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Measuring Out-of-Field Dose to The Whole Brain In Radiotherapy

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ABSTRACT

The aim of this study is to measure out-of-field lens and thyroid doses in whole brain radiotherapy with thermoluminescence dosimeters (TLD) and compare them with treatment planning system (TPS) calculation values.
Before Computed Tomography (CT), TLDs were placed on the lens and thyroid surfaces of the rando phantom and then the phantom was scanned with CT. Data was transferred from CT to RayStation™ TPSs and then target volume and critical organs were determined. The treatment plan was created. TLDs were placed on the lenses and thyroid for out-of-field dose measurement.
For the right lens, the mean value of TLD measurements were 188.3±2.2 cGy and the mean values of TPS measurement were 192.0±0.2 cGy. The average TLD measurement for the left lens was 190.2±0.5 cGy, and the average TPS dose reading was 192.0±0.1 cGy. For doses in the thyroid region, which is further from the target, the TLD measurement and TPS reading averages were 44.9±5.2 cGy and 40.9±6.3 cGy, respectively. Accordingly, right lens point doses calculated from TPS were 1.93% higher than TLD measurements. For the left lens, this difference in the same direction was determined as 0.93%. Within the thyroid region, TLD measurements were observed to be higher than TPS readings.
We measured out-of-field doses via TLDs and found that TPS calculations for thyroid were 8.90% lower than the measured dose. The results we obtained from our study are guiding in estimating out-of-field lens and thyroid doses in 3DCRT whole brain irradiation.

Keywords: 1.Lens, 2.Out-of-Field, 3.Thyroid, 4.TLD, 5.TPS

Introduction

More than 50% of cancer patients need radiotherapy (1). In recent years, there have been improvements in various medical fields and technologies, leading to advancement in patient's health. Significant progress has also been achieves in understanding the radiobiological effects of radiotherapy (2). Radiotherapy aims to prevent the surrounding tissues from receiving high doses while providing the dose delivered to the tumor volume (3). Knowing prognostic factors in light of current treatment modalities is important in predicting the response to the applied treatment modality (4). Radiotherapy treatment techniques for whole brain radiation therapy (WBRT) treatment had advantages and disadvantages according to each other for target volume and critical organ doses such as lenses, eyes, and optical nerves (5). External radiotherapy must meet the recommendation of the International Commission on Radiation Units and Measurement (ICRU), which says that the whole volume of the target must obtain a homogeneous radiation tolerance of 95-107% (3). Whole-brain radiotherapy has been demonstrated to extend the survival of patients with brain metastases from around 1-2 months to 3-6 months (6). The mechanism of pain palliation after radiotherapy is still not fully defined because, the use of different tumor types and scoring methods in the studies (7). During radiotherapy, tumor destruction is achieved using ionizing radiation that causes cell death. Additionally, unintended doses of radiation outside the target area can also be harmful. This may be important not only for critical tissues close to the target volume but also for tissues far from the primary area due to scattering or leakage. This is the most important case for pediatric patients. The longer survival expectancy of pediatric patients means that the likelihood of radiation-induced side effects increases. The increasing interest in out-of-field doses in linear accelerators used for therapeutic purposes began in the 1970s.

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Recently, there has been more interest in critical organ doses other than the target volume[8]. Studies have shown that doses received outside the treatment area are underestimated and that this difference reaches up to 100% as we move away from the target volume (9, 10). In this case, predictions may not be adequately understood in terms of both secondary cancer risks and potential deterministic effects on organs. The risk of radiation-induced secondary cancer is considered a late effect of radiotherapy resulting from primary cancer treatment (11, 12). This may be due to the possibility of the treatment planning system (TPS) reading the scattered radiation dose less accurately, especially as one moves out of the field (9). Accuracy in dose distribution is very important in radiotherapy. One way to verify the actual dose given to each patient in treatment is with in-vivo dosimeters. Such an application can contribute to confirming the accuracy of dose distribution expected from radiotherapy treatments and can play important roles in quality control processes. That is why many international reports recommend in-vivo dosimetry to ensure dose accuracy in external radiotherapy (13-18). Silicon diode and thermoluminescence dosimeters are well-established devices used in many applications, both phantom and in-vivo (19-21). In-vivo dosimeters are generally among the recommended dosimeters because they have been used in radiotherapy for many years. They are generally used to measure input and output doses by being placed on the patient surface or to control the dose to risky organs such as lenses outside the area. For areas larger than and equal to 2x2 cm^2, the relative differences between TLD and Monte Carlo (MC) on the phantom surface were less than 2%; this difference may be due to the smaller volume cross-sectional area and, hence, lower exposure to electron contamination. The volume effect is probably the main reason for the differences seen between the face-down TLD, electron field diode (EFD), and MC gold standard. Importantly, placing a TLD chip face-down is much more practical for in-vivo dosimetry (13). Today, measurements, TPSs, and simulations such as MC are used to determine the external radiotherapy dose (22). Although these methods are successful in dose evaluations in the treatment area, difficulties may be encountered in areas outside the field. It has been reported that TPSs contain significant uncertainties in dose calculations outside the field (23). The literature shows us that commercial TPSs are not sufficient to accurately calculate the dose in out-of-field (24). Ana Cravo Sa et al., reported in their study that TPSs calculated 92% less dose than TLD measurements and MC calculations (25). Another example, Howell and colleagues reported that, compared to TLD and Eclipse's TPS using the Analytical Anisotropic Algorithm (AAA) had a 55% lower dose at 11.25 cm outside from the field (10). TLDs offer measurement for a wide range of doses. Interference of TLD measurements with radiation can be corrected by an energy-dependent calibration factor. This correction factor can be obtained from a MC simulation of the photon energy spectrum. The disadvantage of this method is that it is based on simulations obtained from the expected photon energy spectrum (26-28).

Cataracts in the eye may occur as a result of aging, trauma, surgery, and radiation exposure (29). Radiation-induced cataracts were already thought to have deterministic effects (30). In the past, the eye lens dose limit for occupational exposure was 150 millisieverts (mSv) per year. However, when we look at the latest epidemiological studies (29, 31), the International Commission on Radiological Protection (ICRP) reduced the dose limit for lenses from 150 mSv to 20 mSv per year on average for certain periods of 5 years, provided that it does not exceed 1000 mSv in any year[32]. Lens doses are an important issue in radiotherapy. Studies of Radiation Therapy Oncology Group (RTOG) 0539 and 0825 recommend that the dose limit be kept at 7 Gy (33, 34).

The aim of this study is to measure the lens doses and the doses received by the thyroid from out-of-field organs with TLDs and compare them with TPS values in whole-brain radiotherapy using standard right-left opposing fields. Thus, it is aimed at better evaluating end-of-treatment side effects with more accurate out-of-field doses in all brain patients, especially children.

Materials and Methods

Simulation and Target Volume Delineations: Before CT, TLDs were placed on the lenses and thyroid surfaces, and these TLDs that did not create artifacts were contoured. For TPS and dose measurements from the same point, the extra TLDs we had were used as markers that would not create artifacts. Then, the phantom was placed on a Siemens Spirit (Siemens, Germany) computerized tomography device in the supine position and scanned with 3 mm slice intervals. The data was transferred from CT via Digital Imaging and Communication in Medicine

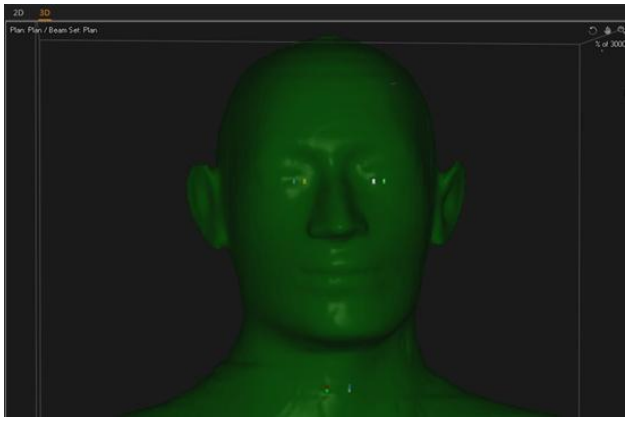

Fig. 1. TLD dose measurement points on the phantom

(DICOM) to RayStation™ TPS (RaySearch Laboratories AB, Stockholm, Sweden). Then, the target volume, the whole brain, and critical organs were delineated.

Treatment Planning: In the treatment planning, conventional right-left opposite fields are used. The plan was created by the physicist to receive a dose of 30 Gy in 10 fractions to the whole brain target. A margin was given to multi-leaf collimators so that the treatment plan covered the whole brain by 5 mm from the right-left opposite areas. In Figure 2, the DRR image of the treatment areas is shown from the front. The plan was made so that 95% of the target volume would receive 95% of the dose. Additionally, it was ensured that the maximum plan dose did not exceed 110%. 6 MV (million-volt) photon energy was selected in the plan. Point doses were taken from RayStatiton TPS using the Collapse Cone algorithm for 8 TLD measurement points.

Thermoluminescence Dosimetry: In this study, Mg and Ti doped TLDs were used. TLDs are LiF: Mg, Ti (TLD-100), a LiF material in the form of a 3.2 mm x 3.2 mm x 0.9 mm chip. TLD is tissue equivalent and has an effective atomic number of 8.14. They are preferred in dose measurements due to their high sensitivity. Other reasons for preference are its small size and wide dose distribution. TLDs were subjected to a series of irradiation and baking protocols before calibration. Our 23 TLDs were irradiated on a Siemens Artiste device calibrated to deliver a dose of 1 cGy at 1 MU in 1.6 cm depth. Element correction coefficient (ECC) and reading calibration factor (RCF) factors of each TLD were obtained. As a result of calibration, 8 TLDs with 1% sensitivity were used in dose measurements. 23 TLD were calibrated, but measurements were made with 8 of them with a sensitivity of ±1%.

Harshaw 3500 (Harshaw-Bicron, USA) TLD reader was used to read the irradiated TLDs.

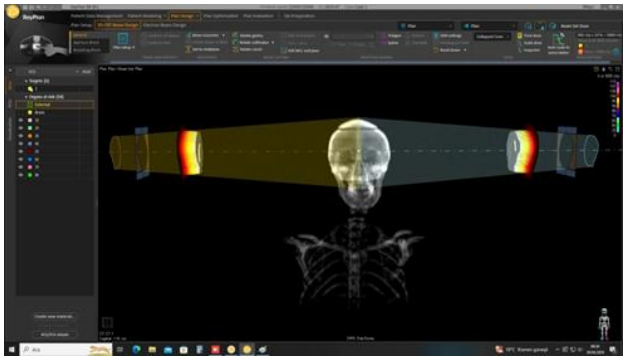

Fig. 2. Preliminary DRR image of treatment areas obtained from planning

TLDs were subjected to the annealing process for reuse. The annealing process was applied for 1 hour at 400 ºC and 2 hours at 100 ºC. TLDs were heated at 100 ºC for 10 minutes before reading.

Defining Measurement Points On The Phantom: TLD procedures were performed in a rando phantom (The anthropomorphic RANDO phantom) made of human tissue equivalent materials such as the patient's bone, soft tissue, and lung. For out-of-field dose measurement, TLDs were placed on the skin surface of the lenses and thyroid area. 2 TLDs were placed on each lens surface, and 4 TLDs were placed on the thyroid area surface. To reduce dose measurement uncertainty, dose measurement was repeated three times, and skin doses were determined by taking the averages. Positions of TLDs on the phantom is also shown in Figure 1.

Dose Measurements: The anthropomorphic Rando phantom was placed on the table of the linear accelerator as in the simulation. Before irradiation, a port image of the phantom was taken. After correct positioning, 8 TLDs were placed as in the CT simulation. The prescribed treatment dose was given as 3 Gy for a fraction, and this process was repeated three times. After taking point doses from the plan made on the phantom, the results obtained from TLD measurements were compared for the same points as a total dose of 30 Gy, which is the daily dose multiplied by ten fractions.

Results

The percentage difference and standard deviation between the measurement averages made with TLD irradiations and the point doses taken from TPS are shown in Table 1. For the right lens, the TLD measurement average readings were 188.3±2.2 cGy, and the TPS measurement average readings were 192.0±0.2 cGy. For the left lens,

Table 1: Measured and calculated mean dose of lens and thyroid

Parameters	TLD (cGy) (Mean±SD)	TPS (cGy) (Mean±SD)	ΔMean
Right Lens	188.3±2.2	192.0±0.2	1.93%
Left Lens	190.2±0.5	192.0±0.1	0.93%
Thyroid	44.9±5.2	40.9±6.3	8.90%

the TLD measurement average was 190.2±0.5 cGy, while the TPS dose reading average was found to be 192.0±0.1 cGy. As for the doses in the thyroid region, which are further away from the target, the TLD and TPS measurement and reading averages were 44.9±5.2 cGy and 40.9 cGy, respectively. Accordingly, the right lens point doses calculated from TPS were 1.93% higher than TLD measurements. For the left lens, this difference in the same direction was found to be 0.93%. For the thyroid region, TLD measurements were found to be higher than TPS readings, and the difference increased to 8.9%. From the results, the differences between TLD and TPS for the lens area close to the treatment area remain below 2%, while the reading differences between TLD and TPS for the thyroid further away from the treatment area reach 8.9%. Again, from the table, although the TPS readings of the out-of-field dose zone lenses close to the treatment area were higher than the TLD measurements, the TLD measurements in the out-of-field thyroid region far from the treatment area were significantly higher than the TPS readings.

Discussion

The lens is one of the organs most sensitive to radiation and is a dose-limiting factor in brain radiotherapy planning. It is recommended that the radiation dose be below 1 Gy for lenses[35]. RTOG requires the maximum dose of the lens to be less than 5-7 Gy (36, 37). The occurrence of secondary primary thyroid cancer has been reported after radiotherapy for many primary cancers, including brain tumors. The close proximity of the thyroid to the brain may cause it to receive the highest dose outside the field edge (38, 39). Tubiana et al. and Xu et al. reported that secondary primary thyroid cancers can be seen at doses of 100 mGy and above (40, 41). Accurate knowledge of out-of-field doses becomes more important due to epidemiological evidence that radiation exposure increases the likelihood of developing cancer (8). The fact that a wide dose distribution of approximately 10 mGy-60 Gy occurs in organs outside the field of radiotherapy gives us the opportunity to examine the side effects of human irradiation (42). Although there are out-of-field dose measurements for whole brain irradiation in the literature, no studies have been found on the comparison of field dose calculations and TLD measurements with RayStation TPS. In our study, we made a whole brain 3DCRT plan from opposed lateral fields with the human tissue equivalent phantom. We compared the measured doses with the calculated TPS doses by placing TLDs in the thyroid area and lens area. The calculated average doses for the lens region close to the target tissue are 1.93% higher than the measured average doses, while the measured average dose for the thyroid far from the target is 8.9% higher than the calculated dose.

The evaluation of out-of-field doses is critical. Because it both involves the risk of secondary cancer and may cause deterministic side effects on the risky organ (23, 43). The reason for fear of extra out-of-field doses in general is that epidemiological evidence shows an increased likelihood of developing cancer as a result of radiation exposure (8). Out-of-field doses are a combination of leakage and scattering of the collimator and the patient (44). The difference in measurements at the same distances outside the treatment area is related to the location of the area relative to the measurement point in the phantom (45, 46). Garrett et al. found larger out-of-field doses at smaller distances from the central axis (CAX) in irradiations with larger field sizes (47). However, the dependence on field size decreases as leakage becomes more significant as we move away from CAX. (46, 48, 49).

Jessie Y. Huang et al. made IMRT treatment plans on the anthropomorphic phantom for brain treatment to investigate out-of-field doses. They used 6 MV photon beams with Pinnacle TPS for IMRT plans and found TPS results to be lower than TLD measurement results in all measurements. And they found that this decrease got worse as they moved away from the treated area. As a result, they found the dose calculated by TPS to be at least 30% lower than the measured dose on average (8). We found that the value

calculated by TPS and the average values measured by TLD were close to each other for the lens region, which is very close to the treatment area in WBRT irradiation. On the other hand, in a region further outside the area, such as the thyroid region, we found the difference between the values we calculated from TPS and the average values we obtained from TLD measurements to be 8.9%. Our TPS results were lower than those of the measured doses.

Ana Cravo Sa et al., in their right brain radiotherapy study with an anthropomorphic phantom receiving 54 Gy, compared TPS calculation, MNCP6 calculation, and TLD measurements. They found the relative differences between TLD measurements and MCNP6 calculations (14.3%) to be significantly lower than the average relative differences between TLD measurements and TPS calculations (55.8%). In organs such as the thyroid and eye that are approximately 13 cm close to the PTV, the relative difference in TLD and MNCP6 varies up to approximately 15%, and the relative difference in TLD and TPS varies up to approximately 43%, while in organs that are more than 13 cm away from the PTV, the relative difference varies up to 21.2% and 92.0%, respectively (25). In our study, we found the difference between TLD measurements and TPS calculations for the eye region to be around 2% and the difference for the more distant thyroid region to be around 8.9%. Looking at this, we see that the differences between TPS calculations and TLD measurement results increase as we move away from the target tissue in both studies.

Elmtalab et al. made a 3DCRT treatment plan with 15 MV for glioblastoma radiotherapy with a tissue equivalent and homogeneous phantom and measured out-of-field doses with TLD. In the plan, they prescribed a dose of 54 Gy to PTV. While they found the difference between the calculations made with Prowess TPS that used the Siemens Artiste linear accelerator and the TLD measurements to be 16.4% lower for the eye region, they found this difference to be 24.3% lower for the thyroid critical organ, which is in the more distant region (50). In our study, we saw that this difference increased up to 8.9% as we moved out of the area, such as the thyroid.

Mohammed Taghi et al. compared the out-of-field doses on the Rando phantom for TPS and TLDs for out-of-field regions. They found that the calculated dose in out-of-field areas was lower than the measured doses. While they found the doses in the treatment area to be less than ±5% with TPS, they found that the ratio of the doses calculated with TPS to the TLD measurement doses multiplied by 100, and the reading range outside the area varied from 26.08% to 292.98%. As a result, they reported that the calculated doses were estimated to be 35% lower on average[51]. In our results, the values of out-of-field doses for the thyroid calculated by TPS were lower than those measured by TLD, and the difference was around 8.9%.

Howell et al. made a plan using a Varian linear accelerator and 6 MV photons with a pediatric-sized anthropomorphic phantom for a historic mantle field on Eclipse TPS and compared the out-of-field doses with TLD measurements. They reported that TPS calculated the dose 40% ± 20% less than the dose measured at long distances from the treatment area, and when the distance increased, TPS calculated a lower dose with increasing distance (10). In our study, the doses measured at the lens points close to the treatment area were close to the TPS's calculated doses, but the average dose calculated by TPS in more distant areas, such as the thyroid area, was 8.90% lower than the average dose measured by TLD. This is also consistent with the data that, as found by Howell et al., the dose calculation of TPS is lower than TLD measurements as you move away from the area.

In our study, we created the whole brain treatment plan in the form of opposed lateral beams that we made for the anthropomorphic phantom with the RayStation TPS and irradiated this plan with the Siemens Artiste linear accelerator. We measured doses away from the treatment site for thyroid via TLDs, and we found that TPS calculations were 8.90% lower than the measured dose as we moved away from out-of-field. This tells us that we should take into account the measurement results as well as the results obtained from the data calculated with TPS in organs such as the lens and thyroid, where it is more important to have extra-field doses into consideration. Many similar studies in the literature on out-of-area doses, using different measurement methods, have shown that TPS shows calculated doses lower as you move out of the area. The results we obtained from our study provide guidance for estimating out-of-field lens and thyroid doses in 3DCRT whole brain irradiation.

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