



Reirradiation for Recurrent Scalp Angiosarcoma: Dosimetric Advantage of PBT over VMAT and EBT

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Abstract

Purpose: Reirradiation in the scalp area can be challenging given the proximity to organs at risk (OARs), such as the eye and brain. Our aim is to evaluate the dosimetric differences of volumetric modulated arc therapy (VMAT) and electron beam therapy (EBT) compared with 3-dimensional proton beam therapy (PBT).

Patients and Methods: We evaluated a patient with recurrent angiosarcoma of the left temporal scalp after prior surgical resections and radiation therapy to 60 Gy in 30 fractions who needed reirradiation. We generated VMAT, EBT, and PBT plans using the Pinnacle Treatment Planning System (TPS). Both VMAT and EBT plans used a skin bolus, whereas no bolus was used for the proton plan. Doses to the OARs, including cochlea, eyes, lens, lacrimal glands, optic nerves, optic chiasm, pituitary gland, and underlying brain, were compared.

Results: The reirradiation treatment dose was 60 Gy(RBE). Target volume coverage was comparable in all plans. Compared with VMAT and EBT, the PBT plan showed reductions in mean and maximum doses to all OARs. Without the use of protons, several OARs would have exceeded dose tolerance utilizing VMAT or electrons. Dose reduction of up to 100% was achieved for central and contralateral OARs.

Conclusion: Compared with VMAT and EBT, PBT resulted in dose reductions to all OARs, while maintaining excellent target coverage. PBT showed a significant advantage in treating superficially located skin cancers, such as angiosarcoma, without the need for a bolus. PBT can be considered in the upfront treatment and certainly in the reirradiation setting.

Keywords: proton beam therapy; Bragg peak; angiosarcoma; organ at risk prevention; periorbital tumors

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Introduction

Angiosarcoma is a rare malignancy that develops from cells that make up the walls of blood vessels. It can occur anywhere throughout the body but most commonly occurs in the skin, breast, liver, spleen, and deep tissues. Of the different categories of angiosarcoma, primary cutaneous angiosarcoma is the most common (28% of cases) and primarily affects the scalp and upper forehead [1]. Proximity to critical organs at risk (OARs) in the periorbital area, such as the eye, lacrimal gland, cochlea, lens, optic nerve, optic chiasm, pituitary gland, and brain, increases risk of collateral morbidity for any treatment of primary cutaneous angiosarcoma. Successful surgical resection is critical for meaningful prognosis of this disease. However, a negative histologic margin found in the postoperative setting is not reliable because of the dependence on a single histologic sample [2]. Therefore, adjuvant treatments are being investigated. Adjuvant radiation therapy (RT) has been introduced and is being optimized for better clinical outcomes.

Previously, protons have been used within the orbital location for the management of ocular melanomas [3, 4], choroidal metastases [5], and orbital rhabdomyosarcomas [6] with excellent results. The role of photons and electron RT in the treatment of orbital and periorbital lesions is well established [7–9]. Compared with electrons and photons, protons achieve steep lateral dose fall-off, which can be controlled based on the depth of the lesion. The fall-off is more rapid with superficial lesions than with deeper lesions [10], making it a more ideal form of radiation for periorbital lesions. Scalp angiosarcoma lies within the parameters for skin cancers with high risk for collateral morbidity upon treatment. The aim of our study was to evaluate the effectiveness of 3-dimensional proton beam therapy compared with electron beam therapy (EBT) and volumetric modulated arc therapy (VMAT) across the parameters of collateral irradiation to surrounding OARs.

Patients and Methods

Case Presentation

A 65-year-old woman initially presented in 2012 with cutaneous angiosarcoma of the scalp at the left temple area. Upon diagnosis, the patient underwent a radical excision of the scalp lesion and a pericranial flap. Pathology revealed a high-grade angiosarcoma that was 3.5 cm at the greatest dimension. A finding of positive surgical margin resulted in a wide resection and flap reconstruction 2 months later. Pathological tests revealed no residual malignancy. Three months later, the patient completed postoperative RT to the scalp to a total dose of 60 Gy in 30 fractions using Tomotherapy® (Accuray, Sunnyvale, CA) without any adjuvant chemotherapy.

She was monitored over the next 4 years with repeated computed tomography (CT) of the neck, chest, abdomen, and pelvis for restaging purposes. In late 2016, a lesion was noted on her left frontal scalp, and biopsy revealed recurrent angiosarcoma. Two months later, the patient underwent extensive excision of the left-sided scalp lesion, left superficial parotidectomy, left supraomohyoid neck dissection, resection of the portion of frontal and parietal bone, anterior lateral thigh myocutaneous free flap, and a split-thickness skin graft to the scalp. Pathological tests revealed post-RT changes along with recurrent cutaneous angiosarcoma. The tumor involved the dermis and ulcerated the epidermis; it was 0.4 cm thick and approximately 1.5 cm at the greatest horizontal dimension. Intraparotid lymph nodes and left neck lymph nodes were dissected, and 0/2 and 0/17 were involved, respectively. The tumor board considered adjuvant reirradiation therapy. Given the previous history of radiation, the 1.5 cm tumor size of recurrence, and the negative margins, retreatment RT was not recommended. Potential risks (damage to OARs) outweighed potential benefits.

About 21 months later, a new pink lesion was noted on the left temple area, which was concerning for recurrence. Biopsy and pathological tests revealed atypical vascular proliferation, suggestive of angiosarcoma. The patient then underwent repeated surgical excision and had a left radial forearm free-flap reconstruction for left temple recurrence. At this time, adjuvant RT of 60 Gy in 30 fractions was recommended. To reduce reirradiation-related toxicities to OARs, proton therapy, VMAT and EBT were considered.

The patient's head was immobilized with a thermoplastic mask. The area at risk was outlined with wire. Two CT stimulations, 1 with bolus of 1 cm (VMAT/EBT) and 1 without bolus (proton beam therapy [PBT]) were then performed. The clinical target volume was contoured based on the clinical and pathologic areas at risk for microscopic disease. A uniform expansion was placed to generate a planning target volume (PTV) for both photon and electron planning. The institutional standard for proton planning does not include a PTV expansion as setup/tissue uncertainty is accounted for in the planning technique and algorithm. Pinnacle TPS version 16.2 (Philips, Andover, MA) was used to generate EBT, VMAT (using convolution and superposition algorithm), and PBT (using pencil beam algorithm) plans, which were then compared. EBT had

Table. Comparison of proton versus electron and VMAT with decreases in absolute mean and cumulative doses with protons.

OARs	Mean dose (Gy)				Cumulative reirradiation dose (Gy)		
	Proton	Electron	VMAT	TomoTherapy	Proton	Electron	VMAT
Left eye	0.35	28.25	4.33	9.51	9.86	37.76	13.84
Left lens	0.01	15.75	3.7	3.58	3.59	19.33	7.28
Left lacrimal gland	8.04	53.89	12.06	14.93	22.97	68.82	26.99
Left optic nerve	0	3.91	3.65	10.63	10.63	14.54	14.28
Left cochlea	3.05	0.86	3.37	3.05	6.1	3.91	6.42
Right eye	0	0.73	1.37	3.57	3.57	4.3	4.94
Right lens	0	0.91	1.3	1.7	1.7	2.61	3
Right lacrimal gland	0	0.54	1.04	6.21	6.21	6.75	7.25
Right optic nerve	0	0.64	1.18	7.02	7.02	7.66	8.2
Right cochlea	0	0.67	1.8	1.25	1.25	1.92	3.05
Optic chiasm	0	0.77	1.2	11.97	11.97	12.74	13.17
Brain avoidance	0.41	3.36	4.68	13.61	14.02	16.97	18.29
Pituitary gland	0	0.77	1.55	7.33	7.33	8.1	8.88

Abbreviations: VMAT, volumetric modulated arc therapy; OAR, organ at risk.

a beam energy of 9 MeV while VMAT had a beam energy of 6 MV with modulation of 46 control points with a single arc. Elekta Versa HD™ machine (Elekta, Stockholm, Sweden) was used for both EBT and VMAT beams. PBT was delivered using Mevion S250™ (Mevion Medical Systems, Littleton, MA) with a CTV target range and modulation was 2.6 g/cm³. Single beam with distal margin = (0.035 x CTV distal) + 3.5 mm; proximal margin = (0.035 x CTV proximal) + 3 mm; lateral margin = 3 mm; aperture margin = 12 mm. Distance from patient surface to the snout (air gap) was 47 mm.

The institutional review board determined that the proposed activity is not research involving human subjects; therefore, institutional review board review and approval was not required.

Results

The patient received an adjuvant reirradiation treatment dose of 60 Gy(RBE) over 30 fractions. Proton irradiation yielded an overall decrease in OARs exposure as measured by dose compared with EBT or VMAT (Table).

From a qualitative perspective, proton radiation yielded a conformal plan compared with EBT or VMAT (Figure).

The precision of proton therapy served to reduce the exposure of OARs to radiation.

Six months after PBT, the patient showed no evidence of recurrence by physical exam and positron emission tomography. She had some dryness of the eyelid that was managed with topical therapy and had no other toxicity.

Discussion

Treatment of periorbital tumors depends on the tumor’s histology, size, location, and extent of invasion. The development of an optimal treatment regimen for each patient involves close interdisciplinary coordination between surgeons and radiation oncologists. The goal of RT is to achieve tumor control while preserving OARs, especially when surgery involves high risk of morbidity. Furthermore, surgery may not be ideal for larger tumors, recurrent disease, deeply invasive tumors, tumors with perineural invasion, or tumors with orbital invasion [11].

Electron beam energies of 6–9 MeV and orthovoltage x-rays [12–14] are often used to treat dermal malignancies occurring in or adjacent to the orbit and face with good efficacy and cosmesis. In the case of recurrence after RT, surgical excision should be considered. If the recurrence is marginal or adjacent to the previously treated field or if the required reconstruction is complex or mutilating, additional RT can be considered [15].

Use of RT in the periorbital location has been previously reported. Petsuksiri and colleagues [16] reported a 5-year local control rate of 88% in 42 eyelid squamous cell carcinomas treated with x-rays (45-250 kv) and electrons (6-12 MeV) to a median of 50–55.25 Gy [16]. In another study of 850 patients with eyelid cancer treated with either contact therapy, conventional RT, or electrons (45–70 Gy), Schlienger and colleagues [7] reported a 5-year local control rate of 97.5%.

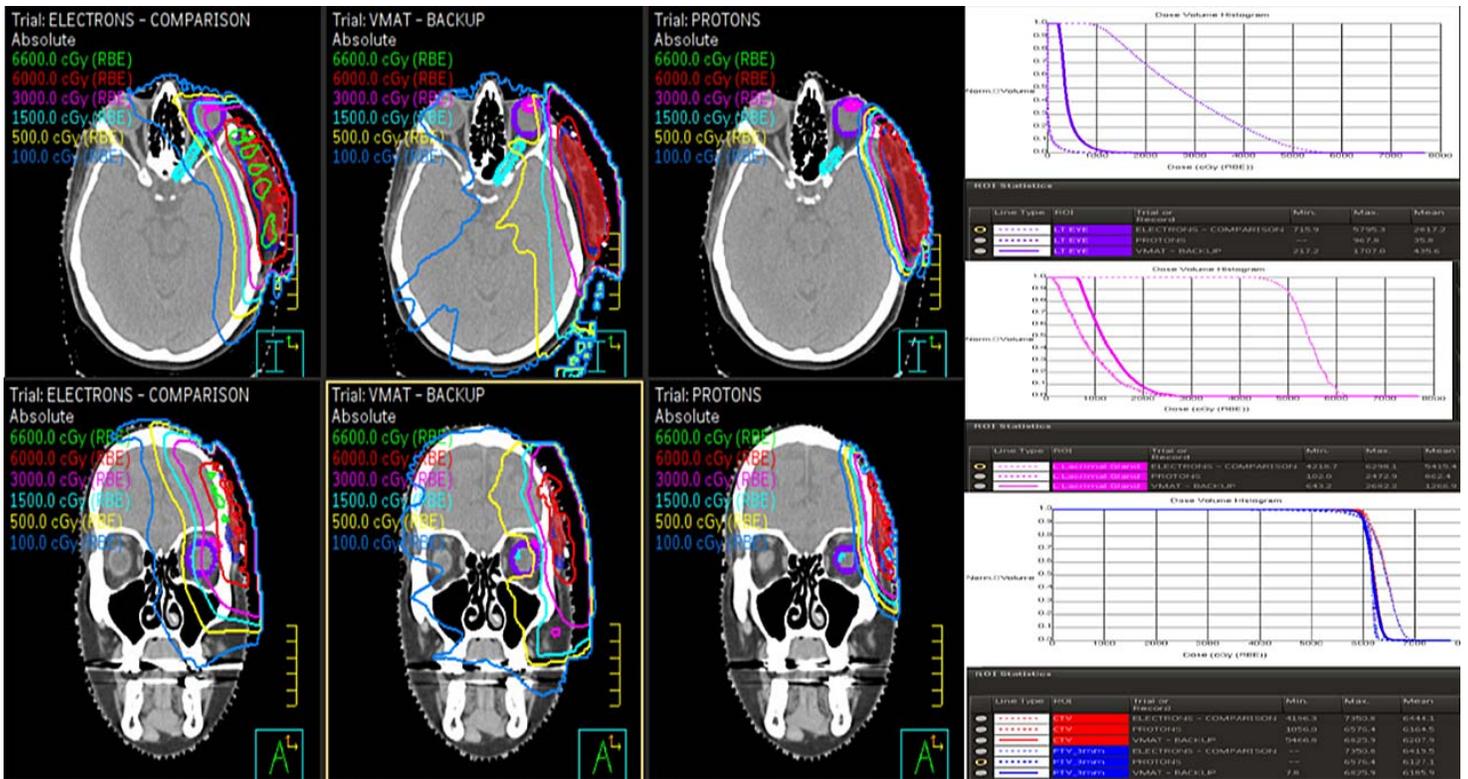


Figure. Comparison of proton versus electron and volumetric modulated arc therapy reirradiation plans on computed tomography.

However, with the use of RT, there is a risk of morbidity. Tissues at risk for toxicity from RT include the eye, lacrimal gland, cochlea, lens, optic nerve, optic chiasm, pituitary gland, and brain. Radiation-induced ocular morbidity encompasses a spectrum from transient eyelid-erythema to complete loss of vision, with or without loss of the globe [17]. PBT has particular physical properties that could be advantageous over other RTs. Protons are charged particles that can be energized. Upon entering a region, protons retain most of their energy and deposit it near the end of their trajectory during an interval known as the Bragg peak. By irradiating a region with protons of different energies and accelerations, coordinating the Bragg peaks to align with the full dimensions of a lesion could be helpful in minimizing radiation to OARs near the lesion. Compared with other modalities, protons are known to improve the therapeutic ratio and are expected to decrease toxicity in the treatment of head and neck tumors [18]. Furthermore, the lower entrance dose decreases collateral damage, resulting in potential reduction of unintended toxicities to OARs [19, 20].

In terms of our case of recurrent angiosarcoma, the total dose of 60 Gy(RBE) was achieved with excellent sparing of the OARs with acceptable toxicities. Specifically, the range of absolute mean and cumulative doses, of 0–8.04 Gy(RBE) and 1.7–22.97 Gy(RBE), respectively, when using protons compared with EBT (0.54–53.89 Gy(RBE) and 1.92–68.82 Gy(RBE), respectively) and of VMAT (1.2–12.06 Gy(RBE) and 3.0–26.99 Gy(RBE), respectively) suggests a clear therapeutic gain when using protons. The limitations of our case report are that we evaluated just 1 person, implying perhaps limited extrapolation. Nonetheless, we believe our case report adds to the current literature and clinical experience with PBT as a unique modality that may lead to better outcomes in reducing toxicities to OARs.

While recurrence and reducing toxicities to OARs were the focus in this case, another concern is subclinical metastasis. A direction of future investigation includes chemoradiotherapy by use of taxanes, such as paclitaxel, for cytotoxic, radiosensitizing, and maintenance therapy purposes, although side effects might be more severe [21, 22]. Additionally, current genomic work on cutaneous angiosarcomas reveals complexities that suggest further investigation into personalized medicine and immune system targets. This work also suggests the need to evaluate new drugs that target genome-related molecules [21, 22].

PBT shows a significant advantage in treating superficially located skin cancers, such as angiosarcoma, without the need for a bolus. PBT, compared with VMAT and EBT, resulted in dose reductions to all OARs while maintaining excellent target coverage. PBT could be considered in the upfront treatment and certainly in the reirradiation setting.

ADDITIONAL INFORMATION AND DECLARATIONS

Conflicts of Interest: The authors have no relevant conflicts of interest to disclose.

Ethical approval: The institutional review board determined that the proposed activity was not research involving human subjects; therefore, institutional review board review and approval was not required.

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