



PHYSICS

2021 ESTRO Physics Workshop: Science in Development

22-23 October 2021, online

Physics aspects of FLASH therapy

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The workshop to consider physics aspects of FLASH radiotherapy began with an introductory session on 28 May and three preparatory sessions at the beginning of October before it culminated in an online meeting on 20-21 October 2021. The event was attended by 32 participants from Europe and North America and five vendors (IBA, Varian, SIT, IntraOp and RaySearch). The purpose of this workshop was to investigate the physics aspects of ultra-high dose rate (UHDR) radiation and to discuss how it was incorporated into a clinical environment. The provision of UHDR radiation causes an in vivo biological response, known as FLASH, which is found to maintain anti-tumour efficacy without causing the usual tissue complications that occur with standard dose rates.

The workshop was planned to cover various areas: dosimetry measurements in UHDR conditions; clinical implementation with emphasis on safety and regulation; and integration of UHDR into treatment planning and its clinical effects. However, after the preliminary sessions, it became clear that participants wanted to focus on certain overarching topics. These were:

- terminology: such that we address the same things and make sure that reporting of experiments is more transparent;
- clinical implementation with focus on safety and regulation; and
- guidelines for UHDR experiments.

Working groups were created to cover these topics.

An additional topic discussed was the creation of an ESTRO FLASH consortium. The idea is to develop a platform where different professions involved in FLASH therapy would find a space to share data (including negative ones) and to stimulate new experiments. A working group will be created with interested persons (contact any chairperson) to prepare a formal demand to the ESTRO board.

Several speakers were invited to the event:

- Magdalena Bazalova-Carter (University of British Columbia), who spoke on the challenges of clinical implementation of FLASH therapy;
- Robert Stewart (University of Washington), whose topic was Monte Carlo modelling of the effects of oxygen on DNA damage;
- Kristoffer Petersson (University of Oxford), who spoke on dosimetry in UHDR electron beams;
- Pierre Montay-Gruel (University of Antwerp), who chose to talk about the new biology challenges of FLASH radiotherapy in radiation research;
- Anna Vella (University of Oxford), whose topic was macroscopic Monte Carlo simulations for FLASH radiotherapy; and
- Wilko Verbakel (University of Amsterdam), who talked about treatment planning for proton transmission beam FLASH and particularly, influences of the dose rate and machine parameters.

Terminology

The working group (WG) that was created to consider this topic will start work on a white paper that will focus on harmonisation of terminology in FLASH radiotherapy and provide recommendations regarding which beam and irradiation parameters should be mandated to be reported in scientific publications. Through this content, it will define the steps that are necessary to improve reproducibility in radiation research studies.

Clinical implementation

Participants in this WG have started to draft recommendations for the clinical implementation of UHDR radiotherapy, with a focus on patient safety, reporting and radiation protection.

The group aims to include in its paper:

- ways to harmonise and standardise all aspects of clinical implementation that are related to patient safety, reporting and radiation protection; and
- ways to help medical physicists to implement UHDR clinically in radiotherapy.

The WG hopes that this document will be the basis of a process to steer proactively the establishment of new regulations that cover the mode of use of UHDR in radiotherapy.

This paper should not overlap with the work of other WGs or projects, such as the European metrology programme for innovation and research (EMPIR) project that is considering metrology for advanced radiotherapy using particle beams with ultra-high pulse dose rates (UHDpulse) or the work on UHDR dosimetry that is being performed by the American Association of Physicists in Medicine (AAPM) with the relevant European Society for Radiotherapy and Oncology (ESTRO) task group.

We aim to ask for endorsement of this work from the International Atomic Energy Agency (IAEA) and AAPM.

Guidelines for UHDR experiments

This WG will prepare a white paper that will detail the type of experiments that should be performed to understand the implications of UHDR in the clinic and, if possible, to provide an environment in which the ramifications of treatments can be quantified. The white paper could be used as a means to obtain funds for this type of experiment. These experiments are required as the concepts of concern to radiation physicists are not covered in experiments that are performed currently by radiation biologists.

Subjects that would be part of such experiments were identified as:

- exploration of the parameter space (volume effects, dose rate, total dose, pulse structure (height, length, pulse repetition frequency), fractionation/ impact of pauses, oxygen status, radiation quality (electrons, protons, etc.));
- mechanism of action (underlying physics); and
- high-level models.



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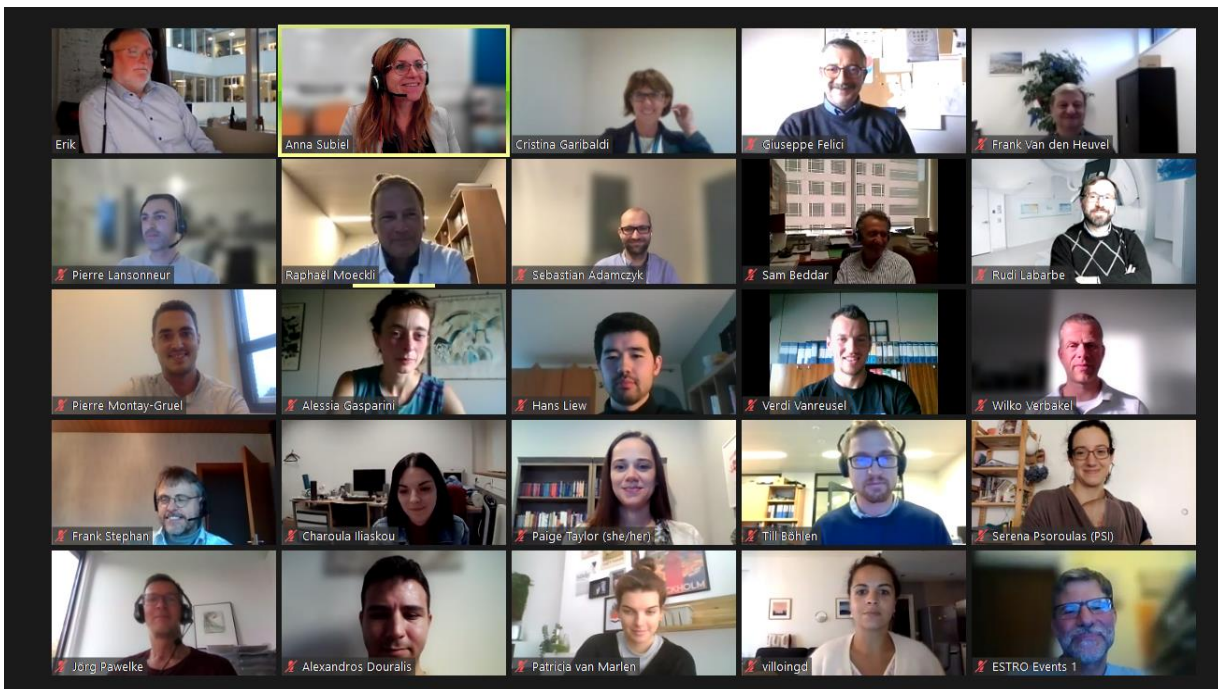
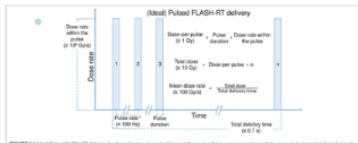
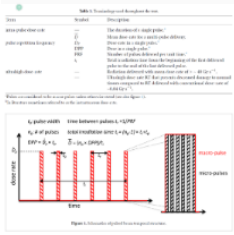


Figure 1. Some participants in the ESTRO Physics Workshop 2021 - physics aspects of FLASH radiotherapy



Definition of beam parameters

machine specific parameters



Quantity	Description	Unit	Value	Reference
n_{part}	Number of particles per bunch		~10 ¹⁰	
n_{bunch}	Number of bunches per train		~100	
n_{train}	Number of trains per session		~10	
n_{spot}	Number of spots per train		~10	
n_{beam}	Number of beams per session		~10	

- **Particle type:** electrons, protons, which ions, X-rays
- **Beam energy** for particle beams or **Photon energy** for X-rays
- **FWHM_y^{min}** – minimum transverse spot size, e.g. for studying microbeams and their effect and for defining the step size for scanning the beam during the treatment time $T_{treatment}$
- **FWHM_y^{max}** – maximum transverse spot size, e.g. for defining which maximum area that can be covered by one bunch and for defining the step size for scanning the beam during the treatment time $T_{treatment}$

Facility name	location	particle type	t_{bunch}	t_{train}	t_{spot}	n_{bunch}	beam energy	FWHM _y ^{min}	FWHM _y ^{max}
PITZ	DESY, Zeuthen (SE of Berlin)	e ⁻	0.1 – 60 ps	0.2 – 10 μs	0 – 1 ms	0.1 – 1 s	10 – 5 nC	7 – 22 MeV, asked for 250 MeV upgrade	~100 μm ~3 cm, more with more drift and/or larger exit window
ARES	DESY, Hamburg	e ⁻	< 5 – few ps	0.02 s	none, i.e. single bunches	0.1 – 1 s	50 – 200 pC, upgrade to 3 nC	160 MeV	similar

application specific parameters

- (dose/dose rate at the target site)
- measured
- additional info from TPS/log files

e.g. calculation of dose rate distribution per voxel

Dose-rate calculations for scanning beams

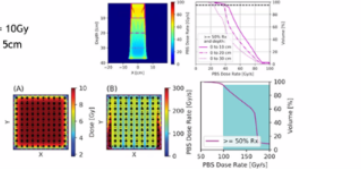
- **Spot dose-rate distribution:** % of local dose delivered above a dose-rate threshold.
 - Exclude scanning; use dose contributions from all spots
- **Dose Averaged Dose-Rate distribution:**

$$DADR = \frac{\sum_{i=1}^N (d_i/w_i) (d_i/B_i)}{\sum_{i=1}^N d_i/w_i}$$
- **PBS dose-rate:** dose from first till last contribution above threshold / total time for this, including scanning
- **Average dose-rate:** total dose per beam / total time per beam



DR Volume Histogram: should be included in TP

- Dose = 10Gy
- 5cm x 5cm



Dose Averaged Dose-Rate

- Dose Averaged Dose-Rate (DADR):
- 3D dose-rate distributions for IMPT
- Instantaneous dose-rates (no dead times considered)

$$DADR = \frac{\sum_{i=1}^N (d_i/w_i) (d_i/B_i)}{\sum_{i=1}^N d_i/w_i}$$

Labels: d_i = dose contribution spot i , w_i = spot weight, B_i = dose influence matrix, d_i = dose influence matrix, B_i = beam intensity.

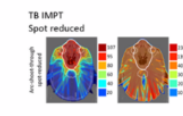


Figure 2. Snapshot of one of the whiteboards that was created during the terminology discussion