# The FLUKA code for application of Monte Carlo methods to promote high precision ion beam therapy

*K. Parodi[1], S. Brons[1], F. Cerutti[2], A. Ferrari[2], A. Mairani[1,3], H. Paganetti[4], F. Sommerer[1,2]*
[1]Heidelberg Ion Therapy Center, Heidelberg, Germany, [2]CERN, Geneva, Switzerland,
[3]INFN, Section of Milan, Milan, Italy, [4]Massachusetts General Hospital, Boston, USA

**Abstract**

Monte Carlo (MC) methods are increasingly being utilized to support several aspects of commissioning and clinical operation of ion beam therapy facilities. In this contribution two emerging areas of MC applications are outlined. The value of MC modeling to promote accurate treatment planning is addressed via examples of application of the FLUKA code to proton and carbon ion therapy at the Heidelberg Ion Beam Therapy Center in Heidelberg, Germany, and at the Proton Therapy Center of Massachusetts General Hospital (MGH) Boston, USA. These include generation of basic data for input into the treatment planning system (TPS) and validation of the TPS analytical pencil-beam dose computations. Moreover, we review the implementation of PET/CT (Positron-Emission-Tomography / Computed-Tomography) imaging for in-vivo verification of proton therapy at MGH. Here, MC is used to calculate irradiation-induced positron-emitter production in tissue for comparison with the $\beta^+$-activity measurement in order to infer indirect information on the actual dose delivery.

## 1 Introduction

The application of light ion beams (from protons up to carbon ions) to external beam radiotherapy is currently rapidly increasing worldwide. The main rationale is the favorable ionization energy-loss of swift charged ions in matter, resulting in the characteristic dose maximum at the end of their range, known as Bragg-peak [1]. Proper spatial superimposition of several Bragg-peaks of different depth and amplitude enables optimal conformation of the delivered dose to the tumor volume, with better sparing of surrounding healthy tissue in comparison to conventional photon and electron radiation. However, this physical advantage can be exploited clinically to its maximum extent only if millimeter accuracy in the localization of the beam stopping point and lateral field position in human tissue is guaranteed. This demands precise range measurements in representative tissue-equivalent materials as well as accurate calculation tools for realistic description of the electromagnetic and nuclear interactions of the ion beam in the heterogeneous patient tissue. Besides, non-invasive imaging techniques for in-vivo verification of the actual beam delivery and, in particular, of the beam range in the patient would be highly beneficial. Nuclear interactions resulting in detectable emerging secondary radiation currently offer the only possibility for this purpose for a timely evaluation during or shortly after irradiation. An already established technique is Positron-Emission-Tomography [2], which exploits the coincident detection of the emerging annihilation photons following the radioactive decay of $\beta^+$-active isotopes formed along the beam path. Due to the different physical processes involved, the pattern of activation induced as a by-product of the therapeutic irradiation is correlated but not proportional to the dose delivery. Treatment verification can be achieved by comparing the measured activity distribution with a calculated one [2], which requires an accurate description of fragmentation reaction channels yielding $\beta^+$-emitters.

Monte Carlo (MC) methods offer powerful computational tools for detailed and realistic description of radiation transport and interaction with matter. Although the intensive computational time still prevents the applicability to the complex task of inverse dose optimization for daily clinical use in ion beam therapy, MC methods are being increasingly utilized at state-of-the-art facilities to promote high precision ion beam therapy. This contribution addresses two emerging and inter-connected areas of research on Monte Carlo and Positron-Emission-Tomography (PET), both aiming to enhance the precision of ion beam therapy in clinical practice for improved quality of patient care. It first illustrates the role of Monte Carlo modeling to support accurate ion beam treatment planning, showing examples of applications at the Heidelberg Ion Beam Therapy Center (HIT) in Heidelberg, Germany, and at the Francis H. Burr Proton Therapy Center of the Massachusetts General Hospital (MGH) Boston, USA. These include the generation of physical basic data required as input by the treatment planning system (TPS), and forward re-calculation of treatment plans for verification of the TPS analytical dose computation in water and in the patient anatomy as given by Computed-Tomography (CT) images. Moreover, we discuss the dedicated MC environment which has been implemented for the first pre-clinical and clinical quantitative study on the feasibility and value of post-radiation PET/CT imaging for in-vivo verification of proton therapy at MGH.

## 2 Material and methods

All the applications presented in this work are based on the usage of FLUKA [3,4], which is a general purpose MC transport and interaction code originally designed for high energy physics but since 1991 extended to cover a wider range of energies and related applications including radiation therapy. In particular, recent efforts of the FLUKA developing team have enhanced the capabilities of the code towards light ion transport, including the complex handling of nucleus-nucleus interactions in the entire energy range of therapeutic relevance [5,6], with the low energy models of [6] only available in a beta version of the code provided to the users upon request. Moreover, the code is capable to handle arbitrarily complex geometries, comprising voxels for easy import of CT scans with an optimised algorithm for minimum memory requirements and fast tracking performances.

For all the investigated applications of FLUKA to ion beam therapy, the suggested usage of default physics and transport settings for hadrontherapy-oriented problems was adopted (cf. definition of the "DEFAULTS" option in the FLUKA manual [4]). In addition, the most updated event generators were activated for accurate handling of nuclear interactions and evaporation, including detailed transport of all heavy recoils and ions. Further freely configurable transport thresholds for hadronic and electromagnetic radiation were chosen as described in [7] to enable time-efficient tracking performances with reasonable accuracy at the requested millimetre spatial scale. Adjustable input parameters like primary beam momentum spread and ionization potential of water were selected according to available experimental information or via identification of the optimal MC configuration settings yielding the best agreement with available experimental data (e.g., depth-dose distributions in water [8]).

For simulation of scanned [9] ion beam delivery at HIT, the FLUKA *source.f* user-routine (offering the possibility to specify arbitrary primary beam properties [4]) was customised for interpretation of the beam control file of the irradiation, which specifies energy, focus (i.e., transversal profile), direction and number of ions dynamically delivered to each scan position within the treatment field. For passive beam irradiation at MGH, the *source.f* user-routine was made able to read the binary phase-space input file specifying position, energy and cosine directors of the primary protons [7], as produced by a separate Geant4 [10] MC simulation accurately modeling the entire treatment head with the patient- and field-specific beam modifiers [11]. Starting from the described beam source information, ion transport in the patient CT was implemented using the CT stoichiometric calibration of Refs. [12,13] for material assignment, together with the newly implemented "CORRFACT" option [4] for forcing the program to follow the same semi-empirical CT-range calibration curve as the TPS

[7]. For other studies using phantom targets or investigating interaction in additional beamline elements, standard combinatorial geometry definition and known elemental composition and density of the materials were used in the simulation of particle transport.
For dose calculations, the built-in scoring algorithms offered by FLUKA were utilised [4,7]. For scoring the spatial distribution of irradiation-induced positron emitters, the proton beam fluence was combined with experimental cross-sections of the main reaction channels yielding $\beta^+$-emitters as described in [7]. The resulting PET activation maps were finally obtained by introducing the imaging system response function and scaling factors accounting for the time course of irradiation and imaging as well as biological washout [13,14].

## 3 Results and discussion

FLUKA-based MC calculations have provided the parameters of the synchrotron accelerator library as well as the basic input data for the TPS (Syngo PT Planning, Siemens AG) which will be used for clinical operation at the HIT facility [15]. The FLUKA-generated accelerator library comprises the 255 proton and carbon ion pencil-beam energies made available for treatment, providing Bragg-Peaks with a depth separation of 1mm (1.5mm at the higher energies) in water, and the corresponding lateral beam dimensions at the isocentre of the treatment unit after broadening in the fixed beamline elements and air gap. The FLUKA-generated TPS physical basic data consist of laterally integrated depth-dose profiles in water calculated for each of the 255 proton and carbon ion beam energies with and without the ripple filter [16], which is used to broaden the Bragg-peaks for reduction of the number of overlapping mono-energetic beams in depth. In addition, energy- and depth-dependent fragment spectra have been calculated in water for initial carbon ion beam energies sampled in steps of 10 MeV/u in the [80,440] MeV/u interval [17], to support the TPS biological calculations based on the Local-Effect-Model developed at GSI Darmstadt [18]. An example of a subset of basic data depth-dose distributions is shown in figure 1 for protons and carbon ions. In general, very good agreement has been observed between FLUKA calculations and experimental depth-dose distributions measured at representative beam energies in water [8], thus supporting the reliability of the electromagnetic and nuclear models of the code for applications to ion beam therapy in line with previous investigations [19,20].

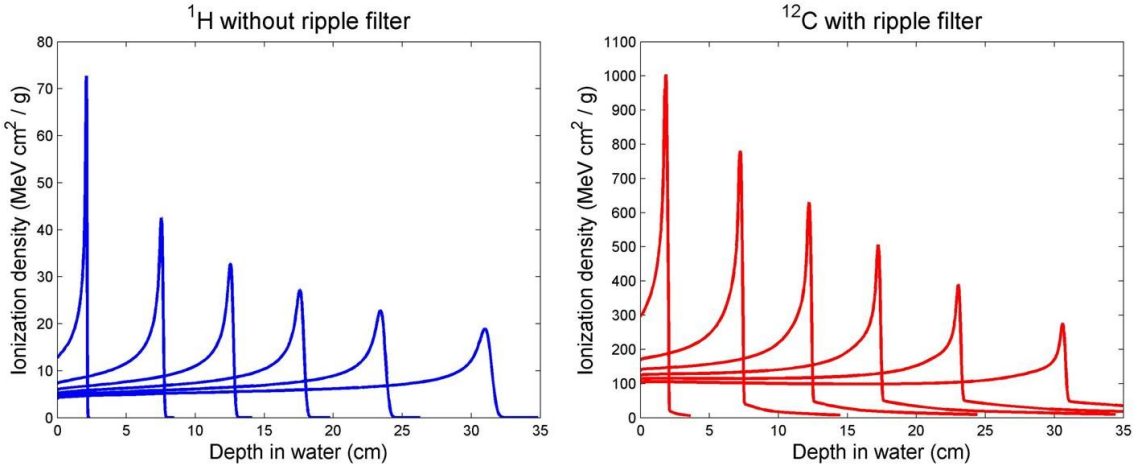


Figure 1: Example of FLUKA-calculated depth-dose distributions in water input into the Syngo treatment planning system at HIT for representative 6 energies spanning the entire interval covered by the FLUKA-generated accelerator library of 255 energy steps for protons without ripple filter (left) and $^{12}$C ions with ripple filter (right).

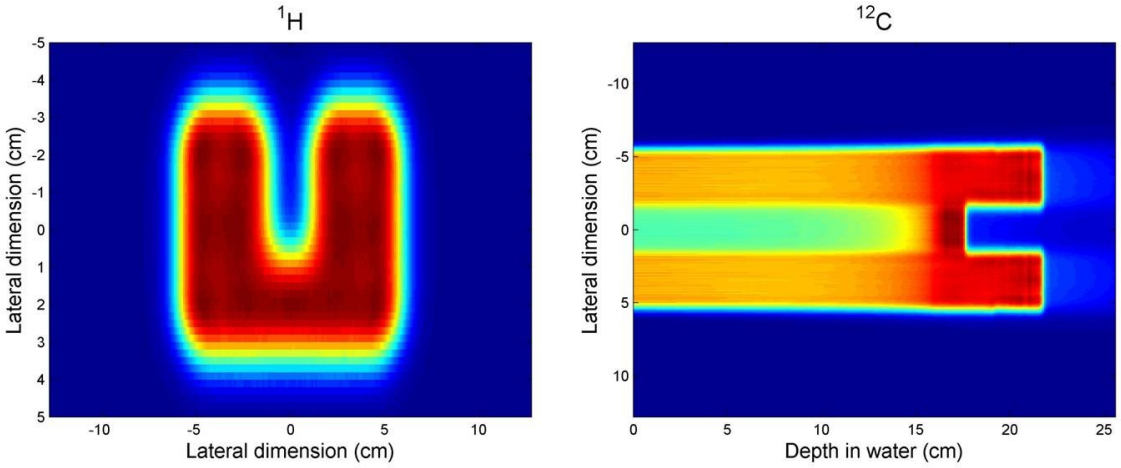


Figure 2: Example of FLUKA re-calculations of scanned ion beam treatment plans in water for different U-shaped target volumes for protons (left, in beam-eye-view) and carbon ions (right, along the penetration depth).

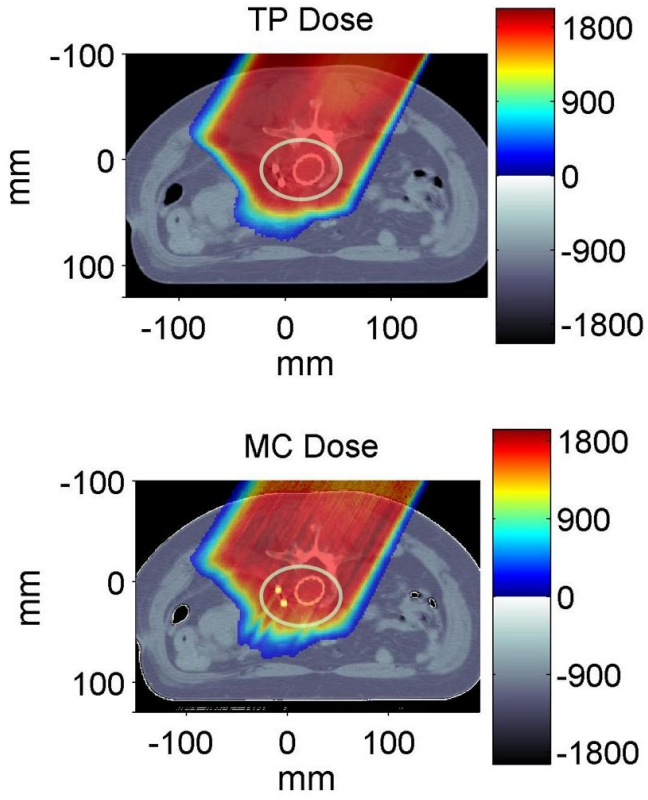


Figure 3: Comparison between the planned ("TP dose": XiO) and FLUKA-calculated ("MC dose") dose distribution for one proton field delivered to a patient with metallic implants (marked by a circle) in the treatment volume at MGH. The absolute dose distribution in mGy is shown in colourwash display (cf. [7] for the absolute scaling of both calculated distributions), whereas the grey-scale of the planning-CT is in arbitrary units for display purposes. Discrepancies between the two dose distributions are observed in the distal part of the treatment field involving interaction of the beam with the implants.

An example of application of FLUKA to forward re-calculation of scanned proton and carbon ion treatment plans in water is illustrated in figure 2. Corresponding point-wise dosimetric measurements indicated an agreement with the FLUKA-calculated distributions within the experimental uncertainties of few percents (data not shown here). Spread-out Bragg-Peaks delivered by the passive beam system at MGH could be also reproduced in fairly good agreement with ionization chamber measurements in water [13]. Re-calculations [7] of treatment plans on the patient CT also showed in general good agreement with the TPS dose distributions (XiO, Computerized Medical Systems Inc.), except in cases with large tissue inhomogeneities or metallic implants (figure 3) which are more sensitive to the approximations introduced by the TPS pencil-like beam algorithms [7,14]. These findings are in line with similar investigations performed with other MC codes [21].

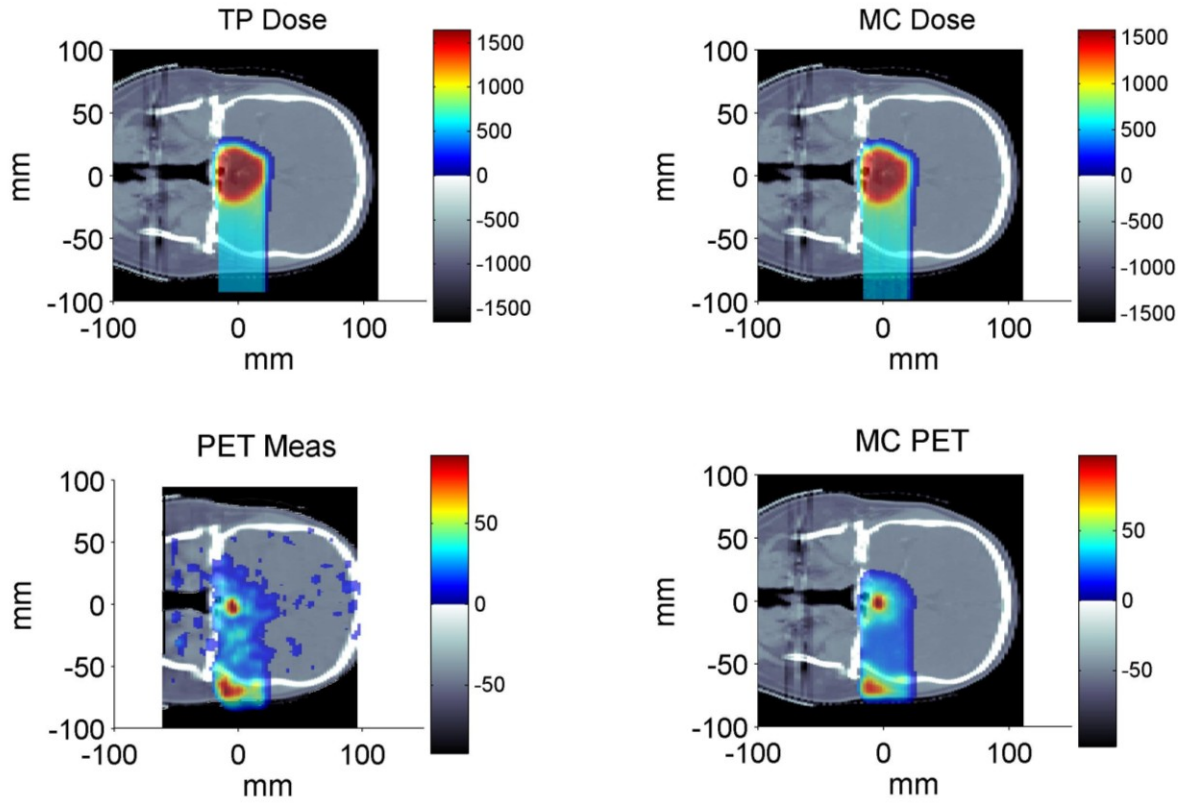


Figure 4: Example of measured ("PET Meas") and FLUKA-calculated ("MC PET") activity distributions (bottom row, shown as Bq/ml in colourwash display superimposed onto the arbitrary rescaled imaging- and planning- CTs, respectively) for a pituitary adenoma patient receiving two orthogonal proton fields followed by PET/CT imaging after a standard treatment fraction at MGH. In the upper row the FLUKA-calculated dose distribution is additionally compared to the treatment plan (XiO) to assess the consistency of the two dose calculation models. Here, the meaning of the colour bar is the same as in figure 3.

MC-calculated activity distributions are compared to measured PET images in figure 4 for a case of pituitary adenoma tumour scanned for 30 min starting about 18 min after complete delivery of a standard proton treatment with a total fraction dose of 1.8 GyE [14]. As discussed in [13,14], promising agreement could be obtained between calculated and measured $\beta^+$-activity distributions in phantom materials and anatomical sites of unambiguously defined composition and reduced influence of washout processes. Therefore, investigations on the usage of FLUKA for application to PET

monitoring of a wider spectrum of primary ions are ongoing [22]. Moreover, MC has been proven to provide a very powerful method for studying the correlation between dose deposition and positron-emitter yield to support the development of analytical models for fast calculation of $\beta^+$-production. In the "filtering approach" of [23], FLUKA-calculated depth-distributions of dose and positron-emitters for mono-energetic proton beams stopped in representative homogeneous materials were used to determine proper reaction-dependent filter functions to be convolved with the planned dose for very fast prediction of $\beta^+$-activation. Following the promising results of this analytical framework for calculation of the long-lived $^{11}C$ activity contribution in offline PET/CT imaging of phantom materials [23] and clinical cases (figure 5), additional MC-data are being currently studied for the extension of the method to include also the major reaction channels of short-lived emitters for application to in-beam and in-room PET acquisition strategies in proton therapy [24].

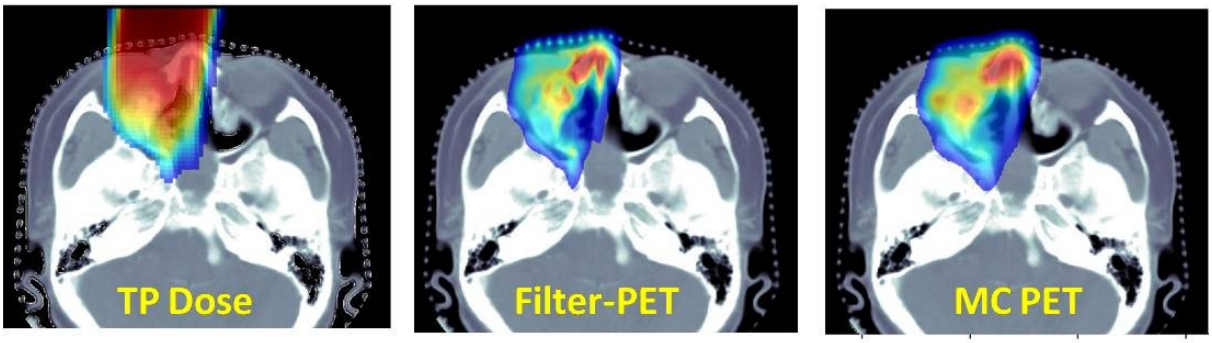


Figure 5: Application of the one-dimensional filtering approach of [23] (i.e., convolution of the planned dose "TP dose" with a proper filter function) along the direction of beam penetration for fast calculation of $^{11}C$-activation ("Filter-PET") in a clinical case of PET/CT imaging after proton irradiation at MGH. The results are found in fairly good agreement with the $\beta^+$-activity distribution obtained from a full-blown FLUKA-based Monte Carlo calculation ("MC PET").

## 4 Conclusion and outlook

Despite the still too long computational times for inverse dose optimization and daily clinical use, MC methods are very valuable tools to support all the main aspects of ion beam delivery, treatment planning and dedicated quality assurance techniques, including the imaging of emerging secondary radiation for surrogate information on the actual dose delivery. So far, very promising results have been achieved with the FLUKA code, making us concluding that it represents a suitable choice for transport of therapeutic proton and carbon ion beams. We do foresee that the application of MC will spread among the ion therapy community and play an increasing role in promoting high precision ion beam therapy.

## Acknowledgement

We wish to thank the physicist team at HIT – in particular T. Haberer, J. Naumann, B. Hasch, P. Heeg, M. Winter, B. Ackermann, O. Nairz, S. Klemm, I. Rinaldi, M. Ellerbrock and O. Jäkel - for fruitful discussions and support on dosimetric measurement, and the people involved in the PET project at MGH Boston – in particular T. Bortfeld and H. Shih for the incessant motivation in its challenging startup phase.

## References


[1] R.R. Wilson, Radiological Use of Fast Protons, *Radiol* **47** (1946) 487

[2] W. Enghardt, P. Crespo, F. Fiedler, R. Hinz, K. Parodi, J. Pawelke and F. Pönisch, Charged hadron tumour therapy monitoring by means of PET, *Nucl Instrum Meth A* **525** (2004) 284

[3] G. Battistoni, S. Muraro, P.R. Sala, F. Cerutti, A. Ferrari, S. Roesler, A. Fassò and J. Ranft, The FLUKA code: Description and benchmarking, *Proceedings of the Hadronic Shower Simulation Workshop 2006*, Fermilab 6-8 September 2006, in: M. Albrow and R. Raja, AIP Conference Proceeding **896** (2007) 31

[4] A. Ferrari, P.R. Sala, A. Fassò and J. Ranft, FLUKA: a multi-particle transport code *CERN Yellow Report 2005-10, INFN/TC_05/11, SLAC-R-773* Geneva (2005)

[5] H. Sorge, H. Stoecker and W. Greiner, Relativistic quantum molecular dynamics approach to nuclear collisions at ultrarelativistic energies, *Nucl. Phys. A* **498** (1989) 567c

[6] F. Cerutti et al, *Ricerca Scientifica e Educazione Permanente,* Suppl **126** (2006) 507

[7] K. Parodi, A. Ferrari, F. Sommerer and H. Paganetti, Clinical CT-based calculations of dose and positron emitter distributions in proton therapy using the FLUKA Monte Carlo code, *Phys. Med. Biol.* **52** (2007) 3369

[8] K. Parodi et al, Bragg curve measurements to support high precision ion beam therapy, *Book of Abstract of the Heavy ions in therapy and space symposium*, Cologne, July 6-10, 2009

[9] T. Haberer, W. Becher, D. Schardt and G. Kraft, Magnetic scanning system for heavy ion therapy *Nucl Instrum Methods Phys Res A* **330** (1993) 296-305

[10] S. Agostinelli et al, GEANT4 – a simulation toolkit *Nucl. Instrum. Meth. A* **506** (2003) 250-303

[11] H. Paganetti, H. Jiang, S.-Y. Lee and H. Kooy, Accurate Monte Carlo simulations for nozzle design, commissioning and quality assurance for a proton radiation therapy facility *Med. Phys.* **31** (2004) 2107-18

[12] W. Schneider, T. Bortfeld and W. Schlegel, Correlation between CT numbers and tissue parameters needed for Monte Carlo simulations of clinical dose distributions *Phys. Med. Biol.* **45** (2000) 459-78

[13] K. Parodi et al, PET/CT imaging for treatment verification after proton therapy: a study with plastic phantoms and metallic implants, *Med. Phys.* **34** (2007) 419

[14] K. Parodi et al, Patient study on in-vivo verification of beam delivery and range using PET/CT imaging after proton therapy *Int. J. Radiat. Oncol. Biol. Phys.* **68** (2007) 920

[15] K. Parodi, A. Mairani et al, The application of the FLUKA Monte Carlo code to basic data generation for clinical treatment planning of scanned proton and carbon ion therapy, to be presented at the *European Workshop on Monte Carlo Treatment Planning* to be held in Cardiff, UK, 19th-21st October, 2009

[16] U. Weber and G. Kraft, Design and construction of a ripple filter for a smoothed depth dose distribution in conformal particle therapy *Phys Med Biol* **44** (1999) 2765

[17] A. Mairani et al, From nuclear reactions modeling to biological effective dose calculations: the FLUKA Monte Carlo code for carbon ion therapy, to be presented at the *European Workshop on Monte Carlo Treatment Planning* to be held in Cardiff, UK, 19th-21st October, 2009

[18] M. Krämer and M. Scholz, Treatment planning for heavy-ion radiotherapy: calculation and optimization of biologically effective dose, *Phys. Med. Biol.* **45** (2000) 3319

[19] M. Biaggi et al, Physical and biophysical characteristics of a fully modulated 72 MeV therapeutic proton beam: model predications and experimental data, *Nucl Instrum Methods Phys Res B* **159** (1999) 89

[20] F. Sommerer, K. Parodi, A. Ferrari et al, Investigating the accuracy of the FLUKA code for transport of therapeutic ion beams in matter, *Phys. Med. Biol.* **51** (2006) 4385

[21] H. Paganetti, H, Jiang, K. Parodi et al, Clinical implementation of Monte Carlo dose calculation in proton beam therapy, *Phys. Med. Biol.* **53** (2008) 4825

[22] F. Sommerer et al, In-beam PET monitoring of mono-energetic $^{16}O$ and $^{12}C$ beams: experiments and FLUKA simulations for homogeneous targets**,** *Phys. Med. Biol.* **54** (2009) 3979

[23] K. Parodi and T. Bortfeld, A filtering approach based on Gaussian–powerlaw convolutions for local PET verification of proton radiotherapy, *Phys. Med. Biol.* **51** (2006) 1991

[24] F. Attanasi, A. Knopf, K. Parodi et al, Validation of an Analytical 1D filtering of the dose distribution for the calculation of the expected PET distributions in proton therapy, *Med. Phys.* **36** (2009) 2814