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Technical note

Dose intercomparison at Italian hadrontherapy centers

F. Guida[a,b,1], A. Barbato[a,b], M. Ciocca[c], M. Schwarz[d], S. Lorentini[d], E. Mastella[c], G.A.P. Cirrone[e], G. Petringa[e,f], M. Liotta[g], P. Tarabelli De Fatis[g], M. Masi[a,b,2], G. Mettivier[a,b,*], P. Russo[a,b]

[a] Università di Napoli Federico II, Dipartimento di Fisica "Ettore Pancini", Napoli, Italy
[b] INFN Sezione di Napoli, Napoli, Italy
[c] CNAO, Pavia, Italy
[d] Centro di Protonterapia, APSS, Trento, Italy
[e] INFN-LNS, Catania, Italy
[f] Università di Catania, Dipartimento di Fisica ed Astronomia, Catania, Italy
[g] Istituti Clinici Scientifici Maugeri, Pavia, Italy

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ABSTRACT

Purpose: To perform the first dosimetric intercomparison for proton beams in Italy using ionization chambers, according to the IAEA TRS-398 code of practice.

Methods: Measurement sites included: National Center for Oncological Hadron Therapy (CNAO, Pavia), Center for Proton Therapy (CTP, Trento) and Center for Hadron Therapy and for advanced Nuclear Applications (CATANA, Catania). For comparison we also included a 6 MV photon beam produced at Istituti Clinici Scientifici Maugeri (ICSM, Pavia). For proton beams, both single pseudo-monoenergetic layers (in order to obtain a planned dose of 2 Gy at the reference depth of 2 cm in a water phantom) and Spread-out Bragg peaks (SOBP) have been delivered. Measurements were performed with a PTW Farmer 30010-1 and a PTW Advanced Markus type 34,045 ionization chamber.

Results: Data obtained at CATANA, CNAO and CPT in terms of absorbed dose to water depth show good consistency within the experimental uncertainties, with a weighted mean of 1.99 ± 0.01 Gy and a standard error of 0.003 Gy, with reference to a nominal dose of 2 Gy as designed by the treatment planning system.

Conclusions: The results showed a standard deviation of less than 1% for single layer and SOBP beams, for all chambers and a percent deviation less than 1.5% for single layer measurements. The weighted means of the absorbed doses for clinical proton beams (118.19 MeV and 173.61 MeV) are consistent within less than 1%. These results agree within the 1.5% difference considered acceptable for national dose intercomparison.

1. Introduction

In a clinical treatment for tumour eradication, an accuracy of ± 5% at the 1σ level is generally required in the delivery of dose to a target volume, as concluded by the International Commission on Radiation Units and Measurement (ICRU) in its Report 24 for beams of X- or gamma-rays in radiotherapy [1]. For hadrontherapy, establishing primary standards of absorbed dose to water for proton (and carbon ion) beams represents an open field of investigation, since beams/institutions are not available/ready yet. Only few intercomparison studies [2–4] have been performed in proton beams using protocols (i.e. Task Groups 20 and 21 by AAPM [5,6]) based on the determination of air kerma, rather than on the determination of absorbed dose to water as recommended in IAEA TRS-398 [7].

Previous dose intercomparison investigations among proton facilities were performed by Vatnitsky *et al.* [2] following Task Group 20 by AAPM and including thirteen international institutions; by Kecperik [4] following IAEA TRS 277; and by Baume *et al.* [3] using the TRS-398 protocol, the same used in this work.

Vatnitsky et al. [2] performed an intercomparison to estimate the consistency of absorbed dose delivered to patients among the participating facilities and to evaluate the differences in absorbed dose determination due to differences in ^{60}Co-based ionization chamber calibration protocols. They used ionization chambers with ^{60}Co calibration factors traceable to standard laboratories, and institution-specific conversion factors and dose protocols, in order to obtain absorbed dose

* Corresponding author at: Università di Napoli Federico II, Dipartimento di Fisica "Ettore Pancini", Via Cintia, 21, 80126 Napoli, Italy.
E-mail address: mettivier@na.infn.it (G. Mettivier).

[1] Present address: Università di Padova, Dipartimento di Fisica e Astronomia "Galileo Galilei", Padova, Italy.
[2] Present address: Università di Roma Tor Vergata, Scuola di Specializzazione in Fisica Medica, Roma, Italy.

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within 3% of the mean value of all the absorbed dose for center.

In 2007 Baumer et al. [4] compared four facilities in Germany which employed spot scanning proton beams and they found that the agreement in terms of determined dose (less than 0.9%) and range (less than 0.4 mm) was well within the inherent uncertainties of the dosimetry equipment.

In Kacperek et al. [4] the intercomparison involved four international centers providing proton eye therapy beams in order to compare results for four Markus ionization chambers and six cylindrical chambers. The proton dosimetry comparison was performed in two proton beam conditions: at full incident energy (corresponding to the entrance dose of the pure Bragg peak) and at a depth of 15 mm in a fully modulated beam. The results showed a standard deviation less than 1% for both beam conditions for all chambers, and a maximum difference of approximately 3%. The Markus chamber group showed a difference in the mean dose of 1.1% from the thimble chamber group, for both beam conditions [4].

In this scenario, in this Technical Note we aimed at performing the first intercomparison study on nominal doses calculated by the treatment planning system (TPS) at the three Italian hadrontherapy centers presently in clinical operation.

2. Materials and Methods

Absorbed dose to water is obtained from measurements in a (photon or proton) beam with an ionization chamber calibrated in a ^{60}Co beam as follows:

$$D_{w,Q} = M_Q \cdot N_{D,w,Q_0} \cdot k_{Q,Q_0}$$

where M_Q is the reading of the electrometer corrected for all the influence quantities, $N_{D,w,Q_0}$is a calibration factor in terms of absorbed dose to water (measured in air using a ^{60}Co beam) and k_{Q,Q_0} is a factor that corrects for the effects of the differences between the reference beam quality Q_0 and the actual used quality Q [7].

As stated in the protocol TRS-398 [7], any difference from the reference conditions should be corrected using correction factors for pressure and temperature (k_{TP}), polarity (k_{pol}) and collection efficiency (k_s)

$$M_Q = M_{raw} \cdot k_{TP} \cdot k_s \cdot k_{pol}$$

where M_{raw} is the reading on the dosimeter without corrections.

The difference between the effective point of measurement (P_{ref}) of the PTW Farmer chamber and the reference depth of measurement (z_{ref}) is accounted for by shifting the chamber by a proper compensating amount as suggested in the literature [7]. For both the plane parallel ionization chamber (i.e PTW Advanced Markus) and the Farmer chamber the water-equivalent thickness of the waterproofing sleeves (such as the chamber holders) was taken into account in the z_{ref}.

Three proton therapy centers participated in the intercomparison study: Centro Nazionale di Adroterapia Oncologica (CNAO), Pavia, Italy; Centro di Protonterapia di Trento (CPT), Trento, Italy; Centro di AdroTerapia ed Applicazioni Nucleari Avanzate (CATANA), Catania, Italy. A fourth center, Istituti Clinici Scientifici Maugeri (ICSM), Pavia, Italy, provided dosimetry for a clinical photon beam at 6 MV, here performed for comparison sake. In order to compare nominal doses calculated by the TPS, in each center we used the same experimental setup (ionization chambers and dosimeter) and water phantoms with equivalent specifications. At the ICSM and CNAO centers we used a PTW 41,023 water phantom, at CPT an IBA WP34 water phantom while at CATANA a custom-made water phantom. This last phantom had a size of 300 × 300 × 300 mm^3, made of 10-mm thick PMMA walls and with a 150 × 150 mm^2 entrance window with a reduced thickness of 3 mm. We used two different ionization chambers: a PTW Farmer type 30010–1 (cylindrical chamber with a sensitive volume of 0.6 cm^3) and a PTW Advanced Markus type 34,045 (plane-parallel chamber with a sensitive volume 0.02 cm^3), readout by a PTW Unidos E dosimeter

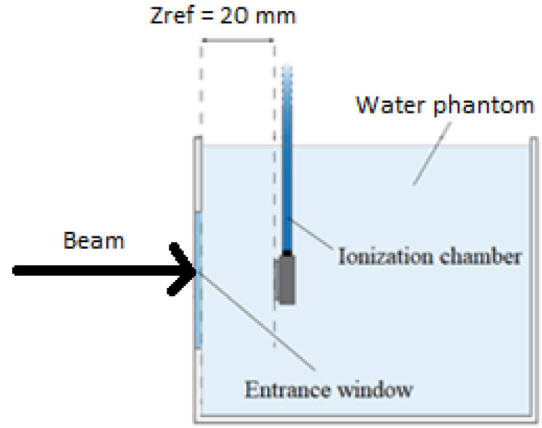

Fig. 1. Experimental setup used for reference dosimetry in water. The reference depth z_{ref} is 20 mm.

(PTW, Freiburg, Germany). The electrometer and the ionization chambers were calibrated in a ^{60}Co beam at temperature T_0 = 20 °C and atmospheric pressure P_0 = 1013.25 hPa. The factory-provided calibration factor was $N_{D,W,Qo}$ = 5.381 × 10^7 Gy/C for the Farmer chamber (Calibration Certificate No. 1,500,445 by PTW) and $N_{D,W,Qo}$ = 1.480 × 10^9 Gy/C (Calibration Certificate No. 1,802,180 by PTW) for the Advanced Markus chamber, respectively, with an associated uncertainty of 1.1% (K = 2), as stated in the calibration certificates.

The beam central axis was aligned with the center of the entrance window of the water phantom (Fig. 1). For each ionization chamber, the measurement position was set at a reference depth of 20 mm in water. To take into account the effective point of measurements, for the Farmer chamber, we corrected for the chamber axis displacement factor equivalent to 0.75 times its internal radius r_{cyl} [7,15]. For the plane parallel ionization chamber (PTW Advanced Markus), as indicated in the TRS-398 protocol [7], the inner surface of the entrance window was set in the reference point.

In each measurement session we delivered a proton beam, either as a single monoenergetic layer (with the ion chamber positioned at plateau region of the Bragg curve) with a nominal dose of 2 Gy at the reference depth z_{ref} = 20 mm in the water phantom (Fig. 1), or as a Spread Out Bragg Peak (SOBP), with measurements performed in the center of SOBP depth in water with a nominal dose of 2 Gy, (cfr. Table 1-3). To convert absorbed dose to water into biological equivalent dose, every TPS keeps into account a fixed relative biological effectiveness (RBE) of 1.1.

The CATANA facility is based on a passive transport system of a 62 MeV proton beam [8] and because of this system of dose delivery, only measurements at the center of SOBP were possible, according to Table 1. The values of k_s and k_{pol} for the Farmer chamber are the same used in [9] whereas for the Advanced Markus chamber they have been calculated according to IAEA TRS-398. Each measurement was repeated three times, and the result shown is their average value, with estimated overall relative standard uncertainty for protons (2.0% for Farmer chamber measurements and 2.3% for Advanced Markus chamber measurements), as reported in TRS-398 [7].

Table 1
Data for absorbed dose to water determination at CATANA facility.

SOBP measurements	CATANA facility
Center of SOBP depth in water (mm)	24
SOBP width (mm)	30
Nominal dose (Gy) @z_{ref} = 24 mm	2
Reference uniform field diameter (mm)	40

Table 2
Data for absorbed dose to water determinations at CNAO.

Single layer measurements	CNAO center	
Nominal energy (MeV)	118.19	173.61
Bragg peak depth in water (mm)	100	200
R80 (mm)	101	201
Nominal dose (Gy) @ z_{ref} = 20 mm	2	2
Reference uniform field (mm^2)	60 × 60	60 × 60
Center of SOBP measurements		
Center of SOBP depth in water (mm)	90	
SOBP width (mm)	60	
Nominal dose (Gy) @ z_{ref} = 90 mm	2	
Reference uniform field (mm^2)	60 × 60	

Table 3
Data for absorbed dose to water determination at CTP.

Single layer measurements	CTP center	
Nominal energy (MeV)	118	173
Bragg peak depth in water (mm)	100	200
R80 (mm)	103.5	202
Nominal dose (Gy) @ z_{ref} = 20 mm	2	2
Reference uniform field (mm^2)	60 × 60	60 × 60
Center of SOBP measurements		
Center of SOBP depth in water (mm)	90	
SOBP width (mm)	60	
Nominal dose (Gy) @ z_{ref} = 90 mm	2	
Reference uniform field (mm^2)	60 × 60	

Measurements at CNAO [10] have been carried out using the data shown in Table 2. Quality factors for proton k_Q used are the one in IAEA TRS-398 and other coefficients are listed (see Table 5 below). For the single-layers proton beam, selected energies were 118.19 MeV and 173.61 MeV, corresponding to a Bragg peak depth in water of about 100 and 200 mm, respectively, so the measurements were made in the plateau region. Square uniform dose fields of 60 × 60mm^2 were created using 20 × 20 = 400 spots and a scan step of 3 mm [11], with a fluence of 1.5 × 10^8 (118.19 MeV) and 2.03 × 10^8 particle/spot (173.61 MeV), respectively. Two measurements sessions were carried out in 2017 [9] and in 2018.

Measurements at CPT [12,13] were carried out with data reported in Table 3. For the single-layer proton beams, we generated squared uniform dose fields of 60 × 60 mm^2 using 25 × 25 = 625 spots and a scan step of 2.4 mm. Two measurements sessions were carried out in 2017 [9] and in 2018, respectively, and the data are reported separately.

Measurements at I.C.S. Maugeri were carried out with data in Table 4. For the Farmer chamber 30,010 the correction factors were assumed to be equal to those one used at facility for reference dosimetry, made with PTW Farmer 30,013 (with same specifications of our Chamber). For Advanced Markus k_s and k_p coefficients were determined using ref. [14] and knowing the dose per pulse of our beam. k_q factor was provided with a cross-calibration by direct comparison of ADW Markus against our reference calibrated chamber. A summary of all coefficients is presented in Table 5. At ICSM center, a uniform 100 × 100 mm^2 square field of 6 MV photons was delivered.

3. Results

Table 6 shows measured data specifying of the facility, the beam type, energy and associated error. The dose has been obtained following the indication of TRS-398: for each beam measurements have been performed and then corrected with coefficients listed in Table 5.

Table 4
Data for absorbed dose to water determination at ICSM (photon beam).

Nominal beam quality (MV)	6
Nominal dose (Gy) @ z_{ref} = 20 mm	2
Reference uniform field (mm^2)	100 × 100

Fig. 2 shows measurements performed in proton beams (and photon beam, for comparison), for the PTW Farmer type ionization chamber TM 30010–1. The weighted mean of these data for proton beams is 1.99 ± 0.02 Gy with a standard error of 0.006 Gy (where standard error = σ/√N). The data from ICSM center are also shown (for photon beams a smaller relative standard uncertainty of 1.5%, vs. 2.0% for protons, is indicated in TRS-398 [7]). The maximum percent deviation for this chamber is less than 2%. The mean shows a good agreement (less than 1%) within the 1.5% difference considered acceptable for national dose intercomparison performed with a single ionization chamber [3].

Fig. 3 shows measurements performed with photon and proton beams with the PTW Advanced Markus 34,045 type ionization chamber. The data from ICSM are used as a reference even if the use of parallel plate chamber like the one used in this work is not advisable, according to TRS-398. The weighted mean is 1.99 ± 0.02 Gy with a standard error of 0.007 Gy. Data show a good consistency with respect to the nominal dose. The maximum percentual deviation (at the 1 σ level) of the mean from the reference dose (2 Gy) for this chamber is less than less than 1% as in the previous case.

4. Discussion

Absorbed dose to water determination was successfully performed at three Italian proton therapy facilities, using both Farmer and planes parallels ionization chamber type. Results show that the weighted mean for a series of measurements, carried out both for single pseudo monoenergetic layers and SOBP beams at various energies, was 1.99 ± 0.02 Gy, and 1.99 ± 0.02 Gy respectively for Farmer and Markus chamber, with a standard error of 0.007 Gy. Pooling all data for proton beams, the weighted mean was 1.99 ± 0.01 Gy with a standard error of 0.003 Gy. Hence, these weighted mean values are within 0.55% when compared to TPS designed dose (2 Gy nominal). All dose values were within ± 1.5% from the 2 Gy target, in agreement with the indication of TRS-398 [7].

We also found a very good agreement between single layer measurements and data collected in the middle of SOBP beams as reported by previous studies [2–4].

A future development could be represented by an intercomparison performed rather than in reference conditions, such as reported in this note, as an end-to-end test, like the ones proposed in the recent past [16–18]. This kind of test verifies if all the stages from preparation imaging, passing through treatment planning to plan delivery are adequately implemented. In order to do so, different kinds of phantoms, such as anthropomorphic ones, should be employed, as in [18]. In that work the authors used two anthropomorphic heterogeneous (head and pelvis) phantoms to perform an end-to-end procedure at MedAustron hadrotherapy center. In addition to the dose comparison in the plastic phantoms they compared dose determined with a Farmer chamber and with alanine pellets.

Indeed, another step could be using a solid-state dosimeter: alanine (EPR) or TLD, even if dose rate and linear energy transfer (LET) effects of the scanning beam might be present and need to be taken into account when analyzing the detector response [17]. Alanine electron paramagnetic resonance (EPR) represents an independent dosimeter since the monitor chambers of the beam delivery system and the beam simulated in TPS are calibrated against ionization chamber dosimetry. Since alanine EPRs are solid state dosimeters, their response depends explicitly on the charge, the fluence and the energy of the particle which constitute the mixed radiation field.

Since a systematic deviation was found between the alanine dosimetry and the ionization chamber ones [18], another possible step could be to investigate this deviation both with measurements and with

Table 5
Coefficients used for dose measurements at the various centers.

Center	Beam	Chamber	N_{dw} (Gy/C) × 10^8	$k_{Q,Qo}$	k_s	k_{pol}	$k_{P,T}$
CATANA	SOBP	Farmer	0.5381	1.032	1.003	1.001	1.030
		A. Markus	14.8	1.005	1.000	1.001	1.030
CNAO	SOBP	Farmer	0.5381	1.029	1.003	1.001	1.012
	single layer			1.029	1.003	1.001	1.012
	SOBP	A. Markus	14.8	1.003	1.000	1.001	1.012
	single layer			1.003	1.000	1.001	1.012
CPT	SOBP	Farmer	0.5381	1.029	1.003	1.001	1.035
	single layer			1.029	1.003	1.001	1.035
	SOBP	A. Markus	14.8	1.029	1.000	1.001	1.035
	single layer			1.029	1.000	1.001	1.035
ICSM	photon 6 MV	Farmer	0.5381	0.991	1.003	1.003	1.015
		A. Markus	14.8	1.001	1.003	1.000	1.015

Table 6
Summary of all measurements carried out in 2018.

Facility	Beam	Energy	Chamber	Dose (Gy)
CNAO	protons	SOBP	Farmer	1.98 ± 0.04
		118.19 MeV	Farmer	1.97 ± 0.04
		173.61 MeV	Farmer	2.00 ± 0.04
		SOBP	Adv. Markus	1.97 ± 0.05
		118.19 MeV	Adv. Markus	1.98 ± 0.05
		173.61 MeV	Adv. Markus	1.98 ± 0.05
CATANA	protons	SOBP	Farmer	2.02 ± 0.04
		SOBP	Adv. Markus	2.02 ± 0.05
CPT	protons	SOBP	Farmer	1.98 ± 0.04
		118.19 MeV	Farmer	1.97 ± 0.04
		173.61 MeV	Farmer	1.98 ± 0.04
		SOBP	Adv. Markus	2.00 ± 0.05
		118.19 MeV	Adv. Markus	1.97 ± 0.05
		173.61 MeV	Adv. Markus	1.97 ± 0.05
ICSM	photons	6 MV	Adv. Markus	1.98 ± 0.03
		6 MV	Farmer	2.00 ± 0.03

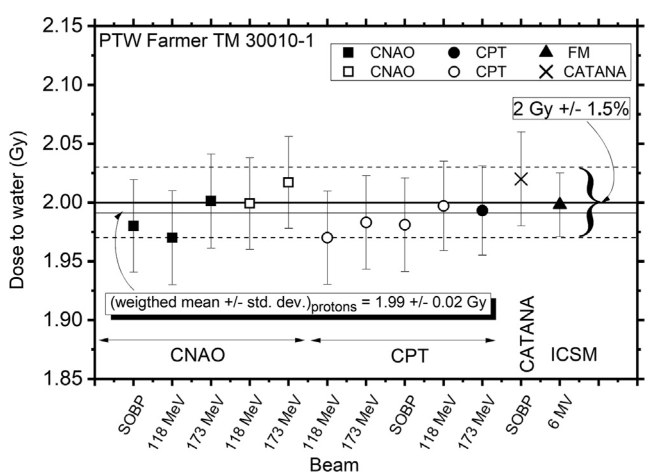

Fig. 2. Absorbed dose to water derived from Farmer chamber measurements at the three proton therapy centers (CNAO, CPT, CATANA). Measurements carried out in 2017 are represented as full square, circle and triangle. The weighted mean for the proton beam data is 1.99 ± 0.02 Gy with a standard error of 0.006 Gy. Data at the photon therapy center ICSM are shown for comparison.

Monte Carlo simulations.

5. Conclusions

In this work, performed within the MC-INFN project, we investigated the consistency, within the experimental uncertainties, of nominal doses delivered at three Italian proton therapy facilities. We performed two sessions of measurement, in 2017 and in 2018, with two

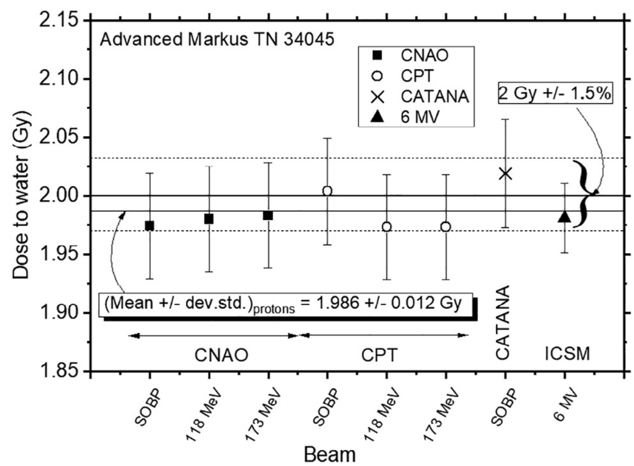

Fig. 3. Absorbed dose to water values derived from Advanced Markus chamber measurements at the three proton therapy centers (CNAO, CPT, CATANA). The weighted mean for the proton beam data is 1.99 ± 0.01 Gy with a standard error of 0.007 Gy. Data at the photon therapy center ICSM are shown for comparison.

ionization chamber types (i.e. Farmer and plane parallel), following reccomendations of report TRS-398 by IAEA. Measurements with megavoltage photons at a conventional radiotherapy center were included for comparison sake. The results show a good agreement with the previous literature results and with nominal doses designed by TPS.

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