

OPTICS DESIGN AND BEAM DYNAMICS SIMULATION FOR A VHEE RADIOBIOLOGY BEAM LINE AT PRAE ACCELERATOR

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Abstract

The Platform for Research and Applications with Electrons (PRAE) is a multidisciplinary R&D facility gathering subatomic physics, instrumentation, radiobiology and clinical research around a high-performance electron accelerator with beam energies up to 70 MeV. In this paper we report the complete optics design and performance evaluation of a Very High Energy Electron (VHEE) innovative radiobiology study, in particular by using Grid mini-beam and FLASH methodologies, which could represent a major breakthrough in Radiation Therapy (RT) treatment modality.

INTRODUCTION

Currently most widely used RT modality is the conventional linear accelerator delivering 6-10 MV photon beams and, in a small proportion, 3-25 MeV electron beams. Higher energy photon beams (e.g. up to 25 MV) are or have been in use for clinical targets, but are not widely used RT techniques and generate neutrons. Currently, there is a growing interest in the biomedical community for VHEE beams ranging from 50 to 300 MeV [1, 2]. Increasing the energy above 70 MeV presents the following advantages: i) the penetration becomes deeper and the transverse penumbra sharper thus allowing a more precise treatment of deeper tumors ii) the small diameter VHEE beams can be scanned avoiding mechanical solutions such as the multileaf collimator iii) a rather smaller sensitivity to tissue heterogeneity can be achieved with VHEE beams under certain conditions [3] iv) VHEE accelerators may be constructed at significantly lower cost than current proton facilities. The VHEE could be of particular interest for treating deep, large or small tumours with several distinct beam entrances within the same radiotherapy session, performing better than current photon-based treatments in terms of doses delivered to surrounding healthy tissues [2]. This would allow to treat patients with VHEE beam directly or with innovative ways of dose delivery, with an increase of the normal tissue tolerance like Grid therapy mini-beams [4] or ultra-high dose rates FLASH beam [5], in a more convenient manner with VHEE compared to conventional photon beams.

In the following, the design of a VHEE accelerator is illustrated, including the RF gun, the linac and a beam line dedicated to pre-clinical studies. Subsequently the interactions of different aspects of the VHEE with materials

are shown. The platform layout and performance has been optimized to enable radiation biologists and radiation oncologists to investigate the molecular and cellular impacts of VHEE beams on normal tissues (e.g. brain, lung, gut) as well as tumours and compare these effects to conventional radiation therapies (e.g. 5-25 MeV electrons and 6-10 MV photons).

VHEE ACCELERATOR: RF GUN, LINAC AND RADIOBIOLOGY BEAM LINE

The PRAE accelerator consists of a photo-injector, an acceleration section and two beam lines with the corresponding experimental setups: the subatomic physics in the direct line and the instrumentation and radiobiology platform sharing the deviated line, as shown in Figure 1. The RF gun is located on the left of this figure. The cyan box shows the first HG linac. After the linac, a quadrupole doublet is used to focus the beam. A drift space of about 4 meters is left for a second HG linac which can boost the electron energy to 140 MeV in future. A quadrupole triplet is used to confine the beam as well as allowing to measure the beam emittance. After the triplet, a dogleg with two 30° dipole magnets (pink boxes) are used to deviate the beam following the building constrains and providing a separated area for the radiobiology experiments. Between the dipoles three quadrupoles are used to match the dispersion and beta function. Finally, another quadrupole triplet is used to achieve the beam requirements for the Grid mini-beams and FLASH modalities.

RF Gun and Linac

Since the Grid mini-beam requires a low-emittance beam (5 mm mrad is assumed), a photo-injector has been chosen as the electron source. The photo-injector consists of a normal conducting RF gun, a drive-laser and two focusing solenoids. To obtain high-charge (1nC) per bunch, a metallic magnesium photocathode will be used. The RF gun is a S-band (3GHz) gun, made of 2.5 copper cells, magnetically coupled to a waveguide. To get an emittance lower than 5 mm mrad for the high bunch charge, an accelerating field of 80 MV/m is required, which means a RF power of 5 MW in a 3 μ s pulse. The electron energy gain at the exit of the gun will be about 5 MeV. Using the magnesium cathode, a laser with wave length of 266 nm is adopted. The pulse length for the laser is chosen as 3 ps. After the RF gun, an instrumentation

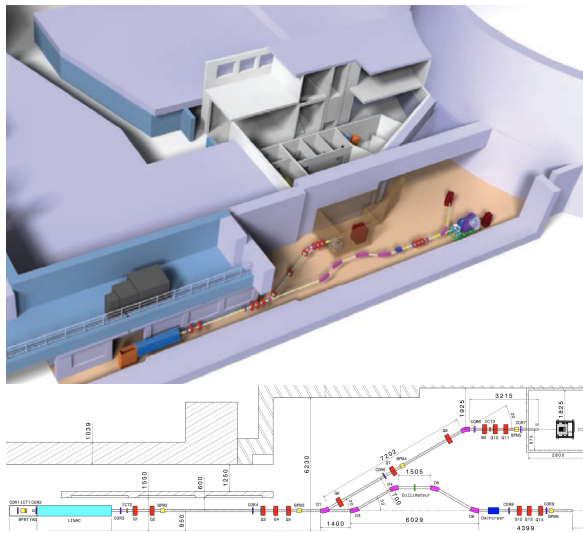


Figure 1: PRAE accelerator layout

section to measure and control the beam, including ICT, BPM and dipole corrector is located. The distance between the RF gun and the linac has been optimized (1.67 m) to provide minimum emittance.

To make the machine more reliable and compact, a High Gradient (HG) S-band linac is chosen. The HG accelerating structure will be a travelling wave (TW), quasi-constant gradient section and will operate at 3 GHz (30 °C in vacuum) in the $2\pi/3$ mode. The RF design consists of 97-cells (95 regular cells + 2 coupling cells), with a length of 3.47 m. Such structure will provide an energy gain of 65 MeV for an input peak power of 30 MW. The structure is being fabricated by Research Instruments [6].

First preliminary simulations for the injector are described in [7], a new campaign of simulations has been launched to optimize globally the RF gun and the linac to get the smallest emittance to match the requirement of Grid mini-beams. The simulations have been realised using ASTRA [8] for the RF gun and RFTrack [9] for the linac.

The Radiobiology Beam Line: Grid Mini-Beam and FLASH

The radiobiology beam line has been designed with a large flexibility to achieve the beam requirements of the Grid mini-beams and FLASH:

- Grid mini-beam: transverse beam sizes of less than $700 \mu\text{m}$ with low beam divergence, [10, 11].
- FLASH: transverse beam sizes of around 10 mm with a dose of 10 Gy with beam on time 100 ms (5 bunches at 50 Hz), i.e. 100 Gy/s, [12].

In the following, the Grid mini-beam with three different energies (70, 140 and 300 MeV) and the FLASH for 70 MeV are illustrated. For each energy, we first use the program MADX [13] to match the beam line in order to provide proper beam properties. Then the simulated beam from the

RF gun and linac will be tracked along the beam line by the program PLACET [14]. The phase space at the end of the beam line are shown for each case. Geant4 [15] is used to simulate the transport of the beam in air and for simulating biological samples water is used.

The Grid Mini-Beam Figure 2 shows the optics beam line in the top, the beam envelope along the beam line is less than 2 mm. The phase space at the end of the radiobiology beam line is shown in the bottom. The beam sizes at the end of the beam line are $\sigma_x = 207 \mu\text{m}$ and $\sigma_y = 240 \mu\text{m}$. Similar optics have been calculated for the 140 and 300 MeV energies.

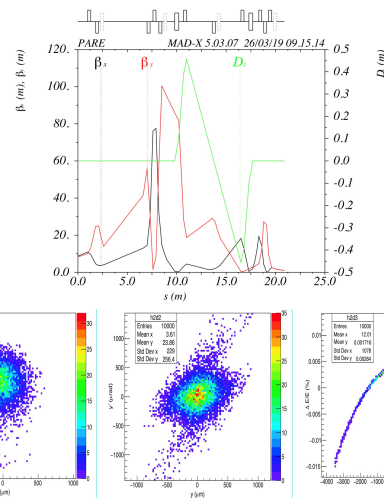


Figure 2: Beam optics and phase space at the end of the beam line, for 70 MeV Grid mini-beam

The interaction with the beam with 10 cm of air and 30 cm of water are shown in Figure 3 for 70, 140 and 300 MeV. The beam in the air gap of 10 cm will not diverge greatly because it reaches the beam waist at the exit of vacuum beam pipe. The beam sizes after the air box are $\sigma_x = 250, 200, 340 \mu\text{m}$ and $\sigma_y = 290, 170, 330 \mu\text{m}$ respectively for 70, 140 and 300 MeV. When the beam enters the water, it will interact strongly: the energy will be reduced and the beam size will be enlarged. In the 70 MeV case the beam sizes become $\sigma_x = 5.5 \text{ mm}$, $\sigma_y = 5.5 \text{ mm}$ after traversing 9 cm of water. At 15 cm in water, they become $\sigma_x = 17.3 \text{ mm}$, $\sigma_y = 17.4 \text{ mm}$. For 140 MeV the maximum dose deposition is at around 19 cm. The beam sizes become $\sigma_x = 3.3 \text{ mm}$, $\sigma_y = 3.3 \text{ mm}$ after traversing 9 cm of water. At 15 cm in water, they become $\sigma_x = 7.5 \text{ mm}$, $\sigma_y = 7.6 \text{ mm}$. We could observe that the most intensive energy deposition region shifts a little to the depth compared to the 70 MeV beam. After several centimetres, the region of energy deposition become large. In the 300 MeV case the beam sizes become $\sigma_x = 2.0 \text{ mm}$, $\sigma_y = 2.0$ after 9 cm of water. At 15cm in water, they become $\sigma_x = 4.1 \text{ mm}$, $\sigma_y = 5.2 \text{ mm}$. We could observe that at this energy the most intensive energy deposition region shifts deeper compared to the 140 MeV beam. The divergence of the 300 MeV beam at 30 cm water depth is very limited.

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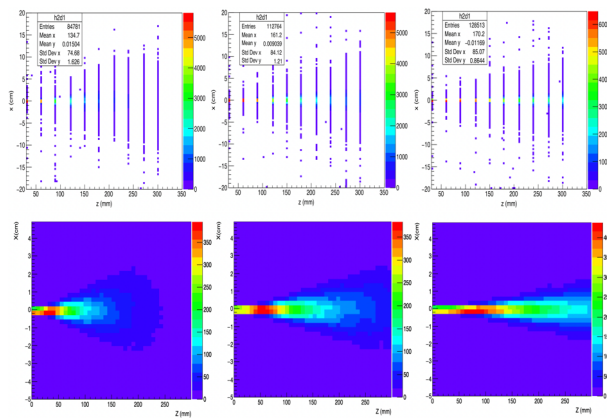


Figure 3: Horizontal beam profile along the longitudinal direction (top) and energy deposition on the x - z plane (bottom) in the water box for 70, 140 and 300 MeV Grid mini-beam respectively.

The FLASH Beam In order to obtain the 10×10 mm transverse beam size, the dispersion from the dipoles dog-leg will be used. Two methods are used to generated the FLASH beam. For the first method in the horizontal plane, we can keep the dispersion unclosed, but in the vertical plane, there is no dispersion generated for a beam without coupling. So the quadrupole in the middle of dog-leg is changed to a skew quadrupole, which can couple the horizontal dispersion to the vertical plane. The second method consists of using the dispersion only in the horizontal plane, generating a large divergence in the vertical plane. The beam optics for the two methods are shown in Figure 4. In a similar way as in the Grid mini-beam GEANT4 has been used to simulate the interaction with the beam with air and water. In this case an air box of 1 meter and water box of 30 cm are used. The results for a 70 MeV beam are shown in Figure 5. In Method 1 after 1 meter of air the beam will not diverge because the beam is tuned to have a small divergence. The beam sizes after the air box are $\sigma_x=11.4$ mm and $\sigma_y=12.0$ mm. When the beam enters the water, it will diverge quickly. The maximum dose deposition is the same as for the Grid mini-beam, i.e. around 10 cm. The beam sizes become $\sigma_x=13.6$ mm and $\sigma_y=14.0$ mm after 9 cm of water. At 15 cm in water, they become $\sigma_x=18.2$ mm and $\sigma_y=18.4$ mm. The most intensive energy deposition region is located at the beginning of the water. After several centimetres, the region of energy deposition becomes large. For Method 2 the beam will diverge a lot due to large divergence at the end of the beam line. The beam size after the air box are $\sigma_x=20.3$ mm and $\sigma_y=17.3$ mm. When the beam enters the water, it will not diverge as quickly as for the Grid mini beam because they have already a relative large beam size. The dose profile is the same as the Method 1. The beam sizes become $\sigma_x=21.4$ mm and $\sigma_y=17.6$ mm after 9 cm of water. After 15 cm of water, they become $\sigma_x=24.6$ mm and $\sigma_y=21.6$ mm. The relative large beam also gives a high dose in a relatively large region while the energy being mainly deposited at depths under 15 cm.

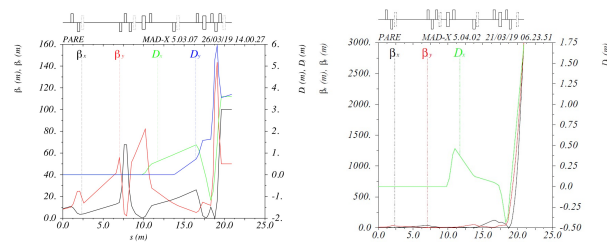


Figure 4: FLASH beam optics for Method 1 (left) and Method 2 (right).

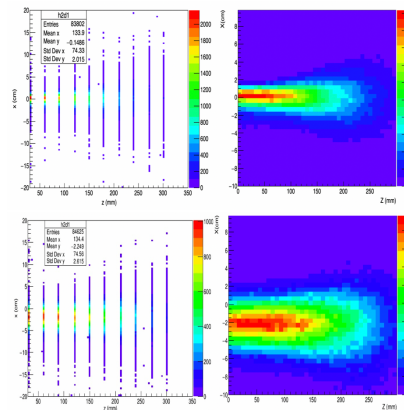


Figure 5: Horizontal beam profile along the longitudinal direction (left) and energy deposition on the x - z plane (right) in the water box for 70 MeV FLASH beam for Method 1 (top) and Method 2 (bottom).

SUMMARY

VHEE as a novel RT technique is being investigated and is showing very promising simulation and first experimental results. Here we are considering two new ways of dose delivery to mitigate the RT effects in healthy cells: the spatial fractionation with Grid mini-beams and FLASH high-dose rate ultra-short delivery time. Beam optics design and performance simulations to create a radiobiology experiment with Grid mini-beams and FLASH ultrahigh dose rate delivery treatment modalities in the same beam line are developed. The results are encouraging and a more in depth technical feasibility study is ongoing in order to demonstrate experimentally these innovative treatment modalities

REFERENCES

- [1] Subiel, A., Moskvin, V., Welsh, G. H., Cipiccia, S., Reboredo, D., Evans, P., Partridge, M., DesRosiers, C., Anania, M. P., Cianchi, A., Mostacci, A., Chiadroni, E., Di Giovenale, D., Villa, F., Pompili, R., Ferrario, M., Belleveglia, M., Di Pirro, G., Gatti, G., Vaccarezza, C., Seitz, B., Isaac, R. C., Brunetti, E., Wiggins, S. M., Ersfeld, B., Islam, M. R., Mendonca, M. S., Sorensen, A., Boyd, M., and Jaroszynski, D. A., "Dosimetry of very high energy electrons (VHEE) for radiotherapy applications: using radiochromic film measurements and Monte Carlo simulations", *Phys Med Biol* 59, pp. 5811-5829, 2014.

- [2] Schuler, E., Eriksson, K., Hynning, E., Hancock, S. L., Hiniker, S. M., Bazalova-Carter, M., Wong, T., Le, Q. T., Loo, B. W., Jr., and Maxim, P. G., "Very high-energy electron (VHEE) beams in radiation therapy; Treatment plan comparison between VHEE, VMAT, and PPBS", *Med Phys* 44, pp. 2544-2555, 2017.
- [3] A. Lagzda, R. M. Jones, D. Angal-Kalinin, J. K. Jones, and K. Kirkby, "Relative Insensitivity to Inhomogeneities on Very High Energy Electron Dose Distributions", in *Proc. 8th Int. Particle Accelerator Conf. (IPAC'17)*, Copenhagen, Denmark, May 2017, pp. 4791-4794. doi:10.18429/JACoW-IPAC2017-THPVA139
- [4] Martinez-Rovira, I., Fois, G., and Prezado, Y., "Dosimetric evaluation of new approaches in GRID therapy using non-conventional radiation sources", *Med Phys* 42, 685-693.
- [5] Favaudon, V., Caplier, L., Monceau, V., Pouzoulet, F., Sanyarath, M., Fouillade, C., Poupon, M. F., Brito, I., Hupe, P., Bourhis, J., Hall, J., Fontaine, J. J., and Vozenin, M. C., "Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumour tissue in mice", *Sci. Transl Med* 6, 245ra293, 2014.
- [6] <https://research-instruments.de/>
- [7] A. Vnuchenko *et al.*, "Start-to-End Beam Dynamic Simulations for PRAE", in *Proc. 9th Int. Particle Accelerator Conf. (IPAC'18)*, Vancouver, Canada, Apr.-May 2018, pp. 495-498. doi:10.18429/JACoW-IPAC2018-MOPML044
- [8] K. Flottmann, ASTRA User Manual. <http://www.desy.de/~mpyf10>
- [9] A. Latina, "RF-Track: Beam Tracking in Field Maps Including Space-Charge Effects, Features and Benchmarks", in *Proc. 28th Linear Accelerator Conf. (LINAC'16)*, East Lansing, MI, USA, Sep. 2016, pp. 104-107. doi:10.18429/JACoW-LINAC2016-MOPRC016
- [10] Prezado, Y., Deman, P., Varlet, P., Jouvion, G., Gil, S., Le Clec, H. C., Bernard, H., Le Duc, G., and Sarun, S., "Tolerance to dose escalation in minibeam radiation therapy applied to normal rat brain: long-term clinical, radiological and histopathological analysis", *Radiat Res* 184, pp. 314-321, 2015.
- [11] Prezado, Y., Sarun, S., Gil, S., Deman, P., Bouchet, A., and Le Duc, G., "Increase of lifespan for glioma-bearing rats by using minibeam radiation therapy", *J Synchrotron Radiat* 19, pp. 60-65, 2012.
- [12] Montay-Gruel, P., Petersson, K., Jaccard, M., Boivin, G., Germond, J. F., Petit, B., Doenlen, R., Favaudon, V., Bochud, F., Bailat, C., Bourhis, J., and Vozenin, M. C., "Irradiation in a flash: Unique sparing of memory in mice after whole brain irradiation with dose rates above 100Gy/s", *Radiother Oncol* 124, pp. 365-369, 2017.
- [13] Methodical Accelerator Design program. <http://madx.web.cern.ch/madx/>
- [14] D. Schulte *et al.*, "PLACET: a program to simulate the drive beams", CERN-PS-2000-028-AE, CLIC-Note-437, CERN, Geneva, Switzerland, 2000.
- [15] S. Agostinelli *et al.*, "Geant4 - a simulation toolki", *NIM A* 506 (2003) 250-303.