A Case of a Cutaneous Angiosarcoma that Demonstrated a Late but Comprehensive Response to Treatment

Libertas Academica
FREEDOM TO RESEARCH

J. J. Calero[1], F. Rodríguez[2], S. Donis[3], B. Robayna[3], O. Hernández[3], J. L. Perez[1] and F. Otón[1]

[1]Department of Radiation Oncology, Hospital Universitario de Canarias, La Laguna, Tenerife, Spain. [2]Department of Medicine Physics and Pharmacology, Universidad de La Laguna, Tenerife, Spain. [3]Department of Medical Physics, Hospital Universitario de Canarias, La Laguna, Tenerife, Spain.

ABSTRACT

INTRODUCTION: A cutaneous angiosarcoma case with visible illness was treated with a modified lateral electron–photon technique (m-LEPT) that demonstrated a late but successful response to treatment.

CASE PRESENTATION: A 74-year-old man presented after surgery with remnants of the tumor at the angiosarcoma bed, which did not stop growing.

MANAGEMENT AND OUTCOME: m-LEPT technique was developed and applied to optimize dosimetry of the scalp. Late complete response was achieved after a disheartening posttreatment clinical state.

DISCUSSION: This is a rare and difficult-to-treat pathology, and hence case studies like this should encourage treatment despite poor early results.

KEYWORDS: cutaneous angiosarcoma, scalp LEPT, radiotherapy, radiotherapy planning

CITATION: Calero et al. A Case of a Cutaneous Angiosarcoma that Demonstrated a Late but Comprehensive Response to Treatment. *Clinical Medicine Reviews in Oncology* 2016:6 1–6 doi: 10.4137/CMRO.S39820.

TYPE: Case Report

RECEIVED: March 31, 2016. **RESUBMITTED:** August 14, 2016. **ACCEPTED FOR PUBLICATION:** August 18, 2016.

ACADEMIC EDITOR: Garry M. Walsh, Editor in Chief

PEER REVIEW: Four peer reviewers contributed to the peer review report. Reviewers' reports totaled 630 words, excluding any confidential comments to the academic editor.

FUNDING: Authors disclose no external funding sources.

COMPETING INTERESTS: Authors disclose no potential conflicts of interest.

CORRESPONDENCE: frguez@ull.edu.es

Paper subject to independent expert blind peer review. All editorial decisions made by independent academic editor. Upon submission manuscript was subject to anti-plagiarism scanning. Prior to publication all authors have given signed confirmation of agreement to article publication and compliance with all applicable ethical and legal requirements, including the accuracy of author and contributor information, disclosure of competing interests and funding sources, compliance with ethical requirements relating to human and animal study participants, and compliance with any copyright requirements of third parties. This journal is a member of the Committee on Publication Ethics (COPE).

Published by Libertas Academica. Learn more about this journal.

Introduction

Malignant neoplasms of the scalp such as cutaneous lymphoma, melanoma, and cutaneous angiosarcoma are rare, and hence scientific literature is scarce and with very little variety in case studies, making it difficult to understand their clinical evolution.

As observed by Wollina et al.[1], cutaneous angiosarcoma is an aggressive vascular tumor that represents 2% of soft tissue sarcoma. They found that 60% arise in skin but can appear in any area of the body and also found that 50% occur in head and neck, often on the scalp of elderly patients.[2]

Due to its aggressiveness, overall prognosis is poor: mean survival is 30 months and the rate of survival is 7.5 months for lung disease that is treated with only palliative chemotherapy.[3] Palliative radiotherapy alone without surgery results in a mean survival of 15 months.[4]

Currently, the treatment of choice is surgery, with adjuvant chemotherapy or radiotherapy when considered necessary. Complete resection is often difficult. Our aim is to review the use of radiotherapy as an adjuvant, looking for possible improvements.

Adjuvant radiotherapy in scalp angiosarcoma cases is a complex technique. It involves a rare target volume, the scalp, which is under the patient's surface and around the skull, only a few millimeters wide. Moreover, tumor localization requires avoidance of some organs at risk (OARs), such as the brain and eyes.

In the scientific literature, there are a few approximations to this treatment challenge with a curved volume. Able et al.[5] and Mellenberg and Schoeppel[6] developed a technique that uses electron fields with a shift and a gap in fields' conjunctions to avoid hotspots in the radiotherapy plan.

The most influential article is the study by Akazawa,[7] who described a technique called lateral electron–photon technique (LEPT). This procedure utilizes opposed lateral photon fields with central blocking to treat the rind of the medial scalp, while two lateral electron fields cover the blocked areas. Two pairs of lateral electron and photon fields are treated for each fraction. The main portions of the lateral scalp are irradiated by the lateral electron field.

The shape of the photon fields must be symmetrical from both sides. The field border between the electron and photon fields is chosen and hence minimal brain tissue is irradiated by the photon fields, while skin surfaces covered by the electron fields are kept from being angulated too greatly away from perpendicular incidence. A treatment central axis is shared by all fields and is located near the center of the curvature of the field junction.

Tung et al.[8] improved dose uniformity of LEPT with an overlap of electron and photon fields. Both techniques have been settled as the treatment of choice for many years. As Lin et al.[9] explained, the importance of a bolus that helps to achieve adequate skin dose is predominant in these treatments.

Later, Bedford et al.[10] observed that Intensity Modulated Radiation Therapy (IMRT) techniques have not improved dosimetry, worsening the dose received by the brain. Meanwhile, Ostheimer et al.[11] established the merits of noncoplanar fields. Liebmann et al.[12] and Wojcicka et al.[13] attempted a helmet brachytherapy technique, without good results. Locke et al.[14] described tomotherapy as a suboptimal treatment because of consequent OAR dose.

Song et al.[15] were one of the few researchers who shared different conclusions about new techniques. They compared helicoidal tomotherapy with Vmat and LEPT: tomotherapy seemed to improve homogeneity and conformity; VMAT maintained low doses in a high percentage of the brain; and LEPT caused minimal low doses to brain, eyes, and chiasma. Jiang et al.[16] stated that IMRT is superior to 3D Conformal Radiation Therapy (3D-CRT), avoiding higher brain doses, and that RapidArc (VMAT technology from Varian) achieved the best conformity.

By sharing this case report, we aim to increase and add information about LEPT, helping to optimize it. Many authors note the early response to treatment or the absence of it. We include 12 months of evolution after radiotherapy with a good late clinical outcome.

Case Presentation

Our case study presented a 74-year-old male with good quality of life. A dark and thick nodule appeared on his scalp. Seven months later, a dermatologist assessed him, describing a big nodule with smaller growths around. A first biopsy study was made and the nodule was identified as dermatofibrosarcoma protuberans.

Four months later, 11 months after the first nodule appeared, extirpation was performed with free margins and a skin graft. This time, however, pathology was described as cutaneous angiosarcoma grade 3. Its shorter margin was at 8 mm, with total resection.

Figure 1. (Left) This angiosarcoma is seen here as a dark adjacent nodule.

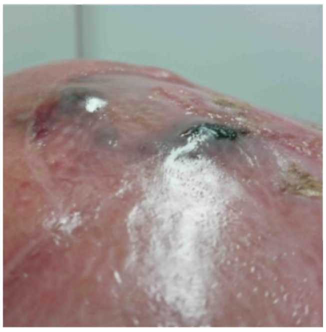

Figure 2. (Right) More prominent nodules are seen at the beginning of radiotherapy, after three chemotherapy cycles.

CT images confirmed no distant metastasis. The patient was seen by the Department of Medical Oncology. Clinical exploration was described as a figure eight-shaped slim area, 12.5 cm long (Fig. 1). In the middle, there was a 2 cm long dark nodule, and two smaller ones (7 mm) were found near it. It seemed like an early relapse. This was why chemotherapy was started two months after intervention. It used paclitaxel 80 mg/m^2, three times per week, every four weeks, for six cycles. Following this, it was determined that after three cycles, the patient would undergo radiotherapy. By then, a local progression was observed with bigger nodules (Fig. 2).

Management

Contouring was done with Focal System software (ver 5.00.04; Elekta Group). We delineated a clinical tumor volume, including the entire scalp outside the skull. The anterior limit was 20 mm from the hairline. Planning tumor volume (PTV) adds a 4 mm margin. The following OARs were contoured: brain, cerebellum, ocular globes, crystallines, chiasma, optical nerves, spinal cord, brain stem, and hippocampus.

Mendenhall et al.[17] described scalp irradiation with doses as high as 50 Gy in adjuvant treatment, 60 Gy if subclinical

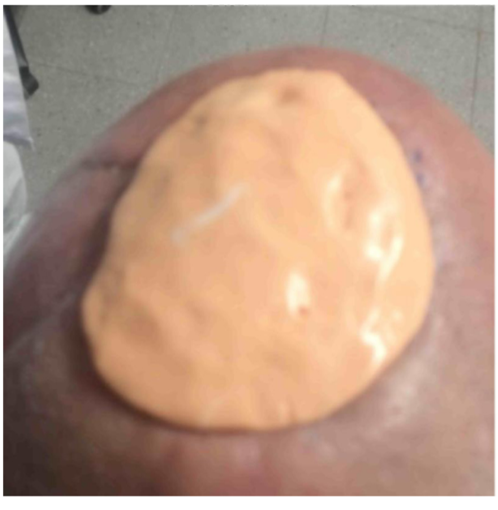

Figure 3. Silicone bolus on tumor's bed.

disease is suspected, or even 70 Gy when gross tumor is present. The chosen dose in this case was 1.8 Gy daily, for 28 sessions, five times a week, until we achieved 50.4 Gy at 95% of PTV (D95%).

Because of the lack of subcutaneous tissue at the tumor's bed, a bolus with its shape was needed to obtain a correct dosimetry (Fig. 3). In addition, another 5 mm bolus also covered the entire scalp. It was made of vinylpolysiloxane. We also added a thermoplastic mask to assure immobilization during treatment (Fig. 4).

An alternate version of the Akazawa's LEPT[7] was developed in our center by our Department of Medical Physics. This modified LEPT (m-LEPT) includes some changes from Akazawa and Tung's technique, aiming a better conformity of the dose:

1. two identical electron beams on each side, 9 and 6 MeV, 70% and 30%, respectively, of the total dose (Fig. 5);
2. multileaf conformed lateral photon fields;

Figure 4. Immobilization with a thermoplastic mask, tumor's bed marked.

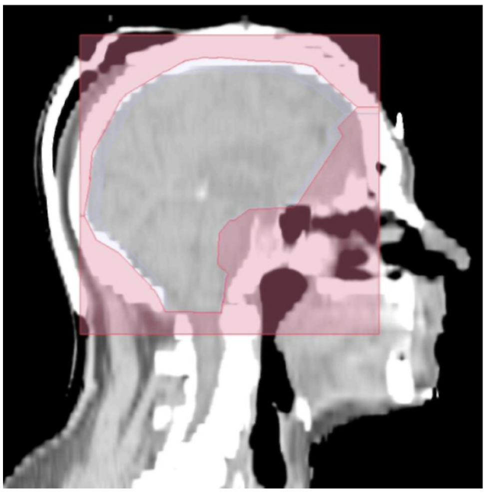

Figure 5. Electron field conformation, brain shaped.

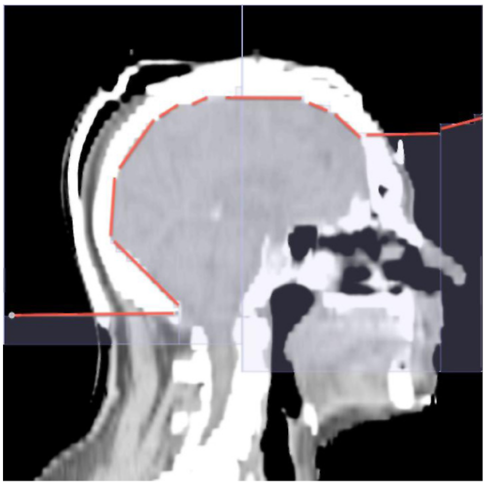

Figure 6. Photon field shape, outside electron one.

Table 1. Gantry angle and MU for each field.

		GANTRY 270º (RIGHT)		GANTRY 90º (LEFT)	
Electron	Field	9 MeV	6 MeV	9 MeV	6 MeV
	MU	150	56	145	57
Photon	Field	Anterior	Posterior	Anterior	Posterior
	MU	88	95	90	96

3. each photon field was divided into two asymmetric ones, anterior and posterior, to adapt to the concavity of the surface to be treated (Fig. 6);
4. electron and photon beams overlapped 3 mm. When 26 Gy was achieved (half treatment), a 1 cm shift was made to reduce hotspots and avoid cold areas.

Gantry angles and monitor unit numbers (MU) for each field are detailed in Table 1.

Dosimetry Analysis

XiO software (version 4.50; CMS software, Elekta Group) was used to plan the treatment. It was given in a Varian Clinac Accelerator 2100 EX (Varian Medical Systems).

Plan conformity was assessed using the following parameters, which were also applied by Ostheimer et al.[11], Wojcicka et al.[13], Song et al.[15], and Jiang et al.[16]:

The Homogeneity Index (HI) was defined in accordance with the International Commission on Radiation Units (ICRU) report 83.

$$\mathrm{IH} = (D_{2\%} - D_{98\%}) / D_{50\%}$$

The Conformation Number (CN)[18] takes into account irradiation of the target volume and irradiation of healthy tissues.

Table 2. PTV conformity values.

	DOSIMETRY	RESULTS
PTV	D_2 (Gy)	60.2
	HI	0.30
	CN	0.63

$$CN=(TV_{95\%})^2/(TV*V_{RI})$$

Dosimetric outcomes are listed in Table 2.

The dose distribution produces hotspots greater than 50.4 Gy ($D_{2\%}$ = 60.2 Gy) in the overlapped regions of electron and photon fields, localized in the top of the head of our patient.

Doses received by all OARs volumes are detailed in Table 3. Brain tissue is a dose-limiting organ for total scalp irradiation. The mean dose to brain was 11.3 Gy in this case.

Dose–volume histograms (DVHs) for target volume and OARs are shown in Figures 7 and 8. Isodose curve is shown in Figure 9, which was considered acceptable.

After 50.4 Gy was achieved, a 10 Gy boost was arranged with a direct 6 MeV electron field, focused on the residual nodules. A dose of 2 Gy per day, five times a week, was given. A total dose of 60.4 Gy was reached at ICRU point.

Table 3. OAR doses detailed.

STRUCTURES	DOSIMETRY	RESULTS
Brain	D_{mean} (Gy)	11.3
	V_{5Gy} (%)	46.94
	V_{10Gy} (%)	33.9
	V_{20Gy} (%)	21.33
	V_{30Gy} (%)	12.12
	V_{40Gy} (%)	4.6
	$D_{1\%}$ (Gy)	47.59
	$D_{99\%}$ (Gy)	1.58
Cerebellum	D_{max} (Gy)	45.57
	D_{mean} (Gy)	13.08
Brainstem	D_{max} (Gy)	2.84
	D_{mean} (Gy)	2.47
Cord	D_{max} (Gy)	2.45
	D_{mean} (Gy)	0.83
Left ocular globe	D_{max} (Gy)	2.12
	D_{mean} (Gy)	1.51
Right ocular globe	D_{max} (Gy)	2.22
	D_{mean} (Gy)	1.46
Left crystalline	D_{max} (Gy)	1.44
	D_{mean} (Gy)	1.38
Right crystalline	D_{max} (Gy)	1.44
	D_{mean} (Gy)	1.35
Left optic nerve	D_{max} (Gy)	1.66
	D_{mean} (Gy)	1.56
Right optic nerve	D_{max} (Gy)	1.79
	D_{mean} (Gy)	1.57
Chiasma	D_{max} (Gy)	1.77
	D_{mean} (Gy)	1.60
Right hyppocampus	Dmax (Gy)	2.88
	Dmean (Gy)	2.51
Hyppocampus left	Dmax (Gy)	3.35
	Dmean (Gy)	2.52

Outcome

After receiving 14 Gy, the patient had grade 1 dermatitis, especially around the scar. At the end of the treatment, a grade 2 generalized dermatitis was observed on the irradiated skin. Symptomatic treatment was performed with hyaluronic acid moisturizing gel (Hialderm from Diafarm Laboratorios).

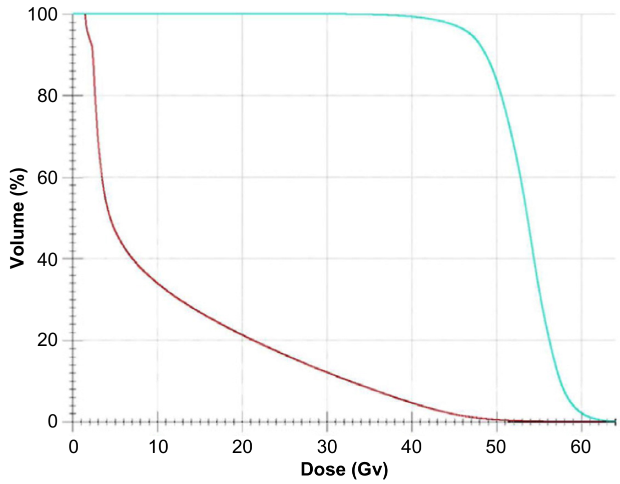

Figure 7. DVHs for PTV (blue) and brain (red).

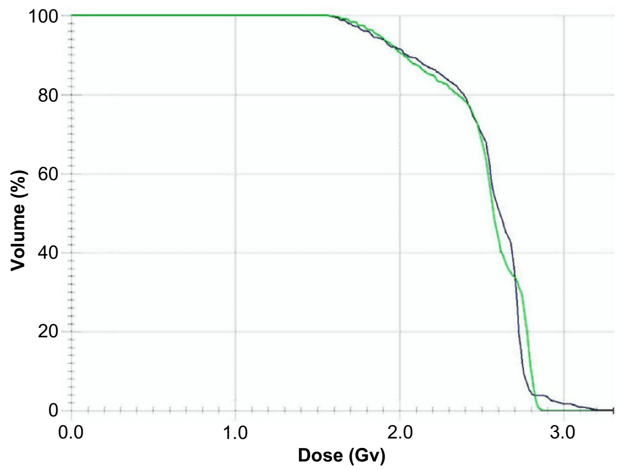

Figure 8. DVHs for left and right hippocampus.

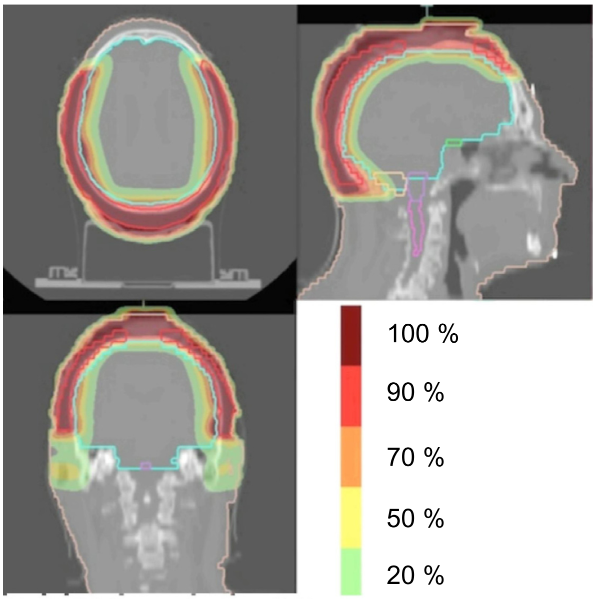

Figure 9. Axial, coronal, and sagittal images of our plan isodose distribution.

Figure 10. Dermatitis grade 1 at the end of the treatment.

Figure 11. Six months after radiotherapy, nodules disappeared.

It is important to highlight that clinically, while on treatment, the dark nodules grew and hardened. One month after the end of radiotherapy, these nodules were still prominent (Fig. 10).

Chemotherapy was continued for three further cycles. Six months after radiotherapy ended, the nodules disappeared (Fig. 11). This was not expected, considering the bad early response. Twelve months after radiotherapy, no sign of disease was observed.

Discussion

In this cutaneous angiosarcoma case, an early relapse was seen after surgery. Clinical evolution supports our radiotherapy indication. Surprisingly, a good outcome came late, six months after treatment, and has lasted for at least six further months.

Because of this, we consider that the time between surgery and radiotherapy is of significant importance to minimize relapse risk. A 50–60 Gy dose seems sufficient and tolerable.

Our technique, called m-LEPT, is suitable and we think that it may improve treatment overall from traditional LEPT. The HI is significantly decreased in our plan compared to traditional LEPT[16] and similar to the one analyzed for IMRT[11] and RapidArc.[16] CN value was slightly higher in the m-LEPT plan than in traditional LEPT[13,15,16] and similar in IMRT[11] and VMAT[15] plans.

It is interesting to note that the role of adjuvant chemotherapy is unclear: it is possible that in our patient it contributed to his clinical evolution. In 1999, Fata et al.[19] observed tumor reduction of angiosarcoma metastasis using paclitaxel. In 2007, Nagano et al.[20] reached the same conclusion in metastatic cases. However, in our case, it is important to highlight the fact that chemotherapy did not have an effect on the tumor in the first three cycles: during chemotherapy, the disease even grew. It was only after radiotherapy that any response was achieved. Further studies comparing adjuvant chemotherapy, radiotherapy, and combinations should be performed to analyze each factor's role.

In contrast to other published cases, we have been able to compile both clinical and esthetic results, 12 months after radiotherapy, with images. We hope this inspires other authors to perform the same to obtain a better understanding of the clinical evolution of cutaneous angiosarcoma.

Acknowledgment

We would like to express our gratitude to Dr. Francisco Padron, dentist, who supported us by providing the silicone bolus. Consent to publish from the patient has been given.

Author Contributions

Conceived and designed the experiments: JJC, JLP, FR. Analyzed the data: SD, OH, BR, JJC. Wrote the first draft of the manuscript: JJC. Contributed to the writing of the manuscript: JJC, FR, SD, BR, OH, JLP, FO. Agree with manuscript results and conclusions: JJC, FR, SD, BR. Jointly developed the structure and arguments for the paper: JJC, FR, SD, BR. Made critical revisions and approved final version: JJC, FR, SD, BR. All authors reviewed and approved of the final manuscript.

REFERENCES

1. Wollina U, Hansel G, Schönlebe J, Averbeck M, Paasch U, Uhl J. Cutaneous angiosarcoma is a rare aggressive malignant vascular tumour of the skin. *J Eur Acad Dermatol Venereol*. 2011;25(8):964–8.
2. Mark RJ, Poen JC, Tran LM, Fu YS, Juillard GF. Angiosarcoma. A report of 67 patients and a review of the literature. *Cancer*. 1996;77(11):2400–6.
3. Maddox JC, Evans HL. Angiosarcoma of skin and soft tissue: a study of forty-four cases. *Cancer*. 1981;48(8):1907–21.
4. Holden CA, Spittle MF, Jones EW. Angiosarcoma of the face and scalp, prognosis and treatment. *Cancer*. 1987;59(5):1046–57.
5. Able CM, Mills MD, McNeese MD, Hogstrom KR. Evaluation of a total scalp electron irradiation technique. *Int J Radiat Oncol Biol Phys*. 1991;21(4):1063–72.
6. Mellenberg DE, Schoeppel SL. Total scalp treatment of mycosis fungoides: the 4 x 4 technique. *Int J Radiat Oncol Biol Phys*. 1993;27(4):953–8.
7. Akazawa C. Treatment of the scalp using photon and electron beams. *Med Dosim*. 1989;14(2):129–31.
8. Tung SS, Shiu AS, Starkschall G, Morrison WH, Hogstrom KR. Dosimetric evaluation of total scalp irradiation using a lateral electron-photon technique. *Int J Radiat Oncol Biol Phys*. 1993;27(1):153–60.
9. Lin SH, Latronico D, Teslow T, Bajaj GK. A highly reproducible bolus immobilization technique for the treatment of scalp malignancies. *Med Dosim*. 2008;33(1):30–35.
10. Bedford JL, Childs PJ, Hansen VN, Warrington AP, Mendes RL, Glees JP. Treatment of extensive scalp lesions with segmental intensity-modulated photon therapy. *Int J Radiat Oncol Biol Phys*. 2005;62(5):1549–58.
11. Ostheimer C, Janich M, Hübsch P, Gerlach R, Vordermark D. The treatment of extensive scalp lesions using coplanar and non-coplanar photon IMRT: a single institution experience. *Radiat Oncol*. 2014;9:82.
12. Liebmann A, Pohlmann S, Heinicke F, Hildebrandt G. Helmet mold-based surface brachytherapy for homogeneous scalp treatment: a case report. *Strahlenther Onkol*. 2007;183(4):211–4.
13. Wojcicka JB, Lasher DE, McAfee SS, Fortier GA. Dosimetric comparison of three different treatment techniques in extensive scalp lesion irradiation. *Radiother Oncol*. 2009;91(2):255–60.
14. Locke J, Low DA, Grigireit T, Chao KS. Potential of tomotherapy for total scalp treatment. *Int J Radiat Oncol Biol Phys*. 2002;52(2):553–9.
15. Song JH, Jung JY, Park HW, et al. Dosimetric comparison of three different treatment modalities for total scalp irradiation: the conventional lateral photon-electron technique, helical tomotherapy, and volumetric-modulated arc therapy. *J Radiat Res*. 2015;56(4):717–26.
16. Jiang H, WeiWei X, ZhiChun H, DeHua K, ALong C, Zhen Y. Target splitting non-coplanar RapidArc radiation therapy for a diffuse sebaceous carcinoma of the scalp: a novel delivery technique. *Radiat Oncol*. 2014;9:204.
17. Mendenhall WM, Mendenhall CM, Werning JW, Reith JD, Mendenhall NP. Cutaneous angiosarcoma. *Am J Clin Oncol*. 2006;9(5):524–8.
18. Feuvret L, Noël G, Mazeron JJ, Bey P. Conformity index: a review. *Int J Radiat Oncol Biol Phys*. 2006;64(2):333–42.
19. Fata F, O'Reilly E, Ilson D, et al. Paclitaxel in the treatment of patients with angiosarcoma of the scalp or face. *Cancer*. 1999;86(10):2034–7.
20. Nagano T, Yamada Y, Ikeda T, Kanki H, Kamo T, Nishigori C. Docetaxel: a therapeutic option in the treatment of cutaneous angiosarcoma: report of 9 patients. *Cancer*. 2007;110(3):648–51.