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Evaluation of the best follow-up period and curative effect for acoustic neuroma treated with a gamma knife

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Abstract ***Objective:*** To determine the best follow-up period with regard to curative effect for acoustic neuroma treated with a gamma knife. ***Methods:*** Sixty cases of acoustic neuroma were treated with a gamma knife. The follow-up period was from 3 to 102 months. Changes in the lesions and peripheral tissues and clinical symptoms were compared and the curative effectiveness of gamma knife treatment was evaluated. ***Results:*** The highest total effective rate (92.3%) was in the third period. There was a significant difference in the tumor size postoperatively. There was no edema in the peripheral tissues surrounding the tumor. It was not obvious that clinical symptoms changed. ***Conclusion:*** In this report, the best follow-up period was 24–36 months. Gamma knife treatment was still effective after 60 months post-operation.

Key words acoustic neuroma; gamma knife; the best follow-up period

Stereotactic radiosurgery (also called gamma knife) was developed in Sweden by Lars Leksell in 1951. At that time, the gamma knife was used in the treatment of intracranial pathology. The acoustic neuroma rate was 8%–12% of intracranial tumors. It was one of the tumors that had been followed-up for the longest period and the effectiveness of treatment with the gamma knife was affirmed [1]. Although there have been many articles, in the past, discussing the effectiveness of treating acoustic neuroma with the gamma knife, the best follow-up period has seldom been discussed. In our treatment and research center, hundreds of cases have been treated since 1994. This report was a study about the best follow-up period.

Materials and methods

Sixty patients, with acoustic neuroma treated with a gamma knife operation (Elketa, Sweden) and followed-up since 1994, were included in this study. There were 33 males and 27 females (age: 20–72 years, mean: 45.7 years). Of the 60 patients, 28 cases underwent surgical intervention before gamma knife treatment and 32 cases did not have surgical intervention before gamma knife surgery. The minimal range of treatment was 13 mm × 7 mm × 8 mm and the maximum range was 60 mm × 39 mm × 55 mm. The follow-up time was from 3 to 102 months. All patients had undergone an MR examination (Siemens Magnetom Impact 1.0 T scanner and Symphony 1.5 T scanner), including an MR plain scan and contrast enhancement scanning (with Gd-DTPA). A neurosurgeon and three MR radiologists, who were familiar with MR examination, analyzed all cases. The spin echo protocol was used. TR/TE time was 500/15 ms. The thickness was 7 mm. In this group the central dose was 20–40 Gy. The marginal dose was 12–14 Gy and that for the brain stem was ≤ 10–14 Gy. The planning area for the cases was around the tumor margin. Postoperative follow-up time was divided into 5 periods: the first was ≤ 12 months, the second was 12–24 months, the third was 24–36 months, the fourth was 36–60 months, and the fifth was > 60 months.

Evaluation criteria

Evaluation of the curative effect seen in different follow-up periods based on MR scans: 1) Efficacy: the diameter decreased or there was no reduction in size but cystic degeneration in the tumor occurred; 2) Stabilization: the diameter showed no change and there was no cystic degeneration in the tumor; 3) Inefficacy: the diameter increased with/without cystic changes.

Comparison of the volume of lesions: The maximum

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Table 1 Comparison of the therapeutic effect at different periods (*n*)

Follow-up period	Efficacy	Stabilization	Inefficacy	Total
≤ 12 months	22 (48.9%)	7 (15.6%)	16 (35.5%)	45
12–24 months	25 (83.3%)	1 (3.3%)	4 (13.3%)	30
24–36 months	12 (92.3%)	0	1 (7.7%)	13
36–60 months	10 (66.7%)	2 (13.3%)	3 (20.0%)	15
> 60 months	8 (42.1%)	8 (42.1%)	3 (15.7%)	19

Table 3 Comparison of clinical symptoms before and after treatment (*n*)

Follow-up period	Severe	No change	Improvement	Total
≤ 12 months	13 (28.9%)	26 (57.8%)	6 (13.3%)	45
12–24 months	6 (20%)	16 (53.3%)	8 (26.7%)	30
24–36 months	1 (7.7%)	7 (53.8%)	5 (38.4%)	13
36–60 months	3 (20.0%)	7 (46.7%)	5 (33.3%)	15
> 60 months	4 (21.1%)	13 (68.4%)	2 (10.5%)	19

size of tumors was measured on horizontal, vertical and sagittal lines in order to estimate and compare the volume of lesions (cm^3) (T1WI, contrast enhancement).

Evaluation of changes of clinical symptoms: based on the patient's self evaluation.

Results

Evaluation of the therapeutic effect at different follow-up periods

The results were shown in Table 1.

Evaluation of MR images

According to the maximum length (horizontal, vertical line, sagittal line), the volume of lesions (cm^3) could be estimated and compared. The paired data average difference *t* test was used (Table 2).

Evaluation of peripheral tissues

None of the patients had edema in peripheral tissues during the follow-up period.

Evaluation of clinical symptoms

The results were shown in Table 3.

Discussion

Evaluation of the effectiveness of gamma knife treatment

The relationship of lesion change to different follow-up periods

The results above-mentioned showed that the highest controlling rate of tumor' growth was in the third period. In that period, the average tumor volume was the smallest of the 5 stages above-mentioned, and it had a significant difference ($P < 0.05$) that the tumor volume altered preoperative and postoperative. Whether the tumor volume decreased or not, 92.3% (12/13 cases) showed some amount of cystic degeneration and necrosis or cicatrix and MR images showed that the tumor volume had decreased or remained stable. An article showed that 63 cases had been followed for 52 months and the gamma knife had a controlling rate on tumor growth of 95% [2]. The control rate was 90% (86/92 cases) based on the research of Zhang *et al* [3]. In another study the control rate was 98%, according to the report of Lunsford *et al* [4] . The follow-up time was ≥ 10 years. The results were a little higher than that in our paper. Although the tumor radiated with higher energy radiation was still there in the images, it would not grow and all of the tumor' cells had evidence of coagulation necrosis. Later the tumor tissues would be replaced by glial scar tissue and part of the tumor would be absorbed. To some extent,the quality of existence would be raised. To compare surgical intervention and the gamma knife, the gamma knife would not keep the tumor out, but it would kill the tumor cells and make them inactive and slow the tumor's developing speed or sometimes stop growth. The gamma knife would make the tumor shrunken, necrotic and scarred. The gamma knife has its special superiority.

The relation of clinical symptoms with different follow-up periods

The main evaluation criterion is the patient's self-evaluation of change in the clinical symptoms. Based on the results above-mentioned, the tumors had some changes in MR images, but the clinical symptoms had little change. Many of the patients felt there was no change in symptoms. In every follow-up period, nearly half or more of them had no improvement in symptoms. A few patients thought that their symptoms had improved. The highest rate was in the third and fourth period, that was 38.4% and 33.3% respectively. There were many reasons. The

Table 2 Comparing the tumor volume (cm^3) before and after treatment ($\chi \pm s$)

	≤ 12 months	12–24 months	24–36 months	36–60 months	> 60 months
n	45	30	13	15	19
Preoperative (cm^3)	31.56 ± 36.9	32.32 ± 41.34	20.75 ± 22.04	28.35 ± 32.65	29.65 ± 37.41
Postoperative (cm^3)	31.48 ± 37.48	19.5 ± 20.97	9.16 ± 8.28	18.78 ± 30.43	19.42 ± 35.53
T value	0.15	1.75	2.95	2.15	2.13
P value	$P > 0.05$	$P > 0.05$	$P < 0.05$	$P < 0.05$	$P < 0.05$

first was that the tumor was very large, the progress of recovery was slow, and the functional damage from the acoustic neuroma was severe and would not improve. The second reason was that the gamma knife belongs to the radiotherapy group. It would bring about radiation damage to all of tissues that they had radiated with rays. It would damage the function and structure of lesions but peripheral tissues also. Perhaps it would be ineffective in recovery of function and so on. A foreign thesis reported that 104 patients were followed for 3 years after being treated with gamma knife and showed that it had no direct interrelation [5], among the factors, such as functional preservation, change of tumor' size, center dose and marginal dose and so on. Therefore, it would be observed and studied and summarized about improvement of clinical symptoms and functional preservation and so on later. Furthermore, improvement of clinical symptoms and functional preservation were evaluated merely according to the patient' subjective feelings, it would not enough to make a summary and gain a precise conclusion. That would have to be done by objective examination.

About the change of peripheral tissues postoperative

It was mainly hydropic change of peripheral tissues (surrounding the tumor) postoperative, including both of the cerebellar hemisphere and brain stem. In the paper, the edematous incidence rate was zero. There was no case in the group that showed hydropic change in the MR images. If inquiring the reasons, perhaps the reasons were that there were fundamental distinctions between the gamma knife and traditional radiotherapy. The principle of the gamma knife was that the gamma knife adopted a single high dosage radial line to damage the target and then intracranial pathological changes (tumor) could be treated. Because the dosage of the radial line was contained primarily in the target region, peripheral tissues surrounding the tumor did not suffer damage. Acoustic neuroma as an extracerebral tumor. When treated with the gamma knife, the tumor' borderline was covered with a 30%–50% isodose curve. The isodose curve had been carefully planned. So, the radial line could destroy the tumor cells effectively and meanwhile the peripheral tissues surrounding the tumor would be protected better because they received very few rays. The dosage to the peripheral tissues was greatly weakened. The impairment of both of the cerebellar hemispheres and the brain stem was slight, or not enough to be found in MR images.

Discussion of the best follow-up period

In the first period (≤ 12 months), the total effective rate was 64.5%. Of that group, 48.9% (22/45 cases) or so began to show changes in the tumor, such as slight cystic degeneration and/or the diameter of tumor contracted slightly. 15.6% (7/45 cases) had no change. In the results abovementioned for the period, with regard to reduction in volume of the tumor, there was no significant difference ($P > 0.05$). Perhaps this is because of the short follow-up time. In the second period (12–24 months), curative effect was appearing gradually. In this stage, the total effective rate was 86.6%. Of that group, 83.3% (25/30 cases) showed changes in the tumor, there was much cystic degeneration and/or the diameter of tumor had contracted obviously, 3.3% (1/30 cases) had no change, and in 13.3% (4/30 cases) the diameter of the tumor enlarged (non-effectiveness). Comparing them, the total effective rate in the second stage was higher than that of the first stage. In the second stage, the total tumor volume was less, but for the group it was not a significant difference ($P > 0.05$). Some individuals manifested a great change but it had no significant difference ($P > 0.05$) on statistical analysis. The authors thought the stage was not the best observing period. The curative effect of gamma knife was not the best in that stage. In the third period (24–36 months), the total effective rate was 92.3% (12/13 cases); it was higher than that of the first and second period. The total effective rate began to descend (80.0%) in the fourth period (36–60 months). It is possible that is due to the length of time postoperative. It had been a long time after treatment with the gamma knife in the stage. For this reason, curative effect was not much better than before. In the fifth period, the total effective rate was much lower than that of the fourth period. Thus, the fourth period and the fifth period were not the best observing periods. On the basis of the results above-mentioned, it could be summed up that the third period (24–36 months postoperative) was the best follow-up period. After this, if the curative effect of gamma knife treatment was not good or below the mark, some other appropriate proposal for treatment would be thought over considered.

Present problems

The gamma knife adopts a single higher dosage radial line to damage the target and achieve the therapeutic purpose. Due to the difficulty of drawing the materials from the tumor, there was little documentation about changes of histopathology. Now the gamma knife has made treatment of acoustic neuroma widespread, but not all acoustic neuromas are suitable to be treated with the gamma knife. At present there are no clearcut standards defining when to use the gamma knife. As an example, if facial nerve function and hearing was be preserved [6], the gamma knife might be considered. The curative effect of the gamma knife needs to be studied further at a later time. The authors considered that: people, such as older men and/or physically weak men, with no severe pressure symptoms, and no ability to tolerate a surgical operation, could be treated with the gamma knife first and the gamma knife would stop the tumor's growth. The part that remained after the surgical operation could be

radiated so that facial nerve function could be preserved as much as possible. The patients with neurofibromatosis and acoustic neuroma on both sides might be treated with the gamma knife. The acoustic neuroma on the side causing hearing loss could be treated first. The patients, with neurofibromatosis as well as other kinds of tumor (such as meningioma and so on, within the brain or intracranial), might select the gamma knife as well. Tumors, with many blood vessels or surrounding important structures or very dangerous to be operated on, ought to be treated with the gamma knife. Past experience indicates larger tumor can be treated if the diameter of the tumor is ≥ 44 mm. It should be pointed out that stereotactic radiosurgery ought to be used for the smaller tumors as far as possible. The decision whether to treat with the gamma knife would be based on rationalization and standardization.

With regard to the curative results for acoustic neuromas treated with the gamma knife, in some cases, it was reported that only rapidly growing tumors evidenced change in size and/or clinical symptoms after being treated with the gamma knife, implying that treatment would not be successful, unless the tumor grew rapidly preoperative. This conclusion seems reasonable given the conditions of the case histories. Further evaluation of the curative effects and conditions is needed to find the best follow-up period for acoustic neuroma treated with the gamma knife.

References

1. Ni TR, Yang WZ, Shi SS, *et al*. Gamma knife radiosurgery for acoustic neurinoma: report of 98 cases. Chin J Minim Invas Neurosurg (Chinese), 2006, 11: 14–15.
2. Kwon Y, Kim JH, Lee DJ, *et al*. Gamma knife treatment of acoustic neurinoma. Stereotact Funct Neurosurg, 1998, 70: 57–64.
3. Zhang GC, Wang ZH, Li YK, *et al*. Analysis of curative effect of gamma-knife radiosurgery on acoustic neuromas. Chin J Clin Neurosurg (Chinese), 2007, 12: 469–470.
4. Lunsford LD, Niranjan A, Flickinger JC, *et al*. Radiosurgery of vestibular schwannomas: summary of experience in 829 cases. J Neurosurg, 2005, 102: 195–199.
5. Thomassin JM, Epron JP, Regis J, *et al*. Preservation of hearing in acoustic neuromas treated by gamma knife surgery. Stereotact-Funct-Neurosurg, 1998, 70 Suppl 1: 74–79.
6. Chen GX, Xu MH, Shen GJ, *et al*. Long-term following up and analysis of curative effect of gamma-knife radiosurgery on acoustic neuromas. Chin J Clin Neurosurg (Chinese), 2007, 12: 400–401.