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Calculated organ doses from selected prostate treatment plans using Monte Carlo simulations and an anatomically realistic computational phantom

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Abstract

There is growing concern about radiation-induced second cancers associated with radiation treatments. Particular attention has been focused on the risk to patients treated with intensity-modulated radiation therapy (IMRT) due primarily to increased monitor units. To address this concern we have combined a detailed medical linear accelerator model of the Varian Clinac 2100 C with anatomically realistic computational phantoms to calculate organ doses from selected treatment plans. This paper describes the application to calculate organ-averaged equivalent doses using a computational phantom for three different treatments of prostate cancer: a 4-field box treatment, the same box treatment plus a 6-field 3D-CRT boost treatment and a 7-field IMRT treatment. The equivalent doses per MU to those organs that have shown a predilection for second cancers were compared between the different treatment techniques. In addition, the dependence of photon and neutron equivalent doses on gantry angle and energy was investigated. The results indicate that the box treatment plus 6-field boost delivered the highest intermediate- and low-level photon doses per treatment MU to the patient primarily due to the elevated patient scatter contribution as a result of an increase in integral dose delivered by this treatment. In most organs the contribution of neutron dose to the total equivalent dose for the 3D-CRT treatments was less than the contribution of photon dose, except for the lung, esophagus, thyroid and brain. The total equivalent dose per MU to each organ was calculated by summing the photon and neutron dose contributions. For all organs non-adjacent to the primary beam, the equivalent doses per MU from the IMRT treatment were less than the doses from the 3D-CRT treatments. This is due to the increase in the integral dose and the added neutron dose to these organs from the 18 MV treatments. However, depending on the application technique and optimization used, the required MU values for IMRT treatments can be two to three times greater than 3D CRT. Therefore, the total equivalent dose in most organs would be higher from the IMRT treatment compared to the box treatment and comparable to the organ doses from the box treatment plus the 6-field boost. This is the first time when organ dose data for an adult male patient of the ICRP reference anatomy have been calculated and documented. The tools presented in this paper can be used to estimate the second cancer risk to patients undergoing radiation treatment.

1. Introduction

Intensity-modulated radiation therapy (IMRT) is becoming a common treatment choice for various cancer sites in patients. The widespread use of IMRT has led to concern about the increase in beam-on time required to deliver modulated radiation fields, and the subsequent increased risk of inducing a treatment-related second cancer in patients outside the treatment volume (Followill *et al* 1997, Brenner *et al* 2000, Hall and Wu 2003, Suit *et al* 2007, Xu *et al* 2008, Tubiana 2009). Several international and national bodies—including the International Committee on Radiological Protection (ICRP) and the National Council on Radiation Protection and Measurement (NCRP) as well as the American Association of Physicists in Medicine (AAPM)—have established committees to make recommendations regarding the long-term side effects associated with relatively new treatment modalities. Even though epidemiological evidence on the increased risk of radiation-induced second cancer from IMRT-specific procedures will not be available for many years (Chaturvedi *et al* 2007), it is imperative to develop accurate dosimetry tools that will help to establish a clear relationship between radiation dose and second cancer risk for IMRT patients (Travis *et al* 2003, Boice 2006, Ron 2006, Xu *et al* 2008).

The most suitable dosimetry quantity to derive epidemiological data is organ-averaged equivalent dose (BEIR 2006, Xu *et al* 2008). Several groups have measured the absorbed dose outside the treatment volume in anthropomorphic phantoms to determine organ-averaged equivalent dose from radiation treatments (Kry *et al* 2005, Vanhavere *et al* 2004, Howell *et al* 2005, Wang and Xu 2008). Many of these studies have focused on treatments for prostate cancer. Kry *et al* (2005) made photon and neutron dose measurements from one 3D-CRT and six IMRT treatments for prostate cancer. The 3D-CRT treatment was delivered with an 18 MV beam. The IMRT treatments were delivered with 6 MV, 10 MV, 15 MV and 18 MV segmental MLCs. The authors reported photon dose equivalent, neutron dose equivalent and total dose equivalent to several points in the patient for all treatment plans considered. Vanhavere *et al* (2004) studied prostate treatments using 6 MV IMRT and 18 MV 3D-CRT procedures. Howell *et al* (2006) also considered treatments for prostate cancer involving both 3D-CRT and IMRT plans. More recent dose measurements from 3D-CRT and IMRT treatments for prostate cancer in a Rando phantom were made by Wang and Xu (2008) at Rensselaer Polytechnic Institute. The group used metal oxide semiconductor field effect transistors (MOSFETs) to measure photon doses outside the treatment field from two 3D-CRT treatments and one IMRT treatment. There are several challenges associated with these types of measurements. Measuring organ-averaged equivalent dose is laborious since it requires placing several dosimeters in cavities that approximate locations of different organs. Consequently, these measurements are also time consuming, and clinical implementation of these procedures on a patient-by-patient basis would be difficult. Finally, measurements are often inaccurate since dosimetry locations are uncertain, patient anatomy in a physical phantom is anatomically simplified, and point-wise measurements can underestimate or overestimate true volume-averaged dose to an organ.

It is well known that Monte Carlo calculations are often less laborious, less time consuming and more accurate than organ dose measurements in anthropomorphic phantoms. Several anatomically realistic computational phantoms are currently available for use in different Monte Carlo codes. In addition, we have previously described the development and validation of a detailed model of a medical linear accelerator for out-of-field dosimetry (Bednarz and Xu 2009). In this paper, we present a computational framework that combines an anatomically realistic computational phantom and a detailed accelerator model to calculate organ-averaged equivalent doses in patients. Typical treatment plans for prostate cancer were considered for this study including a standard 3D-CRT box treatment, a 3D-CRT box treatment plus a 6-field boost and a 7-field IMRT treatment.

2. Methods

2.1. Accelerator modeling

In a previous paper, we presented the development and validation of a detailed representation of a Varian Clinac 2100C (Varian Medical Systems Inc., Palo Alto, CA) accelerator with an 80-leaf multileaf collimator (MLC) (Bednarz and Xu 2009). The agreement between calculated and measured doses for all field sizes considered was within an appropriate acceptance criterion, and it was concluded that the detailed accelerator model could be applied for calculating doses to computational phantoms from radiation treatments (Bednarz and Xu 2009).

2.2. Monte Carlo calculation procedures

The Monte Carlo code MCNPX version 2.5.0 (Pelowitz 2005) was used for all radiation transport simulations in this work. MCNPX allows not only coupled electron–photon transport but also electron–photon–neutron transport including the option of tracking photonuclear production. In MCNPX, point-wise cross-section data are used for all neutral particle interactions. For neutrons, all reactions available in the cross-section dataset are included. For photons, incoherent and coherent scattering, fluorescent emission after photoelectric absorption, pair production with local emission of annihilation photons and bremsstrahlung are included. For electron transport, MCNPX uses a condensed history algorithm. The ITS indexing style was used for all simulations in this study. It has been shown that the ITS indexing style is more accurate than the MCNP indexing style for calculating electron dose distributions (Jeraj *et al* 1999).

Neutron contamination occurs in high-energy radiation therapy beams as a result of photonuclear interactions in the medical accelerator head. Consequently, neutrons will contribute to the out-of-field dose during high-energy treatments, typically from 10 to 18 MV beam energies. Therefore, neutron contamination in the accelerator model was also considered. For photo-neutron simulations, each material was defined by their corresponding isotopic make-up and abundances since the natural material cross-section data for photonuclear interactions are not available. The default LA150u photonuclear cross-section library in MCNPX version 2.5.0 is missing several important cross sections for isotopes of tungsten, lead and other common materials found in the accelerator. Therefore, the photonuclear cross-section libraries were updated to include the newly released ENDF/B-VII photonuclear cross-section datasets. The cross sections included in ENDF/B-VII were based on those provided by the IAEA Coordinated Research Project (CRP) (Chadwick *et al* 2006). The ENDF/B-VII photonuclear datasets were used for all simulations involving neutrons. To account for photo-neutron production in the 18 MV accelerator model, additional simulations had to be completed.

Three common variance reduction techniques in MCNPX were used in all simulations discussed in this paper, which are energy cut-offs, geometry splitting and bremsstrahlung splitting. The energy cut-off in MCNPX is a problem-wide energy level that is specified in the input. Particles are terminated along their track when their energy falls below the energy cut-off; thus, decreasing the time per particle history. For all simulations that did not track photo-neutron production, the photon cut-off (CUT:P) and electron cut-off (CUT:E) values were set to 0.01 and 0.1 MeV, respectively. For photo-neutron simulations the CUT:P and CUT:E values were set to 5 MeV, below the threshold of photonuclear interactions. The CUT:N value varied between simulations. The objective of geometry splitting is to spend more time for sampling in important locations and less time in unimportant locations. To preferentially increase the sampling in a spatial region, cells are given importance. Cell-by-cell importance was set in MCNPX using the IMP: P, E and N cards for photons, electrons

and neutrons, respectively. Bremsstrahlung splitting is a variance-reduction technique where a single photon at each bremsstrahlung event splits into multiple photons. Again, the weights of the photons are adjusted to keep the statistical technique fair.

2.2.1. Conversion from relative dose to absolute dose—All tally results in MCNPX are normalized per source particle. To provide a more meaningful dose quantity, the dose per source particle at a point, $D(x, y, z)$, was converted to the absolute dose, $D_{\text{abs}}(x, y, z)$, in the following manner. First, a water phantom was irradiated with the accelerator beam at a source-to-surface distance (SSD) of 100 cm, and the dose at d_{max} along the CAX, $D_{\text{cax}}^{\text{ref}}$, under reference conditions (10 cm $\times$ 10 cm field size with the MLC retracted) was calculated. Based on this dose, a reference field $f(x, y, z)$ was determined by

$$f(x, y, z) = D(x, y, z) / k D_{\text{cax}}^{\text{ref}}, \quad (1)$$

where k converts $D_{\text{cax}}^{\text{ref}}$ to a reference MU value. Typically accelerators are calibrated in such a way that $k = 1 \text{ MU/1 cGy}$. The absolute dose at a point, $D_{\text{abs}}(x, y, z)$, is therefore given by

$$D_{\text{abs}}(x, y, z) = f(x, y, z) \times U, \quad (2)$$

where U is the total number of MUs delivered for the irradiation under consideration. To normalize the absolute dose per MU, U would be omitted from equation (2). For a treatment involving N fields, the total absolute dose, $D_{\text{abs}}(x, y, z)$, can be determined by

$$D_{\text{abs}}(x, y, z) = \sum_{i=1}^N f_i(x, y, z) \times U_i, \quad (3)$$

where $f_i(x, y, z)$ is the reference field for field i and U_i is the number of MUs delivered for field i .

2.3. Doses to the RPI-adult male from 3D-CRT and IMRT prostate treatments

The accelerator model was integrated with the RPI-adult male computational phantom to calculate intermediate- and low-level equivalent doses to organs outside the primary beam from different 3D-CRT and IMRT treatments for prostate cancer. Three different treatment plans were considered in this study: a 4-field box plan, the same box plan plus a 6-field boost and a 7-field IMRT plan. The methods used to calculate the organ-averaged equivalent doses to the RPI-adult male computational phantom are described in the following sections.

2.3.1. The RPI-adult male computational phantom—To calculate the intermediate- and low-level doses to organs outside of the treatment volume, a whole-body model is required because CT images are typically obtained only for partial body (Zaidi and Xu 2007, Xu and Eckerman 2009). A realistic phantom defined in triangle meshes representing the average adult male has been recently reported by Zhang *et al* (2008). The group adopted 121 organs from a software that contains 3D models of different organs and tissues including a set of detailed bone components (cavity, spongiosa and cortical). An in-house software program was developed to deform these organs using the boundary-representation method (BREP) into an adult male surface model with organ volumes and masses matching those of the ICRP-defined average adult male (ICRP 2002, Na *et al* 2009). Another in-house software program was used to convert the finished surface model into a computational phantom with a resolution of 0.32 cm $\times$ 0.32 cm $\times$ 0.32 cm (Zhang *et al* 2008). The RPI-adult male surface rendering with and without the accelerator model is shown in figure 1.

2.3.2. Treatment setup—Typically, radiation oncology departments use a standard dosimetry protocol to treat prostate cancer. Any deviation from this protocol is to address patient-specific dosimetric concerns. In this paper, we have adopted the standard protocol for prostate treatments used in our department. The first treatment we considered was a 4-field box technique with two sets of opposing fields: AP/PA and RT/LT direction. The AP field is always delivered using a 6 MV beam in an effort to spare as much of the anterior rectum as possible. The other fields are delivered using an 18 MV beam, which helps reduce the dose to the femoral heads. The AP/PA fields typically deliver higher doses than the RT/LT fields. The second treatment we considered was the same box delivery technique plus a 6-field boost. Since an AP field was not used during the boost delivery, all fields were delivered with an 18 MV beam. It should be recognized that 3-field and 5-field boosts are also used in the clinic. The final treatment was a 7-field IMRT treatment. All fields for the IMRT plan were delivered with a 6 MV beam. Table 1 summarizes the treatment plans including the beam energy, gantry angle, field size and treatment depth for all treatment fields in the plans. It should be noted that the field sizes were selected based on dose constraints provided during treatment planning, and were not adjusted to lower the out-of-field dose to organs. It is well understood that the field size is one of many parameters that affects the out-of-field dose (Xu *et al* 2008, Kry *et al* 2006).

2.3.3. Modeling the MLC segments using an equivalent circular field—Both 3D-CRT and IMRT treatments use the MLC to shape the primary beam to match optimized dose distributions determined from treatment planning. 3D-CRT treatments use different field patterns for each gantry angle. This is further complicated in IMRT, which is composed of multiple segments for each gantry angle. Modeling each individual MLC segment can require a large amount of computation time. Therefore, it is advantageous to simplify the MLC configurations for a given gantry angle to a single 'effective' configuration. Simplification of the MLC configurations for a given gantry angle was done using an equivalent circular field determined from the unblocked equivalent square and the percentage of blocked field defined in the treatment plan. For the 3D-CRT treatments the average radius of the equivalent circular field was 2.1 cm and for the IMRT treatment the average radius of the equivalent circular field was 1.5 cm. The use of a small circular field in place of the dynamic MLC segments will account for an appropriate amount of patient scatter at the cost of delivering a non-uniform dose distribution to the target volume. Since we are not concerned about the dose to organs inside the primary beam, this simplification is acceptable.

To validate our method we compared a 24-segment IMRT field with an equivalent circular field representing that same primary beam. A corresponding phase-space file from our detailed accelerator model was resampled into a Geant4-based Monte Carlo framework developed by Hancox *et al* (2008) that includes a complete representation of the MLC capable of delivering dynamic IMRT plans. The out-of-field dose from both the IMRT and equivalent circular field simulations was calculated in a water phantom at a depth of 10 cm in the in-plane direction. A comparison of the 24-segment IMRT field and the equivalent circular field is provided in figure 2. As shown in the figure, the dose from both fields agree very well at distances greater than 10 cm from the central axis. Of course, our model can be improved by representing the detailed configurations of each MLC segment during treatment in order to include dose to in-field organs. Similar to Hancox *et al* (2008), other groups have developed state-of-the-art models that account for dynamic MLC motion (Verhaegen and Liu 2001, Fix *et al* 2001, Siebers *et al* 2002, Ma *et al* 2000, Pawlicki and Ma 2001). While the equivalent circular field does not truly represent the detailed configuration of the MLCs during treatment, the effect of the precise MLC positioning on organ dose is negligible for locations outside the primary beam.

2.3.4. Calculation of organ-averaged equivalent doses—Adopting the treatment plans provided in table 1, the organ-averaged equivalent doses to the RPI-adult male computational phantom were calculated. The organs studied in this work were selected based on proposed recommendations of the ICRP for organs being at risk for second cancer induction: the stomach, colon, liver, lung, esophagus, pancreas, brain, active bone marrow, small intestine, spleen, gall bladder, heart, lymph nodes, kidneys and the thyroid (ICRP 2007). Since we considered only organs that are exposed to intermediate- and low-level doses, organs such as the testis, bladder, skin and prostate, which are in the primary radiation field, were excluded. Portions of the ascending, descending and sigmoid colon receive high radiation doses and were not considered. Thus, the equivalent dose to the colon was approximated by the dose to the transverse colon. The dose to the bone marrow was approximated by adding the doses to the cranium, sternum, ribs and vertebral column since active bone marrow is not directly defined in the RPI-adult male. These bones include a significant amount of active bone marrow that is exposed to intermediate- and low-level doses during prostate treatments (Kry *et al* 2005, Caracappa 2006). The sacrum and pelvis also contain high concentrations of active bone marrow, but since portions of these bones are in the primary radiation fields, they were not considered. The equivalent dose to all lymph nodes was calculated as the weighted average of the dose to the lymph nodes in the head, arms and legs. The lymph nodes in the trunk were not considered because they are also subjected to high radiation doses from the primary beam.

The equivalent dose from photons to all organs and tissues were calculated using the track-length cell energy deposition tally (F6:p) (Pelowitz 2005). Theoretically, this tally provides the collision kerma averaged throughout the organ. In our calculations we assume that outside the primary beam the conditions of electronic equilibrium are satisfied and the dose and kerma are nearly the same (Kry *et al* 2006). To test this assumption we compared absorbed dose and kerma in several organs for a selected number of fields. Our test confirmed that this assumption holds for the treatment plans considered in this study. The advantage of calculating the collision kerma is that for the same number of initial source particles, the relative error of the collision kerma is 2–3 times lower than the absorbed dose. The lower relative error for the collision kerma is due to the difference in how MCNPX records the photon track length energy deposition tally compared to the modified pulse height tally. The track-length energy deposition tally uses a track-length estimator of the photon flux to calculate the energy deposition in a volume. The modified pulse height tallies are updated when an electron is created in the tally volume or when an electron crosses a surface into the tally volume. Consequently, for small tally volumes, non-zero scores occur much less frequently using the modified pulse height tally than the track length tally.

For 3D-CRT treatments involving the 18 MV beam, neutrons are inevitably produced in the accelerator head and patient through photonuclear processes. Therefore, the neutron equivalent doses to organs in the RPI-adult male were also calculated. The neutron equivalent dose depends on an energy dependent radiation-weighting factor. Thus, to calculate the neutron equivalent dose to organs the neutron dose distributions in the organs were convolved with the energy-dependent radiation-weighting factor distribution provided in ICRP 60 (ICRP 1991). A plot of the radiation weighting factors for neutrons as a function of energy is provided in figure 3. The neutron equivalent dose calculations were performed separately from the photon equivalent dose calculations in order to implement variance reduction techniques. These techniques helped to improve the efficiency of the calculations.

A total of 1×10^7 initial electron histories were ran for all simulations of the 18 MV 3D-CRT treatments, while 3×10^7 initial electron histories were ran for all simulations of the 6 MV IMRT treatments. On average each simulation took about 15 CPU hours. The increase in the number of initial electron histories for the IMRT simulations was due to the decrease

in the number of generated photons per electron for the lower energy beam. These numbers are useful since this study is the first time when organ dose data for an adult male patient of ICRP reference anatomy have been calculated and documented.

3. Results and discussion

3.1. Results of organ dose calculations from treatments of prostate cancer using RPI-adult male computational phantom

The total photon organ-averaged equivalent dose normalized per MU to various organs from the box treatment, the box treatment plus a 6-field boost and the 7-field IMRT treatment are provided in table 2. For most organs studied, the normalized photon equivalent dose was highest for the box treatment plus the 6-field boost, followed by the box treatment and the 7-field IMRT treatment. The higher photon doses from the 3D-CRT treatments can be attributed to the increase in integral dose due to the larger field delivered to the treatment site. Subsequently, there was an increase in patient scatter from these treatments compared to the IMRT plan. The differences in organ-averaged equivalent doses can also be attributed to the increase in the number of fields used for box treatment plus the six-field boost compared to the box treatment and the IMRT treatment. The large equivalent doses to the lymph nodes, small intestine and colon can be attributed to the high doses to portions of these organs that were located closest to the primary radiation fields. As seen in table 2, for organs further away from the treatment site the differences between organ doses from the 3D-CRT treatments and the IMRT treatment are less pronounced. This is predominately due to the increased contribution of leakage radiation to these organs. Leakage radiation is much less dependent on the size of treatment field compared to the collimator and patient scatter.

The neutron equivalent doses to important organs from the 3D-CRT treatments are provided in table 3. Since neutrons were not produced during the 6 MV IMRT treatment the last column in table 3 is empty. For most organs the total neutron equivalent dose per MU was much smaller than the photon equivalent dose per MU. The exceptions to this trend included higher neutron equivalent doses to the lung, esophagus, thyroid and brain. The high neutron equivalent dose to these organs can be attributed to the fact that these organs are subjected to large amounts of neutron moderation as a consequence of their position in the body and composition. The average energy of neutrons entering the patient is approximately 0.55 MeV (Bednarz and Xu 2009). The dose in tissue from neutrons of this energy is deposited by recoil ions resulting from inelastic interactions with hydrogen and other light elements. A significant amount of energy loss occurs in these interactions; on average a neutron loses half of its original energy due to primary collisions with hydrogen. Since the range of the recoil ion is in the order of micrometers, most energy deposition from this type of interaction is deposited locally. A 0.55 MeV neutron has a mean free path of about 1.75 cm in tissue and 2.25 cm in bone (Budinger *et al* 1971). The neutron mean free path in tissue is comparable to the depth of superficial organs, such as the thyroid, which explains the high neutron equivalent doses to these organs. In addition, at this energy the neutron weighting factor is near its maximum (see figure 3). Since the brain and lungs are surrounded by bone instead of tissue, these organs received higher neutron doses even though they are located at deeper sites in the body, resulting from the larger mean-free-path of neutrons in bone compared to tissue.

Table 4 provides the total organ-averaged equivalent doses per MU from the 3D-CRT treatments and the IMRT treatment that were calculated by summing the photon and neutron equivalent doses in tables 2 and 3, respectively. For organs outside the primary radiation fields the normalized equivalent doses from the IMRT treatment were less than the doses from the 3D-CRT treatments. This is due to the increase in the integral dose and the added neutron dose to these organs from the 18 MV 3D-CRT treatments. Owing to the fact that the

IMRT treatments require typically 2–3 times greater MU values than those for 3D CRT (Hall and Wu 2003), the total absolute equivalent dose in most organs would be correspondingly higher from the IMRT treatment compared to the box treatment but comparable or less than the doses from the box treatment plus the 6-field boost. The equivalent doses presented in table 4 can be used to assess the risk of inducing second cancers in patients from low- and intermediate-level doses to the organs.

Figures 4(a)–(l) provide equivalent doses to several organs as a function of different gantry angles used to deliver the primary beam for the 3D-CRT and IMRT treatments. Organs that are dispersed throughout the body such as the colon, bone marrow and lymph nodes were not considered. The contribution of neutrons and photons to the equivalent dose is separated for the 18 MV 3D-CRT treatments considered in this study. All doses were normalized per MU to better show the more subtle effects of the incident beams' energy and angle of incidence on intermediate- and low-level organ doses. The dependence of equivalent dose to organs on the gantry angle delivering the primary beam is clear in figures 4(a)–(l). This dependence is due to the position of the organ with respect to the angle of incidence of primary beam on the patient. For organs that are located on the right lateral side of the patient, the equivalent dose is the highest for gantry angles irradiating the right lateral side of the body. The same organs are well shielded when the left lateral side of the body is irradiated so there is a drop in the dose distribution at these corresponding gantry angles. As expected, the opposite effect is true for the organs located on the left lateral side of the patient. Equivalent dose distributions for organs centrally located in the body were relatively uniform, since there is no preferential angle of incidence of the primary beam. The differences between the 4-field and 6-field doses at a common gantry angle are due to the small difference in the equivalent circular field used to define the MLC configurations for the different treatments. These figures demonstrate the usefulness of anatomically realistic computational phantoms in organ dose assessment for radiation treatments.

3.2. Comparison of calculated and measured organ equivalent doses

In this section we compare calculated organ doses presented in this paper with doses measured in an anthropomorphic phantom by Kry *et al* (2005) and Howell *et al* (2006). Kry *et al* measured doses at the center and edge locations of several organs including liver, stomach, lung, esophagus and colon. Similar to this study, Kry *et al* (2005) considered an 18 MV 4-field box treatment with a 6-field boost and a 6 MV IMRT treatment. Howell *et al* (2006) also measured doses at the center of the above organs for a 6 MV IMRT treatment. Table 5 compares our doses with those reported by these authors for selected organs at center locations. Good agreement is seen between our calculations and measured doses provided by Kry *et al* (2005) for the 3D-CRT treatment. It appears that the measured doses reported by Kry *et al* (2005) are systematically higher than the calculated data. A fairly good agreement is also seen between our calculated organ doses and measured doses by Kry *et al* (2005) and Howell *et al* (2006) for the IMRT treatment. The organ doses in this study are slightly lower than those reported by Kry *et al* (2005) and slightly higher than those reported by Howell *et al* (2006). These discrepancies could be due to differences between measured point-wise organ doses and calculated volume-averaged organ doses or differences in the treatment plans. In addition, Howell *et al* (2006) points out that the inconsistencies between their doses and those reported by Kry *et al* (2005) could be attributed to differences in the approximate organ locations used in the different studies. Clearly, the methods presented in this study can provide accurate organ doses and facilitate the management of non-target radiation doses during the planning and retrospective assessment of the treatments.

4. Conclusions

This study made available tools useful in estimating secondary radiation dose and eventually associated cancer risks to patients. It has been repeatedly recognized that organ-averaged equivalent dose is the most suitable quantity to assess radiation-induced second cancer risks (Xu *et al* 2008). In the past, organ-averaged equivalent doses were estimated mostly by measurements, involving dosimeters in several cavities in the anthropomorphic Rando phantom. The tools presented in this paper provide a practical alternative to measuring organ doses. This study shows that organ-averaged equivalent doses can be accurately calculated using anatomically realistic patient models.

The risk of second cancer incidence in patients is a minor concern compared to tumor control and acute toxicity. However, if target coverage and dose sparing to adjacent tissues are comparable between different treatment choices, then consideration of the risk of second cancer incidence could help establish a clear therapeutic benefit for a particular treatment. Furthermore, our methods offer an easy way of comparing different modalities in terms of secondary exposures. Already, a number of emerging treatment modalities are being designed to require much less beam-on time than that of the traditional helical IMRT for the same level of radiation modulation. For example, RapidArc by Varian, is based on volumetric-modulated arc therapy that can be two to eight times faster than Varian's previous dynamic treatments. The tools demonstrated in this work offer an accurate and versatile approach to evaluate and compare various modalities that are evolving rapidly.

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References

- Bednarz B, Xu XG. Monte Carlo modeling of a 6 and 18-MV Varian Clinac medical accelerator for in-field and out-of-field dose calculations: development and validation. *Phys. Med. Biol.* 2009; 54:N43–57. [PubMed: 19141879]
- BEIR. Health risks from exposure to low levels of ionizing radiation BEIR VII, Phase 2 National Research Council. National Academy of Science; 2006.
- Boice, JD, Jr. Ionizing radiation *Cancer Epidemiology and Prevention*. 3rd edn. Schottenfeld, D.; Fraumeni, JF., Jr, editors. Oxford University Press; New York: 2006. p. 259-93.
- Brenner D, Curtis R, Hall E, Ron E. Second malignancies in prostate carcinoma patients after radiotherapy compared with surgery. *Cancer*. 2000; 88:398–406. [PubMed: 10640974]
- Budinger TF, Howerton RJ, Plechaty EF. Neutron radiography and dosimetry. *Phys. Med. Biol.* 1971; 16:439–50. [PubMed: 5559696]
- Caracappa. Dissertation. Rensselaer Polytechnic Institute; Troy, NY: 2006. Development and evaluation of a new algorithm for determining radiation dose to the red bone marrow.
- Chadwick MB, et al. ENDF/B-VII.0: next generation evaluated nuclear data library for nuclear science and technology. *Nucl. Data Sheets*. 2006; 207:2931–3060.
- Chaturvedi. et al. Second cancers among 104760 survivors of cervical cancer: evaluation of long term risk. *J. Natl Cancer Inst.* 2007; 99:1634–43. [PubMed: 17971527]
- Fix MK, et al. Monte Carlo simulation of dynamic MLC based on a multiple source model. *Phys. Med. Biol.* 2001; 46:3241–57. [PubMed: 11768503]
- Followill D, Geis P, Boyer A. Estimate of whole-body dose equivalent produced by beam intensity modulated conformal therapy. *Int. J. Radiat. Oncol. Biol. Phys.* 1997; 38:667–72. [PubMed: 9231693]

- Hall E, Wu C. Radiation-induced second cancers: the impact of 3D-CRT and IMRT. *Int. J. Radiat. Oncol. Biol. Phys.* 2003; 56:83–8. [PubMed: 12694826]
- Hancox C, Seco J, Paganetti H. Geant4 benchmarking for IMRT dose calculations. *Med. Phys.* 2008; 35:2807.
- Howell RM, Ferenci MS, Hertel NE, Fullerton GD. Investigation of secondary neutron dose for 18 MV dynamic MLC IMRT delivery. *Med. Phys.* 2005; 32:786–93. [PubMed: 15839351]
- Howell RM, Hertel NE, Wang Z, Hutchinson J, Fullerton GD. Calculation of effective dose from measurement of secondary neutron spectra and scattered photon dose from dynamic MLC IMRT for 6-MV, 15MV, and 18-MV beam energies. *Med. Phys.* 2006; 33:360–8. [PubMed: 16532941]
- ICRP. ICRP Publication 89. 2002. Basic anatomical and physiological data for use in radiological protection: reference values.
- ICRP. ICRP Publication 60. Pergamon; Oxford: 1991. Recommendations of the International Commission on Radiological Protection.
- ICRP. ICRP Publication 103. Pergamon; Oxford: 2007. Recommendations of the International Commission on Radiological Protection.
- Jeraj R, Keall P, Ostwald P. Comparison between MCNP, EGS4, and experiment for clinical electron beams. *Phys. Med. Biol.* 1999; 44:705–17. [PubMed: 10211804]
- Kry SF, Salehpour M, Followill DS, Stovall M, Kuban DA, White RA, Rosen II. Out-of-field photon and neutron dose equivalents from step-and-shoot intensity-modulated radiation therapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2005; 62:1204–16. [PubMed: 15990026]
- Kry SF, Titt U, Ponisch F, Followill DS, Vassiliev ON, White RA, Mohan R, Salehpour M. A Monte Carlo model for calculating out-of-field dose from a Varian 6-MV beam. *Med. Phys.* 2006; 33:4405–13. [PubMed: 17153419]
- Ma CM, et al. Monte Carlo verification of IMRT dose distributions from a commercial treatment planning system. *Phys. Med. Biol.* 2000; 45:2483–95. [PubMed: 11008950]
- Na, YH.; Zhang, JY.; Ding, AP.; Xu, XG. Mesh-based and anatomically adjustable adult phantoms and a case study in virtual calibration of lung counter for female workers. In: Xu, XG.; Eckerman, KF., editors. *Handbook of Anatomical Models for Radiation Dosimetry*. Taylor & Francis; London: 2009. chapter 14
- Pawlicki T, Ma CM. Monte Carlo simulation for MLC-based intensity-modulated radiotherapy. *Med. Dosim.* 2001; 26:157–68. [PubMed: 11444518]
- Pelowitz, DB. LANL Publication LA-CP-05-0369. LANL; Los Alamos, NM: 2005. MCNPX user's manual.
- Ron E. Childhood cancer—treatment at a cost. *J. Natl Cancer Inst.* 2006; 98:1510–1. [PubMed: 17077348]
- Siebers JV, Lauterbach M, Keall PJ, Mohan R. Incorporating multi-leaf collimator leaf sequencing into iterative IMRT optimization. *Med. Phys.* 2002; 30:533–43.
- Suit H, et al. Secondary carcinogenesis in patients treated with radiation. A review of data on radiation-induced cancers in human, non-human primate, canine and rodent subjects. *Radiat. Res.* 2007; 167:12–42. [PubMed: 17214511]
- Travis LB, et al. Breast cancer following radiotherapy and chemotherapy among young women with Hodgkin disease. *J. Am. Med. Assoc.* 2003; 290:465–75.
- Tubiana M. Can we reduce the incidence of second primary malignancies occurring after radiotherapy? A critical review. *Radiother. Oncol.* 2009; 91:4–15. [PubMed: 19201045]
- Vanhavere F, Huyskens D, Struelens L. Peripheral neutron and gamma doses in radiotherapy with an 18-MV linear accelerator. *Radiat. Prot. Dosim.* 2004; 110:607–12.
- Verhaegen F, Liu HH. Incorporating dynamic collimator motion in Monte Carlo simulations: an application in modeling a dynamic wedge. *Phys. Med. Biol.* 2001; 46:287–96. [PubMed: 11229715]
- Wang B, Xu XG, Kim CH. A Monte Carlo CT Model of the Rando Phantom. *Am. Nucl. Soc. Trans.* 2004; 90:473–4.
- Wang B, Xu XG. Measurements of non-target organ doses using MOSFET dosimeters for selected IMRT and 3DCRT radiation treatment procedures. *Radiat. Prot. Dosim.* 2008; 128:336–42.

- Xu XG, Bednarz B, Paganetti H. A review of dosimetry studies on external-beam radiation treatment with respect to second cancer induction. *Phys. Med. Biol.* 2008; 53:R193–241. [PubMed: 18540047]
- Xu, XG.; Eckerman, KF. *Handbook of Anatomical Models for Radiation Dosimetry*. Taylor & Francis; London: 2009.
- Zaidi H, Xu XG. Computational anthropomorphic models of the human anatomy: the path to realistic Monte Carlo modeling in radiological sciences. *Annu. Rev. Biomed. Eng.* 2007; 9:471–500. [PubMed: 17298237]
- Zhang, J.; Na, Y.; Xu, XG. AAPM Ann. Meeting. Houston, TX: 2008. Development of whole-body phantoms representing an average adult male and female using surface-geometry methods.

Figure 1.
3D rendering of the RPI-adult male computational phantom and accelerator model.

Figure 2.
Comparison of a 24-segment IMRT field with an equivalent circular field in a water phantom at a depth of 10 cm. The dose is normalized per MU.

Figure 3.
Neutron weighting factors provided in ICRP 60 (ICRP 1991).

Figure 4.

Dependence of photon and neutron equivalent doses on gantry angle and energy for several organs including the stomach, liver, lung, esophagus, pancreas, brain, small intestine, spleen, gall bladder, heart, kidneys and thyroid. The 6-MV distribution is from the IMRT treatment. The 18-MV photon and neutron distributions are from the 3D-CRT treatments. Doses for some fields may not be visible due to overlap. Uncertainties of the neutron equivalent dose did not exceed 20% and all photon equivalent doses had uncertainties less than 10%. The small differences between the 4-field and 6-field photon and neutron doses at 90° and 270° can be attributed to slightly different equivalent circular fields used to define the MLC for those fields and differences in the statistical uncertainties in each of the dose values.

Table 1

A 4-field box treatment, a 4-field box treatment plus a 6-field boost and a 7-field IMRT treatment used in this study including beam energy, gantry position, field size and treatment depth.

Beam energy (MeV)	Gantry position (°)	Field size (cm ²)	Treatment depth (cm)
4-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
6-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
7-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

Table 2

Photon equivalent dose per MU to selected organs from the box treatment, the box treatment plus the 6-field boost and the 7-field IMRT treatment for prostate cancer. For the 4-field box plus the 6-field boost we assume that the two treatments use equal amounts of MUs. Accompanying each value is the percent relative error calculated for each value. The percent relative error is the variance of the calculated dose divided by the dose itself.

Organ	Photon equivalent dose ($\mu\text{Sv MU}^{-1}$)		
	4-field box (%)	4-field box + 6-field boost (%)	7-field IMRT (%)
Stomach	7.0 (1.6)	14.1 (1.1)	5.3 (2.9)
Colon	15.0 (1.3)	37.3 (0.9)	11.1 (3.2)
Liver	5.8 (1.2)	11.9 (0.9)	4.9 (2.0)
Lung	2.9 (1.1)	6.0 (1.0)	2.9 (2.0)
Esophagus	1.8 (5.6)	3.7 (3.9)	1.8 (3.2)
Pancreas	4.6 (3.7)	9.6 (2.5)	4.2 (3.5)
Brain	0.9 (3.3)	1.6 (2.4)	1.2 (3.6)
Active bone marrow	2.2 (1.3)	6.8 (0.6)	3.7 (4.3)
Small intestine	54.7 (0.5)	111.0 (0.3)	21.5 (0.8)
Spleen	5.0 (3.1)	10.6 (2.2)	4.3 (3.6)
Gall bladder	6.1 (2.9)	12.5 (2.1)	4.7 (2.5)
Heart	3.3 (1.7)	6.5 (1.3)	3.6 (3.6)
Lymph node	8.7 (4.2)	43.2 (1.2)	7.1 (1.6)
Kidneys	10.0 (1.7)	21.5 (1.2)	5.8 (3.7)
Thyroid	1.6 (10.0)	3.2 (7.1)	1.6 (10.8)

Table 3

Neutron equivalent dose per MU to selected organs from the 4-field box treatment, the 4-field box treatment plus the 6-field boost, and the 7-field IMRT treatment for prostate cancer. For the 4-field box plus the 6-field boost we assume that the two treatments use equal amounts of MUs. Accompanying each value is the relative error calculated for each value.

Organ	Neutron equivalent dose ($\mu\text{Sv MU}^{-1}$)		
	4-field box (%)	4-field box + 6-field boost (%)	7-field IMRT
Stomach	1.1 (13.1)	2.9 (7.3)	–
Colon	1.9 (12.3)	6.8 (7.2)	–
Liver	2.0 (5.4)	6.0 (2.8)	–
Lung	2.9 (4.7)	7.3 (2.7)	–
Esophagus	1.3 (30.4)	4.1 (19.6)	–
Pancreas	3.3 (12.0)	7.1 (8.3)	–
Brain	2.6 (5.5)	4.3 (3.2)	–
Active bone marrow	1.5 (6.8)	4.4 (4.6)	–
Small intestine	1.3 (8.6)	3.8 (4.3)	–
Spleen	3.7 (12.2)	9.6 (4.3)	–
Gall bladder	1.0 (26.6)	2.2 (19.8)	–
Heart	1.3 (9.5)	3.9 (4.9)	–
Lymph node	3.5 (29.3)	12.8 (11.9)	–
Kidneys	3.18 (14.8)	7.1 (8.6)	–
Thyroid	3.8 (11.0)	7.1 (20.7)	–

Table 4

Total equivalent dose per MU to selected organs from the 4-field box treatment, the 4-field box treatment plus the 6-field boost and the 7-field IMRT treatment for prostate cancer. For the 4-field box plus the 6-field boost we assume that the two treatments use equal amounts of MUs. Accompanying each value is the percent relative error calculated for each value.

Organ	Total equivalent dose ($\mu\text{Sv MU}^{-1}$)		
	4-field box (%)	4-field box + 6-field boost (%)	7-field IMRT (%)
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)
Liver	7.8 (1.7)	17.9 (1.1)	4.9 (2.0)
Lung	5.8 (2.4)	13.4 (1.5)	2.9 (2.0)
Esophagus	3.1 (18.3)	7.8 (10.4)	1.8 (3.2)
Pancreas	7.9 (5.6)	16.7 (3.8)	4.2 (3.5)
Brain	3.5 (2.4)	5.9 (2.4)	1.2 (3.6)
Active bone marrow	3.7 (2.9)	11.1 (1.9)	3.7 (4.3)
Small intestine	56.0 (0.5)	114.6 (0.4)	21.5 (0.8)
Spleen	8.7 (2.2)	20.2 (2.3)	4.3 (3.6)
Gall bladder	7.1 (4.5)	14.7 (3.4)	4.7 (2.5)
Heart	4.6 (3.0)	10.4 (2.0)	3.6 (3.6)
Lymph node	12.2 (8.9)	56.0 (2.9)	7.1 (1.6)
Kidneys	13.2 (3.8)	28.6 (2.3)	5.8 (3.7)
Thyroid	5.4 (9.4)	10.3 (17.5)	1.6 (10.8)

Table 5

Comparison of calculated doses from this study with measured doses reported by Kry *et al* (2005) and Howell *et al* (2006).

Organ	Total organ equivalent dose ($\mu\text{Sv MU}^{-1}$)				
	3D CRT (box+boost)		IMRT		
	Our results	Kry <i>et al</i>	Our results	Kry <i>et al</i>	Howell <i>et al</i>
Stomach	17.0	23.6	5.3	8.2	3.3
Colon	44.1	49.4	11.1	19	–
Liver	17.9	24.8	4.6	8.2	3.7
Lung	13.4	17.7	2.9	3.7	2.4
Esophagus	7.8	9.8	1.8	3.2	2.2