

**Article Type: Research Article**

**The influence of nuclear interactions on ionization chamber perturbation factors  
in proton beams: FLUKA simulations supported by a Fano test**

Ana Lourenço\*

*Medical Radiation Science, National Physical Laboratory, Teddington TW11 0LW, United Kingdom and Department of Medical Physics and Biomedical Engineering, University College London, London WC1E 6BT, United Kingdom*

*Email: am.lourenco@ucl.ac.uk*

Hugo Bouchard

*Département de Physique, Université de Montréal, Québec, H3T 1J4, 2900 Boulevard Edouard-Montpetit, Montréal, Canada*

Sebastian Galer

*Medical Radiation Science, National Physical Laboratory, Teddington TW11 0LW, United Kingdom and Department of Medical Physics and Biomedical Engineering, University College London, London WC1E 6BT, United Kingdom*

Gary Royle

*Department of Medical Physics and Biomedical Engineering, University College London, London WC1E 6BT, United Kingdom*

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/mp.13281

This article is protected by copyright. All rights reserved.

Hugo Palmans

*Medical Radiation Science, National Physical Laboratory, Teddington TW11 0LW, United Kingdom and Medical Physics Group, EBG MedAustron GmbH, A-2700 Wiener Neustadt, Austria*

\*Author to whom correspondence should be addressed.

### Abstract

**Purpose:** In all recent protocols for the reference dosimetry of clinical proton beams ionization chamber perturbation factors are assumed to be unity. In this work, such factors were computed using the FLUKA Monte Carlo code for three ionization chamber types, with particular attention to the influence of nuclear interactions.

**Methods:** The accuracy of the transport algorithms implemented in FLUKA was first evaluated by performing a Fano cavity test. Ionization chamber perturbation factors were computed for the PTW-34001 Roos<sup>®</sup> and the PTW-34070 and PTW-34073 Bragg peak<sup>®</sup> chambers for proton beams of 60 to 250 MeV using the same transport parameters that were needed to pass the Fano test.

**Results:** FLUKA was found to pass the Fano test within 0.15%. Ionization chamber simulation results show that the presence of the air cavity and the wall results in dose perturbations of the order of 0.6% and 0.8%, respectively. The perturbation factors are shown to be energy dependent and nuclear interactions must be taken into account for accurate calculation of the ionization chamber's response.

This article is protected by copyright. All rights reserved.

**Conclusion:** Ionization chamber perturbations can amount to 1% in high-energy proton beams and therefore need to be considered in dosimetry procedures.

**Keywords:** proton therapy; proton dosimetry; Monte Carlo simulations; Fano cavity test; ion-chamber perturbation factors

## I. INTRODUCTION

The increased usage of proton beams for radiotherapy has created a demand for improved consistency in reference dosimetry. In older reference dosimetry protocols for clinical proton beams [1, 2, 3, 4] ionization chamber perturbation factors were ignored. In more recent protocols [5, 6], while they are explicitly accounted for in the dosimetry formalism, they are assumed to be unity due to the lack of better information at the time of their publication. Nevertheless, numerous experimental studies have shown that there are differences in response between different types of ionization chambers [7-10] and between ionization chambers and other detectors [11] that are likely due to fluence perturbations in proton beams. Well-designed Monte Carlo (MC) codes can calculate the response of ionization chambers accurately provided correct data on the detector construction materials and dimensions and on the radiological properties of the constituting materials are available. Gomà *et al.* [12] and Sorriaux *et al.* [13] have performed simulations of ionization chambers using PENH and Geant4, respectively. These calculations are very sensitive to transport algorithm parameters, such as step size, and boundary crossing artefacts [14]. The accuracy of the transport algorithms implemented in a specific Monte Carlo code for

Accepted Article

detector response calculations can be evaluated by performing a self-consistency test called the Fano cavity test [15]. This test is based on Fano's theorem, which states that under the condition of a spatially uniform source of ionising particles, the charged particle fluence is uniform and independent of mass density provided the interaction properties are also uniform [16]. The Fano condition is the only non-trivial case for which the transport equation for charged particles traversing a cavity can be solved analytically and it is an important test to determine if particle step and boundary-crossing algorithms in Monte Carlo codes do not cause artefacts as well as to find optimal combinations of parameters for calculating accurate ionization chamber perturbation factors.

The accuracy of electron transport algorithms has been validated in several Monte Carlo codes, such as EGSnrc [17], PENELOPE [18] Geant4 [19]. Sterpin *et al.* [20] have designed a Fano cavity test for proton transport using Geant4 and PENH (PENELOPE extended to protons). Both codes were found to pass the Fano cavity test within 0.1% by using small step sizes. In their work, the transport of electrons was neglected as well as nuclear interactions. However, electrons and nuclear interactions must be taken into account for calculation of ionization chamber response. More recently, Wulff [21] performed a Fano test for proton beams using TOPAS/Geant4 where transport algorithm parameters were optimized to pass the test within 0.1%.

FLUKA is a Monte Carlo simulation package that is continuously being developed and benchmarked and its nuclear models for proton beams have been validated against experimental data [22]. In this work, the accuracy of ion transport

in the FLUKA Monte Carlo code for proton beams (i.e., the mixed charged particle field consisting of primary protons, secondary protons and heavier target fragments) was assessed by performing a Fano cavity test. Using the transport parameter settings necessary to pass the test, ionization chamber perturbation factors were computed for the PTW-34001 Roos<sup>®</sup> and the PTW-34070 and PTW-34073 Bragg peak<sup>®</sup> chambers typically used in clinical proton beams, with particular attention to the influence of nuclear interactions. Moreover, the influence of the new recommendations by ICRU Report 90 [23] for water and graphite I-values on the calculated ionization chamber perturbation factors was investigated.

## II. MATERIALS AND METHODS

### A. Fano cavity test

To implement the Fano cavity test in Monte Carlo the following is required:

- (i) a phantom with homogeneous atomic properties (cross sections, I-value, etc.) but varying mass density;
- (ii) a uniform source, such that the number of emitted particles per unit mass as well as their spectral and angular distributions are constant throughout the geometry.

These two conditions allow the application of Fano's theorem.

Monte Carlo simulations were performed with FLUKA version 2011.2c.5 [24-26].

A routine was written in FLUKA to generate proton sources distributed uniformly in the phantom, proportional to its mass density. For protons the density effect in the stopping power formula is negligible for the clinical energy range. In FLUKA, the

Accepted Article

commands where the user defines the simulations settings are defined as cards. The default card HADROTherapy was used, with delta-ray production set to infinity since it was not the aim of this work to study the accuracy of electron transport in FLUKA. Thus, delta rays were not considered in the simulations and energy transferred to electrons was assumed to be absorbed locally given their very short range (the effects of electron fluence perturbations have been studied in detail in previous publications [9, 10, 27-29]). The energy transport cutoff for protons was set to 10 keV. A step size of 0.01 cm for transport of all generated charged particles was used to correct for boundary crossing artefacts. Simulations were performed for unidirectionally emitted, mono-energetic protons with initial energies of 60 MeV, 150 MeV and 250 MeV.

Figure 1(a) illustrates the simulation geometry, consisting of only water with varying mass density and which is divided in a build-up region and charge particle equilibrium (CPE) region. CPE exists if for each charged particle entering a particular volume, one with equal energy and particle type leaves. There are protons being uniformly generated in the geometry and when  $z = 0 \text{ g.cm}^{-2}$ , there is no CPE because protons are not being generated downstream of this depth thus the build-up region is due to a classical build-up effect of an internal forward directed charged particle source. Protons are being generated from  $z = 0 \text{ g.cm}^{-2}$  and they have a finite range, highly correlated with their initial energy, hence, the build-up region is made large enough to ensure that the CPE region is at a depth beyond the maximum range of the protons generated at  $z = 0 \text{ g cm}^{-2}$ . The secondary charged particles have a range that is shorter than the primary protons thus they reach CPE in the CPE

region as well. Secondary neutrons and gammas do not reach equilibrium. However, the contribution to the total dose from these particles is negligible [30]. Protons scatter much less than electrons due to their heavier mass, therefore,  $x$  and  $y$  dimensions do not need to be as large as the range of the protons generated along the central axis,  $z$ . The field size dimensions,  $x \times y$ , were  $36 \times 36 \text{ cm}^2$  to ensure CPE in the cavity. The ionization chamber geometry was then placed in the CPE region where its materials were overridden with water but keeping the original mass density of the chamber's construction materials. The choice of the depths upstream and downstream of the chamber,  $z_u$  and  $z_d$ , respectively, will be discussed in the following section.

The code accuracy was then tested by comparing the dose scored in the different mass density regions where the dose is expected to be uniform because of the uniform charged particle fluence conditions.

Typically  $10^7$  initial protons were required for each simulation to give a standard uncertainty (type A) of 0.1% or better in the dose ratio. For the large area Bragg peak<sup>®</sup> chamber 6900 CPU hours were required, while for the Roos<sup>®</sup> chamber 13 000 CPU hours were required using the UCL Legion High Performance Computing Facility (Legion@UCL).

## **B. Ionization chamber perturbation factors**

Dose to water,  $D_w$ , is related to dose to air in the ion chamber,  $D_{\text{chamber}}$ , by the stopping power ratio between water and air,  $s_{w,\text{air}}$ , and  $p_{\text{cav}}$  and  $p_{\text{wall}}$  which are perturbation correction factors that account for the non-water equivalence of the air

cavity and the chamber's wall, respectively. Ionization chamber perturbation factors can be determined by calculating the dose in different geometries at water-equivalent depths as illustrated in figure 1(b): (i)  $D_w$  is the dose to water calculated in a thin layer ( $t_w = 0.01$  cm), (ii)  $D_{\text{cavity}}$  is the dose in the air cavity at a depth of measurement  $z_w$  and (iii)  $D_{\text{chamber}}$  is the dose in the air cavity when the full geometry of the ionization chamber is considered with the front face at a depth of  $z_w - \text{WET}$ , where WET is the water-equivalent thickness of the chamber's wall [31]. Thus, ionization perturbation factors were calculated using:

$$p_{\text{wall}} = \frac{D_{\text{cavity}}}{D_{\text{chamber}}} \quad (1)$$

and,

$$p_{\text{cav}} = \frac{D_w}{D_{\text{cavity}} \cdot s_{w,\text{air}}} \quad (2)$$

where,  $s_{w,\text{air}}$  is the water-to-air Bragg-Gray stopping-power ratio:

$$s_{w,\text{air}}(\Phi_{\text{air}}) = \frac{\sum_i \left[ \int_{E_{\text{min},i}}^{E_{\text{max},i}} \Phi_{E,\text{air},i}(E) \cdot \left( \frac{S_i(E)}{\rho} \right)_w \right]}{\sum_i \left[ \int_{E_{\text{min},i}}^{E_{\text{max},i}} \Phi_{E,\text{air},i}(E) \cdot \left( \frac{S_i(E)}{\rho} \right)_{\text{air}} \right]} \quad (3)$$

The integrals are calculated offline from the scored fluence distributions and stopping powers used in the simulation. The combined perturbation  $p_Q$  is then given by:

$$p_Q = p_{\text{wall}} \cdot p_{\text{cav}} \quad (4)$$

Ionization chamber perturbation factors were calculated with FLUKA version 2011.2c.5 [24-26]. The physics settings were the same as those to pass the Fano test. The full geometry of the PTW-34001 Roos<sup>®</sup> and the PTW-34070 and PTW-34073 Bragg peak<sup>®</sup> chambers were modeled according to manufacturer's blueprints. A

mono-energetic mono-directional proton beam of 60 MeV was simulated, where a depth of measurement of  $z_w = 1$  cm was used, while for proton beams of 150 MeV and 250 MeV  $z_w = 2$  cm was used. Calculation of the central axis dose distribution was performed with the PTW-34001 Roos<sup>®</sup> chamber (sensitive radius = 0.78 cm), using a field of  $6 \times 6$  cm<sup>2</sup>. For the large-area PTW-34070 (sensitive radius = 4.08 cm) and PTW-34073 (sensitive radius = 1.98 cm) Bragg peak<sup>®</sup> chambers a pencil beam was used. Proton beams were incident on cylindrical phantoms of water ( $\rho = 1.0$  g.cm<sup>-3</sup> and I-value = 78 eV) with 10 cm radius. Moreover, to study the influence of different subsets of secondary charged particle types three simulations with different charged particle transport parameters were computed for each proton energy considered: (i) elastic and non-elastic nuclear interactions were switched off by setting the energy thresholds for these interactions greater than the primary particle energy, (ii) alpha particles were discarded by zeroing their weight (particles are generated hence the proton loses energy but they are not transported) and (iii) all generated charged particles were transported. The influence of the increased recommended I-value of water and graphite from  $I_w = 75$  eV and  $I_g = 78$  eV [32] to  $I_w = 78$  eV and  $I_g = 81$  eV [23] on the calculated ionization chamber perturbation factors was also investigated.

Simulations were performed at the UCL Legion High Performance Computing Facility (Legion@UCL). Typically  $10^6$  initial protons were required for each simulation to give a standard uncertainty (type A) of 0.05% in the dose scored. For the large area Bragg peak<sup>®</sup> chamber, 1000 CPU hours (narrow beam) were required, while for the Roos<sup>®</sup> chamber 3300 CPU hours were required (broad beam).

### III. RESULTS AND DISCUSSION

#### A. Proton Fano test: boundary crossing artefacts

Figure 2(a) and figure 2(b) show the central axis depth-dose distribution of a uniform-source mono-directional proton beam of 250 MeV in a phantom made of water. Note that the dose is scored within the sensitive volume of the chambers in consideration in this study. The data were obtained using a similar geometry to that shown in figure 1(a), but with a phantom made of water with a density of  $1 \text{ g.cm}^{-3}$  throughout the phantom. After a build-up region of approximately 38 cm (the range of the beam in water), there is charged-particle equilibrium, thus, the CPE region starts at this depth where the dose is uniform. When the phantom was divided into two regions of water (with equal material composition, I-value and density) by placing a boundary at a depth of 45 cm, the results showed an artefact at the boundary, as shown in figure 2(c). In FLUKA, at the scoring level, the proton energy loss is distributed uniformly along the particle step, thus, the energy scored at each depth bin is proportional to the respective step fraction. However, in reality, the stopping power increases non-linearly along the step, and is larger towards the step end. When a boundary falls within that step, the particles are forced to end at the boundary position and therefore the original step is split into two different ones. Considering that for protons the energy loss is variable along the step, the energy loss for the two steps will not be equally distributed. In particular, the first half of the step will have a slightly lower energy loss than the second half. This effect is responsible for the artefacts shown. Moreover, the trajectory of the particles affected by multiple scattering is more curved at the end of the step than at the beginning,

which could also have a small effect. Note that the non-linearity of the stopping power is fully taken into account when particles are transported in FLUKA, however, the scoring considers that the energy loss is uniformly distributed along the step so artefacts appear at boundaries [24-26].

Boundary crossing artefacts were removed by shortening all transport steps down to 0.01 cm (figure 2(d)). This increased significantly the CPU time, thus, small step sizes were only applied to the CPE region. A boundary was created just after the start of the CPE region and the depth upstream of the chamber,  $z_u$ , was made 13 cm for higher-energy beams and 6 cm for lower-energy beams to correct for the scoring artefacts at the latter position. The depth downstream of the chamber,  $z_d$ , was 2 cm since backscattered protons have a negligible effect (figure 1(a)).

### **B. Proton Fano test: cavity response**

Figure 3 shows the ratio between the dose scored in the water-property regions with different mass densities. Overall, FLUKA was found to pass the Fano test within 0.15%. Type-A statistical uncertainties were below 0.05% for the large area Bragg peak<sup>®</sup> chambers while for the Roos<sup>®</sup> chamber statistical uncertainties were of the order of 0.1% due to the small sensitive volume of the chamber.

### **C. Perturbation factors**

Figure 4 shows the Bragg-Gray water-to-air mass stopping power ratio calculated when considering the contribution of different charged particles. The results show that the stopping power ratio for the protons alone (nuclear interactions discarded)

is close to the stopping power ratio for the entire charged particle spectrum, confirming earlier findings [33, 34]. The influence of a 4% increase in the  $I_w$  from 75 eV [31] to 78 eV [23] results in a decrease in the electronic stopping power of water and, consequently, a 0.5% decrease in the water-to-air stopping power ratio confirming the results reported in ICRU Report 90 [23].

Figure 5 shows ionization chamber perturbation factors as a function of proton energy, when considering the transport of different charged particles. When nuclear interactions are discarded perturbation factors are close to unity for all the energies considered. For the PTW-34070 Bragg peak<sup>®</sup> chamber,  $p_{cav}$  was close to unity with the largest deviations from unity of the order of 0.2% (figure 5(a)). These results demonstrate that the presence of the air cavity introduces a negligible perturbation in the medium. For the PTW-34070 Bragg peak<sup>®</sup> chamber,  $p_{cav}$  deviated from unity by 0.6% when all particles were transported (figure 5(b)). Both Bragg peak<sup>®</sup> chambers have an air cavity with a thickness of 2 mm, so the difference between the results of figure 5(a) and figure 5(b) is possibly due to differences in the lateral scattered particles. In the smaller chamber (PTW-34073) a larger fraction of the secondary particles generated in the cavity can escape laterally in comparison with the large chamber (PTW-34070). Moreover, the mean energy of the secondaries also increases with increasing primary proton energy, which explains the energy dependence.

Accepted Article

Deviations from unity were larger for  $p_{\text{wall}}$  (figure 5(d-f)), which was found to be dependent on proton energy. For a 250 MeV beam and considering the transport of all charged particles,  $p_{\text{wall}}$  was significantly different from unity ( $p_{\text{wall}} = 0.992$ ), while for a 60 MeV beam, it deviated less ( $p_{\text{wall}} = 0.996$ ). It is also interesting to note that not only alpha particles contribute to  $p_{\text{wall}}$  but also other secondary particles. Overall,  $p_{\text{wall}}$  factors were below unity. These results suggest that less particles are being stopped in the wall or less particles are being produced in water than in the chamber's wall. The latter is in agreement with the results from Palmans *et al.* [34] where fluence correction factors between water and graphite were below unity when alpha particles were considered; consequently, alpha particles fluence was larger in graphite than in water. Note that the chamber's wall is composed of PMMA which has carbon in its composition.

The influence of the new key data and recommendations by ICRU Report 90 [23] for water and graphite I-values on the calculated ionization chamber perturbation factors is shown in figure 6. The influence of the increased I-value for water and graphite on calculated ionization chamber perturbation factors was found to be negligible, confirming the expectations stated in ICRU Report 90 [23].

#### IV. CONCLUSIONS

The accuracy of particle transport in the FLUKA Monte Carlo code for proton beams was assessed by performing a Fano cavity test. FLUKA was found to pass this test within 0.15%. Ionization chamber perturbation factors were also computed for the PTW-34001 Roos<sup>®</sup> and the PTW-34070 and PTW-34073 Bragg peak<sup>®</sup> chambers

typically used in clinical proton beams. The results show that nuclear interactions must be taken into account for the calculation of ionization chamber response since perturbation corrections amounted to almost 1% when all generated charged particles were transported. Also, perturbation factors were shown to be dependent on the proton energy. These results will feed into the development of data for future codes of practice for the dosimetry of proton beams.

#### **ACKNOWLEDGEMENTS**

The authors acknowledge the use of the UCL Legion High Performance Computing Facility (Legion@UCL), and associated support services, in the completion of this work. We like also to axknowledge the FLUKA mailing list for all the support with FLUKA code, in particular to Alfredo Ferrari, Anton Lechner and Francesco Cerutti. AL was supported by University College London and the UK National Physical Laboratory through the National Measurement System. The authors also wish to thank PTW for providing the blue prints of the ionization chambers for the Monte Carlo simulations.

#### **CONFLICT OF INTEREST DISCLOSURE**

The authors declare that there is no conflict of interest.

[1] AAPM, "Protocol for heavy charged-particle therapy beam dosimetry," American Association of Physics in Medicine Report No. 16 (AAPM, New York, NY, 1986)

[2] S. Vynckier, D. E. Bonnett, and D. T. L. Jones, "Code of practice for clinical proton dosimetry," *Radiotherapy and Oncology* 20, 53–63 (1991)

[3] S. Vynckier, D. E. Bonnett, and D. T. L. Jones, "Supplement to the code of practice for clinical proton dosimetry," *Radiotherapy and Oncology* 32, 174–179 (1994)

[4] ICRU, "Clinical proton dosimetry Part I: Beam production, beam delivery and measurement of absorbed dose," International Commission on Radiation Units and Measurements Report No. 59 (ICRU, Bethesda, MD, 1998)

[5] P. Andreo, D. T. Burns, K. Hohlfeld, M. S. Huq, T. Kanai, F. Laitano, V. G. Smith, and S. Vynckier, Absorbed dose determination in external beam radiotherapy: an international code of practice for dosimetry based on standards of absorbed dose to water. IAEA Technical Report Series TRS-398 (IAEA, Vienna, 2000)

[6] ICRU, *Prescribing, Recording, and Reporting Proton-Beam Therapy ICRU Report 78* (Bethesda, MD: ICRU, 2007)

[7] S. Vatnitsky, J. Siebers, D. Miller, M. Moyers, M. Schaefer, D. Jones, S. Vynckier, Y. Hayakawa, S. Delacroix, U. Isacsson, J. Medin, A. Kacpersek, A. Lomax, A. Coray,

H. Kluge, J. Heese, L. Verhey, I. Daftari, K. Gall, G. Lam, T. Beck, and G. Hartmann, "Proton dosimetry intercomparison," *Radiotherapy and Oncology*, 41, 169-177 (1996)

[8] S. Vatnitsky, M. Moyers, D. Miller, G. Abell, J. M. Slater, E. Pedroni, A. Coray, A. Mazal, W. Newhauser, O. Jäkel, J. Heese, A. Fukumura, Y. Futami, L. Verhey, I. Daftari, E. Grusell, A. Molokanov, and C. Bloch, "Proton dosimetry intercomparison based on the ICRU report 59 protocol," *Radiotherapy and Oncology*, 51, 273-279 (1999)

[9] H. Palmans, F. Verhaegen, J. M. Denis, S. Vynckier, and H. Thierens, "Experimental  $p_{\text{wall}}$  and  $p_{\text{cel}}$  correction factors for ionization chambers in low-energy clinical proton beams," *Physics in Medicine and Biology* 46, 1187-1204 (2001)

[10] H. Palmans, F. Verhaegen, J. M. Denis, and S. Vynckier, "Dosimetry using plane-parallel ionization chambers in a 75 MeV clinical proton beam," *Physics in Medicine and Biology* 47, 2895-905 (2002)

[11] A. Ableitinger, S. Vatnitsky, R. Herrmann, N. Bassler, H. Palmans, P. Sharpe, S. Ecker, N. Chaudhri, O. Jäkel, and D. Georg, "Dosimetry auditing procedure with alanine dosimeters for light ion beam therapy", *Radiotherapy and Oncology* 108, Pages 99-106 (2013)

[12] C Gomà, P Andreo and J Sempau, "Monte Carlo calculation of beam quality correction factors in proton beams using detailed simulation of ionization chambers," *Physics in Medicine and Biology* 61, Pages 2389–406 (2016)

[13] J Sorriaux, M Testa, H Paganetti, D Bertrand, J Lee, H Palmans, S Vynckier and E Sterpin, "Consistency in quality correction factors for ionization chamber dosimetry in scanned proton beam therapy", *Medical Physics* 44, Pages 4919–27 (2017)

[14] B. R. B. Walters, and I. Kawrakow, "Technical note: overprediction of dose with default PRESTA-I boundary crossing in DOSXYZnrc and BEAMnrc", *Medical Physics* 34, 647–650 (2007)

[15] Seco, J., & Verhaegen, F. Chapter 4: Applications of Monte Carlo to radiation dosimetry in *Monte Carlo techniques in radiation therapy*. (Taylor & Francis: 2013)

[16] U. Fano, "Note on the Bragg-Gray Cavity Principle for Measuring Energy Dissipation", *Radiation Research* 1, 237–240 (1954)

[17] I. Kawrakow, "Accurate condensed history Monte Carlo simulation of electron transport. II. Application to ion chamber response simulations", *Medical Physics* 27, 499–513 (2000)

[18] J. Sempau, P. Andreo, J. Aldana, J. Mazurier, F. Salvat, "Electron beam quality correction factors for plane-parallel ionization chambers: Monte Carlo calculations using the PENELOPE system", *Physics in Medicine and Biology* 49, 4427–44 (2004)

[19] E. Poon, J. Seuntjens, and F. Verhaegen, "Consistency test of the electron transport algorithm in the GEANT4 Monte Carlo code", *Physics in Medicine and Biology* 50, 681-694 (2005)

[20] E. Sterpin, J. Sorriaux, K. Souris, S. Vynckier, and H. Bouchard, "A Fano cavity test for Monte Carlo proton transport algorithms", *Medical Physics* 41, 011706 (2014)

[21] J. Wulff, K-S. Baumann, N. Verbeek, C. Baumer, B. Timmermann and K. Zink, "TOPAS/Geant4 configuration for ionization chamber calculations in proton beams", *Physics in Medicine and Biology* 63, 115013 (2018)

[22] I. Rinaldi, A. Ferrari, A. Mairani, H. Paganetti, K. Parodi, P. Sala, "An integral test of FLUKA nuclear models with 160 MeV proton beams in multi-layer Faraday cups", *Physics in Medicine and Biology* 56 4001-11 (2011)

[23] ICRU, *Key Data For Ionizing-Radiation Dosimetry: Measurement Standards And Applications ICRU Report 90* (Bethesda, MD: ICRU, 2016)

[24] S. Roesler, R. Engel, and J. Ranft: "The Monte Carlo Event Generator DPMJET-III" in *Proceedings of the Monte Carlo 2000 Conference*, Lisbon, October 23-26 2000, A. Kling, F. Barao, M. Nakagawa, L. Tavora, P. Vaz eds., Springer-Verlag Berlin, 1033-1038 (2001)

[25] A. Ferrari, P. R. Sala, A. Fassò, and J. Ranft, "FLUKA: a multi-particle transport code", in CERN 2005-10, INFN/TC 05/11, SLAC-R-773 (2005)

[26] T. Böhlen, F. Cerutti, M. Chin, A. Fassò, A. Ferrari, P. Ortega, A. Mairani, P. Sala, G. Smirnov, and V. Vlachoudis, "The FLUKA Code: Developments and Challenges for High Energy and Medical Applications", Nuclear Data Sheets 120, 211–214 (2014)

[27] H. Palmans, and F. Verhaegen, "Monte Carlo study of fluence perturbation effects on cavity dose response in clinical proton beams," Physics in Medicine and Biology 43, 65–89 (1998)

[28] F. Verhaegen, and H. Palmans, "A systematic Monte Carlo study of secondary electron fluence perturbation in clinical proton beams (70–250 MeV) for cylindrical and spherical ion chambers," Medical Physics 28, 2088–2095 (2001)

[29] H. Palmans, "Secondary electron perturbations in Farmer type ion chambers for clinical proton beams," In: Proc. Int. Symp. on Standards, Applications and Quality Assurance in Medical Radiation Dosimetry (Vienna, Austria: IAEA) pp 309–17 (2011)

[30] H. Paganetti, "Nuclear Interactions in proton therapy: Dose and relative biological effect distributions originating from primary and secondary particles," Physics in Medicine and Biology 47, 747–764 (2002)

[31] M. Bailey, D. R. Shipley, and J. W. Manning, "Roos and NACP-02 ion chamber perturbations and water-air stopping-power ratios for clinical electron beams for energies from 4 to 22 MeV", *Physics in Medicine and Biology* 60, 1087 (2015)

[32] ICRU, *Stopping Powers and Ranges for Protons and Alpha Particles ICRU Report 49* (Bethesda, MD: ICRU, 1993)

[33] J. Medin, and P. Andreo, "Monte Carlo calculated stopping-power ratios, water/air, for clinical proton dosimetry (50 - 250 MeV)", *Physics in Medicine and Biology* 42, 89 (1997)

[34] H. Palmans, L. Al-Sulaiti, P. Andreo, D. Shipley, A. Lühr, N. Bassler, J. Martinkovic, J. Dobrovodský, S. Rossomme, R. A. S. Thomas, and A. Kacperek, "Fluence correction factors for graphite calorimetry in a low-energy clinical proton beam: I. Analytical and Monte Carlo simulations", *Physics in Medicine and Biology* 58, 3481-3499 (2013)











