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FAST BEAM DELIVERY FOR FLASH IRRADIATIONS AT THE HZB CYCLOTRON

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Abstract

In the context of radiotherapy, Flash irradiations mean the delivery of high dose rates of more than 40 Gy/s, in a short time of less than one second. The expectation of the radio-oncologists are lesser side effects while maintaining the tumour control when using Flash. Clinically acceptable deviations of the applied dose to the described dose are less than 3%.

Our accelerator control system is well suited for the standard treatment of ocular melanomas with irradiation times of 30 s to 60 s. However, it is too slow for the short times required in Flash. Thus, a dedicated beam delivery control system has been developed, permitting irradiation times down to 7 ms with a maximal dose variation of less than 3%.

INTRODUCTION

Proton Therapy of Ocular Melanoma

Proton therapy of ocular melanoma is a well-established and successful treatment. At the Helmholtz-Zentrum Berlin (HZB), patients are treated in cooperation with Charité – Universitätsmedizin Berlin since 1998. Overall, more than 4500 patients have been treated. The local tumour control is 96% after five years [1, 2, 3].

Protons permit the confinement of the dose to the tumour. At HZB, we use a proton beam with 68 MeV having a range in water of 38 mm. With this energy, the dose drops at the end of the Bragg peak from 90% to 10% within less than 1 mm. This permits the sparing of organs at risk like the optical nerve or the macula.

For eye tumours the typically prescribed total dose is 60 Gy which is applied in four fractions over four days. The irradiation time is 30 s to 60 s.

FLASH Irradiations

While the tumour control using protons for ocular melanoma is excellent, there is still a wish for further improvement: the reduction of side effects. A very vibrant research field for reducing side effects while maintaining tumour control is the so-called FLASH irradiation [4]: the dose rate is increased drastically, at least 40 Gy/s and the irradiation time is less than 1 s. At the moment, neither the ideal dose rate nor the ideal irradiation time is known. The normal dose rate for ocular melanomas is less than 0.5 Gy/s. The huge increase in dose rate provides challenges for the dosimetry like linearity of the dose monitors and saturation effects. The medical physicists require that variations in dose delivery should be less than 3%. Hence, in order to start experiments with FLASH irradiations a new beam delivery control system had to be developed.

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LAYOUT OF THE ACCELERATORS

Figure 1 shows the layout of HZB's accelerator complex for proton therapy. The k130 cyclotron is served by two injectors: either a 6 MV Van-de-Graaff or a 2 MV Tandetron. Besides the treatment room is the experimental room. The control system for the accelerator is based on Vsystem [5].

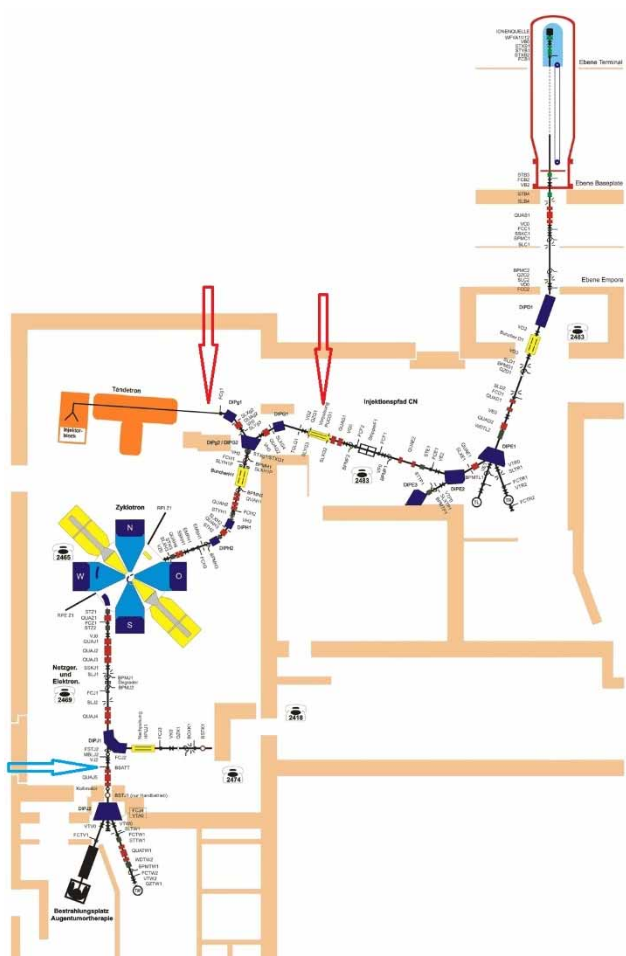

Figure 1: Layout of the proton therapy accelerator complex of HZB. The red arrows mark the position of electrostatic deflectors, the blue arrow the position of the fast beam shutter.

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There are 16 normal Faraday cups (FC) at various positions in the accelerator complex. They serve for intensity measurements as well as beam dumps. Due to their 50 mm stroke, their opening/closing time is 100 ms. For therapy we use a so-called fast beam shutter in front of the treatment room. This opens within 20 ms and closes within 10 ms. These times match well the standard irradiation times of at least 30 s. Furthermore, there are two electrostatic deflectors in front of the cyclotron: They can switch off the beam within 50 ns [6, 7].

EXPERIMENTAL SET-UP

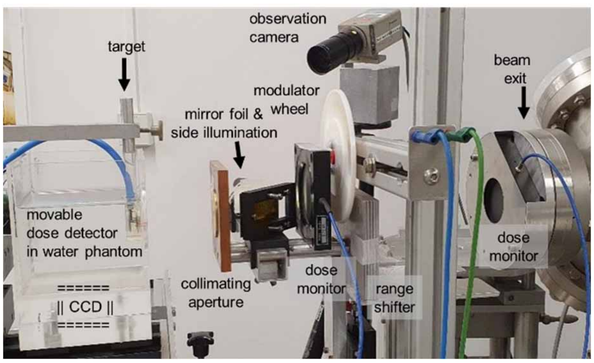

Figure 2: Experimental set-up for the FLASH irradiations, here with water phantom and dosimetry chamber. The proton beam comes from the right.

Figure 2 depicts the set-up in the experimental room [8]. The experiments were performed like in the conventional irradiation with a spread-out Bragg peak (SOBP). The beam with a diameter of about 40 mm exits the vacuum of the beam line via an 80 µm Kapton foil, transverses the first ionisation chamber from PTW Freiburg, and the range shifter. It passes the modulator wheel, which creates the SOBP. Then comes a mirror for visualisation of the beam spot on the samples. A second ionization chamber is used for redundancy. Finally, the x- and y- dimensions of the beam are shaped with an aperture. On the target position either a camera to verify the lateral beam distribution, a water phantom for absolute dosimetry using a Markus chamber with Unidos from PTW Freiburg, or the samples to be irradiated are mounted.

TIMING ISSUES

In an ideal world, the opening or closing of the beam shutters would happen instantaneously and without any delays. In reality, the following times have to be considered:

1. Delay from opening command until the device starts to open.
2. Time of opening.
3. Irradiation time.
4. Delay from closing command until the device starts to close.
5. Closing time

Figure 3 illustrates this with an irradiation time of 500 ms using the fast beam shutter. The overall time for one experiment is one second. For the first 100 ms the Faraday cup just upstream of the fast beam shutter is still in place, then it is opened. To make sure that it really has moved out of the beam path, 200 ms pass before the command of opening the fast shutter is given. It then takes about 40 ms until the device starts to open. The opening

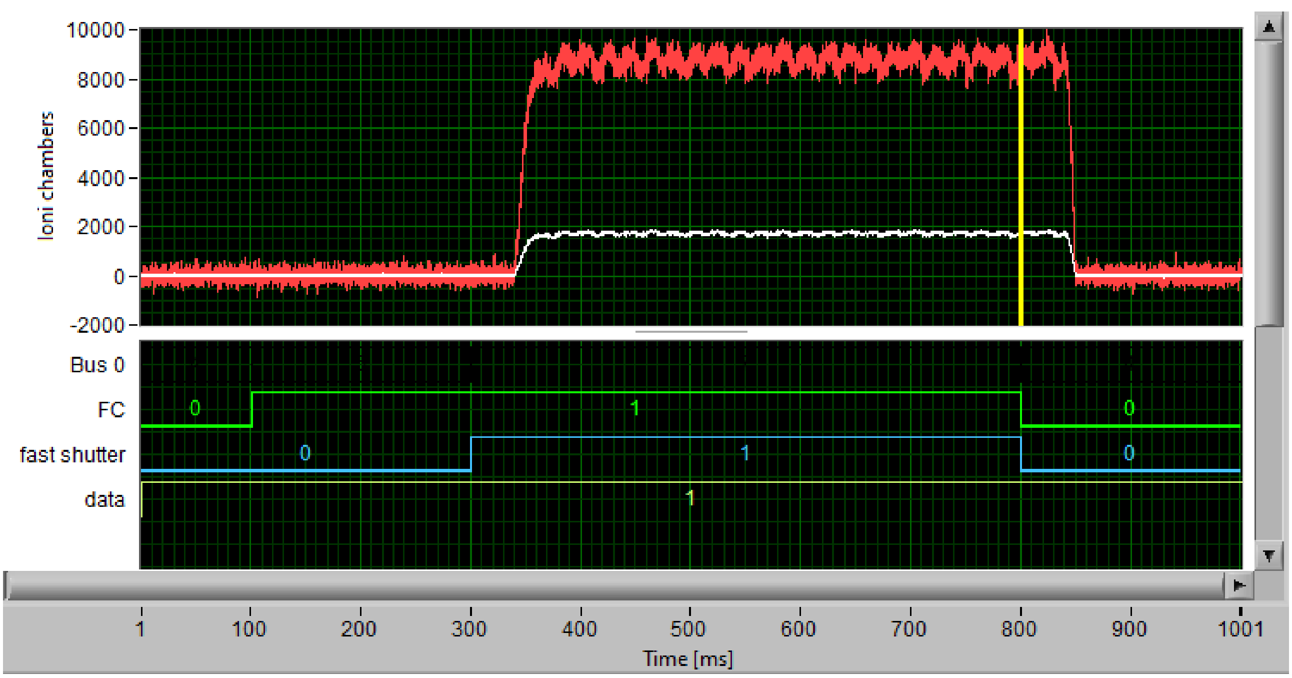

Figure 3: Signals of the experiment over time for an irradiation time of 500 ms using the fast shutter. In the upper part, the signals from the two ionisation chambers (red and white) are displayed in arbitrary units. The lower part shows the switching signals of the Faraday cup (green) and the fust shutter (blue). The vertical yellow line marks the end of the planned irradiation time, in this case 500 ms after the shutter opening command.

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time is about 20 ms, then the full signals in the ionisation chambers are visible. 500 ms after the shutter opening command the signal to close both the Faraday cup and the fast shutter is given. However, it takes again about 40 ms till the devices start closing and 10 ms until the beam is really switched of.

The opening time of 20 ms of the fast beam shutter was the reason to choose 200 ms for the first FLASH experiments [9]. Otherwise, the homogeneity of the lateral dose profile, which has also to fulfil the 3% deviation limit, would be compromised. In a later stage, an electrostatic switch was available on both injector paths, enabling far shorter irradiation times due to shorter switching times and smaller delays.

HARDWARE AND CONTROL LOGIC

The system splits up into an embedded system and a PC which are connected via TCP/IP. The embedded system is a sbRIO 9637 from National Instruments (NI). The ARM Cortex A9 processor runs with NI Linux Real Time with a real time operation system [10]. The real accuracy of the real time clock is 5 ppm. Via a DMA connection the processor has access to the FPGA. The programming platform was LabVIEW. The FPGA samples with 10 kHz, giving a time resolution of 0.1 ms and streams the data every 100 ms to the PC with a two-dimensional array of 1000 x 12 data points. The FPGA processes three analogue

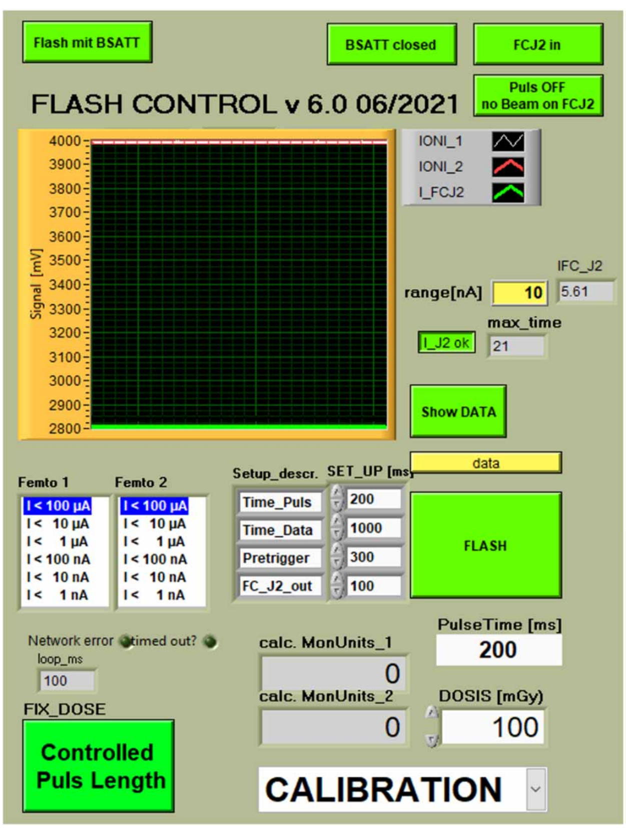

Figure 4: User interface of the FLASH control system for the calibration using the fast shutter just after starting the programme. For more details see text.

signals from the two ionisation chambers and the FC using I/U-converters DLPCA from FEMTO [11]. Thus, the unit of the ionisation chamber signal is mV per 100 µs, considered as counts. The FPGA operates three digital outputs for the signals to open or close the FC, the fast shutter (BSATT), and the electrostatic deflector (pulser).

The PC receives and displays the streamed data. The amplification factors of the I/U converters for the ionisation chambers as well as for the FC are inserted manually. The PC generates the start signal, saves the data into a file, calculates the calibration factors, which correlate the counts of the ionisation chamber to the dose. The PC displays also the user interface (see Fig. 4). In the set-up fields the user defines the following items:

- length of the pulse,
- the data acquisition time,
- the pre-trigger time, which is the time between start of data acquisition and opening command of either fast shutter or electrostatic deflector,
- the time the last FC stays in the beam after beginning of the data acquisition for checks of the beam intensity (FC_J2_out in Fig. 5). This time is also used to determine the background of the ionisation chambers.

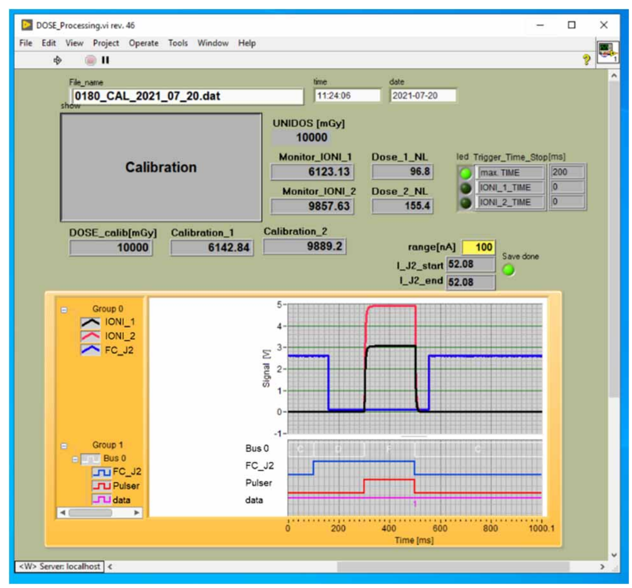

Figure 5: User interface of the FLASH control system displaying the results of the calibration using the electrostatic deflector. A dose of 10 Gy was applied within 200 ms. The calibration factors for the two ionization chambers as well as the excess counts (Dose_1_NL and Dose_2_NL) are displayed. Also, the intensity on the Faraday cup before and after the FLASH pulse is given (I_J2_start and I_J2_end). For more details see text.

The user sees the streamed data of the ionisation chambers and the FC. The PC also displays if the beam intensity is within the limits of the calibration (I_J2_ok). Otherwise, it vetoes the beam (see below). The user chooses which system to use for the FLASH, either the fast shutter or the electrostatic deflector. Finally, the user defines the irradiation mode: calibration, verification or treatment.

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Figure 5 shows the user interface displaying the results after the calibration. For this irradiation, the electrostatic deflector was used. This yields far reaction times (see Fig. 5).

WORKFLOW

The following workflow looks tedious; however, it only takes a few minutes, each irradiation taking only one second.

Calibration

Before starting the calibration mode, the beam intensity is set to the anticipated dose rate. The water bath with the absolute dosimetry is mounted on target position. The user defines a desired, fixed time window between 10 ms and 500 ms. A FLASH is applied, and the measured absolute dose is entered into the user interface. From these data, the system correlates the counts from the ionisation chambers to the dose. Also, the counts of the ionisation chambers after the switch-off signal are determined, the so-called excess counts.

Verification

The verification mode is only accessible after a successful calibration. Instead of a fixed time the user now chooses an application dose with the absolute dosimetry still in place. For safety reasons, this dose has to be slightly smaller than the dose measured during the calibration mode. From the calibration process the system gives the switch-off signal when the counts in the ionisation chamber is equal to the counts corresponding to the desired dose minus the excess counts. Again, the measured absolute dose is entered manually. This step is repeated several times for statistical reasons. If the user is satisfied, he goes to the next step. Otherwise, the calibration procedure has to be repeated.

Treatment Mode

After a successful calibration and verification, the user now enters the treatment mode. The water bath is replaced by the sample to be irradiated. Again, the applied dose must be smaller than the dose measured during the calibration mode. The irradiation is performed if the beam intensity is stable and within the allowed limits (see below).

Safety Measures

The philosophy is that any possible errors lead only to minor changes in the applied dose. If any errors occur, they should preferentially result in a lower dose than intended: whichever ionisation chamber reaches the switch-off level first, this one triggers the stop of the irradiation. Thus, a failure of one chamber dose not result in an excess of dose. In the unlikely event that both ionisation chambers fail simultaneously, the beam is switched off after the time used during the calibration. This is the reason why the dose to be applied should be slightly smaller than the dose measured during the calibration mode with a fixed irradiation time.

To counteract any influences due to beam intensity fluctuations the beam intensity on the Faraday cup in front of the treatment room is monitored for the first 100 ms of each irradiation (see Fig. 5, upper plot, blue line). If it differs more than 5% from the intensity during the calibration mode, the FLASH is vetoed both in verification and in treatment mode.

RESULTS

Table 1 gives the results for various FLASH irradiation times and doses for longer pulses. After the calibration, in the verification mode 20 times a FLASH with the planned dose was applied, and the measured dose and time compared with the planned values. For the times between 20 ms and 200 ms the variation in the applied dose was less than 1.5%. Thus, the requirements of the medical physicists are fulfilled.

Table 1: Comparison of Delivered Dose Versus Planned Dose and Resulting Irradiation Time

Calibration		**Verification**			
t [ms]	**D [Gy]**	**D [Gy] plan**	**D [Gy] real**	**t [ms]**	**ΔD**
200	116.8	105	104.8	182.7	0.19%
150	88.0	79	79.2	138.0	0.25%
100	60.8	55	54.6	94.3	0.73%
50	28.0	25	24.8	43.9	0.80%
40	23.2	21	20.8	37.3	0.95%
30	16.8	15	15.2	26.7	1.33%
20	11.8	11	11.1	19.	0.91%

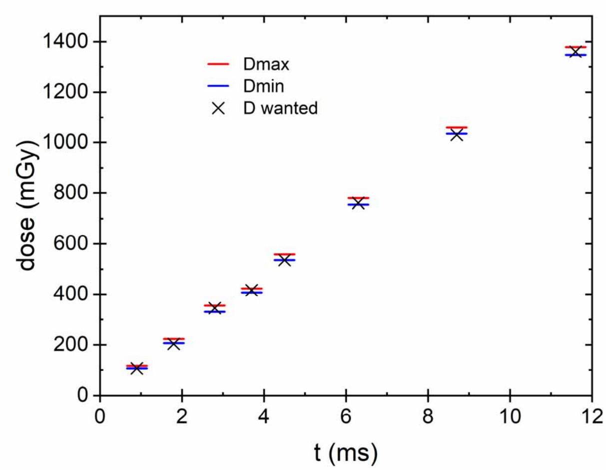

Figure 6: Results for irradiation times below 15 ms showing planned dose (black crosshairs), minimum delivered dose (blue line) and maximum delivered dose (red line) within these 20 shots.

The situation becomes more complicated with shorter irradiation times (see Fig. 6). The average applied dose is well within the required limits. Down to 6 ms irradiation time single shots deviate up to 3%, which is still acceptable. However, the shorter the irradiation times, the larger the errors. At 1 ms and 2 ms the error goes up to nearly 10%.

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This is acceptable for physical experiments, but not for studies on the effect of such irradiations.

The reason for these apparent large errors is the sampling rate: For a shot of 1 ms with 10 kHz sampling, only 10 data points are taken within the FLASH pulse itself which includes the rising flank as well as the falling flank. This is by far not enough.

CONCLUSION

A reliable fast beam delivery system for FLASH irradiations has been installed, implemented, and tested. The system is not certified as a medical device. However, for the implemented security it follows the same philosophy as for medical devices. It has been used for experiments for radiation therapy on cells, organoids, and mice. For times above 6 ms, the reproducibility of the dose application from one irradiation to the next is well within the limits as required by the medical physicists and radiation oncologists.

Irradiations with shorter times are feasible, if the user accepts larger errors: about 5% down to 3 ms, and 10% for smaller times. This can be overcome by increasing the sampling rate and is planned for the near future.

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