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● *Brief Communication*

FRACTIONATED RADIATION THERAPY IN THE TREATMENT OF STAGE III AND IV CEREBELLO-PONTINE ANGLE NEURINOMAS: LONG-TERM RESULTS IN 24 CASES

J. P. MAIRE, M.D.,* M. CAUDRY, M.D.,* V. DARROUZET, M.D.,† J. GUÉRIN, M.D.,‡ R. TROUETTE, M.D.* AND J. P. BÉBÉAR, M.D.†

*Service de Radiothérapie, Hôpital Saint-André, 1 rue Jean Burguet, 33075 Bordeaux cedex, France,
†Service d'Otorhinolaryngologie, Hôpital Pellegrin, place Amélie-Raba-Léon, 33076 Bordeaux cedex,
‡Service de Neurochirurgie, Hôpital Pellegrin, place Amélie-Raba-Léon, 33076 Bordeaux cedex

Purpose: To reevaluate long-term results of frationated radiation therapy (RT) in a previously published series of cerebello-pontine angle neurinomas (CPA).
Methods and Materials: From January 1986 to May 1992, 24 patients with Stage III and IV CPA neurinomas were treated with external fractionated RT; 7 patients had phacomatosis. One patient was irradiated on both sides and indications for radiotherapy were as follows: (a) poor general condition or old age contraindicating surgery, 14 cases; (b) hearing preservation in bilateral neurinomas after contralateral tumor removal, 5 cases; (c) partial resection or high risk of recurrence after subsequent surgery for relapse, 4 cases; (d) nonsurgical relapse, 2 cases. Most patients were irradiated with 9 MV photons. A three- to four-field technique with coned-down portals was used. Doses were calculated on a 95% isodose and were given 5 days a week for a mean total dose of 51 Gy (1.80 Gy/fraction).
Results: Median follow-up from RT was 60 months (7 to 84); five patients died, two with progressive disease. Two patients underwent total tumor removal after RT (one stable and one growing tumor). On the whole, tumor shrinkage was observed in 9 patients (36%), stable disease in 13 (52%), and tumor progression in 3. Hearing was maintained in 3 out of 5 hearing patients with phacomatosis.
Conclusion: Fractionated RT appears to be an effective and well-tolerated treatment for Stage III and IV CPA neurinomas. Hearing can be preserved for a long time.

Neurinomas, Fractionated radiation therapy.

INTRODUCTION

Recently, indications for fractionated radiation therapy (RT) in the treatment of cerebello-pontine angle neurinomas (CPA) have been defined. Wallner *et al.* reported on postoperative irradiation for incompletely excised acoustic neurinomas (20), and Ikeda *et al.* suggested that preoperative irradiation of angioblastic tumors was of great help in obtaining a cleavage plan and hemostasis (8).

In a previously published study of 20 cases (14), we have reassessed the effectiveness of such a treament in Stage III and IV neurinomas and concluded than indications of radiotherapy can be extended to other specific situations in which surgery would lead to increased morbidity: (a) elderly patients in poor general condition or with cardiovascular disease and for whom neuro-anesthesia is contraindicated; (b) patients with phacomatosis previously operated on one side, and in whom a contralateral tumor occurs, while hearing is still satisfactory and is to be preserved. More than 3 years later, we need to verify our preliminary results with a longer follow-up.

METHODS AND MATERIALS

From January 1986 to May 1992, 24 patients with CPA neurinomas (12 males, 12 females) were treated in our department. Ages ranged from 23 to 83 years old (median, 62). Seven patients (median age, 32.3 years) had phacomatosis, of whom one had tuberous sclerosis and six Von-Recklinghausen's disease. One patient was irradiated in both sides (Fig. 1) so that 24 tumors were eighth nerve neurinomas and one was on the glossopharyngeal nerve; 8 were Stage III and 17 were Stage IV. No patients were excluded, but two

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Reprint requests to: Professor Jean Philippe Maire.
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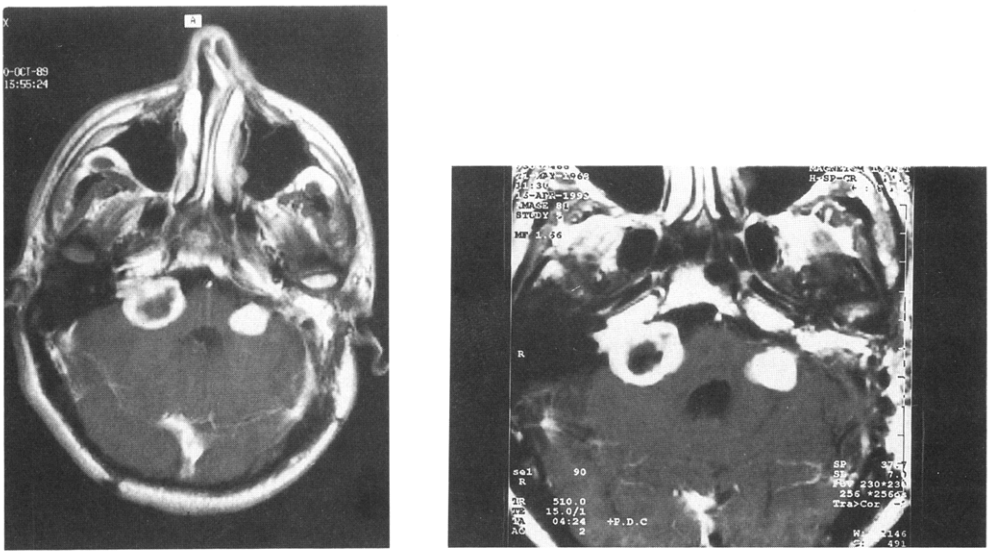

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Fig. 1. A case of bilateral neurinomas in a 23-year-old man with phacomatosis and right Stage IV neurinoma (Case 24) (14). Before irradiation of the right tumor, the previously operated left neurinoma relapsed and, therefore, was reoperated; (a) on the right side, necrotic areas appeared 15 months after irradiation (50 Gy). Hypacousia remains stable, but the patient has experienced three episodes of transient deafness. A second tumor recurrence appeared on the left side 15 months later and was irradiated (45 Gy); (b) there was no tumor progression on both neurinomas 64 months later for the right one, and 45 months later for the left one.

were lost to follow-up. One of these patients (Case 7—Table 1) irradiated in 1988 came from Algeria and the other (Case 10) from Italy; we had information about their outcome only 14 and 24 months after RT.

Before RT, five patients underwent a ventriculo-cardiac shunt, nine benefited from a unilateral excision (three partial, six total), and one totally deaf patient underwent bilateral tumor removal twice on one side.

At the time of RT, 13 patients presented with unilateral deafness and 2 with bilateral deafness (2 phacomatosis); 4 patients had unilateral hypacousia. Of five patients with phacomatosis who had previously been operated on one side, four had hypacousia and one a normal audiogram on the other side. Associated symptoms consisted of tinnitus (four cases), vestibular syndrome (six cases), trijeminal neuralgia (four cases), and brain stem compression with respiratory dysfunction (one case).

Indications for RT were as follows. (a) poor general condition or old age contraindicating surgery, 14 cases; (b) hearing preservation in bilateral neurinomas after contralateral tumor removal, 5 cases; (c) partial excision or high risk of recurrence after subsequent surgery for relapse, 4 cases; (d) nonsurgical tumor recurrence, 2 cases.

On the whole, 25 neurinomas were irradiated in 24 patients with photon beams (5 with ^{60}Co and 20 with 9 MV photons). The target volume was usually delimited by three to four coned-down portals with cerrobend blocks, and technique accuracy was verified with computerized tomographic scan. More recently three-dimensional dosimetry was used (Fig. 2). Doses were calculated on the 95% isodose, 1.80 Gy/fraction, 5 days/week to 48 Gy (4 patients), 50 Gy (16 patients), 55 Gy (4 patients), and 60 Gy (1 patient). During RT, the five patients for whom hearing was to be preserved were hospitalized and underwent weekly audiograms. After treatment, routine clinical examinations, audiograms, Computerized Tomography scan or Nuclear Magnetic Resonance were performed.

RESULTS

Clinical Efficacy

Treatment efficacy was assessed on the basis of regression of associated neurological symptoms. Of six patients with vestibular symptoms, three recovered a normal neurological status. Three of four trijeminal neuralgia disappeared. The patient with brain stem compression and respiratory dysfunction is alive and well more than 7 years later (Case 1).

Radiological Efficacy

Tumor modifications were seen in nine patients (Table 1). In five of them, the tumor became inhomogeneous, consistent with partial tumor necrosis within an elapsed time of 11, 12, 15, 18, and 22 months, without size regression in two cases. Furthermore, a noticeable tumor regression appeared in seven cases, 12, 14, 29, 32, 33, 33, and 60 months after the end of RT (Figs. 3 and 4); in three of these patients, it was associated with tumor necrosis. Three tumors increased in size, 12, 13, and 15 months after RT. Finaly, tumor size and tumor density remained stable in 13 cases including the patient irradiated in both sides (Fig. 1). Four of these cases were detailed in our

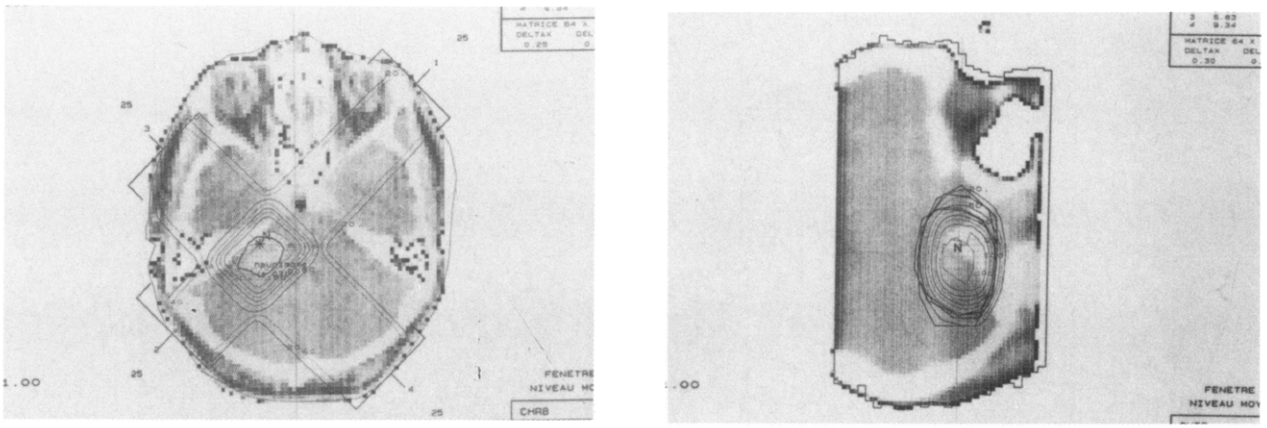

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Fig. 2. An example of 3D dosimetry for a right Stage III CPA neurinoma. (a) transversal, (b) sagittal plan.

previously published series (14). Eighteen-, 48-, and, 72-month actuarial control rates were 82%.

Patient Outcome and Survival

Patients were followed from 7 to 84 months after RT (median, 60 months). Two patients underwent a ventriculo-cardiac shunt for hydrocephalia, while tumor size remained stable (Cases 11 and 12). One patient with persistant trijeminal neuralgia, but with a stable radiological tumor, was operated on 14 months after RT and is still alive more than 6 years later (Case 2); tumor removal was easy and total. Histopathology revealed necrotic areas and fibrosis.

Table 1. Characteristics and follow-up of 24 patients with CPA neurinomas treated with fractionated radiation therapy

n	Age	Sex	Side	Indications for RT	Radiological efficacity	Follow-up (M.)	Clinical status
1	68	m	R	Old age	St + N	84	NED
2	64	f	R	Cardiovasc	St. + Surg.	79	NED
3	77	m	R	Old age	N + PR > 50%	73	DNED
4	45	f	L	Part surg.	St.	64	NED
5	61	m	R	Cardiovasc	PR > 25%	82	NED
6	46	f	Bilat	Tumor Size	Prog.	15	DOD
7	30	m	R	3° Rec + Surg.	St.	24	L.F-up
8	71	f	D	Old age	Prog. + Surg.	68	NED
9	30	m	R	Part surg.	PR > 50%	55	NED
10	27	m	Bilat	2° Rec + Surg.	St	14	L.F-up
11	74	m	R	Old age	St	7	DNED
12	75	f	R	Old age	St	19	DNED
13	77	m	R	Old age	St	67	NED
14	75	f	R	Old age	PR > 75%	84	NED
15	75	f	R	2° Rec no surg.	Prog.	12	DOD
16	83	f	R	Old age	St	20	NED
17	61	m	L	Cardiovasc	N + PR > 25%	24	NED
18	73	f	R	Old age	PR > 25%	32	NED
19	77	f	R	Old age	St	41	NED
20	37	m	L	Hearing pres.	St	75	NED
21	25	f	R	Hearing pres.	St	72	NED
22	23	f	L	Hearing pres.	N + PR > 25%	60	NED
23	43	m	R	Hearing pres.	St	70	NED
24	23	m	(R	Hearing pres.	St + N	64)	NED
			(L	2° Rec no surg.	St	45)	

CPA: Cerebello-pontine angle.
m: Male; F: female; R: right; L: left.
Rec: tumor recurrence; Part Surg.: partial tumor resection.
Surg: surgical exeresis; Hearing Pres.: hearing preservation.
N: tumor changes consistent with necrotic areas.
St: stable tumor size; PR: partial tumor reduction.
Prog.: tumor progression; NED: no clinical evidence of disease.
DNED: dead without evidence of disease; DOD: dead of disease.
L.F-up: lost to follow-up.

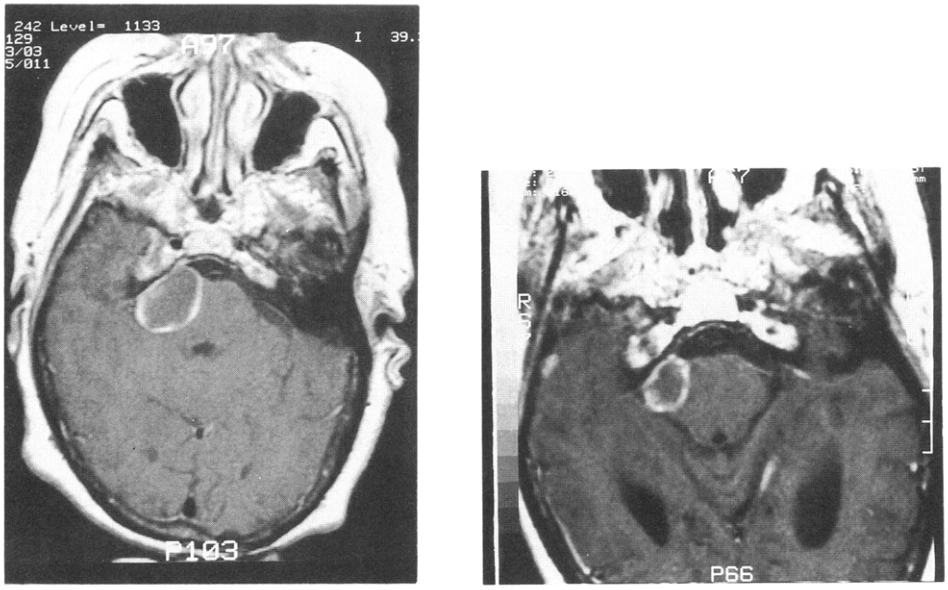

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Fig. 3. A case of tumor regression in a 73-year-old woman (Case 18). (a) Stage IV neurinoma before treatment; (b) Tumor regression was documented 24 months after RT as trigeminal neuralgia regressed.

Another patient with a clinical and radiological tumor progression was operated on 14 months after RT and benefited from a ventriculo-cardiac shunt followed by a total tumor excision (Case 8); histopathology demonstrated active cells with increased vascularity, except in the tumor center where necrotic areas and fibrosis were found. She is alive and well 5 years later. Five patients died: two patients from tumor progression, 12 and 15 months after RT (Cases 6 and 15), and the remaining three patients (74, 75, and 83 years old) from nontumoral causes 7, 19, and 73 months after RT (Cases 3, 11, and 12).

Tolerance and Hearing Evolution

Acute tolerance was good, and only three patients presented radioepithelitis of the external auditory canal. Subacute and late toxicity only concerned hearing.

In the five cases with bilateral tumors and for which hearing preservation was needed, hearing evolution was as follows: (a) in three patients (Cases 20, 23, and 24), hearing was preserved 64, 70, and 75 months after treatment. However, one patient (Case 20) presented with two episodes of transitory deafness 48 h and 5 months after RT, and another one (Case 24), with three episodes of

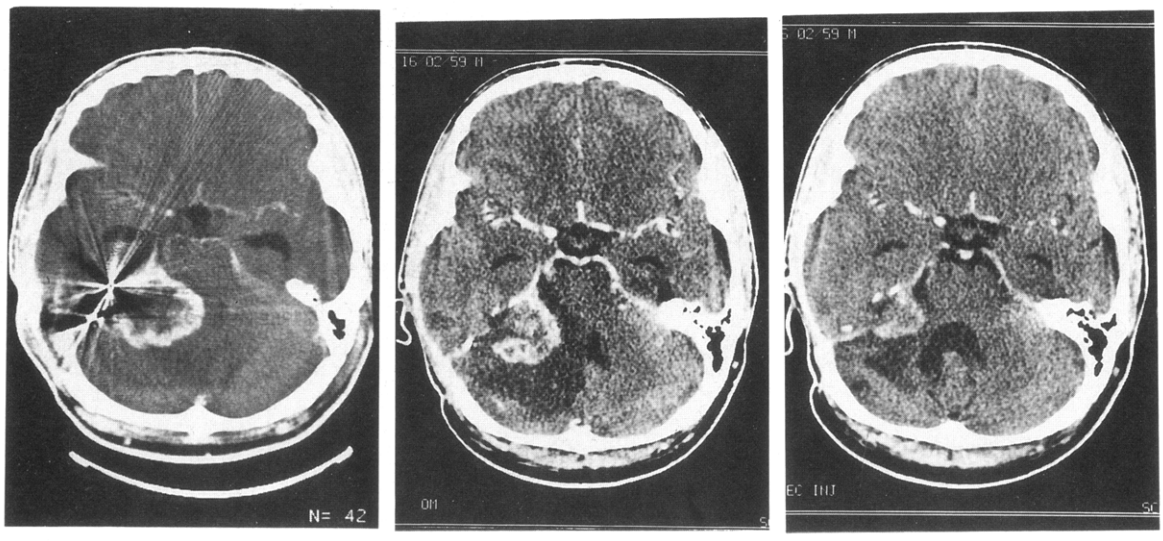

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Fig. 4. A case of tumor regression in a 30-year-old man who underwent partial removal of a right Stage IV neurinoma (Case 9); (a) postoperative CT scan showed a residual mass; (b) 1 year later, tumor decreased in size; (c) 3 years later, tumor regression was greater than 50%.

Table 2. Pure tone average (decibels) and speech discrimination scores (%) prior to radiotherapy and at the time of the last follow-up

Patient number	Before RT		Last Follow-up		Elapsed time (months)
	PTA	SDS	PTA	SDS	
20	10	85	30	75	75
21	80	75	Deaf		2
22	50	50	Deaf		7
23	55	40	80	15	70
24	50	35	70	25	64

transitory deafness 3, 6, and 39 months after RT. (b) The remaining two patients presented definitive deafness. For one patient, this was the only episode, occurring 2 months after RT (Case 22). For the second patient (Case 21), definitive deafness appeared 7 months later, after two episodes of transitory deafness (24 h and 4 months after RT). When deafness appeared, all five patients immediately received methyl-prednisolone and trimetazidine dichlorate. Pure tone average and speach discrimination score before RT and at the time of the last follow-up are given in Table 2.

Three patients with unilateral neurinomas presented contralateral progressive deafness; one patient was irradiated with a two parallel opposed field technique (Case 1), and two with a three-field technique (Cases 3 and 14). The contralateral ear received 55, 30, and 30 Gy, respectively.

DISCUSSION

The effectiveness of fractionated RT was measured by the rate of local control and the risk of complications.

Local Control

With a longer follow-up, our study demonstrates the persistance of effectiveness of fractionated RT for neurinomas of large volume, in situations where surgery was not indicated. Among the 21 nonoperated tumors (including the 2 patients with nonsurgical tumor recurrences), 7 of 11 patients with associated neurological symptoms returned to a normal neurological status within a short time. Only three patients had tumor progression. None of our five patients irradiated for hearing preservation presented tumor progression 60 to 72 months after RT.

Among the four patients with postoperative RT, one patient had a tumor regress 50% in size and is well 4.5 years later (Case 9, Fig. 4) and the three remaining patients did not show any tumor recurrence or progression 12, 24, and 64 months after RT.

On the whole, 9 patients had tumor shrinkage (36%) and 13 had stable disease (52%). Our results are in agreement with those of Wallner *et al.* (20) who reported on 25 patients who received frationated RT after subtotal surgical resection (22 patients) or biopsy (3 patients); of 20 patients who received more than 45 Gy, only 1 relapsed. Routine radiologic follow-up was not available in their series.

Comparisons of our results with those of stereotactic radiosurgery (SRS) are possible because we have a longer radiological follow-up. In the series of Noren *et al.* (17), patients received doses ranging from 18 to 25 Gy, and were followed up from 1 to 13 years; 44% of 115 treated cases had shrinkage of their tumor and 42% had stable disease. Linskey *et al.*(11) reported on gamma knife stereotactic radiosurgery in neurofibromatosis patients with bilateral acoustic neurinomas. The tumor control and regression rates were 89.5% and 21.1%, respectively; doses ranged from 14 to 20 Gy, with a median neuroimaging follow-up of 1.4 years. More recently, Flickinger *et al.* (7) reevaluated their results and confirmed that in 134 treated patients, 4-year actuarial tumor control rate was 89.2%. In the series of Mendenhall *et al.* (16), 32 patients were treated with linear accelerator-based SRS; dose to the periphery of the lesion ranged from 10 to 22.50 Gy, and follow-up ranged from 4 to 59 months. At 3 years, no patient experienced tumors progression, and 78% had tumor shrinkage.

These results are similar to those obtained in the present series. Nevertheless, in SRS series, most patients had tumor size less than 3 cm, while in our study, a majority of patients had tumors greater than 3 cm in size. Is it possible to make a choice between fractionated RT and SRS? In a recent article, Marks (15) discussed the place of SRS in the treatment of neurinomas and concluded that fractionated RT is probably advantageous because clinical and biological studies suggest that the therapeutic ratio of RT is increased with increased fractionations for malignant tumors, as well as for benign tumors. Furthermore, the risk of injury to normal structures will be reduced with fractionation.

Cranial Nerve Tolerance

In a study on tolerance of cranial nerves of the cavernous sinus to large single fractions of RT, Tishler *et al.* (19) analyzed the literature and observed that neuropathies of cranial nerves were seen after fractionated doses greater than 60 Gy. Furthemore, fraction size was found to be the most important parameter in terms of subsequent developpement optic neuropathy if total dose was greater than 50 Gy. Other cranial nerves seem to be less radiosensitive except for the eighth nerve, where reports on their injury are more difficult to interpret because radiation can damage multiple components of the auditory system. Tischler *et al.* (19) concluded from their experience that cranial neuropathies following radiosurgery were not much more frequent than with conventional RT. Nevertheless, in SRS series, the incidence of transitory delayed facial nerve dysfunction ranged from 15 to 36.8%, and the incidence of trigeminal neuropathies from 12 to 32%, but residual poor facial function or trigeminal injury was noted in only 5 to 8% of the patients (7, 11, 12, 16, 17).

Furthermore, the risk of nerve injury was noted to increase with radiation dose (17) and with tumor volume (7). Linskey *et al.* (12) used univariate and multivariate analysis to evaluate the risks of trigeminal and facial neuropathies following SRS in 92 treated patients. Tumor volume, maximum dose, minimum tumor dose, and tumor dose inhomogeneity were analyzed; the risk of damage of these two cranial nerves was significantly correlated with their irradiated length measured with the pons-petrous distance (fifth nerve) and mid-porous transverse tumor diameter (seventh nerve). They concluded that because larger tumors have larger mid-porous transverse diameter and larger pons-petrous distance, radiosurgery should be performed while tumors are still small.

Acute tolerance was good in our series, although most patients presented with very large tumors; furthemore, no patient experienced facial or trigeminal neuropathy.

Hearing Toxicity and Hearing Preservation

Five patients experienced definitive deafness, two on the irradiated tumor side and three on the contralateral ear. Of these three remaining patients, only two received 30 Gy on the contralateral ear, but they were respectively 75 and 77 years old; their old age could explain hearing toxicity, although low radiation doses were delivered. Their cases were discussed in our previously published series (14) and we concluded that a four-field isocentric technique must be proposed in all patients to preserve the contralateral ear and the brain stem, without altering dose homogeneity within the target volume.

On the other hand, in patients with phacomatosis previously operated on one side, and in whom a contralateral tumor occurs, while hearing is still satisfactory and to is be preserved, the problem is identifying and preventing the mechanisms of acute and subacute toxicity. Early vascular lesions are probably responsible for edema and obstruction of the Eustachian tube, as in serous otitis media (2, 6); early delayed injury, which is probably a result of demyelination as described by Boldrey and Sheline, could be evocated (1) and/or so could vascular toxicity of RT on the nerve capillary (6, 9, 10, 13). Nevertheless, it must be underlined that the irradiated eighth nerve is pathologic, and the question remains of how to protect this tumoral nerve in treated patients while they have an evolutive hypacousia. Are corticosteroids able to preclude hearing toxicity, since in animal models, corticosteroids seem to protect capillary endothelium (5)?

Permanent hearing loss (late delayed injury) is a result of nerve demyelinization, fibrosis, and microangiopathy (3, 6, 18). This process is irreversible, and its incidence increases as total dosage and doses per fraction increase (3, 9, 18); therefore, we have recommended reducing the dose per fraction. Wallner *et al.* (20) have observed that the best tumor control rates are obtained with doses over 45 Gy; we had planned to deliver 1.60 Gy per day for a total dose of 46–48 Gy in patients in whom hearing preservation was needed but we have had no indication since that time.

In SRS series, some effective hearing is preserved in one-third to two-thirds of the patients who had pretreatment hearing (7, 11, 17).

Advantages and Disadvantage of Fractionated RT and SRS

In the last decade, SRS had the advantage of stereotactic precision; furthermore, treatment time is short. However, with new immobilization techniques (4) and methods of confirming patient position during treatment such as portal imaging, conformal fractionated RT may be used with much more precision reducing normal brain irradiation. Nevertheless, approximately 6 weeks are necessary to complete treatment.

The rate of facial nerve sequelae after SRS is not quite different than after surgery, while hearing preservation is much more frequent with SRS. In our experience, fractionated RT seems to be as effective as SRS in the treatment of large tumors; its tolerance on normal structures is better, as we have never seen normal cranial nerve injury after fractionated doses of 45 to 50 Gy. It could be concluded from the SRS series than SRS is to be reserved for the treatment of small neurinomas, while fractionated RT is indicated for larger tumors.

CONCLUSION

Fractionated RT is an efficacious and well-tolerated treatment of partially removed or nonoperable Stage III and IV CPA neurinomas. It can replace SRS in the treatment of large tumors, as most facial or trigeminal complications appear in these situations. Hearing can be preserved for a long time.

REFERENCES

1. Boldrey, E.; Sheline, G. E. Delayed transitory clinical manifestations after radiation treatment of intracranial tumors. Acta Radiol. 5:5–10; 1966.
2. Borsany, S. J.; Blanchard, C. L. Ionising radiation and the ear. JAMA 181:958–961; 1962.
3. Chang, C. H. Sensitivity and tolerance of nervous tissues to ionizing radiation. In: Chang, C. H.; Housepian, E. M., eds. Tumors of the central nervous system. Modern radiotherapy in multidisciplinary management. New York: Masson; 1982:215–221.
4. Delannes, M.; Daly, N. J.; Bonnet, J.; Sabatier, J.; Tremoulet, M. Fractionated radiotherapy of small inoperable lesions of the brain using a noninvasive stereotactic frame. Int. J. Radiat. Oncol. Biol. Phys. 21:749–755; 1991.
5. Evans, M. L.; Grahan, M. M.; Mahler, P. A.; Razet, J. R. Use of steroids to suppress vascular response to radiation. Int. J. Radiat. Oncol. Biol. Phys. 13:563–567; 1987.
6. Fajardo, L. F. Organs of special senses. In: Pathology of radiation injury. Masson monograph in diagnostic pathology. New York: Masson; 1982:231–243.

7. Flickinger, J. C.; Lunsdorf, L. D.; Linskey, M. E.; Duma, C. M.; Kondziolka, D. Gamma knife radiosurgery for acoustic tumors: Mltivariate analysis of four year results. Radiother. Oncol. Biol. Phys. 19(Suppl. 1):148; 1990.
8. Ikeda, K.; Ito, H.; Kashihara, K.; Fujisawa, H.; Yamamoto, S. Effective preoperative irradiation of highly vascular cerebellopontine angle neurinomas. Neurosurgery 22:566–573; 1988.
9. Kinsella, T. J.; Weichselbaum, R. R.; Sheline, G. E. Radiation injury of cranial and peripheral nerves. In: Gilbert, H. A.; Kagan, A. R., eds. Radiation damage to the nervous system. New York: Raven Press; 1980:145–153.
10. Krishnan, L.; Krishnan, E. C.; Jewell, W. R. Immediate effect of irradiation on microvasculature. Int. J. Radiat. Oncol. Biol. Phys. 15:147–150; 1988.
11. Linskey, M. E.; Lunsdorf, L. D.; Flickinger, J. C. Tumor control after stereotactic radiosurgery in neurofibromatosis patients with bilateral acoustic tumors. Neurosurgery 31:829–839; 1992.
12. Linskey, M. E.; Flickinger, J. C.; Lunnsdorf, L. D. Cranial nerve length predicts the risk of delayed and trigeminal neuropathies after acoustic tumor stereotactic radiosurgery. Int. J. Radiat. Oncol. Biol. Phys. 25:227–233; 1993.
13. Lundborg, G.; Schildt, B. Microvascular permeability in irradiated rabbits. Acta Radiol. Ther. Phys. Biol. 10:311–320; 1971.
14. Maire, J. Ph.; Floquet, A.; Darrouzet, V.; Guerin, J.; Bebear, J. P.; Caudry, M. Fractionated radiation therapy in the treatment of cerebello-pontine angle neurinomas: Preliminary results in 20 cases. Int. J. Radiat. Oncol. Biol. Phys. 23:147–152; 1992.
15. Marks, L. B. Conventional fractionated radiation therapy vs. radiosurgery for selected benign intracranial lesions (arterious malformations, pituitary adenomas, and acoustic neuromas). J. Neurooncol. 17:223–230; 1993.
16. Mendenhall, W. M.; Friedman, W. A.; Boya, F. J. Linear accelerator-based stereotactic radiosurgery for acoustic schwannomas. Int. J. Radiat. Oncol. Biol. Phys. 28:803–810; 1994.
17. Noren, G.; Arndt, J.; Hindmarsh, T.; Hirsh, A. Stereotactic radiosurgical treatment of acoustic neurinomas. In: Lundsford, L. D., ed. Modern stereotactic radiosurgery. Boston, MA: Martinus Nijhoff Publisher; 1988:481–489.
18. Sheline, G. E.; Wara, W. N.; Smith, V. Therapeutic irradiation and brain injury. Int. J. Radiat. Oncol. Biol. Phys. 6:1215–1128; 1980.
19. Tischler, R. B.; Loeffler, J. S.; Lundsford, L. D.; Duma, C.; Alexander, E., III; Kooy, H. M.; Flickinger, J. Tolerance of cranial nerves of the cavernous sinus to radiosurgery. Int. J. Radiat. Oncol. Biol. Phys. 27:215–221; 1993.
20. Wallner, K. E.; Sheline, G. E.; Pitts, L. H.; Wara, W. M.; Davis, R. L.; Boldrey, E. B. Efficacy of irradiation for incompletely excised acoustic neurilemomas. J. Neurosurg. 67:858–863; 1987.