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Radiation Therapy for Glioblastoma with Limited Resources. Dosimetric Comparison of 3DCRT and IMRT Treatment Planning. A Developing Country Experience

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Introduction

Glioblastomas (GBM) account for about half of all malignant tumors of the central nervous system (CNS) [10]. These are rapidly-growing infiltrative tumors that usually reach large sizes by the time of diagnosis. The standard multidisciplinary treatment of GBM includes maximal safe resection followed by adjuvant radiotherapy (RT) with concurrent and maintenance temozolomide [12].

During the last decades different RT schedules and dose escalation regimes were used [4, 5, 8, 13]. According to this data, the established standard target dose for GBM is 60 Gy, delivered over 6 weeks with 2 Gy per fraction [3]. Radiotherapy volume has also changed during the last decades. Up to the early 1960s the RT volume was the whole brain up to 45–60 Gy [6, 15]. More than 50% of these patients had grade 3–4 neurotoxicity and post-radiation changes mainly in white matter of the brain. In the 1970s, this approach began to be gradually

modified and a two-phase treatment was proposed. At the 1st phase, the whole brain was irradiated to 30–46 Gy, and at the 2nd phase the dose was increased by 20–30 Gy as a boost [1, 7].

After implementation of magnetic-resonance imaging (MRI) into clinical practice and also based on pathological reports this volume was reduced. These studies have shown that GBM recurrence occurs within 1 to 2 cm of a gadolinium-enhancing area on T1-weighted MRI images in approximately 77% of cases. In 18% of cases it is located in the ipsilateral hemisphere at a distance of 4 cm and in 4% of cases – in the contralateral hemisphere [11, 14].

Now the RT volume is defined according to pre- and postsurgical MRI images. GTV is defined as surgical resection cavity plus any residual enhancing tumor (postcontrast T1 weighted MRI scans). CTV is created by adding 1.5–2.0cm to GTV [9].

Currently, considering that approximately 80% of all recurrences in GBM occur in the tumor bed, published studies suggest adding 1 cm to the GTV to define the CTV [2].

Despite the trend towards reducing the radiation volume, it remains relatively extensive. Because of this the target can be near to critical normal structures of the brain (lens, retina, optic nerves, optic chiasma, brainstem, cochlea).

Purpose

The objective of this study is to evaluate and compare the dose distributions in target volumes and organs at risk (OARs) between three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT), with the aim of identifying clinically significant differences.

Materials and Methods

Patients selection

38 patients with diagnosed GBM who received EBRT in our department were included in this study. Tumor was localized in temporal lobe – 17 patients, frontal lobe – 6 patients, parietal lobe – 4 patients, occipital lobe – 1 patient, cerebellum – 2 patients, deep structures – 5 patients and 3 patients had tumors involving two or more lobes of hemisphere.

Radiotherapy Planning

All patients were immobilized in the supine treatment position with thermoplastic masks. CT scan was performed with 2mm thickness from the vertex to the bottom of the third cervical vertebra (C3). MRI using pre- and post-contrast T1-weighted and T2/FLAIR -weighted images were fused for all patients. The gross tumor volume (GTV) and clinical tumor volume (CTV) were contoured according to International Commission on Radiation Units and Measurements

(ICRU) reports 50, 62, 83 and ESTRO-ACROP guideline “target delineation of glioblastomas.” [14]. GTV was defined as surgical resection cavity plus any residual enhancing tumour (postcontrast T1 weighted MRI scans). CTV was created by adding 1.5-2.0cm to GTV. 3–5 mm was added to CTV for creating planning target volume (PTV). There were no differences between 3D-CRT and IMRT for the margin applied. These patients were planned using Varian Eclipse Planning System version 15.1. Normal brain (Brain-PTV), lenses, retinas, optic nerves, optic chiasm, cochleae, brainstem and hippocampi were defined as organs at risk (OARs) and delineated.

The dose limits that defined an acceptable plan included a maximum point dose (Dmax) of 54.0Gy for optic nerves and the chiasm, 45.0Gy for retina, 55.0Gy for brainstem (or D1cc less than 59.0Gy), 45.0Gy for cochlea. In cases where it was possible, we tried to preserve also the hippocampi and lenses as well, but did not “prioritize” these structures over PTV coverage. Acceptable target coverage was defined by a D95 (dose received by 95% of the PTV) of at least 95% of the prescription. Planning was done using dynamic IMRT or 3D-CRT by a linear accelerator, generating 6 MV photons.

All patients received 60 Gy/2 Gy per fraction (30 fractions).

Results and Discussion

We performed a comparative statistical analysis between the 3DCRT and IMRT groups across all evaluated parameters.

The dose distribution and dose-volume histograms (DVH) of the PTV and relevant critical structures were evaluated and compared between the 3D conformal radiation therapy (3DCRT) and IMRT plans. The median PTV volume was 389.1 cc (range: 121.1 – 616.3 cc). The median treatment volume (TV) was 592.60 cc (range: 221.7 – 1015.7 cc) for 3DCRT plans and 396.7 cc (range: 133.1 – 752.4 cc) for IMRT plans ($p<0.05$). The treated volume (TV) isodose 95% in 3DCRT plans was 98.55% (range: 96.0 – 104.2%) compared to 96.3% (range: 92.7 – 97.8%) in IMRT plans ($p<0.05$). The dose received by 98% of the tissue volume (D98%) was 97.75% (range: 89.1–100%) for 3DCRT plans versus 94.70% (range: 90.4 – 99.6%) for IMRT plans ($p<0.05$). The homogeneity index (HI) in 3DCRT plans was 0.08 (range: 0.053-0.161) and 0.06 (range: 0.032 – 0.091) in IMRT plans ($p<0.05$). The conformity index (CI) was 1.59 (range: 0.998–1.83) for 3DCRT plans and 1.04 (range: 0.968-1.517) for IMRT plans ($p<0.05$). The comparison was done also for OAR’s (Table).

The median maximum dose (Dmax) for the brainstem was 59.38 Gy (range: 8.359 – 60.85 Gy) in 3DCRT plans and 56.81 Gy (range: 4.365–58.969 Gy) in IMRT plans. The D1cc for the brainstem in 3DCRT plans was 58.49 Gy (range: 5.375–60.486 Gy) compared to 51.28 Gy (range: 3.452 – 57.109 Gy) in IMRT plans ($p<0.05$). The median Dmax for the right retina in 3DCRT plans was 13.6 Gy (range: 0.752 – 59.192 Gy) and 17.44 Gy (range: 0.956–52.441 Gy) in IMRT plans.

Table 1

Summary of comparison of 3DCRT and IMRT plans

	3D-CRT			IMRT			
	Median	**Range (min-max)**	**Mean**	**Median**	**Range (min-max)**	**Mean**	**P-value**
Prescribed dose	**60**	**60**	**60**	**60**	**60**	**60**	**N/A**
PTV							
Volume (cc)	389.1	121.1 - 616.3	384.26	389.1	121.1 - 616.3	384.26	N/A
TV	592.60	221.7 - 1015.7	599.91	396.7	133.1 - 752.4	403.88	p<0.05
TV isodose 95%	98.55	96.0 - 104.2	98.3	96.3	92.7 - 97.8	96.15	p<0.05
D98 (%)	97.75	89.1 - 100	97.12	94.70	90.4 - 99.6	94.64	p<0.05
D2 (%)	104.8	102.9 - 107.2	104.93	100.05	99.4 - 102.8	100.19	p<0.05
Homogeneity index	0.08	0.053 - 0.161	0.08	0.06	0.032 - 0.091	0.06	p<0.05
Conformity index	1.59	0.998 - 1.83	1.58	1.04	0.968 - 1.517	1.05	p<0.05
OAR's							
Brain-PTV (mean dose)	29.99	19.24 - 41.1	30.27	21.24	11.31 - 30.62	21.78	p<0.05
Brainstem	59.38	8.359 - 60.85	56.54	56.81	4.365 - 58.969	52.43	Not Significant
D1cc brainstem	58.49	5.375 - 60.486	53.75	51.28	3.452 - 57.109	45.88	p<0.05
Right lens	7.98	0.473 - 34.013	8.69	6.53	0.626 - 21.476	7.57	Not Significant
Left lens	7.84	0.839 - 34.258	7.77	6.11	0.550 - 12.028	6.67	Not Significant
Right retina	13.6	0.752 - 59.192	21.1	17.44	0.956 - 52.441	20.51	Not Significant
Left retina	12.05	1.188 - 58.309	21.38	16.78	0.821 - 42.326	18.96	Not Significant
Right optic nerve	34.79	1.576 - 61.191	34.21	20.79	1.206 - 51.403	26.05	p<0.05
Left optic nerve	35.90	1.615 - 61.143	34.28	19.21	1.152 - 54.003	24.0	p<0.05
Optic chiasma	58.82	4.734 - 61.730	51.56	53.46	3.19 - 59.479	44.38	p<0.05
Right cochlea	22.49	1.436 - 59.119	26.92	13.25	0.991 - 55.996	17.58	Not Significant
Left cochlea	18.1	0.997 - 59.830	23.39	10.86	0.824 - 59.026	16.84	Not Significant
Right hippocampus	59.00	17.859 - 61.396	53.89	57.48	4.9 - 61.684	47.06	Not Significant
Left hippocampus	59.55	5.369 - 62.009	53.60	59.52	4.254 - 60.81	55.91	Not Significant

The median Dmax for the left retina was 12.05 Gy (range: 1.188 – 58.309 Gy) for 3DCRT plans and 16.78 Gy (range: 0.821 – 42.326 Gy) for IMRT plans. The dose to the right optic nerve in 3DCRT plans was 34.79 Gy (range: 1.576 –

61.191 Gy) and 20.79 Gy (range: 1.206 – 51.403 Gy) in IMRT plans ($p<0.05$Gy). The dose to the left optic nerve in 3DCRT plans was 35.90 Gy (range: 1.615 – 61.143 Gy) compared to 19.21 Gy (range: 1.152 – 54.003 Gy) in IMRT plans ($p<0.05$Gy). The Dmax for the optic chiasm in 3DCRT plans was 58.82 Gy (range: 4.734 – 61.730 Gy) and 53.46 Gy (range: 3.19 – 59.479 Gy) in IMRT plans ($p<0.05$Gy). Normal brain median mean dose (Brain-PTV) was 29.99 Gy (range: 19.24 – 41.1 Gy) in 3D plans and 21.24 Gy (range: 11.31 – 30.62 Gy) in IMRT plans ($p<0.05$Gy) (Table).The present study compared the dosimetric parameters of 3DCRT and IMRT in glioblastoma radiotherapy planning, focusing on PTV coverage, conformity, homogeneity, and sparing of organs at risk (OARs). Our results demonstrate that while both techniques provided adequate target coverage, IMRT offered superior conformity and better sparing of critical structures, whereas 3DCRT provided slightly higher homogeneity and marginally higher dose coverage.

The treated volume and D98% were significantly larger in 3DCRT plans, indicating more generous coverage of the PTV and surrounding tissues. However, this came at the expense of a higher irradiated volume of normal brain tissue, reflected by a significantly higher median mean dose to the brain outside the PTV (29.99 Gy in 3DCRT vs. 21.24 Gy in IMRT). This finding is consistent with previous reports that IMRT achieves more conformal dose distributions, reducing unnecessary radiation to healthy tissue.

The conformity index was markedly improved in IMRT compared with 3DCRT (1.04 vs. 1.59, $p<0.05$), highlighting IMRT's ability to restrict high-dose regions to the target volume. Conversely, 3DCRT demonstrated a slightly better homogeneity index, suggesting a more uniform dose distribution within the PTV. This aligns with earlier literature indicating that inverse-planned IMRT, while more conformal, can sometimes produce minor hot spots within the target volume.

Evaluation of OARs further supports the advantages of IMRT. Critical visual pathway structures, including the optic nerves and chiasm, received significantly lower doses with IMRT compared to 3DCRT. The brainstem D1cc was also reduced in IMRT plans, underscoring the improved organ sparing achieved by intensity modulation. Interestingly, the maximum doses to the retina were slightly higher in IMRT compared to 3DCRT, although these values remained well within tolerance limits in most cases. These results confirm that IMRT can reduce the risk of late toxicity, particularly visual and neurocognitive complications, which are major concerns in glioblastoma patients requiring high-dose focal irradiation.

Taken together, our findings suggest that the trade-off between conformity and homogeneity must be carefully considered. While 3DCRT may deliver slightly more uniform PTV coverage, the improved OAR protection and lower dose to normal brain tissue provided by IMRT are clinically more meaningful in the context of glioblastoma, where patient prognosis is limited and quality of life preservation is paramount.

Conclusion

This dosimetric comparison between 3DCRT and IMRT in glioblastoma radiotherapy planning demonstrates that IMRT provides superior conformity and significantly better sparing of critical structures, particularly the optic apparatus, brainstem, and normal brain tissue. Although 3DCRT achieves slightly higher homogeneity and marginally greater dose coverage, these advantages are outweighed by the broader high-dose exposure to surrounding healthy tissue.

Given the balance between target coverage and organ protection, IMRT appears to be more favorable technique for glioblastoma radiotherapy, offering a potential reduction in treatment-related toxicity without compromising PTV coverage. Future studies correlating these dosimetric findings with clinical outcomes are warranted to further establish the therapeutic benefits of IMRT over 3DCRT in this patient population.

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Лучевая терапия опухолей основания черепа в условиях ограниченных ресурсов: сравнение планирования трёхмерной конформной и интенсивно-модулированной лучевой терапии. Опыт развивающихся стран

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Глиобластомы составляют приблизительно половину всех злокачественных новообразований ЦНС и 14,2% всех опухолей ЦНС (злокачественных и доброкачественных). Это быстрорастущие инфильтративные опухоли, которые обычно имеют большие размеры на момент постановки диагноза. В настоящее время стандартным методом лечения глиобластом является максимальная резекция и послеоперационная химиолучевая терапия. За последние десятилетия были исследованы эффекты различных доз облучения на контроль опухоли, и были использованы различные технологии.

Целью данного исследования является определение распределения дозы облучения между мишенью и прилегающими здоровыми тканями при использовании различных технологий: трехмерной конформной лучевой терапии (3DCRT) и лучевой терапии с модулированной интенсивностью (IMRT).

В исследование были включены 38 пациентов, проходивших лучевую терапию по поводу опухолей основания черепа в период с 2019 по 2022 гг.

Результаты показали, что IMRT демонстрирует явное преимущество перед 3DCRT с точки зрения распределения дозы и защиты здоровых тканей.

Для подтверждения терапевтической пользы IMRT в этой группе пациентов необходимы дальнейшие исследования, сравнивающие эти дозиметрические данные с клиническими результатами.

Գլիոբլաստոմաների ճառագայթային բուժումը սահմանափակ ռեսուրսներով: Եռաչափ կոնֆորմալ և կարգավորվող ինտենսիվությամբ ճառագայթային բուժման պլանավորման համեմատություն: Զարգացող երկրների փորձը

Մ.Կ. Առուստամյան, Ս.Մ. Ֆազլի, Ս.Վ. Սմոլնիկով, Ա.Ա. Կարապետյան, Է.Ա. Գևորգյան, Ա.Հ. Վարդանյան, Ա.Մ. Բադեյան, Ա.Ա. Ադամյան, Ե.Հ. Գրիգորյան, Լ.Ա. Բաղդասարյան, Ա.Ա. Ավետիսյան, Ս.Վ. Գոլուբ, Կ.Ս. Ղալումյան

Գլիոբլաստոմաները կազմում են ԿՆՀ չարորակ նորագոյացությունների մոտավոր կեսը և ԿՆՀ բոլոր ուռուցքների (չարորակ և բարորակ) 14,2%-ը: Սրանք արագ աճող ինֆիլտրատիվ ուռուցքներ են, որոնք ախտորոշման պահին սովորաբար հասնում են մեծ չափերի: Գլիոբլաստոմաների բուժման ներկայիս ստանդարտն է՝ առավելագույն անվտանգ հեռացում և հետվիրահատական քիմիաճառագայթային բուժում: Վերջին տասնամյակների ընթացքում հետազոտվել է ճառագայթման տարբեր դոզաների ազդեցությունն ուռուցքի հսկողության համար, ինչպես նաև կիրառվել են տարբեր տեխնոլոգիաներ:

Տվյալ հետազոտության նպատակն է պարզել ճառագայթման դոզայի բաշխումը թիրախի և հարակից առողջ հյուսվածքների շրջանում տարբեր տեխնոլոգիաների՝ եռաչափ կոնֆորմալ ճառագայթային թերապիա (ԵԿՃԹ) և կարգավորվող ինտենսիվությամբ ճառագայթային թերապիա (ԿԻՃԹ) կիրառման պարագայում:

Հետազոտության մեջ ընդգրկվել են 2019–2022 թթ. ընթացքում գանգի հիմի ուռուցքներով ճառագայթային բուժում ստացած 38 բուժառու:

Արդյունքների ամփոփումից պարզվեց, որ ԿԻՃԹ-ն ցույց է տալիս ԵԿՃԹ-ի նկատմամբ հստակ առավելություն՝ դեղաքանակի բաշխման և առողջ հյուսվածքների պաշտպանության առումով:

Այս հիվանդների խմբում ԿԻՃԹ-ի թերապևտիկ առավելությունները հաստատելու համար անհրաժեշտ են հետագա ուսումնասիրություններ, որոնք կհամեմատեն այս դոզիմետրիկ տվյալները կլինիկական արդյունքների հետ:

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