$

Otherwise, the PER method terminates. The value of θ was set to 5% in this study. Note that PER also terminates when MIP does not identify a feasible solution.

Although the PER method is able to optimize scanning spot intensities in addition to selecting energies, our primary interest in this study was to determine whether a reduced number of energies would suffice for creating non-degrading IMPT plans. Therefore, PER can be used as a standalone tool prior to clinical treatment planning. With a solution of

selected energies from PER, a treatment planner can choose to use other optimization routines (Fredriksson *et al.*, 2011; Liu *et al.*, 2012; Trofimov and Bortfeld, 2003; Unkelbach *et al.*, 2007) to optimize scanning spot intensities and/or other treatment planning parameters.

2.3. Treatment delivery system and patient study

The proton center at MD Anderson is equipped with a synchrotron and the Hitachi PROBEAT delivery system (Hitachi, Ltd., Tokyo, Japan) (Smith *et al.*, 2009; Gillin *et al.*, 2010). IMPT is delivered via a discrete pencil beam scanning nozzle. The proton pencil beam can use 94 different energies from 72.5 to 221.8 MeV, corresponding to proton ranges between 4.0 to 30.6 g/cm² (Zhu *et al.*, 2010). The spot-scanning speed in the beam transverse plane is approximately 10 m/s for high-energy beams and 20 m/s for low-energy beams. The time required per spot irradiation is approximately 6 ms. Meanwhile, the time required per energy change is approximately 2.1 s (Smith *et al.*, 2009).

In this study, we evaluated six patient cases that had previously been treated at MD Anderson: four cases of prostate cancer, one case of lung cancer, and one case of mesothelioma cancer. The prescribed dose to the planning target volume (PTV) was 76 Gy for the prostate cases, and two parallel opposed beams were used. The prescribed dose to the clinical target volume (CTV) was 60 Gy for the lung case, and three beams were used: 270, 180, and 220. The prescribed dose to the PTV was 50 Gy for the mesothelioma case, and four beams were used: 340, 70, 200, and 100. More details of treatment planning settings are listed in Table 1. For each patient case, the optimized all-energy and reduced-energy plans were compared based on dosimetric measures and required energies and spots for delivering the plans.

In this study, the MIP models were solved using the branch-and-bound algorithm (Wolsey, 1998) in CPLEX v12.1 (IBM, Armonk, New York, USA). The dose was calculated based on our in-house proton dose calculation engine (Li *et al.*, 2011). All patient studies were performed on a Linux computer with an Intel X5650 2.67 GHz six core processor and 24 GB RAM.

3. Results

The results of optimized and reduced proton energy selections from the PER approach for all six patient studies are summarized in Table 2. The numbers of energies per beam selected by PER compared with the numbers per beam used in conventional IMPT planning that employs all available energies. Note that one energy or energy layer is considered to have been selected or used if there is at least one spot with a positive intensity in that energy or energy layer. For the prostate cases, the total number of energies required by the conventional IMPT plans ranged from 37 to 49, whereas the number used in the reduced-energy plan ranged from 30 and 42. This indicates energy reductions of 14.3% ~ 18.9% were achieved by PER. For the lung case, the total number of energies was reduced from 100 to 89 by 11%. For the mesothelioma case, the total number of energies was reduced from 238 to 175 by 26.5%. Note that the mesothelioma case had a particularly larger target than the other cases, and its anatomy is illustrated in Figure 2.

The total delivery time including energy change, spot scanning and gantry movement between fields for the conventional and PER plans are listed in Table 3. The reductions of total delivery time ranged from 0.2 to 2.6 in minute and from 6.5 to 12.1 in percentage. We also simulated the total delivery times based on different speeds of energy switch. Figure 3 shows the total delivery times resulted by the required energy switch times of 0.01, 0.1, 1, 2, 5 s, respectively, for all patient cases. The total IMPT delivery time monotonically increased when the time required for one energy switch increases. In addition, at a slower energy switching speed, there was a larger difference in total delivery time between conventional and PER plans.

The dosimetric performance of the all-energy plan and the reduced-energy plan was compared using dose volume histograms (DVHs). Figure 4 shows the DVHs of major structures for both plans for prostate patient case 1. The DVHs for the PTV agree well, and the DVHs for the rectum, bladder, and femoral heads revealed minor differences between the two plans. Figure 5 shows DVHs of the clinical target volume, total lung, esophagus, and heart for the lung patient case. Each DVH from the reduced-energy plan conformed to the DVH from the all-energy plan completely. Figure 6 shows DVHs of the PTV, esophagus, heart, and spinal cord for the mesothelioma patient case. The minimum, maximum and mean dose levels on targets and normal tissues for all patient cases are listed in Table 4. Note that we used D_{99} (Gy) and D_1 (Gy) as surrogates for minimum and maximum doses, respectively. The differences in those values between conventional and PER plans were no more than 10%. For each of those patient studies, our radiation oncologist (DG) reviewed the two plans and considered them clinically equivalent.

Figure 7 demonstrates the proton energy layers and the number of scanning spots per energy required in both all-energy and reduced-energy plans for the mesothelioma case. Each of the four beams is shown separately. As an example of beam 1, there are 63 energy layers (bars in gray color) required by the conventional all-energy plan, while there are 40 energy layers (bars in black color) required by the optimized reduced-energy plan. In addition, if one energy layer is required by both plans, it is a general trend that the number of scanning spots required by the reduced-energy plan for that layer is equal to or more than the number of spots required by the all-energy plan. However, it is not always the case. For example, the all-energy plan requires more spots than the reduced-energy plan for its energy layers 48 to 52 in beam 2. In all, we observed that 1) the reduced-energy plan always selects a subset of available energies and 2) the reduced-energy plan generally requires at least the same amount of scanning spots as the all-energy plan does for the selected energy levels. Note that patterns similar to those shown in Figure 6 were observed in the prostate cases and the lung case.

4. Discussion

The superior dosimetric benefits of IMPT for various tumor sites have been demonstrated in many recent studies (Zhang et al. 2010, Pugh *et al.*, 2013; Liu *et al.*, 2014; Li *et al.*, 2014; Lomax *et al.*, 2004; Stuschke *et al.*, 2012). The demand for IMPT is rapidly increasing. However, access to IMPT for today's cancer patients is very limited. At MD Anderson, there is only one pencil beam scanning nozzle to deliver IMPT. We operate from 4 a.m. until

midnight every day and still hardly meet the demand. Therefore to improve operation efficiency delivery, the nozzle unitization rate must be optimized. Since switching energies requires a considerable portion of the delivery time, we started investigating the possibility of reducing the number of proton energies used.

This study is a proof of principle demonstrating the feasibility of employing a reduced number of proton energies to deliver non-degraded IMPT plans. Based on patient studies at multiple sites including prostate, lung, and mesothelioma, we observed that it is possible to exclude 11% to 26% of the total number of energies. Previous research (Kang *et al.*, 2008) demonstrated how the active pencil beam scanning system determines a discrete set of proton beam energies for general IMPT delivery. These energies are sampled from a fine grid of 1 mm and are believed to be sufficiently precise to create complex IMPT plans. This study reveals that those energies may be further reduced and optimized to deliver desired dose distributions for individual patients.

The results of this study reflect an important characteristic of IMPT optimization: solution degeneracy, i.e., the existence of different plans (spot intensities and energies) yielding the same or similar dose distribution. As pointed out by many other researchers (Albertini *et al.*, 2007; Albertini *et al.*, 2010; Oelfke and Bortfeld, 2000; Lomax, 1999), IMPT plans may be even more degenerate than intensity-modulated radiation therapy plan (Alber *et al.*, 2002; Jorge *et al.*, 2004; Webb, 2003), because IMPT has one more degree of freedom, i.e., the range of protons, than intensity-modulated radiation therapy. For IMPT plans with multi-field optimization (Pugh *et al.*, 2013), intensities of scanning spots at different two-dimensional positions in different energy layers from different treatment beam angles are independently modulated and optimized. It is likely to find certain treatment plans to achieve desired dose distributions by specifically devising optimization models such as the energy-constrained model we implemented in this study. For example, we observed that a total of 46,901 and 43,738 scanning spots from all energies were required by the all-energy and reduced-energy plans, respectively, for the mesothelioma case. Those spots were also differently allocated. Due to the PER model, the selection of scanning spots in the same energy layer changed because the selection of energies changed (as illustrated in Figure 7), while the resulting dose measures were sustained. However, it may be less likely to find a degenerate solution when the degree of freedom of variables decreases, such as IMPT with single-field optimization (Zhu *et al.*, 2010).

We should note that robustness of IMPT treatment plans against uncertainties is another important aspect. In this study, we utilized our in-house robustness evaluation tool to validate both all- and reduced-energy plans. No marked difference in robustness over sampled uncertainties was found between the two types of plans. Although uncertainties were not specifically included in this study, the proposed model is flexible with different optimization objectives, i.e., different choices of function (6). Therefore, various robust optimization approaches (Fredriksson *et al.*, 2011; Liu *et al.*, 2012; Pflugfelder *et al.*, 2008; Chen *et al.*, 2012; Unkelbach *et al.*, 2009; Unkelbach *et al.*, 2007) can be readily incorporated.

Regarding computational efficiency, the PER model took 20 to 60 minutes to obtain reduced-energy plans while running conventional plan optimization took 5 to 20 minutes for different cases in this study. For clinical purposes, since PER is a mixed integer program, it can be exponentially speeded up by parallel implementation to achieve a similar calculation time required by conventional plan optimization. In addition, a hybrid approach can first start with obtaining the reduced-energy selection, then perform other planning steps such as multi-objective trial and error, robust optimization or evaluation, etc.

The clinical primary benefit of proton energy optimization is improved IMPT delivery efficiency by employing fewer energies. As the treatment delivery time depends significantly on the number of energies used, the percentage by which the energies are reduced is nearly the same percentage by which delivery time is reduced. Thus, this model has good potential to increase patient throughput given that today's IMPT access is highly limited. We also showed that the amount of time saved would be greatest in cases of large tumors. In all, a comprehensive computational framework simultaneously determining parameters such as scanning spots (Cao *et al.*, 2013; Kang *et al.*, 2007), energies, and beam angles (Cao *et al.*, 2012) while minimizing the impact of uncertainties (Fredriksson *et al.*, 2011; Liu *et al.*, 2012; Pflugfelder *et al.*, 2008; Chen *et al.*, 2012) would ultimately achieve more effective and efficient IMPT plans.

It is important to note that the decrease of beam on time incurred by reducing proton energies is greatly dependent on the energy switch speed as demonstrated by this study (see Figure 3). If a fast machine, e.g., 0.1 s per energy switch, is used, the impact of reducing energy layer on beam on time is negligible. If a slow machine, e.g., 5 s per energy switch, is used, the proton energy optimization is much more advantageous and higher decrease in beam on time can be obtained. In other words, adopting a faster machine is more preferable to a new proton center rather than utilizing energy optimization tools on a slower machine in terms of the overall delivery efficiency, if the choice of proton delivery system is allowed.

5. Conclusions

In this study, we demonstrated that it is possible to employ fewer proton energies to achieve non-degraded plan quality in current IMPT planning techniques. An MIP-based iterative approach was introduced to find optimized and reduced energies from all available candidates. The proposed approach was implemented on four prostate cases, one lung case, and one mesothelioma case. With a reduction of approximately 11.0 % to 26.5 % of total energies, we observed that there was no degrading effect on treatment plan quality compared with an all-energy plan based on dose volume measures.

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Figure 1.

Flow chart illustrating the proton energy optimization and reduction method. L^* denotes the incident energy set, and $L \rightarrow$ denotes the optimized energy set from the MIP. The treatment plan with optimized energies $L \rightarrow$ is accepted if the MIP is solved optimally and its cost function value is less than the threshold value.

Figure 2. Computed tomography images for the mesothelioma case in the transverse view (left figure) and the coronal view (right figure). The aquamarine, green, red, and violet contours show the PTV, esophagus, spinal cord, and heart, respectively.

Figure 3.

Total delivery times based on different speeds of energy switch for conventional and PER plans for the prostate, lung and mesothelioma patient cases. Average values are used here for the four prostate cases.

Figure 4.

Comparison of dose volume histograms for IMPT plans with conventional energy setup (solid lines) and PER reduced-energy setup (dashed lines) for prostate case 1.

Figure 5.
Comparison of dose volume histograms for IMPT plans with conventional energy setup (solid lines) and PER reduced-energy setup (dashed lines) for the lung case.

Figure 6.

Comparison of dose volume histograms for IMPT plans with conventional energy setup (solid lines) and PER reduced-energy setup (dashed lines) for the mesothelioma case.

Figure 7. Comparison of numbers of scanning spots delivered in each energy layer for the mesothelioma IMPT plans with conventional all-energy setup (gray bars) and PER reduced-energy setup (dark bars) for all four beams.

Table 1

Patient information and treatment planning parameters.

Patient	PTV (cc)	Number of beams	Beam angles	Maximum energy (MeV)	Number of energies
Prostate 1	90.3	2	90,270	195.6, 198.3	49
Prostate 2	120.1	2	90,270	193.0, 193.0	37
Prostate 3	157.3	2	90,270	198.3, 195.6	39
Prostate 4	233.2	2	90,270	201.0, 203.7	38
Lung	187.8	3	270,180,220	183.5, 155.4, 159.6	100
Mesothelioma	3913.7	4	340,70,200,100	216.8, 206.4, 206.4, 201.1	238

Table 2

Comparison of number of energies obtained from the conventional approach (all available) and the PER approach (reduced) for six IMPT plans.

Plan	Number of Energies		
	All (Conventional)	Reduced (PER)	Reduction
Prostate 1: two-field	19+19=38	14+19=32	15.9%
Prostate 2: two-field	19+18=37	12+18=30	18.9%
Prostate 3: two-field	20+19=39	13+19=32	17.9%
Prostate 4: two-field	24+25=49	23+19=42	14.3%
Lung: three-field	38+36+26=100	35+31+23=89	11.0%
Mesothelioma: three-field	63+59+59+57=238	40+47+51+37=175	26.5%

Table 3

Comparison of total delivery (beam on) time and total number of spots of the conventional and PER IMPT plans for the six patient cases.

Plan	Total Delivery (Beam On) Time in Minute		Total Number of Spots		
	Conventional	PER	Reduction	Conventional	PER
Prostate 1	2.5	2.3	7.6 %	1,688	1,554
Prostate 2	3.1	2.8	9.7 %	2,894	2,605
Prostate 3	3.7	3.4	8.1 %	3,462	3,115
Prostate 4	4.6	4.3	6.5 %	3,735	3,340
Lung	6.1	5.6	8.2 %	2,847	2,649
Mesothelioma	21.5	18.9	12.1 %	46,901	43,738

Table 4

Dose statistics of conventional and PER plans for the six patient cases included in this study. D_n means the minimum dose to n% of the volume and D_{mean} means the mean dose of the volume. All values in this table are in Gy.

Patient	Plan	PTV		Rectum		Bladder		F. Heads	
		D_1	D_{mean}	D_1	D_{mean}	D_1	D_{mean}	D_1	D_{mean}
Prostate 1	Conventional	78.7	75.6	77.7	77.5	78.4	19.2	35.2	25.6
	PER	78.8	75.5	77.7	77.5	78.4	18.7	34.7	27.6
Prostate 2	Conventional	79.7	74.8	78.8	78.6	76.3	6.5	33.6	19.4
	PER	79.7	75.0	78.9	78.8	76.8	6.3	33.7	21.2
Prostate 3	Conventional	80.2	75.8	78.9	78.9	79.2	10.8	32.9	23.1
	PER	79.9	75.2	78.6	78.6	78.6	11.3	33.5	22.9
Prostate 4	Conventional	80.3	75.1	79.0	77.4	79.0	13.4	32.2	22.1
	PER	80.6	75.7	79.3	77.9	79.5	13.6	32.0	21.7
Lung	CTV								
	Total Lung								
	Esophagus								
	Heart								
	<hr/>								
	D_1	D_{99}	D_{mean}	D_1	D_{mean}	D_1	D_{mean}	D_1	D_{mean}
Lung	Conventional	75.4	58.2	65.7	68.9	15.2	67.4	19.6	64.1
	PER	75.3	58.2	66.1	68.9	15.2	66.9	19.5	66.8
Mesothelioma	<hr/>								
	PTV								
	Esophagus								
	Spinal Cord								
	Heart								
	<hr/>								
	D_1	D_{99}	D_{mean}	D_1	D_{mean}	D_1	D_{mean}	D_1	D_{mean}
Mesothelioma	Conventional	61.8	40.1	56.2	53.9	25.1	47.1	23.4	52.5
	PER	62.1	40.2	56.2	53.7	25.0	46.7	23.2	53.3