Draft: Beam Dynamics and Collective Effects in the Generation and Propagation of Structured Beams for Advanced Accelerator-based Radiontherapy

Project Description

1 Starting Point

State of the art and preliminary work

Introduction

Particle accelerators nowadays play a vital role in a multitude of scientific fields. They have become highly complex over time and with them the field of accelerator physics. New developments are continuously pushing the understanding and the technological limits towards increasingly extreme beam properties. In electron accelerators, this includes ultra-short pulses at high intensities in linear accelerators or free electron lasers as well as transversely narrow pulses for ultra-low emittance synchrotron light sources. The extensive research conducted today aims for a deep understanding of the involved beam dynamics occurring in these extreme beam conditions as well as of the diagnostics thereof. The extreme conditions lead to strong effects caused by the coexistence of many particles in the densely populated pulses. These effects are summarized under the term collective effects. They describe self-interaction of particles within the beam as well as the interaction with the environment, both of which are dependent on the actual particle distribution. The study of collective effects is an active research topic and has been the main focus of my research in the last years.

At the same time, the current development of two advanced approaches in accelerator-based radiotherapy (RT) pushes in the same direction of high intensity beams with temporal or spatial structuring. FLASH RT is based on the delivery of very high doses in short pulses and Microbeam RT focuses on spatially fractionated beams. In both methods a significant widening of the therapeutic window is observed. The resulting observed normal tissue sparing effect is expected to improve treatment outcomes and reduce overall toxicity for the patients resulting in a better quality of life. The beam properties used for FLASH and Microbeam RT go beyond the prediction and diagnostic capabilities in conventional RT. One mayor difficulty is the increasing non-linearity in the response of usual dosimetry methods at high dose-rates. The increased requirements on dosimetry as well as on the overall diagnostics and simulation of the beam dynamics in the accelerators used for beam generation open up new challenges and possibilities. These extreme beam properties in the novel radiotherapy methods pose a great opportunity to push the understanding of the involved complex beam dynamics and collective effects in this active and exiting research field.

The proposed project aims at improving the understanding, predictability and control of the accelerator-based particle beams involved in FLASH and Microbeam RT. The entry point will be to extend the research on collective effects in accelerators to cover the beam properties required for FLASH and Microbeam RT, profiting from my expertise in this field. Subsequently, this project will expand the study beyond the particle accelerator into the beam-matter interaction. The influence of collective effects during the transport from the accelerator through matter onto the target, which up until now was sparsely studied, will be explored in detail. Based on these studies the connection from input particle distribution to the dose distribution on target will be explored. Investigating the inverse problem, i.e. determining the required input distribution for a desired dose distribution on target, will allow first tests of targeted beam shaping within this project. The outcome of the project will be a significant contribution to FLASH and Microbeam RT as well as to the general advancement of accelerator physics.

State of the art: radiotherapy

Radiotherapy (RT) has always been a very valuable tool in cancer treatment [1]. In Europe, radiotherapy is recommended as part of the treatment plan for more than 50% of cancer patients [2]. Reducing side effects while maintaining or even enhancing treatment efficacy in the future will improve the quality of life of the patients. Radiotherapy uses ionizing radiation to damage the DNA within the tumor cells, which prevents the cells from reproducing and eventually leads to their death. The external beam radiotherapy (EBRT) is based on accelerator-generated high-energy beams delivering a targeted dose of ionizing radiation to the affected area. As some areas of healthy tissue are unavoidable irradiated the dose rate is carefully chosen to keep a balance between tumor control and normal tissue tolerance. The range between radiation doses that effectively destroy cancer cells while only causing minimal damage to healthy tissue and organs is called the therapeutic window [3]. A widening of this window is one of the main goals of present day radiotherapy research.

FLASH RT is a novel approach which focuses short pulses with very high dose rates to enhance tumor cell lethality while minimizing damage to surrounding healthy tissue. In conventional external beam RT typically around 30 fractions with 1.8 - 2 Gy per fraction are delivered with a dose rate ranging from 0.2 to 20 Gy/min. For FLASH RT, dose rates of more than 40 Gy/s (=2400 Gy/min) were observed to be effective in combination with pulse trains shorter than 500 ms and a total dose of 10 Gy or more [3]. The resulting significant widening of the therapeutic window (see Figure 1) allows a higher dose per fraction than in conventional radiotherapy without causing severe side effects, such as acute normal tissue reactions or long-term complications. Several suspected mechanisms behind the beneficial FLASH effect [6] are being investigated. And while the exact mechanisms are not yet fully determined, the effect has been experimentally demonstrated for irradiation with photons, electrons and ions.

The high dose rates result in difficulties with standard dosimetry techniques showing deviations from the required linear detection efficiency [7]. So is, for example, the Fricke dosimetry nearly

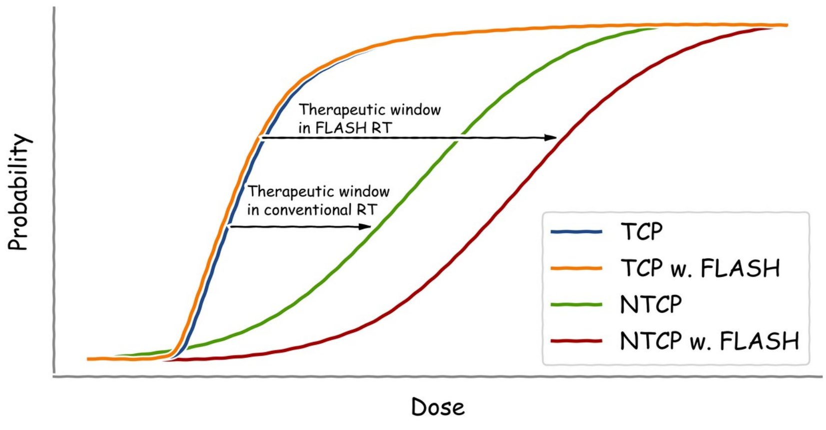

Figure 1: *Sketch of the therapeutic window increasing as normal tissue complication probability (NTCP) is shifted to higher dose for FLASH RT and tumor control probability (TCP) remains.*

independent of does rate up to approximately 2 Gy per pulse, which is exceeded under FLASH conditions. Therefore, the primary standard for dosimetry in conventional electron RT is not applicable to FLASH RT. To this end, the effects leading to the observed deviations between expected and detected dose are under investigation and new dosimetry calibration procedures and detectors are being tested [8]. Recent work has, for example, included further investigations of ion-recombination in ionization chambers including improved ways of calculating the recombination correction factors [9], [10]. In addition, systematic tests of possible, alternative detection mechanisms such as solid-state calorimeters and small-volume and active dosimeters were conducted [7], [11]. Active detectors and real-time diagnostics become increasingly relevant as well for beam monitoring as each of the few high dose pulses carries a non-negligible amount of the total dose described for treatment, increasing the required per shot accuracy as fluctuations in dose per pulse no longer average out. Besides the obvious need to establish accurate dosimetry methods, also the prediction of the expected dose on target can be improved by including collective effects into the simulations. This will be described further in the state of the art: accelerators and collective effects section. For most standard medical accelerators the FLASH beam conditions are challenging if not impossible to achieve, requiring substantial improvement or the development of new dedicated FLASH accelerators [12]. In the mean time, dedicated accelerator facilities with compatible beam conditions are employed as test-beds.

Another possibility to achieve reduced normal tissue damage are spatially structured beams used in **Microbeam Radiotherapy (MRT)** [18]. The spatial intensity modulation at the micrometer scale has shown the potential to widen the therapeutic window. The underlying biological mechanisms are suspected to have significant overlap with the mechanisms behind the FLASH effect due to the similarly high dose and dose rates in the micron-sized individual beamlets in the array of parallel microbeams [18]. Earlier studies with electron GRID radiotherapy [19] and recent studies with protons showed promising results in the sparing of healthy tissue [20]. Nevertheless, most studies on MRT have been conducted with X-rays. The unidirectional microbeams with spot sizes of 25 - 100 µm and a spot spacing of 50 - 200 µm are produced by inserting a multi-slit collimator into an x-ray beam with very small divergence produced at a 3rd generation light source [21]. This dependence on large infrastructure synchrotron sources is one of the main challenges in MRT today. With most research focusing on the modulation of the beam outside the accelerator close to the target area, accelerator-based electron beam modulation remains an open research question.

In summary, it can be concluded, that the high temporal or spatial structuring for both novel radiotherapy methods, FLASH RT and Microbeam RT, leads to an increased complexity in the diagnostics of the beam properties and the dose as well as in the generation. In addition to the capability to generate and diagnose beams for FLASH RT, also the beam dynamics under the extreme beam properties need to be investigated in great detail to understand and simulate the resulting effect on the beam properties on target.

State of the art: accelerators and collective effects

As discussed above, the requirements of new advanced radiotherapy methods on particle accelerators are high and current research on FLASH RT is consequently mainly performed on dedicated accelerator research facilities with a focus on electron accelerators. The additional advantage is the possibility to benefit from the flexibility in operation parameters, such as variable pulse length or intensity, and the higher degree in versatile instrumentation and diagnostics. This allows systematic studies and parameter mappings to assist the search for the best suitable parameter set for a widening of the therapeutic window. Furthermore, at current

RT accelerators, the diagnostic measures focus mainly on the dose detected after the accelerator. The wide range of fast and accurate diagnostics available and employed in research accelerators opens up access to fast and extensive information on the beam properties, such as charge, energy, position, pulse shape, and more. The proposed project will exploit this further than currently done to increase the extend of monitoring and control over the produced pulses [8] and to provide recommendations on the most suited, complementary diagnostics methods for RT.

In general, research accelerators cover a wide variety of different use-cases and machine types, with circular and linear accelerators (linac) being the most common types. Over all, the beam properties can range from continuous beams to bunched beams consisting of particle packages (bunches), from MeV to several GeV or for colliders even TeV beam energies, from artificially elongated bunches with very narrow transverse sizes and divergence (ultra-low emittance [25]) to wider but ultra-short bunches down to femtosecond pulse durations [26]. For electron accelerators, the electrons are either generated via thermionic emission or with a laser pulse on a photo-cathode. The latter case provides control over the pulse length as well as the transverse distribution of the generated initial electron bunch by modulating the incident laser pulse [27]. This offers further possibilities for studies of spatially structured pulses and the possibility for accelerator-based beam modulation of radiotherapy beams will be investigated within this project.

In a continuous effort, research accelerators are characterized to a higher and higher degree with regards to a wide variety of effects including complex contributions to the beam dynamics such as collective effects [13]. In general, the dynamics of accelerated particles is influenced by fields of different origin. External magnetic fields are applied for guiding and focusing the particle beams as well as external electromagnetic fields which are used for the basic acceleration itself but also for fast deflection in the context of diagnostics or for shaping the longitudinal charge distribution by so-called higher harmonic cavities resulting in complex shapes of the electromagnetic potentials. These dynamic boundary conditions lead to complex, non-linear dynamics of the accelerated particles. On top of this, self-generated electromagnetic fields act back on the particles and on the surrounding material. These self-interactions and interactions with the environment depend on the number and distribution of the particles within a bunch and are therefore often referred to as collective effects [28].

Each charged particle is surrounded by its electromagnetic field. The field interacts with all nearby materials such as a vacuum chamber, matter it passes through and also neighboring particles within the same bunch. These interactions can result in a force acting back on the charged particle leading to a change in movement direction or energy. The effective resistance that the charged particle experiences due to these interactions are described with frequency dependent impedances. Furthermore, in the same way one particle affects all neighboring particles, each particle is affected by the superposition of the fields of all other particles within the bunch. The resulting fields are referred to as wake fields and depend directly on the distribution of the charged particles in a bunch as well as on beam energy and the material properties of the surrounding structures. Both quantities are connected, as the impedance Z multiplied by the Fourier-transform of the charge distribution $\tilde{\rho}$ equals the Fourier-transform of the wake field V [28]: $V(t)=\int_{-\infty}^{\infty}\tilde{\rho}(f)Z(f)e^{i2\pi\cdot ft}df$ This equation also directly shows, that depending on the shape and length of the particle distribution, the overlap in frequency with the impedance changes and therefore affects the resulting strength of the self-generated electromagnetic field.

Collective effects cause various issues in accelerator beam dynamics, such as emittance growth, energy loss, beam instabilities, overall degradation of performance and deformation of the temporal and spatial shape of the particle bunch. The mitigation and control of these effects is an ongoing topic in accelerator physics and advanced models and algorithms are developed to predict the influence of collective effects on the particle beams throughout the entire system.
Collective effects have not been considered in the past in conventional accelerator-based RT due to the rather long pulses and therefore low momentary intensity and dose-rates. Furthermore, they are typically not included in calculations of the beam transport through matter often based on Monte Carlo or particle tracking. Common simulation tools include FLUKA [14], EGSnrc [15], BDSIM [16] or the KiT-RT (Kinetic Transport for radiation therapy) framework designed for easy extendibility [17]. The inclusion of collective effects into the beam-matter interaction calculations is going to be an important topic within this project. Examples of collective effects with potential relevance for RT beams include space charge wake fields [29], coherent synchrotron radiation (CSR) [30] and resistive wall wake fields [31] and are present in both circular and linear accelerators. The presence of these effects leads to instabilities like intra-beam scattering, the transverse mode-coupling instability [32], micro-wave instability [31] and the micro-bunching instability [33], all of which I have studied in electron storage rings in the past, as described in the following.

Preliminary work on beam dynamics, collective effects and diagnostics

In the last years, I have performed systematic studies of the longitudinal as well as transverse collective effects and instabilities influencing the electron bunch shape in all dimensions. The main goal of was to investigate phenomena occurring under extreme operation modes to understand and circumvent resulting performance limitations while contributing to the general advancement of the field. The conditions studied included high charge in single bunches, dedicated short bunch-length operation modes at the storage ring KARA [34] and small transverse bunch-size in the ultra-low emittance synchrotron light source MAX IV [31][32], all conditions prone to instabilities leading to dynamic sub-structures in the charge density of the particle bunches.
For the investigations, I conducted experimental studies as well as systematic simulations. My studies of the micro-bunching instability, which occurs at bunch lengths in the order of several picoseconds or less, showed for example, an additional region of instability for certain parameters at lower bunch charge as predicted by the text-book equations [34]. To perform the theoretical calculations, I used the Vlasov-Fokker-Planck solver Inovesa [35], which simulates the longitudinal dynamics under the influence of the coherent synchrotron radiation impedance. To this end, the particle density distribution in the longitudinal phase space is calculated via the Vlasov-Fokker-Planck equation for each time step. I was involved in the scientific conceptualization of the code as well as testing the software and extensive benchmarking against measurements to assess the correctness of the results. Later, I extended the simulation to also include the influence of the geometric and resistive-wall impedance for studies of the micro-wave instability at MAX IV [31]. With these simulations I could very well reproduce the deformations in the longitudinal bunch shape observed experimentally (see Figure 2). This

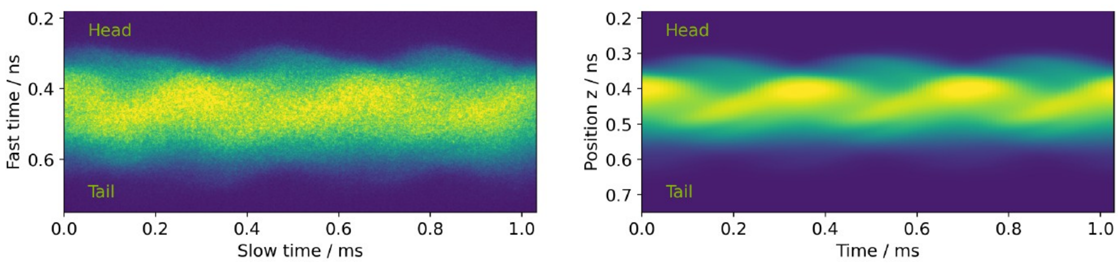

Figure 2: *Measurement (left) and simulation (right) of the longitudinal bunch profile on the vertical axis and the temporal evolution on the horizontal axis.*

again proved the potential of Inovesa to simulate the temporal development of the particle density distribution under the influence of collective effects caused by different types of impedances. Another simulation method capable of calculating the development of a particle bunch under the influence of collective effects is particle tracking, where the individual particle paths are calculated opposed to the particle density in Inovesa. Using the particle tracking tool mbtrack2, I could recently show in simulations as well as in measurements, [40], that for certain settings in the accelerator's magnetic lattice, a single-particle dynamics effect can be used to reduce the impact of the collective effect underlying the transverse mode-coupling instability [32]. This instability is caused by transverse wake fields and is known to lead to drastic beam blow ups resulting in complete loss of the particles. The capability to prevent the resulting particle loss reveals possible ways of combating this instability in future low-emittance electron storage rings. Both simulation methods, particle tracking as well as phase-space density propagation employing the Vlasov-Fokker-Planck equation, are possible options to be explored for the planned calculations of the collective effect influence during the beam transport through matter. Furthermore, there have been efforts in the past at CERN, to calculate beam-matter interaction using covariance matrices [41], which are a common tool used to transport beam properties along the accelerator and also a viable starting point.

Another important aspect in the investigation of collective effects are systematic measurements with a sufficiently high temporal resolution to resolve the resulting dynamics, be it separating the consecutive revolutions of a bunch in a ring based accelerator or resolving the shot to shot differences between consecutive bunches in a linear accelerator. I was part of the team that developed a new ultra-fast readout system, to study the influence of the micro-bunching instability on the emitted CSR and the deformation of the longitudinal bunch shape [36]. The system enabled time-resolved measurements of the CSR intensity emitted by each bunch at every revolution in the synchrotron [37], as well as the synchronization with an electro-optical bunch-profile monitor. The resulting synchronized measurements, together with my simulations using Inovesa, provided further insight, with a high temporal resolution, into the formation of sub-structures in the longitudinal bunch shape causing the observed fluctuations in the emitted CSR [38]. Based on my work, a feedback system has been designed at KIT with the goal to mitigate and control the micro-bunching instability [39]. My experience with the development of the fast readout system as well as the utilization of multiple fast beam diagnostic systems and detectors, such as fast beam current transformers for time resolved charge measurements, beam position monitors, fluorescence screens, fast photo diodes, THz sensitive Schottky diode detectors and more complex systems such as electro-optical bunch profile monitors [42], and synchrotron radiation monitors will be a great basis for the proposed experiments.

The extensive research conducted in the field of accelerator physics today aims for a deep understanding of the involved beam dynamics and collective effects especially in beams under extreme conditions, like short bunch lengths or high intensities and the diagnostics thereof. At the same time, with RT moving to beams with high temporal or spatial structuring for novel methods including FLASH RT or MRT, this research becomes more and more relevant, laying out the program for the proposed project.

Open questions and challenges

In the context of the accelerator-based advanced radiotherapy methods, FLASH RT and Microbeam RT, some of the most pressing open questions and challenges are listed below:

- With the FLASH effect not yet fully understood, the optimal dose and dose-rate parameters are still to be determined. This give rise to the need for flexibility in accelerator parameters to investigate and systematically study the physical limitations on the possible generated beam properties.

- In FLASH and Microbeam RT the accurate knowledge of the beam properties, such as dose distribution on target, is critical, but at the moment limited by the following points.
    - The ultra-high dose-rates result in a non-linear dependence in the dosimetry standards.
    - Time resolved diagnostics to determine the shot to shot accuracy are required due to small number of high dose pulses.
    - High dose-rate, corresponding to high particle densities, increase the expected influence of collective effects on the beam dynamics during generation.
    - Furthermore, the influence of collective effects during the beam transport through matter needs to be investigated to understand the resulting limitations as well as the deformation of the resulting dose distribution.
- Investigations are to be conducted of the possibilities and opportunities that accelerator-based modulation of electron beams could provide.

In general, a sound understanding of the effects involved in the dynamics of temporally and spatially structured RT beams is required for the generation, the propagation as well as the detection of the resulting high dose-rate pulses. Identifying the contributing collective effects and shedding more light onto their deforming influence is therefore crucial to accurately predict the particle, and therefore dose distribution on target.