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THE DEEP ELECTRON FLASH THERAPY FACILITY

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Abstract

The "FLASH" effect is currently a topic of considerable interest in radio-oncology. We present the design of a novel VHEE linac, to be built and installed at CHUV (Lausanne), capable of producing electron beams which deliver radiation at dose rates and time scales consistent with the FLASH effect. The design is based on X-band radio-frequency technology, developed at CERN for the CLIC study. The e-beam properties correspond to a CHUV specification and would allow large, deep seated, tumours to be treated. Construction of DEFT (DEEP Electron FLASH Therapy) will be assured by the company THERYQ in the context of a CHUV-CERN-THERYQ collaboration.

INTRODUCTION

Radiation therapy (RT) constitutes one of the main pillars in cancer treatment, together with surgery and chemo/immuno therapy [1–3]. The conflicting requirement of sparing the healthy tissues that surround the tumor while maximizing the effectiveness in tumor control has pushed RT technologies towards fractionated dose administration together with highly conformal dose delivery systems. Besides MV photon beams, which are the workhorse of modern external beam RT, other therapeutically used particle species include protons, light ions, and electrons <25 MeV. While such modern high-precision RT treatments can provide acceptable clinical outcomes with limited side effects for many patients [1, 3] there is still a clinical care gap and a resulting clinical need for numerous cancer patients.

For such cases, hope is being generated by the observation that doses delivered at ultra-high dose rates (UHDR, average dose rate $\gtrsim$50 Gy/s) can produce a sparing effect on healthy tissues while maintaining the effectiveness on tumoral cells compared to irradiations delivered at conventional dose rates (average dose rate ~0.05 Gy/s) [4, 5]. This increase of the therapeutic index by the ultra-fast dose delivery, commonly referred to as "FLASH effect", was initially observed in the 70's, first proposed in 2014 and has since then been independently confirmed in numerous studies using different radiation modalities and preclinical models [4–7].

The adoption of the high-gradient RF technology developed at CERN for the realization of the high-energy linear collider CLIC appeared to be the logical choice for designing a compact FLASH-RT device capable of producing penetrating very high-energy electron (VHEE, 100 - 250 MeV) beams at UHDR to treat deep-seated tumors. In addition, supporting experiments are being carried out at the CERN facility CLEAR in relation to the creation and detection of UHDR and to the characterization of the FLASH effect.

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MEDICAL BACKGROUND

The potential implications of FLASH-RT in clinical practice are profound. Conventional radiotherapy, while effective, often necessitates a delicate balance between delivering sufficient doses to eradicate tumors and minimizing exposure to surrounding healthy tissues. This balance becomes particularly challenging when treating tumors located close to critical structures and/or large and non-curable cancers such as glioblastomas for which there is a huge unmet clinical need. FLASH-RT, on the other hand, with its potential to elicit a biological selectivity between tumors and healthy tissues, may offer a breakthrough in overcoming these limitations. The reduced toxicity induced by the FLASH effect on the healthy tissue could allow for higher therapeutic doses, potentially improving either local control and overall survival rates or reducing treatment side effects for challenging cancers.

Status of Preclinical and Clinical FLASH Research at CHUV

Extensive preclinical evidence supports the potential of FLASH-RT to enhance the therapeutic ratio of RT by delivering treatments at UHDR [5–7]. In 2018, CHUV successfully conducted the first human treatment using UHDR electrons, marking a significant milestone in the clinical application of FLASH-RT [8, 9]. The patient, treated for cutaneous lymphoma, showed excellent tumor control with minimal side effects, demonstrating the feasibility and potential benefits of FLASH-RT in clinical settings. Building on this success, CHUV has initiated two human clinical trials: a dose escalation trial (IMPulse, NCT04986696) for metastasized melanoma and a Phase II trial (LANCE, NCT05724875) aimed at evaluating the treatment of localized cutaneous squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) with FLASH-RT in comparison with standard of care RT. Both trials show promising preliminary outcomes.

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Need for Technological Innovations

Despite the promising results, a significant challenge remains in treating deep-seated tumors conformally at UHDR. The clinical transfer described above has been realized utilizing devices generating 4-10 MeV broad electron beams at UHDR. While such beams may target superficial tumors extending to a depth of 1-2 cm, they are not sufficiently penetrating for treating the bulk of lesions encountered in clinical radiation oncology. To fully realize the potential of FLASH-RT, there is, therefore, a critical need to develop compact FLASH-RT devices capable of delivering dosimetrically conformal treatments to deep-seated tumors at UHDR [10, 11].

EXPERIMENTAL ACTIVITY AT CLEAR

The CERN Linear Accelerator for Research (CLEAR) is a 3 GHz electron linac, capable of accelerating beams of variable charge and pulse rate up to the energy of 200 MeV, making it an ideal tool for studying different aspects related to FLASH radiotherapy with VHEE at UHDR. Two in-air test areas and three in-vacuum spaces are available for experiments.

In the last couple of years, a large fraction of the available beam time in CLEAR has been dedicated to studies of medical application-related issues [12].

VHEE and FLASH Studies at CLEAR

Several experiments were performed in collaboration with international universities from UK, Germany, Canada and Switzerland and the Lausanne and Geneva University hospitals (CHUV and HUG). Three types of samples were irradiated: water samples for chemistry, plasmids, and Zebra Fish Eggs (ZFE). The goal is to compare the effects of ultra-high dose rates with conventional dose rates on controlled samples. Details about the experimental setup and working procedure are given in [13] and at this conference [12]. A recent publication [14] shows how pBR322 plasmid DNA was successfully used in CLEAR experiments as a biological model to study DNA damage at UHDR. UHDR irradiated plasmid had reduced amounts of DNA single-strand breaks (SSBs) compared to conventional dose rates.

Dosimetry Studies

Reliable dosimetry is crucial in clinical radiotherapy, and the development of the FLASH technique shows that conventional active dosimeters, like ion chambers, have non-linear response and tend to saturate at UHDR. A combination of real-time with high-resolution dosimetry at UHDR is a substantial challenge. Experiments performed at CLEAR, in collaboration with the universities of Oxford and Groningen, could demonstrate initial results in the use of optical fibers as Cherenkov radiation emitters, radiation which is then collected by a photo-detector based on a photomultiplier tube or a CCD camera. Initial measurements show a remarkable response linearity for a large range of dose rates [15]. Very promising results were also obtained by employing plastic scintillator detectors (PSD). Dose rates up to $1.2\,10^9$ Gy/s were investigated, showing again an excellent linearity in the system response.

Dose Uniformity Studies

Preliminary experiments were performed at CLEAR to validate the generation of a transversely uniform electron beam by a Gaussian laser pulse on a photoinjector. The production scheme was created and tested in numerical simulations. The balance between space-charge repulsive forces and solenoid focusing leads to a uniform distribution. Initial tests, adopting a bunch charge of 200 pC, could demonstrate that, despite power limitations in the klystron driving the CLEAR photoinjector, the process to obtain a uniform distribution is correctly understood [16, 17]. Further, more systematic experimental studies should be undertaken to validate the technique.

THE COLLABORATION SET-UP

CERN is a big science organization whose know-how and technologies, developed for particle physics research, find many applications in society, such as in radiotherapy. CERN aims at maximising “the technological and knowledge return to [CERN’s] Member States and promotes CERN’s image as a centre of excellence for technology” [18]. CERN actively seeks medical and industrial partners to co-develop solutions that address unmet clinical needs.

Based on the aforementioned pre-clinical and clinical research at CHUV and the formulation of concrete requirements towards a VHEE FLASH-RT facility, CHUV and CERN entered into a first collaboration agreement in 2020 for the development of a Conceptual Design Report (CDR) that assesses the feasibility of such a facility. In 2021, following the successful delivery of the CDR, CERN and CHUV renewed their collaboration to develop a Technical Design Report (TDR), which provides comprehensive detail of a VHEE FLASH-RT device.

CERN and CHUV extended the collaboration to an industrial partner, the company THERYQ, a spin-off of PMB-ALCEN, in 2022. The addition of industry to a previously academic project aims at a review of the TDR towards an industrialized and medically certifiable device, FLASHDEEP^{TM}, and the construction of a first prototype at CHUV.

FACILITY DESIGN

The main requirements for the DEFT accelerator design concern the beam energy, which is at least 100 MeV, the high electron charge that must be delivered within a well-defined, but still adjustable, time structure and the wide irradiation field, to be able to treat large tumors. Compactness is crucial for such an accelerator whose final destination is the existing Lausanne University Hospital CHUV, with the associated space limitations.

The design has been made compatible with future upgrades, with the possibility of three beams simultaneously

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irradiating the tumor volume at three different energies and from three directions for enhanced irradiation conformality. The first stage that is described here considers a single-beam delivery line.

The required technology and expertise were developed in the frame of the CLIC study for the realization of a TeV-scale linear collider, which aims at producing high current electron beam collisions resulting in high integrated luminosity at the physics experiment. They were extensively tested in specific experiments in different laboratories worldwide and in a dedicated facility built at CERN called CTF3, obtaining their validation within the scientific community. That knowledge and the same technology were adopted for the design of the DEFT accelerator.

The X-band Technology

The X-band technology, which allowed the push of the maximum gradient of the CLIC accelerating structures up to the level of 100 MV/m, was the adopted choice for the DEFT accelerator [19]. In the case of the DEFT design, the maximum accelerating gradient was limited to a lower value, in order to reach high efficiency and to assure a high level of reliability together with the compact dimensions provided at the chosen frequency of 12 GHz.

Over the years, CERN developed an extensive knowledge of X-band technology and its applications by designing and testing high gradient accelerating structures, compression and correction cavities operating at these frequencies and all the required waveguide components whose design is now in the public domain. This knowledge was developed and benchmarked at specific test stations, built in collaboration with industrial partners and operated at CERN, known as X-boxes, that operate with RF power sources ranging from 6 up to 50 MW peak power.

The accelerating cell features higher order mode damping as it was developed for the CLIC Main Linac accelerating structure, and it is sketched in Fig. 1. Each CLIC cell features bent waveguides with damping material that are used to absorb long-range wakefields produced by the high current accelerated beams. The shape of the outer wall of the cell is optimized to reduce the surface magnetic field. The iris has an elliptical shape to minimize the surface electric field and the modified Poynting Vector, S_c.

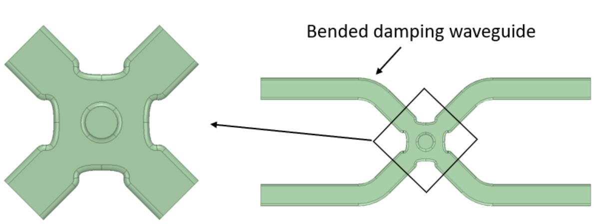

Figure 1: Geometry of the internal (vacuum) volume of a regular cell.

The Injector Design and Laser System

A crucial region of the accelerator is the injector, where the particle beam is produced and its characteristics are defined.

The electron beam is produced in the S-band photo-injector similar to that of CLEAR and accelerated to the energy of 7 MeV. The bunch spacing is 333.3 ps and several bunch trains can be delivered, adding up to a total charge of up to few uC within one treatment.

The crucial requirement of achieving dose homogeneity at the patient's position over a large field forced the design into a new approach, where the combined effects of the RF Gun accelerating field, beam space charge forces and the magnetic field generated by the solenoid were used to produce a uniform beam distribution at the accelerator entrance [16]. The beam loading and wakefield effects in the accelerator had to be carefully taken into consideration to assure the transport of such a uniform beam distribution to the high energy end of the Linac. A specific beam dynamics code, RF-Track [20] developed at CERN, was employed to design and optimise the DEFT beamline and to study the impact of imperfections and collective effects on the beam. This code was developed to meet the specifications of the DEFT project.

Figure 2 shows the bunch transverse profile at the end of the gun, where the average energy of the beam is about 7 MeV.

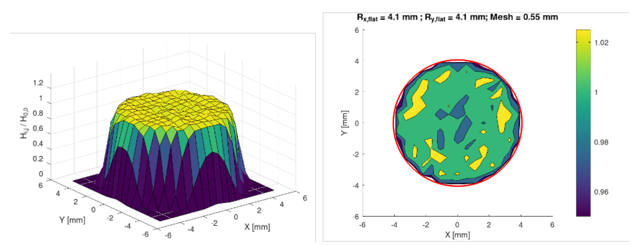

Figure 2: Bunch transverse profile (left) and 2D density histogram (right) at longitudinal position *S*=1.3 m from the cathode (the linac start), normalised to the average density.

CERN operates photo-injectors in the CLEAR facility and in the AWAKE experiment, which have inspired the solution adopted in DEFT. The beam is generated in a Cs_2Te cathode illuminated by a Nd:YLF laser operated in the UV wavelength range for optimum photoemission, with up to 1 µJ delivered per bunch in the pulse train. The typical laser characteristics are summarized in Table 1.

The extracted electrons are then accelerated by the RF Gun field developed in the 2.5-cell S-band structure. The peak field at the cathode surface can range between 80 MV/m and 110 MV/m.

The injector area is very densely populated with beam diagnostics, corrector magnets and vacuum pumping. In order to preserve high values of quantum efficiency (QE) in the photocathode, a vacuum pressure in the range of $< 10^{-10}$ mbar must be assured. A profile monitor is located at the entrance of the first accelerating structure to

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Table 1: Front-end Laser Main Performance Parameters

Laser parameter	Value range
Laser gain medium	Nd:YLF
Wavelength	1030 - 1047 nm
Operation mode	CW mode-locked
Pulse rep rate (locked)	1.5 GHz ± few Hz
P_{ave} oscillator	~100 mW
P_{ave} pre-amplifier	~10 W
Timing jitter	< 0.3 ps RMS [0.001 - 100 MHz]
Beam quality	$M^2 = 1.1$
Power stability	<0.5% (after warm-up time)

assess the beam position and uniformity at that point. The layout of the DEFT injector is provided in Fig. 3.

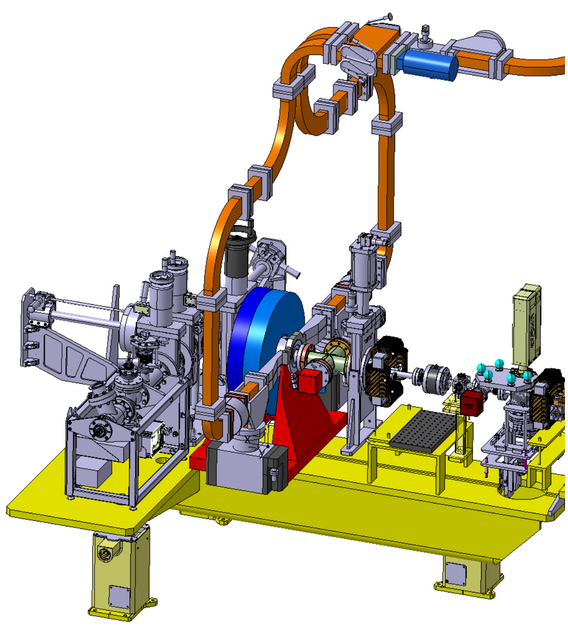

Figure 3: Layout of the DEFT injector region.

The Acceleration and Beam Delivery System

At the Injector output the electron beam has an energy of 7 MeV and it is accelerated to its final energy of above 100 MeV by eight X-band accelerating structures. The accelerating structures are made of waveguide damped cells, as already mentioned, with two coupling cells at the two ends.

The eight accelerating structures are organized in two groups of four, each group making a module. Each module can be independently aligned with an accuracy of ±0.1 mm.

Two X-band power plants feed the two modules. As in the CLIC klystron-based scheme, the RF power from the two klystrons is initially combined and sent to a chain of spherical correction cavities to properly shape the resulting RF pulse and then to an RF pulse compressor of the type Barrel Open Cavity (BOC) [21], to increase the initial peak power by a factor of about four.

The RF power is then split and delivered to the two modules and distributed to the individual accelerating cavities.

The relevant parameters of the RF pulse compression system are summarized in Table 2.

Table 2: Parameters of the Pulse Compression System

Parameter	Value
Power gain	4.35
Compression ratio	10.035
$\tau_r + \tau_f$ [ns]	229
P_t/P_0	0.306
Pulse compression efficiency [%]	43.34

Most of the RF network is made of WR90 waveguides that were modified to double height, to minimize power losses [22].

A quadrupole doublet after the first module matches the beam to the second accelerator module. At the output of the second module the accelerated beam is injected into the final beam delivery system (BDS). This section is designed to assure the conservation of the dose homogeneity at the patient within the required 3% while the beam is allowed to expand up to the specified field area. The BDS is made of quadrupoles, steering magnets and some important beam instrumentation.

Integration Requirements

The study for the integration of the facility into its bunker was led by well defined constraints such as the need of directly connecting the facility to the existing hospital while keeping it under the road level, to maintain the present hospital access. The treatment area benefits from a direct access from the Radio-Oncology Department of the CHUV hospital. The linac and beam delivery extend over a length of about 15 m. The whole facility has a footprint of 900 m^2, including the area for the technical infrastructure, and is built on two levels.

The building has been designed to limit the radiation dose level outside the perimeter of the shielded area below the level of 20 µSv/week. Realistic commissioning and irradiation scenarios were considered to design the shielding, providing a worst case radiation load of 1.3×10^{17} e^-/week during accelerator set-up and development. A schematic view of the linac with the patient area and the klystron gallery is shown in Fig. 4.

THE PATIENT AREA

Downstream of the Beam Delivery System (BDS) the accelerated electron beam exits the vacuum chamber to air through a thin window in the patient room, which is equipped with a Beam Conforming System (BCS) and a Patient Positioning System (PPS).

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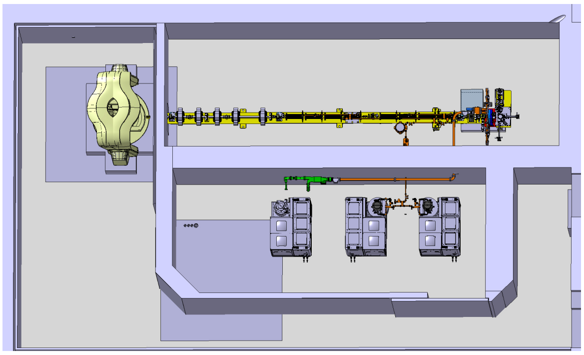

Figure 4: View of the DEFT Linac and treatment room.

The BCS shapes the beam delivered by the BDS by means of a multi-leaf collimator as in Fig. 5, to make the deposited dose area conform to the targeted tumor.

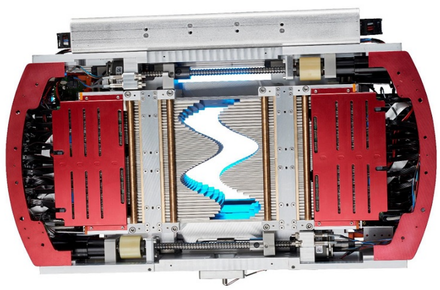

Figure 5: View of the DEFT multi-leaf collimator.

The BCS also integrates redundant beam current detectors to monitor the transverse uniformity of the beam and the delivered dose rate. The PPS includes a patient support which maintains, positions and orients the patient with 5 degrees of freedom in an upright posture with respect to a fixed reference point, the so-called isocenter, which is defined as the intersection of the fixed horizontal beam axis and the vertical axis of rotation of the patient support.

An upright Computed Tomography (CT) scanner is installed at the same location of the patient support as shown in Fig. 6, acquiring 3D images of the tumor with the patient at the isocenter, allowing to precisely plan the radiation therapy treatment.

The CT scanner may be used again when the patient is in place and ready for treatment, to verify his/her position vs. the planned treatment position. A stereoscopic imaging system is needed to optimize the patient position with respect to the isocenter and the beam axis. The stereoscopic imaging system consists of two pairs of kV x-ray tubes and flat panel x-ray detectors to provide 2D images on horizontal axes that converge at the isocenter. The 2D images from the stereoscopic imaging system are compared with the corresponding 2D images reconstructed from the latest CT scan, the Digitally Reconstructed Radiographic (DRR) images, and the patient's position may be corrected accordingly, if needed. The spatial accuracy of the dose delivery is expected to be better than 1 mm, also thanks to the fast dose delivery of the FLASH treatment.

Figure 6: Vertical CT scanner for patient positioning in upright position (https://www.leocancercare.com/).

OVERVIEW AND CONCLUSIONS

The challenge of the DEFT project is to combine a design that provides flexibility in adapting to different operational regimes, like in every research facility, with a set of specifications suitable for its realization in industry and for clinical use. The initial design work, developed at CHUV and CERN, evolved into a staged concept for which the company THERYQ joined the two original partners. The present design has focused on the first stage: a single and straight beamline, with the possibility left to introduce a scanning beam later and a multi-beamline layout in its final configuration.

All critical items are now specified and we are ready to start their detailed technical design, which will eventually lead to their fabrication. Some parts of the equipment have already been ordered in industry. The civil engineering works have started and they are expected to be completed in early 2025. The installation of the technical infrastructure will follow and the delivery of the building is now scheduled for summer 2025. First equipment orders were sent by THERYQ and the integration work is quickly converging to freeze the machine design, the fabrication of critical components will start in the next months.

First pre-clinical experiments are expected to start in 2027, while clinical use will be subject to the time frame required by the medical certification process and by the initial terms of usage of the facility.

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REFERENCES

[1] M. B. Barton *et al.*, "Estimating the demand for radiotherapy from the evidence: A review of changes from 2003 to 2012", *Radiotherapy and Oncology*, Jul. 2014. doi:10.1016/j.radonc.2014.03.024

[2] J. M. Borras *et al.*, "The optimal utilization proportion of external beam radiotherapy in European countries", *Radiotherapy and Oncology*, Jun. 2015. doi:10.1016/j.radonc.2015.04.018

[3] T. Mee *et al.*, "The use of radiotherapy, surgery and chemotherapy in the curative treatment of cancer", *Br. J. Radiol.*, Dec. 2023. doi:10.1259/bjr.20230334

[4] V. Favaudon *et al.*, "Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice", *Sci. Transl. Med.*, Jul. 2014. doi:10.1126/scitranslmed.3008973

[5] M. Vozenin *et al.*, "Towards clinical translation of FLASH radiotherapy", *Nat. Rev. Clin. Oncol*, Dec. 2022. doi:10.1038/s41571-022-00697-z

[6] T.T. Böhlen *et al.*, "Normal Tissue Sparing by FLASH as a Function of Single-Fraction Dose", *Int. J. Radiat. Oncol. Biol. Phys*, Dec. 2022. doi:10.1016/j.ijrobp.2022.05.038

[7] T.T. Böhlen *et al.*, "Effect of Conventional and Ultrahigh Dose Rate FLASH Irradiations on Preclinical Tumor Models", *Int. J. Radiat. Oncol. Biol. Phys*, Jun. 2023. doi:10.1016/j.ijrobp.2023.05.045

[8] J. Bourhis *et al.*, "Treatment of a first patient with FLASH-radiotherapy", *Radiother. Oncol.*, Oct. 2019. doi:10.1016/j.radonc.2019.06.019

[9] O. Gaide *et al.*, "Comparison of ultra-high versus conventional dose rate radiotherapy in a patient with cutaneous lymphoma", *Radiother. Oncol.*, Jan. 2022. doi:10.1016/j.radonc.2021.12.045

[10] R. Schulte *et al.*, "Transformative Technology for FLASH Radiation Therapy", *Applied Sciences*, Apr. 2023. doi:10.3390/app13085021

[11] M. G. Ronga *et al.*, "Back to the Future: Very High-Energy Electrons (VHEEs) and Their Potential Application in Radiation Therapy", *Cancers*, Sep. 2021. doi:10.3390/cancers13194942

[12] R. Corsini *et al.*, "Medical activities in CLEAR: studies towards radiotherapy using Very High Energy Electrons (VHEE) in the FLASH regime", presented at LINAC'24, Chicago, US, Aug. 2024, paper THPB018, this conference.

[13] P. Korysko *et al.*, "VHEE and Ultra-High Dose Rate Radiotherapy Studies in the CLEAR User Facility", in *IPAC'23*, Venice, Italy, May 2023. doi:10.18429/JACoW-IPAC2023-THPM078

[14] H.C. Wanstall *et al.*, "VHEE FLASH sparing effect measured at CLEAR, CERN with DNA damage of pBR322 plasmid as a biological endpoint", *Sci Rep*, 14, 14803, 2014. doi:10.1038/s41598-024-65055-8

[15] J. Bateman *et al.*, "A Novel Fibre Optic Monitor for VHEE UHDR Beam Monitoring: First Tests at CLEAR", in *IPAC'23*, Venice, Italy, May 2023. doi:10.18429/JACoW-IPAC2023-THPL041

[16] A. Malyzhenkov *et al.*, "Experimental Generation of transversely uniform bunches at the CLEAR facility at CERN", in *IPAC'23*, Venice, Italy, May 2023. doi:10.18429/JACoW-IPAC2023-TUPL119

[17] A. Malyzhenkov *et al.*, "Bubble-beam accelerators: breaking the paradigm", in *IPAC'24*, Knoxville, USA, May 2024.

[18] G. Anelli *et al.*, "CERN: the study of the infinitesimally small and the rise of Big Science", *Big Science in the 21st Century*, 2023. doi:10.1088/978-0-7503-3631-4ch2

[19] M. Aicheler *et al.*, "The Compact Linear Collider (CLIC) - Project Implementation Plan", *CERN-2018-010-M*, Dec. 2018. doi:10.48550/arXiv.1903.08655

[20] A. Latina, "RF-Track Reference Manual" doi:10.5281/zenodo.4580369,June2020

[21] P. Wang, A. Grudiev, "RF design of the pulse compression system for the klystron-based CLIC main linac", in *IPAC'23*, Venice, Italy. May 2023. doi:10.18429/JACoW-IPAC2023-WEPA115

[22] P. Wang *et al.*, "Design of the RF waveguide network for the klystron-based CLIC main linac RF module", *Nucl. Instr. Meth. A*, 169410, 2024. doi:10.1016/j.nima.2024.169410