BIOSCIENCES BIOTECHNOLOGY RESEARCH ASIA, March 2015. Vol. **12**(Spl. Edn. 1), p. 71-77

Calculation of Organs Doses and Secondary Cancer Risk during Mantle Field Radiotherapy for Hodgkin's Lymphoma

Mansour Zabihzadeh[1, 2], Zahra Shakarami[1*], Mohammad JavadTahmasebi Birgani[1, 2], Hojattollah Shahbazian[2] and MohammadAli Behrooz[1]

[1]Department of Medical Physics, School of Medicine,
Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[2]Department of Radiotherapy and Radiation Oncology, Golestan Hospital,
Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

DOI: http://dx.doi.org/10.13005/bbra/1607

(Received: 05 February 2015; accepted: 10 March 2015)

Occurrence of radiation-induced secondary cancer risk following mantle field radiotherapy for Hodgkin's lymphoma (HL) patients with long survival demands well-established radiotherapy strategy. Organs doses and resulted secondary cancer risk due to out-of field photons were calculated during mantle field radiotherapy for Hl patient. The male and female mathematical phantom of the Oak Ridge National Laboratory (ORNL)and validated 6MV photon beam of a Varian 2300 C/D were modeled by MCNPX 2.4.0 MC code. Using suitable lungs and thyroid shields for AP and PA fields, the organ specific absorbed doses, effective dose, and secondary cancer risk were calculated following to mantle field radiotherapy for HL. Among the out-of-field organs, the nose, eyes, head and neck's skins and sinuses have the higher received doses. The total effective doses and secondary cancer risk for a male and female were estimated to be 199, 234 mSv and 1.72%, 1.87% respectively. During mantle field radiotherapy for Hodgkin's lymphoma, accurately estimations of organs dose near to the field's edge and suitable shielding of critical in-field organs are crucial factor to establish an optimal treatment plan.

Keywords: Hodgkin lymphoma (HL), Mantle Field Radiotherapy, Secondary Cancer Risk, Monte Carlo Simulation.

Second cancer resulting from radiation treatment of the first cancer has been showed by several publication[1]. Patient survival following to application of new modalities and techniques in the treatment of cancer has been increased the possibility of developing a radiation induced second cancer[2-5]. Determination of the cancer risk factor could be useful factor to establish an optimal treatment planning (TP).

Hodgkin lymphoma (HL) is one of the curable malignant. A patient is treated with anterior and posterior mantle fields, using 4, 6, or 10 MV photons. A dose of 36-44Gy is delivered to PTV while lung and thyroid are shielded with Cerrobend block during radiation therapy[6, 7]. Usually mantle fields are extensive and include many critical organs from mandible to diaphragm. HL is most common in young people (15-35 age), and many of them live several decades after successful treatment; thus the possibility of developing a radiation induced second cancer is increased[8-10].

Most previous investigations estimated organ doses and second cancer risk from radiation treatment of prostate, breast, lung and nasopharynx. According our knowledge from

* To whom all correspondence should be addressed.
Tel: (+98)930-3171073
E-mails: z.shakarami91@gmail.com;
shakarami.z@ajums.ac.ir

literatures, there is not any Monte Carlo (MC) calculation or measurement study about organ doses and second cancer risk for whole body following to HL radiationtherapy[14]. Only some studies have been calculated cancer risk for some of organ such as lung, breast and thyroid using TLD dosimetry[9] or follow up patients for years after treatment[6-8]. Using of Monte Carlo calculations has became a valuable method in radiation therapy dosimetry and implemented in pioneer MC based treatment planning system (TPS). In our study, the average dose delivered to each organ, the effective dose and the secondary cancer risk following to radiation therapy HL with mantle field were calculated by the Monte Carlo method.

MATERIALS AND METHODS

The Monte Carlo code MCNPX version 2.4.0[15] was used to model photon beams form the Varian 2300C/D Linac for 6 MV. MCNPX is a well-known general-purpose Monte Carlo code developed at Los Alamos National Laboratories. Using the tabulated interaction cross sections for most neutral and charged particles (<150 MeV) radiation transport of these particles can be simulated in radiation therapy applications. Figure 2 shows the schematic diagram of the simulated geometry for the Varian 2300C/D Linac. The model included the bremsstrahlung target, the primary collimator, vacuum window, the flattening filter, the monitor ion chamber, the mirror, and the upper and lower jaws. The incident electrons had a Gaussian energy distribution with a full width of half maximum (FWHM) of 1 MeV that was centered at 6 MeV. The electron beam radial intensity distribution was also set to a Gaussian with the FWHM of 1.1 mm for 6 MV. During calculating of the depth doses and dose profiles, the cut-off energy was determined as 0.01 and 0.521 MeV for the photons and electrons, respectively. For depth dose calculations within the water phantom, a cylinder with a radius of one-tenth the size of the open field size was defined and divided into scoring cells with 2 mm height along the beam central axis. For beam profile calculations, the primary cylinder was positioned at the predefined depth vertically to the beam central axis with the radius of 2 mm.

The mathematical phantom of the Oak Ridge National Laboratory (ORNL)[16] was used to estimate of organs dose, Figure 2. The male and female ORNL phantom was investigated in MC simulations, separately.

The phantom located at SSD=100 cm. As regarding to shape of the Mantle field and in order to properely sheilding of lungs and thyroid, treatment field was 30×30 cm^2. The lungs and thyroid were shielded by 8 cm thickness shaped cerrobend alloy located on block tray (inserted in 46 cm distance from the phantom surface). Irradiation of Hl was simulated by two fields of antero-posterior (AP, 0°) and postero-anterior (PA, 180°). The *F8 tally was used to calculate of absorbed dose by organs. Energy cutoffs of 10 and 521 KeV were used for photon and electrons, respectively. The number of source photon histories needed to achieve a relative error < 5% for all cells was 10^9. The prescription dose was 40 Gy to the planning target volume that is deliverd by AP and PA projections. In a separate simulation by inserting a detector in water phantom at reference depth (i.e 1.5 cm for 6MV) the converting coefficient was calculated to convert the MCNP output to the prescripted MU (munitor unit). Furthermore, in order to estimation of cerrobend alloy shields on the secondary cancer risk Mantle fields were applied without presence of lungs and thyroid shields. The effective dose was calculated according to the ICRP-103 report (*International Commission on Radiation Units & Measurements)* recommendations that is defined as the tissue-weighted sum of the equivalent doses in all organs, give by the equation

$$E = \sum_T W_T \sum_R W_R D_{T,R} \text{ or } E = \sum_T W_T H_T$$

Where W_T is the tissue weighting factor derived from ICRP-103 report and H_T or $W_R D_{T,R}$ is the equivalent dose in the organ[17]. The unit for the effective dose is the same as for absorbed dose, J/kg^{-1}, and its special name is sievert (Sv).The conservative maximal risk of secondary cancer (SC) was calculated for out-of-field organs. Coefficient of secondary cancer risk for each organ were extracted from NCRP-116 report (National Council on Radiation Protection & Measurements)[18]. The whole-body risk of (SC) was taken as the sum of the risks for these organs.

RESULTS

The MC-calculated PDD (percentage depth dose) curves and beam profiles were firstly compared with the measurements to validate our MC model. There was a good agreement between the measurements and calculations for beam profiles and PDD curves (Fig 3). Local differences of less than 1% were seen for PDD values in descending part up to 30cm depth, but it increased up to 6% for the buildup region and for the largest field size; e.g. 40 × 40 cm^2 (Fig. 3a). For beam profiles, local differences less than 2% were seen for flat region, but it increased to 13% for region located out of field (fig. 3b). Readers is referred to our pervious paper to the details of validation of our simulated linac's head (19).

The equivalent dose of out-of-field organs for mantle field with 6MV photon beam followed by dose prescription of 40 Gy to the planning target volume were calculated (see fig 4). Among the out-of-field organs, the nose, eyes, head and neck's skins and sinuses have the higher received doses.

The total effective doses integrated over the out-of-field organs of a male and female were

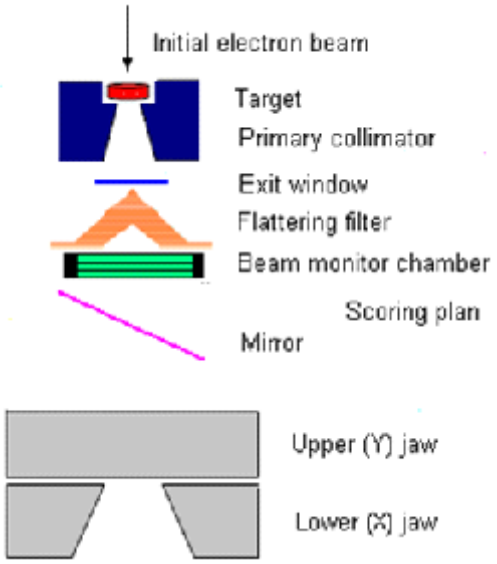

Fig. 1. Schematic diagram of the MC model for the Varian 2300C/D linac geometry.

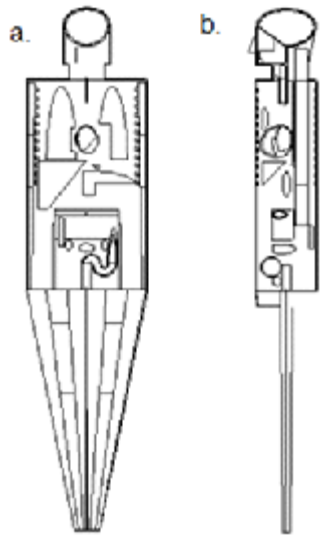

Fig. 2. Mathematical male phantom; **a.**Frontal view at z=0,**b.**Lateral view at x=0.

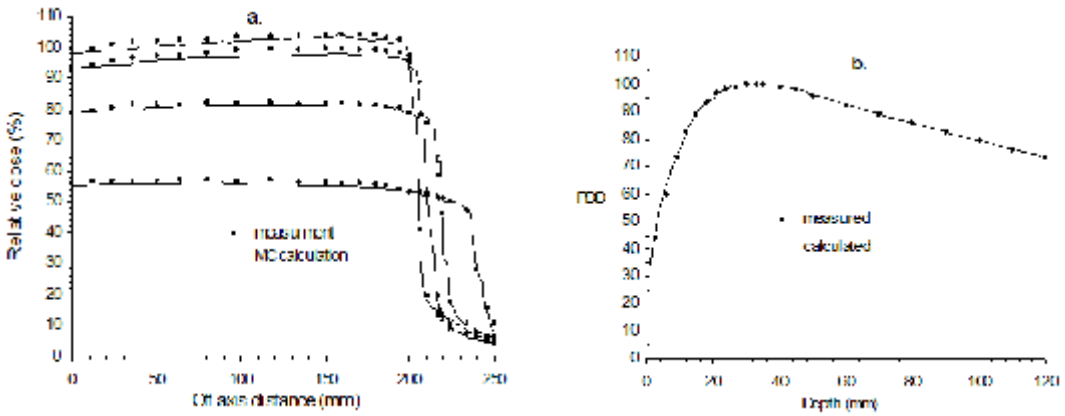

Fig. 3. Comparison of the Monte Carlo calculations with water phantom measurements: a. dose profiles at depths of 3, 5, 10 and 20 cm for the 40×40 cm^2 field size, b. PDD curve for the 10×10 cm^2 field size.

estimated to be 199 and 234 mSv, respectively. Removing of applied shields on lungs and thyroid increase these calculated effective doses up to 343 and 384 mSv.

From figure 5, the higher effective dosesand risks of second cancer were calculated for the nose, eyes and total sinuses due to their adjacency to the primary radiation field and therefore its higher absorbed doses. The skin of female has the larger cross-sectional area for scattered radiation exposures and therefore received higher dose and also higher second cancer risk.

DISCUSSION

The radiation-induced second cancer risk was estimated for AP and PA mantle field with 6MV photon beam. Both male and female phantoms were investigated. The organs located at further distance from the treatment field were received low absorbed dose (i.e. lower portion of leg).

Our results showed that out-of-field organs near the field received higher dose from scatted photons. The out-of-field organs such as the nose wall and contents, eyes, head and neck's skins and total sinuses have the higher received

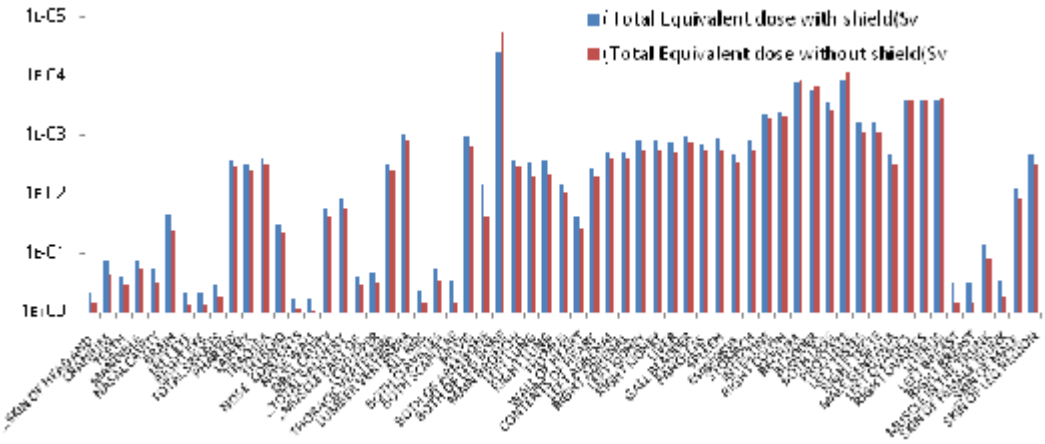

Fig. 4. Out-of-field organs equivalent doses in terms of sieverts per 40-Gy dose during mantle field radiotherapy for Hodgkin's lymphoma with and without shields.

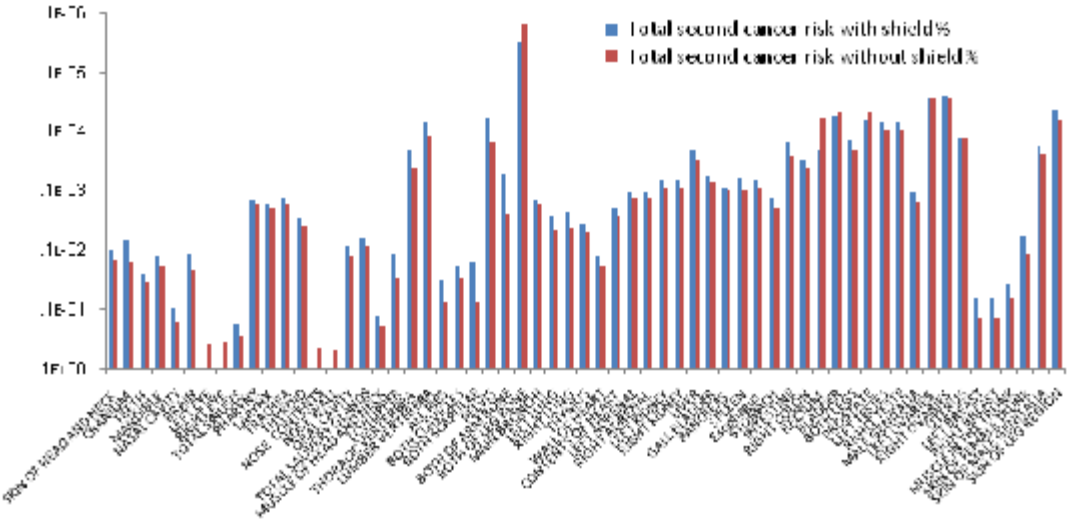

Fig. 5. Fatal cancer risk for various organs in term of a 40 Gy target volume dose during mantle field radiotherapy for Hodgkin's lymphoma from AP and PA mantle fields with and without shields.

doses. The larger dose to the organs adjacent to the applied field edges result higher effective dose and probability of second cancer risk. Therefore accurately estimations of organs dose near to the field's edge are crucial factor to optimise a well-established therapeutic plan. However applying of modern techniques such as intensity modulated radiation therapy (IMRT) provide better coverage of target volume but lead to higher effective dose and secondary cancer risk to patients due to delivering of increased monitor units in comparison to convential radiotherapy[2, 4, 20]. In a study by Koh et al.(2007), the mean dose and risk of second cancer were assessed on 41 patients with Hodgkin disease by 3 modality of treatment. Involved Field Radiation Therapy (IFRT) modality was reduced significantly risk of second cancer[2].

Using of ionization chamber and thermo luminance dosimeters to measuring of dose in form of equivalent dose as function of distance from the field edge[21] could not be an ideal manner. Considering organ specific doses[22] and also nonuniformity of dose distribution due to presence of inhomogenities is essential to prediction of out-of –field doses that could be implemented by MC modeling. In current study the effect of heterogeneities of tissues on mean absorbed dose was investigated by substitution of different materials of female phantom with water in the AP projection. The calculated effective dose of phantom with main material showed an increase of 17% compared to homogeneous water phantom.

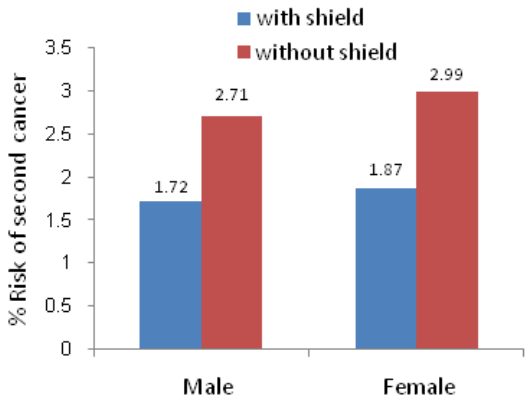

Fig. 6. % total secondary fatal cancer risk for male and female in terms of 40-Gy mantle field radiotherapy for Hodgkin's lymphoma.

Breasts in the case of female phantom with large volume compare to male's breast received considerable dose due to partly locating inside the irradiated field. The fatal cancer risk of breasts for female was calculated about 0.063%. Our finding is in agreement with one measured by Kowalski et al. (1998) that indicate notable radiation dose would be delivered to breast tissue during mantle field irradiation for Hodgkin's disease[9]. The greatest risk of developing secondary breast cancer is reported in <30 years old female during HL treatment and in female who treated with radiotherapy alone[6]. De Bruin et al. (2009) reported Mantle field irradiation results in >2-fold increase in the risk of developing secondary breast cancer compared to administration of radiation to the mediasten with a simular dose (36-44 Gy)[7].

As depicted in figure 6, the total secondary cancer risk followed by mantle field irradiation in AP and PA projections were calculated about 1.72% and 1.87% for male and female, respectively. Swerdlow et al[23] reported the relative risk of secondary cancers as 3.9 and 2.0 after combined modality treatment and chemotherapy alone, respectively. Increasing of the secondary cancer riskto 2.71% and 2.99% by removing of thyroid and breast shields confirms that accurately shielding of these critical organs adjacent to irradiation field is an important factor to decrease the late effect of radiotherapy of Hodgkin's disease.

CONCLUSION

In the current study, the equivalent absorbed dose, effective dose from out-of-field radiation were calculated during mantle field radiotherapy for Hodgkin's lymphoma for male and female.

Our results showed that out-of-field organs near the Mantle field (nose, eyes,…) received higher dose from scattered photons and result higher effective dose and probability of second cancer risk. Therefore accurately estimations of organs dose near to the Mantle field's edge and suitable shielding of critical organs such as lungs and thyroid are crucial factor to optimise a well-established therapeutic plan.

ACKNOWLEDGMENT

This study was supported financially by research affaires of Ahvaz Jundishapur University of medical sciences, Ahvaz, Iran.

REFERENCES

1. Mesbahi A, Seyednejad F, Gasemi-Jangjoo A. Estimation of organs doses and radiation-induced secondary cancer risk from scattered photons for conventional radiation therapy of nasopharynx: a Monte Carlo study. *Jpn J Radiol.* 2010 Jun; **28**(5):398-403. PubMed PMID: 20585932. Epub 2010/06/30. eng.
2. Koh E-S, Tran TH, Heydarian M, Sachs RK, Tsang RW, Brenner DJ, et al. A comparison of mantle versus involved-field radiotherapy for Hodgkin's lymphoma: reduction in normal tissue dose and second cancer risk. Radiation Oncology (London, England). 2007 03/15 11/15/received 03/15/accepted;2:13-. PubMed PMID: PMC1847517.
3. Schneider U, Lomax A, Pemler P, Besserer J, Ross D, Lombriser N, et al. The impact of IMRT and proton radiotherapy on secondary cancer incidence. *Strahlenther Onkol.* 2006 Nov;**182**(11):647-52. PubMed PMID: 17072522. Epub 2006/10/31. eng.
4. Zhang R, Howell RM, Giebeler A, Taddei PJ, Mahajan A, Newhauser WD. Comparison of risk of radiogenic second cancer following photon and proton craniospinal irradiation for a pediatric medulloblastoma patient. *Physics in medicine and biology.* 2013;**58**(4):807.
5. Davis QG, Paulino AC, Miller R, Ting JY. Mantle fields in the era of dynamic multileaf collimation: field shaping and electronic tissue compensation. *Medical Dosimetry.* 2006; B(3):179-83.
6. Crump M, Hodgson D. Secondary breast cancer in Hodgkin's lymphoma survivors. *Journal of Clinical Oncology.* 2009; **27**(26):4229-31.
7. De Bruin ML, Sparidans J, van't Veer MB, Noordijk EM, Louwman MW, Zijlstra JM, et al. Breast cancer risk in female survivors of Hodgkin's lymphoma: lower risk after smaller radiation volumes. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2009 Sep 10;27(26):4239-46. PubMed PMID: 19667275.
8. Schneider U, Lomax A, Lombriser N. Comparative risk assessment of secondary cancer incidence after treatment of Hodgkin's disease with photon and proton radiation. Radiat Res. 2000 Oct;154(4):382-8. PubMed PMID: 11023601. Epub 2000/10/07. eng.
9. Kowalski BS A, Smith MPH S. Measurement of radiation dose delivered to breast tissue during mantle field irradiation for Hodgkin's disease. Medical Dosimetry. 1998;23(1):31-6.
10. Lorigan P, Radford J, Howell A, Thatcher N. Lung cancer after treatment for Hodgkin's lymphoma: a systematic review. The Lancet Oncology. 2005 10//;6(10):773-9.
11. Stathakis S, Li J, Ma CC. Monte Carlo determination of radiation-induced cancer risks for prostate patients undergoing intensity-modulated radiation therapy. *J Appl Clin Med Phys*. 2007; **8**(4):2685. PubMed PMID: 18449157. Epub 2008/05/02. eng.
12. Murray L, Henry A, Hoskin P, Siebert F-A, Venselaar J. Second primary cancers after radiation for prostate cancer: a review of data from planning studies. *Radiation Oncology.* 2013; **8**(1):172.
13. Berris T, Mazonakis M, Stratakis J, Tzedakis A, Fasoulaki A, Damilakis J. Calculation of organ doses from breast cancer radiotherapy: a Monte Carlo study. *Journal of Applied Clinical Medical Physics*. 2013;B(1).
14. Lisik-Habib M, Czernek U, Debska-Szmich S, Krakowska M, Kubicka-Wolkowska J, Potemski P. Secondary cancer in a survivor of Hodgkin's lymphoma: A case report and review of the literature. *Oncology letters*. 2015 Feb; **9**(2):964-6. PubMed PMID: 25621073. Pubmed Central PMCID: 4301521.
15. Walter LS. (Ed.). LANL (Los Alamos National Laboratory) Monte Carlo N-Particle transport code system for multiparticle and high energy applications. Version 240, LA-CP-02-408, Los Alamos National Laboratory. 2002.
16. Cristy M, Eckerman KF. Specific Absorbed Fractions of Energy at Various Ages from Internal Photon Sources. Oak Ridge National Laboratory Report ORNL/TM-8381/VI. 1987.
17. ICRP Report 103. Recommendations of the international commission on radiological protection. *Ann ICRP.* 2007; **37**: 2–3.
18. NCRP Report 116. "Limitation of Exposure to Ionizing Radiation," National Council on Radiation Protection and Measurements. Bethesda, MD. 1993.
19. Allahverdi M, Zabihzadeh M, Ay MR, Mahdavi SR, Mesbahi A, Alijanzadeh H. Monte Carlo estimation of electron contamination in a 18 MV clinical photon beam *IJRR.* 2011;**9**(1):15-28.
20. Kry SF, Salehpour M, Followill DS, Stovall M, Kuban DA, White RA, et al. The calculated risk of fatal secondary malignancies from intensity-

modulated radiation therapy. *Int J Radiat Oncol Biol Phys.* 2005 Jul 15; **62**(4):1195-203. PubMed PMID: 15990025. Epub 2005/07/02. eng.

21. Howell RM, Hertel NE, Wang Z, Hutchinson J, Fullerton GD. Calculation of effective dose from measurements of secondary neutron spectra and scattered photon dose from dynamic MLC IMRT for 6MV, 15MV, and 18MV beam energies. *Medical physics.* 2006;**33**(2):360-8.
22. Walsh L, Rühm W, Kellerer AM. Cancer risk estimates for gamma-rays with regard to organ-specific doses. Radiation and environmental biophysics. 2004;43(4):225-31.
23. Swerdlow AJ, Higgins CD, Smith P, Cunningham D, Hancock BW, Horwich A, et al. Second cancer risk after chemotherapy for Hodgkin's lymphoma: a collaborative British cohort study. *Journal of clinical oncology* : official journal of the American Society of Clinical Oncology. 2011 Nov 1;29(31):4096-104. PubMed PMID: 21969511.