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# Surgical treatment and survival of patients with invasive orbital tumors

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***Background:*** *Intraorbital tumor invasion is not uncommon among craniofacial tumors, and is seen in 27% of cases. Craniofacial malignancies account for 3% of all head and neck tumors. Malignant tumors are more common than benign and comprise about 73% of all craniofacial tumors with intraorbital invasion. Their growth is aggressive and invasive, leading to early postoperative recurrence. The survival of patients with malignant craniofacial tumors depends largely on orbital invasion, and patients demonstrating orbital invasion had a 40% survival rate, while patients without had a survival rate of 72%. Patients with total resection of craniofacial tumors (including those with intraorbital extensions) show higher non-recurrence and survival rates than patients without total resection. Orbital exenteration does not provide patients with better survival rates and worsened the quality of life.*

***Purpose:*** *To assess the outcomes of surgical treatment for, and the survival of patients with, malignant craniofacial tumors growing into the orbit.*

***Material and Methods:*** *We reviewed the outcomes of surgical treatment for, and the survival of 94 patients with, malignant craniofacial tumors growing into the orbit.*

***Results:*** *Destruction of the bony orbital wall only (without periorbital adhesion), was seen in 27/94 cases (28.7%), whereas periorbital invasion, in 67/94 cases (71.3%). The tumor was excised completely with visually clear margins in all cases. Patient survival was affected by the degree of orbital invasion. The recurrence rate after surgery for malignant craniofacial tumors growing into the orbit was 44.7% (40/94 patients). Ten patients had a local intraorbital recurrence after surgery for malignant craniofacial tumors growing into the orbit.*

***Conclusion:*** *Periorbital invasion was seen in 71.3% of patients with malignant craniofacial tumors. There was no significant difference in the survival of patients with malignant craniofacial tumors of different histology. Orbital exenteration does not improve survival and recurrence in patients with malignant craniofacial tumors with orbital invasion. In patients with preoperative periorbital invasion and further intraorbital extension, the recurrence rate was more than three-fold higher than in those showing only destruction of the bony orbital wall preoperatively.*

**Keywords:**

malignant craniofacial tumors, orbital invasion, transbasal approach, subcranial approach, orbital exenteration

## Introduction

Intraorbital invasion is not uncommon among craniofacial tumors, and is seen in 27% of cases. Craniofacial malignancies account for 3% of all head and neck tumors. Malignant tumors are more common than benign and comprise about 73% of all craniofacial tumors with intraorbital invasion. Their growth is aggressive and invasive, leading to early postoperative recurrence. Orbital invasion is most common in malignant craniofacial tumors [1]. Invasion of the orbital cone is believed to be the most common orbital invasion, and it is this that has been associated with a high rate of tumor recurrence [2, 3]. The survival of patients with malignant craniofacial tumors depends largely on orbital invasion, and patients demonstrating orbital invasion had a 41% survival rate, while patients without had a survival rate of 75% [4]. Patients with total resection of craniofacial tumors (including those with intraorbital extensions) show higher non-recurrence and survival rates than patients without total resection [5, 6, 7, 8]. Orbital exenteration did not provide patients with better survival rates and worsened the quality of life [9, 10]. We present our experience with malignant craniofacial tumors and discuss the features of the course of craniofacial tumors growing into the orbit.

**The purpose** of the study was to assess the outcomes of the surgical treatment for, and the survival of patients with, malignant craniofacial tumors growing into the orbit.

## Material and Methods

We retrospectively reviewed the medical records of 253 patients with malignant craniofacial tumors who underwent surgical treatment at the Romodanov Neurosurgery

Institute, Kolomiichenko Institute of Otolaryngology, and Neurosurgery Department of Shupyk Medical Academy of Postgraduate Education (at the premises of Kyiv Regional Clinical Hospital) from 1999 through 2022. Intraorbital invasion was seen in 94 patients. Of these, 35 were women and 59 were men. Patient age ranged from 3 to 72 years, with a mean ± standard deviation of 38.0 ± 11.2 years.

Patients underwent neurological and ophthalmological status assessment, as per routine protocols. In addition, prior to and after surgery, patients underwent a clinical neuroimaging examination involving magnetic resonance imaging (MRI; a Philips Intera 1.5 T machine) (T1-weighted (T1), T1-weighted gadolinium-positive (T1Gd+), T2-weighted (T2), and fluid-attenuated inversion recovery (FLAIR) images) and computed tomography (CT; a Philips Brilliance CT 64-slice machine), particularly, intravenous contrast-enhanced MRI and intravenous contrast-enhanced CT of the brain.

Excised tumors were pathohistologically examined using light microscopy, immunohistochemistry, hematoxylin and eosin staining and iron staining. Images of hematoxylin and eosin staining and immunohistochemistry were acquired on an Axio Lab. A1 microscope using 10x, 20x, 40x and 100x Zeiss A-Plan objectives (Germany) or Axiophot OPTON microscope (Germany).

Our surgical strategy was to perform a simultaneous resection of intracranial and extracranial components of a malignant craniofacial tumor extending into the orbit using one surgical approach by a team of surgeons.

Of the 94 patients involved in the study, 64 received the transbasal Derome approach; 12, the subcranial approach through the frontal sinus (a modification of the transbasal Derome approach); 9, lateral craniofacial resection (5, orbitozygomatic approach; and 4, infratemporal approach); and 9, endoscopic nasal approach. Orbital exenteration was additionally performed in 19/94 cases (20.2%).

Statistica 6 (StatSoft, Tulsa, OK) software was used for statistical analysis. A survival analysis was carried out using the Kaplan-Meier method. Group differences in survival were assessed using the log-rank test.

This study involved human participants and was approved by the local Bioethics Committee. Informed consent was not obtained due to the retrospective study design. The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. No animals were involved in the study.

### Results

We identified seven histologic types of craniofacial tumors in study patients (Table 1). The most common histologic type was cancers (50 patients), followed by sarcoma (11 patients) and adenocarcinoma (11 patients). Eight patients had esthesioneuroblastoma, 6 patients, cartilaginous and osseous tumors, and 6 patients, neuroblastoma. Sympathetic ganglion and nerve-derived tumors were the least common histological type (2 patients).

Figure 2 shows the primary sites of growth malignant craniofacial tumors with intraorbital extension. The most common primary site was the ethmoid labyrinth (70 cases), followed by maxillary sinus (10 cases), nasal cavity (4 cases), floor of the middle cranial fossa (3 cases), frontal sinus (3 cases), pterygopalatine fossa (2 cases), sphenoid sinus (1 case), and sphenoid bone wings (1 case).

Invasive orbital tumors manifested local ocular symptoms and signs like exophthalmos (48 patients), eyelid edema (27 patients) and orbital pain (15 patients). Other ocular findings included limited motility (35

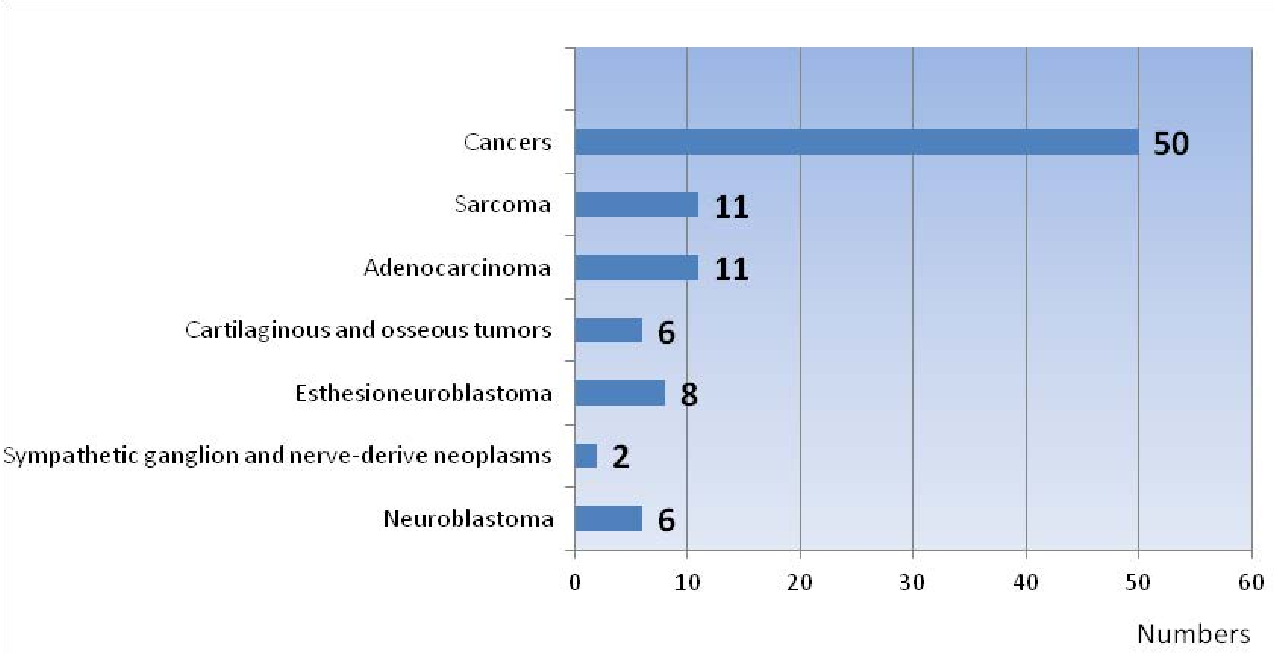


**Fig. 1**. Distribution of histological types of malignant craniofacial tumors

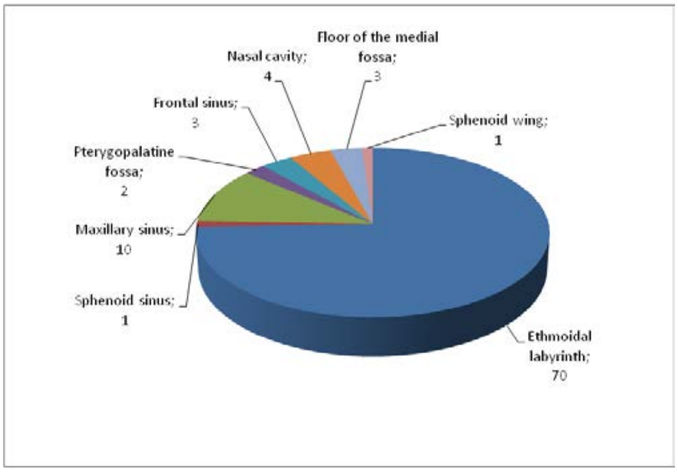


**Fig. 2.** Primary sites of malignant craniofacial tumors (numbers of cases)

patients), visual acuity loss (14 patients), and amaurosis (vision loss or weakness that occurs without an apparent lesion affecting the eye, 11 patients).

Of note that, postoperatively, such local ocular symptoms and signs as exophthalmos, eyelid edema, and orbital pain subsided completely. However, all patients who preoperatively had had visual acuity loss and amaurosis had these findings postoperatively. In addition, all patients who had had limited ocular motility preoperatively, were found to have a loss of ocular motility of different severity postoperatively. Moreover, one patient with no preoperative loss of ocular motility was found to have a loss of ocular motility postoperatively.

There were two general routes of intraorbital extension of craniofacial tumors. The first route, destruction of the bony orbital wall (without periorbital adhesion), was seen in 27/94 cases (28.7%), including 22 cases with destruction of the medial orbital wall, 3 cases with destruction of the lateral orbital wall, and 2 cases with destruction of the upper orbital wall. The second route, periorbital invasion (periorbital adhesion and ingrowth which may be followed by the invasion of the orbital muscles and fat in case of further intraorbital ingrowth), was seen in 67/94 cases (71.3%), including 13 cases with periorbital invasion (periorbital adhesion only); 52 cases with periorbital invasion and further growth, including total orbital lesions with the involvement of the orbital muscle cone and retrobulbar space; and 2 cases with periorbital invasion and further growth with the involvement of the orbital muscle cone only.

Complete resection with clear margins was achieved in all study cases through various types of craniofacial surgery (Table 1).

The transbasal Derome approach (including bifrontal craniotomy with resection of the upper orbital margin) was performed in 64 cases. This approach allowed for a simultaneous resection of intracranial and extracranial tumor components. If the destruction of the bony orbital wall was present (27 cases), in order to remove the orbiral tumor, the tumor was dissected from the periorbit, and a clearcut dissection plane was obtained, which was not considered as a periorbital ingrowth. If local periorbital growth only was present (13 cases), the periorbit was excised. If periorbital invasion and further ingrowth was present (52 cases), the periorbit with tumor-affected periorbital muscles and fat were excised with a clear margin of healthy tissue. In 19/94 cases, orbital exenteration was additionally performed which enabled complete tumor resection. We, however, found that orbital exenteration did not provide patients with better survival rates but worsened the quality of life (Fig. 5). We used orbital exenteration in our early cases of surgery for a craniofacial malignancy with intraorbital extension if there was evidence of periorbital ingrowth. At present, we remove such a tumor via the creation of a dissection plane between the tumor and healthy orbital tissue. Compared to surgery with auxiliary orbital exenteration, this improved patient's quality of life without worsening in survival ($p = 0.15$; Fig. 5).

**Table 1.** Type of surgery in orbital tumor invasion

| Type of surgery | Number of patients, n |
|---|---|
| Bifrontal craniotomy with supraorbital advancement (the transbasal Derome approach) | 64 |
| Subcranial approach through the frontal sinus | 12 |
| Endoscopic nasal approach | 9 |
| Lateral craniofacial resection (5, orbitozygomatic approach; and 6, infratemporal approach) | 9 |

The subcranial approach through the frontal sinus (a modification of the transbasal Derome approach) was used in 12 cases. In this approach, after the skin was incised along the supraorbital ridges, a periosteal flap from the frontal region was created for closure of the postoperative bone defect in the floor of the anterior cranial fossa. Thereafter, an oscillation saw was used to trephine the anterior wall of the frontal sinus, and the posterior wall of the frontal sinus is removed. The subcranial approach allowed us to achieve the same extent of surgical resection as in the transbasal Derome approach. This approach is, however, less traumatic and easier than the transbasal Derome approach. In the subcranial approach, an oscillation drill was used to cut the bone outside the frontal sinus if visualization was limited when the tumor had a lateral extension or the frontal sinus was small. The aforementioned approaches were used in case of primary tumor growth in the medial floor of the anterior cranial fossa (the ethmoid labyrinth, sphenoid sinus and frontal sinus) or in the presence of a significant intracranial component. The subcranial approach and transbasal Derome approach enabled removing malignant craniofacial tumors invading the orbit.

If primary tumor growth was observed in the lateral cranial base (the pterygopalatine fossa and floor of the middle cranial fossa), a radical tumor excision was facilitated by a lateral craniofacial resection. A lateral craniofacial resection was performed as a resection of the floor of the middle cranial fossa and pterional resection or orbitozygomatic resection. The lateral and superior orbital walls were additionally removed to enable complete visualization of the intraorbital extension. In 9 cases, a lateral craniofacial resection was used for simultaneous removal of the intracranial and extracranial components of a lateral cranial base tumor and affected superior and lateral orbital regions.

The superior orbital wall was removed if visualization of tumor extension to the posterior orbit was insufficient, which enabled the removal of the affected regions in the orbital muscle cone and retrobulbar space.

Endoscopic nasal approach was used in 9 cases in which the tumor had a significant extracranial component extending into the medial orbit.

After surgery, patients were followed up at discharge and each 2 to 6 months thereafter. Outcome measures were radicality of resection and postoperative complications.

Complications were seen in 14/94 patients (15%). It was treated conservatively with lumbar drainage, and fistulas closed within 2 weeks of starting lumbar drainage. Meningoencephalitis was seen in 10 patients and was successfully treated within 3 weeks of establishing a diagnosis of meningoencephalitis and correcting the antibiotic therapy.

**Survival**

Figure 3 shows cumulated survival of patients by intraorbital tumor growth. Patients with no intraorbital tumor growth (curve 1) had higher survival than those with periorbital tumor growth (curve 2) based on log-rank tests, and the difference tended to be significant (p = 0.09). It may be supposed that the diagnostic assessment of periorbital growth (but not that of the destruction of the medial orbital wall) is important for the development of surgical strategy. Therefore, prevention of periorbital tumor ingrowth (tumor detection at the stage of destruction of the medial orbital wall) is an important factor in the improvement in the survival of patients with this disorder.

Figure 4 shows cumulated survival of patients by histology. There was no significant difference in the survival of patients with malignant craniofacial tumors of different histology (p = 0.45). Malignant craniofacial tumors show aggressive invasive growth, which promotes early local recurrence. It is this that determines oncological survival of patients.

Figure 5 shows cumulated survival of patients by orbital exenteration. There was no significant difference in the survival between those who received versus those who did not receive orbital exenteration (p = 0.15), although patients with no intraorbital tumor growth had higher survival than those with periorbital tumor growth based on log-rank tests (p = 0.09).

In the current study, the recurrence rate after surgery for malignant craniofacial tumors growing into the orbit was 44.7% (40/94 patients). Ten patients had a local intraorbital recurrence after surgery for malignant craniofacial tumors growing into the orbit. Of these, nine had growth into the periorbit and further intraorbital extension, and one, destruction of the bony orbital wall. Therefore, growth into the periorbit can be considered a major cause of the recurrence, and a recurrence was seen in 9/67 patients (13.5%) who received surgery for malignant craniofacial tumors growing into the periorbit. Of the 27 patients who received surgery for malignant craniofacial tumors with destruction of the bony orbital wall, only one (3.7%) experienced a recurrence. Of the 19 patients who received orbital exenteration in addition to surgery for malignant craniofacial tumors, 7 (37%) experienced a recurrence. Patients who received surgery for malignant craniofacial tumors with intraorbital extension experienced a recurrence in the nasal cavity and paranasal sinuses (13

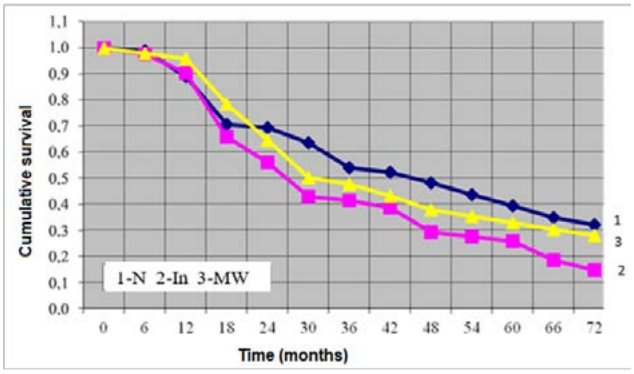


**Fig. 3.** Survival by intraorbital tumor growth among patients with malignant craniofacial tumors (1-N, no extension to the orbit; 2-In, periorbital growth and further intraorbital extension; 3-MW, destruction of the medial orbital wall)

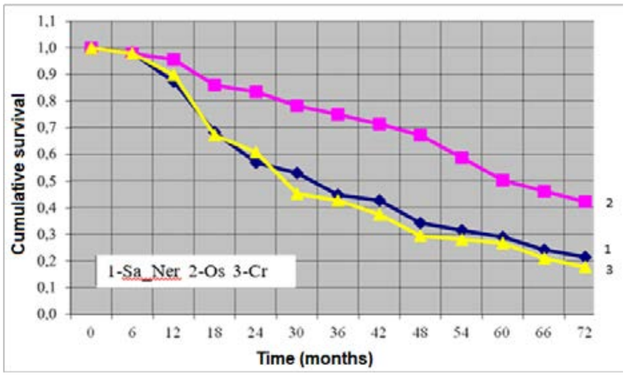


**Fig. 4.** Postoperative survival by histology among patients with malignant craniofacial tumors (1-Sa_Ner, sarcoma and sympathetic ganglion and nerve-derived tumors; 2-Os, osseous tumors; 3-Cr, cancers)

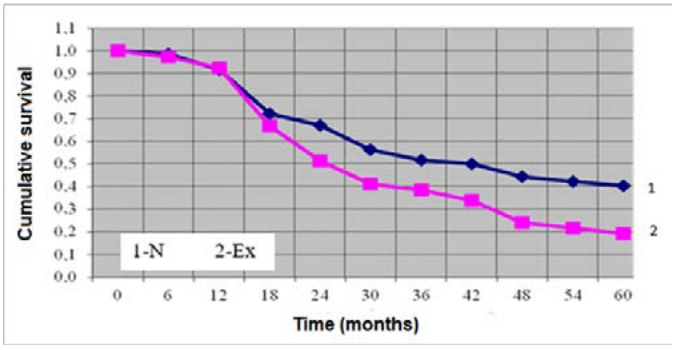


**Fig. 5.** Postoperative survival by the presence of orbital exenteration among patients with malignant craniofacial tumors (1-N, no orbital exenteration; 2-Ex, orbital exenteration)

cases), intracerebral recurrence (11 cases), and distant metastasis (2 cases).

## Discussion

Patients with total resection of craniofacial tumors (including those with intraorbital extensions) show higher non-recurrence and survival rates than patients without total resection [11, 12, 13, 14, 15, 16]. We found that the radicality of resection of invasive orbital tumors clearly depended on the degree of ingrowth into the orbit. We found orbital invasion in 70 of 94 patients with malignant craniofacial tumors originating in the ethmoid labyrinth. In the current study of malignant craniofacial tumors with intraorbital invasion, periorbital adhesion and/or ingrowth was seen in most cases (67/94 cases or 71.3%). These included 13 cases with periorbital adhesion only; 52 cases with periorbital invasion and further growth, including total orbital lesions with the involvement of the orbital muscle cone and retrobulbar space; and 2 cases with periorbital invasion and further growth with the involvement of the orbital muscle cone only. Destruction of the bony orbital wall was seen in 27/94 cases (28.7%), including 22 cases with destruction of the medial orbital wall, 3 cases with destruction of the lateral orbital wall, and 2 cases with destruction of the upper orbital wall. These findings are in agreement with those by others [17, 18]. In the current case series, the tumor was excised completely with visually clear margins in all cases. The transbasal Derome approach was most commonly used (64/94 cases) and allowed complete visualization of the upper and medial walls of the orbit. Raso and Gusmão [19] also reported that the transbasal Derome is still important in skull base tumors with apparent intracranial extension.

Previously, radical resection of the floor of the anterior fossa and medial fossa, radical maxillectomy, orbital exenteration and partial maxillectomy were the techniques mostly used in primary growth and apparent extracranial components of malignant lateral skull base tumors and their lateral extensions [20]. In the current study, we used lateral craniofacial resections, which allowed complete visualization of the tumors. The orbitozygomatic approach (5 cases) was used if the extracranial extension (particularly to the pterygopalatine and infratemporal fossae) was more apparent than the intracranial extension, whereas the infratemporal approach (4 cases) was used if there was a significant intracranial extension of the tumor [21].

Pure endoscopic endonasal approaches have been widely used in managing malignant craniofacial tumors, partially due to lower rate of surgical trauma compared to transbasal approaches. We believe that the difficulties in utilizing pure endoscopic endonasal approaches are associated with significant intracranial tumor extension (e.g., lateral tumor extension into the orbital roof) and vascular involvement in the tumor [22, 23, 24]. We used endoscopic endonasal approaches (9 cases) in cases with a significant extracranial tumor component, when the destruction of the external cranial base (including orbital wall destruction) was more pronounced than tumor growth in the dura mater.

We found that in patients with preoperative destruction of only the bony orbital wall (27 cases), survival was higher than in patients with preoperative periorbital growth and further intraorbital extension (67 cases) ($p = 0.09$) (Fig. 3). Others [25] reported that intraorbital invasion was significantly associated with local recurrence, and, consequently, is important for the subsequent course of the disease.

At the early phase of the study, we increased the radicality of the procedures via orbital exenteration (19 cases). We, however, found that orbital exenteration did not provide patients with better survival rates ($p = 0.15$) (Fig. 6) and substantially worsened postoperative quality of life. This is in agreement with findings of others [26, 27].

We also found that there was no significant difference in the survival of patients with malignant craniofacial tumors of different histology ($p = 0.45$) (Figure 4). Since in the current study, most patients (50/94 cases) were those with cancers, survival for the total study sample shifts towards cancers, and smaller numbers of patients with adenocarcinoma (11/94) and esthesioneuroblastoma (8/94) have no statistically significant effect on survival for the total study sample. The histology of the primary tumor has been reported to be a predictor of survival. Patients with esthesioneuroblastoma show the highest overall survival, followed by patients with adenocarcinoma and patients with malignant cancers of different grades [28]. For example, in the current study, a patient with esthesioneuroblastoma survived for 14 years after diagnosis, whereas patients with adenocarcinoma survived not more than 8 years, and patients with squamous cell carcinoma, not more than 6 years after diagnosis.

For invasive orbital tumors, recurrence is associated with residual tumor components in the orbital cone [29, 30, 31]. In the current study, a local intraorbital recurrence in the orbital cone was seen in 10 patients. Of these, 9 patients showed periorbital invasion and further intraorbital extension, and one patient, only destruction of the bony orbital wall. In addition, in patients with preoperative periorbital invasion and further intraorbital extension, the recurrence rate (9/67) was higher than in those showing only destruction of the bony orbital wall preoperatively (1/27).

### Conclusion

First, periorbital invasion was seen in 71.3% of patients with malignant craniofacial tumors.

Second, there was no significant difference in the survival of patients with malignant craniofacial tumors of different histology.

Third, orbital exenteration does not improve survival and recurrence in patients with malignant craniofacial tumors with orbital invasion.

Finally, in patients with preoperative periorbital invasion and further intraorbital extension, the recurrence rate was more than three-fold higher than in those showing only destruction of the bony orbital wall preoperatively.

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**Disclosures**

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***Study participants:*** *The study was conducted with human participants. This study was approved by the local bioethics committee. Due to the retrospective nature of the study, no informed consent forms were obtained. The study was conducted in accordance with the Declaration of Helsinki. No animals were included in this study.*