Title: Comparison of the peripheral doses from different IMRT techniques for pediatric head and neck radiation therapy

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ABSTRACT

Intensity-modulated radiation therapy (IMRT) can deliver high and homogeneous doses to the target area while limiting doses to organs at risk. We used a pediatric phantom to simulate the treatment of a head and neck tumor in a child. The peripheral doses were examined for three different IMRT techniques [dynamic multileaf collimator (DMLC), segmental multileaf collimator (SMLC), and volumetric modulated arc therapy (VMAT)]. Peripheral doses were evaluated taking thyroid, breast, ovary, and testis as the points of interest. Doses were determined using a radio-photoluminescence glass dosimeter, and the COMPASS system was used for three-dimensional dose evaluation. VMAT achieved the lowest peripheral doses because it had the highest monitor unit efficiency. However, doses in the vicinity of the irradiated field, i.e., the thyroid, could be relatively high, depending on the VMAT collimator angle. DMLC and SMLC had a large area of relatively high peripheral doses in the breast region.

INTRODUCTION

Intensity-modulated radiation therapy (IMRT) that uses multi-leaf collimators (MLCs) can deliver high and homogeneous doses to the target area while limiting doses to surrounding normal tissue. A major difference of IMRT from the conventional method, such as three-dimensional conformal radiation therapy (3D-CRT), is the shielding of organs at risk (OARs) in the irradiation field by using the MLC. However, the volume exposed to lower doses in peripheral fields may be increased compared to conventional techniques. Two studies have shown that IMRT to the head and neck regions gave a smaller peripheral dose to the thyroid, which is located close to the irradiation field, than 3D-CRT did [1, 2]. However, it is not entirely clear whether peripheral radiation exposure from IMRT is higher than that from conventional radiation therapies, 3D-CRT [3-10]. The problem of the peripheral dose is more serious for children. Because of their small body size, the sparing of OARs is more difficult than for adults, and peripheral low doses will affect a larger volume fraction of the whole body. Soft-tissue sarcomas, frequently treated with postoperative radiotherapy, have shown a 10%–15% absolute increase in 5-year survival rates in the United States from 1975 to 1995 [11]. Rhabdomyosarcoma is the most common soft tissue sarcoma in pediatric patients. Lockney et al. [12] reported that late radiation toxicities are commonly seen in pediatric rhabdomyosarcoma survivors treated with IMRT to the head and neck.

According to previous studies, the monitor unit (MU) value plays an important roles in the peripheral doses of IMRT in addition to MLC leakage and radiation-scattered in the patient's body. Since IMRT techniques produce many small radiation fields in order to create a modulated field, they require larger MU values. Indeed, the MUs of IMRTs were reported to be approximately several fold larger than that of 3D-CRT [4, 5]. Larger MU values, which require the radiation delivery system to be energized for a longer time, can result in larger peripheral doses [5].

Supporting this notion, higher MUs are reported to have resulted in larger peripheral doses [4]. However, Mansur et al. [1] argued that larger MUs are not necessarily related to larger peripheral doses, and reported an important role of internal scattered radiation, which is associated with the distance between the irradiation field and the risk organs, and the depth of the OAR in the body. They reported that peripheral doses tend to be larger if risk organs are located closer to the irradiation field [1]. Leakage radiation is related to the structures of the gantry head, including the MLC, the flattening filter, and the jaws. Their thickness and structure, and the materials used in their construction are important [5, 13].

The peripheral dose of IMRT techniques are affected by the factors described above. Three types of IMRT techniques with MLC are, in increasing order of dynamic parameter change, segmental MLC (SMLC), dynamic MLC (DMLC), and volumetric modulated arc therapy (VMAT). We suspect that VMAT, a new type of IMRT technique, is to require low MUs and to result in lower peripheral doses on average. In the present study, peripheral doses from secondary photons were measured for the three IMRT techniques. These measured peripheral doses were compared with the doses evaluated using a pediatric phantom.

MATERIALS AND METHODS

We compared three different IMRT techniques (DMLC, SMLC, and VMAT) using the Novalis™ TX Radiation Therapy System developed by Varian (Varian Medical Systems, Palo Alto, CA, USA) and BrainLab (Kirchheim, Germany). This system uses a 120-leaf MLC (height: 6.8 cm, thickness: 2.5 mm and 5 mm for central and outer parts, respectively, max field size: 22 cm× 40 cm) (HD120MLC™, Varian Medical Systems). As a reference, 3D-CRT was used on the same machine.

The American Association of Physicists in Medicine (AAPM) Task Group 119 (TG-119) proposed a set of test cases called multi-target, mock prostate, mock head and neck, and C-shape to ascertain the overall accuracy of IMRT planning [14]. In the present study, the mock head and neck plan was used as the benchmark. Treatment plans were created using the Eclipse Treatment Planning System (Varian Medical Systems).

Before a patient undergoes IMRT, the treatment regimen must be planned in detail. Doses were calculated using the Analytical Anisotropic Algorithm (AAA) ver. 10, a treatment planning system (TPS). In an ordinary clinical setting for pediatric head and neck radiation therapy, photon energies is of 6 MV X-Rays. Kry et al. [4] reported that the choice of 10 MV X-Rays for IMRT treatment may be more advantageous for the patient's long-term health in a study of prostate cancer. In our experiment, photon energies of 6 and 10 MV X-Rays were used for comparison. The prescribed dose was 50 Gy delivered in 25 fractions. For all plans, a grid size of 2.5 mm was used as the default value for dose calculation. All treatment plans were ensured to meet TG 119 requirements, including dose volume constraint, dose prescription, and dose goals. For the head and neck planning treatment volume (PTV), dose goals were specified as D99, D90, and D20. For normal structures, D50 was used for parotid and maximum dose was used for spinal cord [14].

The treatment plans were defined so that the different IMRT techniques gave similar dose–volume histograms (DVHs). Table 1 shows the doses that satisfy the requirements of AAPM TG-119 for DVH parameters of the target region that were used in the present study. The beam arrangements were set to achieve the required DVH parameters and to insure similar DVH slopes for the PTV and major OARs in the irradiation field (the parotid gland and the spinal cord) for the three IMRT techniques. The present study used collimator angle of 30° to reduce tongue-and-groove effects, which cannot be ignored in the case of VMAT since a leaf may move back and forth repeatedly and extend into the radiation field for a prolonged time during VMAT delivery. Note that DMLC has IMRT delivery with a sliding window technique in which the leaves move only once across each treatment field and, therefore, tongue-and-groove dose effects are small [15]. In the case of SMLC, its IMRT delivery is a step and shoot and does not involve a sliding window. In an ordinary clinical setting using VMAT, the collimator angle of 0° is not used because of 1) a technical difficulty in achieving an ideal distribution of radiation for the target region; and 2) physical characteristics producing more harmful effects of leaf. In our experiment, the collimator angles of 0° and 30°were used for comparison. Note that, in the cases of DMLC and SMLC, the collimator angle is always fixed to 0°. Typical beam arrangements were as follows: for DMLC, nine fields at 40° intervals, collimator angle (0°); for SMLC, nine fields at 40° intervals, collimator angle (0°); for VMAT, two arcs (–179° to 181°) with collimator angles of 30° and 330°, and two arcs (–179° to 181°) with a collimator angle of 0°; and for 3D-CRT, one arc (160° to 240°) with a collimator angle of 0°. In this study, 3D-CRT was used as a reference. Since the DVH setting of AAPM TG-119 is for IMRT planning and it is not achievable when using 3D-CRT, the DVH for 3D-CRT was set as close as possible to the targeted value. Phantom mapping was conducted using a pediatric therapy whole body phantom (PH-38, Kyoto Kagaku, Kyoto, Japan) (Figure 1). The pediatric phantom had a height of 60 cm.

Dosimetric assessment was made using a model GD-302M radio-photoluminescence glass dosimeter (Asahi Techno Glass Corporation, Shizuoka, Japan). The size of the model GD-302M is 1.5 mm in diameter and 12 mm in length. The dose reading of the glass dosimeter is automatically done by the FGD-1000 reader (Asahi Techno Glass Corporation, Shizuoka, Japan). Standard calibration is executed in order to secure traceability of dose read-out value, and it determines the dose equivalent of internal calibration glass inside the reader. Dose calibration is automatically performed with the standard irradiation glass element and the sensitivity calibration with the internal calibration glass element. This dosimetric system can be readout with two modes; standard-dose range (10 μGy-10 Gy) or high-dose range (1-500 Gy). In this study, standard-dose range was used for peripheral photon doses. Araki et al. [16] reported that the energy dependence of glass dosimeter is within 2% for photon energies of a ^{60}Co beam, 4 MV and 10 MV X-rays beams. The dosimeters were placed in four points of interest including the thyroid, breast, ovary, and testis. The distances from the isocenter to the points of interest were 6, 15, 32, and 40 cm, respectively. The dosimeters were placed at 2 cm depth in the case of the thyroid, at 4 cm depth in the ovary, and at the body surface in the case of breast and testis and covered with 5 mm thick bolus for electronic equilibrium. The whole process of measuring was repeated five times.

We evaluated the real peripheral dose distributions, which might not be predicted correctly by the TPS, using COMPASS (IBA Dosimetry, Schwarzenbruck, Germany). A collapsed cone superposition algorithm was used for dose calculation by COMPASS Ver. 3. This system acts as an independent secondary TPS that allows the calculation of dose distributions based on a commissioned beam model (describing, for example, the beam spectrum, leakage radiation, head scattering, and lateral profiles), the plan, segmentation, and patient computed tomography (CT) data (the latter three were imported via DICOM or Digital Imaging and Communication in Medicine). COMPASS adjusts the resulting doses to the measurements obtained from the 2D ion-chamber array (2D-IC array MatriXX, IBA Dosimetry) that is attached to the gantry head (Figure 2). In this way, the actual effects of collimator leakage, tongue-and-groove effects, and penumbra as well as the complex interplay between leaf position, gantry and collimator angle, and the dose rate in highly dynamic treatments can be evaluated for the real delivery of irradiation [17, 18].

The measured peripheral doses ware compared by Kruskal-Wallis test and Mann-Whitney U test among three IMRT techniques and two collimator angles, respectively. Steel-Dwass test was conducted for multiple comparison. Correlations between the measurements of glass dosimeters and COMPASS results were examined by Spearman's rho test. All statistical analyses, except Steel-Dwass test, were performed using STATA version 14.0 (StataCorp, Texas, USA). Steel-Dwass test was conducted by R version 3.2.2 (R Foundation for Statistical Computing, Austria).

RESULTS

Table 1 presents absorbed doses calculated using relevant TG-119 DVH-derived parameters on the basis of TPS for the target and the OARs in the irradiation field (the spinal cord and parotid gland) for photon energies of 6 and 10 MV X-Rays. The results were very similar for all energies and IMRT techniques as expected. Table 2 presents MU values for each technique and shows that the differences in MU efficiency are very pronounced for the various techniques. The MU values were highest for DMLC and then, in decreasing order, lower for SMLC, VMAT, and 3D-CRT. Moreover, MU values were higher for 6 MV X-rays than for 10 MV X-rays. The non-modulated technique (3D-CRT) had the highest MU efficiency, but it was quite noticeable that VMAT was about 3 times more efficient than DMLC was.

Table 3 summarizes the peripheral doses measured using radio-photoluminescence glass dosimeters for 6 and 10 MV X-rays. The doses for the organs far from the target (i.e., breast, testes, and ovary) were the lowest for 3D-CRT, and the results for modulated techniques were lowest for VMAT: the other IMRT techniques gave about 2-2.5 times the dose for VMAT to these distant organs. The doses of both DMLC and SMLC were significantly higher than those of VMAT in all comparisons ($p = 0.024$ for all comparisons by Steel-Dwass test). Furthermore, the doses of DMLC were also higher than those of SMLC in these sites ($p = 0.024$ for all comparisons by Steel-Dwass test). However, the dose in the peripheral area close to the target (i.e., the thyroid) was higher for VMAT than for the other IMRT techniques. However, the differences between the thyroid doses for all modalities were less pronounced than those for the outer periphery, and the differences between 6 and 10 MV X-rays were not very large.

The results of COMPASS for one fraction dose showed strong correlations with the measurements made using the glass dosimeter for both 6 and 10 MV X-Rays (Figure 3).

Figure 4 presents the peripheral dose distributions measured by COMPASS for both 6 and 10 MV X-Rays. For VMAT, relatively high doses were measured in the area close to the irradiation field, and lower but non-negligible irradiation was detected even in distant areas. The measured dose distributions for DMLC and SMLC showed extensive areas with relatively high doses in the breast region. For DMLC, some breast areas received doses higher than 2Gy. For VMAT, relatively high dose areas were found in the area close to the irradiation field. The peripheral doses for VMAT were similar to those of 3D-CRT and were lower than those for DMLC and SMLC.

Table 4 shows the results of dose measurements for VMAT with collimator angles of 30° and 0°. A 30° angle is frequently used in clinical settings. VMAT treatment plans for collimator angles of 30° and 0° are shown in Figure 5, and the peripheral dose distributions measured by COMPASS are presented in Figures 6. For a collimator angle of 30° as above, low doses were found over wider areas than for other IMRT techniques, and the dose in the vicinity of the irradiation field was high in Figures 4. In contrast, for a 0° collimator angle, peripheral dose in the vicinity of the irradiation field was low, and the extent of the low-dose areas were similar to those for 3D-CRT. Moreover, the dose area was smaller than for a 30° collimator angle. However, the 0° collimator angle resulted in higher peripheral doses in areas other than the thyroid (Figure 6).

DISCUSSION

In the present study, we used a pediatric phantom and showed that the peripheral doses varied for different IMRT techniques for pediatric head and neck radiation therapy. One-fraction dose measurements using radio-photoluminescence glass dosimeters showed that peripheral doses to the breast, ovary, and testis were highest for DMLC and then lower for SMLC, VMAT, and 3D-CRT, in that order, indicating that peripheral doses delivered by IMRTs are strongly dependent on the number of MUs used for the irradiation. Note that the MU efficiencies were lowest for DMLC and then higher for SMLC, VMAT, and 3D-CRT, in that order. However, the peripheral doses in the thyroid were, from highest to lowest, in the order of VMAT, DMLC, SMLC, and 3D-CRT. The dose to the thyroid region, which is located close to the irradiation field, can be affected by direct irradiation and by internal scattered radiation. Because of the large number of possibilities regarding the shape of the irradiation field, the collimator angle, and jaw shapes, the thyroid dose can be strongly affected by the treatment plan.

The use of the COMPASS system enabled us to evaluate the 3D distribution of peripheral doses. The analysis carried out with COMPASS revealed that VMAT leads to areas with a relatively high peripheral dose in the vicinity of the irradiation field (Figure 4). In the low-dose areas, however, doses were similar to those observed for 3D-CRT. The COMPASS system (total fraction doses) also showed that DMLC and SMLC, which used more than 1000 MUs, have a large area of relatively high peripheral doses in the breast region. It is of note that for DMLC, some parts of the breast region received a dose greater than 2 Gy. Mansur et al. [1] have also reported that DMLC and 3D-CRT resulted in relatively high doses for the breast. Sharma et al. [19] reported that the collimator scatter and transmission re-increased at the location of 12cm from the isocenter. In this study, the distance of breast region from isocenter was approximately 15 cm, and thus, the breast might be strongly affected by the radiation scatter and transmission from MLCs and Jaws. Since the mammary gland is known to have a high risk of radiation-induced cancer [20], the risk of secondary cancer associated with radiation is a concern especially for girls and young women, because the risk is higher for these patients than for older women.

When it comes to the risk of radiation-induced cancer, two aspects must be considered: first, as indicated by the United Nations Scientific Committee on the Effects of Atomic Radiation [21], children are more sensitive to radiation than adults are with respect to approximately 25% of cancer types, including leukemia and thyroid, skin, breast, and brain cancer. Second, the time span from radiation exposure to the development of cancer can be long, and therefore the longer life expectancy of children results in a higher lifetime risk for secondary cancer. Hall [5] argued that an increase of secondary cancer risk in the order of 1.5%–3% can be regarded as acceptable for adults, but this figure is considered too high for children.

When the VMAT collimator angle was set to 0°, the thyroid doses became lower than those for DMLC and SMLC (Table 3 and 4). As shown in Figure 5, when compared with 0°, the areas of shielding by the jaw are reduced in the case of 30°, and as a result, the doses in the vicinity of the irradiation field for 0°became lower than those for a 30° collimator angle. However, the breast doses were not affected evidently. Because the presence of the jaw made the irradiation field narrower, the scattered dose from the jaw was increased slightly, making the average dose in the low-dose area higher. Setting the collimator angle to 0° in VMAT is good from the viewpoint of making the dose in the vicinity of the irradiation field smaller. However, in clinical settings, the distribution of the dose and the DVH in risk organs in the irradiated field should be considered when the collimator angle is determined.

VMAT has a very good MU efficiency. Whereas DMLC and SMLC modify the dose intensity by MLC shielding only, VMAT can additionally modify dose rates and the gantry speed, resulting in a lower number of MUs than DMLC or SMLC [22]; therefore, the peripheral doses are lower for VMAT than for the other IMRT techniques. This advantage for VMAT was also evident in a study of cervical cancer patients reported by Jia et al. [23], in which VMAT resulted in lower peripheral doses than did SMLC. In our study, the doses for ovary and testis, which are located far from the isocenter, can be considered to be proportional to the radiation leakage through the MLC leaves.

The MU efficiency also depends on the photon energy; therefore, the number of MUs for 10 X-Rays is usually lower than that for 6 MV X-Rays. Taylor et al. [24] reported that lower-energy beams tend to result in greater peripheral photon doses than higher-energy modes. This is because lower-energy photons are less forward-scattered than higher-energy photons. Kry et al. [4] compared 6 and 10 MV X-Rays and reported that the 10 MV X-Rays resulted in lower peripheral doses. However, in the present study, the peripheral doses for 10 MV X-Rays were only slightly lower than those for 6 MV X-Rays except the breast region. 10 MV X-Rays were relatively high peripheral doses in the breast region. Zygmanski et al. [25] reported the scatter at 10 MV X-Rays is almost the same as at 6 MV X-Rays. Compare to 6 MV X-Rays, the MU values of 10 MV X-Rays were lower, which results in lower leakage doses in 10 MV X-Rays. On the contrary, the higher energy increases scatter doses from collimator head. Thus, it is hard to estimate which peripheral dose is higher between 6 and 10 MV X-Rays.

An additional problem related to 10 MV X-Rays is the presence of secondary neutrons. Secondary neutrons, which are generated by the nuclear interactions between X-rays and materials, can be produced with acceleration voltages of 10 MV X-Rays or higher [3, 4].

Although the strong correlation between the measurements made using glass dosimetry and the COMPASS system proved the high reliability of the COMPASS results, the values for the pelvic region should be interpreted with care because this area is more than 30 cm away from the isocenter, and so accuracy cannot be guaranteed by this system. Another limitation is that the results can be affected by target organs, the shape of the irradiation field, the types of linear accelerator and MLC, and TPS algorism.

CONCLUSION

The present study used a pediatric phantom and showed that the peripheral doses were affected by the use of different IMRT techniques for pediatric head and neck radiation therapy. VMAT had the lowest peripheral doses because its MU efficiency was quite high. However, doses in the vicinity of the irradiation field, such as the thyroid, could be relatively high for VMAT, depending on the collimator angle. For DMLC and SMLC techniques, radiation transmitted through the closed collimator leaves resulted in higher doses to the peripheral areas. Moreover, the doses to the breast for these techniques were higher than that for VMAT. The problem of the peripheral dose is more serious for children than for adults because children have higher radiation sensitivity and longer life expectancies; therefore, TPS plan for children should be carefully evaluated. According to our results, for female children of similar stature to that of the phantom used in this study, VMAT should be the technique of choice.

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