ABSORBED DOSE UNCERTAINTY ESTIMATION FOR PROTON THERAPY

by

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Successful radiotherapy treatment depends on the absorbed dose evaluation and the possibility to define metrological characteristics of the therapy beam. Radiotherapy requires tumor dose delivery with expanded uncertainty less than 5 %. It is particularly important to reduce uncertainty during therapy beam calibration as well as to apply all necessary ionization chamber correction factors. Absorbed dose to water was determined using ionometric method. Calibration was performed in reference cobalt beam. Combined standard uncertainty of the calculated absorbed dose to water in 65 MeV proton beam was 1.97% while the obtained expanded uncertainty of absorbed dose for the same beam quality was 5.02%. The uncertainty estimation method has been developed within the project TESLA.

Key words: protons, absorbed dose, therapy, uncertainty

INTRODUCTION

The TESLA Accelerator Installation (TAI), in the Laboratory of Physics of the Vinča Institute of Nuclear Sciences, is planned to be a large scale facility for production, acceleration and use of ions in science and medicine. It consists of a compact isochronous cyclotron (VINCY cyclotron), two similar electron cyclotron resonance heavy ion sources (mVINIS ion source and nVINIS ion source), a volume positive or negative light ion source (pVINIS ion source), and a number of low energy and high energy experimental channels. In the high energy channels ion beams from the pVINIS ion source or nVINIS ion source accelerated in the VINCY cyclotron will be used [1, 2]. The VINCY Cyclotron gives, *e. g*., the beams of H^- ions with the energies of 15, 30, and 65 MeV, the beam of $^4He^{2+}$ ions with the energy of 7 MeV per nucleon, and the beam of $^{40}Ar^{15+}$ ions with the energy of 3 MeV per nucleon. The programs of intended TAI use include basic and applied research in physics, chemistry and biology, development of materials and nuclear technologies, production of radionuclides and radiopharmaceuticals, and proton therapy. The available proton energy, up to 73 MeV, will enable the therapy of tumors lying down to about 4 cm. The proton therapy channel will enable very successful treatment of eye tumors, *e. g*., eye melanoma, one of the most dangerous cancers, as well as degeneration of macula lutea, a very frequent cause of blindness with older persons [1].

Application of proton beam for carcinoma treatment is based on deposition of proton energy in tumor volume followed by minimal beam scattering. Depth dose distribution is characterized by relative low dose in entrance part of the beam followed by narrow high dose at the end of the range. This increased dose is energy dependant Bragg peak which enables irradiation of very small localized lesions.

Successful radiotherapy treatment strongly depends on accurate absorbed dose delivered to the patient. Precise radiotherapy requires possibility of application of dose to target volume with expanded uncertainty less than 5% (normal distribution is applied) [3, 4]. Taking into account all possible sources of uncertainty, expanded uncertainty of 3% for absorbed dose measurement is desirable. The other factors which have influence on expanded uncertainty cover the uncertainties in tumor homogeneity, localization and geometry and all other factors presented by uncertainty of Type B. It is particularly important to reduce uncertainty during the beam calibration and to establish complete traceability chain. Dosimetry techniques at any facility must be consistent with those at other facilities if clinical data are intended to be compared.

Following the tendency in metrology that calibration has to be under conditions as close as possible to real situation, International Atomic Energy Agency

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(IAEA) has launched protocol IAEA TRS 398 dedicated to absorbed dose determination and calibration in radiotherapy. This protocol is based upon a cobalt-60 dose-to-water calibration traceable to a national standard. The same concept is recommended by the International Commission on Radiation Units and Measurement, ICRU 78 and ICRU 59 in the frame of European charged heavy particle dosimetry (ECHED) [5-7].

In the process of uncertainty evaluation we used the existing international recommendations, results of international and bilateral regional intercomparisons in which we participated as the valid national regulatory framework. There are only two national regulatory documents related to proton dosimetry. These are: Hierarchy scheme and methods for absorbed dose standard instruments used in proton beam (Official gazette SFRJ, No. 45, 1994) and Hierarchy scheme and transfer methods of absorbed dose standards for proton beam (Gazette of FBMPM, No. 2, 1994).

METHODS AND MATERIALS

Absorbed dose is the main physical quantity in radiotherapy and it should be determined to get quantitative correlation between ionizing radiation and its effects in tissue. The concept of residual range (R_{res}) is used as a parameter of proton beam quality which can be easily measured. This quantity slightly underestimates the stopping power ratios in the middle of the spread out Bragg peak (SOBP) but this effect is unlikely to exceed 0.3%. SOBP defines the therapeutic radiation distribution. Appropriate energy modulation spreads out the Bragg peak over the extent of the tumor in depth to match the contours of tumors [8, 9].

Residual range is defined by eq. (1) as

$$R_{res} \quad R_p \quad z \tag{1}$$

where z is the measurement depth and R_p – the practical range expressed in g/cm^2. Practical range defines the depth at which Bragg peak or SOBP decreases to 10% of its maximum value [5, 9].

The relation ship between the initial energy $E_0(z = 0)$ and the range R in the medium is given approximately by eq. (2)

$$R_p \quad \alpha E_0^p \tag{2}$$

For energy of our interest the value of $p = 1.8$. Factor α is approximately proportional to the square root of the effective atomic mass of the absorbing medium (Bragg-Kleeman rule) [9].

The depth dose distribution can be presented by eq. (3) in a simplified form

$$D(z) \quad D_1(z) \quad D_2(z) \quad a_1(R_p \quad z)^{\frac{1}{p}\ 1} \quad a_2(R_p \quad z)^{\frac{1}{p}} \tag{3}$$

where $D_1(z)$ is the dose contribution from those protons that have no nuclear interactions. It is proportional to the stopping power and exhibits to some degree the form of a Bragg curve, as it increases monotonically from $z = 0$ to $z = R_p$ and has a peak at R_p. D_2(z) represents the dose delivered by the relatively small fraction of protons that have nuclear interactions. It decreases monotonically and becomes zero at $z = R_p$ [9]

Theory of dosimetric principles

Determination of absorbed dose for heavy charged-particle beam includes the knowledge of the types of charged particles, their fluence spectra and the stopping power S of the absorber material at the point of interest. For particles of energy E, if delta ray equilibrium is established, the dose in a small mass m inside a homogeneous medium is given by the eq. (4) [10-12]. It is assumed that the energy loss in the material is small compared to E (*i. e.*, all particles are "crossers") and that no nuclear reactions take place in m

$$D_m \quad \sum_{i\ 0}^{n} \Phi_i(E)\, \frac{S(\overline{E}_i)}{\rho}_i \tag{4}$$

where i is an index to sum over the different types of contributing particles, (the mass stopping power is the kerma factor for charged particles). The integral $\Phi_i \quad \Phi_i(E)\mathrm{d}E$ is the total number of particles per unit area of type i passing through the absorber, and $\overline{E}_i \quad E\Phi_i(E)\mathrm{d}E / \Phi_i(E)\mathrm{d}E$ is the average energy [10-12].

Equation (4) provides the theoretical basis for determining the absorbed dose in a patient. Measurements of deposited energy or ionization with instruments such as calorimeters or ionization chambers allow the determination of dose in the materials used in the construction of the instrument. Further, it is necessary to convert the results to an estimate of the absorbed dose in tissue. For this reason it is desirable to use tissue-equivalent (TE) materials in the construction of the instruments whenever possible, so that corrections and, most importantly, the uncertainties in the corrections will be small and may be energy independent. If the dose in the dosimeter, D_d, has been measured, the dose in the patient (tissue), D_t, can be calculated by eq. (5)

$$D_t \quad D_d \frac{\sum_{i\ 1\ 0}^{n\ \infty} \Phi_i(E)\, \frac{S(E)}{\rho}_i \mathrm{d}E}{\sum_{i\ 1\ 0}^{n\ \infty} \Phi_i(E)\, \frac{S(E)}{\rho}_{i\ d} \mathrm{d}E} \tag{5}$$

where the fluence in the patient and the dosimeter (the latter denoted by index d) may be different. The measurement of D_d therefore is not sufficient to determine D_t if the fluence spectra $\Phi_i(E)$ are not known for all the particles [10-12]. If the fluencies are not well

known it is recommended that several estimates of the integrals in eq. 5 be made with various possible values of $\Phi_i(E)$ so that the uncertainty of the ratio can be estimated.

Absorbed dose determination

Absorbed dose estimation is based on the concept of calibration factor $N_{D,w}$ determined in water in reference beam quality Q_0 (^{60}Co gamma beam). The correction factor k_{Q,Q_0} for the beam qualities different from the reference one can be calculated easily [5, 13-15]. Ionometric method is inherently relative and consists of calibrated ionization chamber and tissue-equivalent, usually water, phantom [5].

Absorbed dose in proton beam quality Q at the reference depth in the water, z_{ref}, is given in eq. (6)

$$D_{w,Q} \quad M_Q \Pi k N_{D,w,Q_0} k_{Q,Q_0} \tag{6}$$

where M_Q is the electrometer reading at z_{ref} corrected for influential quantities k, N_{D,w,Q_0} – the calibration factor in terms of absorbed dose obtained in reference beam quality Q_0, and k_{Q,Q_0} – the correction for chamber response in radiation beam different from the reference one [5, 9], given by eq. (7)

$$k_{Q,Q_0} \quad \frac{(S_{w,air})_Q \quad \frac{W_{air}}{e} \quad {}_Q p_Q}{(S_{w,air})_{Q_0} \quad \frac{W_{air}}{e} \quad {}_{Q_0} p_Q} \tag{7}$$

where $S_{w,air}$ is the stopping power ratio in water and air for certain beam quality Q and the reference beam quality Q_0, $W_{air/e}$ – the mean energy for ion pair production in dry air, for certain beam quality Q and for the reference one Q_0, and p_Q and p_{Q_0} – the correction factors due to perturbation for the beam quality Q and for the reference beam quality Q_o, respectively. [5, 9]

All correction factors applied with electrometer reading M represent the consequences of approximations and assumptions introduced in ionization chamber cavity theories. Therefore, we considered the following correction factors given in eq. (8)

$$\Pi k \quad k_{TP} k_{elec} k_{pol} k_s k_\tau p_{cel} p_Q \tag{8}$$

The meaning of the factors in eq. (8) are: k_{TP} is the chamber air density correction for temperature and pressure different from reference values (20 °C and 1013 mbar), k_{elec} – the correction which take into account electrometer calibration factor if the chamber and electrometer were calibrated separately, k_{pol} – the correction of chamber response in the case of changed bias polarization, k_s – the correction for recombination losses; k – the source position correction (up to 0.1%), p_{cel} – the correction on central electrode influences on chamber response (in our case, for proton energies up to 75 MeV, the value is equal to one with standard uncertainty of 0.4 %), and p_Q – the total perturbation factor expressed as

$$p_Q = p_{cav} p_{dis} p_{wall} \tag{9}$$

where p_{cav} is the correction that takes into account air cavity effects as are scattered electrons, p_{dis} – the takes into account replacement of water volume by air, relevant only for cylindrical chambers, and p_{wall} – the correction introduced if wall chamber material is not equal to sleeve and phantom material, factor was obtained using Monte Carlo method.

Uncertainty estimation

The uncertainty evaluation is performed according to international standards, international recommendations as well as measurement good practice documents published in reference National metrological institutes (NMI) [16-18]

$$u_c(y) \quad \sqrt{\sum_{i\ 1}^{N} \frac{\delta f}{\delta x_i} u(x_i)^2} \tag{10}$$

where f is the function $f(x_1, x_2, ...)$ describing the measurement quantity, and x_i and $u(x_i)$ are the represent respectively the independent variables related to the measurand and its Type A and Type B standard uncertainties. Expanded uncertainty is given by eq. (11)

$$U(y_1) \quad k u_c(y) \tag{11}$$

For the normal distribution the value of the coverage factor $k = 2$ produces an interval having level of confidence $p = 95.45\%$ [16-18].

Instrumentation

In our investigations we used two different types if ionization chambers.

– Cavity ionization chamber type ND 1006 (volume 0.2535 cm^3) manufactured at National Office of Measurement (OMH), Hungary. Accompanying current integrator type NP 3000 (manufactured also in OMH) with current range from 10^{-12}A to10^{-7} A (electrical charge range 10^{-10}C to 10^{-6}C). Absorbed dose calibration factor in cobalt beam was obtained during comparison at Bureau International des Poids et Mesures (BIPM) in Sevres, France. Calibration factor value was $N_{D,w}$ = = 122.7 Gyμ/C (standard uncertainty less than 0.3%) ND 1006 is waterproof chamber, used with 0.5 mm waterproofing sleeve made of poly-methyl methacrylate (PMMA). The air gap between the chamber wall and the waterproofing

sleeve was 0.25 mm, sufficient to allow the air pressure in the chamber to equilibrate.

– Graphite cavity ionization chamber Farmer type NE 2571, nominal volume of 0.69 cm^3. Calibration factor in cobalt gamma beam (4.5418 10^7 Gy/C) was obtained in comparison with ND 1006. Accompanying electrometer was radiotherapy electrometer Type 35040 manufactured by Kithley, USA.

Chambers were positioned with the stem perpendicular to the beam direction. Collecting voltage was applied to the electrode of the chamber at least 30 minutes before any measurements were made. The ionization current measured from the chamber was corrected for the leakage current. This correction was less than 1 10^{-4} in relative value.

RESULTS AND DISCUSSION

All results for both chambers were related to depth in water of 5 g/cm^2. Measurement reproducibility was better than 2 $^{-4}$ from 90 repeated measurements in phantom.

The absorbed dose to water rate is determined by an ionometric method using eq. (12)

$$\dot{D}_{\text{water}} \quad \frac{I}{m}\frac{W}{e}\overline{s_{\text{c,a}}}\ \overline{\frac{\mu_{\text{en}}}{\rho}}_{\text{w,c}} \Psi_{\text{w,c}}(1\ \ \varepsilon)_{\text{w,c}}\Pi k_{\text{i}} \quad (12)$$

where I/m is the ionization current per unit mass of air measured by ionization chamber, W – the average energy spent by an electron of charge e to produce an ion pair in dry air, $\overline{s_{\text{c,a}}}$ – the mean stopping powers ratio for graphite and air, $(\overline{\mu_{\text{en}}}/\rho)_{\text{w,c}}$ – the ratio of the mean mass energy absorption coefficients, $\Psi_{\text{w,c}}$ – the ratio of photon energy fluencies, $(1+\varepsilon)_{\text{w,c}}$ – the ratio of absorbed dose to collision component of kerma, and k_{i} – the product of correction factors applied to the current integrator or electrometer readings: k_{cav} is the correction factor for the inadequacy of the chamber with the ideal Bragg-Gray cavity k_{s} – the correction factor for recombination losses, k_{ps} – the correction factor for the influence of the Perspex support on the chamber, k_{pf} – the correction factor for the front face of the water phantom which is not water-equivalent, k_{rn} – the correction factor for the non-uniformity of the beam, and k_{h} – the correction factor for humidity [19]. The mass of the air (m) can be obtained by multiplying cavity volume with the air density: $m = v\rho$

We performed calibration of Farmer chamber in reference cobalt beam before the establishment of its use in proton dosimetry. The values of physical constants and correction factors are given together with their uncertainties in tab. 1. Uncertainty of $R = D_{\text{ND1006}}/D_{\text{NE2571}}$ is also given in tab. 1.

Table 1. Uncertainty budget in absorbed dose transfer from ND 1006 to Farmer chamber

Quantity	ND 1006			NE 2571			R	
	Value	u_{A}[%]	u_{B} [%]	Value	u_{A}[%]	u_{B} [%]	u_{A}[%]	u_{B} [%]
Physical constants								
Dry air density [kgm^{-3}]*	1.2930	–	0.01	1.2930	–	0.01	–	–
W/e [JC^{-1}]	33.97	–	–	33.97	–		–	–
$\overline{s_{\text{c,a}}}$	1.0030	–	0.11**	1.0030	–	0.11**	–	–
$(\overline{\mu_{\text{en}}}/\rho)_{\text{w,c}}$	1.1125	0.01	0.14	1.1125	0.01	0.14	–	–
$\Psi_{\text{w,c}}$	1.0065	0.04	0.06	1.0065	0.04	0.06	–	–
$(1\ \ \varepsilon)_{\text{w,c}}$	1.0015	–	0.06	1.0015	–	0.06	–	–
Correction factors	–	–	–	–	–	–	–	–
p_{Q} perturbation	1.1107	0.05	0.17	0.9920	0.05	0.30	0.02	0.30
k_{ps} (PMMA envelope)	0.9994	0.01	0.01	0.9994	0.01	0.01	–	0.01
p_{cav} (air cavity)	0.9900	0.03	0.04	0.9900	0.03	0.04	0.01	–
k_{pf} (phantom window)	0.9996	–	0.01	0.9996	–	0.01	0.01	–
k_{rn} (radial non-uniformity)	1.0051	0.01	0.03	1.0051	0.01	0.03	0.01	–
k_{s} (recombin. losses)	1.0015	0.01	0.01	1.0014	0.01	0.30	0.03	–
k_{h} (humidity)	0.9970	–	0.03	0.9970	–	0.03	0.01	0.30
k_{PT}	–	–	0.20	–	–	0.20	–	–
Measurement chamber	–	–	–	–	–	–	–	–
Volume [cm^3]	0.27	0.19	0.03	0.69	0.20	0.50	0.20	0.50
I (ionization current) (A)	–	0.01	0.04	–	0.01	0.50	0.01	0.50
SCD [cm] (source to chamber distance)	–	–	0.03	–	–	0.30	–	–
Depth in water	–	0.02	0.6	–	0.02	0.06	–	–
Quadratic summation	–	0.22	0.46	–	0.22	0.93	0.20	0.77
Combined standard uncertainty of D_{w}	0.51			0.96			0.79	
Expanded uncertainty (k = 2)	1.02			1.92			1.58	

* At 20 °C and 101.325 kPa, ** combined uncertainty of the production $W / e\overline{s_{\text{c,a}}}$

Reference conditions for all the results presented here were: temperature of 200 °C and a pressure of 101.325 Pa (1013 mbar). It was assumed that the humidity in the ionization chamber is the same as that in the ambient room air and the ionization current was corrected for humidity.

Evaluation of absorbed dose uncertainty for the proton beam

Standard relative uncertainties of $D_{w,Q}$ were estimated for the reference depth in water and for clinical proton beam based on chamber calibration in ^{60}Co gamma radiation. Values for $s_{w,air}$ in proton beams are derived from the proton beam quality specified by R_{res} given by eq. (13)

$$s_{w,air} \quad a \quad bR_{res} \quad \frac{c}{R_{res}} \tag{13}$$

where are $a = 1.137$, b = –4.3 10^{-5}, and $c = 1.84$ 10^{-3} [5].

Uncertainty budget for absorbed dose determination in proton beam using NE 2571 chamber is given in tab. 2.

Estimated relative standard uncertainties of absorbed dose in water at the reference depth for clinical proton beam based on a chamber calibration in ^{60}Co gamma radiation are given in tab. 3. Expanded uncertainty is also given. All data are applied for Farmer ionization chamber type NE 2571.

Type A uncertainties were evaluated by statistical analysis of series of 90 observations. Type A component of uncertainty is a measure of the repeatability of a result under constant conditions and can be assumed to have a normal probability distribution [18].

Type B uncertainties were evaluated using BIPM and OMH intercomparison results, previous measurement data, manufacturer's specifications, data provided in calibration and other certificates, uncertainties assigned to reference data found in published documents.

Both types of evaluation are based on probability distributions, and the uncertainty components resulting from either type are quantified by variances or standard deviations.

The normal probability distribution (Laplace-Gauss distribution) was assumed for all correction factors and quantities for which Type A uncertainties were stated. For uncertainty components evaluated as Type B we assumed rectangular distribution

The combined standard uncertainty of the output quantity, $u(y)$, is derived by the summation in quadrature of all Type A and Type B standard uncertainties due to the input parameters. It is generally a standard deviation with a normal probability distribution unless one component dominates the combined effect of all other contributions. The uncertainty of measurand y is calculated using expression [18]

$$u_i(y) \quad \frac{\delta x_i}{\text{divisor}} \quad \frac{c_i}{y} \tag{14}$$

where x_i – input quantity, c_i – sensitivity coefficient, y output quantity, divisor has the value of $3^{1/2}$ for rectangular and 1 for normal distribution.

Table 2. Uncertainty budget for absorbed dose determination in proton beam using NE 2571 chamber

Quantity	Value	u_A [%]	u_B [%]
Physical constants			
Dry air density (0 0C, 1013 mbar) [kg/m^3]	1.2930	–	0.01
$(\overline{u_{en}}/\rho)_{w.c}$	1.1122	–	0.14
$S_{w,air}$ (calculated)	0.143	–	1.10
W_{air}/e [J/C]	34.23	–	0.50
Correction factors			
$p_Q = p_{cav}\, p_{dis}\, p_{wall}\, p_{cel}$ (total perturbation factor) p_{cav}	0.9900	–	0.30
p_{dis}	0.9870	–	0.40
p_{wall}	1.0000	–	0.80
p_{cel}	1.0030	–	0.40
k_{ps} (PMMA sleeve)	0.9994	0.08	0.50
k_{pf} (phantom window)	0.9996	–	0.01
k_s (recombination losses)	1.0016	0.08	0.80
k_{elec} (electrometer calibration factor)	1.0000	–	0.20
k_{pol} (polarity effects)	1.0000	0.02	0.30
k_h (humidity)	0.9970	–	0.03
Measurements			
v (chamber volume, ionometric method) [cm^3]	0.6875	0.22	0.50
Quadratic summation	–	0.25	1.95
Combined uncertainty 1.97%			

Table 3. Estimated relative standard uncertainties of absorbed dose in water for linical proton beam based on ^{60}Co calibration

Source of uncertainty	u_A [%]	u_B [%]
$N_{D,w,Q0}$ (chamber calibration factor obtained in ^{60}Co reference beam)	0.20	0.77
$k_{p,T}$ (correction for reference conditions)	0.08	0.60
Influence factors k_{rn} (radial non-uniformity of the user's beam) k_{an} (axial non-uniformity of the user's beam) SCD (source to chamber distance)	 0.03 0.03 0.03	 0.40 0.40 0.40
Position in phantom Depth in water	0.01 0.08	0.50 0.60
Absorbed dose in proton beam	0.25	1.95
Long-term stability of the dosimeter Electrometer reading	– 0.02	0.10 0.40
k_Q (beam quality correction)	–	0.40
Quadratic summation Combined uncertainty: 2.51% Expanded uncertainty: 5.02% (k = 2)	0.35	2.49

Under standard conditions (0 °C and 1013 mbar), the density of dry air (ρ_{air}) is 1.29299 kg/m^3 Practically, the value of 1.2930 kg/m^3 was adopted. Assuming that variation shows a rectangular distribution, the uncertainty obtained is 0.01% [14, 20]. This uncertainty is included in the calculation of the air mass m.

The recombination losses are related to the strength of the irradiation field. We obtained correction factor for recombination losses k_s by using the dual voltage measurement technique (normal chamber operating voltage and half of this value). The value of k_s was obtained as mean value of 25 repeated measurements under the same geometrical and irradiating conditions. The uncertainty of Type B, evaluated from experimental data was higher due to uncertainties of additional voltage divider.

The correction factor for the front face of the water phantom made of PMMA (kpf) is taken from the BIPM references and its value is taken to be 0.9996. [19, 20] The front face of the water phantom is made of PMMA and is 0.476 g/cm^2 in thickness. The uncertainty is 0.01% by Type B evaluation method. For ñPMMA we adopted the value of 1.19 g/cm^3 [20].

For non-waterproof chambers a waterproofing sleeve should be used, made of PMMA (0.5 mm in thickness) . The air gap between the chamber wall and the waterproofing sleeve of 0.25 mm is sufficient to allow the air pressure in the chamber to equilibrate. The same waterproofing sleeve that was used for calibration of the user's ionization chamber should also be used for reference dosimetry. Standard chamber ND 1006 is waterproof but we usually used waterproofing sleeve made in BIPM workshop for our own chamber. The same material, design, and thickness were used for making waterproofing sleeve in our phantom manufactured by workshop of Institute of Oncology and Radiology from Belgrade, Serbia. We decided to use our own correction factor obtained indirectly using ND 1006 performing 90 repeated measurements of absorbed dose in water at the reference depth with waterproofing sleeve and series of 90 repeated measurements without it.

The correction factor for humidity k_h was taken from BIPM conditions and its value of 0.9970 was adopted. The corresponding uncertainty of 0.03%, is evaluated by Type B only.

According to the available literature the value of W_{air}/e = 34.23 J/C and a standard uncertainty of 0.4% are recommended for proton dosimetry [5, 21-22].

Special attention was paid to evaluate the correction for the perturbation. The results of measurements for cylindrical ionization chambers show relative perturbation effects that are limited to 0.5-1%, resulting in perturbation correction factors that are larger than unity compared with an NE2571 ionization chamber. The central electrode perturbation correction factor for an aluminum electrode in a Farmer-type geometry was found to be unity within the experimental uncertainties [23-25].

Uncertainties evaluated as Type B and associated to $s_{w,air}$, W_{air}/e, p_{cav}, p_{dis}, p_{wall}, and p_{cel} are taken from published documents [5, 23-27].

CONCLUSIONS

Proton therapy is associated with significant benefits in terms of normal tissue sparing and radiation dose distribution. Currently, proton therapy centers designed specifically for treatment of cancer patients exist in most regions of the United States, as well as several areas in Europe and Asia. The metrological significance of proton therapy must be considered. Accurate determination of proton dose and penetration range is critical in proton therapy. The main challenge of proton therapy is to measure the precise depth dose in water. In this study, we have considered the

pure metrological model for uncertainty evaluation of absorbed dose in water measured by cylindrical ionization chambers in 65 MeV clinical proton beam. In this work, we relied on the experiences we have had in legal metrology and international intercomparisons.

Several major problems then arise: the measured quantity is given for a finite volume and not at a point; the sensitive medium differs, in most cases, from the medium of interest; all the other components of the detector, such as external walls, perturb the field of ionizing radiation impinging the sensitive volume. All these effects must be corrected for, using experimental procedures or calculation. For protons the situation is more complicated, because there the contribution from low energy δ-electrons is much higher than in case of primary electrons. Due to the complexity of the interactions and phenomena considered, the experimental determination of correction factors involved in the use of ionization chambers is not always possible or precise, and the interpretation of some experiments is far from being straightforward. This is the reason why we used Monte Carlo code to estimate the value of some correction factors simulating interactions of radiation with matter. Application of Monte Carlo is well known and progressively accepted by metrologists.

For estimation of wall correction factor we applied traditional linear extrapolation method although this correction to zero wall thickness is an over-correction because the mean centre of electron production is somewhere in the wall and the radiation which interacts at this depth is not attenuated by the total wall thickness. This method must be replaced by more precise MC simulations to investigate the influence of non-elastic nuclear interactions on depth dose data and for quantifying perturbation correction factors for ionization chambers.

We strongly recommend the application of numerical simulation. Nevertheless, the codes have to be applied with special care in the field of metrology, as the evaluation of type B uncertainties resulting from the models used and from the cross section databases are not obvious.

Through the above discussion, the cavity ionization chamber has been defined for its measurement parameters and determined for its physical constants and correction factors. Thus, the absolute measurement of the absorbed dose to water in proton beam can be performed. According to the ISO GUM analysis method, the expanded uncertainty of absorbed dose determination is 5.02%, while, expanded uncertainty of calibration factor obtained in NMI is 1.58%. This measurement system has the capabilities to provide the calibration traceability of absorbed dose to water in proton beam in Serbia.

Metrology of clinical proton beam must be improved. This enforces the need for the availability of metrological standards and methods more adapted to the actual clinical conditions and expressed in quantities as close as possible to the quantities used by the medical physicists in clinical practice.

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ПРОЦЕНА АПСОРБОВАНЕ ДОЗЕ У ПРОТОНСКОЈ ТЕРАПИЈИ

Успешан радиотерапијски третман зависи од процене апсорбоване дозе код пацијента и могућности дефинисања метролошких карактеристика терапијског снопа. Радиотерапија захтева да се тумору испоручи доза одређена са проширеном мерном несигурношћу мањом од 5%. Од посебног је значаја смањење мерне несигурности при калибрацији терапијског снопа као и примена свих релевантних корекционих фактора код јонизационе коморе. Апсорбовану дозу у води смо одређивали јонометријском методом док је калибрација извршена у референтном снопу кобалта. Комбинована стандардна мерна несигурност прорачунате апсорбоване дозе у води у снопу протона енергије 65 MeV је 1.97% док је добијена проширена мерна несигурност одређивања дозе у снопу истог квалитета 5,02%. Метод за процену мерне несигурности је развијен у оквиру потреба пројекта ТЕСЛА.

Кључне речи: протони, апсорбована доза, терапија, мерна несигурност