Monte Carlo simulations of neutron spectral fluence, radiation weighting factor and ambient dose equivalent for a passively scattered proton therapy unit

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Abstract
Stray neutron exposures pose a potential risk for the development of secondary cancer in patients receiving proton therapy. However, the behavior of the ambient dose equivalent is not fully understood, including dependences on neutron spectral fluence, radiation weighting factor and proton treatment beam characteristics. The objective of this work, therefore, was to estimate neutron exposures resulting from the use of a passively scattered proton treatment unit. In particular, we studied the characteristics of the neutron spectral fluence, radiation weighting factor and ambient dose equivalent with Monte Carlo simulations. The neutron spectral fluence contained two pronounced peaks, one a low-energy peak with a mode around 1 MeV and one a high-energy peak that ranged from about 10 MeV up to the proton energy. The mean radiation weighting factors varied only slightly, from 8.8 to 10.3, with proton energy and location for a closed-aperture configuration. For unmodulated proton beams stopped in a closed aperture, the ambient dose equivalent from neutrons per therapeutic absorbed dose ($H^{*}(10)/D$) calculated free-in-air ranged from about 0.3 mSv/Gy for a small scattered field of 100 MeV proton energy to 19 mSv/Gy for a large scattered field of 250 MeV proton energy, revealing strong dependences on proton energy and field size. Comparisons of in-air calculations with in-phantom calculations indicated that the in-air method yielded a conservative estimation of stray neutron radiation exposure for a prostate cancer patient.

(Some figures in this article are in colour only in the electronic version)
1. Introduction

Proton radiation therapy is of increasing interest because of its ability to deliver dose to tumors while sparing most normal tissues nearby. Most proton therapy units in current use employ a passive scattering nozzle (Koehler et al 1975, Gottschalk et al 1991), in which the incoming beam is spread out in depth by a range modulator and laterally by a scatter foil to deliver a uniform dose to the target. However, the dosimetric advantages of proton beams may be negated to some extent by the generation of stray neutrons in proton therapy, which may affect the whole-body exposures and thereby increase patients’ risk of developing secondary cancers. Stray neutron radiation from passively scattered nozzles is larger than that from active scanning nozzles (Kanai et al 1980, Pedroni et al 1995, Tilly et al 2007) because passive scattering nozzles have more material components in the beam path and, thus, more neutrons are produced. The additional stray radiation exposure is of particular concern for patients who have good prognoses with relatively long expected survival times because their lifetime risk of radiation-induced secondary cancers could be increased markedly (Lee et al 2005, Gibbs et al 2006, Miralbell et al 2002).

A wide range of neutron exposures from proton therapy units has been reported (Binns and Hough 1997, Agosteo et al 1998, Yan et al 2002, Schneider et al 2002, Roy and Sandison 2004, Polf and Newhauser 2005, Polf et al 2005, Fontenot et al 2005, Jiang et al 2005, Mesoloras et al 2006, Tayama et al 2006, Zheng et al 2007a, 2007b, Wroe et al 2007). The neutron dose equivalent per therapeutic dose, \( \frac{H}{D} \), has been shown to depend strongly on proton energy, field size, range modulation width and other treatment conditions (Mesoloras et al 2006, Zheng et al 2007b), all of which contribute to these wide differences. Disparity in data can also be attributed to the various measurement and simulation techniques employed and their large associated uncertainties. In our previously published papers (Zheng et al 2007a, 2007b), we described a method to estimate the neutron dose equivalent by measuring or simulating the in-air fluence for a nozzle with a closed-aperture nozzle configuration. However, at the time of those studies, treatment options (that is, combinations of range modulator, second scatterer and proton energy) involving low-energy protons or small scattered field sizes were not available for simulation. Thus, neutron exposures for these treatment options had not been studied. In addition, it would be useful to study the neutron spectra and radiation weighting factors for the complete set of nozzle options to better understand and estimate neutron exposures.

One aim of the present work, therefore, was to use Monte Carlo simulations to estimate the neutron exposures resulting from all nozzle configuration options of the passively scattered proton therapy system in use at our institution. In addition, we studied the neutron spectral fluence and radiation weighting factors resulting from these configurations. We also determined how the neutron exposures were affected by the collimated field size (as determined by the final beam-limiting aperture) and the spread-out Bragg peak (SOBP) width. Finally, we estimated the degree of conservativeness of the free-in-air approach in a case study by comparing the ambient dose equivalent per therapeutic absorbed dose (\( \frac{H^*(10)}{D} \)) determined free-in-air to the effective dose per therapeutic absorbed dose (\( \frac{E}{D} \)) value determined in a realistic anthropomorphic phantom.

2. Methods and materials

2.1. Modeling of the beam delivery apparatus

The passively scattered system in our treatment unit was manufactured by Hitachi America, Ltd (Brisbane, CA). By selecting different scattering foils, it delivers three lateral scattered field
Figure 1. Monte Carlo model of the passively scattered treatment nozzle configured with a medium-field-size option and a medium snout. The proton beams enter the nozzle from the left through a vacuum window (A) and then pass through a beam profile monitor (B), a scattering-power-compensated range-modulator wheel (C), a second scatterer (D), a range shifter assembly (E), backup and primary monitors (F), shielding plates (G), a snout (H) and a final collimator or aperture (I). The location of the isocenter is indicated by I. The open circles outside the nozzle represent the positions of neutron receptors (J). There are eight possible proton energies and three scattered field sizes, corresponding to 24 options.

sizes—small, medium and large, corresponding to maximum uncollimated field diameters at the isocentric plane of 14.1 cm, 25.5 cm and 35.4 cm, respectively—with the field size chosen according to a tumor diameter (Newhauser and Smith 2003). For each of the three scattered field sizes, there are eight options, each of which corresponds to a unique combination of proton beam energy, range modulator wheel and second scatterer to obtain the proton beam penetration depth. The proton energies entering the nozzle for the eight options are 100, 120, 140, 160, 180, 200, 225 and 250 MeV. For each incident proton energy, the proton beam is modulated in depth by a range modulator wheel, spread out laterally by a scattering foil and finely adjusted for the penetration range by a stack of insertable range shifter blades. The corresponding snout (small, medium or large) holds an aperture to further collimate the field’s size and shape (i.e. small collimated fields are up to $10 \times 10$ cm$^2$ in area, medium collimated fields range from $10 \times 18$ cm$^2$ to $18 \times 18$ cm$^2$ and large collimated fields vary from $18 \times 18$ cm$^2$ to $25 \times 25$ cm$^2$).

We used the MCNPX Monte Carlo radiation transport code (version 2.6) (Pelowitz 2005) to simulate the proton therapy beam delivery system. MCNPX is a general-purpose code and has been extensively benchmarked against measurements in proton therapy applications (Polf and Newhauser 2005, Polf et al 2005, Fontenot et al 2005, Herault et al 2005, Tayama et al 2006, Newhauser et al 2005, 2007). For energies from 1 keV to 150 MeV, previously evaluated nuclear interaction cross-section libraries were used (Chadwick et al 1999); above 150 MeV, hadronic cross sections were estimated using the Bertini intranuclear-cascade model (Bertini 1969) for nucleons and pions and the ISABEL model (Yariv and Fraenkel 1979) for other particle types. The cutoff energy for proton transport was 1 MeV. A F4 card was used to tally neutron fluence for sphere cells of 12 cm in diameter. An in-house code was used to automatically generate MCNPX input files that model the proton treatment nozzles (Zheng et al 2006). Figure 1 shows an example of the MCNPX modeling of the nozzle and the layout of the neutron receptors. More details on the nozzle and its modeling can be found in Zheng et al (2007a, 2007b) and Newhauser et al (2007).
2.2. Calculation of radiation weighting factors

The biological effect of radiation is strongly dependent on the particle type and energy. To account for the relative detriment of different types of radiation, the radiation weighting factor, $w_R$, was introduced for calculating radiological protection quantities in the International Commission on Radiological Protection (ICRP) Publication 60 (1991). In proton therapy, the predominant component of stray radiation is from neutrons. The $w_R$ value for neutrons varies with energy and is higher than $w_R$ values for photons and electrons because of neutrons’ relatively large biological effects on tissue. Figure 2 shows a recent estimate of $w_R$ as a function of neutron energy, as reported by the ICRP (2003).

For exposures from a spectrum of neutron energies, a mean radiation weighting factor, $\bar{w}_R$, can be used.

$$\bar{w}_R = \frac{\sum_{i=1}^{n} w_{R_i} \cdot \Phi_i}{\sum_{i=1}^{n} \Phi_i}$$

where $w_{R_i}$ is the radiation weighting factor according to ICRP Publication 92 (ICRP 2003) and $\Phi_i$ is the neutron fluence from the Monte Carlo simulation for the $i$th energy bin.

In this work, the radiation weighting factor was used to calculate the organ equivalent dose (see section 2.4), and the fluence-to-ambient-dose-equivalent conversion factor was used to calculate the ambient dose equivalent (see section 2.3).

2.3. Calculation of ambient neutron dose equivalent per therapeutic dose

Since some radiation protection quantities are difficult to measure, operational quantities are commonly used instead to conservatively estimate the protection quantities. The operational quantity we calculated in our work was the ambient dose equivalent, $H^*(10)$. This value is defined as the dose equivalent that would be produced by the corresponding expanded and aligned field in the ICRU (International Commission on Radiation Units and Measurements) sphere (30 cm in diameter) at a depth of 10 mm on the radius opposing the direction of the
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aligned field (ICRP 1991). $H^*(10)$ can be calculated as the product of the neutron fluence, $\Phi$, and the fluence-to-dose-equivalent conversion coefficient, $H^*(10)/\Phi$. In our calculations, the $H^*(10)/\Phi$ values, which vary with the neutron energy, were taken from ICRP Publication 74 (1996). By summarizing the products of the neutron fluence per incident proton, $\Phi_i/p$, and $H^*(10)/\Phi_i$ over all energy bins, the ambient neutron dose equivalent per proton, $H^*(10)/p$, at each receptor location was obtained by

$$H^*(10)/p = \sum_{i=1}^{n} (H^*(10)/\Phi_i) \cdot \Phi_i/p,$$

where $i$ and $n$ are the index and the total number of neutron energy bins, respectively, $(H^*(10)/\Phi_i)$ and $\Phi_i/p$ are the ambient dose equivalent per unit neutron fluence for neutrons and the neutron fluence per incident proton in the $i$th energy bin from simulations, respectively.

In previous work (Zheng et al 2007a, 2007b, Fontenot et al 2005, Polf et al 2005, Yan et al 2002), the neutron dose equivalent was denoted as $H$ and fluence-to-dose-equivalent coefficients, $H/\Phi$, were taken from the National Council on Radiation Protection and Measurements (NCRP) Report 38 (1971), which is still used in many state regulations. To compare current data with those from previous work, we also calculated the $H$ values based on NCRP Report 38.

The therapeutic absorbed dose per proton ($D/p$) was obtained at the location of the maximum absorbed dose in a water phantom along the central axis of a pristine peak or an SOBP in a cell of 1.6 cm$^3$ volume in a separate simulation, as described previously (Zheng 2007a, 2007b). $H^*(10)/D$ was obtained by dividing the $H^*(10)/p$ value from equation (2) by the $D/p$ value. Similarly, we calculated $H/D$ with fluence-to-dose-equivalent conversion coefficients from NCRP Report 38 (1971).

2.4. Calculation of effective dose

We used the closed-aperture, free-in-air method described above because it is simple and is expected to be suited for conservatively estimating $H/D$ or $H^*(10)/D$ values. This method may be used with data from Monte Carlo simulations, analytical models (Zheng 2007a, 2007b) or measurements. The main advantage of the in-air method is that the complexities attributable to patient factors are avoided, including such variables as neutron production and attenuation in the patient, variations inherent in the use of customized range compensators and apertures and variations in the patient size and location with respect to the nozzle. However, the approach was expected to lead to a potential overestimation of the true neutron exposure received by a patient. To estimate the degree of overestimation, we compared $H^*(10)/D$ results from the simple in-air method with $E/D$ values from more realistic simulations of a patient treatment that included an stylized anthropomorphic phantom (male adult, 1.76 m tall, cf Billings and Yucker 1973, Fontenot et al in preparation) and customized range compensators and apertures for the same nozzle and simulation parameters.

To calculate $E$ per proton ($E/p$), we simulated a prostate treatment of an anthropomorphic phantom using treatment-specific nozzle configurations (e.g. beam range, modulation, snout position and range shifter setting) and hardware (e.g. aperture and range compensator) extracted from a typical patient treatment plan. Absorbed dose from secondary neutrons and photons was estimated for each of the following sensitive organs: bladder, colon, bone marrow, lung, stomach, breast, liver, esophagus, thyroid, skin, bone surface, gonads and the remainder. Radiation weighting factors from ICRP Publication 92 (2003) were applied to tallied doses to obtain the equivalent dose for each organ.

$$H_T/p = \bar{w}_R D_T / p$$ (3)
where $\bar{w}_R$ is the mean weighting factor based on the neutron fluence crossing the organ surface, $D_T/p$ and $H_T/p$ are the absorbed dose and dose equivalent per proton averaged over organ or tissue $T$ from simulations, respectively.

$$E/p = \sum_T w_T H_T/p,$$

where $w_T$ is the tissue weighting factor from ICRP Publication 92 (2003). $E/p$ was then divided by the therapeutic dose per proton, $D/p$, which was tallied in the target organ (here prostate) to obtain $E/D$.

### 3. Results

#### 3.1. Neutron spectral fluence

**3.1.1. Neutron spectral fluence for various proton energies.** We studied the neutron spectral fluence for medium field options of different proton energies at the nozzle entrance, as shown in figure 3(a). There were two pronounced peaks in all neutron spectra, joining each other at about 10 MeV neutron energy. The low-energy peak was similar in shape for all proton energies, with neutron energies ranging from 0 to about 10 MeV (mode $\sim 1$ MeV). These low-energy neutrons were mainly produced from evaporation processes and were isotropically distributed. The high-energy neutron peak started from 10 MeV and extended up to the incident proton energy, with the mode varying with the proton energy. The high-energy peak contained forward-peaked neutrons from direct (nucleon–nucleon) reactions produced in intranuclear cascades and neutrons ejected from the compound-nucleus and pre-equilibrium processes.

The neutron spectral ambient dose equivalent is shown in figure 3(b). Similar to the neutron spectral fluence, these data had two peaks. Because $H^*(10)/\Phi$ values are small for neutrons of less than 100 keV, contributions from neutrons of less than 100 keV were almost negligible. For neutrons of higher energies, $H^*(10)/\Phi$ values are relatively large,
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which means that the high-energy peak contributed more than the low-energy peak to the total neutron ambient dose equivalent.

3.1.2. Neutron spectral fluence at various off-axis distances. Figure 4 shows the neutron spectral fluences at various off-axis distances for the medium field option with a proton energy of 250 MeV. The relative contributions of the high-energy and low-energy peaks varied with the off-axis distance. The closer to the central axis, the more the high-energy peak contributed to the total value. This was because the high-energy neutrons produced in the intranuclear cascade were forward peaked and thus fell off rapidly as the distance from the beam axis increased; the low-energy neutrons from the evaporation process were emitted isotropically, and thus they varied only slightly with the off-axis distance.

3.2. Radiation weighting factors

Figure 5(a) shows the mean radiation weighting factor as a function of proton energy for small, medium and large field options at the isocenter, 100 cm lateral to isocenter and 100 cm downstream. For each field size at any location, \( \bar{w}_R \) decreased almost linearly with proton energy. However, the variation of the mean radiation weighting factor versus proton energy was relatively small, less than 10% when proton energies varied from 100 MeV to 250 MeV. At a given proton energy, it appeared that \( \bar{w}_R \) had a weak dependence on the field size, but a stronger dependence on the location, with \( \bar{w}_R \) at 100 cm lateral to isocenter being largest and \( \bar{w}_R \) at 100 cm downstream smallest. Overall, \( \bar{w}_R \) varied only slightly, between 8.8 and 10.3, for all proton energies and locations considered.

Because the radiation weighting factor is a function of neutron energy, we also studied the mean neutron energy at the isocenter, 100 cm lateral to the isocenter and 100 cm downstream as a function of proton energy for small, medium and large field options, as shown in figure 5(b). The mean neutron energy increased almost linearly with the incident proton energy. At isocenter and 100 cm downstream, there were more forward-peaked high-energy neutrons than at 100 cm laterally; therefore, the average neutron energy was higher. At 100 cm lateral to isocenter, most of the neutrons were isotropic low-energy neutrons; therefore, the mean energy was lower.
3.3. \(H^*(10)/D\) values for unmodulated beams with a closed aperture

Figure 6 shows the simulated \(H^*(10)/D\) values for all 24 nozzle configuration options, revealing that \(H^*(10)/D\) increased strongly with increasing proton energy. When neutron fluence-to-dose-equivalent conversion coefficients from ICRP Publication 74 (1996) were used, the \(H^*(10)/D\) values at isocenter ranged from about 0.3 mSv/Gy for a small field with proton energy of 100 MeV to about 19 mSv/Gy for a large field with a proton energy of 250 MeV. \(H^*(10)/D\) also strongly depended on the scattered field size, such that at a given energy, \(H^*(10)/D\) was highest for the large scattered field option and lowest for the small scattered field option.
We also calculated the $H/D$ values for all nozzle configuration options using the conversion coefficients in NCRP Report 38 (1971) and then compared the results with those from calculations done using ICRP Publication 74 coefficients. As shown in figure 6, $H/D$ values at isocenter that were calculated using fluence-to-dose equivalent conversion coefficients from NCRP Report 38 were slightly higher than the corresponding $H^*(10)/D$ values calculated using coefficients from ICRP Publication 74. It is important to note, however, that the overall difference was relatively small, typically less than 15%. It should also be noted that $H/D$ values calculated according to coefficients from NCRP Report 38 can be slightly lower than $H^*(10)/D$ values calculated according to the coefficients in ICRP Publication 74 if neutrons of lower energy (<10 MeV) dominate, as is the case at locations far from the field edges.

The two sets of fluence-to-dose-equivalent conversion coefficients from NCRP Report 38 and ICRP Publication 74 are plotted in figure 7 for comparison. Relative to coefficients from NCRP Report 38, the coefficients from ICRP Publication 74 are almost the same for neutron energies below 10 keV, differ only slightly at neutron energies between 10 keV and 20 MeV and are much lower at energies above 20 MeV. These coefficients take into account neutron kerma factors, radiobiological effects and other factors, and the coefficients are not directly proportional to the radiation weighing factor in figure 2.

3.4. $H^*(10)/D$ values as a function of the final collimating aperture size

To assess the influence of the proton final collimating aperture on $H^*(10)/D$, we varied the aperture size (i.e. final collimated field size) from $0 \times 0$ cm$^2$ (closed aperture) to $10 \times 10$ cm$^2$ for a small scattered field option, from $10 \times 10$ cm$^2$ to $18 \times 18$ cm$^2$ for a medium scattered field option and from $18 \times 18$ cm$^2$ to $25 \times 25$ cm$^2$ for a large scattered field option. The $H^*(10)/D$ value as a function of the aperture size is shown in figure 8. For each scattered field size, the $H^*(10)/D$ value decreased almost linearly as the aperture size (area) increased; this relationship held because as the aperture grew wider, more protons passed through it without any neutrons being produced (note that no phantom or other beam stopper was present outside
When examining the effects of various scattered field sizes for a fixed aperture size, we found that the smaller scattered field always generated the lower $H^*(10)/D$ value and the larger scattered field the higher one. For example, given an aperture size of $10 \times 10$ cm$^2$, the neutron dose produced by a medium scattered field would be 65% more than that produced by a small scattered field; similarly, at an aperture size of $18 \times 18$ cm$^2$, about 85% more neutrons would be produced by a large scattered field than a medium scattered field. This phenomenon highlights the advantage of designing a nozzle system that can produce different scattered field sizes by using different scattered foils. While a single large scattered field beam could be collimated to deliver smaller fields, the neutron exposure to a patient and the lateral penumbra width would be larger than necessary.

3.5. $H^*(10)/D$ value as a function of the SOBP width

Figure 9(a) shows the relative $H^*(10)/D$ value as a function of SOBP width ($m$) for small, medium and large field options. For clarity of presentation, the values were normalized to unit value at $m = 0$ (i.e. the value for an unmodulated beam). The relationship between $H^*(10)/D$ and $m$ was almost identical for all options simulated. In particular, the $H^*(10)/D$ value was lowest for the unmodulated beam, increased rapidly when the SOBP width was increased to 6 cm and then increased slowly as the SOBP width increased above that value. The $H^*(10)/D$ value for a 16 cm SOBP width was about double that for an unmodulated beam. Figure 9(b) shows $H^*(10)$ and $1/D$ (per proton) as separate functions of $m$, normalized to unit value at $m = 0$. $H^*(10)$ decreased slowly with $m$, with a total decline of about 20% from $m = 0$ to $m = 16$ cm. $1/D$ increased (or $D$ decreased) at a relatively faster rate as $m$ increased, with a final value at $m = 16$ cm about 250% of that at $m = 0$. The decrease of $D$ with increasing $m$ can mainly be explained by the fact that as the SOBP width increases, more protons are needed to deliver dose to a larger volume.
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Figure 9. (a) $H^*(10)/D$ as a function of the SOBP width, $m$, and (b) $H^*(10)$ and $1/D$ per proton as separate functions of $m$, at isocenter for small, medium and large scattered field options in simulations of 250 MeV proton beams, normalized to unit value at $m = 0$ (i.e. an unmodulated beam).

3.6. Comparison of in-air and in-phantom results

To estimate the degree of overestimation arising from free-in-air calculations, we compared $H^*(10)/D$ results from the simple in-air method with the $E/D$ obtained from more realistic simulations of a patient treatment that included an anthropomorphic phantom and customized range compensators and apertures. To facilitate the comparison, we used the same nozzle configuration for the in-air and in-phantom simulations, i.e. a medium field option for a beam with a proton energy of 250 MeV. The calculated effective dose per absorbed dose, $E/D$, was about 8 mSv/Gy, with the majority of effective dose contributed by neutrons (about 85–90%) and the other by photos (about 10–15%). The corresponding $H^*(10)/D$ value from the in-air method (i.e. using the same nozzle configuration but with a closed aperture, no range compensator and no phantom) was about 17 mSv/Gy. This result demonstrates that the in-air method is indeed conservative and predicts neutron dose values within a factor of about 2 of those calculated in the in-phantom simulation for a prostate cancer case.

We also compared the neutron spectral fluences at isocenter obtained in air with a closed aperture to those obtained in a water phantom (13 cm in depth) and an anthropomorphic phantom (16 cm in depth) with an open aperture (figure 10). While the high-energy peaks were very similar, the low-energy peak was largely attenuated in a phantom. Since the mode of the low-energy peak in air was at about 1 MeV, at which point the radiation weighting factor was largest, attenuation of the peak reduced the mean radiation weighting factor by about 30% in the phantom relative to air.

4. Discussion

Our results show that the neutron spectral fluence contained two pronounced peaks, the relative contributions of which depended on the location of the neutron receptor and the proton energy. Mean radiation weighting factors did not vary much with proton energy and location for a closed-aperture configuration. The calculated $H^*(10)/D$ values ranged from about 0.3 to 19 mSv/Gy in all simulated beam configuration options for unmodulated beams from the passively scattered proton therapy system at our institution. We found that $H^*(10)/D$ values were strongly dependent on proton energy, scattered field size, aperture size and SOBP width.
We also found that the in-air method provided a conservative estimate of the stray radiation exposure to an individual patient undergoing proton therapy for prostate cancer.

Our data are consistent with most previously published results. The simulated neutron spectral fluences were consistent with the measured spectral fluence published by Yan et al (2002) and our previous simulation results (Zheng et al 2007a). Our findings on neutron dose equivalent as a function of proton energy and aperture size are similar to the general behavior described by Mesoloras et al (2006). The radiation weighting factors reported here are consistent with those reported in our previous studies (Zheng et al 2007a, 2007b). However, our $H^\ast(10)/D$ or $H/D$ calculations were not affected because we used the fluence-to-dose-equivalent conversion coefficients and not the radiation weighting factors.

The analysis of $H^\ast(10)/D$ dependence on proton energy, aperture size and SOBP width extends the results of our previous studies (Zheng et al 2007a, 2007b). $H^\ast(10)/D$ values in the present study were slightly lower than those we found previously, mainly because here we used a more detailed model of the treatment nozzle that included more shielding and because we used fluence-to-dose-equivalent conversion coefficients from ICRP Publication 74 (ICRP 1997) instead of NCRP Report 38 (NCRP 1971). As it turned out, the influence of the choice of conversion coefficients was relatively small, typically less than 15%, suggesting that the results from previous analyses that utilized NCRP Report 38 data can be directly compared with those from studies that used coefficients from ICRP Publication 74.

Despite our improvements in modeling and simulations of more beam configuration options, we have not yet fully confirmed our simulations with measurements. However, our Monte Carlo models were previously benchmarked against measurements (Polf and Newhauser 2005, Polf et al 2005, Fontenot et al 2005), and preliminary measurements (Gillin 2007 personal communications) showed that the difference between simulated and measured values was less than a factor of about 2, i.e. within the measurement uncertainties.
The statistical uncertainties for simulations are no more than 5% for ambient dose equivalent calculations in air and no more than 10% for effective dose calculations in phantom. As we have modeled the nozzle geometry in detail and with sufficient accuracy, the uncertainties due to geometry model error are minor compared to other uncertainties, such as those from physics model error and cross-section approximation, a detailed discussion on which is out of the scope of this study. Second, our study used a closed aperture to replace the patient as a beam stopper; therefore, patient-specific components were not modeled in the simulations. While this might limit the application of this approach for assessing individual patient cases, the goal of this work was to provide a simple method to estimate $H^*(10)/D$ for a wide range of treatment fields. We indeed found that the free-in-air method is a good surrogate for phantom simulations with a 250 MeV proton energy in that it provides a conservative estimate of $E/D$ values in anatomic phantom for prostate cancer with an accuracy within a factor of about 2. Another key matter that remains to be investigated is the degree of conservativeness for a wide variety of patients and treatment techniques. For example, the in-air method may produce less conservative $H^*(10)/D$ values for low-energy beams because neutrons are produced in the more upstream part of the closed aperture due to the shorter proton penetration range and are then shielded more by the closed aperture.

The neutron spectral fluence and radiation weighting factors presented in this study allow us to better understand and estimate the neutron dose equivalent received by patients during passively scattered proton therapy. The $H^*(10)/D$ values obtained for our proton therapy system suggest that neutron exposures vary in a wide range depending on treatment conditions. Therefore, both treatment conditions and individual patient factors must be considered in evaluating the risk of neutron exposure in a patient receiving proton therapy. Knowing the influence of various treatment factors (e.g. proton energy, field size and SOBP width) on the neutron ambient dose equivalent will be valuable in developing strategies to minimize secondary neutron exposures and, thus, the resulting risk of late effects in patients receiving proton therapy.

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