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Scientific Article

Multiple energy extraction reduces beam delivery time for a synchrotron-based proton spot-scanning system

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Abstract

Purpose: Multiple energy extraction (MEE) is a technology that was recently introduced by Hitachi for its spot-scanning proton treatment system, which allows multiple energies to be delivered in a single synchrotron spill. The purpose of this paper is to investigate how much beam delivery time (BDT) can be reduced with MEE compared with single energy extraction (SEE), in which one energy is delivered per spill.

Methods and Materials: A recently developed model based on BDT measurements of our synchrotron's delivery performance was used to compute BDT. The total BDT for 2694 beam deliveries in a cohort of 79 patients treated at our institution was computed in both SEE and 9 MEE configurations to determine BDT reduction. The cohort BDT reduction was also calculated for hypothetical accelerators with increased deliverable charge and compared with the results of our current delivery system.

Results: A vendor-provided MEE configuration with 4 energy layers per spill reduced the total BDT on average by 35% (41 seconds) compared with SEE, with up to 65% BDT reduction for individual fields. Adding an MEE layer reduced the total BDT by <1% of SEE BDT. However, improving charge recapture efficiency increased BDT savings by up to 42% of SEE BDT.

Conclusions: The MEE delivery technique reduced the total BDT by 35%. Increasing the charge per spill and charge recapture efficiency is necessary to further reduce BDT and thereby take full advantage of our MEE system's potential to improve treatment delivery efficiency and operational throughput.

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Introduction

Conflicts of interest: None.

* Corresponding author. Mayo Clinic Arizona, Phoenix, AZ 85054. *E-mail address:* Shen.Jiajian@mayo.edu (J. Shen). Pencil-beam scanning (PBS) is becoming the delivery technique of choice for therapeutic proton beams because it offers superior dose conformality through intensity

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modulation without the patient-specific hardware required by passive scattering proton therapy.^{1,2} With PBS, treatment volumes are irradiated spot by spot in the lateral directions using steering magnets, and beam energy selection allows dose to be delivered throughout the depth of the target volume.³ Our institution uses the Hitachi ProBeatV synchrotron-based PBS system to treat patients in four gantry rooms. The number of patients that can be treated each day in a spot-scanning proton treatment center is determined by a large number of factors, including the time spent imaging, positioning, and irradiating each patient.^{4,5} One way to decrease treatment time and increase patient throughput is to reduce the beam delivery time (BDT).

In the usual method of synchrotron-based PBS field delivery, called single energy extraction (SEE), only one proton energy is delivered per spill. Therefore, SEE delivery requires at least one accelerator cycle for each energy layer in a field; inevitably these numerous reaccelerations contribute a large fraction of BDT. Even if relatively few protons are delivered on an energy layer, the synchrotron must discard all remaining protons and accelerate new protons before beam delivery can continue on the next energy layer. This frequent loss of potentially deliverable proton charge and unnecessary cycling makes SEE a suboptimal delivery technique that fails to fully utilize the synchrotron's performance capabilities.

Multiple energy extraction (MEE) is an advanced technology that was originally developed and demonstrated at the Heavy Ion Medical Accelerator in Chiba^{6,7} and has recently been implemented into Hitachi's ProBeatV PBS system. The MEE delivery technique uses incremental beam deceleration during extraction to deliver multiple discrete energies within a single spill. The ability to deliver several energy layers per spill reduces the time spent reaccelerating the beam during patient treatment.

Overall time savings will be significant whenever the majority of BDT consists of acceleration and deceleration. Rapid beam delivery with MEE will decrease BDT and have a positive impact on patient throughput, especially at treatment centers with multiple gantry rooms that are served by one accelerator. Reducing the number of pauses during beam delivery is also known to mitigate the interplay effect in intensity modulated proton therapy that results from treating moving targets.⁸

The synchrotron-based beam delivery process is complex, and several limiting factors may affect BDT reduction from MEE.^{9,10} Synchrotron-based systems have a maximum extraction time during which a stable beam can be maintained as well as a maximum amount of deliverable charge available per spill. If either of these limiting factors is exceeded, the accelerator must reset and begin a new cycle. Additional cycles necessitated by these limiting factors can counteract the theoretical time savings gained by MEE delivery. The reduction in MEE performance due to synchrotron limitations depends not only on beam parameters but also on the spot-scanning patterns and charge distributions of fields. For these reasons, evaluating MEE as a means to reduce total beam-on time at a clinic requires a highly representative sample of treatment fields.

In this article, we present a comprehensive quantitative analysis of potential BDT reduction from upgrading our synchrotron to MEE delivery. First, our BDT reduction model was validated by measuring patient treatment fields delivered using SEE and MEE delivery techniques. This model was then used to calculate BDT for all proton treatments delivered at our institution over a period of two months in both SEE and 9 different MEE configurations. Finally, we investigated the effect of hypothetical improvements in accelerator performance, such as increasing the available charge per spill. These scenarios provided insight into how future synchrotron improvements would affect the amount of BDT saved with the MEE delivery technique.

Methods and materials

Beam extraction in MEE

The ProBeatV currently provides discrete spot scanning in which the beam is turned off between spot deliveries.^{3,11} Figure 1A depicts beam energy over 4 accelerator cycles of a discrete spot-scanning system using the SEE delivery technique. After the beam has been accelerated to the desired energy E_i , spot delivery for that energy layer is initiated. The process of spot delivery is shown on the inset graph of the charge delivery rate. The time required to irradiate one spot is called the spot spill time.

After the desired number of MU for a spot is delivered, the beam pauses while being steered to the next spot position. This beam-off time between spot deliveries is called the spot-switch time, which varies only slightly with distance between consecutive spots. After the position is verified, irradiation of the next spot is initialized. This sequence continues until all spots within the energy layer are delivered. Any protons that remain in the synchrotron ring are decelerated and discarded, after which a new batch of protons is accelerated to the next energy E_{i+1} .

The exact SEE layer switch time τ_{SEE} required to decelerate and then reaccelerate the beam depends on the energy but is approximately 2 seconds.¹⁰ Layer switch time has been reported to make up >70% of the total BDT for most treatment volumes.⁴ Therefore, the total layer switch time is typically the largest component of BDT with the SEE technique.

The MEE delivery technique allows mid-spill switching between proton energies. After completing delivery of one energy layer, a portion of the residual charge is decelerated to the subsequent energy level instead of being discarded. An MEE delivery cycle for the same 4 energy layers from Figure 1A is shown in Figure 1B. The 4 individual flat-tops within the spill (one for each energy layer) are separated by MEE layer switch times τ_{MEE} . To indicate



Figure 1 Four energy layers are delivered in (A) single energy extraction (SEE) and (b) multiple energy extraction (MEE). With the SEE delivery technique, only one proton energy can be extracted for each of the 4 accelerator cycles shown. The MEE delivery technique allows protons of 4 different energies to be extracted with 3 intervening MEE layer switch times τ_{MEE} . The MEE layer switch time is much shorter than the SEE layer switch time (approximately one-tenth of the duration for our system), so the total delivery time for these 4 energy layers is reduced by switching to MEE delivery.

that these energy layers are part of the same spill, we use the notation $E_{i,j}$ to denote the *j*th energy layer of a spill initiated on energy level *i*.

A comparison of Figures 1A and 1B illustrates the amount of time that can be saved by switching from SEE to MEE. The MEE technique reduces BDT by replacing several long SEE layer switch times τ_{SEE} with much shorter MEE layer switch times τ_{MEE} . The MEE layer switch time τ_{MEE} for our system is 0.2 seconds, so each SEE layer switch time replaced represents a BDT savings of approximately 1.8 seconds, or roughly 90%. Layer switch time makes up a majority of BDT for most fields; thus, replacing many SEE layer switch times with MEE layer switch times can meaningfully reduce the total BDT (Fig 1).

MEE design graphs

The MEE delivery system offered by the vendor has a finite number of MEE layers that can be distributed among the synchrotron energies. For spills initiated at a particular energy, the MEE layers assigned to that energy are the layers that can be delivered before a synchrotron reset is required. The function that maps each energy level to the number of deliverable MEE layers is called the MEE design. The MEE design in which all energies have the same number of layers *n* is called the uniform MEE design MEE_n . MEE designs may also be nonuniform.

The MEE design shown in Figure 2 is the uniformdesign MEE_4 , which is the vendor-specific default for our system. Our PBS system can deliver 97 distinct energies, ranging from 71.3 MeV to 228.8 MeV, which are labeled on box axes from highest to lowest energy using the integers from 1 to 97. The empty red circles represent the initial energy layer of a spill. The blue diagonal line intersects all energy layers on which spills are initiated. The solid red circles in a column represent the additional MEE layers that can be delivered during the same spill. As seen on the lower-left inset plot, a spill that is initiated on energy level 1 can continue on to energies 2, 3, and 4 before an accelerator reset is required (Fig 2).

BDT calculation for MEE

The total BDT for a field is computed from the three components of beam delivery as described earlier. The first component (spot spill time) is the total beam-on time required to deliver every spot in the field. The second component (spot switch time) is the total amount of time required to realign the beam laterally. The sum of spot spill time and spot switch time is the total extraction time. The final component is the layer switch time, which is the total amount of beam-off time that occurs between energy layers during field delivery, including both SEE and MEE layer switches. The total BDT for a field is the sum of the spot spill time, the spot switch time, and the layer switch time.

An accurate BDT calculation method based on experimentally determined beam parameters has been developed recently for our PBS system.¹⁰ This method can compute



Figure 2 A graphical representation of the uniform multiple energy extraction (MEE) design with 4 MEE layers per spill (MEE_4). Columns correspond to spills with different initial energies, and the points in each column show the MEE layers that can be delivered within that spill. The solid blue diagonal line intersects the initial spill layers. In the single energy extraction delivery mode, only the layers indicated by the empty red circles on this line can be delivered. Solid red circles correspond to the additional MEE layers that can be delivered. The enumerated energy levels are ordered from highest (228.8 MeV) to lowest (71.3 MeV) energy.

each component of a field's BDT in SEE delivery using the spot pattern and beam parameters. The SEE BDT model can be used to compute BDT for MEE delivery with some modifications, primarily to the formula for layer switch time. The layer switch time in this modified BDT model is given by the formula:

$$T_{LSw} = \sum_{i=1}^{N_L} \left(\delta_{S_i} + m_{EX_i} + n_{MU_i} \right) \tau_{SEE} + \left(1 - \delta_{S_i} \right) \tau_{MEE}$$
(1)

where N_L is the total number of energy layers in the field, and the δ_{S_i} are binary variables whose values depend on how each energy layer was initiated before spot delivery. If a new spill starts at the beginning of the layer, an SEE layer switch time is added to the total using $\delta_{S_i} = 1$. On the other hand, if the layer is the continuation of an ongoing MEE spill, then the intervening MEE layer switch time is added with $\delta_{S_i} = 0$. The value of each δ_{S_i} can be determined from the MEE design (Fig 2). Initial spill layers (ie, the empty red circles on the blue line) have $\delta_{S_i} = 1$, and additional MEE layers in the spill that are represented by solid circles have $\delta_{S_i} = 0$ instead.

In the BDT model, the integers m_{EX_i} and n_{MU_i} correspond to the two reasons why an accelerator reset may be required before the end of a layer: exceeding the maximum extraction time and running out of deliverable protons in the accelerator ring, respectively. If a layer can be delivered without exceeding the extraction time and charge limits, the variables m_{EX_i} and n_{MU_i} are equal to 0. They will only take non-zero values on layers in which the accelerator runs out of charge or the maximum extraction time is exceeded during a spill. If a reset is caused by reaching either of these limits, a new spill must be initiated on that layer to deliver the remaining spots. Therefore, the variables m_{EX_i} and n_{MU_i} count the SEE layer switch times that are added to the BDT on each layer due to exceeding the synchrotron's physical limits. The sums of m_{EX_i} or n_{MU_i} over all energy layers divided by the total number of spills determine the fraction of spills that end in aborts of either type. These fractions of aborted spills can be used to measure the relative influence of each limiting factor on MEE delivery efficiency.

For our system, the maximum extraction time is 8 seconds, and the charge limit is approximately 2 nC (or

approximately 19.4 MU in our definition). However, both spot delivery and mid-spill deceleration using the MEE technique perturb the phase space of the beam. As a result, only a fraction of the charge left over from the previous energy layer can be recaptured after deceleration. The ratio of deliverable charge after deceleration to the residual charge before deceleration is known as the charge recapture efficiency. Our delivery system's average recapture efficiency of approximately 50% is achieved in part by reducing the spill rate. Nevertheless, a large portion of the residual charge that could potentially be used in MEE delivery is lost during beam deceleration.

Patient population characteristics

Our patient cohort included all patients treated with the SEE technique over a period of two months at our institution between late December 2016 and late February 2017. A summary of this cohort is shown in the Table 1 (79 patients, 237 unique fields, 2694 delivered beams). The average MU per patient is provided in the third column to indicate relative treatment volume for each major site, and the average SEE BDT for all beam deliveries in each treatment site can be found in the sixth column. The Table 1 also provides statistics on the average MU per layer and average number of spots per layer for fields, which are important measures related to the effectiveness of MEE in reducing BDT.

BDT calculation in various MEE configurations

Total BDT was calculated using a MATLAB (The MathWorks, Natick, MA) script that applied our BDT model to each beam delivery in the patient cohort. The values of δ_{s_i} for each energy layer were determined by the chosen MEE design. After completing a layer, the script checked whether the following layer was an available MEE layer; if this was the case, then the script set $\delta_{s_i} = 0$ and continued the spill. The maximum extraction time and charge per spill were also checked for each spot delivery. The accelerator was immediately reset whenever either of these limits was reached, which prevented some treatment fields from utilizing all MEE layers in an MEE design.

Validation of BDT model for the MEE delivery technique

To validate the BDT model, a sample of 30 treatment fields that was representative of both the cohort treatment sites and the dynamic range of BDT reduction was selected from the patient cohort. The SEE and MEE delivery times for each field were measured with a timer. The observed reduction in BDT was then compared to the BDT reduction predicted by the model.

		L CU		I /			
Patients (n)	Average MU/patient (MU)	Unique fields (n)	Beam deliveries (n)	Average SEE BDT (s)	Average layers/field	Average MU/layer (MU)	Average spots/layer
5	483.12 ± 86.86	14	205	150.81 ± 31.03	45.64 ± 6.46	4.95 ± 1.76	251.46 ± 108.06
8	123.74 ± 55.75	29	234	102.57 ± 24.22	44.17 ± 9.40	0.83 ± 0.50	81.66 ± 48.65
2	941.48 ± 84.33	10	111	189.63 ± 66.44	58.91 ± 17.59	3.97 ± 2.16	243.99 ± 107.19
9	261.22 ± 62.72	15	160	153.96 ± 30.72	57.64 ± 6.38	1.92 ± 1.33	166.03 ± 84.22
23	54.71 ± 17.23	49	513	70.62 ± 14.59	28.01 ± 6.62	1.90 ± 0.60	100.81 ± 29.60
2	348.34 ± 38.96	7	LL	112.16 ± 57.57	40.57 ± 18.65	1.97 ± 0.76	164.39 ± 68.82
1	348.14	3	57	139.61 ± 53.85	52.33 ± 8.26	1.92 ± 1.90	144.06 ± 143.29
13	133.92 ± 50.07	45	672	98.59 ± 23.82	41.07 ± 10.49	1.44 ± 0.76	83.40 ± 62.59
5	387.76 ± 54.19	18	214	136.54 ± 19.79	50.50 ± 9.20	2.93 ± 1.21	136.91 ± 42.42
3	242.09 ± 57.40	6	105	175.79 ± 26.20	67.21 ± 9.94	1.81 ± 0.47	170.24 ± 49.18
4	390.61 ± 336.92	18	128	172.85 ± 38.45	60.09 ± 6.97	3.33 ± 2.98	165.21 ± 133.97
7	230.11 ± 174.56	20	218	112.08 ± 41.41	41.91 ± 12.84	2.21 ± 1.33	127.77 ± 59.53
7 9	211.88 ± 205.45	237	2694	116.52 ± 46.81	43.88 ± 14.47	2.18 ± 1.64	129.59 ± 88.80
extraction. eries are grou	uped by treatment site. Ave	erage single er	hergy extraction be	am delivery time refe	ars to the mean calc	ulated single energy extra over new lover are field en	lection delivery time
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are related to the beam delivery time reduction that can be achieved.

Our analysis of BDT reduction by MEE included the uniform MEE designs from MEE_2 through MEE_{10} (9 total). This was done to determine whether adding more deliverable energy layers to the vendor-specific default MEE design would provide a substantial BDT reduction. For each of these MEE designs, the fraction of the total cohort spills that were aborted due to running out of charge, the fraction of spills that were aborted due to running out of extraction time, and the fraction of spills that completed delivery on all available MEE layers (ie, normal spills) were recorded to measure the influence of the limiting factors.

BDT calculation with increased maximum charge and recapture efficiency

Synchrotron physical limits on charge and extraction time per spill prevented the realization of potential BDT savings. The influence of the limiting factors was analyzed by calculating cohort BDT reduction for hypothetical scenarios with relaxed system limits. First, charge recapture efficiency was increased to 60%, 80%, and then 100%. From the 100% charge recapture efficiency scenario, charge per spill was doubled and then the extraction time was also doubled. In addition, the total BDT for each design was calculated in an ideal scenario with infinite charge and extraction time.

MEE reduces beam delivery time

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Results

BDT model validation

The results of the BDT model validation test are provided in Figure 3. The points indicate the calculated and measured BDT savings for the 30 fields in the validation sample. Perfect agreement between prediction and measurement is shown by the solid line, and the dashed lines indicate a 10% difference from the measured value. The average and standard deviation of the error in calculated BDT reduction was $-0.12\% \pm 3.47\%$; the average error in calculated BDT for SEE delivery was -0.92 ± 1.72 seconds; and the average error in calculated BDT for MEE delivery was -1.50 ± 4.35 seconds (Fig 3).

BDT reduction for patient cohort

BDT reduction with current delivery system

In Figure 4, we present the total BDT savings of the 2694 beam deliveries in our patient cohort for the uniform MEE designs MEE_2 through MEE_{10} . The vertical axis indicates BDT reduction as a percentage of SEE delivery time, and the horizontal axis corresponds to the number of MEE layers in the MEE_n uniform design. Each set of connected points was calculated with different synchrotron



Figure 3 The beam delivery time (BDT) reduction calculated in our model compared with the BDT reduction measured in our system for a validation sample of 30 cohort treatment fields. Fields in this sample were representative of the full range of treatment sites and BDT reduction in the full cohort. Each point indicates the calculated and measured BDT reduction for one field. The solid line corresponds to perfect agreement with the measurement, and the dotted lines indicate a difference of $\pm 10\%$ field single energy extraction BDT. The average error in calculated BDT reduction (Δ_{BDT}), single energy extraction BDT (Δ_{SEE}), and multiple energy extraction BDT (Δ_{MEE}) are also provided.



Figure 4 The reduction in total cohort beam delivery time (BDT) relative to single energy extraction when delivered with uniform multiple energy extraction (MEE) designs with *n* MEE layers per spill (MEE_n). Each connected set of points corresponds to a scenario with different synchrotron physical limits. The current scenario with 2nC per spill and an average of 46.5% charge recapture efficiency (circles) is shown at the bottom of the figure and the BDT savings limit from the ideal scenario without limiting factors (pentagons) is shown at the top. The average single energy extraction BDT per delivery was 117 seconds.

physical limits. The cohort average SEE delivery time (117 seconds) can be used to convert percent BDT savings to absolute time savings per beam delivery.

The circles at the bottom of this figure correspond to BDT savings given our current synchrotron physical limits, for which the vendor-default MEE_4 design saved 34.5% (41 seconds) of SEE BDT. The MEE_5 design saved 35.1% of SEE BDT, and MEE layers beyond the fifth had virtually no effect on BDT. For example, the MEE_{10} design saved 35.2% of SEE BDT, an improvement of only 0.6% over MEE_4 savings. For the MEE_4 design at current system limits, about two-thirds of spills had charge aborts, but none of the spills was aborted due to exceeding the maximum extraction time (Fig 4).

Future improvement in BDT reduction for patient cohort

The additional sets of points in Figure 4 correspond to hypothetical scenarios with improved system limits. The diamond, square, and cross symbols represent BDT savings for charge recapture efficiencies of 60%, 80%, and 100%, respectively. The results made it clear that increasing charge recapture efficiency was an efficient method to increase BDT savings from MEE delivery. At 100% charge recapture efficiency, the BDT savings with the vendor-default MEE_4 design increased to 42.4% of SEE BDT. However, doubling the charge per spill (plus symbols) after reaching 100% charge recapture efficiency had little additional effect on BDT. However, when the extraction time was also doubled (triangle symbols), the BDT was further reduced.

The pentagon symbols at the top of the graph correspond to infinite charge and extraction time; these points represent the theoretical limit of BDT savings without these two limiting factors. In this scenario, increasing the number of MEE layers from 4 to 10 increased BDT savings from 44.1% to 53.7% of SEE BDT (from 51.4 seconds to 62.5 seconds saved per beam delivery).

BDT reduction for individual fields by average MU per layer

Figure 5 shows BDT savings in our current system for individual beam deliveries in our cohort. The BDT savings



Figure 5 The beam delivery time reduction for each beam delivery in the cohort plotted against average MU delivered per energy layer. The points show a beam delivery time reduction for each beam delivery with our current multiple energy extraction system.

are plotted against the average MU per layer for each field. The beam delivery that experienced the most reduction in BDT (>60%) had very little MU per layer. Conversely, the deliveries with almost no reduction in BDT had a much larger average MU per layer (Fig 5).

Discussion

The cost of a proton facility is high, and maximizing patient throughput is important. MEE is a promising technology that can reduce treatment time through more efficient beam delivery. Our study is the first to quantitatively model BDT savings with a clinic patient cohort using a model that was validated by measurements. However, a quantitative determination of BDT savings is complicated because MEE delivery is affected by charge limits, extraction time limits, and charge recapture efficiency. Hence, the MEE model was more complex, and the standard deviation in prediction error for the MEE model (Fig 3) was approximately 2.5 times greater than for the SEE model. Nevertheless, the average deviation from MEE measurements (-1.5 seconds) was small and comparable with that of SEE (-0.9 seconds). Therefore, the accuracy of overall BDT savings was ensured by the large number of beam deliveries. Our results show that the vendor-provided design MEE_4 can reduce total beam-on time by approximately 35% (41 seconds per beam delivery), which will support greater access to proton treatment, particularly at multipleroom treatment facilities.

The secondary aim of this study was to determine whether improved system limits would result in more BDT reduction from the MEE technique. Figure 4 shows that the vendor-provided MEE_4 design is optimal for our current synchrotron because MEE layers added to this design cannot provide significant BDT savings. The large fraction of spills that experience a charge abort indicated that this saturation was caused by a lack of deliverable charge. The charge limitation of the current system was also demonstrated in Figure 5, in which there was almost no BDT savings for beams with very high average MU per layer. Therefore, further reduction in BDT required either increasing the charge recapture efficiency or increasing the total charge per spill to offset recapture efficiency losses between the MEE layers. However, Figure 4 also showed that increasing deliverable charge can only improve BDT savings to a certain level, where the extraction time limit becomes the dominant limiting factor. Without the influence of the limiting factors, the MEE_{10} design with unlimited charge and extraction time reduced BDT by 54% (63 seconds per beam delivery). Reducing BDT beyond this point would require increasing the spill rate and decreasing the spot switch time (eg, by switching to continuous spot scanning).

The quantitative results presented in this paper are specific to our proton system. However, it is possible to provide qualitative results that are applicable to other synchrotronbased treatment centers with spot-scanning beam capabilities. In general, the BDT reduction due to MEE increases if layer switch time becomes a larger portion of the total BDT. PBS systems with longer extraction times and more deliverable charge per spill would see improved BDT savings that approach the ideal level of MEE performance. If fields delivered at a treatment center have a relatively high average MU and number of spots per layer, less BDT savings should be expected. When constructing an MEE design, it is important to remember that the first few MEE layers added to an energy level will provide the most BDT savings. As a result of the intrinsically decreasing savings and the saturation caused by limiting factors, each additional MEE layer added to an energy level provides less (or possibly no) benefit within the overall design.

Shorter layer switch times have been reported to reduce the severity of interplay effects caused by treatment volume motion.⁸ For spot spacings that are smaller than half of the spot sigma, dose homogeneity and effective uniform dose to the treatment volume are shown to have a significant inverse relationship to layer switch time. This suggests that the reduction in average layer switch time that results from MEE should also reduce intensity modulated proton therapy interplay effects. However, further studies are required to make a precise determination of MEE's influence in this regard.

We restricted our study to the uniform designs MEE_n because they represent the simplest scenarios and illustrate the general mechanism behind BDT savings with MEE delivery. In some situations, nonuniform MEE designs may save significantly more BDT compared with the optimal uniform design. A thorough investigation of BDT reduction in nonuniform designs is needed to determine how much additional time savings could be achieved for a representative set of treatment fields.

Conclusions

MEE is a technology that has great potential to reduce beam delivery time for spot-scanning proton therapy. The MEE_4 design reduced total beam-on time by 35% (41 seconds per beam delivery) for a sample of clinic patients. Delivery time reduction for individual fields varies and is typically larger for fields with a lower average MU per layer.

Future synchrotron upgrades that increase the total charge per spill, charge recapture efficiency, and maximum extraction time will be necessary to take full advantage of the potential MEE benefits.

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References

1. Smith AR. Vision 20/20: Proton therapy. *Med Phys.* 2009;36:556-568.

- Lomax AJ, Bohringer T, Bolsi A, et al. Treatment planning and verification of proton therapy using spot scanning: Initial experiences. *Med Phys.* 2004;31:3150-3157.
- Gillin MT, Sahoo N, Bues M, et al. Commissioning of the discrete spot scanning proton beam delivery system at the University of Texas MD Anderson Cancer Center, Proton Therapy Center, Houston. *Med Phys.* 2010;37:154-163.
- Suzuki K, Palmer MB, Sahoo N, et al. Quantitative analysis of treatment process time and throughput capacity for spot scanning proton therapy. *Med Phys.* 2016;43:3975-3986.
- Suzuki K, Gillin MT, Sahoo N, Zhu XR, Lee AK, Lippy D. Quantitative analysis of beam delivery parameters and treatment process time for proton beam therapy. *Med Phys.* 2011;38:4329-4337.
- Iwata Y, Kadowaki T, Uchiyama H, et al. Multiple-energy operation with extended flattops at HIMAC. *Nucl Instrum Methods Phys Res.* 2010;624:33-38.
- Mizushima K, Katagiri K, Iwata Y, et al. Experimental studies of systematic multiple-energy operation at HIMAC synchrotron. *Nucl Instrum Methods Phys Res.* 2014;331:243-247.
- Dowdell S, Grassberger C, Sharp GC, Paganetti H. Interplay effects in proton scanning for lung: A 4D Monte Carlo study assessing the impact of tumor and beam delivery parameters. *Phys Med Biol.* 2013;58:4137-4156.
- Smith A, Gillin M, Bues M, et al. The MD Anderson proton therapy system. *Med Phys.* 2009;36:4068-4083.
- Shen J, Tryggestad E, Younkin JE, et al. Technical note: Using experimentally determined proton spot scanning timing parameters to accurately model beam delivery time. *Med Phys.* 2017;44:5081-5088.
- Pedroni E, Bacher R, Blattmann H, et al. The 200-MeV proton therapy project at the Paul Scherrer Institute: Conceptual design and practical realization. *Med Phys.* 1995;22:37-53.