Simulation of a Radiobiology Facility for the Centre for the Clinical Application of Particles

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Abstract

The Centre for the Clinical Application of Particles is an interdisciplinary collaboration to develop the technologies, systems, techniques and capabilities necessary to deliver a paradigm shift in the clinical exploitation of particles.

The CCAP aims to deliver a broad programme of measurement of the radiobiological effect of particle beams and systematic studies of radiobiological mechanisms using a laser-driven ion source. The design of the facility is being studied and requires simulation of novel accelerator components, detector simulation and simulation of the ion beam interaction with cells. BDSIM, which is an accelerator simulation tool based on Geant4, has been used to perform particle tracking simulations to verify the beam optics design. The results obtained from the BDSIM simulation show that the evolution of the beam envelope agrees well with the beam optics design.

Keywords: Radiobiology, laser, ion, beam

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1. Introduction

Proton and other light ion beams are attractive options for radiotherapy as, in comparison to photons, there is little (ions) or no (protons) dose deposited beyond the distal tumour edge. In addition, as the dose is primarily deposited at the maximum range of the beam, treatment can be conformed to the tumour volume. Proton beam treatment planning assumes that the relative biological effectiveness (RBE) is a factor of 1.1 [1] larger than the effect that would be achieved if the same dose was delivered using photons. However, this is an average value that can vary with tissue type. A detailed systematic study of the biophysical effects of the interaction of protons with different tissue types would enable enhanced treatment planning. Such studies are especially needed in the case of ion beam radiotherapy.

The Centre for the Clinical Application of Particles (CCAP) at Imperial College London is composed of clinical oncologists, medical physicists, accelerator and instrumentation scientists and radiobiologists from: Imperial College London; Imperial College Healthcare NHS Trust; The Institute of Cancer Research; John Adams Institute for Accelerator Science; and the Oxford Institute for Radiation Oncology. The mission of the CCAP is to: "Develop the technologies, systems, techniques and capabilities necessary to deliver a paradigm shift in the clinical exploitation of particles."

One focus of the CCAP's programme is the Laser Accelerator for Radiobiological Applications (LARA). LARA will prove the principal of the novel technologies required for future therapy facilities by developing a proton and light ion beam radiobiology facility for in vitro and in vivo studies. Conventional proton and ion sources produce particles with energies of tens of keV/u. At such low energies, the Coulomb repulsion between the particles that make up the beam limit the beam-current that can be captured and accelerated. Laser accelerated ions can be generated at higher energies (1×10^4 keV or more) and therefore do not suffer the same limitations, allowing injection into a strong focusing particle capture system. Using this approach for LARA will make it possible to deliver multiple ion species from a single source while overcoming beam intensity limitations. Coupling the laser source with a novel accelerator system will provide a facility that can produce intense beams (and thus ultra-high dose rates) of protons and ions from helium to carbon to deliver a definitive programme of radiobiology. The legacy of this programme will be the demonstration of the technologies required to drive a step-change in the provision of proton and light ion therapy, and a system capable of delivering the comprehensive set of experimental data that is essential to underpin and enhance the clinical use of proton and light ion therapy.

This paper will present the concept of the first stage of LARA that will be used for in vitro studies. Initial tracking simulations using BDSIM [2], which is an accelerator simulation tool based on Geant4 [3], have been performed to verify the beam-line design parameters and determine the energy deposition in the cell layer.

2. The Laser Accelerator for Radiobiological Applications (LARA)

The first stage of LARA will use a laser-driven ion beam for detailed systematic studies of in vitro radiobiology. Figure 2 shows the LARA beam-line as implemented in BDSIM, which consists of: a capture system; upstream matching; a vertical 90° bend that provides energy and ion selection; downstream matching; and the end station which includes a vacuum window and the cell sample and container. The capture section is based on Gabor lenses that provide compact capture and focusing of the large divergence and large energy spread of the laser-driven ion beam. The upstream matching section is a quadrupole focusing channel used to match the beam from the capture section to the section that performs energy and ion selection. Two 45° dipole bends and collimators are used to select particles of the required momentum. The gap between the two dipoles is large enough to place a Wien filter for velocity selection, if it is needed. The downstream matching section then transports the beam such that at the entrance of the end station (i.e. the vacuum window) the beam has a very small divergence and occupies the 10 mm diameter aperture.

2.1. Laser Source

The laser uses the principle of target normal sheath acceleration to generate an ion beam. Figure 2 shows the basic principle where a high intensity laser pulse is fired at a thin target at an angle of 45° which causes an ion beam (consisting of protons and carbon ions) to be generated from the contaminants on the back surface of the target. See [4] for a more detailed explanation of sheath acceleration. Using this method generates a high-intensity beam composed of a variety of ions but with a very large energy spread and large angular divergence. A typical energy and angle distribution of a 15 MeV proton beam, from an EPOCH [5] simulation, is shown in Figure 3.

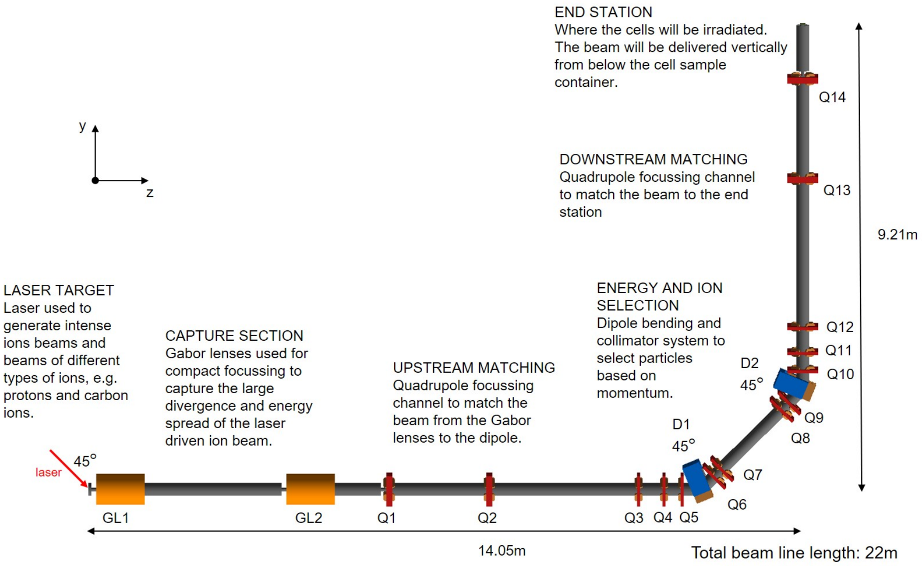

Figure 1: The LARA beam-line as implemented in BDSIM. The direction of the laser beam used to generate the beam is marked and the various sections are annotated.

In order to compare the tracking simulations with the optics design of the LARA beam-line, an idealised cylindrically symmetric beam was generated by BDSIM using the parameters given in Table 1. The combination of small Twiss beta and relatively large emittance means the beam has a small spot size but a very large divergence. The parameters used are an estimate of the beam produced by the laser. The actual beam parameters will be dependent on the laser system that will be purchased for LARA.

Alpha	0
Beta	$71 \times 10^{-6}\,\mathrm{m}$
Emittance	$4 \times 10^{-8}\pi\,\mathrm{m\,rad}$
Kinetic energy	$15\,\mathrm{MeV}$

Table 1: Beam parameters used to generate an input beam for tracking with BDSIM. The parameters alpha and beta are the Twiss parameters. Since the beam is assumed to be initially cylindrically symmetric, beta, alpha and the emittance are the same for both the x and y planes.

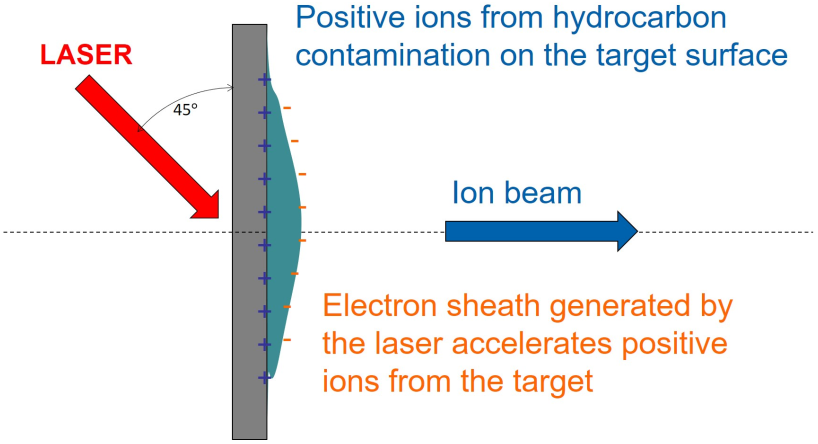

Figure 2: Schematic diagram illustrating the principle used to generate the ion beam.

2.2. Capture

The ion beam generated from the laser target is captured by a series of Gabor lenses. A Gabor lens uses a confined electron plasma to produce an electro-static focusing field. Figure 4 shows the key components of the Gabor lens. The magnetic field produced by the solenoid coils causes the electrons to exhibit spiral trajectories parallel to the axis of the lens, thus confining them in the radial direction. The voltage applied to the anode generates the charge separation that produces the focusing field and the ground plates at the ends confines the electron cloud in the longitudinal direction.

A prototype of the lens has been built and tested using a 1 MeV proton beam at the Surrey Ion Beam Centre, see [6]. Following these tests the prototype has been upgraded and is now being recommissioned at Imperial. It is planned that the upgraded lens will be tested using a laser-driven ion beam at Imperial.

2.3. Beam Transport

The beam transport section includes the upstream matching, 90° vertical bend and the downstream matching, all of which use conventional quadrupole and dipole magnets. The 90° bend is performed using two 45° dipole magnets where the drift between the magnets is long enough for an optional Wien filter to be inserted, which would allow selection of particles based on their velocity.

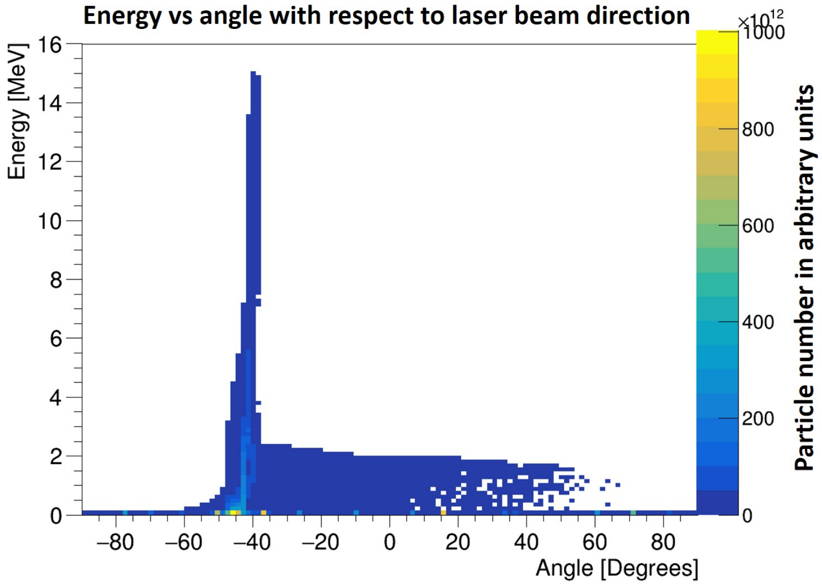

Figure 3: Distribution of energy and angle from a 15 MeV proton beam simulation using EPOCH. In this simulation 0 degrees is the direction of the laser.

2.4. End Station

The beam is delivered vertically into the end station, which is where the cells will be irradiated. Vertical delivery of the beam allows the use of conventional cell sample containers, see Figure 5, that provide breathable wells where the cell sample is grown on the bottom of a well filled with cell nutrient liquid. Since the beam energy is low, any unnecessary material in the beam path may prevent the beam reaching the cell layer. Increasing the beam energy is possible but would require a more costly laser system. Figure 6 shows the materials in the path of the beam. For the simulation only the area of the beam aperture was considered, i.e. a cylinder 10 mm in diameter. The scintillating fibre layer will be used to monitor the beam in real time pulse-by-pulse.

3. Results

The Gabor lens was implemented in BDSIM using a solenoid of equivalent focusing strength. Figure 7 shows a comparison of the beta function (which gives the beam envelope as a function of distance along the beam-line)

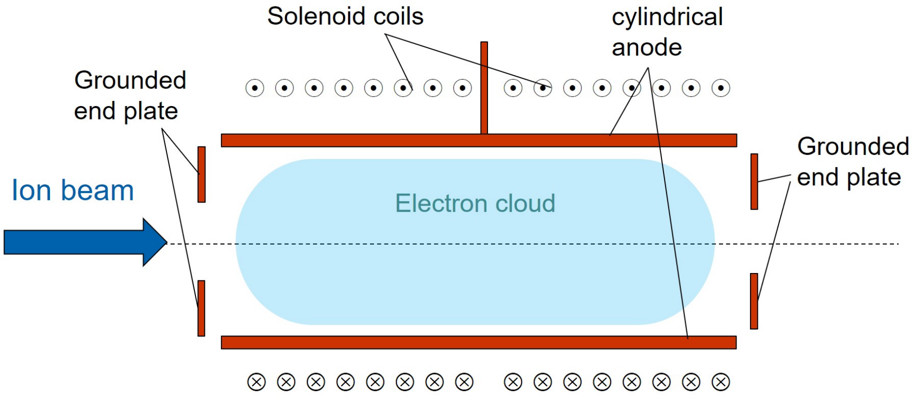

Figure 4: Schematic diagram of the Gabor lens.

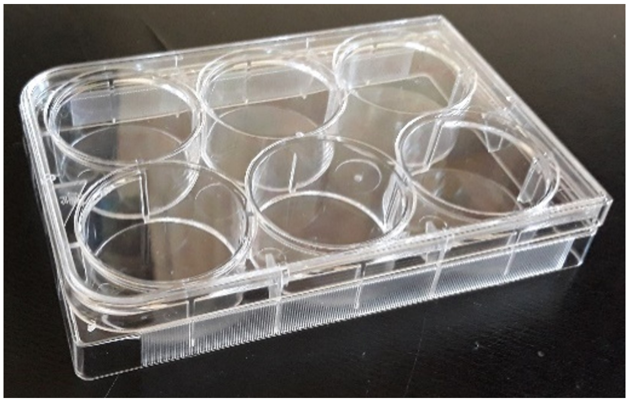

Figure 5: A typical six well cell sample holder.

from the beam optics design, which was performed using an in-house code called BeamOptics, and the beta values after each element in the BDSIM simulation. The figure shows good agreement between the calculated beta from BeamOptics and beta from the tracking simulations performed using BDSIM. In the future, the Gabor lens will be simulated to produce a 3-D electro-magnetic field map that can then be used for tracking in BDSIM.

Figure 8 shows the comparison of the beta function from BeamOptics and BDSIM for the beam transport section. The beta functions show good agreement and at the end of the transport section the beta function is flat, which means the divergence of the beam in the end station will be small. Figure 9 zooms in on the beta functions in the bending region. There can

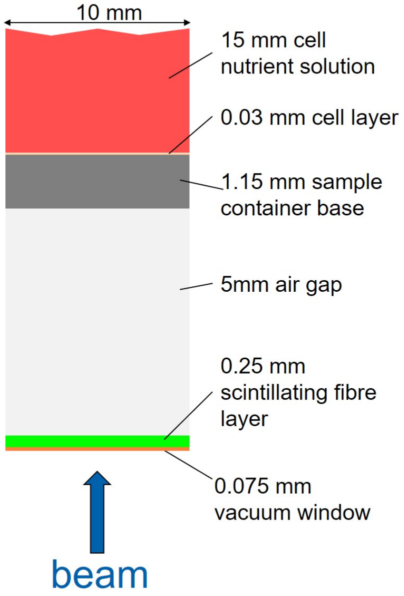

Figure 6: Design of the end station simulated with BDSIM.

be seen a small mismatch in the beta functions in the x-direction. This is probably due to differences in the treatment of edge focusing in BeamOptics and BDSIM and is currently under investigation, though this does not affect the beam significantly since the beta functions are in good agreement downstream.

BDSIM was used to extract the energy deposited in the different material layers, which is shown in Figure 10 for three different beam energies. This shows that a beam with kinetic energy of 10 MeV does not reach the cell layer but the 12 MeV beam has the Bragg peak (i.e. where most of the energy is deposited) at the position of the cell layer. However, this would not allow investigating the radiobiological effect of irradiating a sample located before the Bragg peak. Thus the design kinetic energy of 15 MeV has been chosen since it will also contain a significant number of particles in the range 10-15 MeV allowing irradiation with a variety of energies.

4. Discussion and Conclusions

The CCAP has proposed a concept for a new facility to perform detailed systematic studies of cell irradiation. The facility will use novel accelerator

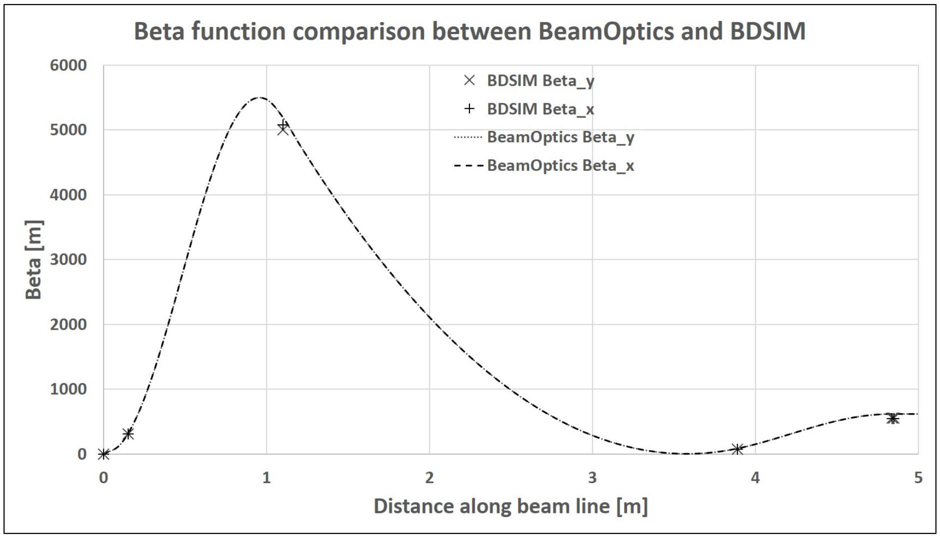

Figure 7: Comparison of the beta function from the beam optics design code BeamOptics and the beta values extracted from the BDSIM simulation.

technology to deliver intense beams of protons and ions from helium to carbon. The optics design of the beam-line has been verified by comparing the beam envelope calculations from BeamOptics with particle tracking simulations using BDSIM. The energy deposition in the end station has also been investigated and this shows that for the current design 15 MeV is a good choice for the nominal beam energy allowing irradiating the cells before and within the region of the Bragg peak.

Further work is on-going to finalise the design of LARA including investigating a more compact beam transport channel and designing LARA Stage II that will include an accelerator to deliver higher beam energies for in vivo studies.

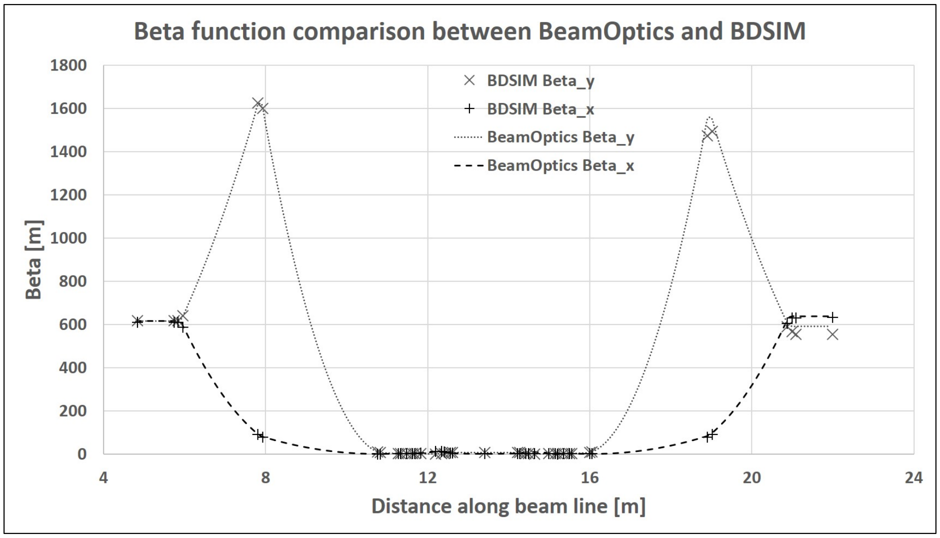

Figure 8: Comparison of the beta functions from BeamOptics and BDSIM for the beam transport section.

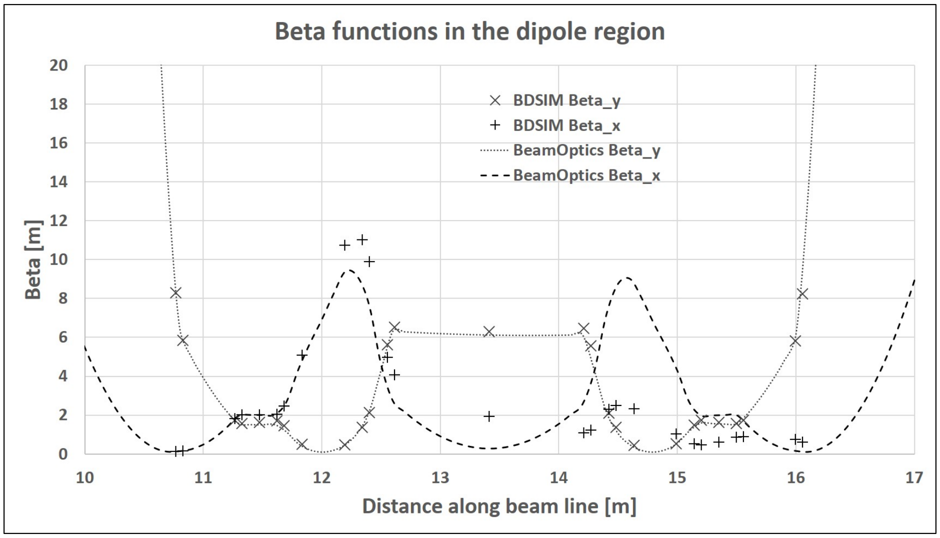

Figure 9: Comparison of the beta functions in the 90° bend region.

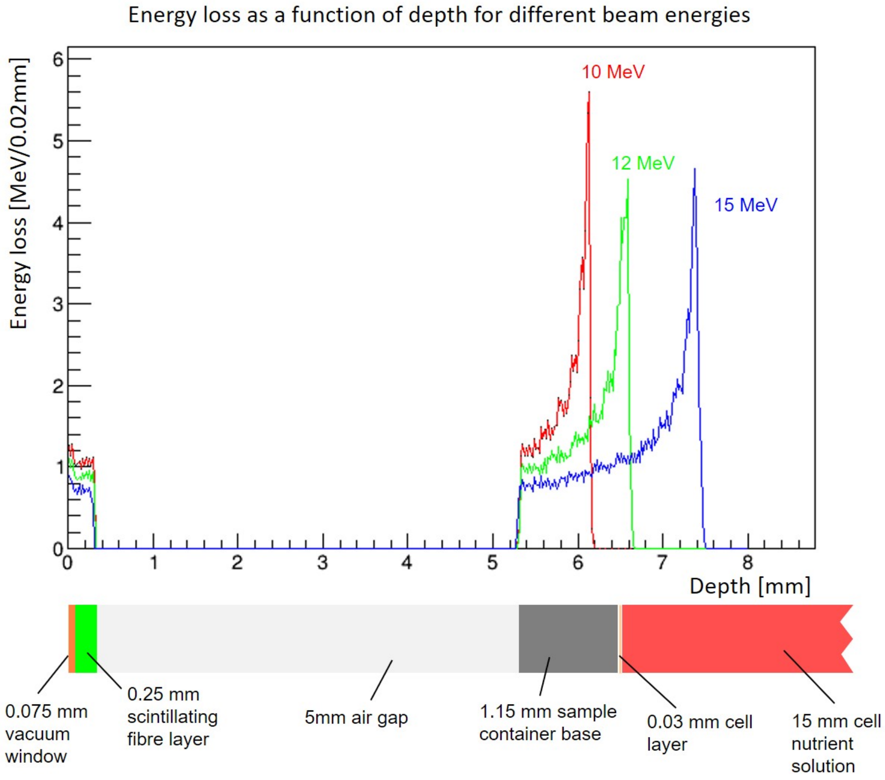

Figure 10: Energy loss as a function of depth in the end station for three different beam energies 10 MeV, 12 MeV and 15 MeV. The strip below the graph shows the material composition of the end station to scale.

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References

[1] H. Paganetti, Relative biological effectiveness (rbe) values for proton beam therapy. variations as a function of biological endpoint, dose, and linear energy transfer, Phys. Med. Biol. 59 (2014) R419.

[2] I. Agapov, G. A. Blair, S. Malton, L. Deacon, BDSIM: A particle tracking code for accelerator beam-line simulations including particle-matter interactions, Nucl. Instrum. Meth. A606 (2009) 708–712.

[3] J. Allison, K. Amako, J. Apostolakis, P. Arce, M. Asai, T. Aso, E. Bagli, A. Bagulya, S. Banerjee, G. Barrand, B. Beck, A. Bogdanov, D. Brandt, J. Brown, H. Burkhardt, P. Canal, D. Cano-Ott, S. Chauvie, K. Cho, G. Cirrone, G. Cooperman, M. Corts-Giraldo, G. Cosmo, G. Cuttone, G. Depaola, L. Desorgher, X. Dong, A. Dotti, V. Elvira, G. Folger, Z. Francis, A. Galoyan, L. Garnier, M. Gayer, K. Genser, V. Grichine, S. Guatelli, P. Guye, P. Gumplinger, A. Howard, I. Hivnov, S. Hwang, S. Incerti, A. Ivanchenko, V. Ivanchenko, F. Jones, S. Jun, P. Kaitaniemi, N. Karakatsanis, M. Karamitros, M. Kelsey, A. Kimura, T. Koi, H. Kurashige, A. Lechner, S. Lee, F. Longo, M. Maire, D. Mancusi, A. Mantero, E. Mendoza, B. Morgan, K. Murakami, T. Nikitina, L. Pandola, P. Paprocki, J. Perl, I. Petrovi, M. Pia, W. Pokorski, J. Quesada, M. Raine, M. Reis, A. Ribon, A. R. Fira, F. Romano, G. Russo, G. Santin, T. Sasaki, D. Sawkey, J. Shin, I. Strakovsky, A. Taborda, S. Tanaka, B. Tom, T. Toshito, H. Tran, P. Truscott, L. Urban, V. Uzhinsky, J. Verbeke, M. Verderi, B. Wendt, H. Wenzel, D. Wright, D. Wright, T. Yamashita, J. Yarba, H. Yoshida, Recent developments in geant4, Nuclear Instruments and Methods in Physics Research Section A: Accelerators,

Spectrometers, Detectors and Associated Equipment 835 (2016) 186 – 225.

[4] M. Borghesi, Laser-driven ion acceleration: State of the art and emerging mechanisms, Nucl. Instrum. Meth. A740 (2014) 6–9.

[5] T. D. Arber, K. Bennett, C. S. Brady, A. Lawrence-Douglas, M. G. Ramsay, N. J. Sircombe, P. Gillies, R. G. Evans, H. Schmitz, A. R. Bell, C. P. Ridgers, Contemporary particle-in-cell approach to laser-plasma modelling, Plasma Physics and Controlled Fusion 57 (2015) 113001.

[6] P. A. Posocco, M. Merchant, J. Pozimski, Y. Xia, First Test of The Imperial College Gabor (Plasma) Lens prototype at the Surrey Ion Beam centre, in: Proceedings, 7th International Particle Accelerator Conference (IPAC 2016): Busan, Korea, May 8-13, 2016, p. TUPMY024.