CRANIOFACIAL RESECTION FOR ANTERIOR SKULL BASE TUMORS

Narayan Sundaresan, MD, and Jatin P. Shah, MD

We present the results of treatment of 30 patients with anterior skull base tumors operated on over an 11-year period. At the time of surgery, intracranial invasion was present in 10 patients. Histology revealed epithelial tumors in 18 patients, sarcoma in 6, esthesioneuroblastoma in 4, and 2 miscellaneous histologies. The overall median survival was 5 years and varied according to histology and grade of tumor. Currently malignancies involving the skull base can be successfully resected using a craniofacial approach, with minimum operative mortality. Limited intracranial invasion need not necessarily represent a major contraindication of this procedure if morbidity can be kept to a minimum.
HEAD & NECK SURGERY 10:219–224, 1988

Over the past decade, the value of a simultaneous craniofacial surgical approach in the management of tumors involving the skull base has been adequately demonstrated in several series.[1–15] Major advantages of the combined surgical approach include wide exposure of the complex anatomic structures, complete visualization allowing "en bloc" excision of malignant tumors, as well as adequate reconstruction of the resulting skull base defect to prevent cerebrospinal fluid leakage and its associated complications. In additon, the use of computed tomographic (CT) scans as well as magnetic resonance imaging (MRI) have helped further to improve patient selection by noninvasive means.[16–20] As a result, current mortality rates for craniofacial operations are low (less than 5%) and surgical morbidity acceptable (approximately 10–15%).

Despite the innovations in surgical technique and widespread acceptance of the value of surgery in eradicating all gross disease in solid tumors, indications for craniofacial resection in the definitive treatment of ethmoid-antral malignancies have never been clearly defined.[21–27] The selection of initial treatment largely reflects the philosophy of the individual institution or surgeon. Traditionally accepted anatomic criteria for surgery include disease approaching the skull base but limited to the sinuses (with or without unilateral orbital extension), no evidence of intracranial extension or distance metastases, and lack of invasion of the pterygoid plates and middle fossa. In view of the current emphasis on the use of external radiotherapy (RT) in the management of ethmoid sinus malignancies in many centers, most patients referred for craniofacial surgery are those in whom previous treatment has failed. In such patients, surgery is often relegated to salvage those with persistent or recurrent disease. We believe that a reappraisal of the traditional indications for surgery are warranted, and represent an analysis of our experience with craniofacial resection for tumors involving the skull base of the anterior cranial fossa.

Presented at the New York Head and Neck Society Meeting, New York, January 14, 1987.
From St. Lukes/Roosevelt Hospital Center, New York, New York (Dr Sundaresan), and Memorial Sloan-Kettering Cancer Center, New York, New York (Dr. Shah).
Address reprint requests to Dr Sundaresan at 53 E 67th Street, New York, NY 10021
Accepted for publication May 5, 1987.

0148-6403/88/0402-0219 $04.00/6

MATERIALS AND METHODS

Over an 11-year period (1975–1985) inclusive), 30 patients with tumors involving the anterior skull base underwent combined craniofacial surgery by the authors. Only patients with midline skull base tumors (involving the cribriform plate) were included, and thus four patients with orbital tumors and secondary intracranial invasion were excluded. In addition, we excluded four patients who underwent initial intracranial exploration as part of a proposed craniofacial procedure, but in whom the findings of tumor extension beyond safe limits precluded resection. Selection criteria for considering patients for this procedure included the radiographic demonstration of tumor involvement of the cribriform plate, with or without unilateral orbital extension; tumor extension into the cavernous sinus or middle fossa were considered contraindications, but patients with intracranial invasion into the frontal lobes were considered for this procedure if there were no medical contraindications for surgery.

Of the 30 patients, there were 19 males and 11 females, ranging in age from 14 to 75 years (median 55 years). The various pathologic entities included epithelial tumors in 18 patients (squamous carcinoma—four; adenocarcinoma—eight; and undifferentiated carcinoma—six), sarcoma in six patients (rhabdomyosarcoma—three; Paget's sarcoma—one; chondrosarcoma—one; and postradiation sarcoma—one) esthesioneuroblastoma in four patients, neuroendocrine tumor in one, and giant ossifying fibroma in one. The tumors were limited to the ethmoid sinus complexes without invasion of the dura or orbit in 15 patients; in five patients, disease was present within the orbit, and in 10 patients, intracranial invasion through the dura was noted. Of these, two patients also had metastatic disease in the neck.

Due to the referral nature of our institution, the majority of patients (53%) had received prior treatment that had failed. Nine patients had undergone prior surgical resection and RT, four patients had progressive symptoms after RT and chemotherapy, and three patients had undergone surgical resection alone and presented with symptomatic clinical tumor recurrence. Review of the RT data showed that irradiation was accomplished in all patients either with a cobalt 60 unit or a linear accelerator, and the target volumes included all demonstrable tumors, nasal cavities, and radiologically opacified sinuses. Treatment techniques included anterior and lateral or oblique lateral fields with wedge filters, with the eye shielded. The target-absorbed dose was calculated to vary from 45–70 Gray delivered over a 4 to 6 week period.

The clinical presentation at initial evaluation was generally consistent with that reported for paranasal sinus malignancies.[29–32] The majority of patients had pain associated with nasal discharge or stuffiness, with the duration of symptoms varying from 2 to 6 months before diagnosis. Epistaxis was reported by five patients and ocular or visual symptoms with associated proptosis was seen in five. Signs of frontal lobe dysfunction (reduction in higher integrative functions with lethargy) was noted in three patients, with these symptoms corresponding to the degree of intracranial invasion and edema noted on CT scans.

In the earlier patients, radiologic evaluation consisted of a combination of pluridirectional tomography, radionuclide bone scans, and cerebral angiography to document extent of intracranial invasion. In patients seen more recently, these studies were completely replaced by regular axial and coronal CT scans with bone windows. Contrast enhancement was limited to those with suspected intracranial invasion. Except for sinus films and skull x-rays, no additional radiographic studies were performed. All patients underwent complete rhinoscopy and biopsy confirmation of malignancy before consideration of the craniofacial procedure.

After surgery, follow-up CT scans and clinical evaluations were performed on all patients at regular 3-month intervals. In those patients in whom prior RT had failed, chemotherapy was offered; eight patients elected this procedure. Follow-up survival analysis was performed using the Kaplan-Meier product limit method, and comparison between individual subgroups was performed using the log-rank test.

CRANIOFACIAL RESECTION

The technical details of our craniofacial approach have been previously published and are briefly summarized here.[8,33] All patients underwent preoperative nasal cultures and were placed on corticosteroid therapy and antibiotics 48 h before surgery. Our standard antibiotic protocol included the use of oxacillin (1 g intravenously every 6 h) and gentamycin (60 mg intravenously every 8 hours), which was continued for 72 hours after the operation. In patients requiring palatal resection, consultation with the max-

illo-facial prosthodontist for prefabrication of a palatal prosthesis was obtained.

After induction of general anesthesia, spinal drainage and mannitol were routinely used; this allowed the intracranial portion of the operation to be performed with minimal or no retraction of the frontal lobes. The first phase of the operation was a standard bifrontal craniotomy, at which time a vascularized pericranial flap for reconstruction of the skull base was obtained. Once the bone flap was removed, the decision to proceed by an intra- or extradural route depended on whether intracranial extension was present. All intracranial tumor was resected in those in whom the intracerebral tumor was deemed resectable. The posterior limit of the resection ended at the planum sphenoidale, which was drilled to expose the sphenoid sinus. Using a high speed drill, cuts were then made through the cribriform plate and roof of the orbit to free the tumor from above. This completed the cranial portion of the operation.

The second phase of the operation began with a Weber-Ferguson incision for maxillectomy. If there was tumor extension within the antrum, a total maxillectomy and ethmoidectomy were performed. If there was no tumor within the antrum, a medial maxillectomy with palatal fenestration that removed only the hard palate on that side was performed for easier access. Using combined dissection, the specimen was mobilized from below while being guided by the neurosurgeon from above. The resected en bloc specimen usually included the tumor, the entire cribriform plate, and the superior and middle turbinates on each side.

Reconstruction of the defect in the skull base was done as follows: the dural defects were primarily closed or repaired by a free graft of temporalis muscle and fascia. The pedicled flap of periosteum was laid over the bony defect in the floor and secured both to the basal dura and anchored to the bone. Against this periosteal falp, the split thickness skin graft was applied from below. The antral defect was also lined with the skin graft held in place with a snug packing of Xerofoam gauze, which was supported in place by the dental obturator. The craniotomy and facial incisions were then closed in routine fashion.

The average operating time for this procedure varied from 6 to 8 h, and the average blood loss ranged from 1500 to 2500 ml. In uncomplicated cases, patients were discharged from the hospital between the 10th and 14th days.

RESULTS

Of the 30 patients who underwent this procedure, there was one death within the 30-day period from presumed sepsis. This resulted in a mortality rate of 3%. The surgical morbidity is listed in Table 1. Two patients suffered increased neurologic deficits after the procedure. Of these, one patient developed a postoperative infection in the epidural spaces and became progressively more obtunded and comatose. However, 2 months after the operation, he recovered and is currently neurologically intact. The second patient developed increased deficit from cortical venous thrombosis after extensive resection of the dura and superior sagittal sinus; he also recovered near complete neurologic function. In additon to these complications, six other patients developed postoperative epidural infection resulting in wound sepsis; despite antibiotic therapy, the bifrontal bone flap had to be removed in all these patients. Only one patient developed a cerebrospinal fluid leak with resulting meningitis; this was successfully treated by intravenous antibiotic therapy and spinal drainage alone. Review of the positive bacterial cultures obtained from those patients with infectious complications included *Staphylococcus aureus* (two patients), *S. epidermidis* (one patient), *Escherichia coli* (two patients), and mixed flora (*Enterobacter cloacae* and *S. epidermidis,* one patient); one patient had no organisms despite appropriate cultures. In only one patient was the infecting organism *(S. aureus)* identified by the preoperative nasal culture.

Review of the resected specimen showed a change from the original diagnosis in seven patients: in three patients, the diagnosis of anaplastic carcinoma was revised to rhabdomyocarcoma; in two patients, the diagnosis of undifferentiated carcinoma was changed to esthesioneuroblastoma; in one patient, the diagnosis of neuroendocrine carcinoma was changed to chromophobe adenoma; while in one, the diagnosis of anaplastic

Table 1. Surgical complications.

Morbidity	No.	Outcome
Increased neurological deficit	2	Complete resolution (1) partial resolution (1)
Infections	7	Removal of bone flap required in 6
Meningitis (1)		
Epidural infection (6)		
Total	9 (30%)	

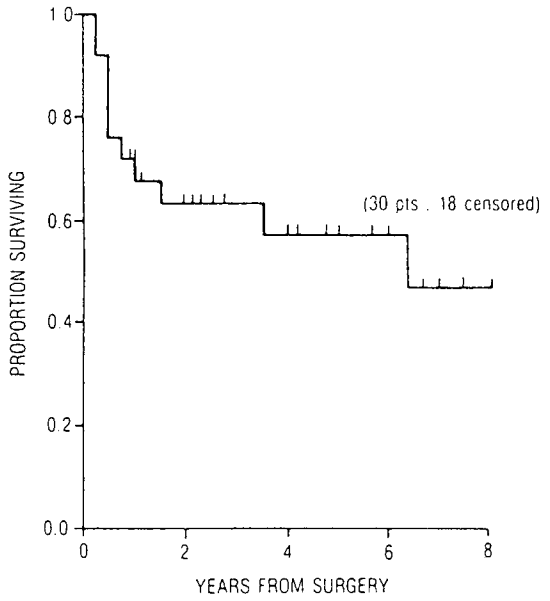

FIGURE 1. Overall survival indicates a median survival of 5 years. Eighteen patients are still alive.

tumor was changed to Paget's sarcoma (malignant fibrous histiocytoma).

Survival analyses are shown in Figures 1–3. The overall actuarial median survival was 60 months; 18 of the patients are still alive. Survival varied according to histology, as illustrated in Figures 2 and 3. The proportion of patients in whom local control was achieved is shown in Table 2; in the entire series, local control was obtained in 19 of 30 patients (63%).

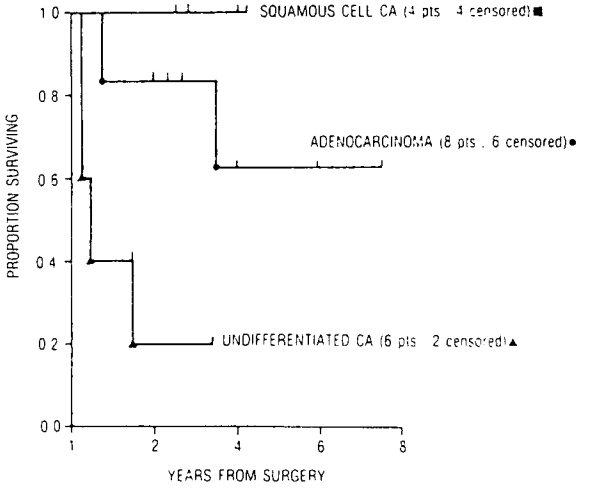

FIGURE 2. Survival by histology: patients with squamous carcinoma and adenocarcinoma had much better survival than those with anaplastic carcinoma, but numbers were too small for statistical significance.

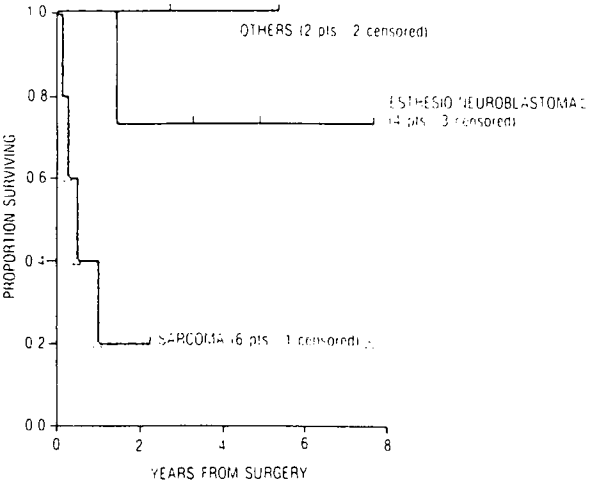

FIGURE 3. Survival by histology: patients with sarcoma had poorer survival than those with well-differentiated epithelial malignancies.

No complications were noted in the four patients in whom the procedure was aborted after the intracranial exploration; however, three of the four patients died within 6 months due to progressive local disease, while one demonstrated a complete response to chemotherapy and is currently a long-term disease-free survivor.

DISCUSSION

The results in our consecutive series of 30 patients confirm the findings reported in other major series, especially those by Ketchum et al,[2,5] that craniofacial resection can currently be accomplished with mortality rates of less than 5%. Our series further suggests that the major cause of morbidity is related to infection in the epidural and parameningeal spaces, which resulted in

Table 2. Local control by histology

Histology	No.	Local control (%)
Squamous carcinoma	4	4
Adenocarcinoma	8	6
Undifferentiated carcinoma	6	2
Sarcoma	6	2
Esthesioneuroblastoma	4	3
Others	2	2
Total	30	19 (63)

the loss of bone flaps in six patients, was the indirect cause of neurologic morbidity in one patient, and resulted in death from sepsis in another. Although the overall morbidity (30%) in this series is considerable, we believe it is acceptable because most patients had far advanced cancers with little alternatives for treatment. Since these complications occurred despite intensive perioperative therapy with antibiotics, we believe that morbidity can be considerably reduced by meticulous reconstruction of the skull base after surgery. Whether the use of vascularized flaps and composite reconstructions of the anterior fossa might reduce this complication is speculative at the present time.[34,35]

In this series, histology and grade of the tumor were the major determinants of survival rather than the presence or absence of intracranial invasion. As shown in Table 2, excellent local control was achieved in well-differentiated adenocarcinomas and squamous carcinomas, but could not be achieved in those with anaplastic epithelial tumors and sarcomas. In all patients, achieving local control directly affected survival, since distant metastases were the cause of death in only one patient. Although the poorer prognosis of patients with anaplastic carcinomas has been noted elsewhere,[36] the final histologic diagnosis was made only after complete resection of the tumor in patients with undifferentiated tumors on biopsy. Before accepting the diagnosis of "anaplastic carcinoma," it is important to rule out other undifferentiated neoplasms with a considerably better prognosis such as lymphoma or esthesioneuroblastoma.[37–39] This is shown in our own series, where the final histologic diagnosis was changed after resection in seven patients. It has been suggested that any undifferentiated neoplasm within the nasal cavity should be considered an esthesioneuroblastoma until electron microscopy and immunohistochemical studies demonstrate either an epithelial tumor or lymphoma.[38,40]

The value of chemotherapy could not be clearly ascertained in view of the different histologies and small number of patients in each subgroup. Only two patients with esthesioneuroblastoma received combination chemotherapy, with disease stabilization in one patient and progression in another. A surprising finding was the poor response of adult onset rhabdomyocarcoma to combination chemotherapy and RT in our patients, since childhood rhabdomyosarcoma represents the paradigm of successful management of tumors with combined modality therapy.[41,42] Since the diagnosis of rhabdomyosarcoma was established only after craniofacial resection in three patients, it is possible that the outcome might have been improved upon if an accurate preoperative diagnosis had been made. We would recommend both preoperative RT and chemotherapy before attempting surgery in this group of patients, since similar strategies have proved successful in children.

Although intracranial invasion clearly affects prognosis adversely, it was less important in this series because most of the patients had well-differentiated malignant or aggressive benign tumors with excellent response to therapy. Since surgical morbidity was no higher in these patients, we believe that limited intracranial invasion should not represent a major contraindication for surgery. In patients with neurologic dysfunction, palliation is an important goal of surgery; in others in whom the prospects of local tumor control exists with either RT or chemotherapy, surgery is important as a debulking procedure. We believe that craniofacial resection is indicated in all patients with esthesioneuroblastoma, since current data (including our own) suggest that tumor extension along the olfactory rootlets is present in all patients despite radiologic studies showing disease limited to the nasal cavity. The value of postoperative RT in those with negative surgical margins cannot be answered in our series, since it was not offered routinely to all patients. However, from the patterns of local failure in this series, we believe that postoperative RT may represent an important surgical adjunct in minimizing local recurrences.

REFERENCES

1. Cheesman AD, Lund VJ, Howard DJ: Craniofacial resection for tumors of the nasal cavity and paranasal sinuses. *Head Neck Surg* 8:429–435, 1985.
2. Jackson IT, Marsh WR, Hide TA: Treatment of tumors involving the anterior cranial fossa. *Head Neck Surg* 6:901–913, 1984.
3. Ketchum AS, Chretien PB, Van Buren JM, et al.: The ethmoid sinus: a re-evaluation of surgical resection. *Am J Surg* 126:469–476, 1973.
4. Ketchum AS, Wilkins RH, Van Buren JM, et al.: A combined intracranial facial approach to the paranasal sinuses. *Am J Surg* 106:698–703, 1963.

5. Ketchum AS, Van Buren JM: Tumors of the paranasal sinuses: a therapeutic challenge. *Am J Surg* 150:406 413, 1985.
6. Malecki J: New trends in frontal sinus surgery. *Acta Otolaryngol* 50:137–143, 1959.
7. Ray BS, McLean JM: Combined intracranial and orbital operation for retinoblastoma. *Arch Ophthalmol* 30:437–445, 1943.
8. Shah JP, Galicich JH: Craniofacial resection for malignant tumors of the ethmoid and anterior skull base. *Arch Otolaryngol* 103:514–517, 1977.
9. Sisson GA: Carcinoma of the paranasal sinuses and craniofacial resection. *J Laryngol Otolaryngol* 90:59–68, 1976.
10. Smith KR, Klopp CT, Williams JM: Surgical treatment of cancer of the frontal sinus and adjacent areas. *Cancer* 7:991–994, 1954.
11. Terz JJ, Young HG, Lawrence WE Jr.: Combined craniofacial resection for locally advanced carcinoma of the head and neck. I. Tumors of the skin and soft tissue. *Am J Surg* 140:613–617, 1980.
12. Terz JJ, Alksne JF, Lawrence W Jr.: Craniofacial resection for tumors invading the pterygoid fossa. *Am J Surg* 118:732–740, 1969.
13. Terz JJ, Young HP, Lawrence W Jr.: Combined craniofacial resection for locally advanced carcinoma of the head and neck. II. Carcinoma of the paranasal sinuses. *Am J Surg* 140:618–624, 1980.
14. Westbury G, Wilson JSP, Richardson A: Combined craniofacial resection for malignant disease. *Am J Surg* 130:463–469, 1975.
15. Bridger GP: Radical surgery for ethmoid cancer. *Arch Otolaryngol* 106:630–634, 1980.
16. Kondo M, Horiuchi M, Shiga E: Computed tomography of malignant tumors of the nasal cavity and paranasal sinuses. *Cancer* 50:226–231, 1982.
17. Parsons C, Hodson W: Computed tomography of paranasal sinus tumors. *Radiology* 132:641–645, 1979.
18. Som PM: The role of CT in the diagnosis of carcinoma of the paranasal sinuses and nasopharynx. *J Otolaryngol* 11:340–348, 1982.
19. Som PM, Lawson W, Biller HF, Langier DF, Sachdev VP, Rigamonti D: Ethmoid sinus disease: CT evaluation in 400 cases. Part III. Craniofacial resection. *Radiology* 159:605–609, 1986.
20. Weber AL, Stanton AC: Malignant tumors of the paranasal sinuses: radiologic, clinical and histopathologic evaluation of 200 cases. *Head Neck Surg* 6:761–776, 1984.
21. Chapman P, Canter RL, Clifford P: The diagnosis and surgical management of olfactory neuroblastoma: the role of craniofacial resection. *J Laryngol Otol* 95:785–799, 1981.
22. Cheng VST, Wang CC: Carcinomas of the paranasal sinuses. *Cancer* 40:3038–3041, 1977.
23. Ellingwood KE, Million RR: Cancer of the nasal cavity and ethmoid sinuses. *Cancer* 43:1517–1525, 1979.
24. Elner A, Koch H: Combined radiological and surgical therapy of cancer of the ethmoid. *Acta Otolaryngol* 78:270–276, 1974.
25. Harrison DFN: A critical evaluation of present day attitudes to the treatment of antro-ethmoidal cancer. *J Otolargynol* 11:148–150, 1982.
26. Jesse RH, Goepfert H, Lindberg RD: Carcinoma of the sinuses: a review of treatment. Cancer of the head and neck. *Europa Medica* 153–159, 1975.
27. Knegt PP, de Jong PC, van Andel JG: Carcinoma of the paranasal sinuses: results of a prospective pilot study. *Cancer* 54:482–488, 1984.
28. American Joint Committee on Cancer: *Manual for Staging of Cancer*. Philadelphia, J. B. Lippincott, pp 23–48, 1983.
29. Bush SE, Baghshaw MA: Carcinoma of the paranasal sinuses. *Cancer* 50:154–158, 1982.
30. Frazell EL, Lewis JS: Cancer of the nasal cavity and accessory sinuses: a report of the management of 416 patients. *Cancer* 16:1293–1301, 1963.
31. Robin PE, Powell DJ, Stansbie JM: Carcinoma of the nasal cavity and paranasal sinuses. Incidence and presentation of different histologic types. *Clin Otolaryngol* 4:431–436, 1979.
32. Saunders SH, Ruff T: Adenocarcinoma of the paranasal sinuses. *J Laryngol Otolaryngol* 90:157–166, 1976.
33. Sundaresan N, Sachdev V, Krol G: Craniofacial resection for paranasal sinus malignancies. In H Schmidek, WB Sweet, eds: *Operative Neurosurgery: Indications, Techniques and Results*. In press, 1987.
34. Rosen M, Simeone DA, Bruce DA: Single stage composite resection and reconstruction of malignant anterior skull base tumors. *Neurosurgery* 18:7–11, 1986.
35. Schuller DE, Goodman JH, Miller CA: Reconstruction of the skull base. *Laryngoscope* 14:1359–1364, 1984.
36. Helliwell TR, Yeoh LH, Still PH: Anaplastic carcinoma of the nose and paranasal sinuses. *Cancer* 58:2030–2045, 1986.
37. Elkon D, Hightower SI, Mengi LL: Esthesioneuroblastoma. *Cancer* 44:1087–1094, 1979.
38. Newbill ET, Johns ME, Cantrell RW: Esthesioneuroblastoma: diagnosis and management. *South Med J* 78:275–282, 1985.
39. Robbins KT, Fuller LM, Vlasak M, et al.: Primary lymphomas of the nasal cavity and paranasal sinuses. *Cancer* 56:814–819, 1985.
40. Kadish S, Goodman M, Wang CC: Olfactory neuroblastoma. *Cancer* 35:1571–1576, 1976.
41. Sutow WW, Lindberg RD, Yehern EA: Three year relapse free survival rates in childhood rhabdomyosarcoma of the head and neck. *Cancer* 49:2217–2221, 1982.
42. Lawrence W, Hays DM: Surgical lessons from the Intergroup Rhabdomyosarcoma Study. *Natl Cancer Inst Monogr* 50:159–163, 1981.