Section: Radiation Oncology

Original Research Article

DOSIMETRIC ANALYSIS OF OPTIC TRACT DOSE IN PATIENTS IRRADIATED FOR PITUITARY ADENOMA AND CRANIOPHARYNGIOMA AND ITS EFFECT ON VISION.

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Abstract

Background: Radiation-induced optic neuropathy is a recognized late complication of radiotherapy for brain and head and neck tumors, yet optimal dosimetric guidelines remain elusive. This study aims to evaluate optic tract dosimetry in patients irradiated for pituitary adenoma and craniopharyngioma and its impact on vision.

Materials and Methods: Twenty-five patients treated between 2020 and 2022 were included. Optic tract dosimetry was assessed using CT simulation images and MRI contouring. Ophthalmological evaluations were conducted pre- and post-radiotherapy. Statistical analysis included Fisher exact test.

Results: Optic tract dosimetry analysis revealed that 20% of the patients exceeded the V50-50% threshold, indicating a significant correlation between optic tract dose and V50-50% (P = 0.0272). Among these patients, 12% exhibited a decline in visual acuity and field of vision. Importantly, none of the patients exceeded the established dose constraints for optic nerve and optic chiasm (Dmax <54 Gy).

Conclusion: Optic tract dosimetry correlated significantly with V50-50%, emphasizing the importance of dose management. Further prospective studies are warranted to optimize vision preservation and local control.

INTRODUCTION

Pituitary adenomas and craniopharyngiomas are among the most common intracranial tumors, often causing significant morbidity due to their proximity to vital structures such as the optic nerve and optic chiasm.[1-3] These tumors frequently manifest with visual impairment and visual field defects, which can be exacerbated by surgical intervention and subsequent radiotherapy. The delicate balance between achieving tumor control and preserving visual function poses a considerable challenge in the management of these patients.[4]

The optic nerve and optic chiasm, integral components of the visual pathway, are particularly susceptible to injury during treatment interventions.[5] Surgical resection, although essential for tumor removal, may inadvertently compromise visual function due to the close proximity of these structures to the tumor mass.[6] Furthermore, adjuvant radiotherapy is often employed to minimize the risk of tumor recurrence; however, the delivery of therapeutic doses to the tumor bed must be carefully balanced with the need to spare surrounding critical structures, including the optic pathway.[7]

In contemporary radiotherapy practice, detailed attention is paid to optimizing treatment plans to minimize the risk of radiation-induced complications while maximizing tumor control.[8] Central to this endeavor is the establishment of dose constraints for critical organs at risk (OARs), such as the optic nerve and optic chiasm.[9] However, while consensus guidelines exist for these structures, there remains a notable gap in our understanding regarding the optimal radiation dose limits for the optic tract in patients with pituitary adenomas and craniopharyngiomas.[10]

The optic tract, comprised of axonal fibers carrying visual information from the retina to the brain, plays a pivotal role in visual processing.[11,12] Despite its significance, the optic tract has received

comparatively less attention in radiotherapy planning, with dose constraints primarily focused on the optic nerve and chiasm. This discrepancy emphasizes the need for comprehensive evaluation of optic tract dosimetry in patients undergoing radiotherapy for pituitary adenomas and craniopharyngiomas.[10,11]

The rationale for investigating optic tract dose in this patient population is twofold. Firstly, optimizing radiation treatment plans to limit unnecessary radiation exposure to the optic tract may mitigate the risk of treatment-related visual impairment, thereby preserving patients' quality of life. Secondly, elucidating the dose-response relationship between optic tract irradiation and visual outcomes can inform the development of evidence-based dose constraints tailored to the unique anatomical and physiological characteristics of these tumors.

Therefore, the primary objective of this study is to perform a dosimetric analysis of optic tract dose in patients irradiated for pituitary adenomas and craniopharyngiomas and to evaluate its impact on visual function. By systematically quantifying optic tract dosimetry and correlating these findings with clinical outcomes, we aim to elucidate the relationship between radiation dose to the optic tract and the incidence and severity of treatment-related visual complications.

Through this research, we seek to address the existing knowledge gap regarding optic tract dosimetry in the context of pituitary adenoma and craniopharyngioma radiotherapy, with the ultimate goal of optimizing treatment planning strategies to safeguard visual function while ensuring effective tumor control. By generating robust evidence on the dosimetric parameters associated with optimal visual outcomes, our findings have the potential to inform clinical practice guidelines and enhance the care provided to patients with these challenging intracranial tumors.

MATERIALS AND METHODS

Study Setting: This study employed a retrospective observational design conducted at the Department of Radiation Oncology, Madras Medical College, Chennai. The study period spanned from the years 2020 to 2022, encompassing patients treated for Craniopharyngioma and pituitary adenoma during this timeframe.

Study Participants: The study included patients who underwent treatment for Craniopharyngioma and pituitary adenoma at our institution between 2020 and 2022. Inclusion criteria encompassed patients with histologically confirmed diagnoses of Craniopharyngioma or pituitary adenoma who underwent both surgical resection and adjuvant radiotherapy. Exclusion criteria comprised patients with incomplete medical records, inadequate follow-up data, or pre-existing visual impairment unrelated to tumor pathology.

Sample Size: A total of 25 patients meeting the inclusion criteria were recruited for this study. The sample size was determined based on the availability of eligible patients within the specified study period. All eligible patients treated for Craniopharyngioma and pituitary adenoma during the study period included in the analysis.

Study Methodology: Preoperative, postoperative, pre-radiotherapy (RT), and post-radiotherapy (RT) vision assessments, including visual acuity and visual field testing, were obtained for each patient. CT simulation images were utilized for treatment planning, with delineation of the optic tract and relevant anatomical structures performed according to the European Particle Therapy Network (EPTN) guidelines (2018). Gross tumor volume (GTV) was contoured using T1-weighted MRI, and a planning target volume (PTV) was generated with a 3mm margin around the GTV.

Treatment planning parameters, including total optic tract volume, optic tract mean dose (Dmean), optic tract maximum dose (Dmax), D1%Gy, V40, V50, and V55 of the optic tract, were evaluated for each patient. All patients underwent radiotherapy utilizing intensity-modulated radiation therapy (IMRT) and RapidArc techniques in conventional fractionation.

Ophthalmological evaluation was conducted to assess the presence of radiation-induced visual impairment in all patients, with findings documented for analysis.

Contouring Optic Tract: Each optic tract was contoured individually, with co-registration performed with T1-weighted MRI for accurate delineation. The optic tract extends from the postero-lateral angle of the optic chiasm anteriorly to the lateral geniculate body posteriorly. It appears linear and hyperintense, running lateral to the hypothalamus and medial to the anterior perforated substance. The visibility of the optic tract is limited beyond the first 10–15 mm from the junction with the optic chiasm, and contouring extends posteriorly until the tract is no longer clearly visible. [Figure 1]

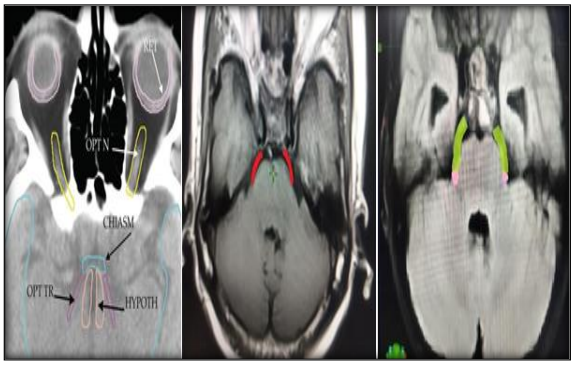

Figure 1: Contouring Optic Tract

Statistical Analysis: Associations between optic tract dose and its impact on vision were evaluated

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using relevant clinical and dosimetric data, including age, comorbidities, total optic tract volume, optic tract Dmean, optic tract Dmax, V40, V50, and V55. Statistical analysis was performed using Fisher's exact test to assess for significant correlations between dose parameters and visual outcomes.

RESULTS

A comprehensive review of the literature revealed a total of 15 studies published between 1983 and 2009, providing detailed descriptions of clinical outcomes and optic toxicity following 2D or 3D radiotherapy (RT) for malignancies of the paranasal sinuses. Additionally, two studies published between 2008 and 2009 reported clinical outcomes and optic toxicity profiles following RT delivered with a combination of 2D/3D RT and intensity-modulated radiation therapy (IMRT). Furthermore, five studies published between 2006 and 2012 reported clinical outcomes and optic toxicity following exclusively IMRT.

In our study, favorable local control of disease was achieved in the majority of patients, manifested by relief of compressive symptoms and improved visual outcomes. Analysis of dose-volume parameters revealed the following observations:

Consistent with findings from previous studies, there appears to be a correlation between the incidence of vision impairment and the radiation dose received by the optic tract. Notably, our study suggests a lower incidence of vision impairment when the optic pathway receives less than 54 Gy. [Figure 2]

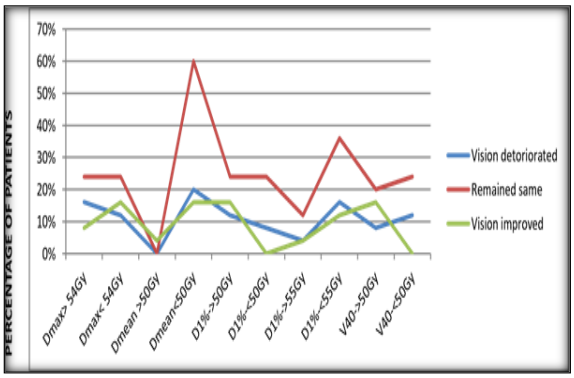

Figure 2: Vision among the study participants

Furthermore, our analysis reveals significant correlations with volume parameters, as summarized in Table 1 below:

These findings highlight the importance of considering both dose and volume parameters when evaluating the risk of radiation-induced optic toxicity and its impact on visual outcomes in patients undergoing radiotherapy for pituitary adenomas and craniopharyngiomas.

Table 1: Correlation between volume parameters

Parameter	Odds Ratio	95% CI	Z Statistic	P Value
Dmax	2.667	0.2774-25.63	0.849	0.3956
Dmean	0.778	0.0283-21.3636	0.149	0.8818
D1% 50 Gy	1.8333	0.2495-13.4702	0.596	0.5514
D1% 55 Gy	1.4167	0.11149-17.0412	0.272	0.7858
V40-50%	0.8148	0.1109-5.9868	0.201	0.8405
V45-50%	1.5556	0.2045-11.8298	0.427	0.6695
V50-50%	13.5	1.3402-135.9887	2.208	0.0272
V55-45%	13.6	0.4750-393.2035	1.526	0.1271

DISCUSSION

Radiation-induced optic neuropathy represents a frequently encountered late complication of radiotherapy in the treatment of brain, head, and neck tumors. While the underlying mechanisms of this condition remain incompletely understood, several prevailing theories highlight the ischemic component as a pivotal factor. It is postulated that radiation-induced optic neuropathy may result from the release of free radicals triggered by radiotherapy, leading to cellular damage. The exact site of primary injury within the optic pathway remains elusive, with potential involvement of vascular endothelial and neuroglial progenitor cells. Another proposed mechanism implicates somatic mutations induced by radiotherapy in glial cells, giving rise to metabolically inefficient cells and subsequent demyelination and neuronal degeneration of endothelial cells.

Lessel et al,[3] proposed the concept of "3-H tissue" as a contributing factor to radiation-induced optic neuropathy, comprising hypovascularity, hypocellularity, and hypoxia. This study suggests that these factors collectively contribute to neuronal degeneration and visual loss. Additionally, Seregard et al,[8] discuss the relationship between damage to the optic pathway and factors such as total radiation dose, volume of the optic pathway irradiated, and fractionation schedule.

It is well-established that the optic nerve and optic chiasm exhibit limited tolerance to radiation doses exceeding 54 Gy. Standard fractionation of 2 Gy per fraction is generally well-tolerated; however, doses higher than this threshold are associated with an increased incidence of optic pathway-related toxicity.

Throughout the literature, radiation-induced optic neuropathy has been extensively investigated across various dose fractionations and radiotherapy techniques. For instance, Bhandare et al,[12]

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conducted a study comparing altered fractionation with standard conventional fractionation, concluding that hyperfractionated radiotherapy with multiple daily doses demonstrated enhanced safety for the critical optic apparatus. Similarly, Girkin et al,[11] compared the development of radiation-induced optic neuropathy between stereotactic radiotherapy and conventional fractionation in suprachiasmatic tumors. Their findings indicated an elevated occurrence of radiation-induced optic neuropathy with single doses ranging from 7 to 14 Gy.

Studies by Speckter et al,[5] and Danesh-Meyer reported the timing of optic pathway toxicity post-radiotherapy. Speckter et al. noted occurrences between 10 to 20 months, with an average of 18 months following treatment. Similarly, Danesh-Meyer observed visual loss within a timeframe ranging from 3 months to 9 years post-radiotherapy, with the majority of patients experiencing symptoms within 3 years of treatment.

In the majority of trials, the observed field defects associated with radiation-induced optic neuropathy include central scotoma, bitemporal hemianopia, or a junctional syndrome characterized by ipsilateral diffuse loss and contralateral temporal hemianopia. These clinical manifestations highlight the significance of understanding the patterns of visual impairment following radiotherapy and the importance of early detection and intervention to optimize patient outcomes.[10,13]

Diagnosis of radiation-induced optic pathway toxicity is primarily one of exclusion, necessitating consideration when visual defects manifest following radiotherapy treatment. Danesh-Meyer,[4] proposed the presence of visual field defects indicative of chiasmatic and optic pathway dysfunction as diagnostic criteria, particularly in the absence of other etiologies. Before attributing symptoms to radiation-induced toxicity, it is imperative to rule out tumor recurrence. Additionally, other potential differentials include arachnoid adhesions surrounding the optic tract or chiasm, as well as giant arteritis.

Imaging plays a crucial role in the diagnosis of radiation-induced optic pathway toxicity. Electrophysiological testing, as suggested by Danesh-Meyer,[4] has demonstrated utility in detecting early signs of radiation damage. While conventional MRI studies often appear normal, T1-weighted images with gadolinium contrast may reveal enhancement of the optic nerve and optic chiasm. However, data regarding the optic tract remain limited. Zhao et al., in a retrospective analysis, reported contrast enhancement on MRI of the optic pathway, along with observations of tortuosity, border irregularity, and atrophy of the optic nerve. These imaging findings contribute to the diagnostic evaluation of radiation-induced optic pathway toxicity, aiding in early detection and management strategies.

Treatment strategies for radiation-induced optic pathway toxicity remain limited due to the incomplete understanding of its pathophysiology. The available literature suggests several therapeutic options, including corticosteroids, hyperbaric oxygen therapy, anticoagulants, and more recently, bevacizumab—a monoclonal antibody targeting vascular endothelial growth factor. However, it is important to note that these treatments have been explored in only a small number of subjects, and to date, there are no double-blind randomized studies validating their efficacy specifically for radiation-induced optic pathway toxicity.[14]

Among these treatment modalities, dexamethasone has been commonly used for radiation-induced neuropathy at dosages ranging from 4-10 mg orally or intravenously per day, with a tapering regimen of 2 to 4 mg every 5 to 7 days.[15] Dexamethasone is believed to mitigate radiation toxicity by reducing edema and potentially reversing damage induced by free radicals during radiotherapy. Nevertheless, no study has definitively demonstrated the efficacy of dexamethasone for radiation-induced optic pathway toxicity.[16]

Furthermore, ACE inhibitors such as Ramipril have shown promise in preventing radiation-induced injury by lowering pro-inflammatory cytokine levels. However, the specific role of ACE inhibitors in mitigating optic pathway toxicity requires further investigation.

In our study, we explored the correlation between clinical and dosimetric parameters with optic tract toxicity. We found that 20% of patients exceeded the V50-50% dose threshold for the optic tract, with 12% experiencing a reduction in visual acuity and field of vision. Conversely, 8% of patients showed improvement in vision, possibly attributable to effective local control of the disease. Importantly, analysis of optic nerve and optic chiasm dosimetry revealed adherence to established dose constraints, with none of the patients exceeding a maximum dose (Dmax) of 54 Gy. Our findings indicate that the observed optic nerve and optic chiasm toxicity was insignificant, as confirmed by the non-significant p-value resulting from the already met dose constraints. Thus, the potential confounding variables of optic nerve and optic chiasm toxicity were effectively excluded from our analysis.

CONCLUSION

This study has unequivocally established a consistent and statistically significant relationship between optic tract dosimetry and the V50Gy 50% cutoff. These results highlight the critical importance of meticulously managing radiation doses to the optic tract to mitigate the potential for adverse effects. Moving forward, it is imperative to conduct further prospective studies with long-term follow-up to comprehensively assess the optimal strategies for preserving vision while enhancing local disease control. By elucidating the most effective approaches to radiation dose management,

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we can strive to improve patient outcomes and minimize the risk of radiation-induced optic pathway toxicity.

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