A comparative study on the risk of second primary cancers in out-of-field organs associated with radiotherapy of localized prostate carcinoma using Monte Carlo-based accelerator and patient models

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Purpose: A physician's decision regarding an ideal treatment approach (i.e., radiation, surgery, and/or hormonal) for prostate carcinoma is traditionally based on a variety of metrics. One of these metrics is the risk of radiation-induced second primary cancer following radiation treatments. The aim of this study was to investigate the significance of second cancer risks in out-of-field organs from 3D-CRT and IMRT treatments of prostate carcinoma compared to baseline cancer risks in these organs.

Methods: Monte Carlo simulations were performed using a detailed medical linear accelerator model and an anatomically realistic adult male whole-body phantom. A four-field box treatment, a four-field box treatment plus a six-field boost, and a seven-field IMRT treatment were simulated. Using BEIR VII risk models, the age-dependent lifetime attributable risks to various organs outside the primary beam with a known predilection for cancer were calculated using organ-averaged equivalent doses.

Results: The four-field box treatment had the lowest treatment-related second primary cancer risks to organs outside the primary beam ranging from 7.3×10^{-9} to $2.54 \times 10^{-5}\%/MU$ depending on the patients age at exposure and second primary cancer site. The risks to organs outside the primary beam from the four-field box and six-field boost and the seven-field IMRT were nearly equivalent. The risks from the four-field box and six-field boost ranged from 1.39×10^{-8} to $1.80 \times 10^{-5}\%/MU$, and from the seven-field IMRT ranged from 1.60×10^{-9} to $1.35 \times 10^{-5}\%/MU$. The second cancer risks in all organs considered from each plan were below the baseline risks.

Conclusions: The treatment-related second cancer risks in organs outside the primary beam due to 3D-CRT and IMRT is small. New risk assessment techniques need to be investigated to address the concern of radiation-induced second cancers from prostate treatments, particularly focusing on risks to organs inside the primary beam. © 2010 American Association of Physicists in Medicine. [DOI: [10.1118/1.3367012](https://doi.org/10.1118/1.3367012)]

Key words: Monte Carlo, second cancer, out-of-field dose

I. INTRODUCTION

Despite high incidence rates of localized prostate carcinoma, a common consensus among physicians regarding the ideal treatment approach still remains to be reached.^{1–6} Traditionally, the choice of treatment (i.e., radiation, surgery, and/or hormonal) is based on several factors including general fitness of the patient, life expectancy, clinical stage of the cancer, and associated toxicities.^{7–10} The risk of developing second primary cancers after radiation treatments is another factor that may be considered.^{7–16} Recently, there has been a renewed concern about radiation-induced second cancers associated with some of the new radiation treatment techniques, such as intensity-modulated radiation therapy (IMRT) and tomotherapy.¹⁵ Compared to conventional techniques, IMRT and tomotherapy aim to improve dose conformity and uniformity at the cost of requiring more fields and longer treatment times, resulting in elevated organ doses outside the treatment field and subsequently higher second can-

cer risks to these organs.^{17–19} For prostate patients, it is still unclear whether the heightened concern of the increased second primary cancer risks to out-of-field organs due to these new treatment techniques is necessary.

Epidemiological studies have concluded that linking second primary cancers in out-of-field organs of prostate carcinoma patients to radiation treatments is difficult.^{8,20} The second cancer risk from radiation treatments is convoluted by genetic and environmental factors. For example, higher incidences of second primary lung cancers could be due to increased smoking rates in radiotherapy patients.⁸ The assessment of second primary cancer risks using dose-dependent risk models has been performed in order to improve our understanding of risks associated with prostate carcinoma treatments.^{17,23–25} The conventional risk assessment technique quantifies second primary cancer risks in regions away from the treatment site in order to comply with the dose limitation imposed by the currently available risk models.^{17,21,23} These models are only valid for doses ranging

from about 0.05 to 2.5 Sv.¹⁵ However, previous attempts to compare treatment-related second primary cancer risks have greatly simplified the patient geometry potentially leading to inaccurate organ doses. In addition, previous attempts have failed to utilize the most relevant risk models. Therefore, there is an important need to accurately assess the second primary cancer risk in prostate carcinoma patients treated with different radiation techniques.²²

The aim of this work is to perform a comparative study investigating the significance of second cancer risks in out-of-field organs from different radiation treatments of prostate carcinoma. We are in a good position to do this study because we have previously combined a newly developed RPI-adult male (RPI-AM) computational phantom and a detailed model of a Varian Clinac accelerator (Varian Medical Systems, Palo Alto, CA) in a Monte Carlo code to calculate volume-averaged organ doses from selected 3D conformal radiation therapy (3D-CRT) and IMRT prostate treatment plans.^{26,27} In this study, we adopt these Monte Carlo-based organ doses with the latest cancer risk data from BEIR VII report²⁸ to estimate radiation-induced second cancer risks associated with treatments for an adult male. This work is meant to provide accurate second cancer risks to organs away from the primary beam of 3D-CRT and IMRT treatments.

II. METHODS AND MATERIALS

II.A. Organ doses in the RPI-adult male computational phantom

In a previous paper, we described the integration of a detailed Varian Clinac linear accelerator model with an anatomically realistic computational phantom of an adult male in the Monte Carlo code MCNPX to calculate organ doses from selected prostate treatment plans.²⁶ The detailed model of the accelerator was developed based on a combination of blueprints provided by the machine manufacturer and information provided in the literature.²⁶ Both beam-line and secondary shielding components were considered. The Monte Carlo model of the accelerator, operating at both 6 and 18 MV beam energies, underwent thorough in-field and out-of-field validation testing where calculated doses were in good agreement with measured doses for all field sizes.²⁶ The whole-body computational phantom used in this work was the RPI-AM phantom that was designed to represent an average adult male patient.²⁹ Over 121 organs and tissues were defined in the model, including a set of detailed bone components (cavity, spongiosa, and cortical). Three-dimensional renderings of the accelerator model and of the RPI-AM model are provided in Fig. 1.

Using the validated accelerator model, organ equivalent doses to the RPI-AM computational phantom were calculated for three different radiation treatments of prostate cancer. The first treatment was a four-field box technique with two sets of opposing fields in the AP/PA and RT/LT directions. The AP field was delivered using a 6 MV beam in an effort to spare as much of the anterior rectum as possible. The other fields were delivered with an 18 MV beam to help

FIG. 1. 3D rendering of the RPI-AM computational phantom and accelerator model.

reduce the dose to the femoral heads. The prescribed dose for the box treatment was 45.0 Gy. The second treatment considered was the same box delivery plus a six-field boost. All fields were delivered with 18 MV beams. The total prescribed dose for the box plus boost treatment was 79.2 Gy. The final treatment was a seven-field IMRT treatment using 6 MV beams. The prescribed dose for the IMRT treatment was 76.0 Gy. Table I summarizes these plans in detail. The equivalent doses per monitor unit (MU) were calculated in several organs that have shown a predilection for cancer.²⁸ These organs include the stomach, colon, liver, lung, esophagus, pancreas, brain, active bone marrow, small intestine,

TABLE I. A four-field box treatment, a four-field box treatment plus a six-field boost and a seven-field IMRT treatment used in this study including beam energy, gantry position, field size, and treatment depth.

	Beam energy (MeV)	Gantry position (deg)	Field size (cm ²)	Tumor depth (cm)
Four-field box	6	0	7 × 9.54	11.7
	18	90	7 × 7.96	15.4
	18	180	7 × 9.96	8.38
	18	270	7 × 7.64	16.6
Six-field boost	18	45	7 × 10.46	14.0
	18	90	7 × 7.96	15.4
	18	135	7 × 9.96	13.3
	18	225	7 × 10.46	13.5
	18	270	7 × 7.64	16.6
	18	315	10 × 10	14.8
Seven-field IMRT	6	0	8 × 10	11.7
	6	51	8.5 × 10	14.6
	6	102	8.5 × 9	15.0
	6	154	8.5 × 10.5	11.0
	6	206	8.5 × 10	11.0
	6	257	8.5 × 9.5	16.1
	6	308	8 × 10	15.6
	6			

spleen, gall bladder, heart, lymph nodes, kidneys, and thyroid. Only organs outside of the primary radiation beam were considered. Therefore, organs such as the testis, bladder, skin, and prostate were excluded. The equivalent dose to the colon was approximated by the dose to the transverse colon. Finally, the equivalent dose to the lymph nodes was approximated as the weighted average of the dose to the lymph nodules in the head, arms, and leg. Also note that for the 18 MV beams, the neutron doses were multiplied by an energy-dependent radiation weighting factor from ICRP-60.³⁴

II.B. Second cancer risk calculations

Second cancer risks from 3D-CRT and IMRT treatments were calculated using the BEIR VII methodology.²⁸ Details of this methodology can be found in Chapter 12 of the BEIR VII report, but we will briefly describe it below. This approach was first adopted by Zacharatou Jarlskog and Paganetti²⁵ to calculate risk from proton therapy and later used for other risk analysis studies.^{19,30}

The relationship between the risk of second cancer induction in exposed populations and the unexposed populations can be quantified by their difference known as the excess absolute risk (EAR) or their ratio known as the relative risk (RR). Typically, the excess relative risk (ERR) is used instead of RR, where the ERR is equivalent to $RR - 1$. In this study, the age-dependent organ-specific ERRs and EARs were calculated for a variety of sites. The BEIR VII report defines the ERR and EAR as a function of attained age (a) (Ref. 28)

$$\text{ERR and EAR}(s, t, a, D) = \rho(D) \cdot \beta_s \cdot \exp(\gamma e) \cdot a^\eta, \quad (1)$$

where e is the age at treatment, D is the total dose equivalent received, s is the gender of the patient, and t is the time since the treatment. For solid tumor sites, the parameter $\rho(D)$ is a linear function of dose. The model parameters β_s and η are provided for several organs in the BEIR VII report and are typically an order of magnitude different for the EAR and ERR. The parameter γ modifies the exponential to reflect the fact that the ERR decreases with increasing age at exposure for those exposed less than 30 yr of age. However, the BEIR committee suggests that for patients over 30 at the time of the treatment, the exponential is replaced by unity.²⁸ Normalizing the attained age to the reference age of 60 the ERR becomes

$$\text{ERR and EAR}(s, t, a, D) = D \cdot \beta_s \cdot (a/60)^\eta. \quad (2)$$

Using the values of ERR and EAR, we also calculated the lifetime attributable risk (LAR), which is defined as the probability that an irradiated individual will develop a cancer during their lifetime.²⁸ The BEIR VII recommends calculating LAR as a weighted average (on a logarithmic scale) between the ERR and EAR and is calculated by

$$\text{LAR}(D, e) = \left(\int_{a+L}^{100} M(D, e, a)_{\text{ERR}} \cdot S(a)/S(e) da \right)^{0.7} \times \left(\int_{a+L}^{100} M(D, e, a)_{\text{EAR}} \cdot S(a)/S(e) da \right)^{0.3}, \quad (3)$$

where

$$M(D, e, a)_{\text{ERR}} = \text{ERR}(D, e, a) \cdot \lambda_l^c \quad \text{and}$$

$$M(D, e, a)_{\text{EAR}} = \text{EAR}(D, e, a) \quad (4)$$

and $S(a)/S(e)$ is the probability of the patient surviving from their age at exposure (e) to their attained age (a) and were determined by the life-span tables provided by Anderson and DeTurk.³¹ The latent period (L) recommended by BIER VII is 5 yr for solid cancer. The parameters λ_l^c can be considered the baseline cancer risk for the exposed individual and were based on data presented in the SEER Cancer Statistics Review.³² For most organs, the weights of 0.7 and 0.3 are recommended by the BEIR VII committee for the ERR and EAR integrals, respectively. These weights were chosen because there is stronger support for relative risk than absolute risk transport and the ERR models are likely less vulnerable to epidemiological biases.²⁸ For lung cancer risk, the logarithmic weights of 0.7 and 0.3 were reversed in Eq. (3) because of evidence that the interaction of smoking and radiation effects in atomic bomb survivors is additive.²⁸ Also, for thyroid cancer there is no EAR model and the LAR was calculated by using only the ERR.

In order to correct the ERR and LAR for dose fractionation during 3D-CRT and IMRT treatments the ERR and LAR were each divided by the nominal dose and dose rate effectiveness factor (DDREF) of 1.5 as suggested by the BEIR VII report. Only the photon contribution to the dose was corrected since the neutrons are considered high LET radiation. The DDREF is used to extrapolate data from acute high dose rate exposures to low dose and low dose rate exposures.

III. RESULTS

The total organ equivalent doses calculated in a previous paper were used to estimate the radiation-induced second cancer risk to patients undergoing treatments for prostate cancer. The equivalent doses to organs outside of the primary beam from a four-field 3D-CRT treatment, a four-field 3D-CRT treatment with a six-field boost, and a seven-field IMRT treatment are provided in Table II. All data are normalized per treatment MU.

Table III provides LAR normalized per MU (%/MU) for a variety of organs outside of the primary beam from the three different treatment plans considered. This table can be used as a guide for clinicians and researchers who would like to estimate the second cancer risks to these organs from these treatments. Several general conclusions can be drawn from this table. The LAR decreases as a function of age at exposure, which is a general feature of the risk model. This is

TABLE II. Total dose equivalent per MU to selected organs from a four-field and six-field 3D-CRT and a seven-field IMRT treatment for prostate cancer. Accompanying each value is the percent relative error calculated for each value.

Organ	Total equivalent dose ($\mu\text{Sv}/\text{MU}$)		
	Four-field box	Four-field box+Six-field boost	Seven-field IMRT
Brain	3.5 (2.4)	5.9 (2.4)	1.2 (3.6)
Thyroid	5.4 (9.4)	10.2 (17.5)	1.6 (10.8)
Esophagus	3.1 (18.3)	7.8 (10.4)	1.8 (3.2)
Lung	5.8 (2.4)	13.4 (1.5)	2.9 (2.0)
Spleen	10.1 (2.2)	20.2 (2.3)	4.3 (3.6)
Stomach	8.1 (2.2)	17.0 (1.5)	5.3 (2.9)
Colon	16.9 (1.8)	44.1 (1.4)	11.1 (3.2)
Pancreas	7.9 (5.6)	16.7 (3.8)	4.2 (3.5)
Liver	7.8 (1.7)	17.9 (1.1)	4.9 (2.0)
Kidneys	13.2 (3.8)	28.6 (2.3)	5.8 (3.7)
Lymph node	12.1 (8.9)	56.0 (2.9)	7.1 (1.6)

intuitive since older patients are less likely to live long enough to develop a second primary cancer. Also, for a given treatment plan, the organs with the highest risks are typically closer to the primary beam suggesting that higher radiation doses contribute to higher second cancer risks. However, this is not always the case. For example, even though the thyroid receives higher dose than the brain, the second cancer risk in the thyroid is lower than the brain for all treatments.

Not apparent in Table III are the differences in risks between different treatment plans. Figure 2 provides the absolute LARs to different organs for an adult male exposed at 60 yr of age. The normalized LARs provided above were multiplied by the total number MUs expected for the treatments under consideration. According to our plans, clinically relevant MU values of 9450, 16 290, and 41 160 were used for the box treatment, the box treatment plus boost, and the IMRT treatment, respectively. As seen in the figure, for most organs (seven out of 11 sites) the four-field box plus six-field boost treatment resulted in the largest risks, followed by the IMRT and the four-field box treatment. However, for some sites the IMRT had the highest associated risks (four out of 11 sites). In addition to LARs, Fig. 2 also provides the age-specific baseline risk taken from the SEER Cancer Statistics Review.³² The baseline cancer risk is defined as the probability of developing cancer in a particular cancer site over a lifetime of 100 yr. As the figure illustrates, the baseline risks greatly exceed the second cancer risks for each organ site under consideration.

IV. DISCUSSION

The criteria for selecting the best treatment of prostate carcinoma include multiple factors.¹⁰ Clinicians have long acknowledged the associated second primary cancer risks from radiation treatments,^{7–13} but there are mixed opinions on the significance of these risks relative to other metrics especially in out-of-field organs. Epidemiological studies

have reported elevated second primary cancer risks in radiotherapy patients compared to surgery patients, but linking these risks to radiation exposure is challenging due to confounding genetic and environmental risk factors. On the other hand, risk models in combination with organ dose data are useful tools to estimate second primary cancer risks.

Our study examined the risk to organs outside the primary beam from different radiation treatments of prostate carcinoma. Detailed Monte Carlo simulations show that the LARs, due to radiation exposure to several organs outside of the primary beam, are less than the baseline risks to these organs for three different prostate radiotherapy treatments. Based on these results, we feel that the conventional risk assessment technique overemphasizes the treatment-related second cancer risks to organs outside the treatment field where the risks are much lower than the baseline risks for the patient. Even though the risks to organs within the treatment field are presumably less than the baseline risk, we strongly suggest that more consideration be given to these organs when the risks from prostate treatments are assessed, especially when treatment options are debated. To deal with the challenge of high dose regions in the primary beam, modifications to the standard dose-response relationship have been attempted and utilized.^{18,19,33}

IV.A. Comparison of second cancer risks from different treatments

Another outcome of this study was a comparison of the second cancer risks outside of the primary beam between 3D-CRT and IMRT treatments. Previous studies suggest that IMRT treatments are always associated with elevated doses outside the primary beam compared to 3D-CRT treatments.¹⁴ However, as shown in this study, this relationship does not hold for all 3D-CRT and IMRT treatments. For both conventional treatments, 18 MV beams were used to help reduce dose to the femoral heads for all fields except the AP field, which used a 6 MV beam to spare dose to the anterior rectum. Each of the seven fields in the IMRT treatment used 6 MV beams. Similar to previous studies, organs outside the primary beam had higher risks from the IMRT treatment compared to the 3D-CRT box treatment.¹⁷ However, the risks in most sites were comparable between the 3D-CRT box plus boost treatment and the IMRT treatment, wherein seven out of 11 sites the 3D-CRT box plus boost treatment risk was only slightly higher than the IMRT treatment risks. In general, the risks were higher in organs further away from the treatment field from the 3D-CRT box plus boost treatment. The larger risks from the 3D-CRT box plus boost treatment could be due to differences in beam energy, particularly since the 18 MV beam in the 3D-CRT treatments produces neutrons. Unlike photons, neutrons are not corrected for fractionation and neutron doses are not divided by a DDREF. Therefore, the neutron dose in organs may be significant, particularly in organs further away from the treatment volume where the photon dose once corrected for fractionation is less dominant. Also, most of these organs are located at shallower depths compared to organs in the abdominal re-

TABLE III. This table shows the LAR as a function of organ and age at exposure (yr) for the three different treatments considered, including the four-field box treatment, the four-field box treatment plus the six-field boost, and the seven-field IMRT treatment.

		LAR (%/MU)				
		Age at exposure (yr)				
		40	50	60	70	80
Four-field box	Organ					
	Brain	8.26×10^{-6}	6.72×10^{-6}	4.70×10^{-6}	2.74×10^{-6}	1.10×10^{-6}
	Thyroid	2.19×10^{-7}	7.30×10^{-8}	2.19×10^{-8}	7.30×10^{-9}	0.00×10^{00}
	Esophagus	6.45×10^{-6}	5.25×10^{-6}	3.68×10^{-6}	2.14×10^{-6}	8.63×10^{-7}
	Lung	7.54×10^{-6}	7.32×10^{-6}	6.45×10^{-6}	4.71×10^{-6}	2.47×10^{-6}
	Spleen	1.81×10^{-5}	1.48×10^{-5}	1.03×10^{-5}	6.01×10^{-6}	2.43×10^{-6}
	Stomach	2.34×10^{-6}	2.16×10^{-6}	1.73×10^{-6}	1.21×10^{-6}	6.06×10^{-7}
	Colon	2.18×10^{-5}	2.02×10^{-5}	1.68×10^{-5}	1.16×10^{-5}	5.36×10^{-6}
	Liver	1.85×10^{-6}	1.67×10^{-6}	1.23×10^{-6}	7.04×10^{-7}	2.64×10^{-7}
	Pancreas	1.64×10^{-5}	1.34×10^{-5}	9.36×10^{-6}	5.44×10^{-6}	2.20×10^{-6}
	Kidneys	2.54×10^{-5}	2.07×10^{-5}	1.45×10^{-5}	8.42×10^{-6}	3.40×10^{-6}
Four-field box+Six-field boost	Lymph node	2.40×10^{-5}	1.95×10^{-5}	1.37×10^{-5}	7.95×10^{-6}	3.21×10^{-6}
	Brain	1.38×10^{-5}	1.13×10^{-5}	3.94×10^{-6}	4.59×10^{-6}	1.85×10^{-6}
	Thyroid	4.16×10^{-7}	1.39×10^{-7}	2.08×10^{-8}	1.39×10^{-8}	0.00×10^{00}
	Esophagus	1.69×10^{-5}	1.38×10^{-5}	4.83×10^{-6}	5.61×10^{-6}	2.27×10^{-6}
	Lung	1.76×10^{-5}	1.71×10^{-5}	7.54×10^{-6}	1.10×10^{-5}	5.76×10^{-6}
	Spleen	4.30×10^{-5}	3.50×10^{-5}	1.23×10^{-5}	1.43×10^{-5}	5.75×10^{-6}
	Stomach	4.98×10^{-6}	4.61×10^{-6}	1.85×10^{-6}	2.58×10^{-6}	1.29×10^{-6}
	Colon	5.80×10^{-5}	5.37×10^{-5}	2.23×10^{-5}	3.09×10^{-5}	1.43×10^{-5}
	Liver	4.39×10^{-6}	3.97×10^{-6}	1.46×10^{-6}	1.67×10^{-6}	6.27×10^{-7}
	Pancreas	3.48×10^{-5}	2.84×10^{-5}	9.92×10^{-6}	1.15×10^{-5}	4.66×10^{-6}
	Kidneys	5.53×10^{-5}	4.50×10^{-5}	1.58×10^{-5}	1.83×10^{-5}	7.39×10^{-6}
Seven-field IMRT	Lymph node	1.07×10^{-4}	8.74×10^{-5}	3.06×10^{-5}	3.56×10^{-5}	1.44×10^{-5}
	Brain	2.06×10^{-6}	1.68×10^{-6}	1.18×10^{-6}	6.84×10^{-7}	2.76×10^{-7}
	Thyroid	4.80×10^{-8}	1.60×10^{-8}	4.80×10^{-9}	1.60×10^{-9}	0.00×10^{00}
	Esophagus	3.10×10^{-6}	2.52×10^{-6}	1.76×10^{-6}	1.03×10^{-6}	4.14×10^{-7}
	Lung	3.02×10^{-6}	2.93×10^{-6}	2.58×10^{-6}	1.89×10^{-6}	9.86×10^{-7}
	Spleen	7.40×10^{-6}	6.02×10^{-6}	4.21×10^{-6}	2.45×10^{-6}	9.89×10^{-7}
	Stomach	1.43×10^{-6}	1.33×10^{-6}	1.06×10^{-6}	7.42×10^{-7}	3.71×10^{-7}
	Colon	1.35×10^{-5}	1.25×10^{-5}	1.04×10^{-5}	7.22×10^{-6}	3.33×10^{-6}
	Liver	1.03×10^{-6}	9.31×10^{-7}	6.86×10^{-7}	3.92×10^{-7}	1.47×10^{-7}
	Pancreas	7.22×10^{-6}	5.88×10^{-6}	4.12×10^{-6}	2.39×10^{-6}	9.66×10^{-7}
	Kidneys	9.98×10^{-6}	8.12×10^{-6}	5.68×10^{-6}	3.31×10^{-6}	1.33×10^{-6}
	Lymph node	1.22×10^{-5}	9.94×10^{-6}	6.96×10^{-6}	4.05×10^{-6}	1.63×10^{-6}

gion closer to the primary beam. Neutrons are most likely to deposit energy at shallower depths in a patient.²⁷ The elevated neutron doses in superficial organs from the 3D-CRT box plus boost treatment contributed to the total organ doses that exceeded the total doses to these organs during the IMRT treatment, as shown in Figs. 3(a)–3(c).

IV.B. Comparison of calculated risks with other studies

There are apparent differences between our risk estimates and those provided by others.^{17,24} These differences can be explained by differences in the dosimetric methods and risk models that were used in these studies. A comparison of organ doses between our study and doses provided by Kry *et*

*al.*¹⁷ are provided in Table IV. Similar to Kry *et al.*,¹⁷ many groups have estimated second cancer risks based on pointwise dose measurements in physical anthropomorphic phantoms. Measurements of this nature can be extremely laborious, requiring placement of several dosimeters in cavities representing individual organs. Consequently, clinical implementation of these measurements on a patient-by-patient basis would be difficult. Also, measurements in phantoms can often be inaccurate since dosimetry locations can be uncertain, patient anatomy is unrealistic, and pointwise measurements can overestimate or underestimate the true volume-averaged organ dose. In this study, we used a detailed computational adult male phantom to calculate organ-averaged equivalent doses. Other studies have estimated the

FIG. 2. LARs for different anatomical sites outside of the primary beam for an adult prostate patient exposed at 60 yr of age. Also provided is the age-specific baseline risk for the same individual taken from the SEER Cancer Statistics Review (Ref. 32).

scatter and leakage radiation based on parameterized models or single measurement points. Our study used a validated Monte Carlo model of the medical accelerator to calculate the dose contributions from these sources. The differences in the dosimetry methods some of the differences in the estimated risks even though similar treatments were studied.

Table V provides a comparison of organ-specific risks from various treatments between our calculations and those provided by Kry *et al.*¹⁷ Another factor contributing to the discrepancies between our results and risks reported by others is due to differences in risk models. The most utilized risk model for second cancer assessment from radiation treatments has been that of the International Commission on Radiological Protection (ICRP) in the form of fatal cancer risk coefficients.³⁴ However, fatal cancer risk coefficients have major limitations when applied to radiotherapy treatments, particularly in the case of prostate treatments.¹⁵ By definition, risk coefficients are averaged over both sexes and all ages, which can be problematic when applied to specific cancer patients. In addition, the end point for these coefficients is cancer mortality, even though cancer incidence is arguably more accurate and clinically relevant. For prostate cancer patients, there are obvious shortcomings when using ICRP risk coefficients since these patients are always male and on average over 65 yr of age. On the other hand, the recently

TABLE IV. Comparison of organ doses from this study with calculated organ doses reported by Kry *et al.* (Ref. 17).

Organ	Dose ($\mu\text{Sv}/\text{MU}$)			
	3D-CRT (box+boost)		IMRT	
	Our results	Kry <i>et al.</i>	Our results	Kry <i>et al.</i>
Stomach	17.0	23.6	5.3	8.2
Colon	44.1	49.4	11.1	19.0
Esophagus	7.8	9.8	1.8	3.2
Thyroid	10.2	13.0	1.6	2.5

(a)

(b)

(c)

FIG. 3. Contribution from photons and neutrons to LARs from the (a) box treatment, (b) box plus boost treatment, and (c) IMRT treatment.

released BEIR VII report improves on these limitations by providing age-dependent sex-specific risk models, as well as providing the option of determining cancer incidence and cancer mortality risks.²⁸ The large differences between risks in Table V is most likely due to the conservativeness of the ICRP risk models where risk coefficient are averaged over all sexes and ages. This hypothesis is supported by a recent report by Kry *et al.*³⁵ that shows a significant reduction in the calculated risk using the BEIR VII risk coefficients.

IV.C. Uncertainties

Finally, we discuss the uncertainties associated with the second cancer risk data provided in this paper. The statistical errors in the volume-averaged organ doses are provided in

TABLE V. Comparison of calculated risks from this study with calculated risks reported by Kry *et al.* (Ref. 17).

Organ	Organ-specific risk (%)			
	3D-CRT (box+boost)		IMRT	
	Our results	Kry <i>et al.</i>	Our results	Kry <i>et al.</i>
Stomach	0.03	1.3	0.04	2.1
Colon	0.3	2.6	0.4	4.8
Esophagus	0.07	0.5	0.07	0.8
Thyroid	3.1×10^{-4}	0.7	1.92×10^{-4}	0.6

Table I. The errors are small for a majority of the organs (less than 5%). However, for a few organs that are located at larger distances from the field edge the errors exceed 10%. In addition, for organ doses that contain contributions from neutrons, another source of uncertainty is from the radiation weighting factor. We used radiation weighting factors recommended by ICRP, which provides a continuous neutron weighting factor as a function of neutron energy.³⁶ The radiation weighting factor is derived from RBE values, and there are large uncertainties associated with neutron RBE values because of limited human and animal data to draw upon.³⁷ Uncertainties in the neutron RBE value reaching 50% have been reported.³⁰

The largest source of uncertainty extends from the risk model, particularly in the fitting parameters and the assumption that the linear dependence of the solid cancer risks on dose extends to the low dose range (<0.05 Sv).²⁸ A majority of the epidemiological data used to produce the fitting parameters is based on atomic bomb survivor data. There are many confounding factors that limit the accuracy of this data. For example, the smoking incidence among the atomic bomb survivors is not well documented. Overall, the uncertainties in the fitting parameters of the risk model likely exceed 50%.²⁸

V. CONCLUSION

The second primary cancer risks were calculated in adult males undergoing radiotherapy treatments for prostate carcinoma. Detailed Monte Carlo simulations involving multiple treatment plans showed that the 3D-CRT box treatment had the lowest associated risks, and the risks were comparable between 3D-CRT box treatment plus boost and an IMRT treatment. In all sites considered, the overall second primary cancer risks were lower than the baseline risks, which were derived from the SEER Cancer Statistics Review. These findings suggest that risks to organs outside of the treatment volume are minimal and that new risk assessment techniques need to be investigated to address the increasing concern of radiation-induced second cancers from prostate treatments. In future works, we will consider risks to organs in the primary beam from prostate treatments. The risks to organs inside the primary radiation field from prostate radiotherapy treatments will be assessed using risk models such as those

proposed by Schneider *et al.*,³³ thus providing a more useful metric to aid in the decision-making process toward an optimal treatment choice.

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