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# Conservative Management of Acoustic Neuromas

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Improved diagnostic screening, most notably auditory evoked brain stem response testing and more sophisticated and generally available imaging as well as a better informed population, have resulted in increasing numbers of smaller and less symptomatic acoustic neuromas being diagnosed [1].

Advances in surgical technique, anesthesia, and perioperative care have dramatically reduced both operative mortality and morbidity. Although the mortality associated with acoustic neuroma excision was on the order of 80% in the early 1900s, this figure has been reduced to approximately 1% in most current series. Lower cranial nerve palsy and significant residual trigeminal hypesthesia is now a rare and generally isolated event [2,3].

As a result, several authors have suggested that all tumors, with few exceptions, should be removed following diagnosis [4,5]. Others have proposed that a more expectant attitude is an acceptable alternative to immediate surgical excision [6–9].

A conservative (non–tumor excision) strategy is based on the premise that surgical removal may pose a greater risk. It assumes that given the nature of acoustic neuroma clinical behavior, ie, pattern of growth, these tumors will not result in either mortality or significant morbidity within the expected life span of a given individual.

The ability to predict a tumor's potential for growth would clearly be of benefit in the assessment of such a treatment strategy. A number of studies have been undertaken to answer this question. Studies of individuals with acoustic neuromas have been carried out to define their rate and pattern of growth. Overall tumor growth is generally considered slow [10]. Annual rates of growth of 0.2 cm per year or less have been noted in the majority of cases followed [11,12]. Importantly 40% or more of tumors studied had no growth, and in several cases, demonstrable tumor shrinkage occurred [13–15]. Very importantly, however, several studies have unequivocally identified a percentage of patients in whom tumor growth is relatively rapid, i.e., exceeding 0.2 cm per year [16,17].

A number of patients have been successfully followed for up to 10 years without appreciable change in symptoms [7]. Such studies confirm the feasibility of adopting a conservative course of management in selected patients. If a strategy could be developed that reliably predicts the future growth of acoustic neuromas, a more rational approach in the management of these patients would evolve. A conservative policy that ultimately results in a large tumor, causing significant disability in an older patient who has been followed for years, is undesirable.

Most clinical studies have used serial imaging as a method of determining tumor growth. Annual tumor growth rate has in many instances become the predominant factor in considering future tumor enlargement [6]. No statistically significant correlation between tumor size and patient age at the time of presentation has been found [7,15].

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Other parameters have been used to predict tumor growth. Attempts have been made to correlate the percentage of tumor cells undergoing mitosis to the clinical course of affected individuals. The use of 5-bromo-deoxyuridine followed by immunolocalization has supported the clinical impression of the overall slow growth of acoustic tumors [18]. Flow cytometric study has defined a variable mitotic rate, suggesting a variable growth pattern [19]. Immunohistochemical study, using the monoclonal antibody KI-67, has revealed a high mitotic rate associated with a faster growing tumor [20]. In the clinical studies published to date, however, no correlation was found between presenting tumor size and the rate of cell proliferation. In one study, a number of tumors studied with flow cytometry were found to have proliferative potential equivalent to some malignant tumors. The usefulness of such a comparison is unclear, given the inability to correlate this laboratory finding to actual tumor behavior. Clearly factors other than actual cellular turnover rates influence changing tumor size. Hemorrhage, cystic degeneration, and scarring also play a role.

If a nontreatment management strategy is to be a serious alternative in the management of patients with acoustic neuromas, a definition of selection criteria, guidelines as to follow-up, and clinical assessment and imaging parameters are crucial. In an attempt to answer some of these concerns, a prospective study was initiated at Sunnybrook Health Science Centre, University of Toronto, in 1978, to follow a select group of mostly older patients with unilateral, previously untreated acoustic neuromas.

## Study group

Four hundred seventy-four patients with acoustic neuromas were seen at Sunnybrook Health Science Centre, between the years 1976 and 1991. A conservative approach (non–tumor excision) was adopted in 56 individuals with unilateral acoustic neuromas. All patients with recurrent or persistent tumors following previous surgery as well as those with bilateral tumors have been excluded. Of the 56 patients in whom conservative management was embarked on, six were excluded for lack of good quality computed tomography (CT) images.

Our study group therefore consisted of 50 patients, 34 of whom were female and 16 male, with an age range of 50 to 83 years (mean = 68.1). Thirty-nine were 65 or over. Table 1 details the reasons for selecting a conservative course of management. Note that of the patients under age 65, extenuating circumstances and refusal were responsible for the decision. Of particular interest are two individuals, one age 50 with an acoustic tumor in the only-hearing ear (the other ear having been deafened following mastoid surgery), and one age 60, who had severe Meniere's disease in the opposite ear.

Table 1
Rationale for conservative management (n = 50)

| Rationale | Age ≥ 65 years | 60–64 | 50–59 |
|---|---|---|---|
| Age | 23 | — | — |
| Age and medical problems | 13 | — | — |
| Medical problems | — | 2 | — |
| Refusal | 3 | 4 | 3 |
| Tumor in only or better hearing ear | — | 1 | 1 |

In patients selected or who themselves have opted for conservative management of their tumor, a follow-up policy has been adopted that includes regular full neurotologic examination together with serial CT scanning at 6-month intervals. In those patients followed for a number of years in whom there has been no clinical or radiologic evidence of tumor growth, the follow-up interval has been extended to 1 year. Conventional contrast-enhanced CT examination of the posterior cranial fossa using either 5-mm or 1.5-mm slices through the internal auditory canal has been the most frequently used method to monitor tumor growth during the follow-up period. In two individuals with lesions confined to the internal auditory canal, either air/CT meatography or more recently magnetic resonance imaging (MRI) has been used to monitor tumor growth. MRI was used to monitor one such patient in this series.

All scans were assessed, and all measurements related to tumor size were carried out by one neuroradiologist (EEK). The radiologist was unaware of the patients' clinical status and future management plans. All measurements were made more than once to validate their accuracy. In this study, the reliability coefficient obtained was 0.998, for simple replication. A value of 1 represents 100% repeatability/accuracy.

Tumor size would be best expressed by an exact measurement of tumor volume [17]. Because this has not been possible, a conservative method has been adopted whereby the mean of the maximum anteroposterior and mediolateral

dimensions of the cerebellopontine angle mass is used to represent tumor size. As described, internal auditory canal tumor content was not included in the measurement. The method and rationale for use of this technique are described in detail in a previous publication [7]. All patients included in this study had at least two CT scans (range 2 to 18), of sufficient quality to allow accurate measurements to be made. The period of follow-up in each case includes only the interval from the first to the last scan from which accurate measurement was possible. Clinical follow-up outside these limits during which scans were judged to be of poor quality has been excluded. Although this has inevitably led to a shortened follow-up interval (mean follow-up 41.7 months; range 7 to 152 months), a more accurate assessment of tumor growth has been ensured. For instance, the individual followed for the longest time in our study had a CT scan over 2 years earlier, which because of its poor quality rendered it inadmissible. This reduced the follow-up period in her instance from 181 to 152 months. Twenty-eight patients have been followed for 3 or more years, with 10 for more than 5 years.

## Data Analysis

Annual tumor growth rate was calculated in two ways (Fig. 1). Method 1 uses the initial and final tumor size divided by the number of years of follow-up. Thus it does not take variability of growth within the total follow-up time into account. Method 2 accounts for growth variability. It is the mean of the individual annual growth rates obtained between each interval of assessment during the follow-up period.

Tumor size was measured to 0.001 cm using a micrometer. This value was rounded off to the nearest 0.01 cm (0.1 mm). Although the reproducibility of these measurements was demonstrated, for reasons of clinical significance, a tumor was judged to have changed in size only if the total growth was 0.1 cm or more. The calculated growth rate, however, was the total growth divided by the number of years of follow-up and as such could be less than 0.1 cm per year.

In an effort to determine whether tumor growth is constant or significantly variable in the same individual, a measure of change in growth rate between consecutive follow-up intervals was

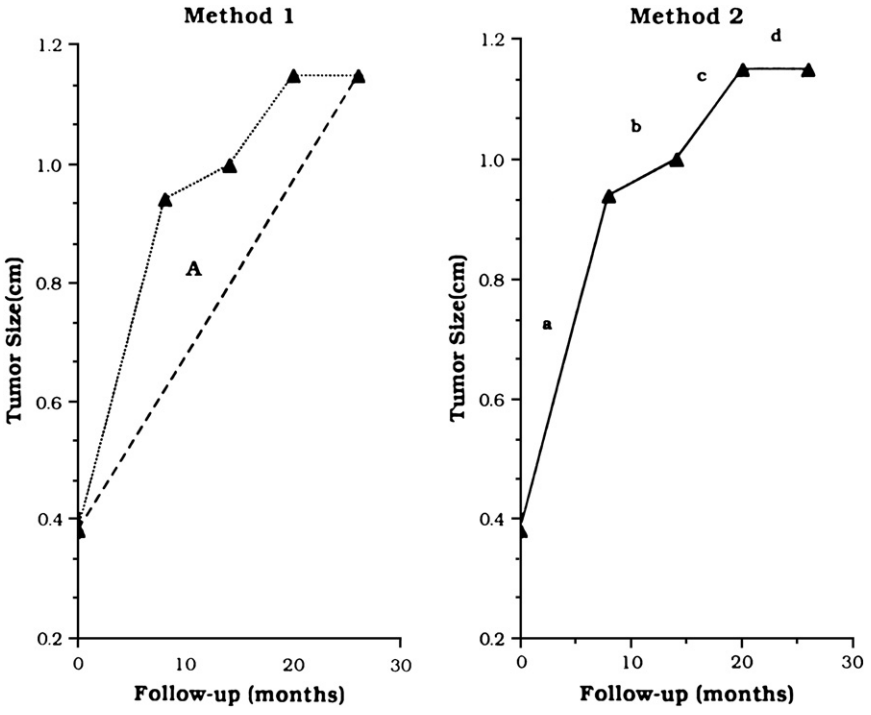


Fig. 1. Calculation of tumor growth rate. (Method 1) Growth rate is calculated as the difference between the first and last measurement and expressed in cm/yr; (Method 2) growth rate is calculated as the mean of individual measurements taken between the first and last study.

also calculated (growth variability). This was determined in 30 of the 50 patients. Small growth variability values represent constant growth, whereas large changes indicate significant variability, whether it be an increase or decrease in size (Fig. 2). Multiple regression analysis was also used to determine whether age or initial tumor size was related to subsequent growth.

## Results

### *Growth rate*

Using method 1, the mean annual growth rate for the study group was determined to be 0.11 cm per year, whereas method 2, which took into account variations in yearly growth, was 0.11 cm per year. All growth rates subsequently referred to are those obtained by method 1, which is easier to calculate. These rates range between an actual reduction in tumor size of 0.51 cm per year to an increase of 0.98 cm per year. Fig. 3 illustrates the distribution of growth rates of tumors for all patients. Note that the majority of patients demonstrate little, if any, growth. These findings are summarized in Table 2. Fully 78% of individuals had a growth rate of less than 0.2 cm per year. In nine patients, the tumor was noted to decrease in size (range of –0.51 to –0.01 cm per year). The CT images in Fig. 4 illustrate a reduction in tumor size from 2.2 cm to 1.05 cm, a 1.15 cm decrease over a 5.5 year follow-up period. Seventeen patients had no measurable change in tumor size. The interval CT scans of one such individual, followed for nearly 13 years (presently age 85), is shown in Fig. 5. Measurable tumor growth occurred in 24 patients (range 0.01 to 0.98 cm per year). The others are as listed in Table 2.

The maximum growth measured was 1.15 cm over a 14-month interval in a 66-year-old woman. Tumor size increased from 1.45 cm to 2.6 cm (Fig. 6). Although less dramatic, in terms of absolute size, another patient, age 65, realized a threefold increase over a 9-month period (0.38 to 1.0 cm) (Fig. 7). In the patients followed for more than 3 years and more than 5 years, the growth rates were +0.04 cm per year and –0.02 cm per year, respectively.

### *Growth variability*

The mean variation in growth rate for the 30 tumors studied is 0.13. The distribution, illustrated in Fig. 8, indicates that the majority

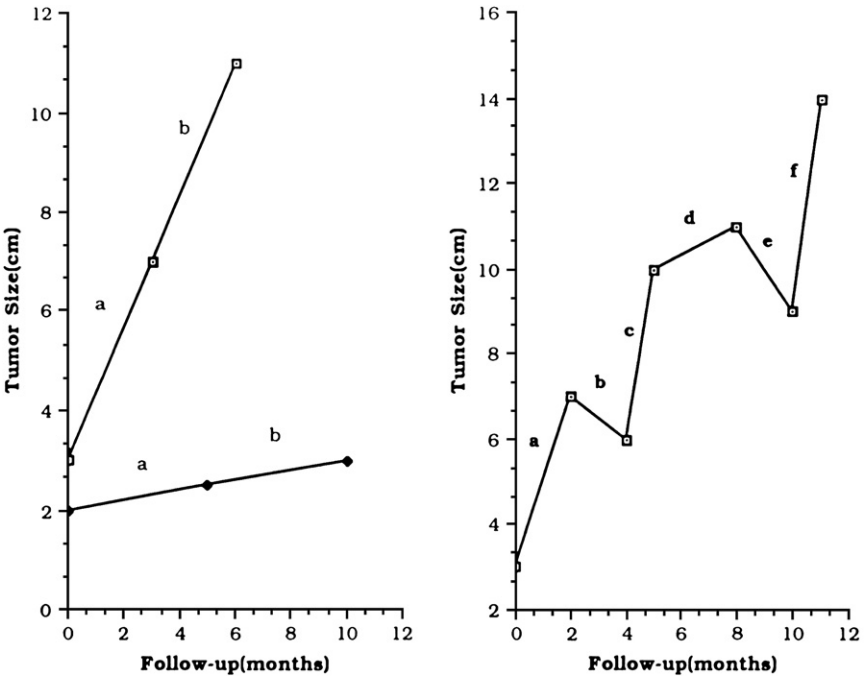


Fig. 2. Examples of growth rate patterns illustrating significant differences in the variability of growth. (*Left*) Constant rate of growth in a fast and slow (*bottom line*) growing tumor; (*Right*) a highly variable rate of growth in a single tumor.

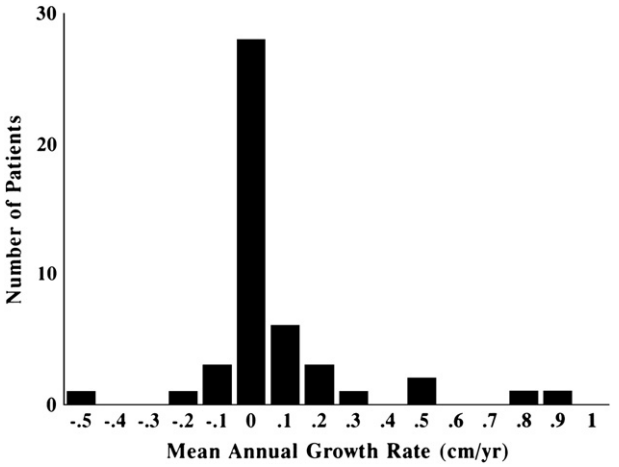


Fig. 3. Distribution of annual growth rates of study group (N = 50). Note that 0 growth includes rate changes between −0.099 and +0.099 cm/y. (See Table 2 for summary.)

of tumors demonstrate little or no variation in their growth rate, that is to say, a constant pattern of growth occurs regardless of the absolute rate.

*Other factors affecting growth*

Multiple regression analysis showed that there was no relationship between either the age of the patient or the initial tumor size with the annual growth rate. Of interest, a significant correlation was noted between patient age and tumor size. That is, the older the patient, the larger the tumor at presentation.

*Outcome of follow-up*

*Patients with tumor growth less than 0.2 cm per year (n = 39)*

Table 3 lists the outcome of the 39 patients in whom tumor growth has been less than 0.2 cm per year.

*No surgical intervention (n = 37).* Of the 39 patients, 37 have not required any form of operative intervention. The mean follow-up for this group is 48.2 months. Thirty-four are known to be alive and well, of whom 29 remain currently under review. The other five have been contacted by phone but decline to attend further clinical and CT evaluation. Apart from a progression of their unilateral hearing loss, all patients remain asymptomatic.

One patient has died during the follow-up period. Death was from causes unrelated to the acoustic tumor.

*Surgical intervention (n = 2).* Two patients have had a ventriculoperitoneal shunt inserted because of the development of associated significant hydrocephalus (mean tumor size 2.6 cm). In one patient, this was performed shortly after presentation. The shunt required revision 6 years later because of recurrent ataxia associated with increasing hydrocephalus. Clinical symptoms with associated hydrocephalus necessitated a shunt in the second patient 2 years after diagnosis, in spite of no obvious tumor enlargement.

Table 2
Annual growth rate of tumors (n = 50)

| | |
|---|---|
| Measurable reduction with ≥ 0.1 cm net change | |
| ≤ 0.1 cm/y | 4 (8%) |
| > 0.1 cm/y | 5 (10%) |
| No growth | 17 (34%) |
| Growth with ≥ 0.1 cm net change | |
| ≤ 0.1 cm/y | 7 (14%) |
| > 0.1 cm/y | 6 (12%) |
| ≥ 0.2 cm/y | 11 (22%) |

*Patients with growth rate greater than 0.2 cm per year (n = 11)*

The outcome of patients with tumor growth exceeding 0.2 cm per year is listed in Table 4.

*No surgical intervention (n = 2).* Despite a documented tumor growth of more than 0.2 cm per year, no surgery has been carried out to date on two patients. One has refused surgery (age 68, tumor presently 2.7 cm, growth rate 0.26 cm per year); the other underwent stereotactic irradiation.

*Surgical intervention (n = 9).* Nine patients have undergone planned translabyrinthine removal of

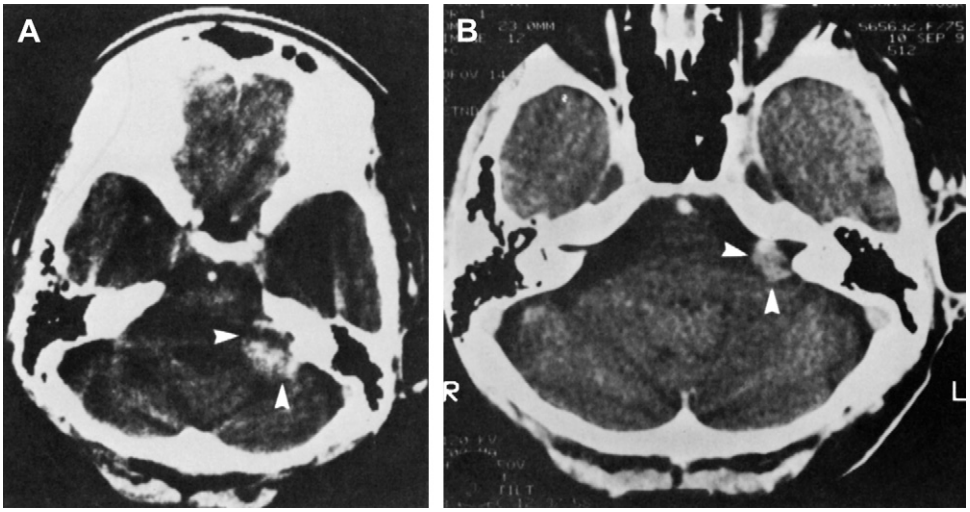


Fig. 4. Enhanced axial computed tomography images. Tumor demonstrating reduction in size over 7 years of follow-up. (*A*) Tumor measures 2.2 cm in May, 1984; (*B*) tumor measures 1.05 cm in September, 1991.

their tumors because of significant growth documented by repeat CT imaging. Complete removal was undertaken in seven, whereas deliberate subtotal excision was carried out in the other two (tumors measuring 3.63 and 2.6 cm). Five of the 11 patients with growth rates exceeding 0.2 cm per year developed either symptoms or signs referrable to their tumors. Three experienced increasing ataxia, one in combination with bidirectional gaze paretic nystagmus, whereas the other two developed varying degrees of trigeminal hypesthesia. Based on the onset of advancing symptoms, one would have expected these five patients to demonstrate enlargement of their tumors radiologically. Interestingly tumor enlargement was noted only in three individuals. Symptoms were in these cases due to developing hydrocephalus.

The mean tumor size in patients experiencing an increase in neurotologic signs was 2.64 cm, compared with 1.77 cm for those who did not.

*Long term follow-up*

A group of 28 elderly individuals have now been followed with good quality CT imaging for longer than 3 years. Ten of these patients have been followed for longer than 5 years. The mean

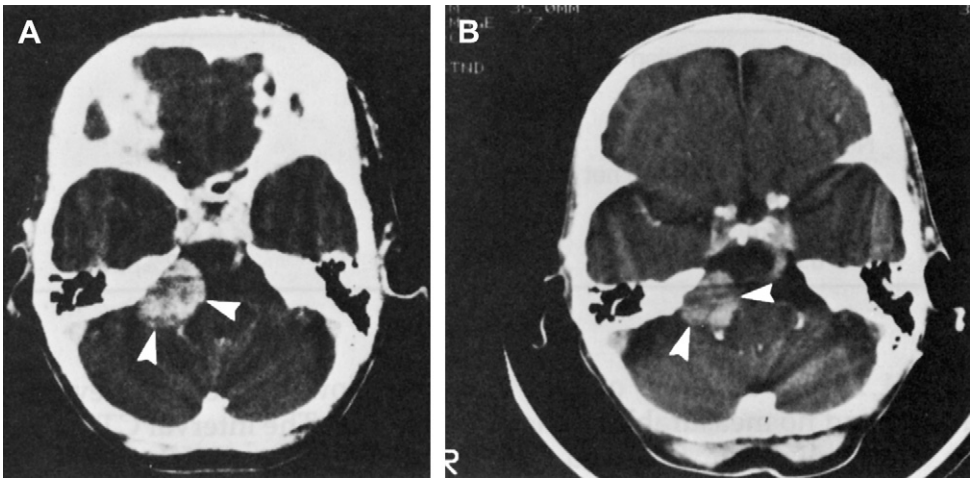


Fig. 5. Enhanced axial computed tomography images. Tumor demonstrating no change in size over a 13-year follow-up. (*A*) Scan from October, 1978; (*B*) scan from May 1991.

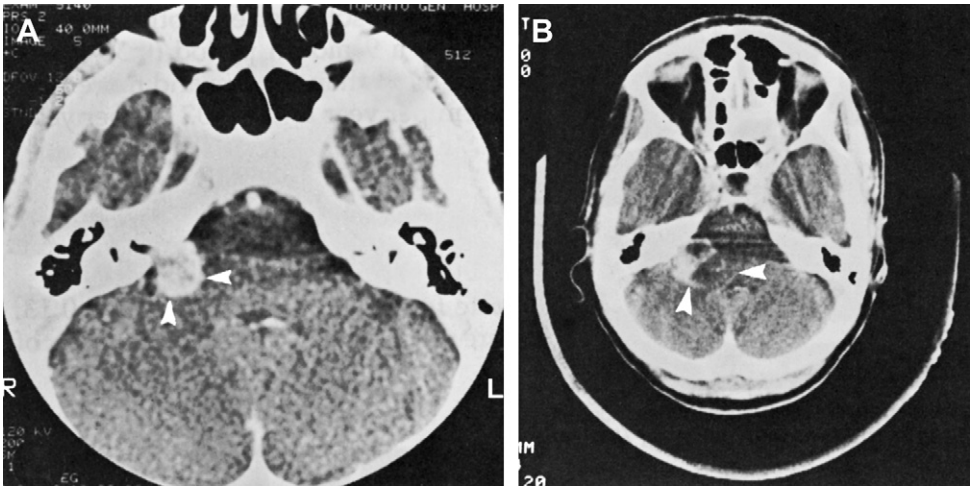


Fig. 6. Enhanced axial computed tomography images. Tumor demonstrating rapid growth rate of 0.98 cm/yr, (1.15 cm increase in 14 months). (*A*) 1.45 cm in November, 1985; (*B*) 2.6 cm in January, 1987.

growth rates of +0.04 and –0.02 cm per year, respectively, reflects little growth occurring in the tumors of these particular patients. No tumor followed for longer than 3 years and with an established pattern of slow growth has ever in our experience begun to grow rapidly and assume a more aggressive behavior, necessitating a change from a policy of observation to that of surgical intervention.

## Discussion

In light of these findings, is an expectant attitude (ie, non–tumor removal) reasonable in the management of the selected individual with an acoustic neuroma? Clearly a non interventional management policy is dependent on (1) patient compliance; (2) a predictable growth pattern; (3) a non invasive, easily obtainable method of assessing tumor size; and (4) reassurance that overall surgical treatment outcome has not been compromised, should it become necessary.

The results of this study confirm the results of others, in that the majority of acoustic neuromas grow slowly. The mean growth rate of tumors in this population (0.11 cm per year) is not significantly different from that of others. Our current findings, however, as well as those of others confirm a wide variation in individual tumor growth. We emphasize that the use of a single

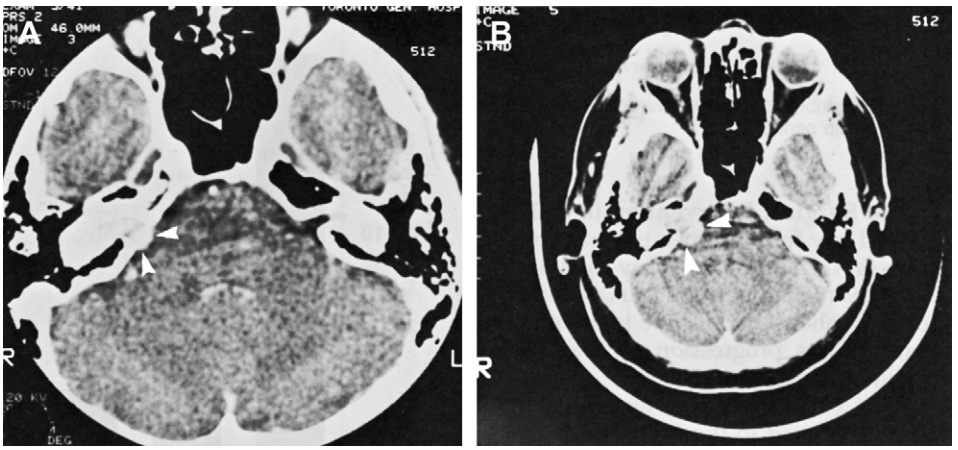


Fig. 7. Enhanced axial computed tomography images. Rapidly growing tumor; note threefold increase in size in 9 months. (*A*) 0.38 cm in August 1985; (*B*) 1 cm in May 1986.

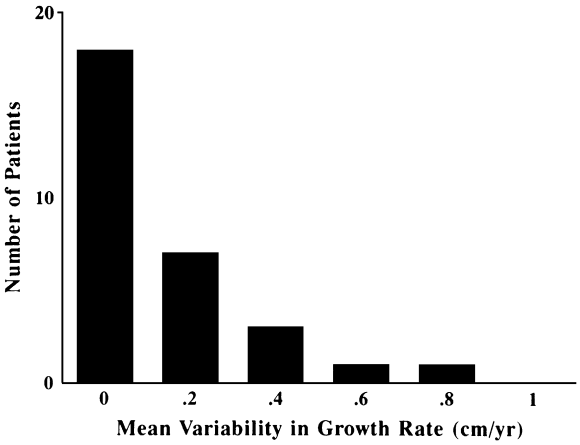


Fig. 8. Distribution of growth variability (n = 30). Lower values = constant rate of growth over follow-up period.

figure to estimate future tumor size is inappropriate. Our data indicate that a growth rate of 0.2 cm or greater was realized in only 22% of our patients. Excluding patients with growth rates greater than 0.2 cm per year, the mean annual growth rate for tumors in those individuals with measurable enlargement is 0.07 cm per year. Projected over 20 years, a time frame that exceeds the mean expected survival of 16 years in our elderly study population, this would equal a further growth of 1.4 cm [21].

In patients who have been followed for more than 3 years and more than 5 years, growth rates in our current study are +0.04 cm per year and −0.02 cm per year, respectively. This suggests that even allowing for an extended life span, few patients with small tumors would require surgery.

Results of analysis of growth variability indicate that the rate of growth of the individual tumor is relatively constant. The rate of growth at the start of follow-up predicted the future growth rate. No significant tumor enlargement occurred once a pattern of slow or absent growth had been established during the period of 3 or more years. This is corroborated by other authors. Consequently it seems reasonable to suggest that tumor behavior will become apparent within a relatively short period of observation subsequent to diagnosis, often within the first 18 months. Two of our patients underwent tumor excision after a longer interval. This was the result of their initial deference of surgery, however.

Aside from tumor growth rate, no other factor, including the size of the tumor at presentation, was found to be useful in predicting tumor growth. In isolated instances, large tumors were observed to become smaller, whereas small tumors were observed to grow rapidly. Explanations for such growth in addition to cell multiplication include hemorrhage into the tumor as well as cystic degeneration. The latter finding is by no means a feature peculiar to large or fast-growing tumors and is found in small tumors as well as those that have demonstrated little tendency to grow.

### *Factors that should be considered before adopting a nontreatment strategy*

#### *Age*

Advanced age, in itself, is not a contraindication to successful surgical removal of acoustic neuromas. A small tumor in an otherwise fit and

Table 3
Patients with growth rates < 0.2 cm/y (n = 39)

| | |
|---|---|
| Mean rate of growth—<0.01 cm/y (no growth) | |
| Mean age—69.7 y | |
| Mean follow-up—46.7 mo | |
| Disposition | |
| Alive and well | 34 |
| Decreased (unrelated cause) | 1 |
| Lost to follow-up | 2 |
| Surgery (ventriculoperitoneal shunt) | 2 |

Table 4
patients with growth rates >0.2 cm/y n = 11)

| | |
|---|---|
| Mean rate of growth—0.52 cm/y (range 0.26–0.9) | |
| Mean age—68.8 y | |
| Mean follow-up—14 mo | |
| Disposition | |
| Tumor excision | 9 |
| Refused surgery | 1 |
| Gamma knife | 1 |

active elderly individual is as easily removed as one in a young patient, with the subsequent recovery profile frequently indistinguishable from that of a young patient. In those individuals who are elderly and are reluctant to proceed to tumor removal, however, a reasonable alternative is to adopt an expectant attitude with the understanding that close, ongoing monitoring is initially required.

To date, no similar study of the natural history of acoustic neuromas in younger individuals has been published. Consequently young patients who opt for a nontreatment course should be advised of the need for even closer scrutiny with the understanding that surgery will be recommended in the event of demonstrated growth.

*Tumor size at presentation*

To date, tumor size at the time of diagnosis and subsequent rate of growth are statistically unrelated. In those instances, however, in which tumor size is responsible for ataxia, obstructive hydrocephalus, and significant trigeminal hypesthesia, it would seem prudent to recommend excision.

*Special extenuating circumstances*

In those individuals with an acoustic neuroma affecting the only-hearing ear or a tumor located on the side of the only-seeing eye, concern with respect to deafness and facial weakness is advised. Such individuals at outset are candidates for an initial conservative course of management.

*General health*

Individuals who are in generally poor health and in whom tumor surgery poses a much greater risk than normal, should be considered for noninterventional management.

*Incidental tumors*

The cited incidence of acoustic neuroma in the general population, as determined by cadaveric temporal bone studies, is estimated to be approximately 1% [22,23]. A generally accepted study cites the incidence of clinically apparent acoustic neuromas as eight tumors per million population [24]. Given recent advances in contrast-enhanced MRI, it seems reasonable to assume that heretofore unsuspected tumors will be identified. Removal of such clinically silent tumors without hearing loss is highly unlikely. In such an instance, documented growth or onset of hearing loss before advocating removal would seem advisable.

## Summary

The results of this study and others document the biologic behavior of acoustic neuromas. In view of the evidence presented, which describes both variable rates of individual tumor growth and spontaneous regression in size, it would seem prudent that before selecting a nonsurgical treatment modality, the growth rate for the particular tumor in question should be established. To date, none of the literature that addresses the use of focused irradiation has attempted to do so.

Our study as well as those of others suggests that the growth rate of acoustic neuromas becomes predictable over time. Based on this observation, a conservative (nontumor excision) management strategy is proposed for selected individuals.

Patients to whom this management philosophy has been recommended or who themselves have chosen this option are seen twice yearly. Each visit consists of a thorough neurotologic examination as well as high-definition CT or MRI. Careful comparison of the clinical course as well as calculation of the tumor size is carried out in each instance. If the clinical course and rate of tumor growth remain unchanged over a 3-year follow-up, annual assessments are recommended. In the event of tumor enlargement, surgery may or may not be recommended, depending on the rate of growth and the age of the patient. Our experience suggests that a rate of growth equal to or exceeding 0.2 cm per year constitutes an indication for tumor removal.

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