MC ESTIMATION OF OUT-OF-FIELD ORGAN DOSES FROM SCATTERED PHOTONS, PHOTONEUTRONS, AND CAPTURE GAMMA RAYS IN PROSTATE RADIATION THERAPY

by

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In the current study, the out-of-field organ and effective dose for external radiation therapy of prostate cancer was estimated by the MCNPX Monte Carlo code and a mathematical phantom. Organ doses from scattered photons, photoneutrons, and capture gamma rays were calculated for an 18 MV photon beam. Our results show that scattered photons are the main contributors in out-of-field patient doses. The resulting effective doses from scattered photons, neutrons, and capture gamma rays amounted to 723 mSv, 134 mSv, and 45 mSv per a 72 Gy prostate dose, respectively. In conventional treatment, the total effective dose from the three radiations in the current study was 902 mSv per a 72 Gy tumor dose. Taking into account that the risk factor for a secondary cancer of an adult male patient is 2% per Sv, the probability of secondary cancer risks of 1.8% and 6.3% were obtained for the conventional and intensity-modulated treatment of the prostate, respectively. Our study suggests that, taking into account all contributors to organ doses – including scattered photons, neutrons, and capture gamma rays – out-of-field dose calculations can provide a more realistic estimation for secondary cancer risk analysis, as well as a wider range of therapeutic techniques for comparison.

Key words: radiation therapy, prostate, secondary cancer risk, MCNPX code

INTRODUCTION

Radiation therapy of prostate cancer is one of the more effective techniques in treating prostate malignancies. Both conventional and intensity-modulated methods have resulted in relatively successful outcomes for prostate cancer patients. The application of intensity-modulated radiation therapy (IMRT) and three-dimensional conformal therapy in the treatment of prostate cancer has resulted in higher tumor dose administration, accompanied by a lower normal tissue dose [1]. Using modern external radiation therapies, the 5-year freedom from relapse in patients with the T_1/T_2 disease (T_1 through T_4 describe the tumor size and status of spreading) has been reported as amounting to 65-85% [2]. Despite a greater dose of radiation delivered by these methods, the toxicity of the therapies has decreased considerably, because a smaller volume of the normal rectum receives high doses [2]. Thus, compared to other types of cancers, the disease-free period and survival rate in prostate cancer cases have increased dramatically. By increasing the life span of prostate cancer patients, the probability of secondary cancer risks from received out-of-field doses could prove to be significant [3]. In recent years, several studies have reported on the whole body effective dose from radiation therapy treatments [4-12]. It was found that using a multi-leaf collimator can decrease the amount of scattered photons and, consequently, cause a moderate reduction in out-of-field photon doses. In radiation therapy of the prostate, high energy photons are employed to provide the required penetration of the pelvic region. On the other hand, photoneutrons are produced in high energy photons (>10 MeV) and become a significant source for unwanted, out-of-field exposure for the prostate patient [13]. These neutrons with an effective energy range of 2 MeV have an average quality factor of 20 [14]. Numerous studies have been performed to identify the characteristics of the patient received dose by out-of-field photons and neutrons [1, 4, 6, 9, 15-18]. In addition to experimental investigations which were carried out using anthropomorphic phantoms and di-

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odes and thermoluminance dosimeters, some *in-vivo* studies have also proved that, with high energy photons, the dose received by the patient can be even higher, due to photoneutrons in conventional treatments. In recent studies, the Monte Carlo (MC) method and mathematical phantoms have shown their capabilities in estimating organ specific doses from photons and neutrons [19, 20]. In a MC study on prostate cancer, the contribution of scattered photons has been determined using the MC method, but neutron doses were not calculated [9]. In a study by Kry *et al*. [5], organ doses from scattered photons and neutrons were measured using a Rando phantom and thermoluminance dosimeters for different conventional and IMRT treatments of the prostate. In addition to this, neutrons captured in the body tissue of the patient and concrete walls of the room can generate gamma photons which may have a significant effect on the patient out-of-field dose and the effective dose of prostate cancer patients under radiation therapy involving high energy photon beams [19, 21, 22].

The aim of the current study was to calculate the specific organ doses and the effective dose from scattered photons, photoneutrons and capture gamma rays for conventional and IMRT treatments of the prostate with 18 MV photon beams using a MIRD-based mathematical phantom and the MCNPX MC code.

METHODS AND MATERIALS

Linac simulation and beam modeling

A Varian 2300C/D linac with a multi-leaf collimator (MLC) (80-leafs) was simulated for calculations in the current study (fig. 1). The MLC axis was along the lateral axis of the patient. A validated model of linac for an 18 MV photon beam was used in the study [23, 24]. The MLC leafs were set to build a circular beam with a diameter of 10 cm at the isocenter. This arrangement was used for all four beams in conventional treatments. To calculate the dose to the organs outside the treatment volume, two components should be considered. First, the scattered photons from the target volume and leakage radiation from the linac head have to be taken into account. The second component is related to the photoneutrons produced mainly in the linac head [21, 25]. To validate our model for photon leakage, a water phantom was located under the linac head at a distance of 100 cm from the photon source. A sphere with a diameter of 5 cm, at a distance of 1 m from the source outside the field size of 0 cm × 0 cm was defined and the photon dose tallied by a *F8 tally. The ratio of this dose to the dose in the water phantom at d_{max} for a 10 cm × 10 cm field size was considered as leakage radiation [9]. It amounted to 0.07%, less than the 0.1% limit for clinical linacs. The simulation also confirmed the suitability of the lead shielding for our linac model. To simulate real

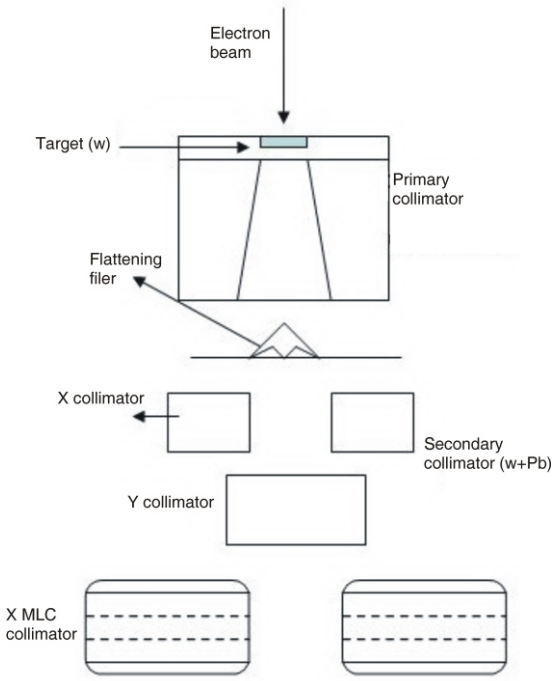

Figure 1. Schematic representaton of Varian 2300 C/D 18 MV MC model used in the current study

treatment conditions, a treatment room with a dimension of 6 m × 6 m × 4 m was simulated and the mathematical phantom and linac situated in the center of the treatment room (fig. 2).

Monte Carlo modeling for prostate treatment

The MIRD-based anthropomorphic phantom was built using MCNP4X MC code 2.4.0. [26]. The phantom resembled an adult man weighing 70 kg (fig. 3). An 18 MV photon beam model of Varian 2300 C/D was used to irradiate the prostate of the phantom. A

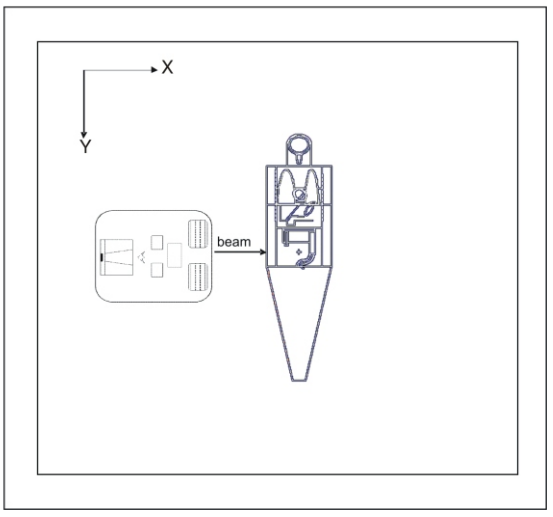

Figure 2. Simulated geometry of Varian 2300 C/D linac head, mathematical phantom and treatment room walls

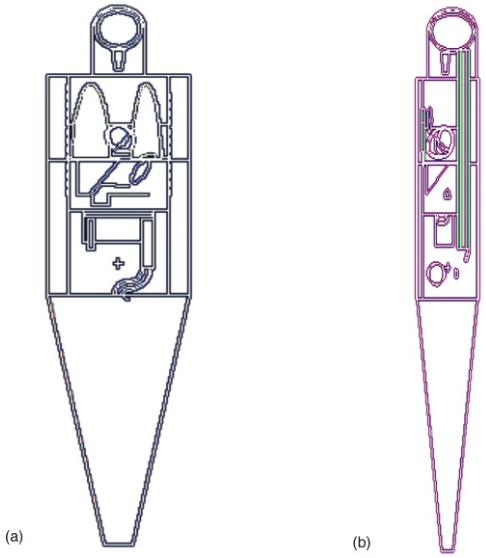

Figure 3. Representation of a mathematical male phantom plotted by the MCNPX MC code
(a) frontal view at z = 0, (b) lateral view at x = 0

four-field box technique, including two lateral fields, an anterior and a posterior one, was simulated. The average organ dose from the four fields was calculated and, based on these values, the effective dose was calculated. The rectum and bladder were partially irradiated by the direct beam.

A spherical cell with a radius of 2 cm at the approximate location of the prostate within the bladder and rectum was defined to resemble the prostate tumor and score the deposited energy at the isocenter. To avoid the primary radiation effect on the estimated effective dose, the rectum dose and irradiated part of the skin were excluded from effective dose calculations. The mathematical model was positioned at a source-to-axis distance of 100 cm from the photon source.

Dose depositions from scattered photon capture gamma rays were tallied in the selected organs of the mathematical phantom by a *F8 tally which scores the deposited energy in terms of MeV [26]. Using the mass of each organ in terms of kg and converting the energy from MeV to joule, the absorbed energy was calculated for each organ. For neutron dose calculation in the selected organs, the F6 tally which scores an energy deposition averaging a cell in terms of MeV/g was used. The simulations were performed in two steps. In the first one, the input file was run for photon dose calculations. Energy cut-offs of 10 keV and 500 keV were used for photons and electrons, respectively. In the second run, the energy deposited by photoneutrons and capture gamma rays was simulated. In order to obtain more accurate results, the statistical uncertainty of MC results for the tumor dose was less than 1%, but it varied for different organs in the out-of-field region. In general, the statistical uncertainty of MC results for all calculations was less than 3%. For cancer risk calculations, tissue weighing factors and the coefficient of cancer risk were derived from ICRP 103 (tab. 1) [14].

Table 1. Tissue weighting factor and nominal risk coefficient used in the current study for equivalent dose calculations derived from ICRP 103 [14]

Tissue	Tissue weighting factor	Nominal risk coefficient [cases per 10000 persons per Sv]
Thyroid	0.04	33
Lung	0.12	114
Esophagus	0.04	15
Stomach	0.12	79
Liver	0.04	30
Spleen	0.12	–
Pancreas	0.12	–
Kidney	0.12	–
Adrenals	0.12	–
Small intestine	0.12	–
Large intestine	0.12	–
Bladder	0.04	43
Testes	0.08	20
Skin	0.01	1000
Bone marrow	0.12	42

Effective dose estimation for IMRT treatments

The effective dose calculated for conventional treatment was then used for IMRT effective dose calculations using a modulation scaling factor. The results of previous studies suggest that an increase in the effective dose could be explained by the increase in the number of monitor units required for IMRT [5, 9, 10, 19, 27]. In other words, the relative increase in the out-of-field dose attributable to IMRT can, partly, be explained by the increase in the modulation scaling factor (MSF). In the current study, the MSF of 3.5 for an IMRT with 7 beams relative to the conventional box technique was used for dose calculations, as reported by a similar previous study [9]. In all simulations, including conventional and IMRT treatmens, a dose of 72 Gy was prescribed for the target volume, including a sphere resembling a prostate and an interior wall of a rectum. In accordance with previous studies and taking into consideration the new ICRP guidelines, 2% per Sv was considered in order to determine secondary cancer risk for elderly patients undergoing prostate radiation therapy [9, 14, 28].

RESULTS

Out-of-field organ equivalent doses from scattered photons, photoneutrons and capture gamma rays

Table 2. Scattered photon, neutron, and capture gamma dose equivalents for prostate cancer irradiation with an 18 MV photon averaged for the four field-box technique. Photon and neutron doses for the rectum are excluded from the calculations

Tissue or organ	Photon equivalent dose [μSv/Gy]	Neutron equivalent dose [μSv/Gy]	Capture gamma equivalent dose [μSv/Gy]	Accumulated equivalent dose from photons and neutrons [μSv/Gy]
Thyroid	4.5	13.2	4.3	22
Lungs	6.4	3.4	1.1	10.9
Esophagus	8.4	10.5	1.3	20.2
Stomach	26.9	8.7	3.8	39.4
Liver	37.3	12.9	3.3	53.5
Spleen	29.9	10.9	6.8	44.4
Pancreas	34.3	13.1	3.6	51
Kidney	32.3	14.0	2.5	48.8
Adrenals	16.2	8.8	2.1	27.1
Small intestine	29.0	14.7	4.2	47.9
Large intestine	53.4	10.9	5.3	69.6
Bladder	–	55.1	6.7	61.8
Testes	47.6	28.7	3.2	79.5
Skin	24.6	45.1	1.8	71.5
Bone marrow	20.1	17.1	2.7	39.9

are shown in tab. 2. Also, the total equivalent dose for a number of selected organs is shown in the last column of tab. 2.

It should be taken into account that other studies [9] and international authorities [14] have pointed out that organ doses cannot be used for absolute survival and hazard predictions. However, in accordance with previous studies, when considering the newly developed techniques, organ doses can be exploited in benefit-risk analysis. According to ICRP103, "there are situations in which the use of an effective dose is not appropriate and individual organ and tissue absorbed doses should be used instead. These include epidemiological studies, assessments of the probability of cancer, assessments of the possibility of tissue reactions, or assessments of doses when treatment or medical surveillance are needed". However, in some previous studies, the risks of secondary prostate cancer have been estimated for cases based on ICRP60 and NCRP116 provided tissue and radiation weighting factors and cancer risk [28, 29]. To compare our results with the reported data, the effective prostate dose was calculated and secondary cancer risk for some selected organs tabulated in tab. 3. Additionally, the effective dose was calculated using the ICRP 103 tissue weighting factor and MC calculated organ doses. The resulting effective doses from scattered photons, neutrons, and capture gamma rays were 723 mSv, 134 mSv, and 45 mSv for a 72 Gy prostate dose, respectively. The photon equivalent dose was 5.4 and 16 times higher than neutron and capture gamma rays equivalent doses, respectively. The total effective dose from the three components studied in the current study was 902 mSv for a 72 Gy tumor dose.

Table 3. Organ equivalent dose in terms of Sv and the probability of secondary cancer (cases per 10000 persons) per a 72 Gy prostate dose

Organ	Equivalent dose (SV) per 72 Gy tumor dose	Number of cases per 10000 person
Thyroid	1.58E-02	0.5
Lungs	7.85E-03	0.9
Esophagus	1.45E-02	0.2
Stomach	2.84E-02	2.2
Liver	3.85E-02	1.2
Bladder	4.45E-02	1.9
Testes	5.72E-02	1.1
Skin	5.15E-02	51.5
Bone marrow	2.87E-02	1.2

As stated previously, the organ and effective dose for IMRT treatments can be estimated by multiplying the MSF and the derived effective dose for conventional treatments. Effective dose calculations were determined for 7 beam IMRT treatments using a MSF of 3.5 provided by the similar studies of Stathakis *et al*. [9], and Howell *et al.* (2005) [17]. An effective dose of 3157 mSv was obtained for IMRT treatment. Taking into account the secondary cancer risk of 2% per Sv for an adult male patient, a probability of a secondary cancer risk of 1.8% and 6.3% was obtained for conventional and IMRT prostate treatments.

DISCUSSION

As seen in tab. 2, distant organs receive a higher neutron equivalent dose than the photon equivalent dose while, for the organs close to the primary beam, the photon equivalent dose dominates. It should be mentioned that the radiation weighting factor of 20 was used in equivalent dose calculations for neutrons, while a factor of 1 was used for photons. The radiation weighting factor for neutrons was a rounded average value considering the mean energy of 0.3-0.8 MeV neutrons produced in radiation therapy according to the ICRP103 report. The equivalent dose from capture gamma rays was smaller in comparison to the one of scattered photons and neutrons. However, if we consider the radiation weighting factor of 20 for neutrons, it can be concluded that the absorbed dose from capture gamma rays is higher than the neutron dose in relatively deep organs. In our study, the photon equiva-

lent dose was higher than the neutron equivalent dose in all organs except for the thyroid. It is in close agreement with the results of Reft *et al*. [27]. Moreover, the results are in close agreement with the results of Barquero *et al*. [19]. They calculated the absorbed organ dose from neutrons and capture gamma rays using a mathematical phantom for an 18 MV photon beam. However, they did not estimate the contribution of scattered photons in the organ absorbed dose. Also, the effective dose was not calculated in their study. Our results for the organ absorbed dose from scattered photons and neutrons are comparable with the measurements of Kry *et al.* on an anthropomorphic phantom [5]. In another study, Vanhavere *et al*. studied the out-of-field organ doses from an 18 MV prostate treatment and the results showed that the organs far away from the prostate, such as the thyroid, receive higher neutron than photon doses [10].

According to our findings which were tabulated in tab. 3, higher secondary cancer risks are obtained for skin, stomach, bladder, liver, and bone marrow. Based on this, it was concluded that both the equivalent dose and nominal risk coefficients are higher for these organs, especially for the skin. However, for the testes the dose is higher than for other organs, because of its proximity to the prostate. But, because of the smaller nominal risk coefficient for testes, the resulting secondary cancer risk is smaller in comparison to those of other organs, such as the bladder or liver.

Data derived from epidemiological studies have shown that an exposure to ionizing radiation above 50 mSv to 100 mSv increases the risk of secondary cancers such as prostate cancer and breast cancer in patients up to 30 years following the primary treatment [30]. Furthermore, studies have shown that induced cancers increase with time after radiation therapy. In the case of elderly prostate patients, induced cancers increase for about 1.5% at a time distance of 10 years after treatment [31]. So, our estimated cancer risk of 1.8% is comparable with previous results. A statistically significant and very small increase in secondary cancer risk after radiation therapy has been reported by several investigations [18, 30, 32]. In cases of prostate cancer, secondary lung cancers show an increase of 4% to 6% compared to prostate surgery. In a study by Followill *et al*, attributable secondary cancer likelihood was estimated as high as 4.5% and 8.4% for IMRT with 18 and 25 MV photon beams, respectively [4].

Although equivalent doses for specific organs have been published in previous studies, only one or two radiations participating in the total out-of-field absorbed dose were reported. For example, Kry *et al*. showed that neutrons are a significant contributor to out-of-field organ doses and that the estimated risk for conventional and IMRT from neutrons amounted to 1.7% and 5.1%, respectively [6]. A similar study on IMRT by an 18 MV beam revealed that the dose equivalent from photoneutrons could lead to a 2% likelihood of secondary cancer for a 70 Gy tumor dose [33]. However, it is worth mentioning that a cancer risk coefficient of 5% per Sv was used in theses studies. In the MC study by Stathakis *et al*. on conventional and IMRT of prostate cancer, the scattered photon dose was calculated and a whole body equivalent dose of 780 and 1450 mSv for a 72 Gy tumor dose obtained. Our effective dose from photons was very similar to their reported value for conventional prostate treatment. However, they did not calculate the neutron dose contribution and based on previous studies [5], it was assumed that the neutron dose could be 2 mSv to 5 mSv for the same number of MU used in their study. Based od this, they concluded that this might cause an increase of 4% to 10% in cancer risk to the prostate patient.

The results of the study by *in vivo* measurement show that, for prostate patients treated with 18 MV IMRT, the out-of-field photon dose equivalent was up to 7 times greater than the neutron dose equivalent and that the neutron dose equivalent varied by 2 mSv/Gy to 6 mSv/Gy for different therapy machines. In our study, the photon equivalent dose was 5.4 times higher than the neutron equivalent dose which was slightly smaller, but in agreement with the study.

CONCLUSIONS

Our results have shown that the photon equivalent dose is the dominant source of the out-of-field effective dose for patients undergoing prostate radiation therapy. But the neutron equivalent dose is another strong contributor. Also, the effect of capture gamma rays cannot be neglected for 18 MV beam treatments. Developments in cancer treatments and, consequently, the increase in the life span of patients might permit secondary cancers to appear after primary treatment. Therefore, in order to find a practical strategy for solving this problem in the near future, we believe that it is necessary to have estimations on patients' effective doses from different radiation therapy techniques so as to make reliable risk-benefit comparisons between radiotherapy techniques. Otherwise, our study suggests that for out-of-field dose calculations in radiotherapy techniques employing high energy photon beams, taking into consideration all contributors in organ doses including scattered photons, neutrons, and capture gamma rays, can provide more realistic estimations for secondary cancer risk analysis and reliable comparison of different techniques.

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Мохамад МОХАМАДЗАДЕХ, Асгхар МЕСБАХИ

МОНТЕ КАРЛО ПРОЦЕНА ДОЗА У ОКОЛНИМ ОРГАНИМА КОЈЕ ПОТИЧУ ОД РАСЕЈАНИХ ФОТОНА, ФОТОНЕУТРОНА И ГАМА ЗАХВАТА У РАДИОТЕРАПИЈИ ПРОСТАТЕ

У раду су процењене ефективне дозе за органе који су изван директног поља зрачења, у случају радијационе терапије канцера простате, применом MCNPX Монте Карло кода и одговарајућег математичког модела примењеног фантома. Дозе у органима које потичу од расејаних фотона, фотонеутрона и гама захвата прорачунате су за случај 18 MeV-ског фотонског снопа. Наши резултати показују да главни допринос дозе у деловима тела који нису директно изложени снопу потиче од расејаних фотона. Укупна ефективна доза која потиче од расејаних фотона, неутрона и гама захвата износи 723 mSv, 134 mSv и 45 mSv при предатој дози простате од 72 Gy. За конвенционални третман разматран у овом раду, укупна ефективна доза која потиче од ове три компоненте зрачења износи 902 mSv за дозу од 72 Gy која је предата тумору. Имајући у виду податак да ризик од секундарног канцера код одраслог пацијента мушког пола износи 2% по сиверту, према нашим резултатима вероватноће добијања секундарног канцера износе 1,8% и 6,3% у случају третирања канцера простате конвенционалном и интензитет-модулисаном техником, респективно. Наша анализа показује да, приликом прорачуна дозе органа који нису деректно изложени снопу, узимање у обзир свих врста доприноса који потичу од расејаних фотона, неутрона и гама захвата, пружа много реалистичнију процену ризика од појаве секундарног канцера.

Кључне речи: радиотерапија, простата, ризик секундарног канцера, MCNPX програм