A Comprehensive Monte Carlo Study of Out-Of-Field Secondary Neutron Spectra in a Scanned-Beam Proton Therapy Gantry Room

F S Englbrecht¹, S Trinkl^{2,3}, V Mares², W Rühm², M. Wielunski², J J Wilkens^{3,5}, M Hillbrand⁴ and K Parodi^{*1} 5 ¹ LMU Munich, Faculty of Physics, Department of Medical Physics, Munich, Germany 6 ² Helmholtz Zentrum München, Institute of Radiation Protection, Neuherberg, Germany 7 ³ Technical University of Munich, Physics Department, Garching, Germany 8 ⁴ Rinecker Proton Therapy Center, Munich, Germany 9 ⁵ Technical University of Munich, Department of Radiation Oncology, School of Medicine and 10 Klinikum rechts der Isar, Munich, Germany 11 Version typeset October 13, 2020 12 *Author to whom correspondence should be addressed. email: franz.englbrecht@lmu.de 13 14 Abstract 15 **Purpose:** To simulate secondary neutron radiation fields that had been measured at 16 different relative positions during phantom irradiation inside a scanning proton therapy 17 gantry treatment room. Further, to identify origin, energy distribution, and angular 18 emission of the secondary neutrons as a function of proton beam energy. 19 20 Methods: The FLUKA Monte Carlo code was used to model the relevant parts of 21 the treatment room in a scanned pencil beam proton therapy gantry including shield-22 ing walls, floor, major metallic gantry-components, patient table, and a homogeneous 23 PMMA target. The proton beams were modeled based on experimental beam ranges 24 in water and spot shapes in air. Neutron energy spectra were simulated at 0° , 45° . 25 90° and 135° relative to the beam axis at 2 m distance from isocenter, monoenergetic 26 $11 \times 11 \,\mathrm{cm}^2$ fields from 200 MeV, 140 MeV, 75 MeV initial proton beams, as well as for 27 118 MeV protons with a 5 cm thick PMMA range shifter. The total neutron spectra 28 were scored for these four positions and proton energies. FLUKA neutron spectra simu-29 lations were crosschecked with Geant4 simulations using initial proton beam properties 30 from FLUKA-generated phase spaces. Additionally, the room-components generating 31 secondary neutrons in the room and their contributions to the total spectrum were 32 identified and quantified. 33 **Results:** FLUKA and Geant4 simulated neutron spectra showed good general agree-34 ment with published measurements in the whole simulated neutron energy range of 35 10^{-10} to 10^3 MeV. As in previous studies, high-energy (E ≥ 19.6 MeV) neutrons from 36

the phantom are most prevalent along 0°, while thermalized $(1 \text{ meV} \le \text{E} < 0.4 \text{ eV})$ and fast $(100 \text{ keV} \le \text{E} < 19.4 \text{ MeV})$ neutrons dominate the spectra in the lateral and backscatter direction. The iron of the large bending magnet and its counterweight
 mounted on the gantry were identified as the most determinant sources of secondary
 fast-neutrons, which have been lacking in simplified room simulations.

Conclusions: The results helped disentangle the origin of secondary neutrons and their dominant contributions and were strengthened by the fact that a cross comparison was made using two independent Monte Carlo codes. The complexity of such room model can in future limited using the result. They may further be generalized in that they can be used for an assessment of neutron fields, possibly even at facilities where detailed neutron measurements and simulations cannot be performed. They may also help to design future proton therapy facilities and to reduce unwanted radiation doses from secondary neutrons to patients.

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⁵² I. Introduction

It has been suggested that proton therapy could enable better tumor control probabilities and demonstrated to do so in treatment of cancers of the central nervous system, for head and neck cancers, and tumors inside the eye¹. Recently, data from ion therapy irradiation of prostate cancer suggesting lower risk of subsequent secondary cancer for ion therapy have been reported². Compared with conventional radiation treatments employing photons, proton beam therapy enables to spatially confine the therapeutic radiation dose to the targeted tumor volume and reduce the integral out-of-field dose to healthy tissue.

Although most of the kinetic energy of a clinical proton beam is deposited in tissue via 60 electromagnetic interactions with atomic electrons³, proton induced nuclear reactions can 61 generate unwanted secondary radiation like stray neutrons within the beam line elements, 62 the structures of the gantry room, and even within the patients themselves^{4,5}. Although the 63 stray neutron dose is much lower in magnitude compared to the therapeutic proton dose, 64 it penetrates the whole body of the patient and can be up to 20-times more biologically 65 effective⁶. Unwanted neutrons, especially relevant for pediatric or re-irradiation patients, 66 can deposit their kinetic energy inside the patient far outside the desired treatment volume 67 and increase the risk of secondary cancer ^{4,7,8}. Although neutron contribution is typically 68 neglected in current treatment planning systems, there are efforts ongoing to integrate the 69 information of risk estimation in the planning process, which will require also the room 70 $model^{9,10}$. 71

In order to make quantitative assessments in calculating the prompt dose rates for 72 shielding design of treatment rooms, the systematic knowledge of the neutron spectrum is 73 essential. These spectra are used to calculate effective doses for a given incident neutron field 74 by applying fluence to effective dose conversion coefficients that vary with neutron energy¹¹. 75 In the context of radiation protection, it has been reported that the radiation quality factor 76 w_R of neutrons is largest for epithermal, fast and high-energy neutrons in the interval 10 keV 77 to 10^2 MeV, which is a 10-times increased w_R compared to $w_R = 2 - 3$ elsewhere (Fig. 1) 78 or $w_R = 1$ for photon radiation^{6,11}. Moreover, these quality factors, although conceived 79 for radioprotection purposes, have been already used as a reasonable approximation for the 80 estimation of biological effectiveness for organ equivalent dose calculations in proton therapy, 81 e.g., Rechner et al. and Zheng et al.^{10,12}. 82

Like the system used in this study, most modern active spot scanning proton therapy 83 systems employ an isochronous cyclotron with a fixed extraction energy of $230 - 250 \,\mathrm{MeV}$ 84 and an energy degrading system several meters upstream of the treatment nozzle 13,14 . By 85 placing this strongest source of secondary neutrons in a separately shielded area (the energy 86 degrader), actively scanned proton therapy has been reported to reduce the secondary neu-87 tron ambient dose exposure to patients by up to one order of magnitude in comparison to 88 delivery techniques based on passive scattering devices placed in the treatment nozzle for 89 beam shaping 15,16,17. 90

Detailed room models were used in Monte Carlo simulations to study the out-of-field 91 dose and optimization of the treatment room design 18,19,20 . To a lesser extent and mostly 92 modeling passively scattered proton beam facilities, the spectra and number of secondary 93 neutrons were studied^{16,21,22,23}. The studies used models of the gantry and treatment room, 94 but the mostly vague description of used materials and the treatment field specific collimators 95 and compensators have so far hindered generalizing the results. Recently, literature is start-96 ing to provide more detailed simulation models and spectra studies coupled to measurements 97 for the Mevion S250 gentry-mounted passively scattered proton system^{24,25,26}. 98

Because active beam scanning has begun to replace passive beam delivery techniques, 99 and literature on secondary neutrons from active treatment facilities is still sparse, we per-100 formed a detailed Monte Carlo analysis for monoenergetic treatment fields in order to enable 101 comparative studies of the contributions of the gantry and room elements on the secondary 102 neutron generation^{18,27,28,29}. We expect spot scanning facilities to be more uniform in design 103 and the present neutron spectra to be better intercomparable, because the spot scanning 104 technique does not place field-specific material into the beam path³⁰. In this case, the pa-105 tient will therefore be the main source of secondary neutrons and a detailed study of the spot 106 scanning room and gantry elements is desirable^{31,32,33}. Of the modeled Varian ProBeam[®] 107 therapy system, 17 rooms were in operation and 20 were under construction in $2019^{34,35}$. 108

Although the purpose of the previously published studies on ambient dose equivalent from neutrons did not include the detailed validation of the Monte Carlo (MC) simulation models of the respective treatment facilities, the obtained measurement and simulation data showed that large differences may occur^{17,20}. For a scattering facility which causes neutrons to be mostly generated in the passive beam modulators and field shaping apartures and



Figure 1: Radiation weighting factor w_R used in radiological protection¹¹. not in the room itself, Farah et al. already reported that elements as the bending magnet 114 and mechanical gantry structure should be adjusted to minimize such discrepancies between 115 measurement and simulation²⁰. For the measurements underlying the presented simulation 116 study, the authors chose a physically accessible quantity, the energy resolved neutron flu-117 ence $\phi(E)$, which will be abbreviated as *neutron spectrum* in this article. Nuclear reaction 118 cross sections needed for MC simulations are strongly dependent on neutron energy as is 119 the simulated secondary radiation field^{36,37}. With monoenergetic proton fields, this facili-120 tated a quantitative and objective evaluation of the secondary neutron spectra as well as 121 the dependence on the proton beam energy and the specific setting of the treatment room 122 geometry. Monoenergetic proton fields were chosen in the measurement campaign in order 123 to distinguish the influence of proton beam energy, as well as the influence of the individual 124 treatment room components and the phantom itself on the secondary radiation field. In fact, 125 nuclear reaction channels become enabled energetically when the neutron energy changes due 126 to scattering or resonances of neutron production in materials influencing the field of sec-127 ondary particles. Previous studies reported differences of a factor of 2-4 in ambient dose 128 equivalent, also originating from approximations in the beamline and room modeling^{28,38}. 129 In order to investigate the reasons for such differences, the influence of room components on 130 the neutron spectra measured by Trinkl et al. was simulated systematically. 131

The report is divided into two main simulation campaigns. First, the FLUKA MC code was used to reproduce published neutron spectra measured by our team at the clinical Varian ProBeam[®] pencil beam scanning facility^{39,40}. Simulated FLUKA spectra were cross-checked using Geant4 MC simulations using FLUKA generated phase spaces as input⁴¹. In a second step, the validated FLUKA room model was also used to study the contributions of the
modeled treatment room elements and concrete shielding to the full neutron spectrum.

138 II. Methods

¹³⁹ II.A. Previously measured secondary neutron spectra

Neutron spectra had been measured using an extended-range Bonner sphere spectrometer 140 (ERBSS) inside a gantry treatment room at the Rinecker Proton Therapy Center (RPTC) 141 in Munich, Germany³⁷. RPTC uses a Varian ProBeam[®] nozzle for pencil beam spot scan-142 ning delivery^{14,42}. The ERBSS uses ³He spherical proportional counters placed inside of 143 polyethylene spheres of different radii (some of them with lead shells) in order to reliably 144 measure neutron spectra in the energy range from thermal up to high-energy neutrons³². 145 The Bonner spheres had been placed at 0° , 45° , 90° and 135° at 2 m distance from the 146 isocenter, relative to the incident direction of the proton beam, in a horizontal plane (See 147 figs. 1a, 1b of the supplementary material⁴³ for a photograph and a drawing of the mea-148 surement setup). Monoenergetic irradiation fields of $11 \times 11 \text{ cm}^2$ lateral size at initial beam 149 energies of 200 MeV, 140 MeV, 118 MeV and 75 MeV had been delivered to a PMMA slab 150 phantom $(30 \text{ cm} \times 30 \text{ cm} \times 30 \text{ cm})$. The 118 MeV field was irradiated using a 5 cm PMMA 151 range shifter to generate the same proton beam range in water as a 75 MeV beam. For each 152 energy, we had unfolded neutron spectra for the four angular positions in the possible range 153 of 10^{-9} MeV to 10^4 MeV³⁷ using 10 log-equidistant intervals per decade. 154

The results showed a strong dependence of the secondary neutron field on the angular 155 measurement position and proton beam energy. Comparison of the neutron spectra from 156 simple bare phantom simulations without room model, which had been used as input for 157 the ERBSS unfolding, to the measurement results showed considerable differences. The 158 differences were especially notable in interval of increased biological effectiveness (Fig. 1). 159 It was evident that the influence of the treatment room dominates the characteristics of the 160 secondary neutron field (See Fig. 3 and Fig. 4 by Trinkl et al.³⁷). In order to clarify the 161 origin of the secondary neutrons and systematically understand the room influence on the 162 different components of the neutron spectrum, we modeled the RPTC treatment room and 163 re-simulated the experiments. 164

¹⁶⁵ II.B. FLUKA beam model

We used the FLUKA Monte Carlo code to perform the treatment room simulations because the code has been extensively used in shielding calculations, radiation protection and dosimetry^{39,44}. A detailed FLUKA model of the RPTC nozzle⁴⁵ was previously benchmarked against measured depth-dose distributions in water and lateral spot shape measurements in air with sub-mm accuracy. The model in this study was extended by the shielding walls and room components (see section II.E.), instead of simply using an idealistic proton beam model based on estimates of proton beam energy, energy spread, and spot shape.

173 II.C. Detailed treatment room model

In contrast to a previous Monte Carlo study by Hofmann et al. modeling the cyclotron and energy selection system area of the facility⁴⁶, we modeled the inside of a clinical gantry room (Fig. 2) employing the modern proton pencil beam spot scanning technique. In addition to the literature, information was also provided by the local medical physics department^{13,14,45}.

Two meter thick walls, enclosing the treatment room $(11 \times 11 \times 20 \text{ m}^3)$ and made of 178 standard concrete from the FLUKA material database, formed the outer mantle (Fig. 2 179 bottom). Standard air was used to fill the shelter. The entrance maze included the concrete 180 floor. The gantry was split into two main model components: a gantry wheel and gantry 181 cone. The section of the floor accommodating the patient support device and table was 182 included as a 1 cm plate of standard iron in FLUKA and extends 130 cm cm into the inner 183 gantry wheel. The wheel consists of two concentric 2 cm thick iron cylinder shells of 5.08 m 184 radius (inner shell) and 6 m radius (outer shell) (See Fig. 2 top). The size of the gantry 185 cone matched the installed, cone shaped, complex back support structure of the gantry. For 186 simplification, the cone model reproduces just the outer dimension and no internal structure. 187 It was modeled as solid iron of reduced density $\rho_{cone} = 2 \,\mathrm{g/cm^3}$ in order to reproduce the 188 actual weight¹⁴. The bending magnet of the gantry was included as a massive cube of iron. 189 On the opposite site of the outer gantry wheel, the counterweight of the bending magnet 190 was modeled based on the exact geometrical drawing by the manufacturer. The geometry 191 of the counterweight was used to calculate a mass of 18.7 tons of massive iron when using 192 $\rho_{Fe} = 7.874 \,\mathrm{g/cm^3}$. The counterweight edge length was hence set to 133 cm to match the 193

¹⁹⁴ bending magnet mass.

The primary protons were sampled inside a small vacuum region 3 cm upstream of the vacuum window and the beam monitor chambers using the previously published nozzle model⁴⁵. After 86 cm downstream, the protons and generated secondary particles hit the front surface of a PMMA phantom, consistent with the phantom position as used for the ERBSS measurements³⁷. The density of the slab phantom at the isocenter, made of PMMA, was the default value as used by the local medical physics staff for quality assurance procedures. The value of ($\rho_{PMMA} = 1.2 \text{ g/cm}^3$) was dosimetrically verified previously.

²⁰² II.D. Simulation settings

FLUKA uses a multi-group technique for neutron transport in the energy range where neutron cross section tables are used (typically for $E \leq 20 \text{ MeV}$). In the multi-group approach, 260 energy groups are used in the simulation of the elastic and inelastic interactions of neutrons⁴⁷. The total energy spectra of secondary neutrons were obtained using FLUKA multichannel (260 fixed bins in the interval 10^{-9} MeV to 20 MeV, log-equidistant above 208 20 MeV) detectors called 'USRTRACK' scorers.

Four of these spherical 'USRTRACK' detectors of 10 cm radius were placed around the phantom isocenter in the reported ERBSS measurement positions³⁷. Because multiscattering of secondary neutrons down to thermalization is CPU-time consuming, we simulated 3.5×10^9 primary protons for each of the four primary proton beam energies to acquire reasonable statistics in the fixed spectral neutron binning. All simulations used FLUKA Version 2c.3 with settings 'HADROTHErapy'.

Secondly, the FLUKA user routine fluscw.f was used to filter during runtime the 'US-215 RTRACK' spectra, depending on the room element in which a scored secondary neutron 216 had been generated. The neutron origin was accessed using the USDRAW section of the 217 mgdraw.f user routine, which automatically is called at runtime after inelastic interactions. 218 The region of neutron origin was saved in ISPUSR variables during the production reactions 219 occurring, like X(p, xn)Y, X(n, xn)Y or $X(\gamma, xn)Y$. The information on the neutron origin 220 was propagated through the simulation of each neutron trajectory and used for filtering when 221 the neutron entered one of the four detector positions. The individually considered regions 222

²²³ of neutron origin were:

- The bending magnet
- The iron counterweight
- The PMMA phantom
- The two gantry cylinders
- The concrete floor of the maze
- The iron plate ranging into the gantry
- The outer concrete walls enclosing the shelter
- The gantry iron cone of reduced density.

Because the quality of the nuclear models in MC codes is energy dependent, we graphically analyzed the four proton beam energies over the full neutron energy range. For a quantitative evaluation, the neutron spectra subsequently were further binned into four neutron energy intervals, similar to those of the ERBSS data³⁷: Thermal (1 meV \leq E < 0.4 eV), epithermal (0.4 eV \leq E < 100 keV), fast (100 keV \leq E < 19.4 MeV) and high-energy (E \geq 19.6 MeV) (Tables 1).

²³⁸ II.E. Crosscheck of FLUKA results with Geant4 using FLUKA ²³⁹ phase space

Although the FLUKA Monte Carlo code is known to provide accurately benchmarked results in the employed energy range, we used the Geant4 general purpose Monte Carlo code⁴¹ to verify the FLUKA simulation results of our room model. Geant4 was also previously employed in the calculation of particle transport problems and the simulation of secondary neutron spectra^{48,49}.

For the four energies 200 MeV, 140 MeV, 118 MeV and 75 MeV, we generated particle phase space files using the FLUKA user routine mgdraw.f in order to avoid a full remodeling of the nozzle and beam parameters in Geant4. The phase space files were scored at the exit of the treatment nozzle downstream from all beam monitors and the vacuum window and reported on a single particle level: *Particle type, kinetic energy, X- and Y- positions and direction vector*. Geant4 was used with the same physics list as used for previously reported simulations of secondary neutron spectra (QGSP_BIC_HP with G4StandardEMPhysics_option3 and G4NeutronHPThermalScattering)^{37,50}. We set up the same treatment room in Geant4 excluding the nozzle model.

Normalization of the simulation results to absolute dose per treatment Gray for both FLUKA and Geant4 results was obtained by using the established monitor unit to absolute dose relationship established for the nozzle model by Würl et al⁴⁵. The normalized spectra were compared to the spectra from Trinkl et al., who normalized their spectra to the nominal planned Bragg peak dose as reported by the treatment planning system.



Figure 2: *Top:* 3D FLUKA model of the treatment room (Gantry position 90° , beam direction along arrow) containing the most important elements of the manufacturer representation⁵¹ (shown at gantry position 0°).

Bottom: Horizontal cut at floor level (Gantry position 90°). The four points of fluence-scoring are marked as circles.

²⁵⁹ III. Results

²⁶⁰ III.A. Spectra of no room simulation versus full room simulation

In order to evaluate the necessity of a full treatment room model, we first evaluated the US-RTRACK simulated neutron spectra per proton treatment Gray in preliminary simulations without any room components. Only the vacuum window, the beam monitor chambers, airgap and phantom were included and compared to the experimental results of Trinkl et al.³⁷.

It is evident for the exemplary shown 0° and 135° positions of the 200 MeV proton field, that oversimplifying the simulation model by omitting any room components causes mismatches over the whole energy range of the secondary neutrons at both positions (fig. 3).

270 III.B. Simulated full room model spectra compared to measure 271 ments

As a second step, we analyzed the neutron spectra of the full room model and compared 272 these to the measured ERBSS spectra. The neutron spectra for the modeled proton beam 273 therapy scanning nozzle and treatment room for azimuth angles of 0°, 45°, 90° and 135° 274 relative to the beam axis at 2 m distance from isocenter are shown for the $11 \times 11 \text{ cm}^2$ fields 275 at initial beam energies of 200 MeV (Fig. 4), 140 MeV (Fig. 5), 75 MeV (Fig. 7), and 276 118 MeV with the PMMA range shifter of 5 cm thickness (Fig. 6). The fraction of neutrons 277 from the nozzle in our four phase spaces was < 0.6% of all phase space particles. Nearly 278 100% of secondary neutrons hence originated from the treatment room and phantom. 279

In general, our results present similar behavior of the neutron spectra inside treatment rooms over the full energy range: a high-energy peak, elevated fluence in the fast neutron region, a approximately $1/E_n$ slope for the epithermal neutrons and a minor peak in the thermal neutron energy range. Depending on proton energy and measurement angle, the relative contributions of these features to the total spectrum differ. The simulated FLUKA neutron spectra display fine resonances which are not present in the ERBSS data, because the ERBSS used response functions with only 130 log-equidistant energy bins and 18 measured



Figure 3: Bare phantom simulation (dashed line) and previously measured data (solid line) in lethargy notation for forward and 135° backscatter direction³⁷.

count rates to unfold the spectrum in the full energy range, which spanned approx. 11 orders
 of magnitude.

For FLUKA and Geant4, the laterally integrated depth dose profiles in the PMMA phantom were scored. FLUKA and Geant4 using the FLUKA phase space as input agreed in simulation of the 80% distal falloff range R_{80} of the primary proton beam for all four energies better than 1 mm.

²⁹³Minor neutron spectra discrepancies between the measured ERBSS and the FLUKA ²⁹⁴and Geant4 simulations were observed. FLUKA, compared to Geant4 and the ERBSS data, ²⁹⁵tended to display larger fluence in the high-energy interval for 200 MeV, 0° (Fig. 4 top left) ²⁹⁶and 140 MeV, 0° (Fig. 5 top left), whereas FLUKA and ERBSS data agreed but were below ²⁹⁷the measurements for all four proton energies at the 90° off axis position (Fig. 4 - 7 bottom ²⁹⁸left). Larger discrepancies were present for the 118 MeV, 0° range shifter case for Geant4 ²⁹⁹(Fig. 6 top left) and the 75 MeV, 135° FLUKA simulation (Fig. 7 bottom right).

Both codes showed reasonably good agreement with experimental data for the four energies and positions by adequately generating the fast neutron shoulder - often called evaporation peak - in the interval 10^{-1} MeV ≤ 19.4 MeV. For the whole epithermal interval, the simulations were in close agreement and reflected the spectrum in more detail than the approximately $1/E_n$ slope displayed by the ERBSS data.

Depending on the angle of detector position and beam axis, the relative contributions of the high-energy and evaporation peaks systematically varied. For all four energies, the





Figure 4: Measured³⁷ and full-room simulated neutron spectra for the 200 MeV proton field. high-energy peak $(> 19.4 \,\mathrm{MeV})$ was more pronounced for smaller observation angles with 307 respect to the beam axis. This finding agrees with the behavior of the spectra reported by 308 Hohmann et al.³¹ and Mares et al.³². Table 1 displays quantitatively the neutron fraction 309 per energy range. Approximately 50% of neutron fluence for nearly all angles and energies 310 is in the fast neutron range between 10^{-1} MeV and 19.4 MeV. The absolute fluence values 311 per treatment Gray are shown in the most right column of table 1. It is evident that the 312 number of generated secondary neutrons scales with the initial energy of the proton beam. 313 The extreme case is calculated by FLUKA as an increase by a factor of 121 for the 0° 314 measurement position on comparing the proton energies of 75 MeV and 200 MeV (table 1). 315

³¹⁶ III.C. Contribution of room components to neutron energy spec-³¹⁷ trum

Simulated neutron spectra filtered according to the considered possible neutron sources are here presented exemplarily for the highest beam energy of 200 MeV. The figures for all four proton energies are in the supplementary material⁴³.

$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		Position/	Data		Fluence ϕ [%]				Absolute
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Proton	Angle	source	Thermal-n	Epithermal-n	Fast-n	High-n		total
$118 \ \mathrm{MeV} = \ \begin{tabular}{ c c c c c c c c c c c c c $	Energy			$10^{-9} - 4 \times 10^{-7}$	$4 \times 10^{-7} - 10^{-1}$	$10^{-1} - 19.4$	> 19.4	Total	fluence
$118 \text{ MeV} + \begin{array}{ c c c c c c c c c c c c c c c c c c c$				${ m MeV}$	${ m MeV}$	${ m MeV}$	MeV		$[1/(cm^2 \mathrm{Gy})]$
$118 {\rm MeV} + \left \begin{array}{cccccccccccccccccccccccccccccccccccc$			Trinkl et al.	9.3	21.7	46.4	22.6	100	1772
$140 {\rm MeV} + \left[\begin{array}{c ccccccccccccccccccccccccccccccccccc$		1 / 0°	Geant4	11.2	18.8	49.3	20.3	100	1845
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			FLUKA	5.4	15.7	52.1	26.8	100	1790
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			Trinkl et al.	15.7	20.7	44.9	18.4	100	1507
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		$2 / 45^{\circ}$	Geant4	13.0	19.5	53.0	14.4	100	1453
$140 {\rm MeV} + \left[\begin{array}{cccccccccccccccccccccccccccccccccccc$	$75 { m MeV}$		FLUKA	10.3	18.0	51.7	19.9	100	1236
$140 {\rm MeV} + [136] = {\rm Geant4} = 18.0 = 26.7 = 55.1 = 3.1 = 100 = 910 = 100 = 1762 = 1760 = 100 = 1762 = 1760 =$			Trinkl et al.	19.2	25.0	51.7	4.0	100	1210
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		3 / 90°	Geant4	18.0	26.7	55.1	3.1	100	1211
			FLUKA	15.8	26.2	54.3	3.6	100	910
$140 {\rm MeV} + \left[\begin{array}{c c c c c c c c c c c c c c c c c c c $			Trinkl et al.	17.2	27.0	55.3	0.6	100	1762
$140 \text{ MeV} = \begin{array}{c c c c c c c c c c c c c c c c c c c $		$4 / 135^{\circ}$	Geant4	18.8	27.5	53.4	0.3	100	1959
$140 \text{ MeV} + \begin{bmatrix} & Trinkl et al. \\ 1 / 0^{\circ} & Geant4 \\ range \\ shifter \end{bmatrix} (10^{\circ} & Geant4 \\ 118 \text{ MeV} + \\ range \\ shifter \end{bmatrix} (10^{\circ} & Geant4 \\ 118 \text{ MeV} + \\ range \\ shifter \end{bmatrix} (10^{\circ} & Geant4 \\ 118 \text{ MeV} + \\ range \\ shifter \end{bmatrix} (10^{\circ} & Geant4 \\ 118 \text{ MeV} + \\ range \\ shifter \end{bmatrix} (10^{\circ} & Geant4 \\ 118 \text{ MeV} + \\ range \\ 118 \text{ MeV} + \\ range \\ shifter \end{bmatrix} (10^{\circ} & Geant4 \\ 110^{\circ} & $			FLUKA	16.1	28.6	54.7	0.5	100	1266
$140 \text{ MeV} + \begin{bmatrix} 1 / 0^{\circ} & \text{Geant4} & 8.4 & 18.9 & 49.8 & 22.8 & 100 & 7260 \\ & \text{FLUKA} & 3.0 & 13.3 & 48.0 & 35.5 & 100 & 9810 \\ & \text{Trink t et al.} & 8.4 & 18.0 & 44.1 & 29.3 & 100 & 9210 \\ 2 / 45^{\circ} & \text{Geant4} & 7.0 & 14.2 & 50.2 & 28.5 & 100 & 7721 \\ & \text{FLUKA} & 6.0 & 14.9 & 47.5 & 31.6 & 100 & 7621 \\ & \text{Trink t et al.} & 13.8 & 26.8 & 50.4 & 9.0 & 100 & 5106 \\ & 3 / 90^{\circ} & \text{Geant4} & 11.9 & 20.7 & 57.8 & 7.9 & 100 & 4628 \\ & \text{FLUKA} & 11.7 & 24.0 & 56.3 & 7.7 & 100 & 4157 \\ & \text{Trink t et al.} & 13.6 & 28.9 & 55.3 & 1.9 & 100 & 5712 \\ & \text{FLUKA} & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 43937 \\ & \text{Trink t et al.} & 5.0 & 15.4 & 42.1 & 37.4 & 100 & 19779 \\ & 1 / 0^{\circ} & \text{Geant4} & 6.3 & 11.4 & 37.6 & 44.6 & 100 & 19312 \\ & \text{FLUKA} & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 43937 \\ & \text{Trink t et al.} & 5.0 & 15.4 & 42.1 & 37.4 & 100 & 19779 \\ & 1 / 0^{\circ} & \text{Geant4} & 6.3 & 11.4 & 37.6 & 44.6 & 100 & 19312 \\ & \text{FLUKA} & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 43937 \\ & \text{Trink t et al.} & 10.8 & 18.4 & 43.8 & 26.8 & 100 & 11504 \\ & 2 / 45^{\circ} & \text{Geant4} & 10.8 & 18.4 & 43.8 & 26.8 & 100 & 11504 \\ & 2 / 45^{\circ} & \text{Geant4} & 10.8 & 18.4 & 43.8 & 26.8 & 100 & 1005833 \\ & \text{Trink t et al.} & 10.8 & 18.4 & 43.8 & 26.8 & 100 & 105833 \\ & \text{Trink t et al.} & 10.8 & 25.1 & 49.0 & 7.8 & 100 & 7286 \\ & 3 / 90^{\circ} & \text{Geant4} & 16.9 & 21.6 & 54.3 & 7.1 & 100 & 6325 \\ & \text{FLUKA} & 17.2 & 28.3 & 53.2 & 1.3 & 100 & 6391 \\ & \text{Trink t et al.} & 41.1 & 14.3 & 43.4 & 38.0 & 100 & 83625 \\ & \text{FLUKA} & 17.2 & 28.3 & 53.2 & 1.3 & 100 & 6691 \\ & \text{FLUKA} & 17.2 & 28.3 & 53.2 & 1.3 & 100 & 6691 \\ & \text{FLUKA} & 7.2 & 15.6 & 46.2 & 30.9 & 100 & 37338 \\ & 1 / 0^{\circ} & \text{Geant4} & 5.7 & 10.1 & 36.3 & 48.0 & 100 & 83625 \\ & \text{FLUKA} & 7.2 & 15.6 & 46.2 & 30.9 & 100 & 37338 \\ & \text{FLUKA} & 7.2 & 15.6 & 46.2 & 30.9 & 100 & 37338 \\ & \text{FLUKA} & 7.2 & 15.6 & 46.2 & 30.9 & 100 & 37338 \\ & \text{FLUKA} & 7.2 & 15.6 & 46.2 & 30.9 & 100 & 37338 \\ & \text{FLUKA} & 13.6 & 24.0 & 53.3 & 8.9 & 100 & 21092 \\ \end{array} \right.$	118 MeV + range shifter		Trinkl et al.	5.6	20.6	47.1	26.6	100	8926
$118 \text{ MeV} + \left \begin{array}{cccccccccccccccccccccccccccccccccccc$		1 / 0°	Geant4	8.4	18.9	49.8	22.8	100	7260
$140 \text{ MeV} + \begin{bmatrix} 2 / 45^{\circ} & \text{Geant 4} & 1.0 & 14.2 & 50.2 & 28.5 & 100 & 7721 \\ FLUKA & 6.0 & 14.9 & 47.5 & 31.6 & 100 & 7621 \\ FLUKA & 6.0 & 14.9 & 47.5 & 31.6 & 100 & 5106 \\ 3 / 90^{\circ} & \text{Geant 4} & 11.9 & 20.7 & 57.8 & 7.9 & 100 & 4628 \\ FLUKA & 11.7 & 24.0 & 56.3 & 7.7 & 100 & 4157 \\ FLUKA & 11.7 & 24.0 & 56.3 & 7.7 & 100 & 4157 \\ 4 / 135^{\circ} & \text{Geant 4} & 12.3 & 27.6 & 58.3 & 1.9 & 100 & 5192 \\ FLUKA & 12.3 & 27.6 & 58.3 & 1.9 & 100 & 5192 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 4937 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 4937 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 19779 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 19372 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 19372 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 19372 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 19372 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 19372 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 19372 \\ FLUKA & 12.3 & 27.6 & 58.4 & 1.5 & 100 & 19372 \\ FLUKA & 12.4 & 7.9 & 2.88.3 & 49.6 & 100 & 12512 \\ FLUKA & 10.8 & 18.4 & 43.8 & 26.8 & 100 & 11504 \\ 2 / 45^{\circ} & \text{Geant 4} & 9.7 & 14.6 & 46.6 & 29.9 & 100 & 10583 \\ & & & & & & & & & & & & & & & & & & $			FLUKA	3.0	13.3	48.0	35.5	100	9810
$ 118 \text{ MeV} + \left \begin{array}{cccccccccccccccccccccccccccccccccccc$		2 / 45°	Trinkl et al.	8.4	18.0	44.1	29.3	100	9210
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			Geant4	7.0	14.2	50.2	28.5	100	7721
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			FLUKA	6.0	14.9	47.5	31.6	100	7621
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			Trinkl et al.	13.8	26.8	50.4	9.0	100	5106
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		3 / 90°	Geant4	11.9	20.7	57.8	7.9	100	4628
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			FLUKA	11.7	24.0	56.3	7.7	100	4157
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		4 / 135°	Trinkl et al.	13.6	28.9	55.3	1.9	100	5712
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			Geant4	12.3	27.6	58.3	1.9	100	5192
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			FLUKA	12.3	27.6	58.4	1.5	100	4937
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	140 MeV		Trinkl et al.	5.0	15.4	42.1	37.4	100	19779
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		$1 / 0^{\circ}$	Geant4	6.3	11.4	37.6	44.6	100	19312
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			FLUKA	2.7	9.2	38.3	49.6	100	25421
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			Trinkl et al.	10.8	18.4	43.8	26.8	100	11504
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		$2 / 45^{\circ}$	Geant4	9.7	14.6	46.6	28.9	100	9499
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			FLUKA	7.6	15.8	46.6	29.9	100	10583
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			Trinkl et al.	18.0	25.1	49.0	7.8	100	7286
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		$3 / 90^{\circ}$	Geant4	16.9	21.6	54.3	7.1	100	6325
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			FLUKA	14.9	24.0	54.0	7.0	100	6371
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $			Trinkl et al.	19.2	28.9	49.5	2.3	100	7839
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		4 / 135°	Geant4	20.8	25.6	52.3	1.1	100	6929
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			FLUKA	17.2	28.3	53.2	1.3	100	6691
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	200 MeV	1 / 0°	Trinkl et al.	4.1	14.3	43.4	38.0	100	83625
$\begin{array}{c c c c c c c c c c c c c c c c c c c $			Geant4	5.5	10.1	36.3	48.0	100	86736
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			FLUKA	2.2	8.2	36.0	53.5	100	108629
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			Trinkl et al.	9.4	18.4	44.8	27.2	100	43192
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		$2 / 45^{\circ}$	Geant4	9.0	14.0	44.7	32.1	100	34959
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			FLUKA	7.2	15.6	46.2	30.9	100	37338
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			Trinkl et al.	17.0	25.3	48.5	9.1	100	24004
FLUKA 13.6 24.0 53.3 8.9 100 20129 Trinkl et al. 18.6 30.2 49.1 2.0 100 21902		3 / 90°	Geant4	16.2	20.6	54.2	8.9	100	19815
Trinkl et al. 18.6 30.2 49.1 2.0 100 21902			FLUKA	13.6	24.0	53.3	8.9	100	20129
			Trinkl et al.	18.6	30.2	49.1	2.0	100	21902
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$		4 / 135°	Geant4	18.8	26.1	53.5	1.5	100	18122
FLUKA 15.9 29.1 53.3 1.6 100 18320			FLUKA	15.9	29.1	53.3	1.6	100	18320

Table 1: Secondary neutron fluence ϕ measured using the ERBSS³⁷ and that simulated by Geant4 and FLUKA in the present work for the four proton energies at the four detector positions. Data is normalized to the integral neutron fluence in order to compare the fractions.





Figure 5: Measured³⁷ and full-room simulated neutron spectra for the 140 MeV proton field. The secondary neutron spectra, decomposed by the room elements of production, demonstrate a correlation between energy of the neutron and the room element, especially in the high and fast neutron energy intervals between 10² MeV and 10⁻² MeV.

The high-energy peak at 0° relative to the beam axis (Position 1 in fig. 4) can exclusively be attributed to neutrons from the PMMA phantom (Fig. 8 top). For all four positions, the high-energy region of 10 MeV to 10^2 MeV is governed by phantom-induced neutrons, although the total magnitude is reduced for larger beam angles.

In contrast, the origin of the neutrons in the energy interval 10^{-1} MeV to 10 MeV (cp. fig. 1) is more diverse. For 0° (Fig. 8 top), the two consecutive gantry cylinders modeled as iron are the main source of $\approx 70\%$ contributing neutrons. The remaining $\approx 30\%$ are shared by counterweight and gantry cone. For the off-axis positions (Figs. 8 bottom, 9 top, 9 bottom), the gantry fraction reduces relative to all remaining room components, which equally contribute. Additionally, as the scoring positions are further off-axis relative to 0°, neutrons originating from the phantom dominate the fast neutron interval.



Figure 6: Measured³⁷ and full-room simulated neutron spectra for the 118 MeV proton field using a PMMA range shifter of 5 cm thickness.

The neutrons in the interval 10^{-8} MeV and 10^{-1} MeV show no distinct room component as a main origin.

The contribution of the secondary neutrons generated within the concrete floor, the iron floor support plate, the bending magnet and the concrete walls individually is more than one order of magnitude lower than the total number generated across all four scorer positions.



Figure 7: Measured³⁷ and full-room simulated neutron spectra for the 75 MeV proton field.



Figure 8: Total neutron spectrum (dashed line) and room component spectra (solid lines) at 0° (top) and 45° (bottom) for the 200 MeV proton field.



Figure 9: Total neutron spectrum (dashed line) and room component spectra (solid lines) at 90° (top) and 135° (bottom) for the 200 MeV proton field.

³⁴⁰ IV. Discussion

The measured ERBSS neutron spectra showed the evaporation peak around 1 MeV, i.e. at lower energies compared to the peak simulated spectra without room model, which indicates that the produced secondary neutrons scattered and lost energy inside the treatment room before they reached the detector. We hence modeled the whole room in an attempt to reproduce the measured spectra. Note that for a scattering facility, Sayah et al.³³ reported that the lack of treatment room details in MC simulations can lead to errors in the simulated ambient dose equivalent $H^*(10)$ of up to 45%.

For side and backward directions (90° and 135°) the high-energy peak merges with 348 the evaporation peak. This behavior was already experimentally reported for spot-scanning 349 facilities^{37,52}. For all energies and forward angles, the high-energy peak amplitude exceeds the 350 amplitudes of the evaporation and thermal peaks. Especially for the two forward directions 351 $(0^{\circ} \text{ and } 45^{\circ})$, the relative contributions of the high energy interval can change dramatically, 352 as e.g. from 53.5% for $200 \,\mathrm{MeV}, 0^\circ$, to 1.6% for $200 \,\mathrm{MeV}, 135^\circ$. The absolute fluence of 353 thermal neutrons is similar within a factor of two for every initial proton beam energy across 354 all four measurement positions. This was explained in the literature as isotropic scattering 355 of the secondary neutrons from the walls 32 . 356

Our results show that the neutrons contributing to the high-energy peak originate predominantly from the phantom itself while the neutrons generated in gantry cylinders and counterweight mainly contribute to the fast (evaporation) peak. A previous ERBSS measurement campaign, although without detailed modeling investigations, already presumed structures of large atomic number (High-Z) materials like iron in forward direction, namely gantry and counterweight to contribute to neutron production in this energy range³².

At all four measurement positions, the used initial beam energies of 200 MeV, 140 MeV, 118 MeV and 75 MeV show the same magnitude of thermal neutrons (right in tab. 1). As reported previously, these thermalized neutrons originate from high-energy neutrons, which were isotropically scattered multiple times inside the gantry room³². Hence, simulations lacking the treatment room failed to reproduce this spectral component (Fig. 3).

Because the neutrons in the energy range 10^{-8} MeV to 10^{-1} MeV show no distinct room component as a main origin, the directionality of the initial emission appears to be

lost. In contrast, nuclear reactions in the phantom of type X(p,xn)Y directly generate 370 the high-energy neutrons, which are emitted along the 0° beam axis and directly hit the 371 detector at 0° (Fig. 8 top). Such neutrons interact via a next step in inelastic reactions 372 of Fe(n,xn) Fe with the structures of the counterweight (compared to the bending magnet 373 located in backward direction) and the two gantry wheels, which are located in forward 374 direction and all around the patient table, respectively (Fig. 8 and fig. 9). This finding 375 corroborates the explanations by Mares et al., who, based on ERBSS measurements) claimed 376 that the fast neutron component originates from forward scattered neutrons interacting 377 in the iron-rich counterweight³². Furthermore, at the 90° position, there are pronounced 378 contributions in the fast neutron range from the bending magnet, while the contribution 379 from the counterweight is less. 380

Although the contributions of the secondary neutrons generated within the concrete floor, the iron floor support, the bending magnet and the concrete walls individually are more than one order of magnitude lower than the total signal across all four scorer positions, the walls and massive components cannot be neglected in the model, because the neutrons, when generated in the gantry, are scattered multiple times in these components before reaching the scorer positions. In particular, the thermal peak at energies between 10^{-9} MeV and 4×10^{-7} MeV would be lost in this case.

³⁸⁸ V. Conclusion

The present study has confirmed a strong dependence of the secondary neutron field on the 389 angle of observation and incident proton beam energy as discussed in recent publications. 390 The comparison of the simulated neutron spectra produced by geometrically well defined, 391 monoenergetic proton fields with measured ERBSS neutron spectra around a homogeneous 392 PMMA phantom have shown that a room model, although simple, is needed to understand 393 the origin of secondary neutrons in general and their energy dependence in particular. The 394 results of this study, which was based on a systematic investigation of production of sec-395 ondary neutrons from monoenergetic protons at defined geometries, may be generalized in 396 that they can provide a estimation of neutron fields, even at spot-scanning facilities where 397 detailed neutron measurements and simulations cannot be performed. Due to the unavoid-398 able uncertainties from ERBSS measurement unfolding, as well as due to the heterogeneity 399

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of nuclear models, used cross-sections and code differences over 13 orders of magnitude of
neutron energies between different Monte Carlo codes, a cross comparison of the used codes,
FLUKA and Geant4, has been useful.

Identification of the neutron origin has shown that iron-rich room components like the 403 gantry cylinders, the gantry cone and the counterweight contribute most to this energy 404 interval. Of course, massive iron structures are needed for the stability in the whole gantry 405 system, which in turn enables reaching the required sub-mm precision of the proton beam. 406 We propose using Monte Carlo simulations for the design of future pencil beam scanning 407 gentry rooms to investigate options for the reduction of secondary neutrons, although the 408 concept of upright seated proton treatments may be feasible for certain indications without 409 using heavy gantry structures⁵³. Such simulations could influence the decisions on gantry 410 construction material or structure, for example on the choice of massive gantry versus a bird 411 cage gantry like structure. 412

Finally, the presented data can help in including the secondary neutron field in analytical treatment planning systems in order to predict the out-of-field neutron dose to organs far from the treatment field. This is already under investigation for scattering facilities, where a personalized estimate of organ specific neutron equivalent dose may eventually guide medical physicists to create treatment plans which feature reduced risk of late adverse effects^{9,54}.

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422 Conflict of Interest Statement

⁴²³ The authors have no relevant conflicts of interest to disclose.

424 References

- ⁴²⁵ ¹ Allen AM, Pawlicki T, Dong L et al. An evidence based review of proton beam therapy:
 the report of ASTRO's emerging technology committee. *Radiotherapy and Oncology*.
 ⁴²⁷ 2012;103(1):8-11.
- ⁴²⁸ ² Mohamad O, Tabuchi T, Nitta Yet al. Risk of subsequent primary cancers after car-⁴²⁹ bon ion radiotherapy, photon radiotherapy, or surgery for localised prostate cancer: a ⁴³⁰ propensity score-weighted, retrospective, cohort study. *Lancet Oncol.* 2019, 5: 674-685.
- ³ Newhauser WD, Zhang R. The physics of proton therapy. *Phys. Med. Biol.* 2015;60
 R155–R209.
- ⁴ Newhauser WD, Durante M. Assessing the risk of second malignancies after modern
 radiotherapy. *Nature Reviews Cancer.* 2011; 11(6): 438–448.
- ⁵ Hall EJ. The impact of protons on the incidence of second malignancies in radiotherapy.
 Technol Cancer Res Treat. 2007;6(4 Suppl):31-4.
- ⁴³⁷ ⁶ Schneider U, Hälig A, Baiocco G, Lomax T. Neutrons in proton pencil beam scanning:
 ⁴³⁸ parametrization of energy, quality factors and RBE. *Phys. Med. Biol.* 2016;61(16):6231⁴³⁹ 42.
- Ottolenghi A. ANDANTE Multidisciplinary evaluation of the cancer risk from neutrons
 relative to photons using stem cells and the induction of second malignant neoplasms
 following pediatric radiation therapy, www.cordis.europa.eu/result/rcn/182088_en.html
 [Accessed: 10.12.2018]
- ⁸ Hillbrand M, Georg D, Hadner H, Pöttner R, Dieckmann K. Abdominal cancer during
 early childhood: A dosimetric comparison of proton beams to standard and advanced
 photon radiotherapy. *Radiotherapy and Oncology.* 2009;89(2):141-9.
- ⁹ Kollitz E, Han H, Kim CH, Kroll C, Riboldi M, Newhauser W, Dedes G, Parodi K. A
 ⁴⁴⁸ novel hybrid model for out-of-field dose calculation in proton therapy treatment planning.
 ⁴⁴⁹ Int J Part Ther 2020;6(4):285.
- ⁴⁵⁰ Rechner L, Eley JG, Howell RM, Zhang R, Mirkovic D and Newhauser WD. Risk⁴⁵¹ optimized proton therapy to minimize radiogenic second cancers . *Phys. Med. Biol.*⁴⁵² 2015;60:3999-4013.

- ⁴⁵³ ¹¹ International Commission on Radiological Protection. The 2007 Recommenda ⁴⁵⁴ tions of the International Commission on Radiological Protection ICRP 103
 ⁴⁵⁵ www.journals.sagepub.com/doi/pdf/10.1177/ANIB_37_2-4 [Accessed: 10.12.2018]
- ¹² Zheng Y, Fotenot J, Taddei P, Mirkovic D and Newhauser W. Monte Carlo simulations
 of neutron spectral fluence, radiation weighting factor and ambient dose equivalent for
 a passively scattered proton therapy unit *Phys. Med. Biol.* 2008;53:187-201.
- ⁴⁵⁹ ¹³ Schneider RA, Wisser L, Arnold MR et al. Proton therapy with spot scanning:
 the Rinecker Proton Therapy Center in Munich. Nowotwory Journal of Oncology.
 ⁴⁶¹ 2007;57(5):524-532.
- ⁴⁶²¹⁴ Borchert HJ, Mayr M, Schneider RA et al. Proton therapy with spot scanning: the Rinecker Proton Therapy Center in Munich. Part 2: Technical & physical aspects. Nowot ⁴⁶⁴ wory Journal of Oncology. 2008;58(2):116-124.
- ¹⁵ Fontenot J, Taddei P, Zheng Y, Mirkovic D, Jordan T, Newhauser W. Equivalent dose
 ⁴⁶⁶ and effective dose from stray radiation during passively scattered proton radiotherapy
 ⁴⁶⁷ for prostate cancer. *Phys. Med. Biol.* 2008;53(6):1677-88.
- ¹⁶ Perez-Andajar A, Newhauser WD, DeLuca PM. Neutron production from beam ⁴⁶⁹ modifying devices in a modern double scattering proton therapy beam delivery system.
 ⁴⁷⁰ Phys. Med. Biol. 2009;54(4):993–1008.
- ⁴⁷¹ ¹⁷ Schneider U, Agosteo S, Pedroni E, Besserer J. Secondary neutron dose during proton
 ⁴⁷² therapy using spot scanning. Int J Radiat Oncol Biol Phys. 2002;53(1):244-51.
- ⁴⁷³ ¹⁸ Taddei PJ, Fontenot JD, Zheng Y et al. Reducing stray radiation dose to patients re⁴⁷⁴ ceiving passively scattered proton radiotherapy for prostate cancer. *Phys. Med. Biol.*⁴⁷⁵ 2008;53(8):2131-2147.
- Titt U, Newhauser WD. Neutron shielding calculations in a proton therapy facility based
 on Monte Carlo simulations and analytical models: criterion for selecting the method of
 choice. *Radiation Protection Dosimetry*. 2005;115(1-4):144-8.
- Farah J, Martinetti F, Sayah R et al. Monte Carlo modeling of proton therapy installations: a global experimental method to validate secondary neutron dose calculations. *Phys. Med. Biol.* 2014;59:2747–2765.

⁴⁸²²¹ Cywicka-Jakiel T, Stolarczyk L, Swakon J, Olko P, Waligórski MPR. Individual patient
⁴⁸³ shielding for a proton eye therapy facility. *Radiation Measurements*. 2010;45(10):1127⁴⁸⁴ 1129.

Tayama R, Handa H, Hayashi K et al. Benchmark calculations of neutron yields and
 dose equivalent from thick iron target for 52–256 MeV protons. *Nuclear Engineering and Design.* 2002;213(2-3):119-131.

⁴⁸⁸ ²³ Chen KL, Bloch CD, Hill PM, Klein EE. Evaluation of neutron dose equivalent from
 the Mevion S250 proton accelerator: measurements and calculations. *Phys. Med. Biol.* ⁴⁹⁰ 2013;58:8709-8723.

⁴⁹¹²⁴ Baradaran-Ghahfarokhi M, Reynoso F, Darafsheh A et al. A Monte Carlo-based analytic
⁴⁹² model of neutron dose equivalent for a mevion gantry-mounted passively scattered proton
⁴⁹³ system for craniospinal irradiation. *Med. Phys.* 2020;47(9): 4509-4521.

²⁵ Baradaran-Ghahfarokhi M, Reynoso F, Darafsheh A et al. A Monte Carlo based analytic
 ⁴⁹⁴ model of the in-room neutron ambient dose equivalent for a Mevion gantry-mounted
 ⁴⁹⁵ passively scattered proton system . J. Radiol. Prot. 2020;40: 980-996.

⁴⁹⁷²⁶ Howell RM, Burgett EA, Isaacs D et al. Measured Neutron Spectra and Dose Equivalents
⁴⁹⁸ From a Mevion Single-Room, Passively Scattered Proton System Used for Craniospinal
⁴⁹⁹ Irradiation. Int J Radiat Oncol Biol Phys. 2016;1;95(1): 249-284.

²⁷ Brenner DJ, Elliston CD, Hall EJ, Paganetti H. Reduction of the secondary neutron dose
 ⁵⁰¹ in passively scattered proton radiotherapy, using an optimized pre-collimator/collimator.
 ⁵⁰² Phys. Med. Biol. 2009;54(20):6065–6078.

²⁸ Islam MR, Collums TL, Zheng Y, Monson J, Benton ER. Off-axis dose equivalent due
 to secondary neutrons from uniform scanning proton beams during proton radiotherapy.
 Phys. Med. Biol. 2013;58(22):8235-51.

Newhauser WD, Titt U, Dexheimer D, Yan X, Nill S. Neutron shielding verification mea surements and simulations for a 235-MeV proton therapy center. *Nuclear Instruments* and Methods in Physics Research A. 2002;476:80-84.

- page 25
- ³⁰ Arjomandy B, Sahoo N, Cox J, Lee A, Gillin M. Comparison of surface doses
 ⁵¹⁰ from spot scanning and passively scattered proton therapy beams. *Phys. Med. Biol.* ⁵¹¹ 2009;54(14):N295-302.
- ³¹ Hohmann E, Safai S, Bula Ch et al. Investigation of the neutron stray radiation field
 ⁵¹³ produced by irradiating a water phantom with 200-MeV protons. *Nuclear Technology*.
 ⁵¹⁴ 2011;175(1):77-80.
- ³² Mares V, Romero-Exposito M, Farah J et al. A comprehensive spectrometry study of a stray neutron radiation field in scanning proton therapy. *Phys. Med. Biol.* 2016;61(11):4127-40.

 ³³ Sayah R. Evaluations des doses dues aux neutrons secondaires reçues par des patients de différents âges traités par protonthérapie pour des tumeurs intracrâniennes. Université Paris XI. 2013

- ³⁴ Goebel H. Dose Delivery System Of The Varian Probeam System With Continuous
 Beam. Workshop On Innovative Delivery Systems In Particle Therapy. 2017
- ³⁵ Particle therapy facilities under construction www.ptcog.ch/index.php/facilities-under ⁵²³ construction PTCOG Press Releases [Accessed: 11.04.2019]
- ³⁶ Zheng Y, Newhauser W, Klein E, Low D. Monte Carlo simulation of the neutron spectral
 ⁵²⁶ fluence and dose equivalent for use in shielding a proton therapy vault. *Phys. Med. Biol.* ⁵²⁷ 2009;54(22):6943–6957.
- ³⁷ Trinkl S, Mares V, Englbrecht F et al. Systematic out-of-field secondary neutron spectrometry and dosimetry in pencil beam scanning proton therapy. *Phys. Med. Biol.* ⁵³⁰ 2017;44(5):1912-1920.
- ³⁸ Zheng Y, Newhauser W, Fotenot J, Taddei P, Mohan R. Monte Carlo study of
 neutron dose equivalent during passive scattering proton therapy. *Phys. Med. Biol.* ⁵³³ 2007;52(15):4481-96.
- ³⁹ Battistoni G, Cerutti F, Fasso A et al. The FLUKA code: description and benchmarking.
 AIP Conference Proceedings. 2007

⁴⁰ Ferrari A, Sala PR, Fasso A, Ranft J, FLUKA: a multi-particle transport code. CERN 2005-10. 2005;31-49

⁴¹ Agostinelli S et al. Geant4—a simulation toolkit. Nuclear Instruments and Methods
 ⁵³⁹ in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated
 ⁵⁴⁰ Equipment. 2003;506:250-303.

- ⁴² Langer UW, Eley JG, Dong L, Langen K. Comparison of multi-institutional Varian
 ⁵⁴² ProBeam pencil beam scanning proton beam commissioning data. *Radiation Oncology* ⁵⁴³ *Physics.* 2017;18(3):96-107.
- ⁴³ Englbrecht FS, Trinkl S, Mares V et al. Supplemental material for: A Comprehensive
 ⁵⁴⁵ Monte-Carlo Study of Out-Of-Field Secondary Neutron Spectra in a Scanned-Beam
 ⁵⁴⁶ Proton Therapy Treatment Room. Zeitschrift für Medizinische Physik Online 2020.
- ⁴⁴ Boehlen TT, Cerutti F, Chin MPW, et al. The FLUKA code: developments and challenges for high energy and medical applications. *Nuclear Data Sheets*. 2018;120:211-214.
- ⁴⁵ Würl M, Englbrecht FS, Parodi K, Hillbrand M. Dosimetric impact of the low-dose
 ⁵⁵⁰ envelope of scanned proton beams at a probeam facility: comparison of measurements
 ⁵⁵¹ with tps and mc calculations. *Phys. Med. Biol.* 2016;61(2):958-73.
- ⁴⁶ Hofmann, W, Dittrich W. Use of isodose rate pictures for the shielding design of a proton
 therapy centre. *Proc. of shielding aspects of accelerators, targets and irradiation facilities*(SATIF 7). 2004;181-187.
- Ferrari A, Sala PR. The physics of high energy reactions. Nuclear reaction data and
 nuclear reactors physics, design and safety. 1997;1-109.
- ⁴⁸ De Smet V et al. Neutron H*(10) inside a proton therapy facility: comparison between
 Monte Carlo simulations and WENDI-2 measurements. *Radiation Protection Dosimetry*.
 ⁵⁵⁹ 2013;161(1-4):417-21.
- ⁴⁹ Avery S, Ainsley C, Maughan R, McDonough J. Analytical shielding calculations for a
 ⁵⁶¹ proton therapy facility. *Radiation Protection Dosimetry*. 2008;131(2):167-79.
- ⁵⁰ The Geant4 Collaboration. Physics Lists EM constructors in Geant4 10.1. 2015

- ⁵⁶³ ⁵¹ Varian Medical Systems, Inc., Probeam Proton Therapy System
 ⁵⁶⁴ www.varian.com/oncology/products/treatment-delivery/probeam-compact-proton ⁵⁶⁵ therapy-solution [Accessed: 10.08.2016]
- ⁵² Farah J, Mares V, Romero-Exposito M et al. Measurement of stray radiation within a
 scanning proton therapy facility: EURADOS WG9 intercomparison exercise of active
 dosimetry systems. *Medical Physics*. 2015;42(5):2572-84.
- ⁵³ Tami Freeman, Upright treatment could increase patient comfort, reduce proton ther apy costs, *Physics World* www.physicsworld.com/a/upright-treatment-could-increase patient-comfort-reduce-proton-therapy-costs [Accessed: 11.10.2020]
- ⁵⁴ Eley J, Newhauser WD, Homann K et al. Implementation of an analytical model for leak age neutron equivalent dose in a proton radiotherapy planning system. *Cancers (Basel)*.
 ⁵⁷⁴ 2015;7(1):427-38.