JOURNAL OF INTENSE PULSED LASERS AND APPLICATIONS IN ADVANCED PHYSICS Vol. 3, No. 2, p. 15 - 25

Absorbed dose determination in conventional and laser – driven clinical hadron beams

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IAEA TRS 398 recommends for hadron therapy beam energies of 50 to 250 MeV for protons and of 100 to 450 MeV/u for carbon ions. At present these energies are supplied by the conventional accelerators of cyclotron, synchrocyclotron, synchrotron and linac types. As an alternative to conventional accelerator beams that include compact accelerators in the design phase (FFAG, DWA and cyclinac) laser-driven carbon ion/proton therapy beams has appeared. Parameter characterizing the interaction of the clinical beams of charged particles with the target is the absorbed dose in the tumors. This paper presents a measurements procedure for determining absorbed dose in hadron beams by the ionization method with ionization chambers.

(Received May 5, 2013; accepted June 24, 2013)

Keywords: Absorbed dose to water, Ionization chamber, Hadron therapy beam, Hadron dosimetry, Expand uncertainity.

1. Introduction

APOLLON laser system of 10 PW (150 J, 15 fs) [1] which is now under construction on Magurele platform near Bucharest, induced the idea of using it to generate the therapeutic hadrons beams (protons and carbon ions) with energies of 50 to 250 MeV and 100 to 450 MeV/u, respectivelly [2]. In this way it is possible to skip the stage of conventional accelerators (cyclotron, synchrocyclotron, synchrotron and linac types) which also includes compact accelerators in the design phase (FFAG, DWA and cyclinac) and directly pass to the alternative of using the laser-driven carbon ion/proton therapy beams. This alternative is based on the fact that the experimental researches by Target Normal Sheath Acceleration (TNSA) mechanism have showed that protons can be accelerated to kinetic energy of about 65 MeV (3 cm range in water), energy needed to treat eye cancer [3] and carbon C^{6+} ions were accelerated to the energy of 525 MeV (≈ 44 MeV / u, 0.6 cm range in water) in the first experimental demonstration of the mechanism of acceleration Brake-Out Afterburner (BOA) [4].

Computer simulations have demonstrated that by using the mechanism of acceleration Radiation Pressure Acceleration (RPA) for protons the obtained energy was up to 2.5 GeV, two times more than the recommended energy of 250 MeV (≈ 37.4 cm range in water) and for carbon ions C^{6+} the obtained energy was up to 1 GeV/u more than twice the recommended energy of 450 MeV / u (≈ 28.6 cm range in water) [5]. Besides the 10 PW laser operating in the ultrarelativistic regime ($a_L \geq 100$ and $I_L \geq 1\cdot10^{20}$ W/cm^2) becomes a source of neutral and charged particles (electrons, positrons, protons, neutrons, ions etc.). INFLPR has in its inftastructure a Secondary Standard Dosimetry

Laboratory at High Energies - STARDOOR [6], accredited by Romanian Accreditation Association (RENAR) to perform testing and calibration in beams of photons, electrons and high-energy neutrons in accordance with SR EN ISO / IEC 17025:2005. The dosimetric measurements performed by the laboratory are traceable to the reference standard developed and maintained by PTB. The existing laser source requires theoretical research, development of 3D simulation and experimenting to generate therapeutic hadrons beams (protons and carbon ions in the first phase) with energies close to clinical applications using the acceleration mechanism RPA and develop their calibration methods. In this respect, it is mandatory the expansion of the functions of STARDOOR lab for performing clinical testing and calibration in beams of protons and carbon ions. For that the material base is ensured by outfitting the platform with 10 PW laser and lab STARDOOR with cylindrical and plane parallel ionization chambers calibrated in a ^{60}Co beam at PTB. Taking into account the above and the experience gained in international hadrontherapy centers with protons and carbon ions, the reference dosimetry techniques for clinical beams of hadrons - calorimetric dosimetry, chemical dosimetry, ionization dosimetry with Faraday cup and ionization chamber dosimetry - in this paper to measure the absorbed dose to water in clinical hadron beams have chosen the ionization chamber Dosimetry, sometimes called Ionometer method.

2. Proton and carbon ion beams

Generally, heavy charged particle beams for therapy applications are delivered by the conventional particle beam accelerators (such as cyclotrons, synchrotrons and linear accelerators) through direct acceleration of interested particle (primary beam) e.g. protons or through nuclear interaction between accelerated particle and target material from which the desired particle is obtained (secondary beam) for example: carbon ions, π^- meson etc. For laser driven accelerators, proton and ion beams are obtained as secondary beams through the interaction of the laser beam with target abundant in protons or carbon atoms.

2.1 Requirements for Clinical Beam Parameters

The most important physical parameters when starting the design or choosing a charged particle accelerator for radiotherapy, are: the particle beam energy and the extracted beam current formed and transported to the target material. The energy defines the ion range in the patient, while the current provide the absorbed dose in the tumor.

Their values and other parameters of the proton and carbon ion clinical beams are presented in Table 1.

Table 1. Short summary of main parameters.

Beam parameter	Value
Extraction energy E, min.-max. [MeV /u] vs. range in patient 3-38 g/cm^2	50-250 (protons) 100-450 (carbon ions)
Intensity beam [pps]	(1-5)·10^{10} particle /s
Beam monoenergetic [ΔE/E]	≤ 10^{-2}
Repetition rate [Hz]	≥ 5
Average dose rate [Gy/min/liter tumor]	≥ 2
Range modulation [g/cm^2]	step of < 0.5
Range adjustment [g/cm^2]	step of < 0.1
Radiation levels	ALARA

The relationship between range and energy shows that 250 MeV protons have a range in water of 38 cm which corresponds to an energy of carbon ions of 450 MeV/u (5400 MeV) [TRS 398].

2.2. Conventional Hadron Acceleration Methods

Acceleration of heavy charged particles is done in an electric field of the electromagnetic wave. The total energy of a particle, E, is removed at the end of the acceleration process, in this case the proton or carbon ion, is related to the rest energy $E_0 = m_0 \cdot c^2 = E / \gamma$, the kinetic energy $T = m_0 \cdot c^2 \cdot (\gamma-1)$ and momentum $p = m \cdot v = m_0 \cdot \gamma \cdot \beta \cdot c$, through the known relationship of relativistic dynamics, $E^2 = E_O^2 + p^2 \cdot c^2$, where $E = E_o + T$ [7]. Depending on the kinetic energy T, the above relation can be written as an equation as follows: $T^2 + 2TE_o - p^2 \cdot c^2 = 0$. In this equation, the term that highlights the advantages, disadvantages and limitations of the acceleration method is the third term $p \cdot c = E_0 \cdot \beta \cdot \gamma = E \cdot \beta$, cu $\beta = v/c = (T^2+2 \cdot T \cdot E_o)^{1/2}/E$, because it is directly proportional to the total particle energy E. Acceleration of the particle for therapy applications can be done on a circular trajectory in accelerators type cyclotron, synchrocyclotron, isochronous cyclotron and synchrotron or on a linear trajectory in linac.

Acceleration of heavy particles with charge $q = z \cdot e$ and mass $m = A \cdot m_u$ on a circular trajectory of radius R, which requires the existence of a magnetic field with magnetic induction B, is described by relativistic relationship $T^2 + 2T \cdot E_o = (z/A)^2 \cdot (c \cdot B \cdot R)^2$, where the kinetic energy T and the normalized to a nucleon rest energy E_0 are measured in e·V/u, z is the charge state of particles with respect to electron charge e, A is atomic mass of the projectile ion, m_u is the mass atomic unit in kg and c is the speed of light. Easily identify the term: $p \cdot c$ [MeV] = $300 \cdot z \cdot B$ [T] $\cdot R$ [m].

For situations when β<<1 (or T<<2E_o) in nonrelativist regime, accelerated particle energy to extraction trajectory from accelerator is: T_{max} [MeV/nucleon] = $K_b(q/A)^2$, with K_b = 48.244 [MeV/(T·m)^2]·(<B>·R_{ex})^2. For some ion or isobar (A = const), ions maximum energy increases with q^2 hence the source of injection of ions in the hadron collider. Also shown that the energy increases with squared extraction radius, with the square of the magnetic flux density and volume of steel increases with the third power of the radius (184 Berkeley began construction in 1939 as the classical cyclotron, was put into operation in 1946 as synchrocyclotron, p 350 MeV, 1.5 T, 4300 t, 4.7 m diameter Φ) [8], [9]. Product B·R [Tm] indicates the size range trajectory depending on the maximum value of magnetic induction, which can be obtained from the extract radius before saturation for a constant energy of the hadron. To increase the magnetic field from 1.5 T to ≈ 10 T in order to decrease the extraction radius were performed cyclotrons with superconducting magnets (SC). It reduces the size and cost of the accelerator facility.

Cyclotrons produce continuous beams with very high intensity and stability (IBA Cyclotron 235 MeV, 300mA, 220T, 4.34 m - diameter (Φ) [10]). They also possess: simplicity, reliability, lower cost and size and easy operated. Great disadvantage of cyclotrons is that they have fixed extract energy. This disadvantaje was removed using the increasing the magnetic field with radius as for called isochronous cyclotron accelerator (Varian/ ACCEL SC Cyclotron: 250 MeV, 800 nA, 90 t, 3.1m Φ [11]. A Better solution was the operating in pulse mode with a variable radio-frequency, as for synchrocyclotron accelerator type (Still River SC Synchrocyclotron 250 MeV, 10^9 pps, 200 Hz, 20 t, 1.7 Φ [12], [13]).

Synchrotron is an accelerator with a well known technology that produces a pulsed beam with variable energy from MeV to TeV energies. It was developed to eliminate the disadvantages of the cyclotron at relativistic speeds. It has advantages variable energy operation, easy dose management and a relatively low current intensity. All worldwide medical centers use synchrotrons for providing protons beam and carbon ions beam, for e.g. Synchrotron-Hitachi: 70-250 MeV, 10 nA, 0.5 Hz, 23 mC and Synchrotron Siemens: 48-220 MeV for protons and 88-430 MeV / u for carbon ions, 20 m Φ [14].

In the case of the linear accelerators (Linac H^+ 250 MeV, 100-300 μA, 100-300 Hz, 2 t, 28 m [15]) the total energy of the particle E is given by $E^2 = E_o^2 + (eE_{||}ct)^2$, Where's $E_{||}$ is the longitudinal RF electric field, e - electron charge, c-speed of light and electric pulse duration t. In case of conventional linear acceleration, the electric field acceleration is thermally limited and breakthroughs in the linac RF cavities sites, currently about 100 MV / m.

2.3. Laser-Driven Hadron Acceleration Method

Making Petawatt laser (Nd: glass - 1.5 PW, 600 J, 440 fs, 1053 nm, $7 \cdot 10^{20}$ (W/cm^2) and contrast - 10^{-4}) demonstrated that radiation intensities can be obtained order 10^{20} W/cm^2 [16]. These high intensity laser radiation, for example 10^{18} W/cm^2, leading to a peak amplitude of the transverse electric field of a linearly polarized laser pulse E_L (TV/m) = $2.7 \cdot 10^{-9}$ $I^{1/2}$ (W/cm^2) = 2.7 TV/m, which is about four orders of magnitude higher than that obtained in conventional RF linacs.

The dimensionless parameter that characterizes the normalized transverse momentum of electrons oscillation in the laser field is denoted by a_L and is defined as: $a_L = e \cdot E_L/m_e \cdot \omega \cdot c = m_p/m_e(e \cdot E_L/m_e \cdot \omega \cdot c) = 8.5 \cdot 10^{-10}\ \lambda[\mu m] \cdot I^{1/2}$ [W/cm^2], where $m_p = 1836 \cdot m_e$ is the proton rest mass, m_e is the electron rest mass, e is the electron charge, λ and ω are the wavelength and the frequency of the electromagnetic wave and c is the vacuum light speed.

Accelerating the protons to relativistic energies (a_L = 1836) requires an intensity $I = 4.67 \cdot 10^{24}$ W/cm$^2 \cdot$(1μm/λ). Experimental simulations show that plasma collective effects lead to lower intensities, about $I = 10^{21}$ W/cm$^2 \cdot$ (1μm/λ). Method of laser acceleration in ultra-relativistic regime ($a_L \geq 100$) is similar to the method for generating bremsstrahlung radiation in conventional accelerators [17]. Bremsstrahlung radiation occurs at interaction of electron beam accelerated in the linac, betatron, microtron etc. and target made of a material with high atomic number for getting a high conversion factor in bremsstrahlung radiation.

Acceleration methods of TNSA Laser light hadrons, the hadron beam energy is proportional to the square root of the intensity of radiation and method BOA, mention that Coulomb explosion method were obtained for 100 MeV protons [18]. Finally, we believe that laser-piston method proposed by Esirkepov and collaborators [19, 20, 21] and later by A.P.L. Robinson as the RPA, the hadron energy is proportional to the intensity of radiation, provide accelerate hadron in therapy energy range [22, 23, 24, 25].

With the RPA accelerating method, laser beam interacts with a proton or carbon ions-rich target. At the laser radiation pressure, electrons are bounced rapidly in the direction of propagation of the laser beam power $|e \cdot v_e \cdot B_L| \approx e \cdot E_L$, where $B_L = E_L/c$ is the magnetic field of the laser pulse. Due to the mass difference between electrons and ions, it is creating a double layer of electrical charges and therefore there is an longitudinal electric field to separate charge $E_{||} = 2\pi \cdot e \cdot n_e \cdot l < E_L$, which produces accelerating ions.

In longitudinal field $E_{||}$, the total energy of accelerated ions is $E_i = [m_i^2 \cdot c^4 + (e \cdot E_{||} \cdot c \cdot t)^2]^{1/2}$ where m_i is the rest mass of the ion, c - speed of light and pulse duration t laser. To produce protons with kinetic energy of 250 MeV it is necessary that the term $(e \cdot E_{||} \cdot c \cdot t)$ be ≥ 729 MeV in the case of conversion efficiency of laser energy into the energy of protons of 100%. For carbon ions with kinetic energy of 450 MeV/u, the same term with the same efficiency must be ≥ 1020 MeV/u. The feasibility of using controlled laser accelerators in radiotherapy, with advantages and disadvantaged field is presented in the paper [26], [27].

Basic relationship of RPA mechanism to determine the hadron acceleration energy consists of equality between the photon momentum flux of the laser radiation $((2I/c) \cdot (1-\beta_f)/(1+\beta_f))$ and ion and electrons momentum flux generated in the target $(2\rho \cdot c^2 \cdot \beta_f^2 \cdot \gamma_f^2)$. They are noted with I - the intensity of the laser radiation, ρ is the density of the target and β_f - is the normal speed of the piston and c – the vacuum light speed [22], [28]. Ions are accelerated due to radiation pressure; laser radiation energy is transferred to the ions by the charge separation electric field between the two layers, which determine the final kinetic energy of the accelerated ions.

2.4. Quality Parameters of Hadron Beams

The practical range. Beam quality parameter of hadrons resulting from absorbed dose distribution in depth describing the spatial distribution of energy transferred to charged particles environment. The distributions of the proton and carbon ion absorbed doses in - depth (Fig.1) are characterized by a low dose in the plateau area followed by a narrow area of Bragg peak at the end of the practical range, Rp, in the medium. That is defined as the depth to which the dose has decreased to 90 % of the maximum dose.

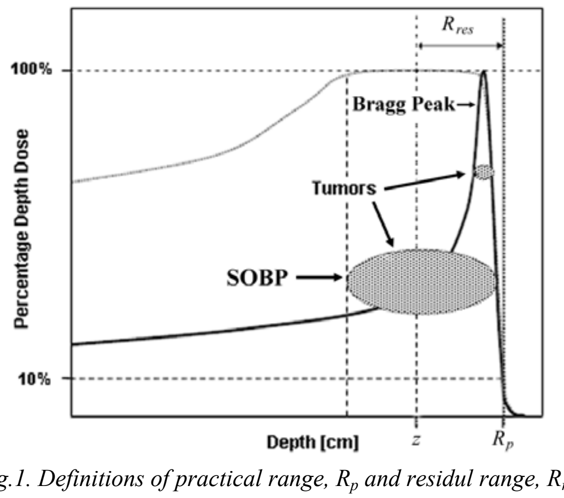

Fig.1. Definitions of practical range, R_p and residul range, R_{res}.

The quality parameter of the hadron beams is considered the residual range, defined as $R_{res} = z - R_p$, where z is the measurement depth in water [2]. Depth absorbed dose distributions according to the depth to water for a proton beam are shown in Fig. 2, in order to see that all tumor location can be achieved by varying the proton energy. They are normalized (at peak) for different incident proton energies [29].

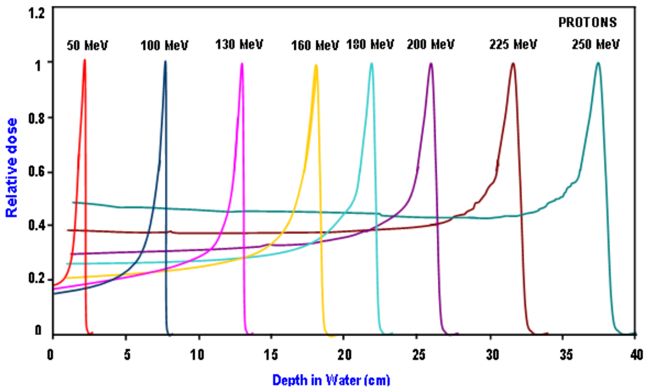

Fig. 2. Relative dose vs. proton depth in water [29].

When the entrance hadron energy in the medium is modulated in order to produce an extended Bragg peak, the ratio plateau to peak decreases but the biological efficacity reduces this disadvantage (see Fig. 3) [30]. Mention that

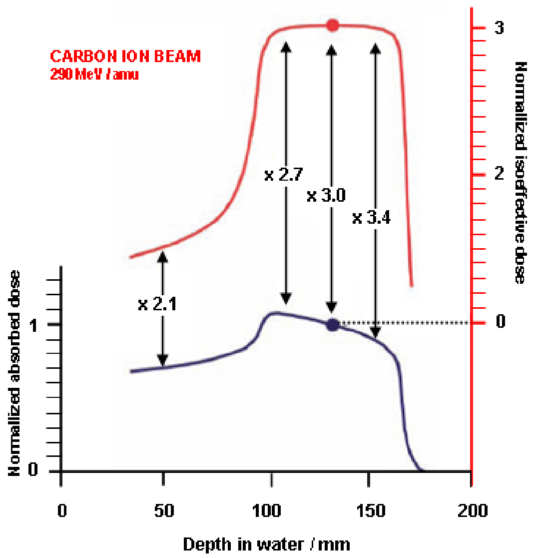

Fig. 3. Biologically equivalent spread out Bragg Peaks (SOBP) [30].

RBE is a ratio of the absorbed dose of a reference radiation to the absorbed dose of a test radiation to produce the same level biological effect, other conditions being equal.

The stopping power. In the case of determining the absorbed dose in an environment other than air, for example, water, it is defined as a product between the particle fluence Φ measured in [particles / cm^2] characterizing the radiation field and the coefficient on the interaction of the particles with the total mass stopping power (S/ρ) measured in [MeV·cm^2 /g] [31]. The calculated values of the water/air stopping power ratios as a function of the depth in water for carbon beams with initial energies

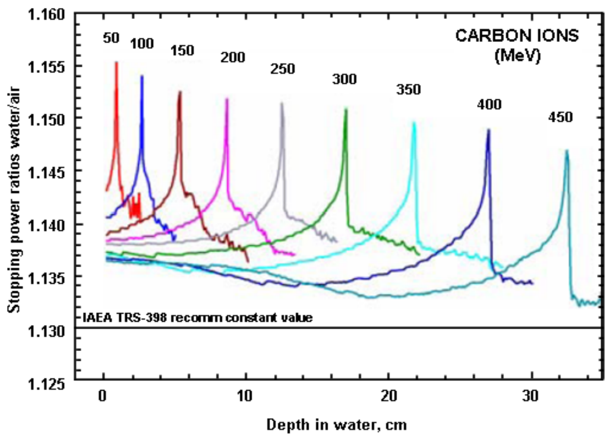

Fig. 4. Stopping-power ratios as a function depth in water for carbon ions [32].

between 50 MeV/u and 450 MeV /u [32] are presented in Fig. 4. The solid line of 1.130 corresponds to the constant $(s_{w,air})_{i.c.}$= 1.13, the value recommended by IAEA TRS 398. This was taken on the basis of reports stopping power by residual ranges calculated by various authors, for protons, carbon ions and other ions and presented in Fig. 5 [2].

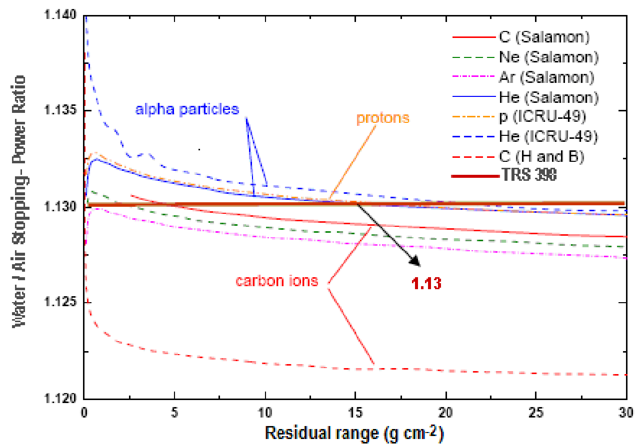

Fig. 5. Stopping-power ratios as a function residual ranges for proton beams and carbon ions [2].

In this case, the mean ratio of mass electronic stopping powers of the water medium to the air, $(S_{w,air})_{Qo}$ =1.133 in the Co-60 calibration beam, IAEA TRS 398 recommended value, calculated by Andreo using mono-energetic electron stopping power data tabulated in ICRU Report 37 [33].

Table 2. Proton stopping power and ranges according to ICRU 49.

E [MeV]	S/ρ {MeVcm²/g}		$S_{w,air,}$	R [g/cm²]	
	H_2O	Air	H_2O/Air	H_2O	Air
50	12.45	10.99	1.133	2.23	2.53
100	7.289	6.443	1.131	7.72	8.74
150	5.445	4.816	1.131	15.8	17.9
200	4.492	3.976	1.130	26.0	29.4
250	3.911	3.462	1.130	37.9	42.9

TRS 398 recommends that values for the water-to-air mass electronic stopping power ratio in the proton beams, $(S_{w,air})_p$ be calculated using the quality parameter R_{res}, in expression $(S_{w,air})_p = a + b \cdot R_{res} + (c/ R_{res})$, where a = 1.137; b = - 4.3·E^{-05} and c = 1.84·E^{-03}.

Therapeutic energies between 50 and 250 MeV have shown that some data, for example, in Table 2 protons ICRU 49 [34], AAPM 16 [35] and for carbon ions assessment using SRIM [36] presented in Table 3.

Table 3. Carbon Ion stopping power and ranges according to SRIM

E [MeV/u]	S/ρ {MeVcm²/mg}		$S_{w,air,}$	R [g/cm²]	
	H_2O	Air	H_2O/Air	H_2O	Air
50	0.446	0.388	1.149	0.74	0.86
100	0.259	0.226	1.145	2.59	2.98
150	0.193	0.169	1.143	5.31	6.09
200	0.159	0.139	1.143	8.76	10.04
250	0.138	0.121	1.142	12.82	14.68
300	0.124	0.109	1.141	17.41	19.91
350	0.115	0.100	1.141	22.44	25.66
400	0.107	0.094	1.141	27.87	31.85
450	0.101	0.089	1.140	33.63	38.43
500	0.097	0.085	1.140	39.70	45.35

At present, TRS 398 recomends the water-to-air mass electronic stopping power ratio in the carbon ions beams a constant value of the $(S_{w,air})_{i.c.}$= 1.13 (Fig. 5). Calculus performed with SRIM gives the value of $(S_{w,air})_{i.c.}$ = 1.14 (Table 3).

Stopping power formulas for heavy charged particles and for electrons and positrons are given in NBSIR 82-2550-A [36] and in ICRU 49 [33].

3. Ionization method and materials

3.1. Ionization Method Principle

Ionization method is used to determinate the dosimetric quantities which characterize the clinical radiation beams used in conventional radiotherapy and hadrohtherapy.

The basic principle of the ionization method with open ionization chambers (not sealed) and closed (sealed) is known [37]. By irradiation of the gas in the sensitive volume V of the ionization chamber with energy fluence Ψ [MeV/cm²] of the radiation beam, is collected a charge (one sign) q [C] measured in volume V filled with ambient air of mass m_{air} and density $\rho_{air} = 1293 \cdot 10^{-3}$g/cm³. Type cylindrical or plan parallel ionization chambers can be used for absolute dosimetry.

The associated method device is very simple and has three main components: the ionization chamber, an electrometer and a power supply. Ionization chamber, filled with gas (usually ambient air) is a radiation detector in which ions generated by the interaction of a radiation beam directly or indirectly ionizing radiation are collected due to the existence of an electric field created between two electrodes, between which it establishes a potential difference. Electrometer is a device that measures very small values of the electrical currents and charge provided by ionization chambers. Measuring device receives electric power through electrical power supply.

Main dosimetric quantities measured or determined by the ionization method with the associated device are: exposure X, air kerma K_{air}, the absorbed dose in air D_{air} and the absorbed dose to water D_w [31]. These quantities are proportional to the measured electrical charge (q [C] = $m \cdot X = (m/\varepsilon) \cdot K_{air} = (m/\varepsilon) \cdot D_{air} = (m/\varepsilon \cdot s_{w,air}) \cdot D_w$) where ε is the deposited energy expressed in joule per number of created charge in coulombs ($\varepsilon \equiv (W_{air}/e)$) and $s_{w,air}$ is the stopping power ratio (STPR) of the particle beam for water and air ($(s_{w,air} = (S/\rho)_w/(S/\rho)_{air}$). Rates of these quantities are proportional to the electric current I (A) measured as electrical charge by electrometer. The common factor is the air mass in the ionization chamber m (= $\rho . V_{ef}$) and ε and η factors that are used for dosimetric quantities assessment. If one of the four quantities (X, K_{air}, D_{air}, D_w) are determined by a ^{60}C beam by primary laboratory but the calibration factors of the ionization chambers are assessed by a secondary standard laboratory, then using conversion relations other three quantities could be calculated. To do this equivalence must determine the factors $\varepsilon \equiv W_{air}/e$ and $\eta \equiv S_{w,air}$. First it is experimentally determined and the second is determined through calculus.

3.2. Average Energy Expended in Air in ^{60}Co Beam

The average energy expended in air per ion pair formed W_{air} is the quotient between the initial kinetic energy T of a charged particle when is completely dissipated in air formed from N particles and the mean number N of ion pairs (i.p.) formed: W_{air} = T/N. The current best estimate for the average value of W_{air} in ^{60}C is 33.97 eV/i.p. or $33.97 \cdot 1.602 \cdot 10^{-19}$ (J/i·p) [2]. Taking into account that electrical charge of the ion pair is $1.602 \cdot 10^{-19}$ (C/i·p.) result that for dry air, W_{air}/e = 33.97 J/C. This value is valid for high energy electron and photon beam [IAEA TRS 398].

The experimental measurements regarding the determination of ε factor in air for another quality of the particle beam, Q, in special for protons are present in Fig. 6.

Based on the analysis of all the experimental measurements conducted by now, for protons TRS 398 recommends the value of ε factor of $(W_{air}/e)_p$ = 34.50 J/C and for the carbon ions, the value of $(W_{air}/e)_{i.c.}$ = 34.23

J/C , for all energies of the protons and carbon ions beams used the therapy.

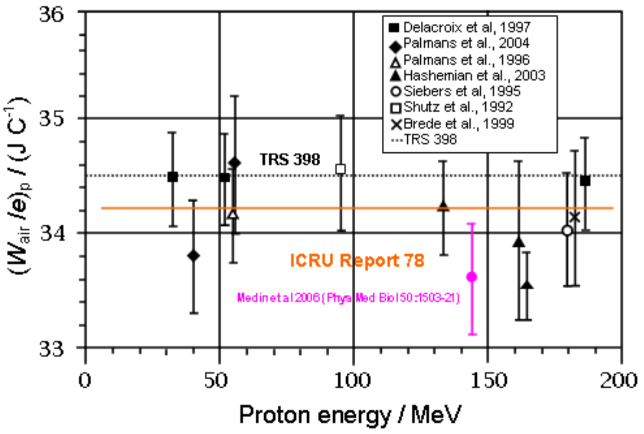

Fig. 6. Ion chambers: $(W_{air}/e)_p$ values from calorimetry

3.3 Conversion of Calibration Factors

The ICRU 59 [39] protocol allows for determinations based on exposure, air kerma, absorbed dose to air and absorbed dose to water calibrations in a ^{60}Co gamma beam [40], [41]. Because with the radiation therapy the absorbed dose measured in Gy is used it is most recommendable that the calibration factor of an ionizing chamber be expressed in [Gy/C].

Yet, in order to compare the medical results of the today and future hadron-based therapy with the results obtained by now with the hadron-based therapy and the conventional therapy and even for verifying the results of the dosimetric measurements, it is necessary that the conversion relations between the calibration factors: $N_{X,Qo}$, $N_{K,Qo}$, $N_{D,air,Qo}$ and $N_{w,Qo}$ defined and measured in the beam of quality Q_o ($\equiv$ ^{60}Co γ rays beam) in order to determine the corresponding 4 dosimetric magnitudes.

Otherwise said, once the calibration factor is determined, one may calculate the equivalent values with the corresponding uncertainties for the other 3 calibration factors. Therefore, is preserved in all the relations Q_o quality.

Calibration Factor at In-air Exposure. X exposure measured in roentgen [R] or [C/kg] has the calibration factor defined by relation $N_{X,Qo} = X_{Qo}/M_{Qo}$ [R/C], where M_{Qo} is the meter reading in [C] at the time of calibration, corrected for temperature, pressure, humidity and ion recombination. The calculation formula for

$$X = (q/m)\cdot\Pi_i\cdot k_i, \tag{1}$$

where $\Pi_i\cdot k_i$ quantity includes all the correction factors required for this type of measurement [42].

The unit of exposure is coulomb per kilogram [C/kg] in SI units and roentgen [R] in the CGS system. 1R = 1esu/cm^3 = 1esu /0.001293g$_{air,STP}$ = $2.580\cdot10^{-4}$ C/kg = $2.09\cdot10^9$ e$^-$/cm^3, where e$^-$ is the symbol for electron. There are two cases: 1. when X_u is measured in [R], it may be expressed in [C/kg], as: X[C/kg]=$2.58\cdot10^{-4}$[C/kg·R]·X_u [R] and 2. when X_u is measured in [C/kg], it may be expressed in [R], as: X[R] = 3876 [R·kg/C] ·X_u [C/kg].

Conversion Relation Between N_X and N_K. Amplifying the exposure with the mean charge for to create a pair of ions (W_{air}/e) one may obtain the calculation relation for the second magnitude called the collision interactions kerma in aer, K_{col} = (W_{air}/e)·X. Viceversa, amplifying the collision kerma K_{col} by (e/W_{air}), i.e. the number of coulombs of charge created per joule of energy deposited, one obtains the charge created per unit mass of air or exposure, X = K_{col}. (e/W_{air}). Marking by g the mean fraction of the energy that is lost by radiation processes, the result for collision kerma is the relation: K_{col} = K_{air} (1-g), where K_{air} = K_{col} + K_{rad} [43, 44, 45]. The SI unit for the air kerma is the gray (Gy), 1Gy = 1 J/kg. Finally one obtains the calculation relation for air kerma, on basis of exposure $X_{Qo,}$ $K_{air,Qo}$ = X_{Qo}·(W_{air} /e)$_{Qo}$ /(1-g) [Gy].

Using the calibration in kerma in air $N_{K,Qo}$= $K_{air,Qo}$ / M_{Qo} [Gy/C], defined in above mentioned manner, results the conversion relation between calibration factors $N_{X,Qo}$ and $N_{K,Qo}$

$$N_{K,Qo}\,[Gy]= N_{X,Qo}\,[C/kg].(W_{air}/e)/(1\text{-}g)\,[J/C]. \tag{2}$$

Calibration factors N_X for exposure (R) can be converted to calibration factors N_K for air kerma (Gy) by (IAEA 277): N_K[Gy](1-g)= N_X[C/kg]·(W_{air}/e)[J/C] and N_K [Gy] = N_X[R]·$2.58\cdot10^{-4}$ [C/kg.R]·33.97 [J/C]·(1/0.997) = N_X[R]·0.00877 [Gy/R].

Calibration Factor in Absorbed Dose to Air. The third quantity is the absorbed dose in air. The SI unit for the absorbed dose is the gray (Gy), 1 Gy = 1 J/kg. In CGS system, the unit for absorbed dose is the rad (radiation absorbed dose), 1 rad = 1erg/g = 0.01 J/kg.

With the balance of the charged particles in the ionizing chamber, the average absorbed dose in air, D_{air}, is equal to the collision kerma in aer K_{col} (= K(1-g)), $D_{air,Qo}$= $K_{air,Qo}$ (1-g)$k_{att}k_mk_{cel}$ [Gy] where the correction factors (k_m , $k_{att,}$ k_{cel}) are defined in [2], [43], [44]. Applying the definition of the calibration factor at the absorbed dose in air $N_{D,air,Qo}$ = $D_{air,Qo}$/M_{Qo} and of kerma calibration factor, the relation (10) becomes the conversion relation between the two factors:

$$N_{D,air,Qo} = N_{K,Qo}\,(1\text{-}g).\,k_{att}k_mk_{cel} \tag{3}$$

or, in function of the calibration factor at exposure $N_{X,Qo}$,

$$N_{D,air,Qo} = X_{Qo}.\,(W_{air}/e)_{Qo}\,N_{K,Qo} \tag{4}$$

The Calibration Factor at the Absorbed Dose to Water. TRS 398 recommends the calibration of the ionizing chamber for the absorbed dose to water $D_{W,Qo}$ in ^{60}Co gamma radiation beam. The absorbed dose to water $D_{W,Qo}$, whose value is known in the calibration beam, may serve in secondary laboratory, for the determination of the calibration factor $N_{D,w,Qo}$ as the ratio of the value of absorbed dose to water $D_{W,Qo}$ at the point of measurement to the reading M_{Qo} under reference conditions, $N_{D,w,Qo} = D_{w,Qo}/M_{Qo}$, [Gy/C]. Knowing the calibration factor on ^{60}Co beam obtain:

$$D_{w,Qo} = M_{Qo} \cdot N_{D,w,Qo}. \quad (5)$$

Absorbed Dose to Water Using Bragg-Gray Theory. According to the cavity theory elaborated by Bragg-Gray [45], the absorbed dose in point P to the water D_w may be obtained by measuring the absorbed dose in air, in the ionizing chamber cavity D_{cav}, with the chamber central point in P, by multiplying it with the stopping power ratio $(S/\rho)_w/ (S/\rho)_{air} = (S/\rho)_{m,cav} = s_{w,air}$, $D_w(P) = D_{air} \cdot s_{w,air}$

In this case, absorbed dose to water becomes

$$D_{w,Qo} = M_{Qo} \cdot N_{D,air,Qo} \cdot s_{w,air} \cdot p_{Qo}, \quad (6)$$

where the correction factors $p_{Qo} = p_{Qo} = p_{cav}\, p_{dis}\, p_{wall}\, p_{cel}$, are presented in detail in [2], [43], [44].

The Relation Between $N_{D,air,Qo}$ and $N_{D,w,Qo}$. The absorbed dose to water, given by the relation (5), based on the calibration factor in water, should be equal with the absorbed dose to water (6) based on Bragg-Gray principle. The conversion relation between the two calibration factors ($N_{D,air,Qo}$ and $N_{D,w,Qo}$) is obtained from the equality of the two absorbed doses:

$$N_{D,w,Qo} = N_{D,air,Qo} \cdot (s_{w,air})_{Qo} \cdot p_{Qo} \quad (7).$$

4. Determination of the absorbed dose in proton and carbon ion beams

4.1. Absorbed Dose for Hadrons in Other Quality Q

The absorbed dose to water in the proton or carbon ion beam of quality Q is given by relation

$$D_{w,Q} = M_Q \cdot N_{D,w,Qo} \cdot k_{Q,Qo}, \quad (8)$$

where M_Q is ionization chamber reading in [C] corrected for influence quantities, $N_{D,w,Qo}$ the absorbed dose to water calibration factor of ionization chamber in a beam of quality Q_o, and $k_{Q,Qo}$ the beam quality correction factor to account for the use of the calibration factor in a different beam quality Q, in our case proton or carbon ion beam, given by the relation

$$k_{Q,Q_0} = \frac{(s_{w,air})_Q \cdot (W_{air}/e) \cdot p_Q}{(s_{w,air})_{Q_0} \cdot (W_{air}/e)_{Q_0} \cdot p_{Q_0}}, \quad (9)$$

where $s_{w,air}$ is the water to air mass collision stopping power ratio, $(W_{air}/e)_p$ is the mean energy required to produce an ion pair in dry air and p_Q is a correction factor accounting the perturbation by the presence of the ion chamber in the phantom [2], [39], [40], [46 - 49].

Equations 1 and 2 may be expressed in the form of the product of three factors [50]:

$$D_{w,Q} = M_Q \frac{N_{D,w,Qo}}{(s_{w,air})_{Q_0} \cdot (W_{air}/e) \cdot p_{Q_0}} (s_{w,air})_Q \cdot (W_{air}/e) \cdot p_Q \quad (10).$$

The first factor represents the corrected reading of the chamber, the second factor represents the factors specific to the calibration beam and the third factor represents the factors specific to the hadron beam. The reference conditions for the determination of the absorbed dose in water for protons and carbon ions are presented in Table 4.

Table 4. Reference conditions for the determination of absorbed dose in proton and ion beams [IAEA TRS 398].

Influence quantity	**Reference values or reference characteristics**	
Particle type	Protons	Carbon ions
Quality beam	Residual range	Residual range
Phantom	water	water
SSD	clinical treatment distance	clinical treatment distance
Field size	10 cm · 10 cm	10 cm · 10 cm
Reference dosimeter	IC thimble or PP	IC thimble or PP
Chamber type	for $R_{res} \geq 0.5$ g·cm^2, IC thimble or PP for $R_{res} < 0.5$ g·cm^2, PP	for SOBP width ≥ 2g·cm^2,IC or PP for SOBP width < 2 g·cm^2, PP
Measurement depth, z_{ref}	middle of the SOBP/plateau	middle of the SOBP/plateau
Calibration quality	Co-60 beam	Co-60 beam
IC calibration factor	$N_{D,w}$ – TRS 398 (N_X,N_K,$N_{D,w}$ICRU59)	$N_{D,w}$ - TRS398

The quality factor $k_{Q,Qo}$ can be measured in both qualities Q and Qo of the beam in a standard laboratory, but, due to the experimental limits, most of the times it is calculated. The values for $k_{Q,Qo}$ were calculated by formula (9) and are presented in TRS 398, in function of the hadron beam quality parameter R_{res}. Table 5 is a synthesis of the parameters of the component formula k_{QQo} factor.

Table 5. Specific factors for Q hadron beams and for the Q_o calibration beam

$k_{Q,Qo}$ parameter	**Value for protons**	**Values for carbon ions**
$(s_{w,air})_{Qo}$	1.133	1.133
$(s_{w,air})_Q$	Function of E	Function of E
$(W_{air}/e)_{Qo}$	33.97 eV	33.97 eV
$(W_{air}/e)_Q$	34.50 eV	34.23 eV
p_{Qo}	1.009	1.009
p_Q	1.0	1.0

4.2. Absorbed Dose for Hadrons When $k_{Q,Qo}$ is Known

Protons. Factor $k_{Q,Qo}$ value for protons are calculated by equation 4 as a function of the beam quality index R_{res}

defined as (IAEA 2000 TRS-398) $R_{res} = R_p - z$, where R_p is the practical range and z is the depth of measurement. R_{res} is related to the most probable energy of the highest proton energy peak in the spectrum. The beam quality correction factor for PTW chambers within STARDOOR laboratory, calibrated at PTB, are given in Table 6 for protons.

Having the calibration factor for PTW ionization chamber determined by PTB with the values in Table 6 or for other types, as per TRS 398 and formula 2, the absorbed dose in the proton beam is determined.

Table 6. Calculated values of k_{QQo} for proton beams [IAEA TRS 398].

Cylindrical chambers	**Beam quality R_{res} (g/cm^2)**				
	0.25	**1**	**10**	**20**	**30**
PTW 31002 flexible	-	1.030	1.028	1.028	1.027
PTW 31014 PinPoint	-	1.026	1.024	1.024	1.023
PTW 23332 rigid	-	1.029	1.027	1.027	1.026
PTW 30010 Farmer	-	1.031	1.029	1.029	1.028
Plan parallel chambers	**Beam quality R_{res} (g/cm^2)**				
	0.25	**1**	**10**	**20**	**30**
Markus	1.009	1.004	1.002	1.002	1.001
Roos	1.008	1.003	1.001	1.001	1.000

Carbon Ions. The values for factor $k_{Q,Qo}$ for carbon ions calculated in case of cy cylindrical and plane-paralel chambers of Markus type within STARDOOR lab, are presented in Table 7.

Table 7. Calculated values for $k_{Q,Qo}$ for heavy ion beams.

Cylindrical chambers	**k_{QQo}**
PTW 23332 rigid	1.029
PTW 30001/30010 Farmer	1.031
PTW 31014 PinPoint	1.026
PTW 34045 Markus	1.004
Plan parallel chambers	**k_{QQo}**
PTW 34001 Roos	1.003
PTW 31010 Farmer	1.003

4.3. The Absorbed Dose for Hadrons When $k_{Q,Qo}$ is Not Known

Protons. In case of proton and carbon ion beams, for the ratio of stopping power water to air TRS 398 recommends the value of $(s_{w,air})_{Qo} = 1.13$ in ^{60}Co gamma radiation according ratios of stopping powers water/air for heavy ions calculated using the computer codes developed by Salamon, Hiraoka and Bichsel. Data for protons and He are from ICRU-49.

To calculate the values of factor $k_{Q,Qo}$, from the denominator of its expression, all the three are known: $(s_{w,air})_{Qo} = 1.133$, $(W_{air}/e)_{Qo} = 33.97$ J/C and the third one is in Table 8 (TRS 398). The table presents only the data for the ionization chambers within STARDOOR lab. For the parameters at factor k_{Qqo} expression denominator, the values recommended in TRS398 are selected, namely: $(W_{air}/e)_{Qp} = 34.23$ J/C, factor $p_Q \approx 1$ and factor $(s_{w,air})_{Qp}$ shall be calculated in function of the hadron kinetic energy.

So, the factors related to the qualities of Co-60 calibration beam are data calculated and presented in TRS 398.

Table 8. Values for the factors p and $s_{w,air}p_{Qo}$ in ^{60}C gamma radiation [IAEA TRS 398].

Ionization chamber type	**p_{dis}**	**p_{wall}**	**p_{cel}**	**$s_{w,air}\ p_{Qo}$**
Cylindrical chamber				
PTW 23323 micro	0.993	1.001	0.993	1.119
PTW 30001/30010 Farmer	0.988	1.001	0.993	1.113
PTW 31002 flexible	0.989	1.001	0.993	1.114
PTW 31014 Pin Point	0.996	0.998	0.993	1.118
Plane-parallel chamber				
PTW 34045 Markus	-	1.009	-	1.144
PTW 34001 Roos	-	1.010	-	1.145

Carbon Ions. Knowing the calibration factor of the ionization chamber in ^{60}Co beam and the other factors which characterize the calibration beam, the quality parameters of the carbon ion beam need to be determined. For carbon ion, TRS 398 recommends the following values: $(W_{air}/e)_{c.i.} = 34.50$ J/C, $p_{Q,c.i.} = 1$ and $(s_{w,air})_{Qp}$ is calculated in function of the carbon ion kinetic energy.

5. Uncertainities

IAEA TRS 398 recommends for calibration beam specific factors *Q_o (≡Co-60) the following uncertainty (U) values* for $s_{w.air}$ in Co-60 beam:
- STPR: $(s_{w.air})_{Qo} = 1.133 \pm 0.1\%$, for dry air and humid;
- the mean energy expanded in air per ion pair formed: $(W_{air}/e)_{Qo} = 33.97$ J/C $\pm$ 0.2%;
- p_{Qo} the calculus method of its is presented in detail in [2].

Regarding proton beams, IAEA TRS 398 recommends the following values:
- $(s_{w.air})_p$ are calculated as a function of the energy and are presented in 2.4 Paragraph;
- $(W_{air}/e)_p = 34.23$ J/C $\pm$ 1.5%, $(W_{air}/e)_p = 34.8$ J/C $\pm$ 0.7% for dry air and humid air, respectively. In the case of proton beam ICRU 59 recommends $(W_{air}/e)_p = 34.80$ J/C $\pm$ 0.7%.
- $p_Q = 1$ for protons.

Estimated relative uncertainity for protons beam are presented in Table 9 [51, 52].

Table 9. Estimate relative uncertainities (in %) for the quality factors for proton beams [IAEA TRS 398].

Protons	**Cylindrical chambers**		**Plane-parallel chambers**	
Component	Protons	^{60}Co+protons	Protons	^{60}Co + protons
$s_{w,air}$	1.0	1.2	1.0	1.2
W_{air}/e	0.4	0.5	0.4	0.5
p_Q(combined)	0.8	1.1	0.7	1.7
Total uncertainy in $k_{Q,Qo}$	-	1.7	-	2.1

In terms of heavy ions beam IAEA TRS 398 recommends the following values:

- $(s_{w,air})_{c.i.}$= 1.13 ± 2% [2];
- $(W_{air}/e)_{c.i.}$ (weighted median) = *34.5 J/C* ± 1.5%;
- $p_{,c.i.}$= 1.0 ± 1% [2], [10];

Estimated relative uncertainity for carbon ion beams are presented in Table 10 [51, 52].

Table 10. Estimate relative uncertainities (in %) for the quality factors for carbon ion beams [IAEA TRS 398].

Light ions	**Cylindrical chambers**		**Plane-parallel chambers**	
Component	Light ions	^{60}Co + light ions	Light ions	^{60}Co + light ions
$s_{w,air}$	2.0	2.1	2.0	2.1
W_{air}/e	1.5	1.5	1.5	1.5
p_Q (combined)	1.0	1.0	1.0	1.8
Total uncertainty in $k_{Q,Qo}$	-	2.8	-	3.2

6. Conclusions

The purpose of this paper is to offer a synthesis of all the data required to determine the absorbed dose in water in proton and carbon ion beams, also satisfying the recommendations in TRS 398.

These preliminary data may be used to elaborate and implement a technical procedure for the determination of the absorbed dose in hadron beams.

For the other data that, by now, could not be found in the specialized literature, until the commissioning of the 10 PW laser, themes for standard R&D project proposals should be elaborated for the measurement of a single parameter – the electric charge.

The energies of protons and carbon ions were selected from the values in TRS 398 considering that they can be obtained in the operation of the 10 PW laser in an ultrarelativistic regime using the radiation pressure acceleration (RPA) mechanism.

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