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Case Report

Endoscopic Resection Followed by Proton Therapy With Pencil Beam Scanning for Skull Base Tumors

Jonathan E. Leeman, MD; Nancy Y. Lee, MD; Ying Zhou, MS; Brian Neal, PhD; Kevin Sine, BS; Viviane Tabar, MD; Marc A. Cohen, MD, MPH

For patients who require postoperative radiotherapy after endoscopic resection of skull base tumors, proton therapy with pencil beam scanning (PBS) may allow sparing of normal tissue compared to intensity-modulated photon radiation (IMRT). We compared PBS and IMRT radiation plans in the preoperative and postoperative settings for two patients with advanced skull base tumors following endoscopic resection. The benefits of PBS over IMRT appear greater in the postoperative setting following endoscopic resection with improved sparing of critical organs at risk. The multidisciplinary approach of endoscopic resection followed by PBS represents a treatment paradigm with potential for improvements in toxicity reduction.

Key Words: Skull base, endoscopic surgery, proton therapy, head and neck cancer.

INTRODUCTION

In the appropriately selected patient, endoscopic resection of anterior skull base tumors offers the ability to perform resection of locally advanced disease in a less invasive manner than traditional open approaches. For patients who require postoperative radiation therapy after endoscopic resection, proton therapy may provide substantial sparing of surrounding normal tissue and superior dosimetry to photon techniques, although the combined approach of endoscopic surgery followed by proton therapy with pencil beam scanning (PBS) has not been formally assessed.

We performed radiation dosimetry comparisons between intensity-modulated photon radiation therapy (IMRT) plans and PBS proton plans in the the preoperative and postoperative setting following endoscopic resection using two illustrative cases.

CASE REPORT

CASE 1

An 80-year-old male presented with locally advanced intestinal-type adenocarcinoma of the ethmoid sinus with extensive involvement of the anterior skull base and paranasal sinuses. After multidisciplinary assessment, the patient underwent endoscopic surgical resection. The patient was then treated with adjuvant proton radiotherapy with PBS to a dose of 6,600 centigrays (cGy) to the tumor bed. Comparison IMRT and PBS plans were constructed with preoperative (Fig. 1) and postoperative (Fig. 2) imaging and target volumes. For preoperative plans, a dose of 7,000 cGy was prescribed to the gross disease and 6,000 cGy to the surrounding areas at risk.

Dose-volume characteristics for the IMRT and PBS plans are shown in Table I. In the preoperative setting, significant reductions in dose were achieved to the brain (mean dose 14.5 Gy IMRT, 8.0 CGE PBS Cobalt Gray Equivalent (CGE), brainstem (maximum dose 60.0 Gy IMRT, 35.8 CGE PBS), temporal lobes (mean doses IMRT 28.6 Gy and 25.9 Gy; PBS 10.7 and 8.5 Gy), lacrimal glands (mean doses IMRT 41.4 Gy and 21.9 Gy; PBS 7.2 CGE and 4.7 CGE), and cochleae (mean doses IMRT 31.7 Gy and 29.3 Gy; PBS 2.7 CGE and 2.7 CGE). In the postoperative setting, these dose reductions were maintained, and significant dose reductions were also achieved for the optic structures (chiasm, right nerve, left nerve dose to 0.03 cc: IMRT 49.1 Gy, 51.3 Gy, 43.3 Gy; PBS 37.4 CGE, 38.0 CGE, 43.1 CGE), amounting to ~20% reduction in dose to the optic tracts overall. In the preoperative setting, these dose reductions were maintained, and significant dose reductions were also achieved for the optic structures (chiasm, right nerve, left nerve dose to 0.03 cc: IMRT 49.1 Gy, 51.3 Gy, 43.3 Gy; PBS 37.4 CGE, 38.0 CGE, 43.1 CGE), amounting to ~20% reduction in dose to the optic tracts overall. In the preoperative and postoperative settings, target coverage was comparable with IMRT or PBS, as assessed by V95 (volume receiving 95% of the prescription dose). As of 14 months following completion of postoperative radiation, the patient remains without evidence of recurrent disease.

CASE 2

A 21-year-old male presented with a locally advanced chondrosarcoma of the sphenoid sinus with...
extensive involvement of the skull base. The patient underwent endoscopic surgical resection. The patient was then treated with adjuvant proton radiotherapy with PBS to a dose of 7,000 cGy to the high-risk tumor bed and 6,000 cGy to surrounding areas at risk. Comparison IMRT and PBS plans were constructed with preoperative (Fig. 3) and postoperative imaging (Fig. 4) and target volumes. For preoperative plans, a dose of 7,000 cGy was prescribed to the gross disease and 6,000 cGy to the surrounding areas at risk.

Dose-volume characteristics for the IMRT and PBS plans are shown in Table II. For the preoperative plans, lower dose was observed to the brain, brainstem, and temporal lobes with PBS (mean doses: IMRT 17.1 Gy, 36.1 Gy, 34 Gy, 37.6 Gy; PBS 12.1 CGE, 13.3 CGE, 17.5 CGE, 25.6 CGE). Lower doses were delivered to the cochlea with PBS (mean doses IMRT 34.9 Gy, 42.7 Gy; PBS 14.5 CGE, 16.1 CGE) as well as the lacrimal glands (IMRT 38.9 Gy and 38.3 Gy; PBS 8.9 CGE and 9.3 CGE). In the postoperative plans, lower mean doses to the brain, brainstem, and cochlea were maintained. In this case, comparable dose was delivered to the optic chiasm and right optic nerve, but dose reduction to the left optic nerve was achieved (D0.03cc IMRT 73.1 Gy; PBS 65.5 Gy) as the left optic nerve was not encompassed by tumor. As of 27 months following completion of postoperative radiation, the patient remains without evidence of recurrent disease.

RESULTS

In both cases, doses to brain, brainstem, temporal lobes, optic structures, and chiasm were significantly reduced following endoscopic resection compared to in the preoperative setting.

Each proton case was planned using five gantry fields, with unique orientations chosen to maximize PTV coverage and organ-at-risk sparing. Spot weights were optimized using multi-field optimization intensity-modulated proton therapy. Beams treating to superficial

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**Fig. 1.** Comparison of IMRT and proton preoperative plans for case 1. IMRT = intensity-modulated photon radiation therapy. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

**Fig. 2.** Comparison of IMRT and proton postoperative plans for case 1 following endoscopic resection. IMRT = intensity-modulated photon radiation therapy. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]
structures included a 7-cm range shifter placed 2 cm away from the patient surface. For the 100 mega-electron volts (MeV) to 180 MeV energy layers used, spot size in air at isocenter $\sigma$ ranged from 7 mm to 4 mm. Photon IMRT plans were generated using the same structure sets and prescription doses as the proton plans. IMRT plans utilized nine coplanar beams from 120 CCW to 240 degrees at 30-degree intervals, plus two anterior oblique beams; all used 6 megavoltage photons.

### DISCUSSION

Advanced tumors of the anterior skull base present a challenging clinical scenario given the proximity and involvement of multiple critical structures, including cranial nerves, optic tracts, brainstem, and temporal lobes. Endoscopic skull base surgery has emerged as an effective approach for resection of selected tumors while having the potential for low treatment-related morbidity. Compared to traditional craniofacial resection, endoscopic surgery...
surgery has been demonstrated to result in lower rates of postoperative complication, shorter mean duration of hospitalization,\(^1\) and less cosmetic deformity.\(^2\) Although there clearly is selection bias, endoscopic surgery may be associated with improved locoregional control and, more broadly, disease-specific and overall survival in the management of sinonasal malignancies.\(^3\)

Following the resection of skull base tumors, adjuvant radiotherapy is often indicated to minimize risk of locoregional recurrence. Proton radiotherapy carries significant advantages over conventional photon-based therapy due to the physical properties of the proton beam. Specifically, due to the deposition of dose at a narrow specified depth known as the Bragg peak, no radiation dose is delivered beyond the target, whereas photon IMRT is inherently limited by delivery of “exit dose” beyond the tumor volume. Head and neck cancers, and skull base tumors in particular, are often intimately associated with sensitive structures and organs such as the optic tracts, the brainstem, temporal lobes, and cranial

<table>
<thead>
<tr>
<th>Organs at Risk</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>Preoperative</th>
<th>Postoperative</th>
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<td></td>
<td>IMRT</td>
<td>Proton</td>
<td>IMRT</td>
<td>Proton</td>
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<tr>
<td>Brain mean dose (Gy)</td>
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<td>11.1</td>
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<td>Brainstem max dose/D0.03 cc (Gy)</td>
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<td>68.5/65.4</td>
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<td>Temporal lobe R max/D0.03 cc (Gy)</td>
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<td>73.8/73.1</td>
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<td>25.2/20.5/16.1</td>
<td>23.8/22.3/22.6</td>
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<td>23.9</td>
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**Target Coverage**

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<tr>
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<th>Proton</th>
<th>IMRT</th>
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<tr>
<td>PTV60 V95 (%)</td>
<td>96.20%</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>PTV70 V95 (%)</td>
<td>86.4%</td>
<td>83.9%</td>
<td>94.6%</td>
<td>94.5%</td>
</tr>
</tbody>
</table>

Gy, gray; IMRT = intensity-modulated photon radiation.; L = left; max = maximum; R = right.
nerves. As a result, the benefits of proton therapy are magnified in the context of skull base tumors due to the ability to spare adjacent critical structures. A systematic review and meta-analysis has demonstrated improved overall survival and disease-free survival with the use of particle therapy for sinonasal tumors compared to photon radiation. Spot-scanning proton therapy has demonstrated, particularly impressive rates of local control for typically radioresistant histologies such as chordoma and chondrosarcoma.

The two cases presented in this study demonstrate the situational advantages of the combined multidisciplinary approach of endoscopic surgery followed by proton radiotherapy. In the first case, a patient with locally advanced intestinal-type adenocarcinoma of the ethmoid sinus with extensive involvement of the anterior skull base underwent resection with an endoscopic approach, followed by adjuvant proton therapy. The lesion is abutting the brainstem and optic chiasm such that a nonoperative radiation-based approach with proton therapy (Fig. 1) results in only moderate sparing of the optics, brainstem, and temporal lobes with proton therapy compared to IMRT. Following endoscopic resection, however, the radiation dose can be reduced (70 Gy–60 Gy). Furthermore, lower maximum doses to the brainstem, optic nerves, and optic chiasm are achieved with protons postoperatively compared to than in the preoperative setting (Table I) (Fig. 2). In this case, because the tumor is only marginally associated with the chiasm and optic nerves, proton therapy allows for significant sparing in the postoperative setting. PBS also delivers markedly lower doses to the temporal lobes, which would be expected to result in lower risk of necrosis. These benefits are achieved while maintaining excellent coverage of the target volume.

The second case describes a patient with a locally advanced chondrosarcoma of the sphenoid sinus with extensive involvement of the skull base who underwent endoscopic resection followed by adjuvant proton therapy. In this case, the optic chiasm is encompassed within the target volume; thus, sparing cannot be technically achieved with protons either in the preoperative or postoperative settings. However, the conformality of PBS allows for carving of dose around the optics in a manner similar to what can be achieved with IMRT (Fig. 4). Meanwhile, as is also true in the first case, significantly less dose in the low to intermediate range is deposited to surrounding normal tissue, mostly brain. This is particularly important in a young patient, such as the one described here, to minimize the risk of secondary malignancy by reducing the volume of irradiated healthy tissue.

**CONCLUSION**

A multidisciplinary approach involving endoscopic resection followed by postoperative proton beam therapy with PBS for anterior skull base tumors represents a treatment paradigm with potential for improvements in neurological sparing and toxicity reduction. Proton therapy with PBS offers particular benefit in terms of dose reduction to organs at risk outside of the planning target volume. Formal comparative studies and clinical trials evaluating this combined approach are needed.

**BIBLIOGRAPHY**