

ACCEPTED MANUSCRIPT • OPEN ACCESS

Study of the over-response of radiochromic films in ultra-high dose rate and dose per pulse electron beams

To cite this article before publication: Felix Horst *et al* 2026 *Phys. Med. Biol.* in press <https://doi.org/10.1088/1361-6560/ae47b6>

Manuscript version: Accepted Manuscript

Accepted Manuscript is “the version of the article accepted for publication including all changes made as a result of the peer review process, and which may also include the addition to the article by IOP Publishing of a header, an article ID, a cover sheet and/or an ‘Accepted Manuscript’ watermark, but excluding any other editing, typesetting or other changes made by IOP Publishing and/or its licensors”

This Accepted Manuscript is © 2026 The Author(s). Published on behalf of Institute of Physics and Engineering in Medicine by IOP Publishing Ltd.



As the Version of Record of this article is going to be / has been published on a gold open access basis under a CC BY 4.0 licence, this Accepted Manuscript is available for reuse under a CC BY 4.0 licence immediately.

Everyone is permitted to use all or part of the original content in this article, provided that they adhere to all the terms of the licence <https://creativecommons.org/licenses/by/4.0>

Although reasonable endeavours have been taken to obtain all necessary permissions from third parties to include their copyrighted content within this article, their full citation and copyright line may not be present in this Accepted Manuscript version. Before using any content from this article, please refer to the Version of Record on IOPscience once published for full citation and copyright details, as permissions may be required. All third party content is fully copyright protected and is not published on a gold open access basis under a CC BY licence, unless that is specifically stated in the figure caption in the Version of Record.

View the [article online](#) for updates and enhancements.

1
2
3
4
5
6
7
8
9
10 **Study of the over-response of radiochromic films in**
11 **ultra-high dose rate and dose per pulse electron**
12 **beams**
13
14
15
16
17
18
19

20 **Felix Horst**

21
22 OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine
23 and University Hospital Carl Gustav Carus, TUD Dresden University of Technology,
24 Helmholtz-Zentrum Dresden-Rossendorf, Dresden, Germany
25
26

27
28 Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiooncology - OncoRay,
29 Dresden, Germany
30

31
32 E-mail: felix.horst@oncoray.de (corresponding author)
33
34
35

36 **Andreas Schüller**

37
38 Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, Germany
39
40

41
42 **Ralf-Peter Kapsch**

43
44 Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, Germany
45
46

47 **Thomas Hackel**

48
49 Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, Germany
50
51
52

53 **Johanna Pehlivan**

54
55 Karlsruhe Institute of Technology (KIT), Institute for Neutron Physics and Reactor
56 Technology, Eggenstein-Leopoldshafen, Germany
57
58
59
60

1
2
3 *Dose rate dependence of radiochromic films*
4

5 **Cathyanne Schott**

6 Université Paris-Saclay, Gustave Roussy, Inserm, Molecular Radiotherapy and
7 Therapeutic Innovation, 94800, Villejuif, France
8
9

10
11
12 **Elke Beyreuther**

13
14 OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine
15 and University Hospital Carl Gustav Carus, TUD Dresden University of Technology,
16 Helmholtz-Zentrum Dresden-Rossendorf, Dresden, Germany
17

18
19 Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiation Physics, Dresden,
20 Germany
21
22

23
24
25 **Jörg Pawelke**

26
27 OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine
28 and University Hospital Carl Gustav Carus, TUD Dresden University of Technology,
29 Helmholtz-Zentrum Dresden-Rossendorf, Dresden, Germany
30

31
32 Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiooncology - OncoRay,
33 Dresden, Germany
34
35

36
37
38 January 29, 2026
39
40

41 **Abstract.**

42
43 Objective: Many pre-clinical experiments on FLASH radiotherapy, in which
44 biological samples are irradiated at conventional and ultra-high dose rate (UHDR),
45 make use of radiochromic films as an absolute dose reference because their response
46 is typically assumed to be dose rate independent. While several previous experiments
47 confirmed this assumption, a recent study with protons found an over-response for
48 Gafchromic EBT3 films at UHDR [doi:10.1002/mp.15526]. If EBT3 is used as a
49 reference in FLASH experiments, the over-response could result in an underdosing
50 that falsely appears as sparing of normal tissue.
51
52

53
54 Approach: To investigate whether the reported dose rate dependence of EBT3 can be
55 reproduced with UHDR electron radiation as well, about 600 EBT3 samples were
56
57
58
59
60

Dose rate dependence of radiochromic films

irradiated at the metrological linear accelerator facility at Physikalisch Technische Bundesanstalt, Braunschweig, and at the ELBE research accelerator at Helmholtz-Zentrum Dresden-Rossendorf, with different beam parameters. As dosimetric reference served a PTW flashDiamond detector which has been verified to show no deviation in the studied UHDR range as well as PTB's alanine dosimetry system. In addition, several OC-1 films, which have been shown to be dose rate independent in previous studies, were irradiated together with EBT3 films.

Main results: EBT3 shows a significant over-response at ultra-high dose per pulse and intra-pulse dose rates. Up to 3 Gy per pulse no significant deviations were observed. However, for larger doses per pulse an over-response was observed that increases with dose per pulse to up to 50%. For OC-1 films no significant effects were found.

Significance: We provide evidence for the over-response of EBT3 films in UHDR electron beams. Therefore, EBT3 films should be used with caution in FLASH experiments.

1. Introduction

The discovery of the FLASH effect, the sparing of normal tissue at the same tumor treatment efficiency when applying a ultra-high dose rate (UHDR) as compared to low conventional dose rates (Favaudon et al. 2014), has stimulated radiobiology and radiochemistry research at many centers worldwide. The UHDR required to observe the FLASH effect in vivo has also turned out to be a challenge for accurate dosimetry (Schüller et al. 2020, Romano et al. 2022). In FLASH experiments, the dosimetry needs to be accurate for the ultra-high (typically > 40 Gy/s) and the low (conventional) dose rate used as reference (typically in the order of a few Gy/min). The single fraction dose required to observe the FLASH effect is typically above 7 Gy (Böhlen et al. 2022).

This high single fraction dose can either be applied with a few intense pulses with doses of a few Gy, as typically delivered by electron linacs, or with a single continuous

Dose rate dependence of radiochromic films

beam pulse as e.g. delivered by isochronous cyclotrons. Ionization chambers, the gold standard for dosimetry in radiotherapy and radiobiology, show considerable deviations as a result of charge losses due to ion recombination at ultra-high dose per pulse, and are therefore only suitable to a limited extent for dosimetry for irradiations with strongly pulsed beams such as those delivered by UHDR electron linear accelerators. Many pre-clinical and radiobiological experiments on the topic of FLASH radiotherapy make use of radiochromic films, most commonly EBT3 (Gafchromic, Ashland Advanced Materials, Bridgewater, USA), as dosimetric reference (Giannini et al. 2024, DeFrancisco & Kim 2025). DeFrancisco & Kim (2025) even concluded that Gafchromic films are the most frequently used detector in electron FLASH studies. They are typically based on a radiation sensitive monomer that is incorporated into a water-soluble polymer matrix coated onto a polyester base and when irradiated they show a dose-dependent color change due to radiation-induced polymerization. Besides the relative 2D information provided by radiochromic films they can also be calibrated in terms of absolute dose (Devic 2011, Liu et al. 2023). Their response is typically believed to be dose rate independent in the range relevant for FLASH radiotherapy (Romano et al. 2022) and therefore they have been applied in many FLASH experiments to adjust or to verify the absolute dose output at UHDR (Konradsson et al. 2020, 2021, Xie et al. 2022, Garty et al. 2022, Lempart et al. 2019). While several previous experiments supported this assumption (Jaccard et al. 2017, Favaudon et al. 2019, Jorge et al. 2019, Togno et al. 2022), a recent study with protons by Villoing et al. (2022) found a significant response enhancement for EBT3 and EBT-XD films at UHDR, i.e. at doses per pulse above 10 Gy at an intra-pulse dose rate of 7.5 kGy/s. Very recently, also Del Sarto et al. (2025), Cayley et al. (2025) and Yasuda et al. (2026) found indications for an over-response of EBT-XD films in experiments with UHDR electrons and protons as

Dose rate dependence of radiochromic films 5

well. Such a dose rate dependence would make the suitability of this type of films as reference in radiobiological FLASH experiments highly questionable if not corrected for. The over-response of the radiochromic films at UHDR as found by Villoing et al. (2022) would result in an underdosing that could falsely appear as sparing of normal tissue. That could make the FLASH effect seem stronger than it actually is or could even give the impression of a FLASH effect when in reality there is no difference in the biological response at UHDR at all. Notably, the magnitude of the over-response of EBT3 films at UHDR reported by Villoing et al. (2022) at an UHDR of 7.5 kGy/s is in the order of the FLASH effect itself ($\sim 20\%$) (Böhlen et al. 2022). For the up to now rarely utilized OC-1 films (OrthoChromic, Hillsborough, NJ, USA) (Lim & Tang 2022) no dose rate dependence was found by Villoing et al. (2022). The radiation-induced polymerization reaction in EBT3 films creates macromolecules with a pre-determined orientation. Therefore, these films show different light absorption characteristics depending on their orientation to the film scanner (Schoenfeld et al. 2014). In addition to the above mentioned response enhancement, Yasuda et al. (2025) also found changes in the orientation effects of EBT3 films irradiated with UHDR proton beams as compared to irradiations at low dose rate.

To investigate whether the over-response of EBT3 can also be reproduced with electron beams and which beam parameters it depends on, extensive experiments were conducted at two different electron linear accelerator facilities. Approximately 600 EBT3 film samples were irradiated over a wide range of dose rates and doses per pulse. Three different independent reference detectors were applied: A flashDiamond (fD), alanine pellets as well as OC-1 films.

2. Material and Methods

Four different measurement campaigns were conducted at two different electron accelerator facilities with different UHDR ranges and beam structures. Specific emphasis was put on the use of suitable and independent reference detectors to compare the radiochromic film response to:

- (i) EBT3 vs. flashDiamond (total doses in the range of 3 – 100 Gy, at five different doses per pulse in the range between 0.1 – 18.5 Gy, at a pulse duration of 2 μ s)
- (ii) EBT3 vs. flashDiamond and alanine (total doses around 15 – 20 Gy where the uncertainties of the used alanine system are minimal, at doses per pulse in the range 0.3 – 20 Gy, at a pulse duration of 1 μ s or 2 μ s)
- (iii) EBT3 vs. flashDiamond and OC-1 (total doses around 30 Gy, at doses per pulse in the range between 0.3 – 33 Gy, at a pulse duration of 2 μ s)
- (iv) EBT3 vs. flashDiamond and OC-1 (irradiation with single pulses at different intra-pulse dose rates between 0.16 Gy/s – 90 kGy/s, variation of the pulse durations leading to doses per pulse in the range between 5 – 100 Gy)

Campaigns (i)-(iii) were conducted at the metrological linear accelerator facility at the Physikalisch-Technische Bundesanstalt (PTB) in Braunschweig, Germany, and (iv) at the Electron Linear accelerator with high Brilliance and low Emittance (ELBE) at Helmholtz-Zentrum Dresden-Rossendorf (HZDR), Dresden, Germany. In the following, more details on the different measurement campaigns are given.

2.1. Irradiation experiments at the metrological electron linac at PTB

Experiments were conducted at the metrological electron linear accelerator facility at PTB. A medical linear accelerator (Elekta Synergy) and a research electron accelerator

Dose rate dependence of radiochromic films

at PTB were used. Both accelerators deliver a pulsed electron beam with a pulse duration of a few microseconds, consisting of a train of electron bunches with a repetition rate of 3 GHz. This is a similar pulse structure as that found in linacs used in clinics for research on FLASH radiotherapy with electrons (e.g. Mobetron, FLASHknife, SIT ElectronFlash (Marinelli et al. 2022), converted medical linacs). EBT3 and OC-1 film samples (size: $40 \times 35 \text{ mm}^2$) were irradiated with electron pulses (20 MeV, $2 \mu\text{s}$ macro pulse duration) over a wide range of total doses (3.5 – 100 Gy) with different intra-pulse dose rates (55 kGy/s - 16.5 MGy/s). The films were irradiated in a water phantom at the depth of maximum dose (30.8 mm). Up to three films were stacked on top of each other and irradiated at the same time in order to increase the measurement statistics. For the majority of the irradiations, the pulse duration was kept constant at $2 \mu\text{s}$ and the dose per pulse was varied via the intra-pulse dose rate, either by varying the charge per pulse provided by the electron gun, or by adding aluminum scattering discs (thickness 6, 2 or 1 mm) at the vacuum exit window of the beamline, or by changing the source to surface distance (SSD) between 90, 70, or 50 cm. In measurement campaign (ii) the dose per pulse was varied by lowering the pulse duration while keeping the intra-pulse dose rate constant in order to disentangle the influence of intra-pulse dose rate and dose per pulse. The films were irradiated with a different number of pulses at a pulse repetition frequency of 5 Hz. At this frequency the individual pulses can be considered as independent for detectors based on radiochemical principles such as radiochromic films. For example, at a dose per pulse of 0.06 Gy, 500 pulses were required to irradiate the film with a total dose of 30 Gy, whereas at 30 Gy per pulse, only a single pulse was delivered. As dosimetric reference served a flashDiamond detector (model 60025, serial number 7610, PTW dosimetry, Freiburg, Germany) that had previously been extensively characterized in this UHDR electron beam, demonstrating a linear response compared

Dose rate dependence of radiochromic films

with alanine (see Figure 2). In measurement campaign (ii), alanine was directly irradiated together with EBT3 films as an another dose rate independent reference (Soliman et al. 2020, Bourguin et al. 2022) in addition to the flashDiamond. The alanine dosimetry system has been shown to be consistent with the PTB water calorimeter primary standard also under ultra-high dose per pulse conditions (Bourguin et al. 2023).

For all measurement campaigns at PTB ((i) - (iii)), an integrating current transformer (Bergoz Instrumentation, Saint Genis Pully, France, ICT in-flange version, turns ratio 50:1) was used to monitor precisely ($\pm 0.1\%$) the charge of the electron pulses (30 – 300 nC) (Schüller et al. 2017). For each setup with respect to SSD, scattering disc and pulse duration, the beam pulse charge was varied and recorded as function of the simultaneously determined dose per pulse, measured by means of the calibrated flashDiamond at the same water depths as chosen for the positioning of the EBT3 films. Calibration functions were then fitted to the data sets, which allowed to convert the measured ICT signal to the actual dose per pulse during the irradiation of the films with low uncertainty ($< 1\%$).

Figure 1a shows a schematic of the experimental setup at PTB. The electron beam passes through the ICT before exiting the vacuum through a titanium window and being scattered by Aluminum plates. The water phantom is positioned at a variable distance from the scatterer to set different doses per pulse. The radiochromic films and the alanine holder are positioned at ~ 3 cm water equivalent depth.

2.2. Irradiation experiments at ELBE research electron linac

In measurement campaign (iv) experiments with a different dose per pulse and dose rate range (5 – 95 Gy per pulse at 1 000 Gy/s, 10 000 Gy/s and 90 000 Gy/s) were performed at the ELBE electron accelerator (Gabriel et al. 2000) using 30 MeV elec-

Dose rate dependence of radiochromic films

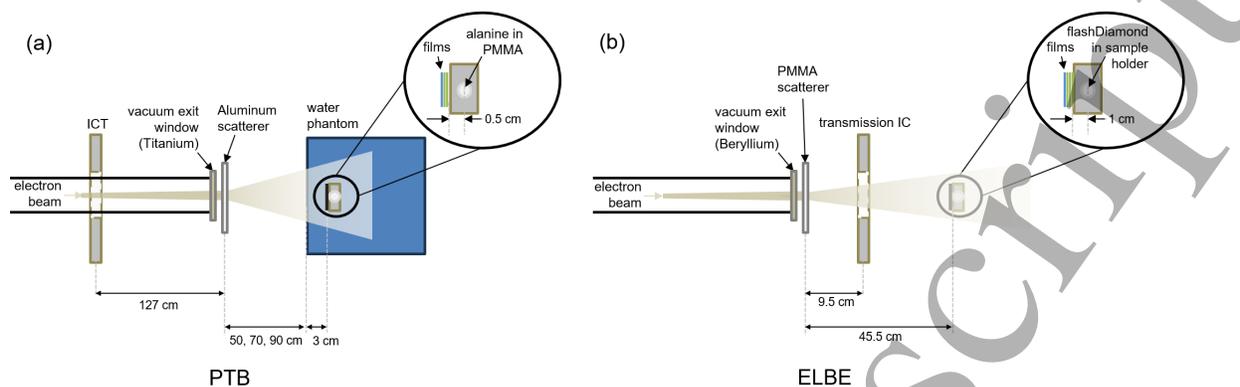


Figure 1: Experimental setup at the research electron linac at PTB (a) and at the ELBE accelerator (b). In the PTB setup, the films and alanine can be replaced by a flashDiamond measuring at the same water depth like the films. The dimensions are not true to scale.

trons, where several radiobiological FLASH experiments have been performed in the past (Pawelke et al. 2021, Karsch et al. 2022, Horst et al. 2023, 2024). All irradiations at ELBE were performed with single pulses, where each pulse was a bunch train consisting of ~ 5 ps electron bunches separated by 77 ns pauses (bunch repetition rate: 13 MHz). The dose rate was adjusted by varying the bunch charge and the dose per pulse was set by varying the number of bunches and thus the pulse duration (length of the bunch train). The lowest dose rate used was in the order of $10 \text{ Gy/min} \approx 0.16 \text{ Gy/s}$. The films were irradiated in air as stacks of EBT3 and OC-1 films (size: $48 \times 50 \text{ mm}^2$). Reference measurements were performed beforehand for every dose per pulse and dose rate setting with a flashDiamond (serial number 220517) right behind the film position positioned at the maximum of the beam spot (Gaussian profile with a $\pm 5\%$ homogeneity over a diameter of 6.5 mm). The readings of the flashDiamond were used to calibrate a transmission ionization chamber (model 7862, PTW Dosimetry, Freiburg, Germany) used as beam monitor for each dose rate and dose per pulse setting.

Figure 1b shows a schematic of the experimental setup at ELBE. The electron beam exits the vacuum through a Beryllium window and is scattered by a thin PMMA plate

Dose rate dependence of radiochromic films

10

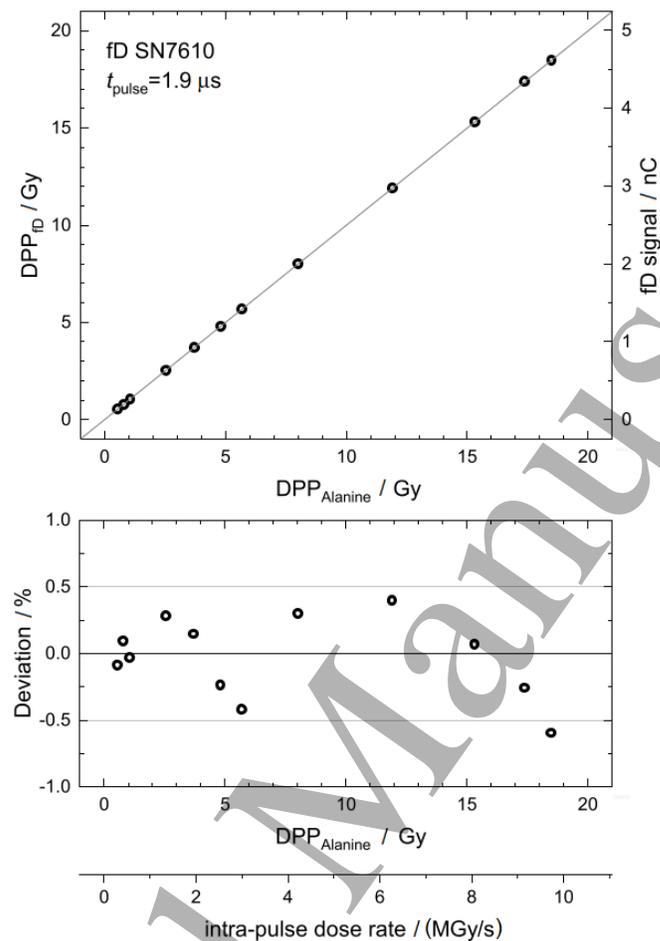


Figure 2: flashDiamond (SN7601) dose reading compared to alanine reference as a function of dose per pulse (DPP) and intra-pulse dose rate obtained in experiments at the PTB metrological electron linear accelerator.

before passing through a transmission ionization chamber. The sample holder which can hold the flashDiamond with the films stuck on top is positioned some centimeters downstream.

Notably, the electron accelerators at PTB and the ELBE research accelerator have very different time structures as shown in Figure 3. The electron beam at PTB is strongly pulsed with 1 – 2 μs macro pulse duration with 3 GHz accelerating radiofrequency and therefore comparable to FLASH electron linacs that are available

Dose rate dependence of radiochromic films

11

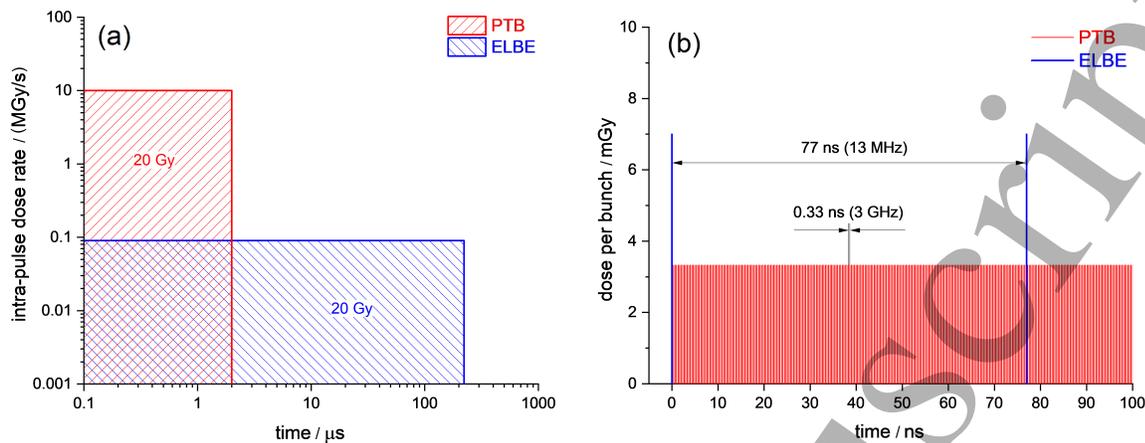


Figure 3: Panel (a): Intra-pulse dose rate and pulse duration at irradiation with 20 Gy per pulse at the research electron linac at PTB compared to the 90 kGy/s dose rate setting of the ELBE accelerator. Panel (b): Bunch time structure of the two electron beams.

for potential clinical applications. The ELBE electron beam, on the other hand, can provide much longer macro pulses (up to seconds or even minutes) which are trains of 5 ps bunches divided by pauses of 77 ns duration (corresponding to 13 MHz bunch repetition frequency).

It was verified beforehand that the flashDiamond detector provides reliable dose readings in the ELBE beam since it has not been tested under similar conditions before. Figure 4 shows the dose reading of the flashDiamond as a function of the number of electron bunches at maximum bunch charge for a measurement series where the length of the bunch train, i.e. the pulse length, was gradually increased while keeping the intra-pulse dose rate constant at 90 kGy/s. The flashDiamond response increases linear with the number of bunches in the pulse as expected and no saturation behavior is observed even at the highest dose per pulse of almost 100 Gy. Therefore, the flashDiamond was found suitable for dosimetry in the electron beam of the ELBE accelerator and could be applied as reference for the radiochromic film studies.

Dose rate dependence of radiochromic films

12

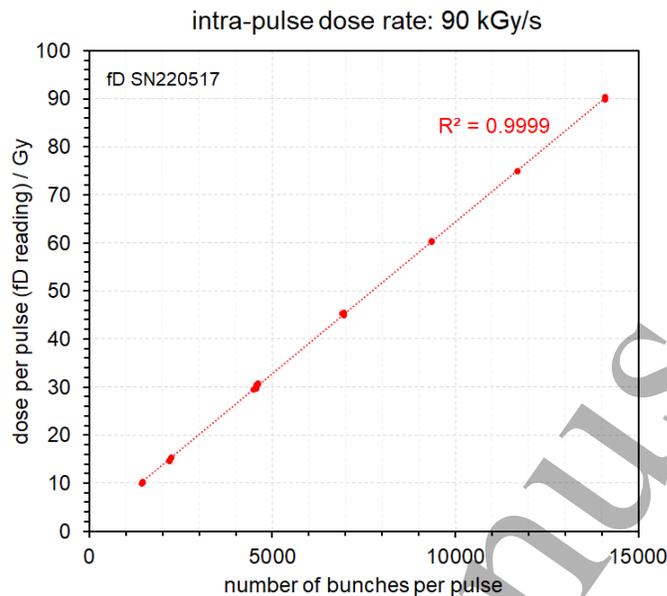


Figure 4: flashDiamond (SN220517) dose reading as a function of the number of electron bunches per pulse obtained in experiments at the ELBE accelerator with its highest dose rate setting.

2.3. Radiochromic films

For the experiments at PTB (measurement campaigns (i)-(iii)), the films were immersed in water while at ELBE (measurement campaign (iv)) they were irradiated free in air. In order to increase the measurements statistics, the films were arranged as stacks consisting of three EBT3 films or one OC-1 film in the front and two EBT3 films behind (at PTB) or one OC-1 film in the front and three EBT3 films behind (at ELBE). The films were all from the same production batch (EBT3 films: LOT 11192002, OC-1 films: LOT # 2-2020507-2). EBT3 films were scanned 48-72 hours after irradiation. OC-1 films were scanned 10 days after irradiation because of their considerably slower darkening as compared to EBT3 films (Villoing et al. 2022, Lim & Tang 2022). An Expression 11000 XL scanner (Epson, Suwa, Japan) was used for scanning all films. The films were oriented in landscape orientation for all scans. From the red-green-blue images, both the red and green channel were analyzed for EBT3 films and only the green channel for OC-1.

1
2 *Dose rate dependence of radiochromic films* 13
3

4 For evaluation of the doses the *netOD*, defined as $netOD = -\log_{10}(OD_D/OD_{0Gy})$ with
5 OD_D being the optical density of the irradiated film and OD_{0Gy} being the optical density
6 of an unirradiated film of the same sheet, was analyzed. EBT3 films were calibrated at
7 the Elekta Synergy linac at PTB operated in 18 MeV electron mode at conventional dose
8 rate (~ 5 Gy/min) by relating the netOD to the absorbed dose to water determined with
9 a reference ionization chamber (Roos Electron Chamber, model 34001, PTW Dosimetry,
10 Freiburg, Germany). This ionization chamber is directly traceable to the German
11 primary standard of absorbed dose to water. OC-1 films were always irradiated together
12 with EBT3 films. Therefore, the OC-1 films were cross-calibrated using the EBT3 data
13 obtained at low dose rate at the PTB research linac (measurement campaigns (i)-(iii))
14 or the ELBE accelerator (measurement campaign (iv)), respectively.
15

16 Some EBT3 films were also scanned with an ArtixScan 2500f (Mikrotek, Hsinchu,
17 Taiwan) scanner at PTB and some OC-1 films also with a Perfection V850 Pro
18 (Epson, Suwa, Japan) scanner at Institute Gustave Roussy. This was done because
19 different scanners have different calibration functions when used for film dosimetry
20 and by using multiple scanner models possible influences of the scanner used can be
21 excluded. Furthermore, at Institute Gustave Roussy the OC-1 film type was already in
22 use previously and therefore the analysis could be done with an established dosimetry
23 system.
24

25 The radiation fields applied have Gaussian lateral profiles (2.8 cm FWHM at ELBE and
26 28.8 – 4.17 cm FWHM, depending on the setup, at PTB). The dose maximum of the 2D
27 dose distributions on the films was analyzed and consequently the reference detectors
28 were positioned at the dose maximum as well.
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

3. Results

3.1. Experiments at PTB

Figure 5 shows the EBT3 calibration functions obtained for the red and green color channels obtained from calibration with conventional dose rates (0.2 mGy per pulse) at the Elekta Synergy linac at PTB for two different scanners (Epson 11000 XL and Microtek ArtixScan 2500f). Using the Epson 11000 XL scanner, the red channel can only be used to evaluate doses up to ~ 20 Gy. At the increased optical density at higher doses, the Epson 11000 XL can hardly distinguish between the different degrees of darkening and the netOD value is almost independent on the dose and saturates at a value of 1.2. However, the Microtek ArtixScan 2500f is still sensitive at higher optical densities (netOD values > 1.2). The slope of the calibration function and thus the sensitivity to dose differences decreases with increasing dose, yet this scanner still allows evaluation of the red channel for dosimetry up to 100 Gy, which is far beyond the dose range specified by the vendor (0.01 Gy – 10 Gy). This aligns with recent updated recommendations on the use of EBT3 films by Liu et al. (2023) who found it suitable up to 50 Gy. By analyzing the green channel of EBT3 films scanned with the EPSON 11000 XL scanner, they can be applied for dosimetry up to 100 Gy also using this scanner, as seen in Figure 5a. In addition to the calibration curves obtained by reference irradiations at the Elekta Synergy medical linac, also values obtained by the results from EBT3 irradiation at the PTB research electron linac operating at 0.1 Gy per 2 μ s pulse and at UHDR of 18.5 Gy per 2 μ s pulse are shown in Figure 5. The netOD values obtained at 0.1 Gy per pulse agree well with those obtained from irradiation with conventional dose rates at the Elekta linac used for determining the calibration function. However, it can be noticed that the data points representing the results from EBT3 irradiation with 18.5 Gy per pulse lie all above the calibration function, and therefore it is evident

Dose rate dependence of radiochromic films

15

that the EBT3 films show an over-response.

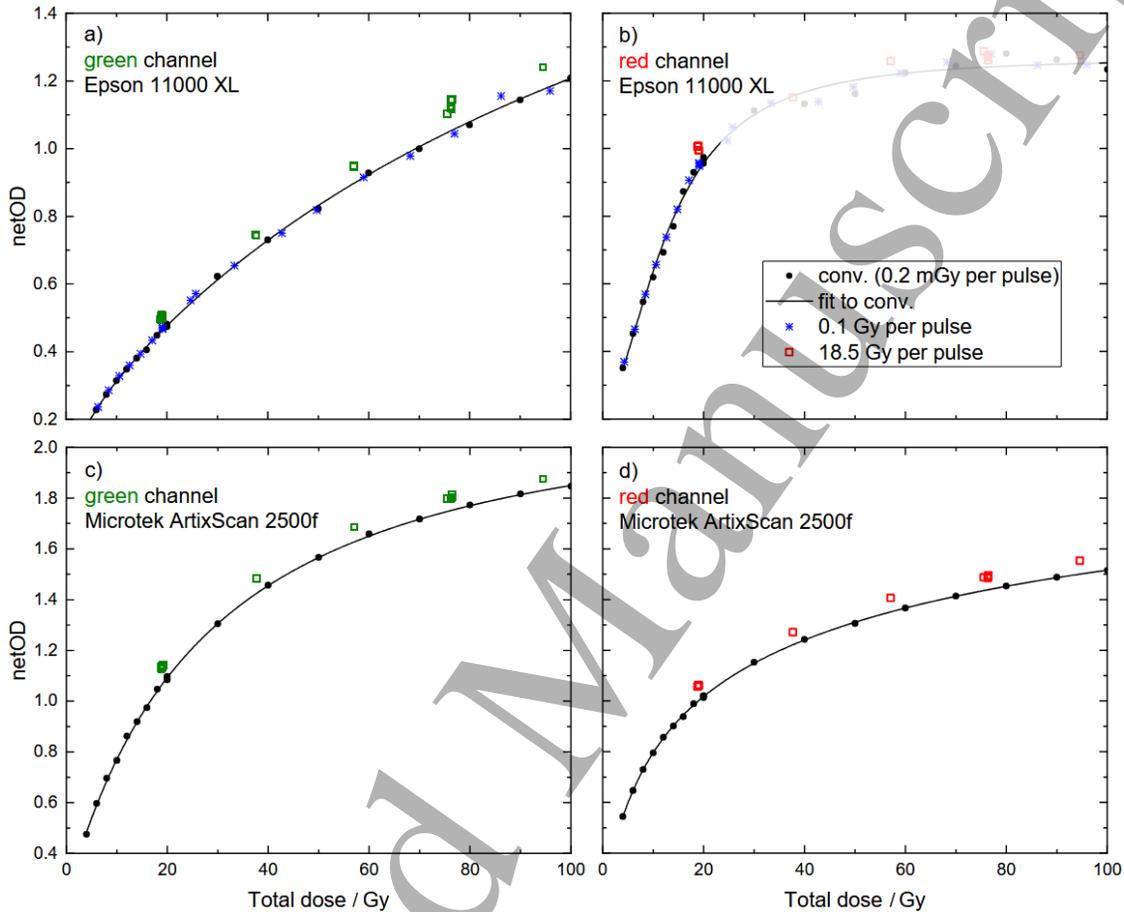


Figure 5: EBT3 calibration for the netOD of the green ((a) and (c)) and red ((b) and (d)) color channel as a function of dose for the reference irradiation at a standard Elekta Synergy linac (conv., black dots represent the measurements and solid lines the calibration functions) as well as for 0.1 Gy per pulse (blue asterisks) and for 18.5 Gy/pulse (squares) at the PTB research electron linac (measurement campaign (i)). The films were scanned using an Epson 11000 XL ((a) and (b)) and a Microtek ArtixScan 2500f scanner ((c) and (d)). For each data point three films that were irradiated together were averaged. In panel (b), the dose range above 20 Gy is greyed out because for the Epson 11000 XL scanner, the red channel can not be used for reliable dosimetry.

The EBT3 dose readings relative to the flashDiamond used as reference for the irradiations at the PTB research linac are shown for the red channel in Figure 6a (only total doses up to 20 Gy for the Epson 11000 XL) and for the green channel in Figure 6b.

Dose rate dependence of radiochromic films

16

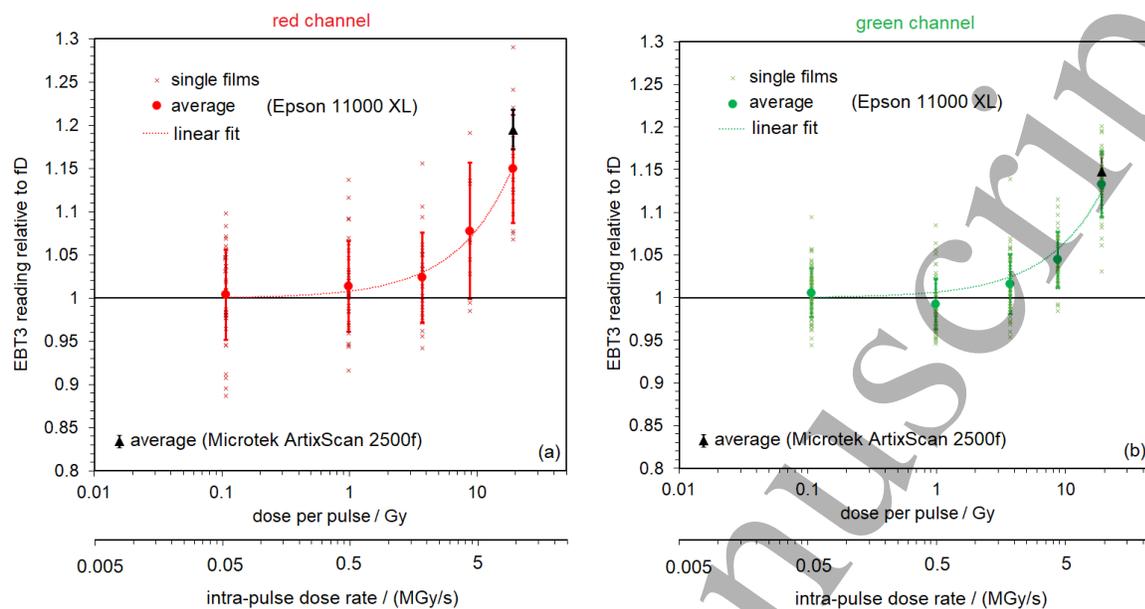


Figure 6: EBT3 dose reading (red channel) (a) and EBT3 dose reading (green channel) (b) relative to the flashDiamond (fD) reference as a function of dose per pulse (measurement campaign (i)). The second x-axis label shows the intra-pulse dose rate in the $2 \mu\text{s}$ pulses from the electron linac. The films irradiated with the highest dose per pulse (18.5 Gy/pulse) were analyzed with two different scanners (Epson 11000 XL, red dots, and Microtek ArtixScan 2500f, black triangles).

For the lowest dose per pulse studied (0.1 Gy/pulse), the average relative response lies at 1 which means that the films behave exactly like during the calibration at the Elekta Synergy linac operated with conventional dose rate. Towards higher doses per pulse the average relative response deviates from 1 and increases up to ~ 1.15 at 18.5 Gy per pulse, indicating a 15% over-response. For the green channel, a significant difference from 1 can be observed for doses per pulse above 8.3 Gy per pulse. The over-response effect seems to be equally pronounced in both color channels. The values at 18.5 Gy/pulse obtained with the two different scanners are also in good agreement with each other. Furthermore, no dependence of the over-response on the total dose at the same dose per pulse was observed.

Dose rate dependence of radiochromic films

17

Figure 7 shows data from measurement campaign (ii) performed at the PTB electron research linac where EBT3 films were irradiated together with alanine (Bourgouin et al. 2022). Figure 7a shows the ratio of the flashDiamond dose reading to the alanine reference as a function of dose per pulse and no significant variation from 1 can be observed. This proves the suitability of the flashDiamond detector as dose rate independent reference.

In contrast to this, the EBT3 readings relative to the alanine reference as a function of dose per pulse shown in Figure 7b exhibit an over-response that increases with increasing dose per pulse. Figure 7c shows the same data points as in Figure 7b but as a function of intra-pulse dose rate. One can observe that the orange data points, where the intra-pulse dose rate was kept constant but the dose per pulse was reduced by halving the pulse duration, only align with the fitted function for the other data points when plotted as a function of dose per pulse (Figure 7b). Notably, these measurements with variation of the pulse duration were performed directly after another without changing anything related to the experimental conditions.

Figure 8 shows data from measurement campaign (iii), also performed at the PTB electron research linac, where EBT3 films were irradiated together with OC1 films with total doses around 30 Gy. Since no dependence of the over-response of EBT3 on the total dose or the color channel was found in the previous experiments only 30 Gy was used, the dose range where the green channel has an optimum sensitivity. In this experiment, OC-1 films were included as well since Villoing et al. (2022) suggested them as a dose rate independent alternative to EBT3.

Figure 8a shows the EBT3 dose reading relative to the flashDiamond reference as a function of dose per pulse. A deviation from 1 can be observed for 3 Gy per pulse and above and at 7 Gy per pulse the mean deviation is already at 6%. Notably, for the

Dose rate dependence of radiochromic films

18

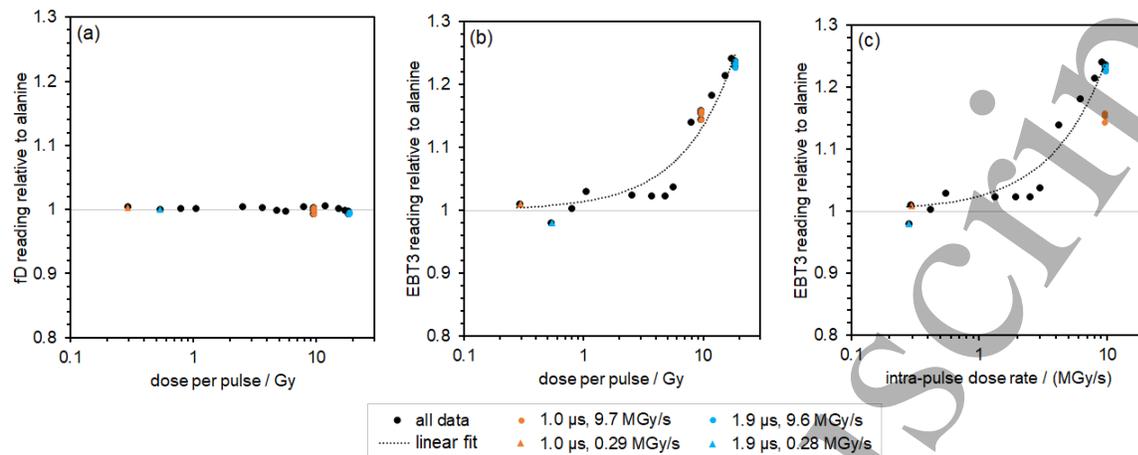


Figure 7: Panel (a): flashDiamond (fD) dose reading relative to the alanine reference as a function of dose per pulse (measurement campaign (ii)). Panel (b): EBT3 dose reading (green channel) relative to the alanine reference as a function of dose per pulse. Panel (c): Same data as in (b) but as a function of intra-pulse dose rate. The orange symbols represent irradiations with 1 μ s pulse duration and the blue symbols irradiations with the same intra-pulse dose rates but with 1.9 μ s pulse duration. The black circles represent all other data points, which were obtained with a fixed pulse duration of 1.9 μ s.

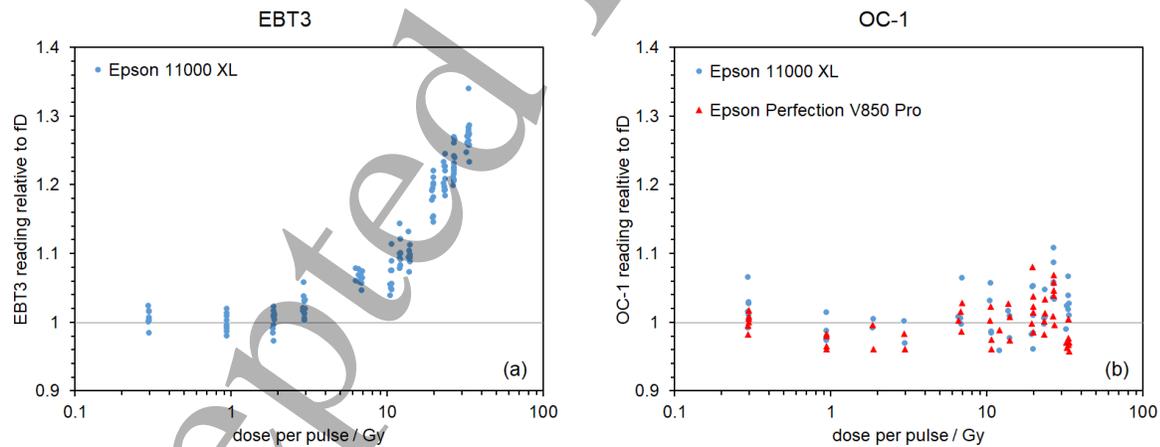


Figure 8: Panel (a): EBT3 dose reading (green channel) relative to the flashDiamond (fD) reference as a function of dose per pulse (measurement campaign (iii)). Panel (b): Dose reading (green channel) of the OC-1 films irradiated together with EBT3 films plotted in panel (a). The OC-1 films were scanned by two different scanners (Epson 11000 XL and Epson Perfection V850 Pro).

Dose rate dependence of radiochromic films

19

highest dose per pulse of 32.5 Gy, the observed over-response is around 25%. As shown in Figure 8b, for OC-1 films irradiated together with the EBT3 films, no over-response or other trend can be observed in our data which confirms the findings by Villoing et al. (2022) from their experiments with continuous proton beams.

3.2. Experiments at ELBE accelerator

In addition to the experiments at the PTB research linac (measurement campaigns (i) - (iii)), providing microsecond electron pulses with intra-pulse dose rates in the M Gy/s range, we also performed experiments at the ELBE research accelerator (measurement campaign (iv)) which offers a different beam parameter range.

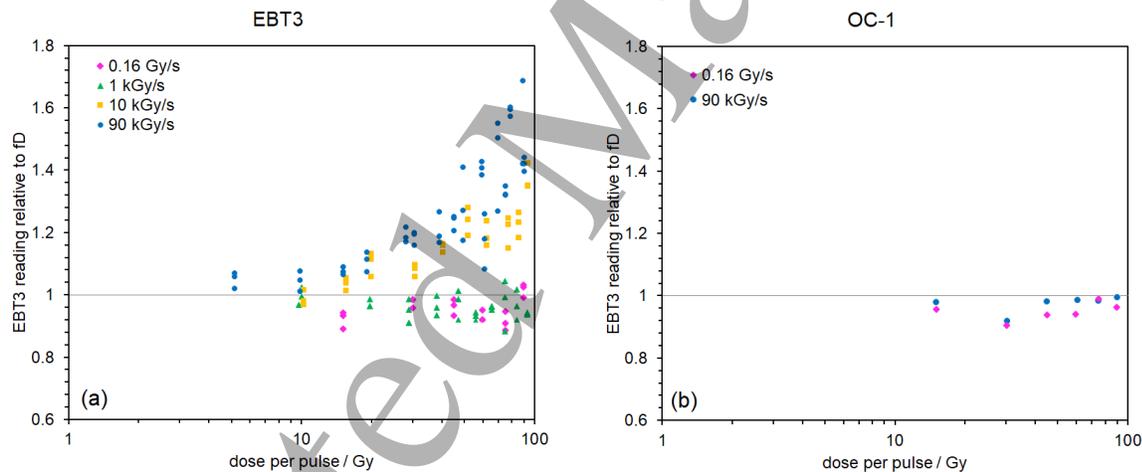


Figure 9: Panel (a): EBT3 dose reading (green channel) relative to the flashDiamond (fD) reference as a function of dose per pulse (measurement campaign (iv)). Panel (b): dose reading (green channel) of the OC-1 films irradiated together with EBT3 films plotted in panel (a). The different symbols indicate different intra-pulse dose rates.

While the highest dose per pulse that could be reached at the PTB linac was 32.5 Gy, at the ELBE accelerator the studied range could be extended up to more than 90 Gy in a single pulse. Figure 9a shows the film reading relative to the flashDiamond reference as a function of dose per pulse obtained for EBT3 films at different intra-pulse dose rates and Figure 9b shows the corresponding data for OC-1 films irradiated

1
2 *Dose rate dependence of radiochromic films* 20
3

4 together with the EBT3 films at lowest and highest intra-pulse dose rates used. At
5
6 0.16 Gy/s, which is in the order of magnitude of the average dose rate of conventional
7
8 radiotherapy devices, no significant trend with increasing dose per pulse can be observed
9
10 for EBT3 nor for OC-1. However, at 90 kGy/s, the EBT3 films show an over-response
11
12 that increases together with the dose per pulse. For an intermediate intra-pulse dose
13
14 rate of 10 kGy/s the EBT3 over-response is still apparent but less pronounced than for
15
16 90 kGy/s. At an intra-pulse dose rate of 1 kGy/s, however, the effect disappears and
17
18 the EBT3 response is again identical to that observed at conventional dose rate.
19
20

21
22 It is noticeable in Figure 9 that the ELBE data points scatter much more compared
23
24 to the data measured at PTB (Figure 6, 7 and 8). The setup and the experimental
25
26 conditions at ELBE do not offer a precision that is as good as the setup at PTB. In
27
28 the irradiation setup at ELBE, the flashDiamond used as reference is placed inside a
29
30 sample holder immersed with water leading to a water equivalent measurement depth
31
32 difference of about 10 mm (see Figure 1b). The radiochromic films were stuck on the
33
34 front face of such sample holders and therefore the flashDiamond measured at a slightly
35
36 larger depth and distance compared to the films. However, the over-response effect in
37
38 the ELBE beam is so strongly pronounced that it is still clearly evident, despite the less
39
40 defined setup as compared to the experiments at PTB.
41
42
43
44
45

46 **4. Discussion**

47
48

49 The data set shown in Figure 5 and Figure 6 confirms the findings by Villoing et al.
50
51 (2022) and clearly shows that the over-response of EBT3 films at UHDR observed in
52
53 their experiments with single pulses of continuous proton beams can also be reproduced
54
55 with electron beams. However, from the data in Figure 5 and Figure 6 one can not
56
57 yet differentiate if the dose per pulse or the intra-pulse dose rate is the driving fac-
58
59
60

Dose rate dependence of radiochromic films 21

tor behind the EBT3 film over-response. Therefore, another experiment (measurement campaign (ii)) was conducted where for some irradiations the pulse duration was halved while the intra-pulse dose rate was kept constant (see Figure 7). The results of these measurements show that the dose per pulse rather than the intra-pulse dose rate seems to be the crucial parameter that determines the magnitude of the EBT3 over-response. However, the following experiments performed at the ELBE accelerator revealed that the intra-pulse dose rate seems to play a role as well (see Figure 9). We hypothesize that a certain combination of intra-pulse dose rate and dose per pulse is necessary for the effect to occur, which would explain why it did not appear in previous studies and was discovered only recently. Our results indicate that up to intra-pulse dose rates of about 1 kGy/s and doses per pulse up to about 2 Gy EBT3 films can be safely applied while at higher dose rates or dose per pulse one should be cautious. That is in agreement with the results by Villoing et al. (2022) who found only minor effects at 1.5 kGy/s while at 7.5 kGy/s they observed an over-response with a magnitude that is quantitatively comparable to the data for 10 kGy/s presented in this work.

The data measured at the PTB research linac and at the ELBE accelerator were analyzed together to better understand the over-response of EBT3 films for certain combinations of intra-pulse dose rate and dose per pulse.

Figure 10a shows the EBT3 dose reading relative to the flashDiamond reference as a function of dose per pulse for the three intra-pulse dose rates where a over-response was observed (same data sets as shown in Figure 8 and Figure 9) together with linear fit functions of the form $y = m \cdot x + 1$ where y is the relative response and x is the dose per pulse in Gy. Figure 10b shows the parameter m as a function of intra-pulse dose rate DR (in Gy/s). For the PTB irradiations, the intra-pulse dose rate was varied to

Dose rate dependence of radiochromic films

22

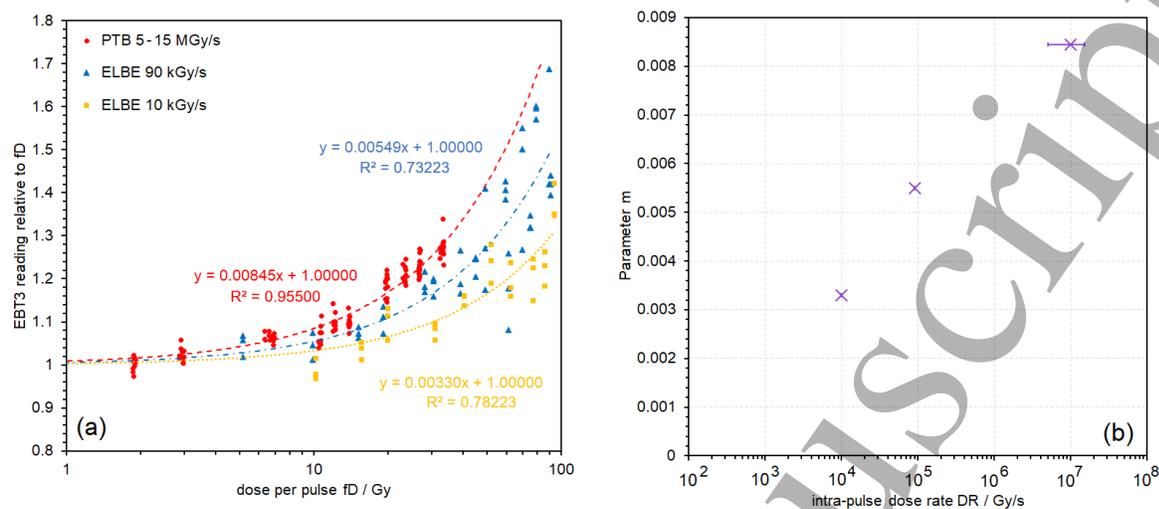


Figure 10: Panel (a): Linear model describing the relative EBT3 reading as a function of dose per pulse for the three intra-pulse dose rates where an over-response was observed. Panel (b): Model parameter m as a function of intra-pulse dose rate.

change the dose per pulse, therefore, an average value of $DR = 10 \pm 5$ MGy/s is used for the plot in Figure 10b. This systematic representation of the EBT3 over-response data shows that the over-response is determined by both the dose per pulse and by the intra-pulse dose rate. For higher intra-pulse dose rates the over-response effect is more pronounced. The functions in Figure 10a can, for instance, be used to estimate if an over-response of EBT3 films is to be expected for certain irradiation parameters, or it could also be applied to retrospectively assess if previous experiments were affected by the EBT3 over-response.

One can observe from the trend in Figure 10b that for intra-pulse dose rates around 1000 Gy/s, the parameter m approaches zero. This means that for FLASH experiments using quasi-continuous proton beams with dose rates considerably lower (~ 100 Gy/s) than the intra-pulse dose rates in pulsed UHDR electron beams, as delivered by clinical proton therapy systems based on isochronous cyclotrons, the application of EBT3 films as reference is probably not a problem. This is in agreement with previous studies

Dose rate dependence of radiochromic films 23

using UHDR proton beams (Togno et al. 2022, Horst et al. 2024). However, at UHDR electron accelerators used for research on the FLASH effect, which typically deliver a few Gy per pulse with intra-pulse dose rates of MGy/s, one should be cautious with EBT3 films and preferably use a different dosimetric reference, e.g. a flashDiamond or alanine. By extrapolating the data presented in this work to other pulsed radiation sources providing even higher intra-pulse dose rates such as laser accelerators (Reimold et al. 2023), the over-response of EBT3 films may become relevant at doses per pulse even lower than 2 Gy.

Radiochromic films are chemical dosimeters, and therefore the cause for the over-response probably lies in the chemical phase of radiation action (time scale $\sim \mu\text{s} - \text{ms}$) where some mechanism that is not yet fully understood amplifies the polymerization reactions that are responsible for the film darkening (Yasuda et al. 2025). While the present study focussed on EBT3 films, also for EBT-XD films Villoing et al. (2022) found an over-response in UHDR proton beams and consequently it can be expected that this film will behave similarly. In fact, indications of this have also already been found using UHDR electron beams (Del Sarto et al. 2025, Cayley et al. 2025). For the new EBT4 films (Akdeniz 2024) no comprehensive study has been conducted, yet. However, since nothing has changed in the basic functioning principle and chemical composition of these films compared to their predecessors (Miura et al. 2023) an over-response at ultra-high dose rate and dose per pulse should be expected for EBT4 as well. Yasuda et al. (2026) found no indications for an over-response of EBT4 at UHDR but used only a 720 Gy/s proton beam for this test.

In addition to the extensive experiments with EBT3 films, also OC-1 films were tested in the present work (see Figure 8 and Figure 9). In line with the findings presented by Villoing et al. (2022), no dose rate dependence was detected in the present

Dose rate dependence of radiochromic films 24

experiments. However, it should be pointed out that OC-1 films, besides their proven dose rate independence, have some properties which might be impractical for routine dosimetry in FLASH experiments. We observed, for instance, a strong sheet-by-sheet variation requiring a sheet individual calibration as well as a rather slow darkening after irradiation that takes several days or even weeks. Furthermore, Villoing et al. (2022) reported an uncertainty for these films up to 13.3% for doses below 10 Gy using the green color channel and their practicality is limited by them not being laminated, making them fragile and difficult to handle. A definit statement concerning the applicability of OC-1 films for routine dosimetry in FLASH experiments would require a more rigorous characterization.

5. Conclusion

The over-response of EBT3 films at ultra high dose rate and dose per pulse was confirmed in experiments at two electron accelerators with different beam pulse structure. For OC-1 films, no dose rate or dose per pulse dependency was detected within the experimental uncertainties which is in agreement with the study by Villoing et al. (2022). However, the suitability of OC-1 for a practical application as dosimeters in FLASH experiments requires further investigation. The range where EBT3 can safely be applied for FLASH dosimetry is at intra-pulse dose rates below 1 kGy/s and doses per pulse up to about 2 Gy. Above that one should expect a significant over-response that depends on the dose per pulse.

Acknowledgements

Part of this research was carried out at ELBE at the Helmholtz-Zentrum Dresden – Rossendorf e. V., a member of the Helmholtz Association. The ELBE operator team is

REFERENCES

25

kindly acknowledged for their assistance during the experiments.

The authors would like to thank Rafael Kranzer from PTW Freiburg for discussions about the applicability of the flashDiamond in the ELBE electron beam, Michael Nasse and the colleagues from the KIT institute IBPT for providing their flashDiamond detector used for the experiments at ELBE, Hans-Peter Schlenvoigt from HZDR for help with laser cutting of the films and Michael Schürer from NCT for support with the experimental setups at ELBE.

The project (24NRM01 FLASH-DOSE) has received funding from the European Partnership on Metrology, co-financed from the European Union's Horizon Europe Research and Innovation Programme and by the Participating States.

References

Akdeniz, Y. (2024), 'Comparative analysis of dosimetric uncertainty using Gafchromic™ EBT4 and EBT3 films in radiochromic film dosimetry', *Radiation Physics and Chemistry* **220**, 111723.

URL: <https://www.sciencedirect.com/science/article/pii/S0969806X24002159>

Bourgouin, A., Hackel, T. & Kapsch, R.-P. (2023), 'The ptb water calorimeter for determining the absolute absorbed dose to water in ultra-high pulse dose rate electron beams', *Physics in Medicine and Biology* **68**(11), 115016.

URL: <https://doi.org/10.1088/1361-6560/acce1d>

Bourgouin, A., Hackel, T., Marinelli, M., Kranzer, R., Schüller, A. & Kapsch, R.-P. (2022), 'Absorbed-dose-to-water measurement using alanine in ultra-high-pulse-dose-rate electron beams', *Physics in Medicine and Biology* **67**(20), 205011.

URL: <https://dx.doi.org/10.1088/1361-6560/ac950b>

REFERENCES

26

Böhlen, T. T., Germond, J.-F., Bourhis, J., Vozenin, M.-C., Ozsahin, E. M., Bochud, F., Bailat, C. & Moeckli, R. (2022), 'Normal tissue sparing by flash as a function of single-fraction dose: A quantitative analysis', *International Journal of Radiation Oncology*Biography*Physics* **114**(5), 1032–1044.

URL: <https://www.sciencedirect.com/science/article/pii/S0360301622005417>

Cayley, J., Engels, E., Charles, T., Bennetto, P., Cameron, M., Poder, J., Hausermann, D., Paino, J., Butler, D., Cutajar, D., Petasecca, M., Rosenfeld, A., Tan, Y.-R. E. & Lerch, M. (2025), 'Establishing Linearity of the MOSkin Detector for Ultra-High Dose-per-Pulse, Very-High-Energy Electron Radiotherapy Using Dose-Rate-Corrected EBT-XD Film', *Applied Sciences* **15**(14).

URL: <https://www.mdpi.com/2076-3417/15/14/8101>

DeFrancisco, J. & Kim, S. (2025), 'A systematic review of electron flash dosimetry and beam control mechanisms utilized with modified non-clinical linacs', *Journal of Applied Clinical Medical Physics* **26**(4), e70051.

URL: <https://aapm.onlinelibrary.wiley.com/doi/abs/10.1002/acm2.70051>

Del Sarto, D., Masturzo, L., Cavalieri, A., Celentano, M., Fuentes, T., Gadducci, G., Giannini, N., Gonnelli, A., Milluzzo, G., Paiar, F., Pensavalle, J. H., Romano, F. & Di Martino, F. (2025), 'A systematic investigation on the response of EBT-XD gafchromic films to varying dose-per-pulse, average dose-rate and instantaneous dose-rate in electron flash beams', *Frontiers in Physics* **Volume 13 - 2025**.

URL: <https://www.frontiersin.org/journals/physics/articles/10.3389/fphy.2025.1474416>

Devic, S. (2011), 'Radiochromic film dosimetry: Past, present, and future', *Physica Medica* **27**(3), 122–134.

URL: <https://www.sciencedirect.com/science/article/pii/S1120179710000578>

Favaudon, V., Caplier, L., Monceau, V., Pouzoulet, F., Sayarath, M., Fouillade,

REFERENCES

27

C., Poupon, M.-F., Brito, I., Hupé, P., Bourhis, J., Hall, J., Fontaine, J.-J. & Vozenin, M.-C. (2014), 'Ultrahigh dose-rate flash irradiation increases the differential response between normal and tumor tissue in mice', *Science Translational Medicine* **6**(245), 245ra93–245ra93.

URL: <https://www.science.org/doi/abs/10.1126/scitranslmed.3008973>

Favaudon, V., Lentz, J.-M., Heinrich, S., Patriarca, A., de Marzi, L., Fouillade, C. & Dutreix, M. (2019), 'Time-resolved dosimetry of pulsed electron beams in very high dose-rate, flash irradiation for radiotherapy preclinical studies', *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* **944**, 162537.

URL: <https://www.sciencedirect.com/science/article/pii/S0168900219310666>

Gabriel, F., Gippner, P., Grosse, E., Janssen, D., Michel, P., Prade, H., Schamlott, A., Seidel, W., Wolf, A. & Wünsch, R. (2000), 'The rossendorf radiation source elbe and its fel projects', *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms* **161-163**, 1143–1147.

URL: <https://www.sciencedirect.com/science/article/pii/S0168583X9900909X>

Garty, G., Obaid, R., Deoli, N. & et al. (2022), 'Ultra-high dose rate flash irradiator at the radiological research accelerator facility', *Scientific Reports* **12**, 22149.

Giannini, N., Gadducci, G., Fuentes, T., Gonnelli, A., Di Martino, F., Puccini, P., Naso, M., Pasqualetti, F., Capaccioli, S. & Paiar, F. (2024), 'Electron flash radiotherapy in vivo studies. a systematic review', *Frontiers in Oncology* **Volume 14 - 2024**.

URL: <https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2024.1373453>

Horst, F., Bodenstern, E., Brand, M., Hans, S., Karsch, L., Lessmann, E., Löck, S., Schürer, M., Pawelke, J. & Beyreuther, E. (2024), 'Dose and dose rate dependence of the tissue sparing effect at ultra-high dose rate studied for proton and electron beams

REFERENCES

28

using the zebrafish embryo model', *Radiotherapy and Oncology* **194**, 110197.

URL: <https://www.sciencedirect.com/science/article/pii/S0167814024001191>

Horst, F., Brand, M., Hans, S., Karsch, L., Lessmann, E., Löck, S., Schürer, M., Pawelke, J. & Beyreuther, E. (2023), 'In regard to böhlen et al.', *International Journal of Radiation Oncology*Biology*Physics* **115**(4), 1006–1007.

URL: <https://www.sciencedirect.com/science/article/pii/S0360301622035295>

Jaccard, M., Petersson, K., Buchillier, T., Germond, J.-F., Durán, M. T., Vozenin, M.-C., Bourhis, J., Bochud, F. O. & Bailat, C. (2017), 'High dose-per-pulse electron beam dosimetry: Usability and dose-rate independence of ebt3 gafchromic films', *Medical Physics* **44**(2), 725–735.

URL: <https://aapm.onlinelibrary.wiley.com/doi/abs/10.1002/mp.12066>

Jorge, P. G., Jaccard, M., Petersson, K., Gondré, M., Durán, M. T., Desorgher, L., Germond, J.-F., Liger, P., Vozenin, M.-C., Bourhis, J., Bochud, F., Moeckli, R. & Bailat, C. (2019), 'Dosimetric and preparation procedures for irradiating biological models with pulsed electron beam at ultra-high dose-rate', *Radiotherapy and Oncology* **139**, 34–39. FLASH radiotherapy International Workshop.

URL: <https://www.sciencedirect.com/science/article/pii/S0167814019304037>

Karsch, L., Pawelke, J., Brand, M., Hans, S., Hideghéty, K., Jansen, J., Lessmann, E., Löck, S., Schürer, M., Schurig, R., Seco, J., Szabó, E. R. & Beyreuther, E. (2022), 'Beam pulse structure and dose rate as determinants for the flash effect observed in zebrafish embryo', *Radiotherapy and Oncology* **173**, 49–54.

URL: <https://www.sciencedirect.com/science/article/pii/S0167814022041317>

Konradsson, E., Arendt, M. L., Bastholm Jensen, K., Børresen, B., Hansen, A. E., Bäck, S., Kristensen, A. T., Munck af Rosenschöld, P., Ceberg, C. & Petersson, K. (2021), 'Establishment and initial experience of clinical flash radiotherapy in canine

REFERENCES

29

cancer patients', *Frontiers in Oncology* **Volume 11 - 2021**.

URL: <https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2021.658004>

Konradsson, E., Ceberg, C., Lempart, M., Blad, B., Bäck, S., Knöös, T. & Petersson, K. (2020), 'Correction for ion recombination in a built-in monitor chamber of a clinical linear accelerator at ultra-high dose rates', *Radiation Research* **194**(6), 580–586.

URL: <https://doi.org/10.1667/RADE-19-00012>

Lempart, M., Blad, B., Adrian, G., Bäck, S., Knöös, T., Ceberg, C. & Petersson, K. (2019), 'Modifying a clinical linear accelerator for delivery of ultra-high dose rate irradiation', *Radiotherapy and Oncology* **139**, 40–45. FLASH radiotherapy International Workshop.

URL: <https://www.sciencedirect.com/science/article/pii/S0167814019300593>

Lim, S. B. & Tang, G. (2022), 'Evaluation of orthochromic oc-1 films for photon radiotherapy application', *Journal of Radiation Research* **64**(1), 105–112.

URL: <https://doi.org/10.1093/jrr/rrac080>

Liu, K., Jorge, P. G., Taylor, R., Moeckli, R. & Schüler, E. (2023), 'Comprehensive evaluation and new recommendations in the use of gafchromic ebt3 film', *Medical Physics* **50**(11), 7252–7262.

URL: <https://aapm.onlinelibrary.wiley.com/doi/abs/10.1002/mp.16593>

Marinelli, M., Felici, G., Galante, F., Gasparini, A., Giuliano, L., Heinrich, S., Pacitti, M., Prestopino, G., Vanreusel, V., Verellen, D., Verona, C. & Verona Rinati, G. (2022), 'Design, realization, and characterization of a novel diamond detector prototype for flash radiotherapy dosimetry', *Medical Physics* **49**(3), 1902–1910.

URL: <https://aapm.onlinelibrary.wiley.com/doi/abs/10.1002/mp.15473>

Miura, H., Ozawa, S., Okazue, T., Enosaki, T. & Nagata, Y. (2023), 'Characterization of scanning orientation and lateral response artifact for EBT4 Gafchromic film', *Journal*

REFERENCES

30

of *Applied Clinical Medical Physics* **24**(8), e13992.

URL: <https://aapm.onlinelibrary.wiley.com/doi/abs/10.1002/acm2.13992>

Pawelke, J., Brand, M., Hans, S., Hideghéty, K., Karsch, L., Lessmann, E., Löck, S., Schürer, M., Szabó, E. R. & Beyreuther, E. (2021), 'Electron dose rate and oxygen depletion protect zebrafish embryos from radiation damage', *Radiotherapy and Oncology* **158**, 7–12.

URL: <https://www.sciencedirect.com/science/article/pii/S0167814021060497>

Reimold, M., Assenbaum, S., Bernert, C., Beyreuther, E., Brack, F.-E., Karsch, L., Kraft, S. D., Kroll, F., Nossula, A., Pawelke, J., Rehwald, M., Schlenvoigt, H.-P., Schramm, U., Umlandt, M. E. P., Zeil, K., Ziegler, T. & Metzkes-Ng, J. (2023), 'Dosimetry for radiobiological in vivo experiments at laser plasma-based proton accelerators', *Physics in Medicine and Biology* **68**(18), 185009.

URL: <https://dx.doi.org/10.1088/1361-6560/acf025>

Romano, F., Bailat, C., Jorge, P. G., Lerch, M. L. F. & Darafsheh, A. (2022), 'Ultra-high dose rate dosimetry: Challenges and opportunities for flash radiation therapy', *Medical Physics* **49**(7), 4912–4932.

Schoenfeld, A. A., Poppinga, D., Harder, D., Doerner, K.-J. & Poppe, B. (2014), 'The artefacts of radiochromic film dosimetry with flatbed scanners and their causation by light scattering from radiation-induced polymers', *Physics in Medicine and Biology* **59**(13), 3575.

URL: <https://doi.org/10.1088/0031-9155/59/13/3575>

Schüller, A., Heinrich, S., Fouillade, C., Subiel, A., De Marzi, L., Romano, F., Peier, P., Trachsel, M., Fleta, C., Kranzer, R., Caresana, M., Salvador, S., Busold, S., Schönfeld, A., McEwen, M., Gomez, F., Solc, J., Bailat, C., Linhart, V., Jakubek, J., Pawelke, J., Borghesi, M., Kapsch, R.-P., Knyziak, A., Boso, A., Olsovcova, V.,

REFERENCES

31

Kottler, C., Poppinga, D., Ambrozova, I., Schmitzer, C.-S., Rossomme, S. & Vozenin, M.-C. (2020), 'The european joint research project uhdpulse – metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates', *Physica Medica* **80**, 134–150.

URL: <https://www.sciencedirect.com/science/article/pii/S1120179720302362>

Schüller, A., Illemann, J., Renner, F., Makowski, C. & Kapsch, R.-P. (2017), 'Traceable charge measurement of the pulses of a 27 MeV electron beam from a linear accelerator', *Journal of Instrumentation* **12**(03), P03003.

URL: <https://doi.org/10.1088/1748-0221/12/03/P03003>

Soliman, Y. S., Pelliccioli, P., Beshir, W., Abdel-Fattah, A. A., Fahim, R. A., Krisch, M. & Bräuer-Krisch, E. (2020), 'A comparative dosimetry study of an alanine dosimeter with a ptw pinpoint chamber at ultra-high dose rates of synchrotron radiation', *Physica Medica* **71**, 161–167.

URL: <https://www.sciencedirect.com/science/article/pii/S1120179720300600>

Togno, M., Nesteruk, K., Schäfer, R., Psoroulas, S., Meer, D., Grossmann, M., Christensen, J., Yukihiro, E., Lomax, A., Weber, D. & Safai, S. (2022), 'Ultra-high dose rate dosimetry for pre-clinical experiments with mm-small proton fields', *Physica Medica* **104**, 101–111.

URL: <https://www.sciencedirect.com/science/article/pii/S1120179722020804>

Villoing, D., Koumeir, C., Bongrand, A., Guertin, A., Haddad, F., Métivier, V., Poirier, F., Potiron, V., Servagent, N., Supiot, S., Delpon, G. & Chiavassa, S. (2022), 'Technical note: Proton beam dosimetry at ultra-high dose rates (FLASH): Evaluation of GAFchromic™ (EBT3, EBT-XD) and OrthoChromic (OC-1) film performances', *Medical Physics* **49**(4), 2732–2745.

URL: <https://aapm.onlinelibrary.wiley.com/doi/abs/10.1002/mp.15526>

REFERENCES

32

Xie, D.-H., Li, Y.-C., Ma, S., Yang, X., Lan, R.-M., Chen, A.-Q., Zhu, H.-Y., Mei, Y., Peng, L.-X., Li, Z.-F., Huang, B.-J., Chen, Y., Huang, X.-Y. & Qian, C.-N. (2022), 'Electron ultra-high dose rate flash irradiation study using a clinical linac: Linac modification, dosimetry, and radiobiological outcome', *Medical Physics* **49**(10), 6728–6738.

URL: <https://aapm.onlinelibrary.wiley.com/doi/abs/10.1002/mp.15920>

Yasuda, H., Bantan, H., Umezawa, M., Yamada, M., Yogo, K. & Toshito, T. (2025), 'Changes in scanning orientation effects of Gafchromic EBT-3 film irradiated with ultra-high dose rate proton beams', *Discover Applied Sciences* **7**, 64.

URL: <https://link.springer.com/article/10.1007/s42452-025-06484-6>

Yasuda, H., Toshito, T., Umezawa, M., Yamada, M., Tanaka, K., Omachi, C., Yogo, K., Bantan, H. & Nakashima, T. (2026), 'Comparative analysis of the responses of EBT-XD and EBT4 films to ultra-high dose rate proton beams', *Radiation Physics and Chemistry* **239**, 113349.

URL: <https://www.sciencedirect.com/science/article/pii/S0969806X25008412>

Accepted Manuscript