Review of Leakage from a Linear Accelerator and Its Side Effects on Cancer Patients

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Abstract

Radiation therapy using external beam radiation therapy (EBRT) is playing an important role for effective treatment of all kinds of tumors. Peripheral dose is the result of leakage and scatter from multileaf collimators devices (MLCs), counts for 2-10% of the maximum dose given to the patient, depending on the machine used and type of treatment. The present review reveals that despite of the recent advancements in linear accelerators (LINAC) and MLC design and technology, the remaining small amount of leakage (peripheral dose) of these devices still has significant side effects on patient's life span and quality of life after treatment. Based on the findings in this review, it is suggested that introduction of additional effective and patient-specific shielding techniques would have great impact on reducing risk of radiating healthy cells and hence adversely side effects on cancer patients.

Keywords: Radiation therapy; Peripheral dose; Patient-specific shielding

Introduction

Cancer is becoming one of the main burdens of human being all over the world. The number of cancer patients is increasing because of the growth and aging of the population, as well as an increasing prevalence of established risk factors such as smoking, overweight, physical inactivity, and changing reproductive patterns associated with urbanization and economic development. GLOBOCAN estimated about 14.1 million new cancer cases and 8.2 million deaths occurred in 2012 worldwide [1]. From the most recent reported statistics, cancer is becoming a major public health problem in the United States and many other parts of the world. It is currently the second leading cause of death in the United States, and is expected to surpass heart diseases as the leading cause of death in the next few years [2]. Radiation therapy is playing an important role for effective treatment of all kinds of tumors [3-6]. External beam radiation therapy (EBRT) is currently utilizing x-ray or electron beam through linear accelerators (LINAC) [7-14]. Figure 1 displays the LINAC unit used at Ellis Fischer Cancer Center of University of Missouri. LINAC therapy allows the oncologist to deliver higher doses of radiation to the tumor with limited damage to the surrounding healthy tissue and/or organs [15]. During radiation therapy, multileaf collimator (MLC) device is used to shape radiation beams coming from LINAC, to conform to boundaries of the treated target (tumor). Despite the recent advancement in the design of MLC, there is still a small amount of radiation, (peripheral dose), is transmitted outside the boundaries of the treated target defined by MLC (Figure 2). Peripheral dose is the result of leakage and scatter from MLC. Peripheral dose counts for 2-10% of the maximum dose given to the patient, depending on the machine used and type of treatment. The existence of MLC designs reduces the peripheral dose by 6% to 50% of open field radiation that are harmful to the healthy tissues [16]. This small amount of leakage could cause serious damage to surrounding health tissues and severe side effects. According to New York State Department of Health, excessive exposure to radiation leakages will cause vomit, cataracts, sterility, secondary cancer, and even fetal death. There is a risk of fetal damage at doses as low as 0.05 Gy, and the risk becomes significant at doses between 0.1 and 0.5 Gy [17]. Followill et al. [18,19] estimated that the percentage likelihood of fatal secondary cancers attributable to a prescribed dose of 70 Gy can be as high as 4.5% for Intensity-Modulated Radiation Therapy (IMRT) with 18 MV photon

Figure 1: Medical Linear Accelerator (LINAC) used for Radiation Therapy at Ellis Fischer Cancer Center University of Missouri, Columbia, MO USA.

beams and up to 8.4% for 25 MV photon beams. One could conclude from the reported survey that the level of leakage (peripheral dose) of existing treatment devices have significant side effects on patient's life span and quality of life after treatment. Additional shielding or blocking devices should be developed to reduce the harmful effects of peripheral doses.

Features of available Multileaf Collimator (MLC)

The overall goal of radiotherapy treatment is a precise delivery of the recommended dose to a target volume [25]. The dosimetric
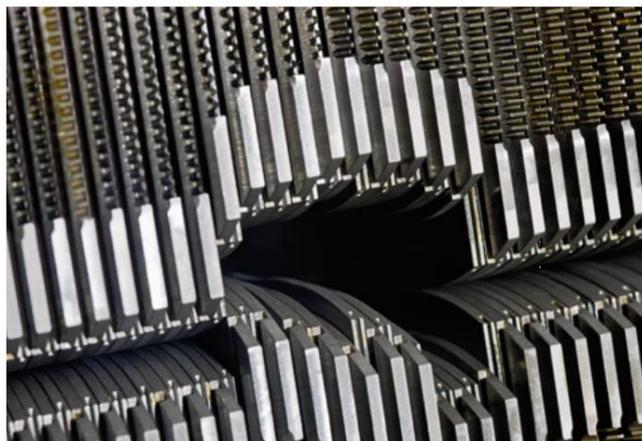
Figure 2: Siemens 160 MLC [20].

Figure 2: (a) 160 MLC with a certain shape open field.
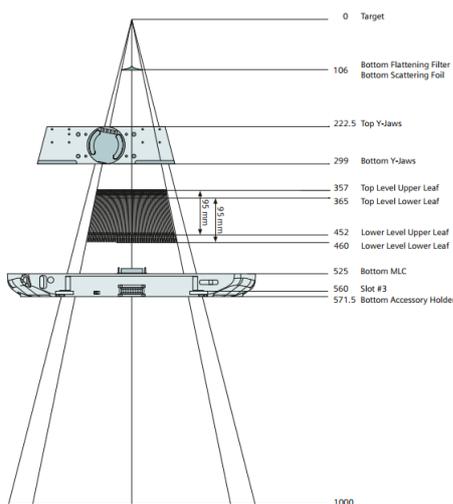
Figure 2: (b) 160 MLC dimensions and ranges.

Figure 3: An illustration of the AgilityTM collimator featuring the leaves and the sculpted diaphragms from the patient's eyen view [28].

characteristic of the new 160 MLCTM mounted on a linear accelerator (ARTISTETM Siemens Medical Solutions) is determined by Tacke et al. Through the dose calculations measured by a diode detector (PTW Diode P, Germany), the maximum observed interleaf leakage was 0.63% for a 100 × 100 mm² field. Subramaniam et al. did a dosimetric comparison with 2.5 mm high definition MLC to the 5 mm millennium multileaf collimator (MMLC), for volumetric-modulated arc therapy (VMAT)-based lung stereotactic body radiotherapy (SBRT), the high dosage spillage, in case of flattening filter-free (FFF) beam, was maximum for 2 cc volume at 2.9% for high definition multileaf collimator (HDMLC) and 3% for MMLC [26]. According to Fogliata et al., the accuracy of photon dose calculation algorithms in regards to out-of-field regions are often ignored regardless of its utmost importance for organs at risk and peripheral dose evaluation. The out-of-field (peripheral) dose is generated from three sources: leakage from the linear accelerator head shielding; radiation scattered from the LINAC head (mainly from flattening filter and collimating system); and internal scatter originating in the patient [27]. A new accelerator collimator, shown in Figure 3, containing a single pair of sculpted diaphragms that is orthogonally mounted to a 160 leaf of multileaf collimator (MLC).
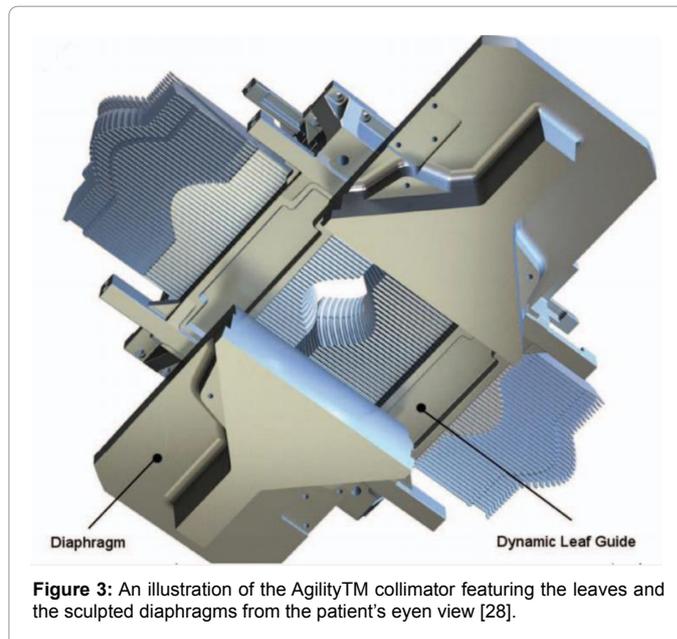
Dosimetric characteristics were evaluated by Thomson et al. [28]. They stated that the maximum transmission through the multileaf collimator, AgilityTM (Elekta AB, Stockholm, Sweden) which incorporates a full field, narrow leaf-pitch MLC), is 0.40% at 6 MV and 0.52% at 10 MV. When there is zero leaf gap, the off-axis intertip transmission is 2.2% for 6 MV and 10 MV. Kragla et al. determined the dosimetric properties of unflattened megavoltage photon beams at 6MV and 10MV of the Elekta Precise LINACs, where the accelerator is equipped with 40 leaf pairs (isocentric leak width 1 cm) and backup jaws that allows for maximum field size of 40 × 40 cm². The mean inter-leaf leakage was 1.7% ± 0.4% and 1.4% ± 0.3% for 6F* and 6U* beams (6F*, 6U*, 6F, 6U, 10F and 10U are the beam labels in reference [29], which are explained by Table 1). For 10F and 10U beams, it was reported that the inter-leakage is 1.7% ± 0.3%, and 1.5% ± 0.3%, respectively [29]. Asnaasharia et al. compared dosimetric characteristics of two MLC systems, Elekta "Synergy S" and Radionics micro-MLC (mMLC), which are frequently used for stereotactic radiosurgery and radiotherapy. It was reported that the maximum leakage percentage of the Radionics mMLC and beam modulator (BM) were 1.2 % and 1.3% maximum, respectively [30]. Moreover, mMLC and BM leaf transmission possibly will contribute to out-of-field dose leakages which will negatively affect normal healthy tissues. Based on numerous studies, LoSasso stated that the average static leakage (mid-leaf and interleaf) from the MLC is approximately 1.5% accounting for the open field dose for a beam of 6 MV and field size of 10 × 10 cm² and for a field sizes of 20 × 20 cm² the percentage leakage increased 20% [31]. Hong et al. presented investigated research in regards to planning and delivery of large IMRT fields using LINAC and MLC technology at 15 MV beams. With Varian 2100EX series, the utilization of film dosimetry estimated the scatter and leakage from MLC contributed approximately 4% of the total dose for the treatment field [32]. Podder et al. investigated the physical characteristics such as the interleaf leakage, transmission through the leaves and the tongue and groove effect of two linear accelerators (BrainLAB's Novalis and Elekta's Synergy-S Beam Modulator). It was determined that the tongue and groove effect of the Novalis is 23% ± 0.9% which is smaller than the Synergy-S of 25 ± 1%. The interleaf leakage and leakage from the leaves directly for synergy-S is 1.6 % ± 0.07% and 0.9% ± 0.04%, respectively,

MUW 6 MV SLH 6 MV MUW 10 MV

	FF	FFF	FF	FEE	FF	FEE
Quality index (TPRzono)	0.686°	0684°	0.681	0.664	0.735	0.714
Ds/Dio (10 x 10 cm²)	1.	1.	1.	1.320	1.	1.
Relative dose rate	1	2.	1	2.	1	2.30
Beam label in this work	sr	611	6 F	6U	10 F	IOU

Table 1: A Relative dose rate: ratio of maximum dose rate of FFF beam and the maximum dose rate of the clinically used beam. b TP820/10 matched for 10×10 cm² field size in reference conditions.

whereas for the Novalis it is 2 ± 0.08% and 1.3 ± 0.05% [33]. Garcia-Garduno et al. utilized GafChromic EBT radiochromic to measure dosimetric characteristics. The measurements were conducted using a Novalis linear accelerator, m3-mMLC that has 26 pairs of tungsten alloy leaves of several different width dimension [34]. The result shows a transmission percentage of the m3-MLC is 0.93 ± 0.05% with a leakage of 1.18 ± 0.11%. Belec et al. performed Monte Carlo calculations of dose distributions of the Varian CL2300 linear accelerator that has a 6 MV photon beam. The transmission percentage was determined to be 1.3% and the leakage percentage was determined as 2.4% [35]. The Siemens 160 MLC developed in 2009, is equipped with 160 leaves with a tungsten leaf thickness of 5 mm over a 40 × 40 cm field. It provides incredibly accurate conformity to the actual tumor shape for homogeneous dose coverage [20]. The 160 MLC was found to improve dosimetric conformity and IMRT delivery efficiency compared to the old model 58-ML [36]. However, the newly developed MLC still has a 2.75% of transmission from inter leaf, intra leaf and through jaws and 0.2% of maximum leakage [20]. Leaking dosage from MLCs measurements conducted by Arnfield, Mark et al. are described for two tungsten alloy MLCs: a Mark II 80-leaf MLC on a Varian 2100C accelerator and a Millennium 120-leaf MLC on a Varian 2100EX accelerator. MLC leakage was measured by film for a series of field sizes. Measured MLC leakage was 1.68% for a 10×10 cm field for both 6 and 18 MV for the 80-leaf MLC. For the 6 MV field, the 1.68% leakage consisted of 1.48% direct transmission and 0.20% leaf scatter [37]. It should be mentioned here that significant inaccuracy in the detectors measurement for the radiation dosage were reported [38]. Lárraga-Gutiérrez et al. concluded that statistically there is a significant difference in RT values amongst different detectors ranging from 3.5 to 12.5%. This variability in measurement could impact dosimetry of IMRT treatment by up to 1.78 Gy to the healthy tissue surrounding the target for a treatment of 60 Gy. This level of dose leakage to healthy tissue could cause severe health risk for patients [38]. Furthermore, most dosimetry measurements only focus on parts of leaking through the MLCs. According to Victor Tello's report, the primary x-ray transmission through the MLCs are nearly 9.5%, with 2% through the leaves, 3% through interleaf transmission, jaws 1% and cerrobend blocks 3.5%. These data are for the MLCs that have 40 pairs of leaves and width of 1cm with 6-7.5 cm of tungsten alloy [39].

Possible side effects from leakage generated at linear accelerator (linac) and other sources

Most of the currently used multileaf collimator (MLC) devices have leakage in the range of 2% to 9.5% of the full radiation dose. In case of using 7000 cGy dose to treat typical cancer patients, their healthy organs and tissues will be exposed to a range of radiation from 140 cGy up to 665 cGy. These level of exposure is more than sixty times what the human body can tolerate (10 cGy) with acceptable adverse side effects. Many papers have reported about Side effects after radiation therapy have been reported by many investigators [40-45]. Different tissues have different radiation tolerance, for example, for orbital tumors, whereas orbital bones, muscle, and fat can tolerate relatively high doses; the lens, eyelashes, retina, and lacrimal system are more radiosensitive [40]. Side effects such as dry eye, eyelash loss, cataract, neovascular glaucoma, radiation retinopathy, and optic neuropathy are all potential local complications of orbital irradiation [16,41-45]. On EU Scientific Seminar 2013, R. Padovani, presented the current status of dosimetry and radiation risk assessment in diagnostic and interventional radiology and future research and regulatory actions. Pathologies such as ESKD (end stage kidney disease), IBD (inflammatory bowel disease), CAD (coronary artery disease) and HT (heart transplant), requires frequency radiological examinations [46]. The existence of large cumulative individual doses is confirmed by this simple analysis of 6 months of radiological records in a hospital (Udine, 2013): (i) 2.4% of CT adult patients have received a DLP of more than 6700 mGycm (corresponding to approximately 100 mSv of effective dose for an adult standard man), (ii) a 28 years old man with 8 CTs has received 210 mSv. A study from Mei-Kang Yuan et al., has associated patients with several head and neck CT examinations with an increased risk of cataracts [47]. As stated by Mike Hanley from www. Xrayrisk.com, it is currently estimated that 62 million CT scans are obtained in the United States each year [48]. A study published 2004 suggested that radiation exposure from medical imaging may be responsible for 1-3% of cancers worldwide [49]. Occurrence of cancer within an irradiated field that was previously treated, clinically persuades medical experts that it is due to radiotherapy (RT) [50]. Little compared quantitatively the cancer risk estimates derived from recent life span study (LSS) cancer data with cancer incidence and mortality risks investigated by a patient population that underwent substantial radiation doses due to treatment for malignant and non-malignant conditions. M. Little minimally updated the studies relating to solid cancer and leukaemia from recently published reviews. It was reported that for solid cancers the ratio of LSS risks: RT risks ranges from 0.52 to 31.89 (Table 2), whereas for leukaemia the ratio of risks ranges from 1.72 to 524 [51-57]. Yuan et al., utilized information from 2 million random surveys of patients enrolled in the Taiwan National Health Insurance Research Database [58-60]. Among 2776 patients who had neck tumors and CT scans were conducted on the patients, the exposed patients exhibited higher overall incidence of cataracts (0.97%), where further stratification of the quantity of CT studies revealed that cataract incidence gradually increased with increased frequency of CT studies (0.79%, 0.93% and 1.45%, respectively) (p=0.0001, adjusted for trend) [60]. Sinnott et al. discussed radiation exposure relative to the thyroid stemming from diagnostic imaging and treatment and potential risks pertaining to the thyroid in childhood exposure due to its sensitivity to radiation at an early age [61]. It showed that radiation-related cancer occur more frequently in children than adults because children tissues are growing and cells are dividing more rapidly when exposing children to the mutagenic effects of ionizing radiation [61]. A radiological accident [62] occurred at the Bialystok Oncology Centre (BOC) in Poland in 2001 that negatively affected 5 patients undergoing radiotherapy. The patients' dosage were significantly higher than required which caused itching and burning sensations. Due to the severity of the over exposure, surgery was conducted in order to relieve the pain or to treat the injuries stemming from the radiation overdose. According to Taylor et al. radiotherapy in most developed countries

Reference	2nd cancer	Age at Ist Pt cancer Controls cancer range(mean)				Age at 2s cancer, (mean)	Dose to Dose to controls, average	Dose to controls, maximum	Study ERR Gy'(95%CI)	BEIR VII ERR	Ratio
Travis et al. [22]	Breast	Hodkins disease	105	266	13-30(22)	41	25	61	0.15 (0.04-033)	11	7.34
Inskip et al. [23]	lung	Breast	61	120	35-72(50)	68	6	23	0.20 (-0.62-1.03)	1.17	5.87
Gilbert et al. [24]	lung	Hodkins disease	227	455	9-81(49)	59	24	60+	0.15 (0.057-0.39)	1.43	9.56
Boice et al. [8]	Bone sarcoma soft tissue	cervix	15	155	<45-65+(45-54)	67	22	10+	0.02 (4.03-0.21)	NA	-
Boice et al. [8]	sarcoma	cervix	46	598	<45-65+(45-54)	67	7	10+	-0.05 (-0.11-0.13)	NA	-
Rubino et al. [25]	sarcoma	Breast	14	98	35-77(55)	62	19	80	0.05 (<0-1.18)	NA	-
Morton et al. [26]	esophagus	Breast	252	488	28-88(59)	74	7	45	0.08 (0.04-0.16)	0.61	7.64
van den Belt-Dusebout et al. [27]	Stomach	Testis & Hodkins disease	42	126	20-50+(34)	51	11	40	0.84 (0.12-15.6)	0.43	0.52
Boice et al. [8]	Colon	cervix	409	759	<45-65+(45-54)	68	24	40+	0.00 (-0.01-0.02)	0.36	-
Boice et al. [8]	Rectum	cervix	488	901	<45-65+(45-54)	68	45	60+	0.02 (0-0.04)	0.1	5.04
Boice et al. [8]	uterine carpus	cervix	313	469	<45-65+(45-54)	68	165	200+	(NA)	NA	-
Boice et al. [8]	ovary	cervix	309	560	<45-65+(45-54)	68	32	60+	0.01 (4.02-0.14)	0.32	31.89
Boice et al. [8]	Bladder	cervix	273	520	<45-65+(45-54)	68	45	60+	0.07 (0.02-0.17)	1.38	19.78

Table 2: Excess relative risks/Gy for second solid cancers among survivors of first cancer predominantly treated in adulthood [58] compared with risk in a similar (age, sex, follow-up matched) Japanese atomic bomb survivor subpopulation, via BEIR VII models [59].

are received by 50 percent of women with breast cancer, and in a random trails of 40,000 women, the beneficial effect of radiotherapy was offset by 30% increase in heart disease death rate due to ischaemic heart disease. Within the UK, majority of women receive tangential radiotherapy that delivers mean heart doses of approximately 1-2 Gy from the left-sided and 1 Gy from right-sided radiotherapy where in the right tangential radiotherapy, the heart received scattered irradiation only [63-67]. Based on the findings, statistics and discussions reported in the present review, it is suggested that introduction of additional effective and patient-specific shielding techniques would have great impact on reducing risk of radiating healthy cells by peripheral doses and hence adversely side effects on cancer patients. At present time, King Abdulaziz University in Saudi Arabia and University of Missouri in USA are collaborating in developing the new technology for the additional patient-specific shielding techniques.

Conclusion

The following conclusions can be drawn from the present review:

1- Radiation therapy using external beam radiation therapy (EBRT) is playing an important role for effective treatment of all kinds of tumors.

2- Peripheral dose is the result of leakage and scatter from multileaf collimators devices (MLCs), counts for 2-10% of the maximum dose given to the patient, depending on the machine used and type of treatment.

3- The present review reveals that despite of the recent advancements in linear accelerators (LINAC) and multileaf collimators devices (MLCs) technology, the remaining small amount of leakage of these devices still has significant side effects on patient's life span and quality of life after treatment.

4- Based on the findings in the present review, further research and development are recommended for establishing additional shielding devices that covers the patient's critical area around the treated target in order to maintain the fetal peripheral dose below acceptable levels.

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