Objective: To evaluate orbital and ophthalmologic function following standardized eye-sparing protocol for treating superior nasal vault malignant neoplasms.

Design: A retrospective review of patients with sinonasal malignant neoplasms who underwent preoperative radiation therapy with or without chemotherapy and craniofacial resection (CFR) with eye preservation. Pretreatment and posttreatment ophthalmologic evaluations were performed.

Results: A total of 59 patients underwent eye-sparing therapy between 1983 and 2005; 36 had invasion of the lamina with or without periorbital resection (61%). The most common abnormality was esthesioneuroblastoma (37 cases; 63%), most of which were Kadish stage C (n = 26). The most common preoperative ophthalmologic findings were motility disturbances (18 cases; 31%), afferent pupillary dysfunction and change in acuity (17 cases; 29%), and proptosis (17 cases; 29%). A total of 36 patients were available for long-term follow-up (mean follow-up, 61 months); 35 of these retained functional vision (97%); and 1 patient had a nonfunctional eye.

Conclusions: Standardized treatment for superior nasal vault malignant neoplasms using an eye-sparing CFR remains a sound approach both oncologically and ophthalmologically. Most patients with advanced disease present with ophthalmologic findings, and most posttreatment eye findings are notable only on detailed examination and either resolve spontaneously in the acute-care setting or do not require surgical repair.

Arch Facial Plast Surg. 2007;9(6):406-411

ADVANCED SUPERIOR NASAL vault malignant neoplasms with orbital involvement have traditionally been treated with radical surgery including craniofacial resection and orbital exenteration.1 With increasing experience, the addition of adjuvant chemoradiation therapy, and the use of more detailed radiographic techniques, eye-sparing procedures performed without compromising local control and survival have been performed.2,3

In 1988, Perry et al4 reported the experience at the University of Virginia in treating superior nasal vault malignant neoplasms with an eye-sparing protocol that included adjuvant chemoradiation therapy, craniofacial resection, and selective periorbital resection as an alternative to traditional orbital exenteration. The findings supported the preservation of the eye in most patients without extensive intraorbital invasion.

In 1996, McCary et al5 added to the initial report with the evaluation of an additional 34 patients treated with the same eyesparing protocol. In patients with sinonasal malignant neoplasms that eroded the lamina and involved the periorbita, the use of preoperative radiotherapy and resection of involved periorbita with frozen section control could be used to spare the eye without compromising oncologic safety.

While prior reports have supported eyesparing techniques in treating advanced lesions from an oncologic standpoint,5-8 few studies have provided a detailed ophthalmologic evaluation of the function of the preserved eye. The present study examines the long-term functional outcomes of eye-sparing therapy.

METHODS

We analyzed the medical records of all patients with superior nasal vault malignant neoplasms treated at the University of Virginia with adjuvant chemoradiation and craniofacial resection between 1979 and 2005. A total of 59 patients were evaluated preoperatively by a single neuroophthalmologist (S.A.N.) between 1983 and 2005. This cohort was obtained from a tumor database maintained by the Department of Otolaryngology–Head and Neck Surgery, which consisted of demographic, clinical, histopathologic, staging, and ophthalmologic examination data (Microsoft Excel 2000; Microsoft Corp, Red-
monday, Washington). Institutional review board approval was obtained.

All patients included in the analysis were treated based on the recommendation of a multidisciplinary team consisting of members from the departments of Otolaryngology–Head and Neck Surgery, Radiation Oncology, Medical Oncology, Neuro-radiology, Neurosurgery, and Neuro-ophthalmology. All patients underwent preoperative computed tomographic and/or magnetic resonance imaging scans to delineate tumor extent. Each patient was staged according to his or her pathologic findings and the extent of disease with respect to the orbit and anterior cranial fossa. The degree of orbital invasion and criteria for orbital exenteration were defined by McCary et al.8 Following neuro-ophthalmologic examination, tumor evaluation, and staging, the patients underwent preoperative radiation therapy with or without chemotherapy followed by craniofacial resection.9 Patients who were not available for follow-up were assessed by outside ophthalmologists using prescribed criteria, and their examination findings were sent to the University of Virginia for evaluation by the attending neuro-ophthalmologist.

Thirty-six patients were evaluated both preoperatively and post-operatively for interval comparison of the ophthalmologic examination findings and to determine treatment results. Eleven patients were lost to follow-up, and 12 patients died. A detailed, formal neuro-ophthalmologic examination was performed and included assessment of (1) previous ophthalmologic disease (to differentiate preexisting findings from findings related to the tumor or to treatment of the tumor), (2) afferent function, (3) efferent function, and (4) adnexal structures and function. Examinations were both qualitative and quantitative.

Afferent examination included evaluation of visual acuity, afferent pupillary defect, decreased central vision, visual field, and the optic disc. Efferent function was determined by evaluating ductions, versions, and alignment. Adnexal structure and function were assessed by evaluating the function of cranial nerves V and VII, globe position, medial canthal tendon position, eyelid position and function (ptosis, lagophthalmos, eyelid retraction, and ectropion/entropion), chemosis, injection, and lacrimal outflow dysfunction. These examination findings were further categorized as functionally important or not. Corrective treatments, if necessary, were performed. Using the scale put forth by Imola and Schramm,7 we classified patients into categories based on functional ophthalmologic status: functional vision without impairment (no persistent sequelae); functional vision with impairment (1 or more postoperative sequelae treatable with ocular therapeutics); and nonfunctional vision (chronic ocular sequelae, blindness, exenteration, or impairments unresolved with ocular intervention).

### RESULTS

The initial cohort (n=82) comprised 51 male (62%) and 31 female (38%) patients ranging in age from 10 to 81 years (mean age, 48 years). Of the 82 patients diagnosed as having a superior nasal vault malignancy and treated at the University of Virginia, 59 patients were evaluated preoperatively, and 36 patients were evaluated both preoperatively and postoperatively by a single attending neuro-ophthalmologist (S.A.N.) between 1983 and 2005.

Most patients in this series had advanced-stage esthesioneuroblastoma, based on the expertise and referral patterns for the Department of Otolaryngology–Head and Neck Surgery at the University of Virginia (Table 1). Of the patients with esthesioneuroblastoma, 26 had Kadish stage C (70%), 10 had Kadish stage B (27%), and 1 had Kadish stage A (3%). Of the patients with squamous cell carcinoma, 3 had T4N0M0 lesions, and the remaining case was staged as a T3N0M0 tumor. Thirty-six patients were found to have pretreatment invasion of the lamina (61%).

Twenty-six patients had preexisting ophthalmologic disease unrelated to the tumor (44%), including strabismus, cataracts, retinal tears, dry eye, posterior vitreous detachment, entropion, and congenital nerve palsies. Fourteen patients had normal findings at preoperative examination (24%). The most common symptom identified as the result of tumor growth was motility disturbance (18 patients; 31%), followed by afferent system dysfunction (17 patients; 29%), proptosis in 17 patients (29%), eyelid abnormalities in 11 patients (19%), and dystopia in 10 patients (17%). Three patients presented with lacrimal outflow obstruction (5%).

Thirty-six patients were available for long-term follow-up (mean follow-up, 61 months; range, 1-214 months with a detailed ophthalmologic examination). Patient characteristics are outlined in Table 2. The remaining patients died (n=12) or were lost to follow-up (n=11). Ten patients were unable to return for follow-up owing to excessive distance from the medical center and preferred to continue routine examinations with their local ophthalmologists.

All patients with malignant disease received adjunctive treatment. Only 2 patients, who had benign disease...
(benign myxoid and ameloblastoma), did not undergo adjuvant treatment. Twenty-six patients received preoperative chemoradiation therapy (72%); 6 patients received preoperative radiation therapy alone (17%); 1 patient received preoperative irradiation and postoperative chemotherapy; and 1 patient received postoperative brachytherapy.

Tumor invasion data are documented in Table 3. Twenty-six patients had bony invasion determined on preoperative imaging and at the time of surgery (72%), and 17 of these patients had bony erosion but no evidence of pathologic involvement of the periorbita as determined by frozen section analysis (65%). A total of 9 patients had bony and peri orbital invasion grossly at surgery and by frozen section analysis (35%), and 11 patients underwent peri orbital resection (31%); 4 patients required reconstruction with temporalis or rectus abdominis fascia (11%).

Most patients had 1 or more ocular sequelae on detailed ophthalmologic examination. The most common posttreatment findings are documented in Table 4. These findings are taken collectively and are not distinguished from preoperative examination findings.

The findings from preoperative and postoperative ophthalmologic examinations were compared, and the numbers of new posttreatment examination findings are identified in Table 5. Fifteen patients presented with previous ophthalmologic findings unrelated to the superior nasal vault tumor (42%). Motility disturbances were the most common preoperative findings, seen in 9 patients preoperatively (22%), and postoperatively, 11 patients were identified with motility disturbances. Eight patients were seen preoperatively with optic nerve dysfunction (22%), while 8 patients developed new optic nerve findings, primarily afferent pupillary defects and visual field changes. No patients lost central visual function secondary to their treatment. Eight patients presented with proptosis (22%), and 5 developed proptosis postoperatively. Five patients presented with abnormal eyelid position (14%), and following treatment, 6 patients developed abnormal eyelid position. Two patients presented with lacrimal outflow obstruction (5%), and 3 patients developed obstruction following treatment. In total, 16 patients developed new orbital abnormalities (44%), and 18 patients developed new ophthalmologic findings (50%).

Eleven patients were identified with persistent disturbances that were bothersome to the patient (31%), and surgical correction was recommended. These therapeutic findings are documented in Table 4. These findings are taken collectively and are not distinguished from preoperative examination findings.

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tic interventions are listed in Table 6. The most common procedure was revision dacryocystorhinostomy, seen in 3 patients; cataract surgery, 2 patients; and hard palate grafting to the eyelid, upper eyelid recession, and ptosis repair in 1 patient each.

Five patients developed locally recurrent disease (14%), and only 2 of these required salvage orbital exenteration unrelated to the initial sparing of the eye (6%). Of these 2 patients, one developed severe fronto base osteoradionecrosis and later required orbital sacrifice; the other patient had extensive disease at the time of surgery, including skull base invasion and residual disease at the optic chiasm. Of the 5 patients with recurrent intraorbital disease, 2 patients had extensive disease intraoperatively. The remaining 3 patients had squamous cell carcinoma (2 patients) or advanced-stage esthesioneuroblastoma. Two patients lost light perception secondary to intraorbital disease. The first patient had extensive disease identified at the time of surgery, and the second patient became symptomatic in long-term follow-up (13 years following initial treatment). Both patients had aggressive, multiply recurrent tumors.

Most important, most patients were unaffected by their ophthalmic sequelae. Using the functional scale put forth by Imola and Schramm,7 we classified patients into categories based on their functional ophthalmologic status: 3 patients retained functional vision without impairment (no persistent sequelae) (8%); 32 retained functional vision with impairment (1 or more postoperative sequelae treatable with ocular therapeutics) (89%); and 1 patient was deemed nonfunctional (chronic ocular sequelae, blindness, exenteration, or unresolved with ocular therapeutics) (3%).

## COMMENT

Over the past 35 years, the indications for orbital preservation and exenteration have evolved. Traditional surgical treatment of paranasal sinus tumors with orbital involvement has been aggressive, oftentimes requiring radical maxillectomy with orbital exenteration. The approach reflected the dismal prognosis for patients with advanced disease and the propensity for local recurrence.10 In 1966, Conley11 acknowledged that the orbit is often at risk owing to its central location and proximity to the paranasal sinuses, but that every rational effort to spare the eye should be taken so long as prognosis and organ function were not jeopardized.

Early efforts to preserve the eye have provided the framework for this current protocol. Several investigators have advocated multimodal therapy in an aggressive approach to orbital preservation. The prevailing conclusion was that preserving the orbit and its contents did not adversely affect patient survival in most cases. However, the degree of orbital invasion, the anatomic barriers to tumor spread, and the indications for orbital sacrifice continued to be controversial.1-3,8,12,13 Key arguments in the comparison between orbital sacrificing vs orbital preserving protocols included the inherent selection bias because more advanced lesions may have been more likely treated with orbital exenteration. Andersen et al4 reported that because of this bias, it was inappropriate to retrospectively compare local recurrence rates between these 2 groups.

Prior reports demonstrated that orbital preservation can be performed even with limited soft tissue invasion. The University of Virginia series continued to define criteria for sparing the eye.1-3 The report evaluated 74 patients who underwent organ-sparing treatment: 41 had invasion of the bony orbit (55%); 14 had invasion of the periorbita (19%); and only 4 patients had recurrent disease (11%). The orbital walls were considered intact if the tumor was abutting the medial wall but without frank invasion or erosion. Invasion was defined in terms of preirradiation and postirradiation computed tomographic or magnetic resonance imaging scans and ultimately by direct evaluation at the time of surgery. As a result of this experience, surgeons have become more aggressive in their willingness to resect larger areas of the periorbita with frozen section control to preserve the orbit and its contents.

With established oncologic safety, and recent efforts toward organ preservation, controversy remains as to whether a functional organ is actually preserved. Andersen et al4 described 58 consecutive patients who underwent anterior fossa craniofacial resection with orbital preservation and reported loss of orbital function to be multifactorial, including loss of globe support due to resection of the orbital floor; exposure keratopathy secondary to eyelid abnormalities or inadequate tear film; and secondary effects from radiation therapy, which included optic neuropathy and poor tear production from damage to lacrimal glands. They noted an overall complication rate of 43.1%, with 8 of the 25 patients developing a nonfunctional eye (32%). The most common ocular complication in their series was lacrimal outflow obstruction, which occurred in 21 of 58 patients (36%). Twelve patients underwent surgery to correct ophthalmologic disturbances, including dacryocystorhinostomy, ectropion repair, drainage of orbital mucocele, and corneal transplantation in 1 patient who experienced a ruptured globe after desiccation.

Stern et al15 recommended strong consideration for orbital exenteration in patients requiring orbital floor resection and/or postoperative irradiation fields that included the eye based on poor ocular function alone. Adequate ocular function was defined as visual acuity of 20/40 or better in the involved eye, use of binocular vision, no incapacitation by pain or other symptoms, and overall adequate function. Their group reported that only 3 of 18 patients with orbital floor resection retained adequate eye function (17%).

### Table 6. Postoperative Ophthalmologic Therapeutics in 36 Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ophthalmologic therapeutics</td>
<td>11 (31)</td>
</tr>
<tr>
<td>Dacryocystorhinostomy</td>
<td>3 (8)</td>
</tr>
<tr>
<td>Cataract surgery</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Hard palate graft (retraction)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Upper eyelid recession</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Paramedian forehead flap</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Ptosis repair</td>
<td>1 (3)</td>
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</table>
Recently, investigators have become more cognizant about eye function following eye-sparing treatment. Imola and Schramm evaluated a group of patients who underwent orbital preservation surgery and graded their function as having no significant dysfunction, functional with impairment, and nonfunctional. Based on their data, 91% of their patients had a useful seeing eye, but 41% of these patients with preserved orbits had 1 or more ocular sequelae. Patients who had significant posttreatment ocular findings were evaluated later by an ophthalmologist.

DeMonte et al compiled more specific ophthalmologic data regarding the extent of resection. They concluded that in most patients, elaborate orbital reconstruction is not necessary after partial excision of the orbital bones. Isolated medial and lateral orbital wall defects or combined superior and lateral orbital wall defects, especially in cases in which the periorbita is intact, do not require primary reconstruction. However, in this series, follow-up appeared to be limited, and multiple types of resection were included in their study.

The present article is part of an ongoing series detailing the treatment of sinonasal malignant neoplasms using a defined eye-sparing protocol. As prior reports from this institution lend support to eye-sparing techniques in treating advanced lesions from an oncologic standpoint, few studies exist to provide detailed, long-term, ophthalmologic evidence describing the function of the preserved eye following cranial facial surgery for advanced superior nasal vault malignant neoplasms.

In the present study, 59 patients were evaluated preoperatively by a single attending neuro-ophthalmologist, and 26 were identified with preexisting ophthalmologic findings unrelated to tumor or treatment (44%). Only 14 patients had normal preoperative examination findings (24%). This is an important consideration in evaluating the ophthalmologic outcome following craniofacial surgery because one must differentiate preexisting issues from postoperative sequelae to accurately assess posttreatment outcome. The most common findings were related to mass effect on the orbit from tumor growth, which manifested as motility disturbances, followed by afferent dysfunction and proptosis, and only a few patients had evidence of preoperative lacrimal outflow obstruction.

Thirty-six patients were available for long-term follow-up. This finding reflects the wide geographic distribution of patients and their choice to continue treatment and observation under the care of their local ophthalmologist or not at all. When the subset of patients who returned for long-term follow-up were evaluated, the most common posttreatment findings were motility disturbances, visual field defects, diplopia, and cataracts. When these findings were analyzed further and compared with the preoperative ophthalmologic findings secondary to the disease process, there was an interval increase in motility disturbances, abnormal eyelid position, and lacrimal outflow obstruction. However, there was a decrease in proptosis following treatment, which reflects an inherent functional benefit of surgical treatment (Figure 1).

A substantial number of patients had advanced disease with invasion of the bony orbit and/or periorbita, identified preoperatively with imaging and intraoperatively with pathologic confirmation. Despite this finding and the fact that many patients on detailed ophthalmologic examination had evidence of posttreatment sequelae, the overwhelming majority of patients retained a functional eye. When the ophthalmologic data were reviewed and categorized according to the system put forth by Imola and Schramm, we found that 8% of patients retained normal function with no adverse sequelae (n=3). Eighty-nine percent of patients had reportable findings on examination (n=32), but they all retained adequate function for daily living. This finding reflects the fact that many issues resolve with time or are cosmetic only. Taken collectively, 97% of patients in this series retained functional vision (n=35). Only 1 patient was determined to have a nonfunctioning eye with no light perception secondary to intraorbital recurrence, and this patient had advanced disease, lamina invasion, and a multiply recurrent tumor.

It is well known that patients with advanced head and neck cancers benefit from a multidisciplinary treatment approach. All but 2 patients in this series (who had benign disease) were treated with adjunctive therapy (94%) consisting of radiation therapy with or without chemotherapy. Analysis of the orbital complications following treatment with multimodality therapy would be incomplete if the entire protocol was not considered in the review.

In addition to the anterior craniofacial resection with manipulation of the visual apparatus and bony orbit, there are also significant orbital and ophthalmic complications following radiation therapy. The locally advanced nature of most paranasal sinus malignant neoplasms as well as proximity of the brain, visual apparatus, and lacrimal glands makes treating them challenging for both surgeon and the radiation oncologist.

Interestingly, the few studies available regarding orbital complications following craniofacial surgery cite radiation therapy as a significant contributor to postoperative complications. When we reevaluated the postoperative data, taking the effect of radiation therapy into consideration, we found that almost half of the ophthalmologic complications could be attributed to radiation therapy, as depicted in Figure 2. Furthermore, posttreatment sequelae can be categorized into complications affecting the orbit vs those affecting the ophthalmic system. In 36 patients available for long-term follow-up, 16 new orbital (44%) and 18 new ophthalmic findings (50%) were identified on detailed examination. The importance
is that surgery tends to produce new orbital findings that are cosmetic, correctable with further surgery, or are of no functional consequence to the patient and are readily identified on detailed examination. Conversely, radiation therapy tends to be more destructive to the visual system.

Just as surgical technique has been refined, there have been similar advances in the delivery of radiation therapy. Chen et al performed a long-term study of clinical outcomes of patients with carcinomas of the nasal cavity and paranasal sinuses who received combined-modality treatment including radiation therapy from 1960 to 2005. They found a significant and progressive improvement in grade 3 and 4 toxicity among patients treated over a 4-decade interval starting in the late 1960s. Additionally, when complications specific to the neuro-ophthalmologic pathway were compared using conventional radiotherapy, 3-dimensional conformal radiotherapy, and intensity-modulated radiotherapy, a significant reduction in incidence was found with the more innovative techniques.

At the University of Virginia, our eye-sparing protocol continues to evolve. The current state of the art in treating paranasal sinus and nasal cavity malignant neoplasms is helical tomotherapy. This technique reflects continued progress in the field in that, compared with intensity-modulated radiotherapy, helical tomotherapy provides equivalent or slightly better normal structure avoidance and more uniform planned treatment volumes. This translates clinically as a continued effort to not only preserve the eye but to also preserve function of the visual pathways.16

Owing to the limited cohort size, retrospective analyses based on multiple surgical approaches, heterogeneous tumor histologic characteristics, varied tumor location, and adjunctive protocols, meaningful data has taken time to accrue. The nature of this disease process and its treatment makes data extrapolation difficult and heavily dependent on institutional experience over extended periods. That being said, orbital exenteration as a component of surgical resection has not been performed in nearly 15 years at our institution.

This study represents a 22-year experience at a single institution using a defined eye-sparing protocol and a basis for comparison of ophthalmologic treatment sequelae for superior nasal vault malignant neoplasms. As sound oncologic evidence exists for orbital preservation, it can now be confirmed that using an eye-sparing protocol has few significant postoperative ophthalmologic impairments, and the vast majority of patients retain adequate function.

Accepted for Publication: August 30, 2007.
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Financial Disclosure: None reported.

Previous Presentation: This article was presented at the North American Skull Base Society Meeting; May 26, 2007; Chicago, Illinois.

REFERENCES