Proton Versus Intensity-Modulated Radiation Therapy: First Dosimetric Comparison for Total Scalp Irradiation

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Abstract

Purpose: Total scalp irradiation (TSI) is used to treat malignancies of the scalp and face, including angiosarcomas, nonmelanoma skin cancers, and cutaneous lymphomas. Owing to the irregularity of the scalp contour and the presence of underlying critical organs at risk (OARs), radiation planning is challenging and technically difficult. To address these complexities, several different radiation therapy techniques have been used. These include the combined lateral photon-electron technique (3DRT), intensity-modulated radiation therapy (IMRT)/volumetric arc therapy (VMAT), helical tomotherapy (HT), and mold-based high-dose-rate brachytherapy (HDR BT). However, the use of proton radiation therapy (PRT) has never been documented.

Materials and Methods: A 71-year-old, immunosuppressed man presented with recurrent nonmelanoma skin cancer of the scalp. He was successfully treated at our center with PRT to deliver TSI. A comparative VMAT treatment plan was generated and dose to critical OARs was compared.

Results: We present the first clinical case report of PRT for TSI and dosimetric comparison to a VMAT plan. The PRT and VMAT plans provided equivalent target volume coverage; however, the PRT plan significantly reduced dose to the brain, hippocampi, and optical apparatus.

Conclusion: TSI planned with PRT is relatively straightforward from a planning perspective and does not require a bolus. It also has the potential to decrease radiation therapy–related toxicity. However, PRT is relatively expensive and not universally available. The uncertainty surrounding the end-range of the proton beam is a consideration. Although there are potential disadvantages to using PRT for TSI, its use should be considered by treating radiation oncologists and referring physicians.

Keywords: proton; radiation therapy; total scalp irradiation

Introduction

Total scalp irradiation (TSI) is used to treat several different scalp and facial malignancies including angiosarcomas, nonmelanoma skin cancers, and cutaneous lymphomas, among others [1–5]. Owing to the irregularity of the scalp contour and the presence of underlying critical organs at risk (OARs), radiation planning is complex and technically difficult. To address this, several different radiation therapy techniques have been developed and used.
Akazawa [6] first described the use of a combined photon-electron technique (3DRT) using 2 nonoverlapping lateral electron fields and 2 lateral photon fields. This technique was later modified by Tung et al [7], who showed superior dosimetry by overlapping the electron and photon fields. More modern and commonly used techniques include intensity-modulated radiation therapy (IMRT) and volumetric arc therapy (VMAT). These techniques eliminate dose inhomogeneity associated with electron-photon field matching and allow for improved treatment of concave and irregular treatment surfaces. Previous dosimetric comparisons have shown that IMRT/VMAT techniques offer superior conformity and decreased dose to underlying OARs [8, 9].

Helical tomotherapy (HT) has also been shown to be a reasonable radiation therapy technique for TSI, owing to its ability to deliver tangential beams to any point on the scalp with no need for field matching [10–13]. Song et al [9] performed a dosimetric comparison of HT to 3DRT and VMAT and found that HT provided the best conformity of all 3 techniques and resulted in the lowest mean brain dose. The use of mold-based, high-dose-rate brachytherapy (HDR BT) has been reported in case reports and small case series [14–17]. Wojcicka et al [8] performed a dosimetric comparison between HDR BT, 3DRT, and IMRT. They found that HDR BT plans were the most conformal; however, doses to critical OARs were higher.

Despite the many different radiation therapy techniques and modalities listed above, the use of proton radiation therapy (PRT) to treat TSI volumes has never been documented in the literature. Proton beams deliver dose according to the “Bragg peak,” meaning dose is delivered to the intended target and then falls off rapidly, leading to little or no exit dose. Owing to these favorable physical characteristics, there is a significant potential to reduce dose to critical, underlying OARs as well as to decrease integral dose.

Here, we report the clinical case and relevant treatment planning considerations of a TSI patient who received pencil beam scanning proton radiation therapy. We also created an equivalent target coverage VMAT plan for dosimetric comparison.

Materials and Methods

Clinical Case Description

A 71-year-old man with a history of liver cirrhosis secondary to nonalcoholic steatohepatitis was referred for consideration of TSI. He underwent a liver transplant in April 2016 and had been receiving immunosuppressive therapy with tacrolimus since.

Approximately 8 months after his transplant, he was found to have skin lesions of the scalp, nose, and left cheek and was treated with surgical resection, which revealed a diagnosis of squamous cell carcinoma with several positive surgical margins. Adjuvant electron radiation therapy was delivered to the central and posterior scalp by using a 6-MeV beam and a dose of 66 Gy in 33 fractions to the 85% isodose line.

Two months later, he developed new scalp lesions, both within and outside of the prior radiation therapy field, which were treated with surgical resection and anterolateral thigh free flap reconstruction. Five months later he was found to have a left temple recurrence treated with Mohs surgery and surgical reconstruction.

Four months after this, he developed worsening erythema along the posterior scalp/free flap suture line. Magnetic resonance imaging (MRI) scan of the brain revealed a nodular soft tissue mass measuring $9.5 \times 11 \times 2.3$ cm that invaded the free flap, occipital bone, superior sagittal sulcus, and dura (Figure 1). Positron emission tomography (PET) scan showed no evidence of distant metastases. A multidisciplinary tumor board reviewed the case and determined the patient was not a candidate for further surgical resection or immunotherapy in light of the extent of disease and his immunosuppression status.

The patient underwent PRT. At 1-month follow-up post treatment, his primary tumor had a complete clinical response on physical examination. Unfortunately, a PET scan revealed suspicious left lung metastases. The patient underwent immunotherapy with gefitinib shortly thereafter.

At the most recent follow-up, 3 months post completion of radiation therapy, the patient continues to have a good local response. MRI shows only postsurgical and radiation therapy changes, with no signs of tumor recurrence.

Results

Proton Radiation Therapy Dose and Volumes

Computed tomography (CT) simulation for radiation therapy was performed. The patient was immobilized by using a 5-point head and neck mask. Intravenous contrast was not administered given his nephrotoxic immunosuppression medications.
Two distinct target volumes were contoured. The initial clinical target volume (CTV1) included the total scalp and was initially prescribed to 50.4 Gy in 42 twice-daily fractions delivered with a minimum of 6 hours between fractions. The boost target volume (CTV2) included the gross disease plus a 2-cm margin to cover microscopic disease. The CTV2 expansion volume was edited to exclude natural boundaries such as adjacent skull, healthy brain tissue, and surrounding air. This volume was dose escalated sequentially to an additional 14.4 Gy, also in twice-daily fractions delivered with a minimum of 6 hours between fractions. All treatment doses were adjusted to account for differences in relative biological effectiveness between PRT and photon radiation therapy and were delivered in photon dose Gray equivalents.

Early in the treatment course the patient experienced increased edema of the scalp, which required refitting of the immobilization mask and treatment re-planning (although beam orientation did not change). The patient started the new radiation therapy plan after completing 14.4 Gy. The patient stopped treatment after 61.2 Gy owing to a rapid tumor response.

**Proton Radiation Therapy Treatment Planning**

The radiation therapy plan was created in the RayStation treatment planning system (Manufacturer, City, State or Country). CTV1 was covered by using 4 noncoplanar treatment fields, including 2 lateral beams oriented at 90° and 270° in the axial plane and angled downwards 15° in the coronal plane. The third beam was angled at 200° in the axial plane and 90° in the sagittal plane, and a fourth beam was angled at 300° in the axial plane and 90° in the sagittal plane (Figure 2).

CTV2 was covered by 3 treatment fields: 2 coplanar beams oriented at 130° and 230° in the axial plane and a third noncoplanar beam angled at 200° in the axial plane and 90° in the sagittal plane.

The proton therapy target coverage goal was that 98% of the total CTV should receive 100% or more of the dose, which was achieved successfully.

**VMAT Treatment Planning**

An equivalent target coverage VMAT plan was also created in the RayStation treatment planning system that used a 1-cm-thickness bolus over the entire scalp and gross disease in order to cover 95% of the total planning target volume (PTV) with 100% of the dose. This plan used 2 full arcs to cover both PTV volumes.

Note should be made that target coverage goals varied slightly between the PRT and VMAT plans. This was due to the local institutional practice to prescribe dose to a robustly optimized CTV when treating with PRT and to prescribe to a PTV when treating with VMAT.
Target and OAR Dosimetric Comparison

PRT and VMAT TSI plans provided equivalent target coverage. Doses to almost all OARs were much lower with the PRT plan, which is shown in the Table. Visual representations of the dosimetric comparison between the PRT and VMAT plans are shown in Figures 3 to 5.
Discussion

TSI with PRT provided excellent target coverage while sparing significant radiation dose to OARs when compared with VMAT, despite the extensive amount of dural involvement in this case. Dosimetric comparisons of TSI planned with 3DRT, IMRT/VMAT, HDR BT, and HT have been reported in the literature [8, 9]; however, to the best of our knowledge this is the first report and dosimetric comparison of TSI with PRT.

TSI delivered with PRT offers additional advantages. Sufficient dose to the skin is easily delivered, eliminating the need for a bolus, which can be difficult to construct and secure on the complex scalp surface. Delivery of TSI with PRT is much simpler than with HDR BT, which requires specialized technical expertise and is not widely available.

There is some question in the scientific literature as to whether decreasing dose to OARs actually leads to improved clinical outcomes in the acute and long-term setting [18, 19]. However, based on normal tissue complication probability models, it is likely that reductions in dose will lead to significant decreases in treatment-related toxicity [20]. In the current study, mean hippocampal dose was reduced from 14.31 Gy to 0.36 Gy (essentially 0). In a study by Gondi et al [21], logistic regression modelling showed that an increase in mean dose from 0.0 to greater than 0.0 Gy led to 14.8 times increased odds of neurocognitive impairment. Increased doses to other critical neurological structures like the brainstem and temporal lobes have also been shown to have higher rates of radionecrosis [22, 23].

PRT is less accessible than IMRT/VMAT and is often more costly [24]. Another important consideration includes the end-range uncertainty of the proton beam. This uncertainty can arise from inaccuracy of CT Hounsfield unit conversion to proton-stopping power, treatment setup uncertainty, and intertreatment changes in patient anatomy [25–27].

**Table.** A comparison of dose received by OARs in PRT vs VMAT.

| Target          | Protons | IMRT (VMAT w/1-cm Bolus) |
|-----------------|---------|---------------------------|
| CTV1            | 99.66% receives 100% | 99.62% receives 100%     |
| OAR             | Protons, cGy | IMRT (VMAT), cGy           |
| Brain (mean)    | 1590    | 2888                      |
| Brain (max)     | 6936    | 6976                      |
| Brain-CTV (mean)| 1062    | 2493                      |
| Brain-CTV (max) | 6936    | 6909                      |
| Brainstem (max) | 40      | 1805                      |
| Hippocampus (max)| 66       | 1734                      |
| Hippocampus (mean)| 36     | 1431                      |
| Cochlea_LT (mean)| 398  | 1438                      |
| Cochlea_LT (max) | 1093    | 1982                      |
| Cochlea_RT (mean)| 181  | 1651                      |
| Cochlea_RT (max) | 966    | 2037                      |
| Lacrimal_LT (mean)| 1864 | 3253                      |
| Lacrimal_LT (max) | 2857   | 4742                      |
| Lacrimal_RT (mean)| 1803  | 3288                      |
| Lacrimal_RT (max) | 2798   | 4366                      |
| Optic chiasm (max)| 21    | 1158                      |
| Optic nerve_LT (max)| 1870 | 4245                      |
| Optic nerve_RT (max)| 1698 | 2653                      |
| Retina_LT (max) | 2638    | 4450                      |
| Retina_RT (max) | 2255    | 3196                      |
| Spinal cord (max)| 103   | 2057                      |
| Temporal lobe_LT (mean)| 898  | 2316                      |
| Temporal lobe_LT (max) | 5355  | 5340                      |
| Temporal lobe_RT (mean)| 1161  | 3222                      |
| Temporal lobe_RT (max) | 5338  | 5819                      |

**Abbreviations:** OAR, organ at risk; PRT, proton radiation therapy; VMAT, volumetric arc therapy; IMRT, intensity-modulated radiation therapy; CTV, clinical target volume; LT, XXX; RT, XXX.
Conclusion

TSI delivered with PRT provides a significant dosimetric advantage when compared to VMAT. Its use should be considered by treating and referring radiation oncologists and other health care providers.

ADDITIONAL INFORMATION AND DECLARATIONS

Conflicts of Interest: Mark Vikas Mishra, MD, reports personal fees from Varian, outside the scope of the submitted work. The authors have no other relevant conflicts of interest to disclose.
Ethical Approval: All patient data have been collected under internal review board (IRB)–approved protocol.

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