Project Description – Emmy Noether Programme

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

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Project Description

1 Starting Point

State of the art and preliminary work

Radiotherapy (RT) has been continuously a very valuable tool in cancer treatment [1] and with the significant advances in the field in over the years, RT promises to contribute even more towards a successful and well tolerable treatment of cancer by reducing side effects while maintaining or even enhancing treatment efficacy in the future and improving the quality of life of the patients.

In Europe, radiotherapy is recommended as part of the treatment plan for around 50% of cancer patients [2]. Scientific and technological advances in a broad spectrum of scientific disciplines are an important cornerstone for developments in radiotherapy due to the high performance requirements on the used technologies. Radiotherapy uses ionizing radiation to damage the DNA within the tumor cells, which prevents the cells from reproducing and eventually leads to their death. One common approach employs high-energy beams of particles or X-rays to irradiate the cancer cells and shrink or destroy the tumors. This non-invasive, targeted approach focuses on delivering a precise and targeted dose of ionizing radiation directly to the affected area, minimizing damage to healthy tissues while effectively treating the selected area. As still small areas of healthy tissue are irradiated in order to ensure the treatment of all cancerous cells, an accurate control of the dose rate is required 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 tissues and organs is called the therapeutic window [3]. In conventional radiotherapy, this requires a carefully balancing of the number of fractions (dose sessions) and the dose per fraction to achieve optimal results and avoiding excessive harm to nearby healthy tissues. A widening of this window is one of the main goals of radiotherapy research.

The external beam radiotherapy (EBRT) is based on particle accelerators to produce the high-energy beams, which can range from X-rays over electrons and protons to helium and carbon ions. The different beam types offer different advantages in their interaction with matter. Photon (x-ray) radiotherapy is the most common form and has been widely studied. More than 90% of radiotherapy patients receive high-energy X-rays produced by bremsstrahlung of electrons accelerated in linear accelerators. The direct usage of electrons is limited to more superficial treatments as they only penetrate a few centimeters into tissue before losing energy. This makes electron radiotherapy particularly suitable for treating superficial or shallow tumors such as skin or lymphoma cancer, while sparing deeper organs. Heavier particles like protons or ions deposit most of their energy immediately before the end of their path through the tissue (Bragg peak), resulting in reduced damage to healthy tissues before and beyond the target area. The requirements on stability and reproducibility of the accelerators providing the radiation beams are very high to ensure that the dose applied to the patient is within 5% of the prescribed treatment dose, requiring a deviation in reference dose of less than 1% for dose absorbed to water. Therefore, precise calibration and dosimetry measurements are required and national standards are defined. For conventional RT, the primary standards have been defined by several national metrology institutions. For conventional MeV electron beams the Fricke dosimetry method is used as primary standard for absorbed dose to water [4]. For proton therapy dosimetry, graphite calorimeters have been well established as primary standard level instruments [5]. Advancements and new concepts of treatment and beam modalities in radiotherapy lead to increasing requirements on dosimetry as well as on the diagnostics and understanding of the beam dynamics in the accelerators used for beam generation. Especially for new approaches including temporally or spatially modulated beams, new effects might need to be considered in the examination and simulation of the beams and their generation. Two advanced approaches to radiotherapy have received considerable attention in the last years and are being investigated in preclinical trials.

FLASH radiotherapy

FLASH RT is a novel approach which focuses on delivering very high doses in an comparably short time frame, typically within milliseconds or less. This technique exploits the unique properties of such short pulses to enhance tumor cell killing while minimizing damage to surrounding healthy tissues. 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 were observed to be effective in combination of pulse trains shorter than 500 ms and a total dose of 10 Gy or more [3]. The observed advantage of FLASH radiotherapy is the significant shift of normal tissue complication probability (NTCP) to higher doses for the very high dose-rates while the tumor control probability (TCP) remains unchanged (see Figure 1). This significant widening of the therapeutic window allows to apply higher dose per fraction than in conventional radiation therapy without causing severe side effects, such as acute normal tissue reactions or long-term complications. Preclinical studies report evidence for a radio-protective effect in healthy tissue during FLASH RT. One suspected underlying mechanism involves the generation of reactive oxygen species (ROS) within tumor cells, which increases the damage taken from high doses of ionizing radiation, while the short pulse duration

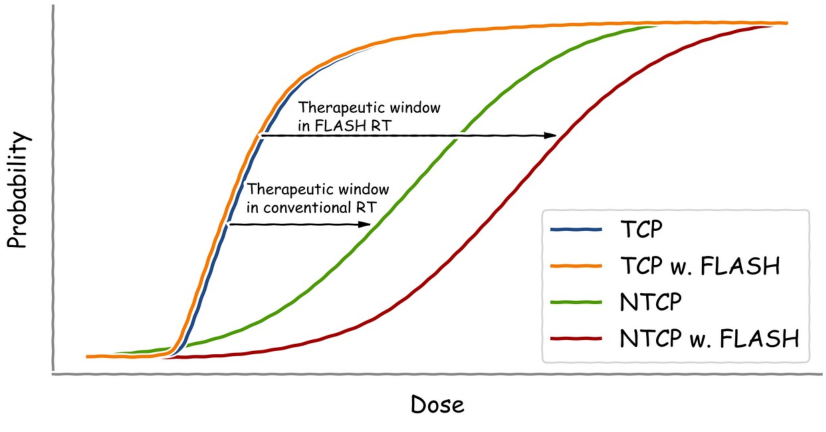

Figure 1: *Sketch of the therapeutic window increasing as normal tissue complication probability (NTCP) is shifted to higher dose for FLASH RT and tumor control probability (TCP) remains.*

in FLASH is hypothesized to allows for a rapid intracellular oxygen depletion resulting in a minimal ROS production in normal tissue, reducing the risk of side effects and enhancing treatment tolerance. Other mechanisms under study investigate the effects of FLASH pulses on DNA damage response, and immunoreaction [6]. While the exact mechanisms behind the beneficial FLASH effect are not yet fully understood, the effect has been experimentally demonstrated to occur for irradiation with photons, electrons and ions. This gives hope that the normal tissue sparing effects could be generally applied and may lead to improved treatment outcomes and reduced overall toxicity for patients with various types of cancer. Furthermore, the reduction in irradiation duration and in necessary repeat treatments could lead to an increase in the total number of patients treated. For this to become possible, several open questions and challenges need to be addressed in addition to further medical research on the optimal parameters such as pulse duration, intensity and energy [6].

One of the main reasons for the many challenges in translating FLASH RT to clinical application is the combination of short pulses and high intensities leading to extreme conditions and phenomena. In the same ways, the positive effect FLASH has on the biological processes differs from the effect of conventional RT requiring further investigation, the FLASH pulses also affect the detection mechanisms of diagnostics as well. The high dose combined with the short pulse makes dose measurements difficult, as different typical dosimetry technics have shown deviations from the required linear detection efficiency [7]. So is, for example, the primary standard of dose absorbed to water via Fricke dosimetry nearly independent on does rate up to approximately 2 Gy per pulse, which while sufficient for conventional electron RT is exceeded under FLASH conditions. This makes the primary standards for dosimetry in conventional RT not directly applicable and forces the definition of new standards. 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 included further investigations of ion-recombination in ionization chambers having an increased effect due to the high dose-rates and extreme time structure of FLASH pulses including improved ways to calculate the recombination correction factors normally used to correct for ion-recombination effects [9], [10]. In addition, systematic tests of possible, alternative detection mechanisms such as solid-state calorimeters and small-volume and active dosimeters have been conducted [7], [11]. Active detectors and real-time diagnostics become as well increasingly relevant 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 pose per pulse are no longer averaged out.

Furthermore, for most standard medical accelerators these beam conditions are challenging to impossible to achieve, requiring substantial improvement or the development of new dedicated FLASH accelerators [12]. Laser-driven particle acceleration based on the use of intense, ultra-short laser pulses could be interesting compact sources for high energy FLASH RT for electrons as well as ions [8]. In the mean time, for development and experiments, dedicated accelerator facilities with compatible beam conditions are a possible test-bed for per-clinical research. In addition to the capability to generate beams for FLASH RT, also the diagnostic and simulation for these types of beams needs to be adjusted and brought up to the high accuracy level necessary for clinical application. At current RT accelerators, diagnostic mostly focuses on the beam after the accelerator. The wide range of fast and accurate accelerator diagnostics available and employed in research accelerators could be exploited further than currently done to increase the extend of monitoring and control over the produced pulses [8].

In general, a sound understanding of the effects involved in the challenging short-pulse dynamics of photons, electron and ions is required for the detection but also the generation and propagation of these short, intense microsecond down to femtosecond pulses. In accelerator physics, the study of dynamics in short pulses is an ongoing topic including effects caused by self-induced electromagnetic fields, causing interaction among the charged beam particles through space charge forces and the excitation of wake fields in the surrounding structures [13]. As theses collective effects describe the interaction between the particles in the beam, they become more and more relevant for increasingly extreme beam properties, such as decreasing pulse length and increasing pulse intensity, as well as in spatial structuring of the beam. They 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 and are typically not included in beam transport through matter calculations with typical simulation tools, often employing Monte Carlo or particle tracking, such as FLUKA [14], EGSnrc [15], BDSIM [16] or the KiT-RT (Kinetic Transport for radiation therapy) framework designed for easy extendibility [17].

Radiotherapy with spatially structured beams

While in FLASH RT the radiation beam is structured longitudinally in short pulses there are also application in RT with spatially structured beams. This equally leads to an increased complexity in the dynamics as well as diagnostics of the beam and dose. One such an approach to RT actively discussed is Microbeam Radiotherapy (MRT). MRT employs spatially fractionated beams and is based on the clinical experience of GRID radiotherapy. The spatial intensity modulation at the micrometer scale has been recognized to have the potential to reduce normal tissue damage [18]. 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 beams in the array of parallel microbeams. Earlier studies with electron GRID radiotherapy have investigated the potential use of electron beams, with centimeter sized grid blocks and a naturally limited penetration depth of the MeV electrons [19]. Recent approaches with protons showed similarly promising results in the sparing of healthy tissue [20]. It was assumed, even so the microbeams spread out in the normal tissue that they stay separated, providing the normal tissue sparing effect, until they reach the tumor where they achieve a homogeneous dose distribution leaving the tumor response unaffected. Most studies on MRT have been conducted with X-rays and microbeam spot sizes of 25 - 100 µm and a spot spacing of 50 - 200 µm. The unidirectional microbeams are mainly produced by inserting a multi-slit collimator into an x-ray beam with very small divergence produced at a 3rd generation light source [21]. One of the main challenge for the clinical utility of MRT are the requirements on the source. X-rays MRT currently relies on large infrastructure synchrotron sources not fully optimized for patient treatment. It is mainly applied at Brookhaven National Laboratory (US), ESRF in Grenoble (France) and the Australian National Synchrotron in Melbourne [18]. MRT could profit from the development of FLASH capable radiotherapy sources as these would be able to achieve the high doses and does rates needed.

An application of radiotherapy with spatially structured beam that is already used in clinical treatment is Electron Conformal Therapy (ECT) [22]. Here, the electron beam is shaped and modulated either in energy or intensity by specialized devices such as multi-leaf collimators, a mask or bolus to match the three-dimensional shape of the tumor and to accommodate for uneven patient surfaces. This allows a precise targeting of the tumor and minimizes exposure to the surrounding healthy tissue. ECT can also be used to achieve an dose distribution as homogeneous as possible. The methods and tools used for modulation are an active field of research. Modulation based on scanning the beam over the target area or by superpositions of several different beam energies are two of the applied possibility as well. Most research focuses on the modulation of the beam outside the accelerator close to the target area which leaves accelerator based modulation an open question.

Particle accelerators, beam dynamics and collective effects

As discussed above, the requirements of new advanced radiotherapy methods on particle accelerators are higher and more complex than most of the currently used standard medical accelerators can fulfill [23]. As medical accelerators need to be robust and reliably to run continuously without to much maintenance in the day to day operation, they are custom tailored to the specific application. Therefore, they typically do not provide the flexibility and a big enough parameter range to study new treatment methods based on different beam properties. Most research on FLASH RT with electrons is consequently done on a few modified medical accelerators or on dedicated research accelerator facilities. Similarly, most studies on Microbeam RT are done on high brilliance synchrotron light sources [18]. The advantage in employing research accelerators is the possibility to benefit from the flexibility in operation parameters and the higher degree in versatile instrumentation and diagnostics. This allows the systematic study and mapping of the best suitable parameter ranges and diagnostic for the new RT method under development before being implemented in a clinical setting.

Research accelerators cover a wide variety of different use-cases and machine types. Circular accelerators where particles can be stored and used for the production of synchrotron radiation and linear accelerators (linac) where the particles are only propagated once through the accelerator and then used for example directly as high energy particle beam are the most common types. A more recently developed accelerator type are plasma accelerators. Where a plasma is used to generate an ultra-high acceleration gradient up to 100 GeV/m using various plasma wave drivers such as for example pulses from a high-brightness laser with a power up to petawatt [24]. In general, most accelerators operate with electrons or protons but also dedicated machines for different ions exist. The beam properties 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 explicitly 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 later 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 could open up the possibility for accelerator based beam modulation of radiotherapy beams.

In a continuous effort, research accelerators are characterized to a higher and higher degree with regards to a wide variety of effects including complex contribution to the beam dynamics such as collective effects which become more and more relevant with the push towards more extreme beam parameters such as short, high intensity pulses or spatially structured beams. Besides the magnetic fields for guidance and focusing of the particle beams also electric fields are used to interact with the particles, for one for the basic acceleration itself but also for fast deflection in the context of diagnostics or for shaping the longitudinal charge distribution within the particle bunch by so-called higher harmonic cavities. All these external influences lead to complex dynamics of the accelerated particles, which can be described and simulated for each particle individually, and are therefore referred to as single-particle dynamics. Additionally to the externally applied fields, also self-generated electromagnetic fields act back on the particles and on the surrounding materials. 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 is referred to as impedance. 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 beam energy and the material properties of the surrounding structures. Both quantities are connected, as the impedance multiplied by the Fourier-transform of the charge distribution results in the Fourier-transform of the wake field [28]. Impedances can 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. To avoid, mitigate or control these effects advanced models and optimization algorithms are developed to predict the influence of collective effects in the particle beams throughout the entire system.

Typical examples of collective effects include space charge wake fields [29], coherent synchrotron radiation (CSR) [30] and restive 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]. The investigation of these effects is ongoing and pushes for the understanding and control of the effects in beams with ever increasing complexity and extreme parameters such as increasingly shorter bunch length or ultra-low transverse emittances and always combined with high intensities. To this effort, I have contributed with 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 my studies was to investigate the phenomena occurring under extreme operation modes, such as high charge in single bunches, dedicated short bunch-length operation modes at the storage ring KARA [34], small transverse bunch-size in the ultra-low emittance synchrotron light source MAX IV [31][32], all resulting in 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. So showed studies of the micro-bunching instability which occurs at bunch length in the order of several picoseconds or less, for example, an additional region of instability for certain parameters at lower bunch charge as predicted by the text-book equations [34]. To perform 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. 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 include also the influence of the geometric and resistive-wall impedance for studies of a longitudinal 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), which allowed the identification of the instability as

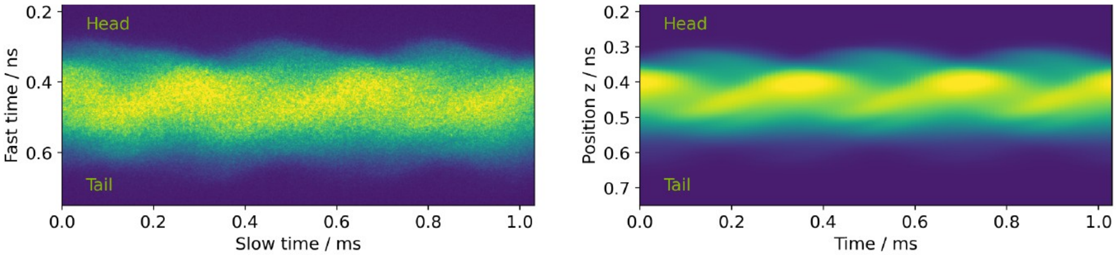

Figure 2: *Measurement (left) and simulation (right) of the longitudinal bunch profile on the vertical axis and the temporal evolution on the horizontal axis.*

micro-wave instability. This also proved the potential of Inovesa to simulated different types of longitudinal instabilities caused by impedances.
Another important aspect in the investigation of collective effects are systematic measurements with a sufficiently high temporal resolution to resolve the resulting dynamic, 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. To study the influence of micro-bunching instability on the emitted CSR and the deformation of the longitudinal bunch shape, I cooperated with the electronics institute IPE (KIT) on the development of a new ultra-fast readout system [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 synchronized measurements provided high resolution measurements giving further insight 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]. Recently, I could show experimentally as well as in simulations, 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 know 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.
The extensive research conducted in the field of accelerator physics today provides 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 method including FLASH RT or MRT, this knowledge becomes more and more relevant. It is therefore the perfect moment to bring these fields together. Accelerator based RT can profit from this knowledge transfer in multiple ways such as in the generation of these extreme beam properties as well as for the evaluation of suitable beam and dose diagnostics which fulfill the high requirements. Last but not least, accelerator based RT can gain from extending the consideration of collective effects beyond the accelerator towards the beam transport through matter. To this end, accelerator research can provide experience with a multitude of tested simulation methods to propagate self-interacting particle beams. With these connections the foundation is laid for the research proposed within this project.

2 Objectives and work programme

2.1 Anticipated total duration of the project

The project is anticipated to run for a total duration of six years consisting of two funding periods (36 + 36 months) in accordance with the Emmy Noether program structure.

2.2 Objectives

The present advances in accelerator based RT, like FLASH RT or Microbeam RT, lead to operation parameters of the used accelerators that can no longer be described by simple linear optics and beam dynamics. In fact, due to the development towards higher intensity combined with shorter pulse lengths and transverse modulations, the consideration of non-linear and complex beam dynamics influenced by collective effects becomes necessary for accelerator RT sources. Not only during the generation in the accelerator but also for the diagnostics and dosimetry as well as for the beam matter interaction on the way to the target the effect of these extreme pulse properties need to be systematically investigated. Further bringing together accelerator science and medical physics through this project is a crucial step and will aid in paving the way towards accurate and predictable generation, diagnostic and metrology of advanced radiotherapy beams based on particle accelerators.

The extreme pulse properties affect many of the open questions to be answered before bringing FLASH and Microbeam RT to clinical use. The high dose-rates achieved by the temporally or spatially structured beams have a strong effect on the underlying mechanisms: from the improved biological interaction with healthy tissue being the main advantage and driving point, to the increased non-linearity in dosimetric measurements, high requirements in beam based diagnostics, and the presence of complex dynamics and self-interaction leading to collective effects in the accelerator generated particle beams. The latter have yet to be investigated in connection with radiotherapy. Thinking further, collective effects acting on the beam can lead to significant deformations of the charge distribution and therefore of the produced dose distribution, resulting in the need for mitigation or compensation and ideally shaping of the generated RT pulse. Which, under certain conditions, might be extendable to generate modulated beams for Microbeam RT and Electron Conformal Therapy directly in the accelerator.

The main goal of the proposed project is to improve the access to information about radiotherapy beam properties and the resulting deposited dose on target as well as control thereof in an effort to bringing these new radiotherapy modalities with more extreme beam parameters closer to clinical application.

To this end, the following four objectives are selected:

I. Increased predictability of RT beam properties on target by development of start-to-end simulation including collective effects

II. Improved insight into the influence of temporal or spatial pulse modulation on detection and diagnostics to ease selection of suitable methods

III. Exploring the possibilities and limitations of accelerator based pulse shaping and modulation

IV. Investigating possible methods and algorithms for calculating the required initial beam distribution from a desired beam shape on target

These objectives will be achieved by investigating the influence of collective effects on the beam generation, beam transport, beam-matter interaction and diagnostics in novel electron radiotherapy methods with temporally and spatially structured beams. Therefore, different interactions of beam particles with one another, described as collective effects, will be considered and incorporated into theoretical calculations and simulations of the transport of the particle beam from start-to-end, not only within the accelerator but also extended to the transport through matter (e.g. air or water). Furthermore, systematic studies on the dependence of different detection mechanisms and diagnostic tools on temporal and spatial pulse shapes combined with varying intensity will give insight into which diagnostic tools are suitable to aid in reliably delivering the desired conditions. The investigation on the possibility to modulate the beam in the accelerator will pursue and compare different methods which could provide different temporal and spacial modulations. It will also entail studies on which modulations can be achieved on the final target when taking the transport through matter into consideration. Employing the improved and extended simulation (from the first objective) to predict the resulting distribution on the target, might allow to consider the effects of the beam transport already during the generation of the beam. And if successful, this could enable the generation of a temporal and spatial particle distribution which preemptively compensates for the deformation expected during the propagation of the particle distribution from generation to the target. As a result, it would become possible to generate (within certain parameter limits) user-definable final particle distributions on the target.

2.3 Work programme incl. proposed research methods

To achieve the objectives of the project, the work program is structured in the following work packages **A**-**C**:

- **A** Complex beam dynamics and collective effects
    1. Beam dynamics and collective effects in accelerator based generation of short or spatially structured RT beams
    2. Beam-matter interaction for high intensity, temporally and spatially structured pulses
    3. Start-to-end simulation including beam dynamics and beam-matter interaction
- **B** Systematic investigation on temporal and spatial pulse shape dependence of detection mechanisms and diagnostic tools
    1. Accelerator beam diagnostics
    2. Dose and dose-rate diagnostics (Dosimetry)
    3. Feasibility of accelerator beam diagnostics outside vacuum
- **C** Beam modulation and beam shaping
    1. Exploration of methods for temporal and spatial shaping of pulses
    2. Evolution of shaped pulses during transport to target
    3. Investigation of methods and limitations to generate custom dose distributions on target

WP A: As new, advanced radiotherapy modalities rely on high intensity, short or spatially structured particle beams, the influence of interactions between the beam particles will be increased compared to conventional radiotherapy. Work package **A** will study the influence of these collective effects on the beam in the accelerator as well as on the beam transport through matter onto the irradiation target. Sub-work package **A1** will focus on the resulting beam dynamics during the beam generation in the accelerator by, firstly, conducting a case study of the influence of collective effects during the beam generation for FLASH and Microbeam RT in proposed, dedicated accelerators (WP **A1a**). Established accelerator simulation tools, such as ASTRA, AT or Ocelott will be as each has a different set of collective effects included. WP **A1b** will use the linear accelerator FLUTE at KIT as a testbed and compare measurements and simulations of different beam parameters resembling the desired RT beam properties. The second sub-work package (WP **A2**) will focus on the influence the extreme beam properties (high intensity, temporally and spatially structured) have on the beam-matter interaction on the way from the accelerator to the target tissue inside the patient. In WP **A2a** the existing models and simulation tools used in beam transport trough matter will be reviewed and in WP **A2b** simulations with a variety of possible beams properties generated by FLUTE will be conducted with codes commonly employed in radiotherapy settings, like BDSIM (Geant4), EGSnrc, FLUKA and the new KiT-RT framework. WP **A2c** will investigate, in the context of beam-matter interaction, how different possible interactions between the beam particles themselves affect the passage through matter. To this end, collective effects known from accelerator physics, such as space charge, intra-beam scattering, transition or coherent synchrotron radiation effects and ion- or electron cloud effects (depending on the beam particle type) are evaluated and their relevance depending on beam properties estimated. As next step, in WP **A3**, the effects will be incorporated into the calculations for the beam transport through matter and combined with simulations of the dynamics in the accelerator to create a start-to-end simulation tool. Multiple option on how the different simulation and calculations are to be combined will be evaluated, in order to find the best implementation method for beam propagation simulation through the accelerator and matter interactions not only for single particles but also taking into account collective effects. Possible methods include Monte Carlo simulations, particle tracking, phase-space density propagation and the application of covariance matrices.

WP B: The extreme beam properties not only affect the beam propagation but also increase the complexity of applicable detection mechanisms and diagnostic tools. WP **B1** will focus on accelerator based beam diagnostic, such as fast beam current transformers, beam position monitors, fluorescence screens and more complex systems such as electro-optical bunch monitors [40], synchrotron or transition radiation monitors among other, with regards to their suitability for and ability to detect high intensity, temporally and spatially structured particle bunches with a high accuracy. Experimental tests are planed in WP **B1a** and can be compared with simulations from WP A1b. This will give input for the assessment in WP **B1b** on the potential of different diagnostic methods as support for RT beam diagnostics with shot to shot resolution and the required adequate resolution and stability for medical applications. Work package **B2** will focus on the effect the high dose rate generated by short beam pulses has on the dosimetry detectors. In WP **B2a**, the ultra-short electron pulses from FLUTE and the ultra-short photon pulses generated at the KIT synchrotron light source with the electron storage ring KARA can be used for experimental tests of different dosimetry methods and their dependence on beam properties such as pulse length, intensity, transverse size and energy. As starting point an advanced Markus chamber and the newly-developed flash-diamond detector [11] will be tested towards the dependence on pulse length. Based on these measurements, also the recent developments of improved theoretical dosimetry correction factors for ion-recombination [9], [10] can be with the ultra-short pulses (WP **B2b**). And work package **B2c** will investigate possibilities for measuring a 2-dimensional dose distribution. For tests of the spatial resolution, the electron beam at FLUTE could be modulated, for example, by using collimators or potentially a mask at the accelerator exit. Furthermore, to measure the 2-dimensional particle distribution, typical accelerator diagnostics such as fluorescence screens for profile monitors will be assess for application outside the accelerator vacuum in WP **B3** as preparation for WP **C**. In this context also detector test of new detector types under development at KIT, for example radiation hard CMOS-pixel detectors [41], could be incorporated.

WP C: This work package aims to understand the physical and theoretical limits of accelerator based beam modulation and shaping for the application in radiotherapy. The first step (WP **C1**) will be exploring different methods for temporal and spatial manipulation of the beam shape. This will be based, firstly, on simulations exploring options more broadly for different possible accelerator types operating as RT sources. One general option would be, for example, to employ the accelerator focusing magnets to modify the bunch shape (WP **C1a**), by over-focusing the beam at the accelerator exit. Secondly, in WP **C1b**, the possibility on modulations of the source distribution, will be experimentally tested by modulating the gun laser spot on the electron-gun with the spatial light modulator set-up a FLUTE [27]. The second step (WP **C2**) includes then the investigation of the evolution of the modulated bunch shape during the transport through the accelerator and through matter on to the target. The investigation of the bunch shape evolution will consist of simulations (WP **C2a**) based on the results in work package **A**, which can then be compared with experimental measurements in WP **C2b**, using the diagnostics tested in WP **B**. WP **C3**, will then investigate how and to what extend it is possible to generate a custom particle distribution and through this dose distribution on target tissue. To this end, WP C3a, will examine possible methods and algorithms for calculating based on a desired final distributions, the required, corresponding initial particle distribution in the accelerator. As this work will build on the work from work package **A3**, especially on the designed start-to-end simulation, the optimal methods will likely depend on the method depend on the algorithm chosen in WP **A3**. Several possible methods can be imagined, ranging from systematically mapping final distributions for a wide variety of initial distributions resulting in a type of catalog, over the analytical or numerical inversion of the transport matrix described in form of covariance matrices, up to employing machine learning algorithms trained on arbitrary bunch shapes propagate through the start-to-end simulation. When this connection between the final and the initial distribution is established, it can be combined with the beam modulation methods established in WP **C1.** WP **C3b** will, as a first step, employ this to compensate the effect the beam transport has in the pulse shape by considering these deformations already during the beam generation. And in WP **C3c** the capability of this method will be tested and the limits in the achievable distributions on target will be explored.

The work of this project will be distributed as follows onto the planned group members with the time schedule shown in the gantt graph below (Figure 3.):
Doctoral student (PhD 1) (starting between month 1 and 6, 3 years duration)
Research topic: Experimental study of the influence of advanced radiotherapy beam properties such as short bunch length, charge, energy and transverse size on accelerator beam dynamics, diagnostics and detected dose
The research will mainly focus on experimental measurements of the effects of extreme beam properties at the linear accelerator FLUTE accompanied by supporting simulations and will contribute to work packages A1b, A2b, B1 and B2a.
Postdoctoral researcher (Postdoc) (starting month 13, 2 year duration)
Research topic: Establishing start-to-end simulation for beam transport of accelerator generated novel RT beams
This will entail exploring methods to propagate structured beams through the accelerator as well as through matter, including not only single particle to matter interactions but also considering collective effects during the beam transport through matter. The research will include the work on WP A2a+c and will be the main contributor for WP A3.
Master student (Master 1) (starting month 31, 1 year duration)
Research topic: Measurements of 2D particle and dose distribution of structured accelerator beam for RT
The experimental work will include the set-up of 2D diagnostics and dose distribution measurements for initial experimental tests of possible beam modulation methods. The work will be based on WP B1+B2. It will cover WP B2c+B3a and involved in the initial steps of WP C1+C2.
Doctoral student (PhD 2) (starting between month 31, 3 years duration):
Research topic: Investigation of methods and algorithms for custom accelerator based beam modulation towards advance radiotherapy
The main focus will be the theoretic work on a solution for WP C3a by finding a exploitable connection between the final particle distribution and the corresponding initial distribution. Therefore the research will build on the start-to-end simulation from WP A3. The work will furthermore contribute to the simulation based tests while also closely collaborating on the experimental tests in WP3b+3c.
Master student (Master 2) (starting month 60, 1 year duration)

Research topic: Experimental tests of targeted beam modulation and pulse shaping for accelerator based radiotherapy

This work will be directly based on the outcome of WP C3a and will perform the experimental prof-of-principle measurements in WP3b+c.

Group leader (6 years):

As group leader, I will be involved in all work packages as a discussion partner and supervisor, and would furthermore take on the following work packages partially or fully:

A1a, A2a (partially), A2c (partially), B1b (partially), B1c (partially), B2b, C1a, C1b (partially), C2a, C2b (partially), C3b (partially).

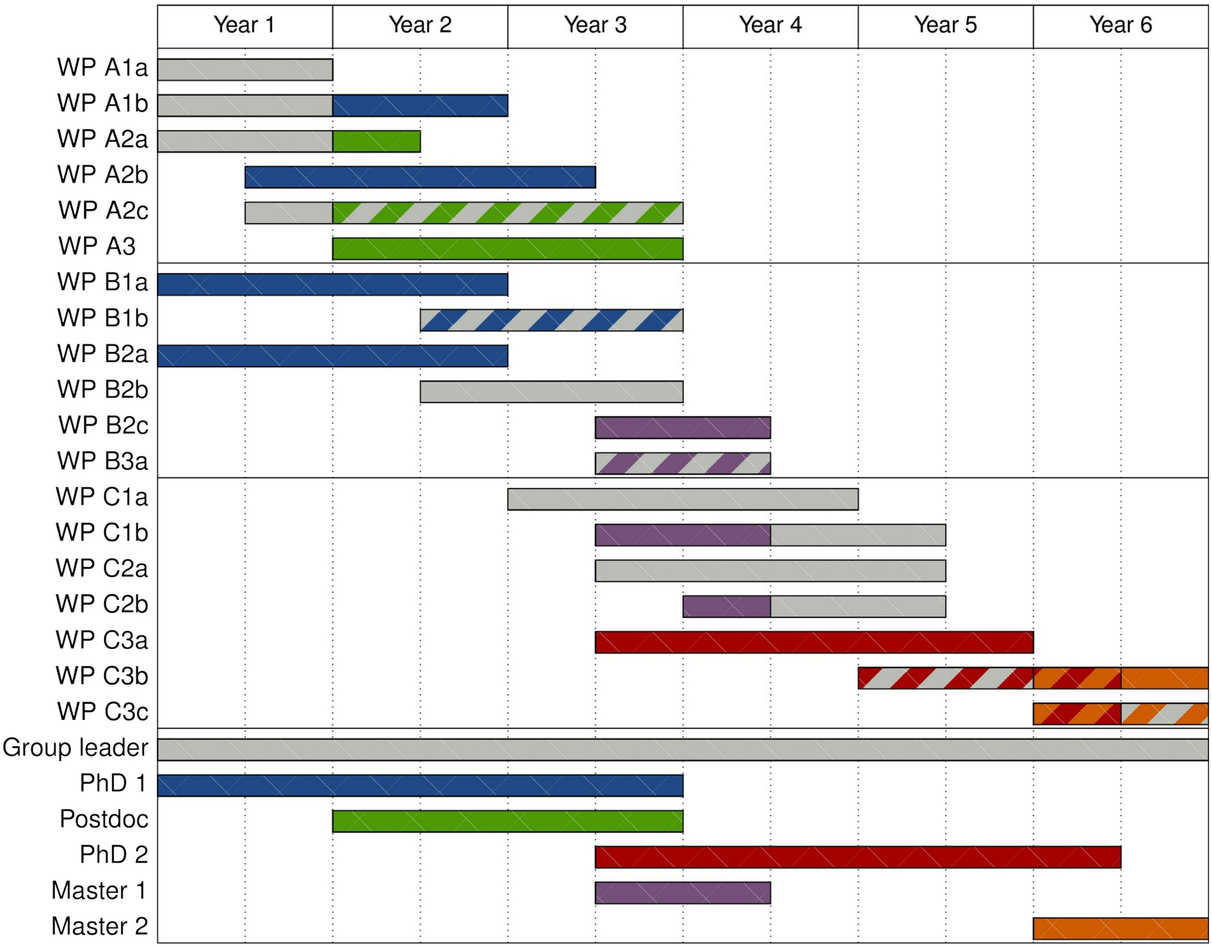

Figure 3: *Time plan showing the individual work packages colorcoded by responsible team member as well as the time frame of each team members within the project.*

2.4 Handling of research data

The research data produced in this project will cover a wide variety of data types, sizes and formats. Measurement data will originate from the multitude of accelerator beam diagnostic system such as charge measurement, beam position information, transversal bunch profiles monitors or gun laser parameters, as well as from dose measurements in the water phantom. Estimating the total amount of measurement data to be generated over the course of the 6 year project duration results in several TBytes due to the multitude of diagnostics continuously running during the accelerator experiments combined with systematic parameter scans including imaging data from 2D profile measurements. Simulation will be conducted with multiple existing simulation tools like EGSnrc, FLUKA, ASTRA or Ocelott. Furthermore, results from theoretical calculations such as self implemented simulation tools are expected and will contribute to the resulting research data as well as the developed software tools themselves. Due to the use of particle tracking simulation tools and the possibility to run simulations on a HPC cluster, the estimated amount of simulation data is also in the range of several TBytes.

The file formats will depend on the diagnostic systems or simulation tools and can range from for example TXT, PNG, JSON or CSV to proprietary file formats such as MAT (Matlab) or custom binary file-formats. If the original format is not easily accessible and/or additional metadata should be saved with the original data, the data will be transferred into files of the hdf5 file-format (Hierarchical Data Format version 5). In the past, I have used the hdf5 file-format extensively and it has proven to be very useful to store complex data, as it is accessible with a wide variety of programming languages (e.g. Python, Matlab, C++) and provides the possibility for internal structuring the stored data in groups, multi-dimensional datasets and amend each substructure with attributes. This allows the collection of connected data, such as the output of different diagnostic tools during one experiment, as well as the addition of metadata. In this way all the information from different sources needed to evaluate measurement results including information about the used instrument types, configuration and settings and furthermore operational parameters of the accelerator. The same principle can be applied to data resulting from calculations and simulations. In this case, it is possible to for example save different derived properties of the simulation output additionally to the simulation results or combine output given in multiple files into one. And furthermore, to keep the context of the simulation and improve the re-usability, all the simulation input parameters and settings can be stored as metadata in the attributes of the hdf5-files. Also in cases, where the stored data is not in SI units conversion factors can be included in the metadata. In cases where the read-out software or the simulation tool will be programmed from scratch, the hdf5 file-format will be used directly.

A consistent filename convention will be implemented including the date (in the human readable date format ISO8601), a short name for the detector respective the simulation tool, and further information. Additional information relevant for later analysis or re-use of the data will be, as mentioned earlier, saved as metadata, either live during the measurement, for example, by reading accelerator parameters provided online from the accelerator control-system (EPICS) (always including Unix timestamps for each added parameter) or, alternatively, added later on in post-processing. All relevant accelerator settings, parameters or properties are by design saved continuously in a Casandra database. A corresponding post-processing workflow can be based on an existing Python framework developed by me which was successfully used to process more than 50 TByte of measurement data during my PhD studies.

To document the conducted experiments, the digital logbook ELOG will be used. Originally developed at the Paul Scherrer Institut (Switzerland) under the GNU Public License, it is used in multiple accelerator facilities as a documentation standard. Small data files can be directly linked to the corresponding entries. Larger files will be stored in structured directories on a file server of the institute and a link to the storage location will be added to the ELOG entry. For documentations exceeding the logging during individual measurements, an instance of a wiki is available at the institute. Sub-spaces for individual teams can be created with corresponding access rights. There, information or discussions regarding multiple measurements or simulations can be stored. Within the framework of scientific research, regular comparisons between simulated and measured data will be performed to ensure consistency and increase data quality. Furthermore regular reference measurements at well known conditions are performed to characterize the detection chains. Regular meetings and discussions on the acquired data will be held to minimize human bias (four eyes principle). For the development of software a GitLab instance will be used. This provides a version controlled and simple possibility to save, transfer and jointly work on source codes. With the usage of GIT (distributed version control system), there is also the possibility to implement basic quality control mechanisms, e.g. git hook frameworks like pre-commit, which check the integrity of the source code before committing. For all python scripts the PEP8 coding-style convention will be respected.

For immediate storage during the runtime of the project, the data will be saved on the institute's own servers which are equipped with backups and allow to manage the access rights via user-groups. A specific group directory would be created with a systematic folder structure to allow the storage of the generated measurement and simulation data sorted by type and date. In addition to ensure minimal data loss every personal pc of group members will be equipped with an external backup hard drive and each member will be instructed to perform regular backups.

For long-term storage and archival of data the multi-petabyte storage systems of the host institution (e.g. LSDF) including the archival on tape storage will be used. A minimum storage period of 10 years is default for these services. Those are provided by the host institution at no cost. In addition, RADAR4KIT, a research data repository, can be used to, to bundle data and metadata, store and archive this data with the possibility to provide public access later on. For publications, high-level derivative data can be added as supplementary material on the journal web-page. For simulation data, produced with publicly available simulation code, the minimal set of parameters to recreate the simulations will be added. The corresponding full data sets can be published in KITopen via RADAR4KIT, receive a DOI and is open access. Software developed in the framework of this project is planned to be open-source and published on services such as GitHub.

Members of the project group will be provided with the possibility to learn the usage of technologies regarding data management used for the project. Due to the continuous availability throughout the project and previous experiences with large data and software management, the applicant will take on the task of coordinating the handling of research data for the project supported by the IT team of the host institute. Since the usage of established storage solutions is foreseen, the long-term storage and archival responsibility after the project ends lies with KIT.

Research data management within the project as well as the used services will conform to the guidelines published by KIT ("Guidelines for Responsible and Sustainable Research Data Management at KIT (RDM Policy)") as well as the DFG code of conduct, and the EU open science policy.

2.5 Relevance of sex, gender and/or diversity

not applicable

2.6 Justification for the choice of host institution(s)

The Karlsruhe Institute of Technology (KIT) would provide an exceptionally well-suited research environment with an unique combination of multidisciplinary research infrastructure and strategic collaborations within the multitude of institutes in complementary research fields as well as with external institutions.

The KIT is one of the eleven "Universities of Excellence" in Germany. It is unique in that it combines a university and a national research laboratory (in the Helmholtz Association) within one entity resulting in one of the biggest science institutions in Europe. These conditions provide the opportunity to combine academic and fundamental research with application-based and goal-oriented research. KIT offers the possibility to profit from the motivation and ingenuity of students and early-carrier researchers and at the same time gives access to large-scale research facilities. The excellent research at KIT covers among others the disciplines of natural and engineering sciences. Interdisciplinary KIT Centers bring together scientists from different institutes to cross-divisionally tackle challenges and research actives connected to the further development and technological improvement of society. This quest naturally leaves KIT striving to push also the advancement of medical technologies. As newest of the nine KIT Centers, the Center “Health Technologies” has recently been established in March 2023 aiming to “provide next generation innovation for the global health challenges of today and tomorrow”.

Another piece of the puzzle is the research bridge “Medical Technology for Health (MTH)” with the aim to combine knowledge from engineering sciences, molecular basic research and bio-informatics with medical expertise to develop better diagnostics and therapy. The bridge is part of the longstanding strategic partnership with the Heidelberg University HEIKA (Heidelberg Karlsruhe Strategic Partnership) which was initiated in order to combine the complementary competencies of the two Universities. Furthermore, a joint master program in biomedical engineering in cooperation with the University Heidelberg is planned to start in the winter semester 24/25 strengthening this important research area by attracting young talents. The initiators behind this program would welcome my contribution towards lectures and supervisions of potential students. Additionally, the former dean (Prof. Dr. Quast) and the current vice-dean (Prof. Dr. Husemann) of the physics faculty have declared their support for my involvement in lectures towards a newly planned module of lectures on physical foundations of technologies.

The close connection to the Heidelberg Ion-Beam Therapy Center (HIT) and the German Cancer Research Center (DKFZ) offers the collaboration with experts in radiotherapy and medical physics, such as Prof. Dr. Oliver Jäkel, and furthermore provides the possibility for experimental studies with protons or ions, which could be conducted at the experimental area of the accelerator complex.

The Accelerator Technology Platform (ATP) at KIT combines KIT internal expertise and infrastructures relevant for accelerator research, development and application. This not only includes the KIT based accelerators FLUTE and KARA (see below), experts in accelerator physics (IBPT) and accelerator relevant technologies like the Magnet Characterization Facilities (MCF) and cryogenic research laboratories, but furthermore it also includes experts and infrastructure on advanced detector technologies studying for example ultra-fast and radiation hard detection systems. With the experimental part of the proposed project relying on the possibility to conduct systematic measurement on accelerators and beams, KIT with the Institute for Beam Physics and Technology (IBPT) is an ideal environment in that it provides easy and extended access for in-house researchers to its electron accelerators. Both accelerators serve as accelerator test facilities for a variety of accelerator physics studies, leading to a high flexibility in available operation modes and beam conditions and the possibility to tailor operation modes to experimental requirements. To this end the accelerators are equipped with extensive, state of the art diagnostics and continuously serve as a test-bed for research towards novel and improved diagnostic methods. The 2.5 GeV storage ring and synchrotron light source KARA (Karlsruhe Research Accelerator) is based on the ANKA (Angströmquelle Karlsruhe) which started operation in 2003 and which has been improved continuously since then. KARA provides short-pulsed x-ray modalities at multiple beam lines. Further more, additional operation modes have been implemented at different electron energies such as for example a short-pulse operation allowing the investigation of the dynamics in short electron bunches as well as the development and tests of novel, fast diagnostic methods. The second accelerator at KIT-IBPT is the linear electron accelerator FLUTE (Ferninfrarot Linac- und Test-Experiment). It is designed to provide ultra-short electron pulses with an energy of around 6 MeV after the low-energy section and with energies of up to 50 MeV and bunch lengths down to femtoseconds after the full accelerator. Furthermore, FLUTE provides coherent radiation in ultra-short, very intense light pulses from terahertz to far-infrared and beyond. The electrons pulses in FLUTE are generated with a femtosecond chirped laser-driven photo-injector. Recent studies include the application of machine learning for accelerator tuning tasks based on reinforcement learning as well as extend the existing diagnostics with virtual diagnostics achieved by surrogate modeling of the electron beam dynamics. Also of great importance is the recent implementation of a spatial light-modulator which allows spatial and temporal shaping of the laser pulse on the photo-cathode and therefore control of the initial electron distribution in the accelerator. Besides the two existing accelerators, two more are planned to be build within the near future. A 50 MeV laser-plasma accelerator is being build as part of the ATHENA project in collaboration with DESY and the Helmholtz Institute Jena (HIJ). This will open the opportunity to test the developed simulation and diagnostic methods to a different type of accelerator and investigate the possibilities and limitations of LPA beams for radiotherapy. Last but not least, an innovative non-equilibrium storage ring with a wide energy acceptance will be build and will be able to accept both, the LPA as well as FLUTE, as injector.

Last but not least, KIT offers a strong background in mathematical and computational science with the Scientific Computing Center (SCC) and KIT Center "MathSEE" (Mathematics in Sciences, Engineering, and Economics). So was the KiT-RT (Kinetic Transport Solver for Radiation Therapy) [17] simulation code recently developed by the research group Computational Science and Mathematical Methods (CSMM).

Even with KIT being my alma mater, I am convinced that KIT offers an unparalleled opportunity, based on the multidisciplinary research environment and the close collaboration with the university Heidelberg and the Heidelberg ion-therapy center and is therefore the best-possible choice as host institution for the proposed project. The direct and timely access to flexible accelerator test-facilities generating ultra-short pulses of high energy electron and photon beams within the same institution is a strong advantage and a perfect fit for the experimental part of the project. The wide variety of research fields included in the new KIT-center “Health Technologies” combined with the collaborations with experts on medical science in Heidelberg promises multidisciplinary input and solution-finding in an inspiring, dynamic and nurturing environment. Embedded in one of Germany’s leading healthcare and technology regions, the proposed project will be especially well positioned to provide an important contribution towards the advancement of novel accelerator based radiotherapy methods.

3 Project- and subject-related list of publications

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4 Supplementary information on the research context

4.1 Ethical and/or legal aspects of the project

1.1.1 General ethical aspects

not applicable

1.1.2 Descriptions of proposed investigations involving humans, human materials or identifiable data

not applicable

1.1.3 Descriptions of proposed investigations involving experiments on animals

not applicable

1.1.4 Descriptions of projects involving genetic resources (or associated traditional knowledge) from a foreign country

not applicable

1.1.5 Explanations regarding any possible safety-related aspects (“Dual Use Research of Concern; foreign trade law)

not applicable

4.2 Employment status information

Brosi, Miriam Katharina employed as Postdoc in the Accelerator Development Group at the MAX IV Laboratory, Lund University in Lund, Sweden. The contract started on the 17th of January 2022 and runs until 16th of January 2025.

4.3 Composition of the project group

not applicable

4.4 Researchers in Germany with whom you have agreed to cooperate on this project

- Prof. Dr Oliver Jäkel (in ch.), Heidelberg University and Heidelberger Ionenstrahl Therapiezentrum (HIT) and Division Head of “Medical Physics in Radiation Oncology” Deutsches Krebsforschungszentrum (DKFZ).
- Prof. Dr. Anke-Susanne Müller, Institute Director, Institute for Beam Physics and Technology, Karlsruhe Institute of Technology.
- Dr. Erik Bründermann, Head of Department: Accelerator Research and Development + Operations II, Institute for Beam Physics and Technology, Karlsruhe Institute of Technology, Honorable Guest Professor of Shizuoka University

- Dr. Lennart Volz, Medical physicist, GSI Helmholtzzentrum für Schwerionenforschung, Darmstadt, expert on ion-based radiotherapy, particle imaging and treatment planning.

4.5 Researchers abroad with whom you have agreed to cooperate on this project

not applicable

4.6 Researchers with whom you have collaborated scientifically within the past three years

- MAX IV Laboratory, Lund University, Sweden:
  - Dr. Pedro Fernandes Tavares
  - Dr. Åke Andersson
- PhLAM, University Lille, France:
  - Prof. Dr. Serge Bielawski
  - Dr. Christophe Szwaj
  - Dr. Eléonore Roussel
- KIT, Karlsruhe, Germany:
  - Prof. Dr. Anke-Susanne Müller
  - Dr. Erik Bründermann
  - Dr. Michele Caselle

4.7 Project-relevant cooperation with commercial enterprises

If applicable, please note the EU guidelines on state aid or contact your research institution in this regard.

not applicable

4.8 Project-relevant participation in commercial enterprises

Information on connections between the project and the production branch of the enterprise

not applicable

4.9 Scientific equipment

List larger instruments that will be available to you for the project. These may include large computer facilities if computing capacity will be needed.

- Far-infrared linac and test experiment (FLUTE)
- Karlsruhe Research Accelerator (KARA)
- HoreKa (Hochleistungsrechner Karlsruhe)
- ?bwUniCluster

more elaboration necessary?

4.10 Other submissions

List any funding proposals for this project and/or major instrumentation previously sub-mitted to a third party.

not applicable

4.11 Other Information

Please use this section for any additional information you feel is relevant which has not been provided elsewhere.

not applicable

5 Requested modules/funds

Explain each item (stating last name, first name)

5.1 Module Junior Research Group Leader

Brosi, Miriam Katharina:
To lead the proposed project in the Emmy Noether program, the funding for the position as junior research group leader is requested for the expected project duration of 6 years consisting of two funding periods (36 + 36 months). The position will be filled by applicant, Miriam Katharina Brosi.

Personnel Cost Category	EUR / year (as of 2024)	EUR / Sum (6 years)*
Head of independent junior research group	100200	648135

*An annual rise of 3% in personnel costs has been included.

5.2 Basic Module

1.1.6 Funding for Staff

For the proposed work program the funding for one postdoctoral researcher, two doctoral students and one to two student workers is requested.

The **postdoctoral researcher** will be employed for two years on a 100% position and is planned to start at the beginning of the second project year (12 month after project start). The planned work will include the incorporation of collective effects into beam-matter interaction and the implementation of a start-to-end simulation combining beam transport simulations in the accelerator with simulations of the transport through matter. A candidate with a strong background in many particle systems or theoretical accelerator physics with experience in simulation programming is envisioned.
The first **doctoral student** will be employed for three years on a 75% position and is planned to start shortly at the project start, latest after half a year (1-6 month after project start). The PhD thesis will be on the topic of: Experimental study of the influence of advanced radiotherapy beam properties such as short bunch length, charge, energy and transverse size on accelerator beam dynamics, diagnostics and detected dose. The candidate should have some experience in experimental work, including setting up and handling sensitive diagnostic hardware.
The second **doctoral student** will be employed for three years on a 75% position. This position should start in the second half of project year 3 (30 month after project start). The work will focus on: Investigation of methods and algorithms for custom accelerator based beam modulation towards advance radiotherapy. A candidate is envisioned with a background in mathematical methods and computational physics.
To allow for some unexpected delays during the work on the PhD thesis, an additional half year per doctoral position is requested, so that the contract could be extended to prevent financial stress for the students during the final stage of their thesis.
Additionally, some funds are requested to employ student assistants for a total of 3 years distributed over the project duration as required and interested students available. The working

time would be adjusted in such a ways that the salary corresponds to a “mini job” according to the customary rates for student assistants at KIT.

Personnel Cost Category	EUR / year (as of 2024)	EUR / Sum (6 years)*
Postdoctoral researcher	86100	180026
Doctoral researcher (75%) (3 year)	59850	184990
Doctoral researcher (75%) (3 year)	59850	196256
Extension possibility for Doctoral researcher (75%) (in total 1 year)	59850	65400
Student assistants (in total 3 years)	9000	28394

*An annual rise of 3% in personnel costs has been included.

1.1.7 Direct Project Costs

[Text]

5.2.1.1 Equipment up to € 10,000, Software and Consumables

-Safety equipment, like small dosimeters to measure area free after irradiation?
5000?
-building material for eg. holders in water target ?? and similar
6000?
- cables, adapter, connectors for readout of detectors…
6000?
- amplifiers, attenuators, for readout
6000?
- humidity measurement device...

- portable external drives for each group member for backup of the working pc 4x1TB SSD (4x100€=400€)
- desktop PC as control and read-out station for new diagnostics 3000€ including at least 4 TB of internal storage
- (personal laptop can be requested? Or? 4X2000€=8000€)
- monitors...
=11400

Unidos electrometer for dosimeter readout ~10.000€
Dosimetry detectors (e.g. mircoDiamond from PTW) 9000-11000 netto
advanced markus chamber, (not for photons but for protons) → 3000-5000€
FlashDiamond detector (from PTW) → ~10.000€ netto
farmer chamber can detect starting from 60keV photons → awaiting price

5.2.1.2 Travel Expenses

- participation in conferences
(1x per doctoral researcher, 2x for postdoc, 4x for me?
- one summer school per doctoral researcher? Topic depending on their interest, e.g. HIDSS4Health. https://www.hidss4health.de summer school

Ask Erik how much ?

5.2.1.3 Visiting Researchers (excluding Mercator Fellows)

not applicable

5.2.1.4 Expenses for Laboratory Animals

not applicable

5.2.1.5 Other Costs

not applicable

5.2.1.6 Project-related Publication Expenses

[Text] ???

1.1.8 Instrumentation

5.2.1.7 Equipment exceeding € 10,000

[Text] waiting for price information on possible 2D detector

water phantom kleines horizontales 6750€ (großes motoriziertes WP → 52000€)

5.2.1.8 Major Instrumentation exceeding € 50,000

not applicable

5.3 Module Temporary Clinician Substitute

Clinician scientists may apply for a temporary substitute position instead of a position as junior research group leader. In addition, this module may be used to finance substitute medical personnel who will assume the patient-care responsibilities of the clinicians participating in your project.

not applicable

5.4 Module Mercator Fellows

not applicable

5.5 Module Workshop Funding

not applicable

5.6 Module Public Relations Funding

not applicable

5.7 Module Standard Allowance for Gender Equality Measures

Please detail what measures are planned to promote diversity and equal opportunities.

not applicable

5.8 Module Family Allowance

not applicable