BULETINUL INSTITUTULUI POLITEHNIC DIN IAŞI
Publicat de
Universitatea Tehnică „Gheorghe Asachi” din Iaşi
Volumul 63 (67), Numărul 4, 2017
Secţia
MATEMATICĂ. MECANICĂ TEORETICĂ. FIZICĂ

DOSIMETRIC EFFECT ON NEURAL STRUCTURES OF SCALP-SPARING IMRT AND VMAT RADIOTHERAPY FOR HIGH-GRADE GLIOMAS

BY

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Received: October 23, 2017
Accepted for publication: December 22, 2017

Abstract. Radiotherapy for brain tumors with hair follicle protection for alopecia reduction has become a viable option with the introduction of inverse planning radiotherapy techniques. The aim of the study was the evaluation of the possibility of reducing the maximum and the medium dose received by the scalp for 3 cases of temporoparietal glioblastoma patients irradiated with a total dose of 60Gy and the effect of applying this constraint on other radiosensitive anatomical structures. In all three cases a reduction in mean doses of 5.5%, 3.2% and 12.5% was achieved using the modulated intensive radiotherapy technique (IMRT) and 5.1%, 0.8% and 22.2% by volumetric modulated arc therapy (VMAT) and a reduction of maximum dose by 18.7%, 9.6% and 8.3% using IMRT technique and by 16.35%, 11% and 16% using VMAT technique with no increase in dose to the other radiosensitive organs including hippocampus involved in cognitive function of patients.

Keywords: scalp sparing; glioblastoma; IMRT; VMAT; neural structures.

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1. Introduction

Transient and permanent alopecia have a psychological impact on radio-treated patient's quality of life.

Brain tumors radiotherapy with hair follicle protection for alopecia reduction has become a viable option by introduction of the inverse planning radiotherapy techniques. Limmer *et al*. has been demonstrating the potential to reduce the scalp dose in the whole brain treatment of brain metastases, by helical tomotherapy from 10 years ago, confirming data from the treatment planning system TPS using thermo-luminescent dosimetry (TLD). In the case of high-grade gliomas, reducing alopecia by protecting the scalp is often difficult due to the presence of the target volume in the vicinity of the scalp (Limmer *et al*., 2007).

The purpose of the study is to evaluate the possibility of inverse planning techniques to reduce the dose to the scalp to reduce alopecia of patients and to assess the dosimetric consequences of applying these constraints on the other OARs.

2. Materials and Methods

For 3 patients with a pathologic diagnosis of glioblastoma multiform (GBM) surgically resected and proposed for adjuvant radiotherapy, CT simulation was performed using a Siemens Somatom AS simulator. The patients were immobilized using a thermoplastic mask system and CT simulation image were reconstructed in 3 mm slice thickness (Fuller *et al*., 2007).

6 alternative treatment plans were proposed for each patient: 2 plans using 3D-CRT (3D conformal) technique, 6 MV or 10 MV energy with 4-7 non-coplanar fields, 2 by IMRT (intensity modulated radiation therapy) technique using 4-7 coplanar fields, 6 MV energy and 2 VMAT (volumetric modulated arc therapy) plans using 2 complete arcs and 6MV energy. Dose prescription for target volume was 60Gy/30 fractions. For all plans, dosimetric constraints for OARs were applied according to the QUANTEC guidelines (quantitative analysis of normal tissue effects in the clinic). For the scalp, dosimetric constraint was applied only for one of the IMRT plans and one of the VMAT plans (0% dose of the scalp <35Gy).

The gross tumor volume (GTV) was delineated using an image fusion and a rigid registration algorithm. The surgical bed delineated using preoperative MRI and the contrast enhanced lesion (identified on postoperative T1-weighted MRI) were included. The clinical target volume (CTV) was defined by adding an isotropic 2-cm margin to the GTV and was edited according to the anatomical barriers. For the planning target volume (PTV), CTV was expanded with 5 mm. Brain, brain stem, optic nerves, hippocampus, eyes and lenses were delineated as organs at risk (OARs). Whole scalp from the surface of the scalp skin to the depth of the cranium was delineated as OAR (Dobbs *et al*., 2009; Song *et al*., 2015).

For glioblastoma cases, the most common primary brain tumor, a net benefit in survival has been proven with post-operative radiation therapy (RT) concurrent with temozolomide (TMZ) for 30 days followed by adjuvant TMZ treatment for another 6 months. Dose escalation above these values did not benefit in survival but increased the risk of toxicity (Barani and Larson, 2015).

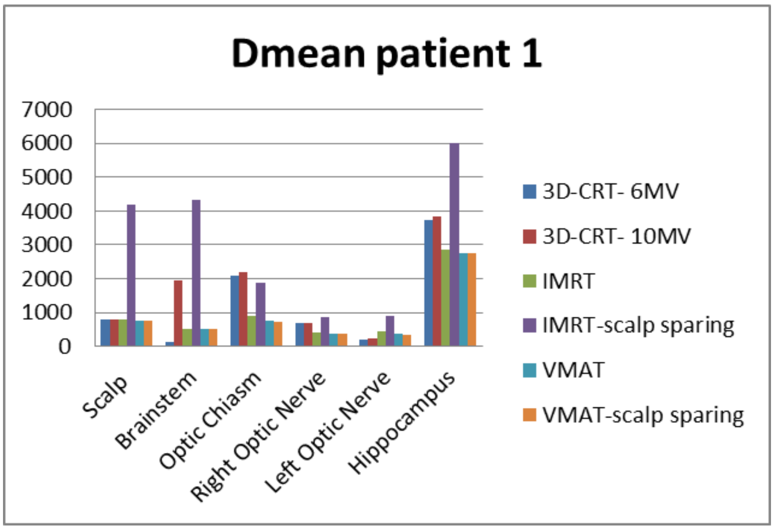

Fig. 1 – OARs mean dose for patient 1 for the five irradiation techniques.

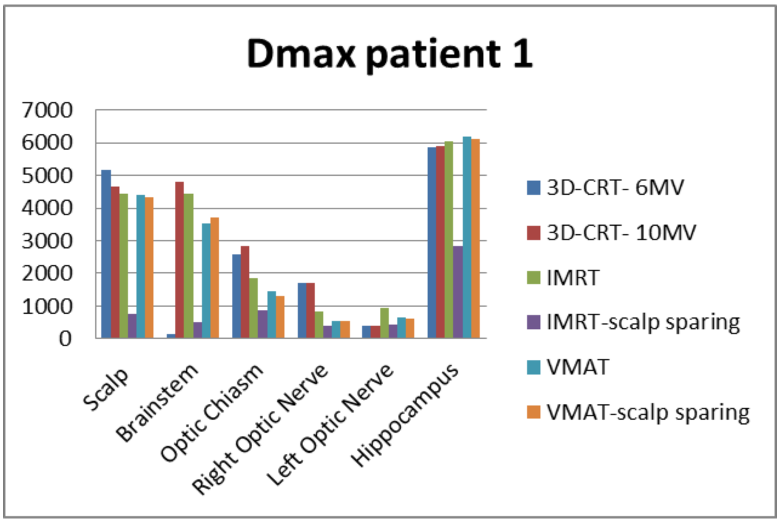

Fig. 2 – OARs maximum dose for patient 1 for the five irradiation techniques.

3. Results

In all three cases the application of a dosimetric constraint on the scalp did not lead to unpredictable increases in mean and maximum doses for other OARs. Hippocampus doses were comparable to those obtained without constraint or lower in some situations. For scalp, the IMRT technique reduced Dmean by 5.5%, 3.2% and 12.5% and Dmax by 18.7%, 9.6% and 8.3% for all three cases compared to the doses obtained using 3D-CRT (6MV energy) technique considered the standard treatment. The VMAT technique reduced Dmean with 5.1%, 0.8% and 22.2% and Dmax with 16.35, 11% and 16% relative to the 3D-CRT (6MV) radiotherapy plans (Figs. 1-6).

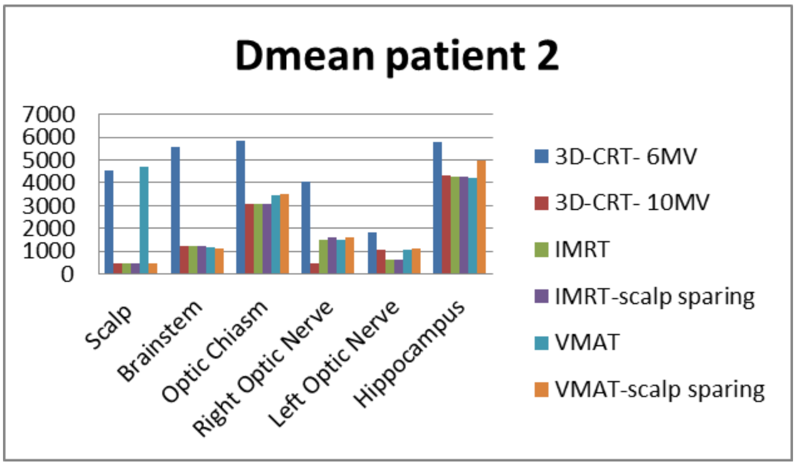

Fig. 3 – OARs mean dose for patient 2 for the five irradiation techniques.

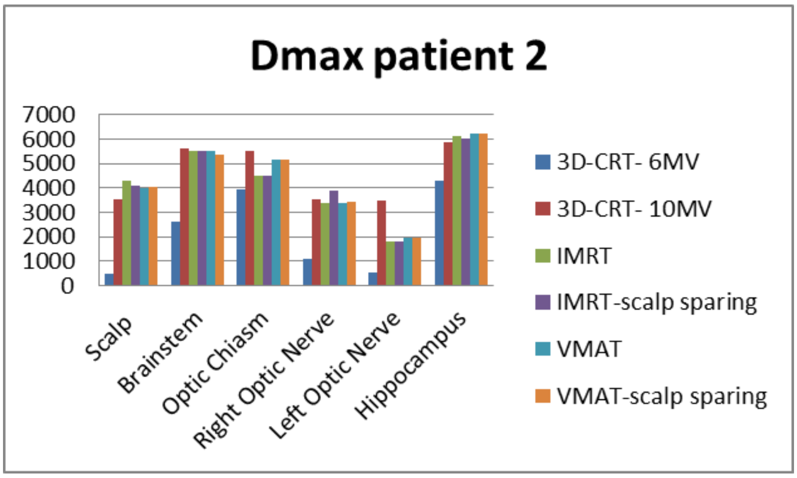

Fig. 4 – OARs maximum dose for patient 2 for the five irradiation techniques.

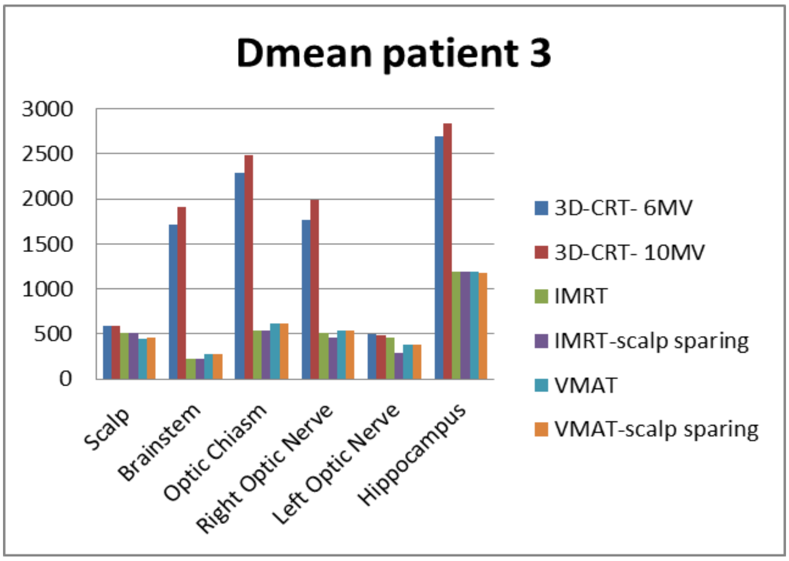

Fig. 5 – OARs mean dose for patient 3 for the five irradiation techniques.

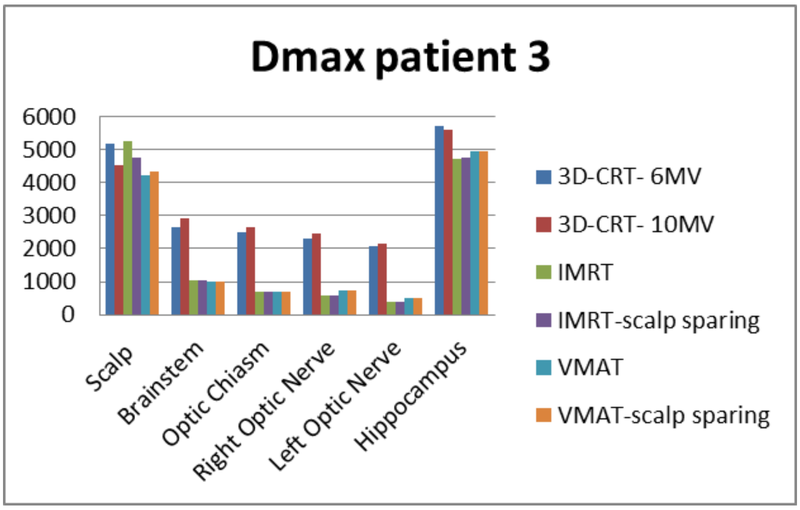

Fig. 6 – OARs maximum dose for patient 3 for the five irradiation techniques.

4. Discussion

Compared to the lateral opposed fields whole brain radiotherapy (OF-WBRT), the VMAT computations clearly predict a mean dose decrease of approximately 25% in the total hair follicle volume. Dose measurements demonstrated the potential of VMAT-WBRT to reduce the subcutaneously absorbed dose by 20.5%. Roberge *et al.*, for comparison, measured a dose reduction of 53% at 1 mm depth with TLD's and calculated a dose reduction of 38% within the first 5 mm of the skin when comparing IMRT to OF-WBRT (De Puysseleyr *et al*., 2014).

When compared to traditional opposed lateral fields, the IMRT plan with combined hippocampal and scalp-sparing constraints was able to significantly reduce the max and mean scalp dose as well as the percentage of scalp receiving 10 and 20Gy by 46% and 35%, respectively, while maintaining acceptable RTOG 0933 hippocampal dose variations. Witek *et al*. concluded that acceptable PTV coverage and sparing of the scalp and hippocampus can be obtained using a 9-field non-coplanar IMRT plan. No significant difference in hippocampal doses between the hippocampal-sparing and hippocampal-scalp-sparing plan was found using IMRT. IMRT was able to reduce the average measured dose to scalp by 53% from 95% of the prescription dose with the conventional plan to 44% with the IMRT plan (Witek *et al*., 2014).

Three field IMRT plans were compared with conventional WBRT plans for 17 irradiated patients for brain metastases. IMRT reduced the mean scalp dose (26.2Gy *vs*. 16.4Gy, $p < 0.001$) and is a feasible technique to reduce alopecia in brain radiotherapy (Kao *et al*., 2015).

Scoccianti *et al*. reports that a Dmax ≤ 35Gy constraint was obtained in all cases using helical tomography, maintaining under the recommended dose limits at OARs but meeting the constraints for the scalp is not always possible for high grade gliomas targets that need to be treated with a total dose of 60Gy (Scoccianti *et al*., 2016).

5. Conclusions

Applying a dosimetric constraint on the scalp, the doses Dmean and Dmax may be reduced using IMRT and VMAT techniques compared to 3D-CRT radiotherapy (considered standard for brain tumors) without increasing the dose to the other OARs. For the hippocampus, the dosimetric evaluation has confirmed that scalp-sparing radiotherapy decreases in most cases or maintains comparable doses for hippocampus and this method can not lead to increased risk of cognitive impairment. The possibility to apply the technique in clinical practice should be evaluated on a larger number of patients and factors such as tumor volume and anatomical localization should be considered.

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EFECTUL DOZIMETRIC ASUPRA STRUCTURILOR NEURONALE ALE RADIOTERAPIEI IMRT ŞI VMAT CARE PROTEJEAZĂ SCALPUL ÎN CAZUL GLIOAMELOR DE GRAD ÎNALT

(Rezumat)

Radioterapia tumorilor cerebrale, cu protecția foliculilor piloși pentru reducerea alopeciei a devenit o opțiune viabilă odată cu introducerea tehnicilor de radioterapie cu planificare inversă. Scopul studiului a fost, evaluarea pe 3 cazuri de glioblastom temporo-parietal iradiat cu doza totala DT = 60Gy, posibilității reducerii dozei maxime și dozei medii primite de foliculii piloși și evaluarea consecințelor

dozimetrice asupra celorlalte organe la risc. În toate cele 3 cazuri s-a obținut pentru scalp o reducere a dozelor medii cu 5,5%, 3,2% și 12,5% prin tehnica IMRT și cu 5,1%, 0,8% și 22,2% prin tehnica VMAT. În cazul dozei maxime s-a obținut o scădere cu 18,7%, 9,6% și 8,3% prin tehnica IMRT și cu 16,35%, 11% și 16% prin tehnica VMAT fără a crește doza la celelalte organe la risc (inclusive hipocampul implicat în menținerea statusului cognitiv al pacienților).