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PAPER

A bi-directional beam-line energy ramping for efficient patient treatment with scanned proton therapy

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Abstract

Objective. The treatment of mobile tumours using Pencil Beam Scanning (PBS) has become more prevalent in the last decade. However, to achieve the same beam delivery quality as for static tumours, treatments have to be combined with motion mitigation techniques, not limited but including, breath hold, gating and re-scanning, which typically prolong treatment time. In this article we present a novel method of bi-directional energy modulation and demonstrate our initial experience in improvement of treatment efficiency. *Approach.* At Paul Scherrer Institute Gantry 2 mobile tumours are treated by combining PBS with gating and volumetric re-scanning (VR), where the target volume is irradiated multiple times. Initial implementation of VR used only descending beam energies, creating a substantial dead time due to the beam-line initialization (ramping) before each re-scan. In 2019 we commissioned an energy meandering strategy that allows us to avoid beam line ramping in-between energy series while maintaining beam delivery quality. *Main results.* The measured beam parameters difference for both energy sequence are in the order of the typical daily variations: 0.2 mm in beam position and 0.2 mm in range. Using machine log files, we performed point-to-point dose difference calculations between original and new applications where we observed dose differences of less than 2%. After three years of operation employing bi-directional energy modulation, we have analysed the individual beam delivery time for 181 patients and have compared this to simulations of the timing behaviour assuming uni-directional energy sequence application. Depending on treatment complexity, we obtained plan delivery time reductions of up to 55%, with a median time gain of 17% for all types of treatments. *Significance.* Bi-directional energy modulation can help improving patient treatment efficiency by reducing delivery times especially for complex and specialised irradiations. It could be implemented in many existing facilities without significant additional hardware upgrades.

1. Introduction

Proton therapy is a radiation modality that, thanks to characteristics of the Bragg peak, allows for an improved dose conformation to the target and significant reduction of dose to normal tissue. Currently the majority of proton therapy facilities worldwide are employing Pencil Beam Scanning (PBS) for the management of cancer treatment (PTCOG 2023). This technique is based on a sequential delivery of proton beams (spots) to the target in three dimensions. Developed in 1996 at Paul Scherrer Institute (PSI) (Pedroni *et al* 1995) it allowed implementation of Intensity Modulated Proton Therapy (Lomax 1999) which was successfully adopted at multiple facilities worldwide for treatment of static tumours.

During the last decade an increasing number of centres started treating mobile tumours using PBS (Trnková *et al* 2018). The therapeutic challenge for those cases is that the delivery of the scanned beam to a moving target may lead to an interplay effect degrading the dose distribution quality within the target volume and in critical structures in vicinity of the tumour (Phillips *et al* 1992, Bert *et al* 2008, Kang *et al* 2017). In order to deliver a conformal 3D dose distribution to the tumour, PBS has to be used in a combination with motion mitigation techniques such as re-scanning, gating or other motion mitigation strategies. Re-scanning is one of the techniques that does not require additional installations, thus is the one most straightforward to implement for routine care within an existing system. Re-scanning algorithms can be divided into two main categories: layered rescanning (LR) and volumetric re-scanning (VR) (Zenklusen *et al* 2010). During LR the prescribed number of repetitions is performed sequentially within each energy layer. For VR the whole tumour is re-scanned multiple times requiring additional magnet initialization before each re-scanning volume which leads to a substantial increase of plan delivery time.

The magnet initialization (ramping) of the beam-line is a standard procedure for all accelerator based therapy systems employing conventional magnets. This ensures a reproducible magnetic field in beam-line magnets that sustains the precise beam delivery to the patient. Without a properly ramped beam-line, magnets may end up with a wrong magnetic field even if the current it set correctly leading to a spot position error. Depending on magnetization history of the system, range errors can reach 1 mm (Pedroni *et al* 2011) and the position can be off by several millimetres. Currently all proton therapy systems change energy in a single direction only. Depending on the power supplies and types of magnets used, typical magnet ramping times may be 10 s or longer. Unfortunately, there is little knowledge available in the literature regarding the issue of ramping time in radiation delivery.

For VR the magnet ramping alone would add one minute or more to a treatment time. For instance, for a patient field with 10 re-scans and 20 energy layers, this would prolong the treatment time by 3 min due to energy switching alone. If VR is implemented on systems with energy changes of more than 1 s, this would lead to even more significant prolongation of treatment times. However, for systems offering an energy changing times better than 150–200 ms, such as our treatment unit (Gantry 2), dead-time using VR would be dominated by ramping.

For large motion amplitudes re-scanning has to be combined with other motion mitigation techniques such as gating or breath-hold in order to obtain a conformal dose distribution. Since 2017 we have been treating moving targets with small motion amplitudes (< 1 cm) applying VR at PSI Gantry 2. In 2019, we introduced gating as a complimentary technique for treatments of larger motion amplitudes (Fattori *et al* 2020). Thanks to fast energy switching times of 100 ms (Pedroni *et al* 2011) the typical irradiation time of one VR volume takes 6–20 s depending on target geometry. Initially, before each re-scanning volume, we had to perform a full beam-line ramping of around 10 s, which was a significant parameter prolonging the patient plan delivery time.

Other beam delivery options which require additional ramping at Gantry 2 are: (i) field patching needed for large targets and (ii) use of the pre-absorber for shallow/superficial targets.

We use patching for tumours with dimensions exceeding the 12×20 cm^2 system's scanning area. Thanks to parallel beam at iso-centre (Pedroni *et al* 2011) patching of several fields is a quite straightforward procedure at Gantry 2. From beam delivery point of view patching however, it is handled the same way as re-scanning, requiring a full beam-line initialization before each patch.

For superficial tumours, the range shifter must be used to position dose spots close to the surface. Here we benefit from the capability of Gantry 2 to remotely insert a pre-absorber of 4.2 cm water equivalent (WE) located in the gantry nozzle. Parameters for beams with and without pre-absorber are integrated into Gantry 2 Treatment Planning System (TPS) and the mixed beam pool (combination of beams with and without pre-absorber) is used for up to 80% of the clinical plans. Since the energy for beams with the pre-absorber needs to be adjusted, we apply the same beam delivery scheme as for re-scanning and field patching and use a full beam-line magnet ramping between parts of the field with and without pre-absorber.

After introducing VR, we had a few patients, which were treated using a combination of re-scanning, mixed beam pool and patching. For these patients the dose plan delivery time was often exceeding 20 min. Therefore in 2019 we clinically commissioned a novel method helping to reduce patient treatment time for such complex cases. We implemented a bi-directional energy operation (energy meandering) that allows us to change energies sequentially in both directions to avoid full beam-line ramping between fields (VR, patching, mixed beam pool). In case of field patching, we still have to wait until the table reaches the required position, but this is typically less than the full beam-line ramping used conventionally.

In this article, we describe the process and results of energy meander commissioning, as well as our experience after 3 years of clinical operation. In section 2, we describe the methods and tools, which we were using during the commissioning. Here we also give a background on challenges triggered by highly dynamic beam delivery and possible solutions. In section 3 first, we present the beam validation and commissioning results, second, we summarize the outcome of the first three years of patient treatment statistics collected using energy meandering and compare it to our initial strategy.

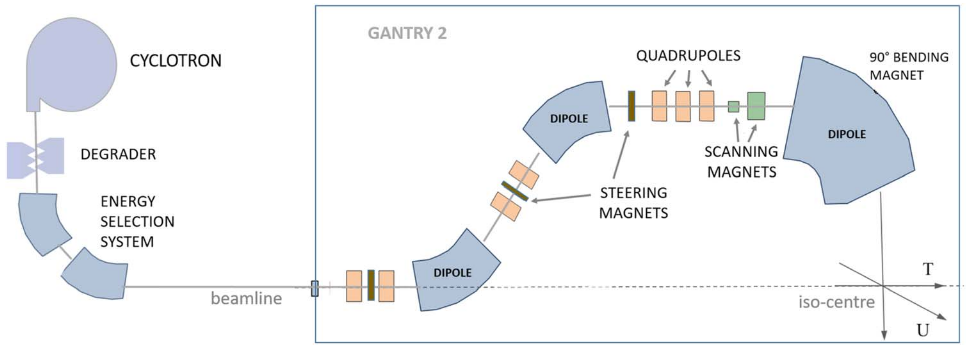

Figure 1. Schematic layout of Gantry 2 system within PROSCAN facility.

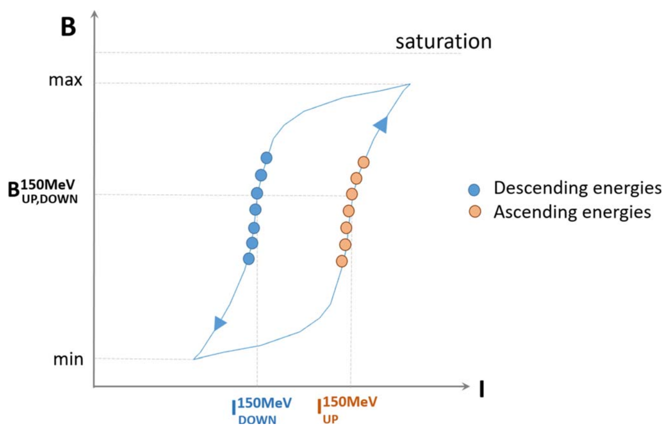

Figure 2. Schematic presentation of a hysteresis loop for a dipole magnet. Note, that B field is proportional to the particle momentum. Blue dots represent positions of energy layers within hysteresis cycle for descending and red dots for ascending energy directions (novel implementation).

2. Materials and methods

In this chapter, we describe the methodology and instrumentation we used to commission the ascending energy sequence as well as methods and tools that we used to perform patient QA and calculate treatment time statistics.

2.1. Beamline settings and hysteresis effect

The PROSCAN facility (Pedroni *et al* 1995) makes use of a cyclotron followed by the degrader and an energy selection system (ESS) as shown in figure 1. The protons are accelerated to an energy of 250 MeV, which, using a degrader, is adjusted right after the accelerator and transported to the patient. To reach all tumour positions within the human body using a gantry equipped with a pre-absorber, the required treatment energies should range from 70 to 230 MeV (4.8–33 cm water equivalent range). All the beam line elements and their power supplies are designed for an energy switching time of less than 100 ms (Pedroni and Bearpark 2004, Kunzi and Jenni 2006, Negrazus *et al* 2008) making the system ideal for VR implementation.

In order to transport each beam of every required energy from the cyclotron to the target a correct magnetic field with a relative precision of 10^{-4} is required for all beam-line dipole magnets. Figure 2 shows a schematic correlation between the magnetic field (B-field) and the magnet current settings within a typical hysteresis cycle of the electromagnet. The same B-field value, which is required for the opposite energy changing directions, corresponds to two different magnet current settings. Moreover, to obtain a stable system operation, the same hysteresis loop between maximal and minimal energy/current settings has to be followed. If those requirements are not fulfilled, even a proper current setting may result in a magnetic field offset leading to a beam position error in the patient. Prior to the treatment, the system status is often unknown, hence a magnet initialization—ramping of the beam line between maximal and minimal energies—has to be performed. After ramping, the system is ready to start at the minimal or the maximal (typical for cyclotron-based systems) energy and the patient field energies are delivered sequentially in one direction. If the energy has to be adjusted for a new field

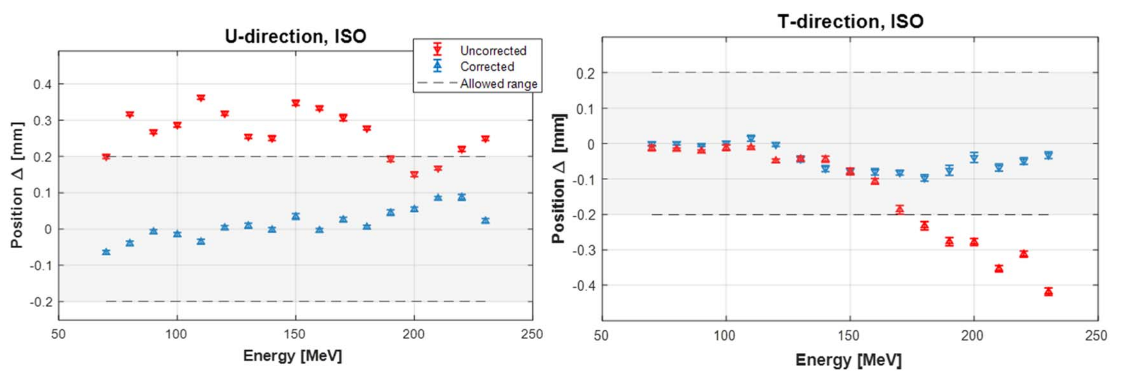

Figure 3. Positions residuals for Gantry 2 in T and U transverse directions before (red markers) and after (blue markers) the fine-tuning. The shaded area show the allowed range for position residuals.

fraction such as a new patch, re-scanning volume or changed pre-absorber position—the full ramping has to be performed.

All beam-line settings for energies from 70 to 230 MeV with 10 MeV step are stored in a table. Using interpolation based on the momentum scaling, we generated beam-line parameters for all clinically required energies.

In 2019, we implemented a bi-directional energy operation based on a concept of stable operation guaranteed by following the proper (full) magnet ramping. The only difference is that we make use of both ramping directions applying patient field fractions using both descending and ascending energies (figure 2). In-between, we only go to a minimum or a maximum energy (depending on the direction) before inversing the scan. Following a strict hysteresis cycle with a full magnet initialization in the beginning helps us to assure the required beam position precision and save up to 10 s per field fraction (Actis *et al* 2018).

2.2. Technical commissioning of bi-directional energy sequence

The operation of Gantry 2 using both energy directions was taken into consideration already at the point of the system design. The detailed description of the whole commissioning procedure can be found in (Pedroni *et al* 2011). We obtained separately two sets of beam-line parameters for ascending and descending energy ramping directions as follows:

Range: using beam optics simulation tools we calculated all beam-line parameters for all clinical energies. Due to the fact that simulations do not take into account magnet hysteresis effect, as a next step, we had to preform small adaptations of the degrader settings to align the beam with the central axis at ESS. Finally, we measured proton range at the iso-centre using a water tank with a large area parallel plate ion chamber to re-label/correlate energies measured at the iso-centre and degrader settings.

Position: using the beam element settings resulting from the beam transport calculation (Pedroni *et al* 2011) we performed fine tuning of the down-stream beam-line part in order to obtain the desired position precision at the iso-centre. Due to time constraints clinical commissioning of the ascending energy sequence was not completed by the beginning of Gantry 2 operations.

Several years later, while implementing bi-directional energy changes we obtained a position deviation of more than 0.2 mm between beams applied using descending and ascending energies at the iso-centre. This is due to minor beam elements setting changes during first years of operation using only descending energies. Thus, we had to realign the beam for ascending energies in order to achieve a better agreement. To do this we used the last set of steering magnets and the last dipole on the gantry. We used steering magnets to correct the position in one of two transverse directions (T) and the U-direction we corrected using the 90° dipole (see figure 1). First, we derived a calibration curve for both elements in order to obtain the correlation factors between magnet's current settings and the beam displacement at the iso-centre. To measure the iso-centre position we used an ionization strip chamber identical to the one in the gantry nozzle (Actis *et al* 2014). Second, based on the measured position deviation between beams applied using opposite energy changing directions, we calculated the required current corrections for the ascending energies. Figure 3 shows the position deviation between ascending and descending energies measured at iso-centre before and after correction.

2.3. Clinical validation of bi-directional energy sequence

In order to enable treatments using energy meandering, we validated the corresponding beam output for all clinically relevant configurations. The pass criteria was to obtain almost identical beam characteristics (were the difference does not exceed daily variations) at the iso-centre making it transparent for the end user and TPS. To do so we validated beam integral depth dose curves over the whole energy range, beam position and shape at iso-centre for all gantry angles and scanning positions. In addition, we had to perform patient specific QA tests to prove that there is no dosimetric difference between the original configurations (using only descending energies) or bi-directional energy sequences.

2.3.1. Beam energy/range

As most of the other therapy systems, Gantry 2 does not have a possibility for on-line range validation during patient treatments. Therefore we perform a detailed range QA on a daily basis (Actis *et al* 2017). Based on knowledge of daily variations we set a tight tolerance of 0.2 mm for the maximal measured range offset between ascending and descending energy directions. Using a water tank with an 8 cm large parallel plate ion chamber we also checked that the 80% fall-off positions do not deviate by more than 1 mm from either ICRU data (ICRU 2007) or from Gantry 2 commissioning data. In addition, we performed a gamma analysis of the full Bragg-peak profile using the 0.5%/0.2 mm global gamma criteria for integral dose evaluation. Employing this technique, we assure that not only the 80% fall-off, but also the entire curves acquired changing the energies in opposite directions match within required criteria.

2.3.2. Beam position

Beam position affects significantly the quality of the final dose distribution at the patient. Unlike beam energy, we monitor this parameter on a spot basis during the patient irradiation using the strip chamber located in the gantry nozzle together with two other dose monitors (Pedroni *et al* 2011, Actis *et al* 2014). For each beam we measure the position in the nozzle and, knowing the beam angle and distance to the iso-centre, calculate the position for this beam in the patient.

As for the difference between beam positions for ascending and descending energy sequences we had to apply strict constraints since we did not want the Gantry 2 TPS having to distinguish between energy directions. A typical day-to-day beam position variation at Gantry 2 is around 0.2 mm depending on accelerator settings. We decided to use this value as the maximal acceptable position deviation between beams produced using ascending and descending energy sequences along the central axis.

For different scanning positions we use an angular dependent position-to-scanner magnet current calibration. Thus, for new (ascending) energy changing direction we validated beam positions at the iso-centre over the full scanning area for various energies and gantry angles, and compared them to values obtained using beam-line settings from the descending energy direction, using standard interlock limit of 1.5 mm (Bula *et al* 2019).

2.3.3. Beam phase space

Even a small change of the beam size or distortion of the beam shape can lead to a dose error of several percent (Moteabbed *et al* 2015). Thus, we had to validate also this parameter during the commissioning of the ascending energy sequence. As a reference data set, we took the original commissioning beam data containing only descending energies and used a CCD camera (Pedroni *et al* 2011) to measure the 2D beam profiles. We acquired beam data in steps of 5 cm over the nominal scanning area of $12 \times 20\ \mathrm{cm}^2$ for energies between 70 and 230 MeV in 10 MeV step. First, we measured and compared the sigma for both, ascending and descending energy sequences collected on the same day, to the commissioning data which we use in our TPS. Typically, expected variations for sigma value are in the order of several percent. We set the pass criteria at 10%, which is the limit that we also apply in our yearly QA procedure. Second, we compared 2D profiles for both energy directions to make sure there is no significant deformation of the spot applied with new beam parameters.

2.4. Dose calculation/Dose in the patient validation

In our clinical workflow, we run two types of patient specific QA procedures. For Patient Specific Quality Assurance (PSQA) we perform a direct measurement of the delivered dose in a water phantom at the selected depth. The patient plan is delivered to a water tank with a PTW array (PTW 2020) mounted below the adjustable water level. We measure a 2D dose distribution and check the dose output to be within 2% with respect to the calculated dose in water based on the nominal plan. For the first delivered fraction of each plan we perform a dose calculation based on machine log files (so called 'log file back-calculation') (Meier *et al* 2015, Scandurra *et al* 2016). Those files are created during the patient irradiation and contain all information about the machine parameters as well as measured dose and position for each proton beam. Using this extensive information, we back-calculate the delivered dose in the patient 3D geometry and compare it to the nominal dose. This tool has demonstrated to be accurate and it is able to pick up small uncertainties in dose delivery (Meier *et al* 2015) at the

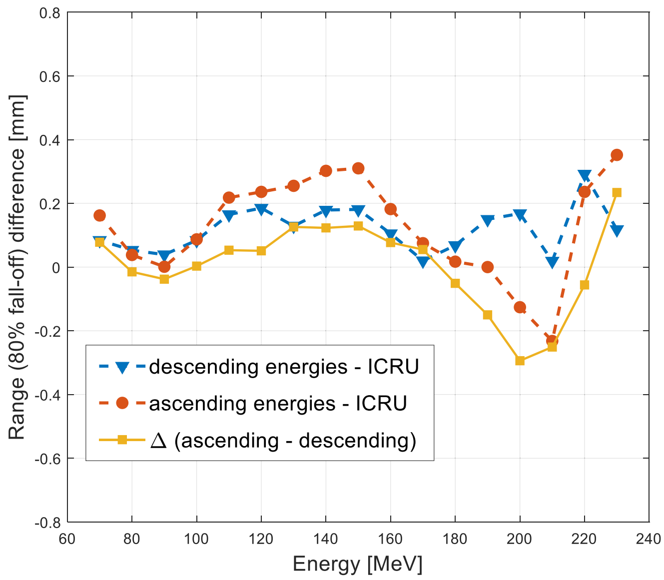

Figure 4. Proton range (80% fall-off) residuals between ICRU data and several data sets: descending energies (blue triangle markers), ascending energies (red circle markers) and range difference between beams acquired in opposite energy directions (yellow square markers).

order of 1 percent caused by reproducibility of the beam position delivery and measurements that can fluctuate up to 0.2 mm.

2.5. Machine time performance in clinical operation

While machine steering files contain all the information about the requested beam delivery (nominal parameters), machine log files contain the actual information about the delivered treatment. Thus we can use log files to extract the actual plan delivery time.

In parallel we developed a timing model which allows us to predict/calculate any plan delivery time based on steering file information without actual delivery. Using the available patient plans, we calculated the plan delivery time for irradiation strategies with energy meandering, as well as for the old beam delivery approach with uni-direction energy changes.

3. Results

We divided this chapter into three parts to present the main results of our work. In the first part we describe the results obtained during the beam validation and clinical commissioning of the ascending energy sequence. In the second part we show how the switch to bi-directional operation affects the patient dosimetry. In the last part, we demonstrate the analysis results obtained using the data from the first three years of clinical operation with main focus on treatment performance improvement using this new beam delivery strategy.

3.1. Beam commissioning and validation results

The commissioning objective was to obtain and validate beam-line parameters for ascending energies, which allow the delivery of almost identical beams to the patient, independently of energy switching direction.

3.1.1. Range

During the validation of ascending energy sequence, we measured dose depth curves, by changing energy between 70 and 230 MeV in 10 MeV steps and calculated the position of the Bragg peak (80% fall-off) for both ascending and descending energy sequences.

Eighty percent fall-off of the ICRU proton range data was used as a reference so we could compare this to our measurement results. Figure 4 shows the residuals between ICRU proton range data and measurements in both energy-changing directions. Both data sets comply very well with recommended ICRU values and the residuals do not exceed 0.4 mm. Here we also show the range difference between beams of the same energy acquired in opposite energy changing directions. The difference for energies less than 200 MeV does not exceed 0.2 mm. For higher energies the residuals are slightly larger. During the validation process however, we noticed that the

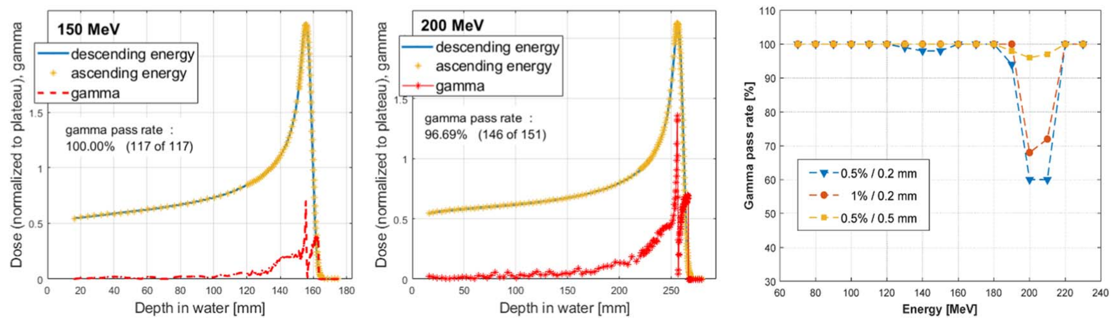

Figure 5. Left and centre: the integral depth dose curves for 150 and 200 MeV beams measured in both energy-changing directions: descending (blue solid line) and ascending (yellow star markers) and resulting gamma pass rate (red dashed line) for 0.5%/0.5 mm global gamma criteria. Right: gamma pass rate for different energies calculated using various global gamma criteria: 0.5%/0.2 mm—blue triangle markers, 1%/0.2 mm—red circle markers, 0.5%/0.5 mm—yellow square markers.

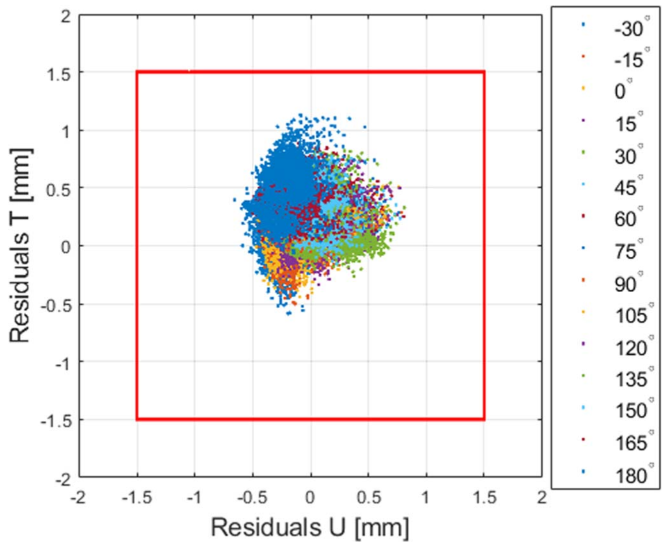

Figure 6. Beam position residuals measured in the nozzle and projected to iso-centre in transverse plane for ascending and descending energy sequences. Markers of the same colour show the measured positions at 17 different energies over the full scanning area of $12 \times 20\ \mathrm{cm}^2$. Measurements performed at different gantry angles are shown in different colours.

measurements at energies above 200 MeV were often showing higher fluctuations and we believe that these larger deviations were a consequence of an increased measurement uncertainty.

Figure 5 (left) shows the 150 MeV Bragg peak profile measured using ascending and descending energy direction. The resulting gamma analysis of all measurement positions over the curve is shown as the red solid line. As one can see from this plot, all data points result in small gamma values, indicating that all curves are well within the 0.5%/0.5 mm tolerance. Thus, for this particular energy the gamma pass rate is 100%. Figure 5 in the centre shows same comparison but for 200 MeV. Here the gamma pass rate is close to 97% which represents our 'worst case' scenario. Analysing the complete data sample of all energies, we obtained gamma pass rates of 100% for energies below 190 MeV and 97%–100% for energies above 190 MeV (figure 5 on the right). Varying the gamma criteria to 0.5%/0.2 mm or 1%/0.2 mm and taking into account our generic tolerance levels, we confirmed that we are most sensitive to range, especially for high energies.

3.1.2. Beam position

As a final spot position test, we validated that Gantry 2 is able to deliver the beam with a required precision at any energy, over the full scanning area and at all gantry angles. Figure 6 shows beam position residuals between measured and nominal values for both energy changing directions over the full Gantry 2 scanning area for 15 different gantry angles. All measured positions stay well within our standard tolerance of 1.5 mm. Moreover, considering each gantry angle separately, more than 95% of dose spots are delivered with a precision of better than 0.5 mm.

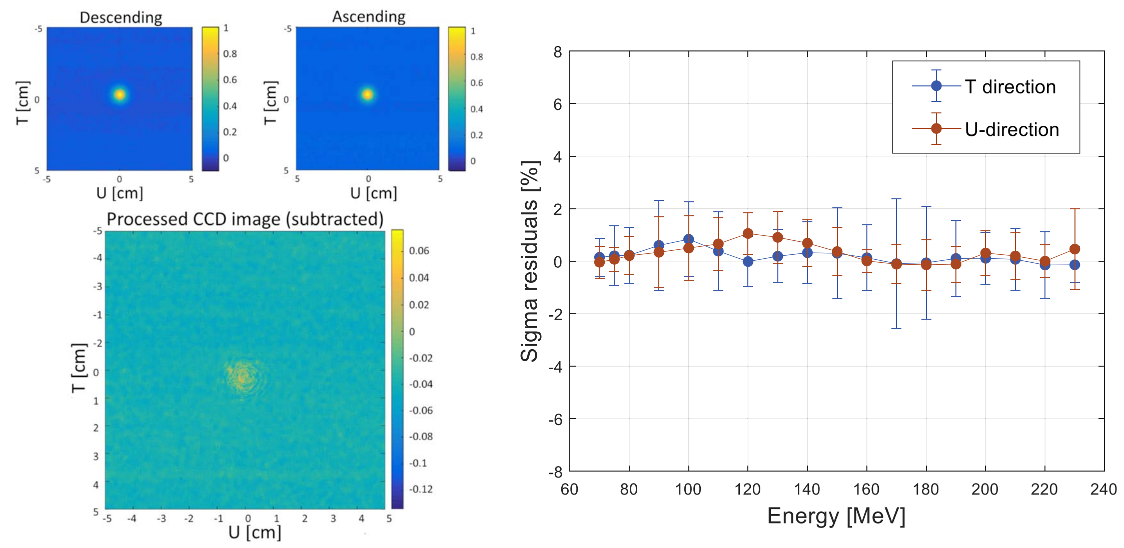

Figure 7. Left: the upper 2D profiles of 100 MeV beam applied using descending and ascending energy directions. The lower plot show the difference of two profiles shown above. Right: Beam sigma residuals (ascending—descending energies) in two transverse directions for ascending and descending energy sequences measured over the whole scanning and energy range in 10 MeV steps. The wiskers show the standard deviation for all measured values in a single energy layer.

3.1.3. Beam phase space

For the assessment of the beam phase space for ascending energies this was compared to the same parameter obtained with the descending energy sequence. In addition, we have verified that the beam sigma in both transverse directions is almost the same (<5% difference), since Gantry 2 beam-line optics is designed such that the beam is almost symmetrical (round) over the whole scanning area for all avaliable gantry angles and energies (Pedroni and Bearpark 2004).

An example beam profile for 100 MeV is shown in figure 7 for both ascending and descending energy sequences. The differential plot at the bottom shows only negligible differences between each energy sequence. On visual validation of all clinical enegies, difference were always below 5%. Figure 7 (right plot) shows beam sigma differences performed using the opposite energy changing directions for the two transverse axes. Tolerances on beam sigma were set at 5%—twice as tight as used for our yearly quality assurance test. For all energies, sigma differences were within tolerance, and differences in the tranversal directions negligible.

As such, we confirmed that differences in beam parameters between acsending and descending energy sequences are negligible and thus, there was no need for an update of the beam model within our TPS.

3.2. Patient dosimetry

As a next step, detailed dosimetry of a set of patient cases was performed, with the objective of validating the dose delivered to the patient using the uni- or bi-directional energy sequences. For this comparison, we selected a group of patients with various indications in order to cover a wide range of clinical scenarios.

At first we performed PSQA measurements at a single depth using a PTW array, for which only negligible dosimetric differences were found between energy meandering and standard (unidirectional) delivery.

Next, dose reconstruction from the log-files was performed (Matter *et al* 2018). Typically, differences here are related to daily fluctuations of beam delivery and position measurement resolution. The magnitude of these could be quantified by analysing patient log files delivered on two sequential days. From this, a typical daily beam position fluctuation of around 0.2 mm results in a dose fluctuation of about 1%.

Figure 8(a)) show the analysis results for two fractions of the same patient delivered on two sequential days. Voxel-by-voxel comparison was performed over each plan. For each combination, we calculated the maximum dose difference and standard deviations, ignoring voxels in air and those with dose below 10%. For most voxels, dose differences are below 0.2%, with a maximum value of 0.8%. For comparison, figure 8(b)) shows the differences for the same plan, but when delivered using the descending energy sequence and energy meandering.

The difference histogram is very similar to the one of the previous comparison, with the dose in most of the voxels not differing by more than 0.2%, although minimum and maximum deviations extend to −1.1% and 1% respectively. Such differences however are still well within clinically acceptable tolerances.

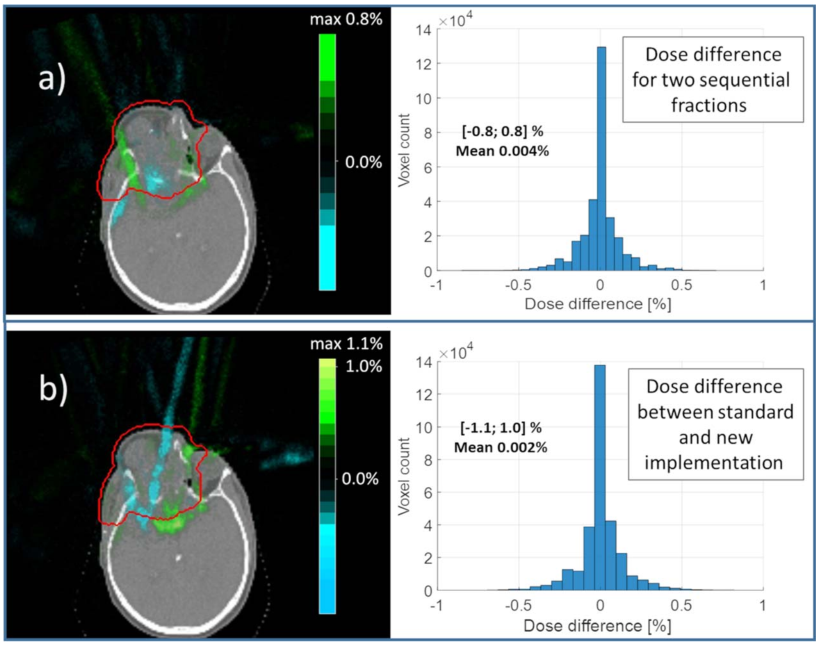

Figure 8. Results from the dose back calculations—back calculated 2D dose difference in a selected energy layer, results from dose voxel comparison for the entire plan. (A) Comparison of the dose calculated from two the same plan delivered on two sequential days. (B)—comparison for the same plan delivered with conventional approach and energy meander.

3.3. Results from the first 3 years of operation

In July 2019, after clinical commissioning was completed, bi-directional energy changes were implemented for patient treatments. During the first three years of operation, 181 patients were treated using energy meandering, most using the mixed beam pool, where a pre-absorber is automatically inserted or extracted during delivery. In addition, some required field patching due to the scanning dimensions extending above the Gantry 2 field size. Finally, some cases were mobile tumours which required re-scanning or/and gating.

The data for the delivered plans were analysed as described in 3.1 based on steering and machine log files. In addition, for all patients, we re-created steering files using the original beam delivery configuration which used the descending only energy sequence. This allowed us to estimate differences in beam delivery time. As a last step, we compared delivery times for the bi- and uni-directional approaches (figure 9). Three different patient categories have been analysed. The first includes all patients treated with re-scanning (no distinction for mixed pool or patching) (22). Second, patients with no re-scanning were split into mixed-pool only (w/o patching) (68) and patching (w or w/o mixed pool) (91). The vertical axis in figure 9 shows the time gain in percent for patient plans delivered using meandering with respect to the uni-directional approach. Median time reductions were 27% (range from 10% to 55%) for re-scanned plans, 17% (range from 0% to 29%) for plans with mixed beam pool modality and 15% (range from 8% to 20%) for plans with field patching. Time reductions were more prominent for plans where the mixed beam pool is used together with re-scanning (time gain goes up to 55%).

The time reduction for mixed pool only plans strongly depends on the size of the tumour. For small tumours, the field delivery time could be less than a full magnet initialization time. In this case, the benefit of energy meandering can be up to 50%. Larger targets require more time for dose delivery making the improvements less prominent. For plans requiring patching however, the effect of energy meandering is almost negligible. This is due to the fact that we allow for a minimal system pause of seven seconds during each patient table move. This pause is just 2–3 s smaller than a standard magnet initialization and in case of longer movements, the timing is identical between new and old approaches. However, most of the patched fields still contain mixed beam pool modalities. This is also consistent with our results. The gain in plan delivery time for patched fields is 15%, which is only 2% less with respect to plans which use only mixed pool modality.

Finally, figure 10 shows an example of delivery time reduction for a large, superficial target. For this case, the fields were delivered with 2 patches, with each patch containing a mixed pool component. Here one can see that even with a pause for table movement (patching), energy meandering reduced delivery time by 15%–20% for each field.

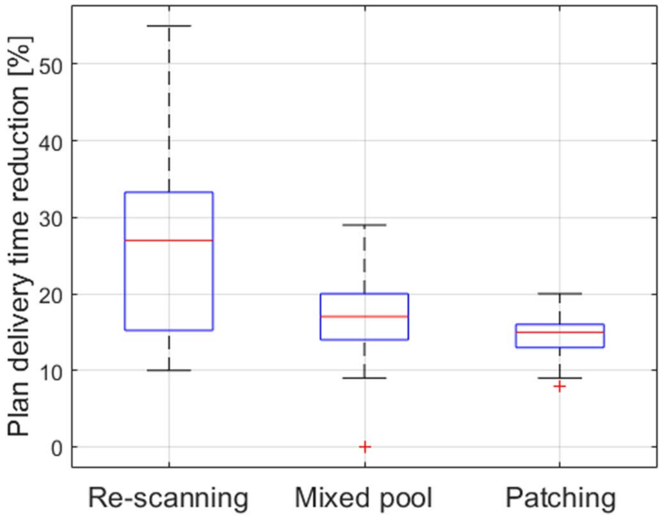

Figure 9. Patient plan delivery time reduction in percent between a new beam delivery approach with energy meander and an old one-directional energy sequence. On each box, the red mark inside indicates the median, and the bottom and top edges of the box indicate the 25 and 75 percentiles, respectively. The whiskers extend to the most extreme data points not considered outliers, and the outliers are plotted individually using the '+' symbol.

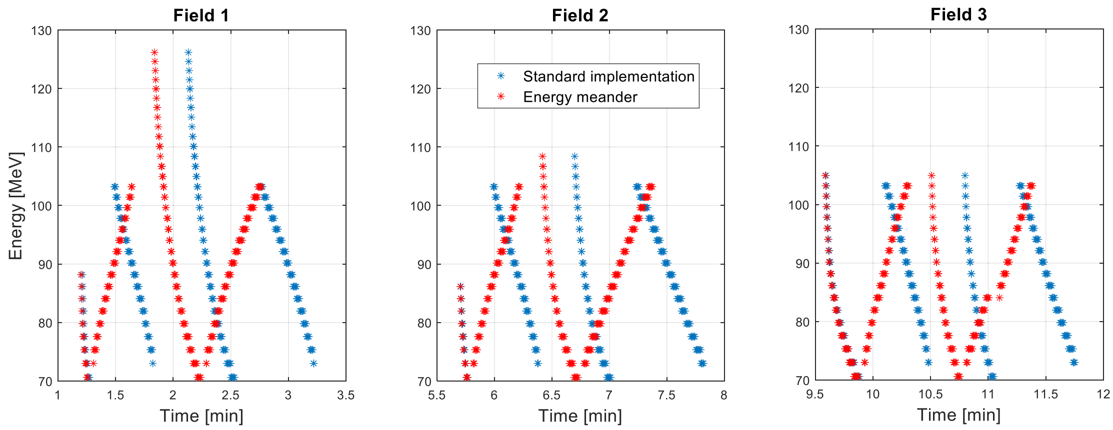

Figure 10. Energy as a function of time for the delivery of a 3-field clinical plan. Blue markers—energies delivered using one-directional energy changes. Red markers—plan delivery using energy meandering (novel technique).

4. Discussion and outlook

In this paper we describe development and commissioning of bi-directional energy meandering, and demonstrate the efficiency of its clinical operation. We commissioned the ascending energy sequence with the main objective of making it transparent to our TPS system, by achieving beam parameters differences that are within machine variability for both ascending and descending energy changes. Dosimetry tests on plans delivered with and without energy meandering showed no effect on the accuracy of the delivered dose. In addition, log-file based dose reconstructions showed dose differences not exceeding 1%–2%, which is comparable to what we obtain for the same plan and type of delivery due to daily beam variations. Since the re-scanning effectiveness depends on the interplay of intra-fractional target motion and beam delivery dynamics (Schätti *et al* 2013), bi-directional energy modulation may differ from one-directional energy application. We did not investigate in detail the impact of the new implementation on motion mitigation, but we believe that using our standard settings for VR and number of volumes the outcome is the same or even better since a patient movement is less probable over a short period of time.

We have also demonstrated that introducing energy meandering, one can avoid additional ramping between scans and significantly improve plan delivery efficiency. However, this strongly depends on therapy system design such as energy switching time and efficiency of dose delivery (van de Water *et al* 2013, Klimpki *et al* 2018, Nesteruk *et al* 2021).

As such, the proposed method is mainly interesting for cyclotron-based therapy systems, where energy switching times range between 80 ms and 1 s if the energy is adjusted upstream. In addition, bi-directional energy operation approach may be especially advantageous for therapy systems with fast energy changes which use VR and/or other modalities which require sequential energy scans, e.g. fields with patching or with mixed pre-absorber positions. Here the time gain through avoiding the additional ramping would strongly depend on the parameters/performance of the system. For instance the IBA Proteus®ONE (Pidikti *et al* 2018) also uses upstream scanning and provides an automated pre-absorber. It also has a restricted scanning range of 20×24 cm^2, which also requires more field patching than for systems with larger scanning ranges. Although the IBA system provides fast lateral scanning, energy switching time is limited to 0.9 s. Implementation of bi-directional energy operation at such a system therefore, assuming the same ramping sequence as at Gantry 2, would lead to a smaller time gain than for our system. For example, for tumours with small extension in depth, one would expect time reductions up to 20%, or more for longer ramping times.

Another option to degrade the cyclotron energy is to install a range shifter down-stream in the nozzle, just before the patient. This is the fastest way to change energy, however comes with the price of an increased spot size and neutron dose to the patient. In addition, down-stream energy switching avoid the problem of hysteresis control described in this paper (Zhao *et al* 2016). However, energy meandering could still be an interesting option to reduce/optimize range shifter travel paths.

The reduction of treatment times demonstrated here, although small, are nevertheless interesting, since they could help to increase patient comfort. The latter is especially important for patients undergoing complex irradiations which may last for more than half of an hour. In addition, during long treatments, the precision of the delivered dose can be affected by intra-fraction motion for patients without anaesthesia. Indeed, there is a trend for the development of compact machines to reduce treatment costs. Typically such systems use smaller scanning fields where, as a consequence, more field patching will be required. At the same time, smaller scanning fields also allow for smaller pre-absorbers, making it easier to automate these and exploit mixed pool delivery. As such, bi-directional energy delivery may become more important in the future.

5. Conclusions

Therapy systems offer currently an impressive speed and flexibility for scanning in the transverse direction. However, in the longitudinal direction, scanning times are still rather slow, even if many advances in energy switching performance were shown in the past years. We believe that the use of a bi-directional energy modulation allows for additional flexibility for PBS proton therapy, and is a step forward towards more optimised and efficient patient treatments.

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Data availability statement

The data cannot be made publicly available upon publication because they contain sensitive personal information. The data that support the findings of this study are available upon reasonable request from the authors.

Author's contributions

OA coordinated the comissioning of bi-directional energy modulation, performed experiments, performed patient statistical analysis and wrote the manuscript. DM performed measurements and data interpretation of of beam parameters for ascending energy changes at early comissioning stage. AM implemented the new energy delivery approach in therapy plan converter. OA and UR analyzed and evaluated beam comissioning data. DM and AB revised the manuscript at all stages. All authors commented on the paper and approved its final form.

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