Literatur 24.)


Abstract
Sixty-eight patients with chordoma or low-grade chondrosarcoma at the base of the skull received fractionated high-dose postoperative radiation delivered with a 160-MeV proton beam. Protons have favorable physical characteristics which allow the delivery of high doses of radiation to these critically located tumors. The methods employed for these treatments are described. These patients have been followed for at least 17 months and for a median of 34 months. The median tumor dose was 69 CGE (cobalt Gy equivalent): CGE is the dose in proton Gy multiplied by 1.1, which is the relative biological effectiveness for protons compared to cobalt-60. The daily dose was 1.8 to 2.1 CGE. For this group the 5-year actuarial local control rate is 82% and disease-free survival rate is 76%. The incidence of treatment-related morbidity has been acceptable.

Abstract
PURPOSE:
To evaluate the outcome of children with base of skull or cervical spine chordomas treated by high dose irradiation.

METHODS AND MATERIALS:
Eighteen children, 4 to 18 years of age, with base of skull or cervical spine chordomas, received fractionated high-dose postoperative radiation using mixed photon and 160 MeV proton beams. The median tumor dose was 69 Cobalt Gray-equivalent (CGE) with a 1.8 CGE daily fraction.

RESULTS:
The median follow-up was 72 months. The 5-year actuarial survival was 68% and the 5-year disease-free survival (DFS) was 63%. The only significant prognostic factor was the location: patients with cervical spine chordomas had a worse survival than those with base of skull lesions (p = 0.008). The incidence of treatment-related morbidity was acceptable: two patients developed a growth hormone deficit corrected by hormone replacement, one temporal lobe necrosis, and one fibrosis of the temporalis muscle, improved by surgery.

CONCLUSION:
Chordomas in children behave similarly to those in adults: children can receive the same high-dose irradiation as adults with acceptable morbidity.

Abstract
Forty-five consecutive patients with chordoma or chondrosarcoma at the base of skull or cervical spine were treated at the University of California Lawrence Berkeley Laboratory (UCLBL) and University of California School of Medicine, San Francisco (UCSF) between November 1977 and October 1986. All patients had undergone a subtotal surgical resection. Twenty-three patients were treated definitively with charged particles, 13 patients were treated with photons and particles, and 9 patients were treated for recurrent disease. Total doses ranged from 36 to 80 Gray equivalent (GyE). Thirty-three patients are alive with a minimum followup of 1 year. The actuarial survival and local control for all patients at 5 years is 62% and 59%, respectively. Patients treated for primary disease had a 78% actuarial local control rate at 2 years, whereas the rate for patients with recurrent disease was 33%. Patients with smaller visible tumor volumes (less than 20 cc) had a significantly better local control rate than patients with larger tumor volumes (80% vs 33% actuarial rate at 5 years). Patients with chondrosarcoma had the highest local control rate, as did patients treated with particles alone. Complications included 3 patients with unilateral visual loss, two patients who became blind, and 4 patients with radiation injury to the brainstem.

Abstract
OBJECT:
Local tumor control, patient survival, and treatment failure outcomes were analyzed to assess treatment efficacy in 58 patients in whom fractionated proton radiation therapy (RT) was administered for skull base chordomas and chondrosarcomas.

METHODS:
Between March 1992 and January 1998, a total of 58 patients who could be evaluated were treated for skull base tumors, 33 for chordoma and 25 for chondrosarcoma. Following various surgical procedures, residual tumor was detected in 91% of patients; 59% demonstrated brainstem involvement. Target dosages ranged from 64.8 and 79.2 (mean 70.7) Co Gy equivalent. The range of follow up was 7 to 75 months (mean 33 months). In 10 patients (17%) the treatment failed locally, resulting in local control rates of 92% (23 of 25 patients) for chondrosarcomas and 76% (25 of 33 patients) for chordomas. Tumor volume and brainstem involvement influenced control rates. All tumors with volumes of 25 ml or less remained locally controlled, compared with 56% of tumors larger than 25 ml (p = 0.02); 94% of patients without brainstem involvement did not experience recurrence; in patients with brainstem involvement (and dose reduction because of brainstem tolerance constraints) the authors achieved a tumor control rate of 53% (p = 0.04). Three patients died of their disease, and one died of intercurrent disease. Actuarial 5-year survival rates were 100% for patients with chondrosarcoma and 79% for patients with chordoma. Grade 3 and 4 late toxicities were observed in four patients (7%) and were symptomatic in three (5%).

CONCLUSIONS:
High-dose proton RT offers excellent chances of lasting tumor control and survival, with acceptable risks. In this series all small- and medium-sized tumors with no demonstrable brainstem involvement have been controlled; all such patients are alive. Surgical debulking enhanced delivery of full tumoricidal doses, but even patients with large tumors and disease abutting crucial normal structures benefited.

Abstract
To define the prognostic factors for local control and overall survival among 100 consecutive patients with chordoma of the base of skull or upper cervical spine treated by fractionated irradiation combining proton and photon beams. Between December 1993 and August 2002, 100 patients (median age: 53 years [8 - 85], M/F sex ratio: 3/2) were treated by a combination of high-energy photons and protons. The proton component was delivered at the Centre de Protonthérapie d’Orsay (CPO) by a 201 MeV beam. The median total dose delivered to the tumor volume was 67 GyECO. With a median follow-up of 31 months [range: 0 - 87], 25 tumours relapsed locally. The 2- and 4-year local control rates were 86.3% (+/-3.9%) and 53.8% (+/-7.5%), respectively. According to multivariate analysis, at least 95% of the tumor volume encompassed by the 95% isodose (p = 0.046; RR: 3.4 95%CI [1.01 - 11.8]) and a minimal dose delivered into the tumor volume <56 GyECO (p = 0.042; RR: 2.3 95%CI [1.03 - 5.2]) were independent prognostic factors of local control. Ten patients died. The 2- and 5-year overall survival rates were 94.3% (+/-2.5%) and 80.5% (+/-7.2%), respectively. According to multivariate analysis, local tumor control (p = 0.005; RR: 21 95%CI [2.2 - 200]) was a prognostic factor of overall survival. For chordomas of the base of the skull and upper cervical spine treated by surgery and irradiation combining photons and protons, the quality of irradiation, reflected by homogeneity of the dose into the tumor volume, is a major factor of local control. Close attention must be paid to minimize the underdosed areas close to critical organs. The role of surgical resection remains paramount, and a trial of dose escalation would have to consider an increase in the dose to critical organs, especially as current results indicate the low toxicity of this treatment.