

Evaluation of Organs at Risk's Dose in External Radiotherapy of Brain Tumors

Hamideh Nazemi-Gelyan¹, Hadi Hasanzadeh¹, Yasha Makhdumi², Sara Abdollahi³, Fatemeh Akbari², Fatemeh Varshoe-Tabrizi², Hamzeh Almasrou², Alireza Nikoofar³, Mostafa Rezaei-Tavirani⁴

Abstract

Background: Radiotherapy plays an important role in the management of most malignant and many benign primary central nervous system (CNS) tumors. Radiotherapy affects both tumor cells and uninvolved normal cells; so, it is important to estimate absorbed dose to organs at risk in this kind of treatment. The aim of this study was to determine the absorbed dose to chiasma, lens, optic nerve, retina, parotid, thyroid and submandibular gland in frontal lobe brain tumors radiotherapy based on treatment planning system (TPS) calculation and direct measurement on the phantom.

Methods: A head and neck phantom was constructed using natural human bone and combination of paraffin wax and Sodium Chloride (NaCl) as tissue-equivalent material. Six cylinders were made of phantom material which had cavities to insert Thermoluminescent Dosimeters (TLDs) at several depths in order to measure absorbed dose to chiasma, lens, optic nerve, retina, parotid, thyroid and submandibular gland. Three routine conventional plans associated with tumors of this region and a new purposed technique were performed on the phantom and dose distribution and absorbed dose to critical organs were compared using treatment planning system (TPS) calculation and direct measurement on the phantom.

Results: Absorbed doses were measured with calibrated TLDs and are expressed in centigray (cGy). In all techniques absorbed dose to all organs except the lenses were at their tolerance dose levels and in the new purposed technique, absorbed dose to chiasma was significantly reduced.

Conclusion: Our findings showed differences in the range of 1-5% in all techniques between TPS calculation and direct measurements for all organs except submandibular glands and thyroid. Because submandibular glands and thyroid are far from primary radiation field, TLD reading in these regions although small but differs from TPS calculation which shows very smaller doses. This might be due to scattered radiation which is not well considered in the TPS. In the new technique, because the chiasma is out of the radiation field, absorbed dose was reduced significantly.

Keywords: Brain tumor; External Radiotherapy; Dosimetry; Phantom

Please cite this article as: Nazemi-Gelyan H, Hasanzadeh H, Makhdumi Y, Abdollahi S, Akbari F, Varshoe-Tabrizi F, et al. Evaluation of Organs at Risk's Dose in External Radiotherapy of Brain Tumors. *Iran J Cancer Prev.* 2015;8(1):47-52.

Introduction

Annually, an estimated 63000 new cases of primary nonmalignant and malignant central nervous system (CNS) tumors are diagnosed in the United States with an estimated 13000 deaths. Most of the primary CNS tumors are located within the frontal, temporal, parietal and occipital lobes of the brain

[1]. There appear to be some difference between the patterns of brain tumor epidemiology in Iran and western countries. In the first report from Iran by Ameli et al. [2], the prevalence of glioma was estimated to be about 45% of all brain tumors, somewhat low in comparison to the western reports, but almost the same as Southeast Asian countries. In

1. Dept. of Medical Physics, Semnan University of Medical Sciences, Semnan, Iran
 2. Reza Radiotherapy Oncology Charity Center, Mashhad, Iran
 3. Dept. of Radiotherapy, Iran University of Medical Sciences, Tehran, Iran
 4. Proteomics Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding Author:

Hadi Hasanzadeh, PhD;
 Assistant Professor of Medical Physics
 Tel: (+98) 2333451337
 Email: hasanzadeh.h@semums.ac.ir
 Received: 25 Oct. 2014
 Accepted: 14 Dec. 2014
Iran J Cancer Prev. 2015; 1:47-52

fact, in Iranian reports of glial tumor subtypes, the majority of lesions are low grade astrocytoma and ependymomas [2, 3] which is very different from western countries, such as the US and France [4].

Radiotherapy plays an important role in the management of most malignant and many benign primary CNS tumors. With the goal of achieving uncomplicated loco-regional tumor control, balancing between benefits and side effects is the art of radiation oncology [1, 5-10]. The most important challenge in radiotherapy is delivering prescribed dose to the tumor and minimize dose to the normal tissues. Emami et al. obtained tolerance radiation dose of 28 critical organs; their findings showed the TD5/5 for lens, optic nerve, retina, chiasma, parotid and thyroid as 10, 50, 45, 50, 32 and 45 gray (Gy), respectively [11]. An absorbed dose of 4 Gy to the lens of eye in three weeks to three months leads to cataract [12]. So in the frontal lobe irradiation, lenses will not save at all and cataract will be induced. In other organs, although organ dose is tolerated, but in order to minimize complications it seems necessary to develop new technique. Two major complications might occur after frontal lobe irradiation; necrosis and visual disturbances which might be due to high dose received by chiasma [13-15].

In this study, for frontal lobe brain tumors three routine conventional radiotherapy techniques were compared in terms of dose distribution and absorbed dose to critical organs using treatment planning system (TPS) calculation and direct measurement in an anthropomorphic phantom. Then a new treatment technique was designed with same criteria as a mentioned above. Due to the high probability of visual disturbances in frontal lobe brain radiotherapy, we tried to reduce absorbed dose to the chiasma significantly considering new fields and bringing out the chiasma from radiation field with overall lower dose to other considered critical organs.

Materials and Methods

Construction of phantom

To construct the phantom, natural bone with Paraffin wax with Sodium Chloride (NaCl) as impurity was used; the effective atomic number and electron density of phantom soft tissue were 6.57 and 3.36×10^{23} (electron g^{-1}), respectively. A hollow cavity and two hollow tubes were considered as the mouse cavity, trachea and esophagus, respectively.

Six cylinders were made from phantom material which had cavities to insert Thermoluminescent Dosimeters (TLDs) at several depths, one for parotid (a transverse one from the left to the right parotid), one for Chiasma (perpendicularly inserted from top of brain), two for eyes and two for thyroids [16] (Figure 1).

TLD measurement technique

Radiation dosimetry was done using cubic lithium fluoride TLD chips (3mm×3mm×1mm). The TLDs (TLD-100, Harshaw, USA) were initially sorted into groups of equal sensitivity. This was accomplished by delivering a known dose (100 cGy) from 6 MV X-ray (*Siemens Primus linac*) and consequently measurement of the output light from each TLD using a TLD reader (Harshaw model 3500 TLD reader, USA). The annealing cycle of TLDs consisted a heat cycle of 1 hour at 400°C and then immediately 2 h at 100°C. Calibration procedure was done by exposing TLD to 6MV photons in the range of 0-250 centigray (cGy). In order to measure dose values, a calibration curve was plotted in which the TLD reading in μc is related to absorbed dose in cGy. Besides, the linear calibration equation which used for dose measurement was fitted on experimental data points (Figure 2) [16-19].

TPS and direct measurement on the phantom

An imaginary 4 cm putative tumor with 2 cm margin was considered in the right frontal lobe of the brain and phantom was CT planned. Three routine conventional techniques associated with frontal lobe brain tumors were considered as two lateral opposite-fields (technique 1), one lateral and an anterior field (technique 2), two lateral opposite-fields and an anterior field (technique 3) [20]. A new conventional technique with the benefits of conventional techniques and significantly reduced dose to chiasma was designed. This technique consists two 6 MV and 18 MV angled AP/PA fields with an oblique field with 18 MV photon beam. In angled AP/PA fields, the chiasma was brought out from radiation field with a couch rotation of 90° and gantry rotation of 10°; plan of the new technique and chiasma are brought in figure 3. The phantom was planned using above techniques (Prowess Panther treatment planning software, California, USA) with a total prescribed dose of 6000 cGy in 30 fractions. After contouring PTV and considered critical organs, dose distribution was obtained and absorbed dose to critical organs was extracted from the Dose Volume Histograms (DVH). As the dose fall-off was

severe in organs closer to PTV, the selected points on plan (ROI) were about the same points where TLDs were placed in the phantom. TLDs were inserted in considered places in the phantom (retina, optic nerve, chiasma, lens, submandibular glands, parotids and thyroid) and the phantom was irradiated with above techniques.

Results

The results of total absorbed dose to selected organs in selected points estimated from TPS and TLD in 30 fractions is presented in figure 4 and table 1.

In the assessed techniques, absorbed dose to all organs except lenses were at their tolerance dose levels and in the new technique, absorbed dose to chiasma is significantly reduced. Among all techniques, technique 2 (one lateral and an anterior field) was the best in terms of dose distribution, because of its localized irradiated volume at the side of brain.

The differences between calculation and measurement in selected techniques are presented in table 2 as percentage difference. As it is obvious, the differences were as high as 70% in organs far enough from considered PTV such as thyroid and submandibular glands, although absorbed doses were not comparable with their tolerance dose. Also in the new technique, differences were in the range of three routine techniques.

Discussion

In clinical radiation therapy, usually TPS is used to estimate dose to different organs; but the obtained values might be different from the actual values depending on the clinical circumstances. Our findings showed differences in the range of 1-5% in all techniques between TPS and direct

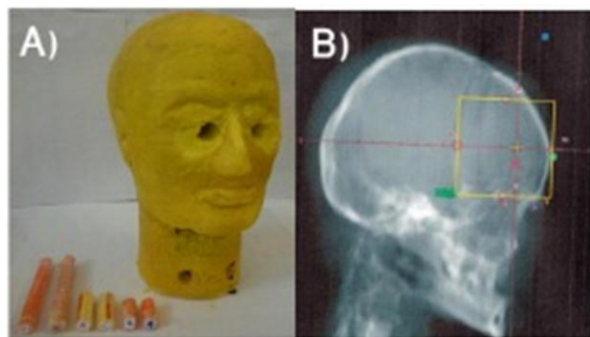


Figure 1. A) Constructed head and neck phantom with TLD applicator; B) beam's eye view (BEV).

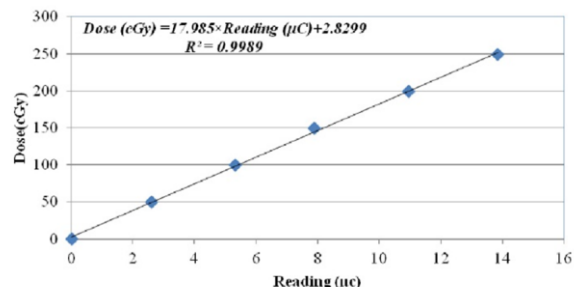


Figure 2. TLD calibration curve with calibration equation and the correlation coefficient.

measurements for all organs except salivary glands and thyroid; although their distance from primary

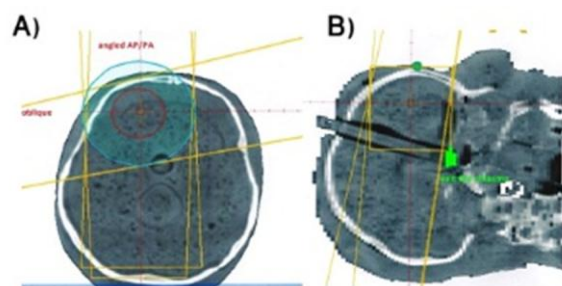


Figure 3. A) New technique consist of angled AP/PA and oblique fields, B) Bringing out the Chiasma.

radiation field causes TLD reading being small, but differs with TPS (about 60%) which showed very smaller doses; this might be due to scattered radiation which is not well considered in the TPS. It has been showed that an increase in parotid irradiated volume from 0% -40% to 90% -100% (carried out in patients who had received a dose of 35-45Gy), results in decreased secretion from 100% to 10% [21].

Due to high probability of cataract induction in lens exposed to 400 cGy in three weeks to three months, and underestimation of doses obtained from plan and measurement at about 5% (~20 cGy), it is important during planning to consider these differences to reduce the incidence of cataract.

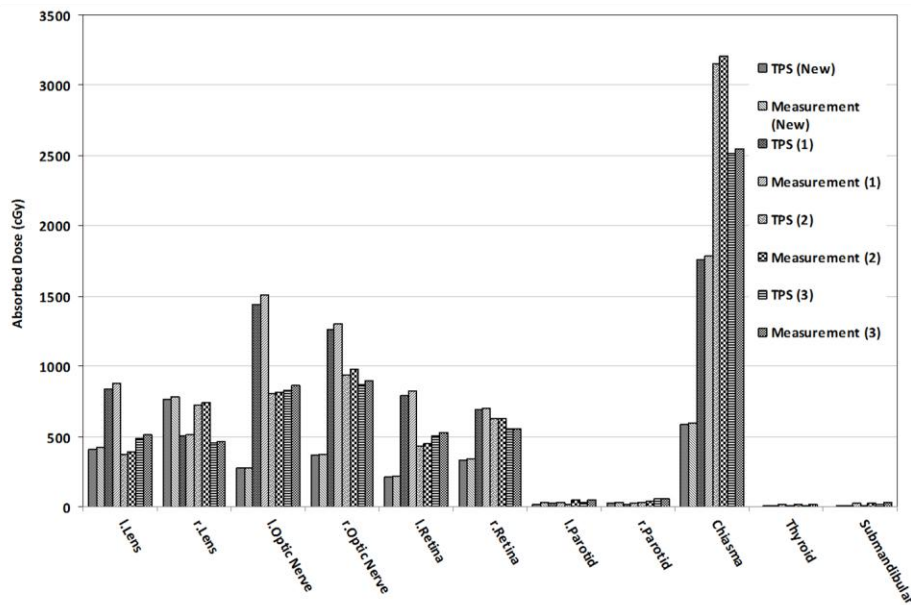


Figure 4. Absorbed dose to selected organs estimated from TPS and measured using TLDs in all technique: two lateral opposite-field (technique 1), one lateral and an anterior (technique 2), two lateral opposite-fields and an anterior (technique 3), angled AP/PA and oblique (new technique).

As showed in table 1, in three routine techniques, chiasma receives high doses (1800 -3000 cGy). As previously has reported [13, 15],

Gensheimer et al. in a review on the outcomes of lacrimal gland adenoid cystic carcinoma treated with neutrons observed severe visual impairment which

Table 1. Total absorbed dose to selected organs estimated from TPS and measured with TLDs in all technique in 30 fractions.

Organ name	Technique 1		Technique2		Technique 3		NewTechnique		TD5/5 (cGy)
	TPS	TLD	TPS	TLD	TPS	TLD	TPS	TLD	
Left lens	838.5	875.2	373.1	393	492	516.8	410.9	423.6	1000
Right lens	502.7	512.8	722.3	741	458.1	466.9	763.1	781.9	1000
Left optic nerve	1444.7	1503.3	807.1	816	826.7	862.9	274	278.2	5000
Right optic nerve	1261.2	1298.8	939.4	957.5	869	897.7	363.1	377.1	5000
Left retina	786.8	823.8	429	451.5	505.4	530.8	212	220.8	4500
Right retina	693.1	701.5	623.7	626.2	551.3	556.8	333.6	345.7	4500
Left parotid	23.3	35.8	20	50	32.8	46.85	15.1	30.2	3200
Right parotid	17.8	22.25	30	42.9	53.7	55.36	25.2	31.5	3200
Chiasma	1762.1	1783.5	3151	3205	2518.9	2544.3	585.9	596.6	5000
Thyroid	7.9	15.8	5	16.6	6.3	19.68	1.5	4.1	4500
Submandibular	12	23.1	10	23.8	16.2	33.1	2.2	4.7	3200

Table 2. Percentage difference between measurement and TPS calculation in selected organs in all techniques

Organ	Technique 1	Technique 2	Technique 3	New Technique
Left lens	4.2%	5%	4.8%	3%
Right lens	2.1%	2.5%	1.9%	2.4%
Left optic nerve	3.9%	1.1%	4.2%	1.5%
Right optic nerve	2.9%	1.9%	3.2%	3.7%
Left retina	4.5%	5%	4.8%	4%
Right retina	1.2%	0.4%	1%	3.5%
Left parotid	35%	60%	30%	50%
Right parotid	20%	30%	3%	20%
chiasma	1.2%	1.7%	1%	1.8%
thyroid	50%	70%	68%	63%
submandibular	48%	58%	51%	53%

might be due to high dose to chiasma. Rischin et al. in studying with Sino-nasal undifferentiated carcinoma treated using three fields (weighted anterior field and two wedged laterals) found that mean dose to the optic chiasm was 54 Gy which exceeded from tolerance dose level [15]; these high doses are in accordance with our study. So, as showed in table 1, in the new technique we could reduce dose to chiasma as low as 596 cGy, and also save other organs better.

It is notable that in presented technique, although sparing other organ at risks, the absorbed dose to chiasma was measured as 596 cGy which showed a considerable dose reduction. This reduction might results in a less complication rate in radiotherapy of brain tumors.

Conclusion

The present study sought estimates of the radiation doses received by organs at risk in the frontal lobe radiotherapy with direct measurement on the anthropomorphic phantom using TLD dosimetry. In addition, a comparison between the estimated values from treatment planning system and direct measurement shows differences in the range of 1.1% to 70% between the estimated and measured values. The dose values of some organs despite the large difference between the two methods, was within their tolerance dose and so there will be no concern about elevated risk of radiation induced adverse effects.

Acknowledgement

This work was a part of Mrs. Nazemi thesis for the degree of MSc in Medical Physics made possible with a grant of deputy of research of Semnan University of Medical Sciences and kind collaboration of Reza Radiotherapy Oncology Charity Center.

Conflict of Interest

The authors have no conflict of interest in this study.

Authors' Contribution

Hadi Hasanzadeh designed the study, gathered and analyzed the data and wrote the paper. Hamide Nazemi Gelyan, Yasha Makhdumi, Alireza Nikoofar, Sara Abdollahi, Fatemeh Akbari, Fatemeh Varshoe Tabrizi and Hamzeh Almasrou contributed to study design, phantom irradiation, treatment planning and Mostafa Rezaei-Tavirani contributed to writing and overall correction of the manuscript.

References

1. Khan FM, Gerbi BJ. Treatment planning in radiation oncology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2012.
2. Ameli N, Hadadian A, Kamalian N. Incidence of intracranial tumors in iran. *Neurosurg Rev.* 1979;2:67-71.
3. Mehrazin M. ABO blood group frequency and brain tumors. *Asian Pac J Cancer Prev.* 2006;7(4):582-4.
4. Alimohamadi SM, Ghodsi SM. Epidemiologic patterns of primary brain tumors in Iran. *Asian Pac J Cancer Prev.* 2008;9:361-2.
5. Jellema AP, Doornaert P, Slotman BJ, Leemans CR, Langendijk JA. Does radiation dose to the salivary

glands and oral cavity predict patient-rated xerostomia and sticky saliva in head and neck cancer patients treated with curative radiotherapy? *Radiother Oncol.* 2005;77(2):164-71.

6. Roesink JM, Moerland MA, Hoekstra A, Rijk PPV, Terhaard CHJ. Scintigraphic assessment of early and late parotid gland function after radiotherapy for head-and-neck cancer: a prospective study of dose-volume response relationships. *Int J Radiat Oncol Biol Phys.* 2004;58(5):1451-60.

7. Pehlivan B, Ares C, Lomax AJ, Stadelmann O, Goitein G, Timmermann B, et al. Temporal lobe toxicity analysis after proton radiation therapy for skull base tumors. *Int J Radiat Oncol Biol Phys.* 2011;83(5):1432-40.

8. Blonigen BJ, Steinmetz RD, Levin L, Lamba MA, Warnick RE, Breneman JC. Irradiated volume as a predictor of brain radionecrosis after linear accelerator stereotactic radiosurgery. *Int J Radiat Oncol Biol Phys.* 2010;77(4):996-1001.

9. Valery CA, Cornu P, Noel G, Duyme M, Boisserie G, Sakka LJ, et al. Predictive factors of radiation necrosis after radiosurgery for cerebral metastases. *Stereotact Funct Neurosurg.* 2003;81(1-4):115-9.

10. Minniti G, Clarke E, Lanzetta G, Osti MF, Trasimeni G, Bozzao A, et al. Stereotactic radiosurgery for brain metastases: analysis of outcome and risk of brain radionecrosis. *Radiat Oncol.* 2011;6:48.

11. Emami B, Lyman J, Brown A, Cola L, Goitein M, Munzenrider JE, et al. Tolerance of normal tissue to therapeutic irradiation. *Int J Radiat Oncol Biol Phys.* 1991;21(1):109-22.

12. Hall EJ, Giaccia Amato J. *Radiobiology for the Radiologist.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

13. Gensheimer MF, Rainey D, Douglas JG, Liao JJ, Laramore GE, Jian-Amadi A, et al. Neutron radiotherapy for adenoid cystic carcinoma of the lacrimal gland. *Ophthal Plast Reconstr Surg.* 2013;29(4):256-60.

14. Oker N, Lang P, Bresson D, George B, Guichard JP, Wassef M, et al. Radionecrosis of the frontal lobe as a consequence of malignant ethmoid tumor management: incidence, diagnosis, risk factors, prevention and management. *Eur Arch Otorhinolaryngol.* 2014;271(12):3223-32.

15. Rischin D, Porceddu S, Peters L, Martin J, Corry J, Weih L. Promising results with chemoradiation in patients with sinonasal undifferentiated carcinoma. *Head Neck.* 2004;26(5):435-41.

16. Hasanzadeh H, Sharafi A, AllahVerdi M, Nikoofar A. Assessment of absorbed dose to thyroid, parotid and ovaries in patients undergoing Gamma Knife radiosurgery. *Phys Med Biol.* 2006;51:4375-83.

17. Khan FM. *the physics of radiation therapy.* Philadelphia: Lippincott Williams & Wilkins; 2009.

18. Costa AM, Barbi GL, Bertucci EC, Ferreira H, Sansavino SZ, Colenci B, et al. In vivo dosimetry with thermoluminescent dosimeters in external photon beam radiotherapy. *Appl Radiat Isot.* 2010;68(4-5):760-2.

19. Rivera. Thermoluminescence in Medical Dosimetry. *Appl Radiat.* 2012;71 Suppl:30-4.

20. Chao KSC, Perez CA, Brady LW. *Radiation Oncology : Management Decisions.* 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2001.

21. Roesink JM, Moerland MA, Battermann JJ, Hordijk GJ, Terhaard CHJ. Quantitative dose-volume response analysis of changes in parotid gland function after radiotherapy in the head-and-neck region. *Int J Radiat Oncol Biol Phys.* 2001;51(4):938-46.