Independent dose per monitor unit review of eight U.S.A. proton treatment facilities

M. F. Moyers^{a)}

Colton, California 92354

G. S. Ibbott, R. L. Grant, P. A. Summers, and D. S. Followill

Department of Radiation Physics, University of Texas – M. D. Anderson Cancer Center, Houston, Texas 77030

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Purpose: Compare the dose per monitor unit at different proton treatment facilities using three different dosimetry methods.

Methods: Measurements of dose per monitor unit were performed by a single group at eight facilities using 11 test beams and up to six different clinical portal treatment sites. These measurements were compared to the facility reported dose per monitor unit values.

Results: Agreement between the measured and reported doses was similar using any of the three dosimetry methods. Use of the ICRU 59 $N_{D,w}$ based method gave results approximately 3% higher than both the ICRU 59 N_X and ICRU 78 (TRS-398) $N_{D,w}$ based methods.

Conclusions: Any single dosimetry method could be used for multi-institution trials with similar conformity between facilities. A multi-institutional trial could support facilities using both the ICRU 59 N_X based and ICRU 78 (TRS-398) $N_{D,w}$ based methods but use of the ICRU 59 $N_{D,w}$ based method should not be allowed simultaneously with the other two until the difference is resolved.

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Key words: proton, dosimetry, calibration

1. INTRODUCTION

Although patients have been treated with proton beams since 1954, the number of treatment facilities has remained small. In 2005, there were only four operating proton treatment facilities in the U.S.A. with one of those only treating eyes. By 2011 that number had increased to nine and more are expected to open in the next few years. With this increased number of proton facilities comes a rising probability that the facilities will enter an increasing number of patients onto multi-institutional cooperative clinical trials. To ensure that the results of these trials are meaningful and not underpowered, it is important that the radiation dose reported by one facility is the same as the dose reported by the other facilities.

As of 2000, all existing proton facilities in the U.S.A. were using the methodology presented in the International Commission of Radiation Units and Measurements (ICRU) Report 59 to measure absorbed dose in proton beams with ionization chambers.¹ The ICRU 59 method had a proven record of success with many of the older facilities around the world having participated in large-scale dosimetry comparisons.^{2,3} In 2000, the International Atomic Energy Agency (IAEA) introduced the new TRS-398 protocol⁴ (it was revised in 2004) but as of 2005, the existing proton facilities in the U.S.A. were still using the method described in the ICRU 59 report.^{5–7} The reluctance to change to the newer protocol was because of many perceived problems with the new protocol and the lack of any comparisons of its use and results by different treatment facilities. Many of the problems with the TRS-398 protocol had to do with protocol specified reference conditions and measurement procedures that did not fit within standard

clinical practice (e.g., water proof chambers versus chamber sleeves, phantom windows, field sizes, plastic phantoms versus water phantoms, recombination correction factors, effective points of measurement, lack of data for commonly used ion chambers, etc.). In 2009 it was observed that most of the newer proton facilities built since 2005 had begun clinical patient treatments using the new TRS-398 protocol despite its procedural shortcomings and lack of demonstrated standardization. It was also noted that, although the new facilities were using the calculation formulas and data from the newer TRS-398 protocol, they were not necessarily using the specified procedures and parameters and instead using ones that were more clinically relevant. In 2007, the ICRU published Report 78 which recommended that the IAEA TRS-398 protocol be adopted as the standard proton dosimetry protocol; however, it did clarify a number of aspects and provided recommendations for its use.⁸ It also provided estimates of uncertainty and an analysis of recent publications that pertained to the TRS-398 protocol. Although several individual facilities had performed their own comparisons between the older and newer dosimetry methods, for example Vatsnitsky *et al.*,⁷ at the beginning of the present study no interinstitutional comparisons of patient portals had been performed comparing the older and newer methods at either the older existing proton facilities or at the newer facilities.

To ensure the constancy of radiation doses used to generate results in multi-institutional clinical trials, the National Cancer Institute (NCI), in conjunction with the Massachusetts General Hospital Federal Share funds, sponsored a proton treatment facility site review program, conducted by the Radiological Physics Center (RPC), to approve proton facilities to

TABLE I. Beam delivery types tested (facilities listed in alphabetical order).

Facility	Lateral spreading	Range modulation	Patient collimation
Loma Linda University	Double scattered	Downstream propellor	Lipowitz aperture
Massachusetts General Hospital	Double scattered	Upstream propellor with beam flux modulation	Brass aperture
Massachusetts General Hospital	Modulated scanning	Energy stacking	None
Midwest Proton Radiation Institute	Uniform scanning	Binary rangesifter	Brass aperture
ProCure, Oklahoma City	Uniform scanning	Upstream radiation head range shifter	Brass aperture
ProCure, Warrensville	Uniform scanning	Upstream radiation head range shifter	Brass aperture
University of Florida	Double scattered	Upstream propellor with beam flux modulation	Brass aperture
University of Florida	Uniform scanning	Upstream radiation head range shifter	Brass aperture
University of Pennsylvania	Double scattered	Upstream propellor with beam flux modulation	Multileaf collimator
University of Texas - M. D. Anderson	Double scattered	Upstream propellor with beam flux gating	Bronze aperture
University of Texas - M. D. Anderson	Modulated scanning	Energy stacking	None

use protons in NCI funded clinical trials. These proton facility site visits included reviews of dosimetry, treatment planning, and imaging capabilities. This report describes the comparison of dose per monitor unit (D/MU) using three different dosimetry methods, as measured by the RPC during its site visits to eight proton facilities.

2. METHODS AND MATERIALS

During 2010, 2011, and 2012, the RPC measured the D/MU in several clinical proton beams at eight proton facilities in the U.S.A. wishing to participate in NCI funded clinical trials. Three of these facilities had more than one beam delivery modality resulting in a total of 11 tested proton beams with varying characteristics as shown in Table I. For two of

the facilities with more than one beam delivery modality, the second beam type was measured during a second site visit resulting in a total of ten site visits. For each proton beam tested, the D/MU was measured for one reference calibration portal (some systems had multiple reference portals) and an assortment of up to five different clinical portals simulating different patient treatment sites, as shown in Table II, to test conformance over a large range of clinically treated conditions. Not all five clinical portal treatment sites were measured at all facilities because some proton facilities were not performing the particular clinical treatments defined in Table II.

For the first five site visits, the D/MU was measured in all proton portals with an Exradin P11 parallel plate ionization chamber (Standard Imaging, Madison, WI) in a water phantom at the depth and position prescribed by the facility.

TABLE II. Characteristics of simulated clinical portal treatment sites measured by the RPC during proton site visits. Numerical values represent the bounds of the parameters. The uncertainty values associated with the D/MU values are given at the one standard deviation level.

Site no.	Clinical portal treatment site	Field size (mm × mm) or diameter	D ₉₀ (mm) ^a	M ₉₀₋₉₀ (mm) ^b	Calibration depth (mm)	Notes on calibration conditions	Avg. D/MU ratio ICRU 59 N _x	Avg. D/MU ratio ICRU 59 N _{D,w}	Avg. D/MU ratio ICRU 78 N _{D,w}
1	Reference	100 dia.–180 dia.	133–200	60–121	99–166	Standard	1.003 ± 0.019	1.038 ± 0.015	0.997 ± 0.012
2	Prostate	60 dia.–100 dia.	244–294	85–120	182–256	Standard	1.009 ± 0.004	1.039 ± 0.004	0.993 ± 0.015
3	Pituitary	18–61 × 43–64	101–171	51–91	59–140	Standard	0.988 ± 0.014	1.017 ± 0.015	0.994 ± 0.020
4	Spine	49–70 × 160–213	55–127	31–66	36–102	Location may not be at the isocenter, depth may not be at the center of range modulation	1.002 ± 0.021	1.031 ± 0.022	0.989 ± 0.022
5	Lung	57–100 × 70–184	151–180	63–154	93–130	Physical depth from surface and water equivalent depth do not match	1.003 ± 0.016	1.033 ± 0.017	0.988 ± 0.020
6	Patch	79 × 79	80	70	50	Location may not be at the isocenter, depth may not be at the center of range modulation	1.028	1.058	1.021

^aD₉₀ ≡ depth corresponding to the distal 90% dose in water.^bM₉₀₋₉₀ ≡ modulation width as defined by the difference in depths between the proximal 90% dose in water and the distal 90% dose in water.

This polystyrene-walled chamber was chosen because it had a large collecting volume (20 mm diameter by 2 mm plate separation) for absolute dose measurements and it could be used for quickly measuring both depth dose distributions and D/MU without altering the phantom setup. For the subsequent site visits, the D/MU was measured in the reference portals using either the Exradin P11 or an Exradin A12 thimble ionization chamber (air-equivalent wall Farmer type) in a water phantom while the D/MU was measured in the sample clinical portals using an IBA MatriXX Evolution (IBA Dosimetry, Bartlett, TN) ionization chamber array for which the central four chambers of the array had been cross-calibrated to the P11 or A12 ion chamber in the facility's reference proton portal. The revised procedure in the second year of the study was followed to expedite measurements of D/MU and lateral dose profiles in the clinical portals which were required for another aspect of the facility site visits. The MatriXX device consists of a square array of 32 by 32 vented parallel plate ionization chambers, each chamber being 4.5 mm in diameter with a 5 mm plate separation giving a collecting volume of 0.08 cm^3 . The lateral distance between chamber centers is 7.62 mm and the surface of the chambers is at a water-equivalent depth of 4 mm below the surface of the device. A bias of 400 volts was applied for all D/MU measurements with the Exradin chambers. For each reference proton portal, a polarity correction factor was determined for the Exradin ion chambers using the method outlined in ICRU 78. Due to the confusion in the proton community regarding application of the approximate two-voltage technique to proton beams, the recombination correction factor was determined by using four different voltages, plotting the MU per charge versus the inverse of the voltage, and determining the factor from the y-intercept of a fit to the data. Both linear and quadratic fits were tested and the fit best matching the data was used to determine the recombination factor therefore bypassing any ambiguity in the use of the two-voltage technique. Moyers and Vatnitsky⁹ have compared calculations of the three different methods of applying the two-voltage technique to several proton beam delivery methods and found that the methods recommended by the ICRU 78 report matched the extrapolation method better than the method many users mistakenly apply when using the TRS-398 protocol directly. On the other hand, the error that a user might make by using the wrong method for the beams tested in this project would be at most 0.4%. The ion chamber collected charge was additionally corrected for ambient pressure and the temperature of the water phantom into which the ionization chamber was placed after allowing a sufficient time for the chamber to equilibrate to the phantom temperature. For the first five site visits where the D/MU was measured with the Exradin ionization chambers, the D/MU was determined using three different calculation methods; the N_X based method from ICRU 59, the $N_{D,w}$ based method from ICRU 59, and the $N_{D,w}$ based method from ICRU 78 (which was based upon IAEA TRS-398). The well-known errors in the ICRU 59 N_X method concerning humidity and chamber wall and chamber cap material mismatch were corrected as typically performed using the AAPM TG-21 method.^{10–12} During the second year of the project (second five site visits) when the scope of the

FIG. 1. Results of D/MU comparisons for the different clinical portal treatment sites, test beams, and dosimetry methods. Red diamonds represent RPC determinations using the ICRU 59 $N_{D,w}$ method. Green crosses represent RPC determinations using the ICRU 59 N_X method. Blue triangles represent RPC determinations using the ICRU 78 (IAEA TRS-398) $N_{D,w}$ method. The numerical values given in the legend represent the average and one standard deviation values for the D/MU ratios for all clinical portal treatment sites and test beams during the first five visits using only the P-11 data. For the ICRU 78 (IAEA TRS 398) $N_{D,w}$ average, the second values given in brackets represent the average and one standard deviation values for all visits and includes the measurements with the A12 and Matrix chambers.

renewed grant was changed to decrease the beam time required to make measurements and the MatriXX was used to measure the D/MU in the clinical portals, only the ICRU 78 (TRS 398) $N_{D,w}$ method was used.

3. RESULTS AND DISCUSSION

The results, the ratio of the RPC measured D/MU to the facility reported D/MU, are plotted in Fig. 1 for all three dosimetry methods. The graph is organized according to the following scheme. Each symbol represents the ratio determined for a given test beam and clinical portal treatment site. The number for the clinical portal treatment site, as given in Table II, is given on the abscissa. The clinical portal treatment site names are also indicated on the graph. For each of the clinical portal treatment sites, the results for each of the 11 test beams is plotted to show the spread in the comparison data.

The average and one standard deviation (s.d.) ratios of RPC measured to facility reported D/MU values for each clinical portal site and dosimetry method are given in Table II. When the results are broken down into these multiple categories, the average and s.d. calculations are based upon less than nine measurements each and typically less than five measurements for the ICRU 59 N_X and $N_{D,w}$ methods performed during the first year; nevertheless, a few comments can be made. The smallest spread between test beams of the ratio of RPC measured to facility reported D/MU for any single clinical portal treatment site and single dosimetry method was for the prostate treatment site. The portals

used for the prostate treatment site used high proton energies and the D/MU was typically specified at the isocenter. The greatest spread in the D/MU ratios for any single treatment site and single dosimetry method was found for the spine and lung treatment sites. The field shapes for the portals used for the spine site were typically long and narrow and the calibration reference point was often upstream of the isocenter thereby deviating from reference conditions more than the other clinical portal treatment sites. The portals used for the lung treatment site had different physical and water equivalent depths and were thus more challenging to obtain a phantom setup equivalent to the treatment plan. The measurements with the P-11 chamber for the pituitary treatment site resulted in an average RPC measurement to facility ratio less than 1 for both the ICRU 59 N_X and ICRU 78 (TRS-398) $N_{D,w}$ methods. This difference might be expected because of the small field sizes of the portals and the large active diameter of the P-11 chamber compared to the active diameters of the chambers used by the facilities to determine the D/MU. Only one measurement was performed for a patch portal because most facilities were not using this technique. The portal selected by the facility had a small diameter and therefore an Exradin A-16 micro thimble chamber (Standard Imaging, Madison, WI) was cross-calibrated to the P-11 chamber in the facility's reference beam and then used for the measurement. This chamber had a collecting volume of only 0.007 cm^3 . The RPC measured D/MU for the patch portal was significantly higher than the facility's reported D/MU.

When the results from all clinical portal treatment sites are combined, better statistics can be realized. Using the data from only the first five facility site visits where the RPC measurements were done with the P-11 chamber, a comparison can be made of the three different dosimetry methods. Using the ICRU 59 N_X method, the average RPC measured dose to facility reported dose ratio was 1.003 with a 1 s.d. of $\pm 1.6\%$. Using the ICRU 59 $N_{D,w}$ method, the average RPC measured dose to facility reported dose ratio was 1.034 with a 1 s.d. of $\pm 1.6\%$. Using the ICRU 78 (TRS-398) $N_{D,w}$ method, the average RPC measured dose to facility reported dose ratio was 0.997 with a 1 s.d. of $\pm 1.6\%$. It is thus seen that the spread of RPC to facility ratios was essentially the same regardless of which of the three methods was used. In addition, the average ratios using the ICRU 59 N_X method and the ICRU 78 (TRS-398) $N_{D,w}$ method were essentially the same within uncertainties. This result is similar to a Japanese intercomparison study of N_X and $N_{D,w}$ methods in reference proton beams.¹³ On the other hand, the ratios determined using the ICRU 59 $N_{D,w}$ method were about 3% higher than with both of the other methods. This difference may be a result of the ICRU 59 calculation method for the k_p chamber factor for the P-11 ionization chamber; similar results may not be found for other chambers having different designs and made of different materials. These results do, however, cast doubts on the use of the ICRU 59 $N_{D,w}$ method for multi-institutional clinical trials. Further studies should be performed with a larger variety of ionization chambers.

When only the results using the ICRU 78 (IAEA TRS-398) $N_{D,w}$ method are considered but including the results from the

Matrix array measurements during the second five facility site visits, the average ratio for all test beams and clinical portal sites was 0.993 with a 1 s.d. of $\pm 1.8\%$, a slightly larger spread than when only the P-11 chamber was used. Although the number of proton test beams in this study is relatively small, this spread of ratios is similar to that found during RPC site visits for x ray and electron beams.¹⁴

4. CONCLUSIONS

Conformity of dose measurements between different facilities participating in multi-institutional clinical trials could be accomplished if all institutions used the same dosimetry method regardless of which of the three methods was used. Good agreement between the ICRU 59 N_X based and the ICRU 78 (TRS-398) $N_{D,w}$ based methods suggests that a facility could use either method for patients entered onto a trial. The results also demonstrate that doses delivered to patients in the past with D/MU based upon the ICRU 59 N_X method and patients treated currently with D/MU based upon the ICRU 78 (TRS-398) $N_{D,w}$ are essentially the same. The difference between the ICRU 59 $N_{D,w}$ based method and the other two methods suggests that the ICRU 59 $N_{D,w}$ based dosimetry method not be used for multi-institutional clinical trials in conjunction with the ICRU 59 N_X based and the ICRU 78 (TRS-398) $N_{D,w}$ based methods until the measured difference is resolved. A related study has recently been performed where investigators from multiple institutions compared multiple ionization chambers irradiated in two beams at a single institution.¹⁵ Preliminary results from that study indicate that some of the discrepancies found in the present study may soon be resolved. Finally, it should be noted that by the time the present study was completed, most proton treatment facilities in the U.S.A. had switched to using the formulas and data from the ICRU 78 (TRS 398) $N_{D,w}$ protocol.

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- ^{a)} Author to whom correspondence should be addressed. Electronic mail: MFMoyers@roadrunner.com
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