Diagn Interv Radiol 2011; 17:209–215

ORIGINAL ARTICLE

Evaluation of the necessity of contrast in the follow-up MRI of schwannomas

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PURPOSE
The purpose of our study was to determine whether gadolinium is necessary in follow-up MRIs for evaluating vestibular schwannomas.

MATERIALS AND METHODS
A retrospective analysis of 49 magnetic resonance imaging (MRI) examinations of 20 vestibular schwannoma patients was performed. Patients received between 1 and 4 follow-up scans, and the mean follow-up period was 15.3 months. Two radiologists independently reviewed the initial and follow-up MRI examinations. Tumor measurements obtained using the constructive interference in steady state (CISS) and contrast-enhanced T1-weighted (T1W) sequences were compared. Both radiologists used both of the sequences to analyze any differences in the tumor sizes measured in consecutive MRI scans.

RESULTS
The linear anteroposterior and transverse tumor diameter measurements obtained by the two observers using both sequences were strongly correlated ($r = 0.962–0.987$, $P < 0.001$). The observers agreed to a very high degree when detecting changes in the tumor size using the CISS sequence ($\kappa = 0.902$, $P = 0.0001$), whereas the agreement with the contrast-enhanced T1W sequence was good but not as good ($\kappa = 0.706$, $P = 0.001$).

CONCLUSION
CISS, as a contrast-free sequence, may be an option in regular follow-up MRIs of vestibular schwannomas.

Key words: • *schwannoma* • *vestibular nerve* • *magnetic resonance imaging*

Vestibular schwannomas are the most common benign neoplasms of the internal acoustic canal and the cerebellopontine angle and originate from the sheath of the eighth cranial nerve (1, 2). They typically grow slowly, usually at a rate of less than 2 mm/year (3). Microsurgical removal, stereotactic or focused radiotherapy and conservative management are used to treat these tumors. Conservative management is preferred in select cases, such as patients with advanced age or small tumor size (3). Magnetic resonance imaging (MRI) is the imaging modality of choice used for both the initial detection and any follow-up scans of vestibular schwannomas. Contrast-enhanced T1-weighted (T1W) imaging is considered the gold standard for detecting lesions in the internal acoustic canal (4). Ultrathin T2-weighted imaging (T2W) with constructive interference in steady state (CISS) and T2W fast spin echo imaging have also been proposed as screening tools for patients with probable intralabyrinthine lesions (4, 5). Vestibular schwannoma growth is determined by performing consecutive MR examinations in which gadolinium-based contrast agents are used (2). However, administration of contrast agents is time consuming and expensive and is also associated with several side effects, such as allergic reactions and nephrogenic systemic fibrosis (NSF) (6, 7). Therefore, it is important to identify the patient population in which contrast agents must be used. In this study, we aimed to determine whether it is possible to use the gadolinium-free CISS sequence alone when following up vestibular schwannomas.

Materials and methods

Patient population

Between January 2005 and January 2010, the medical records of 20 patients with a radiological diagnosis of vestibular schwannoma who underwent consecutive MRI examinations were reviewed. Patients with a history of prior surgery, radiation therapy or neurofibromatosis type 2 were not included in the study. The mean age of the study group, which included 9 men and 11 women, was 51.45 years (age range, 34–70 years). The follow-up duration ranged from 6 months to 27 months. The mean follow-up period was 15.3 months, and 2 scans were available in 13 patients, 3 scans in 5 patients, and 4 scans in 2 patients.

Imaging

MR images were acquired with a 1.5 T MR unit (Symphony, Siemens, Erlangen, Germany) using both a head coil and a neck coil. The MRI protocol included axial T1-weighted spin echo images (TR/TE, 430/10 ms; slice thickness, 3 mm; interslice gap, 0 mm; matrix, 384 x 211; and NEX, 1), TSE T2-weighted images (TR/TE, 4110/104; slice thickness, 3 mm; interslice gap, 0 mm; matrix, 512 x 269; and NEX, 1) and 3D CISS images (TR/TE, 10/5 ms; slice thickness, 1 mm; NEX, 1; matrix, 256 x 192; and

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Received 5 August 2010; revision requested 1 September 2010; revision received 6 October 2010; accepted 6 October 2010.

Published online 28 October 2010
DOI 10.4261/1305-3825.DIR.3786-10.1

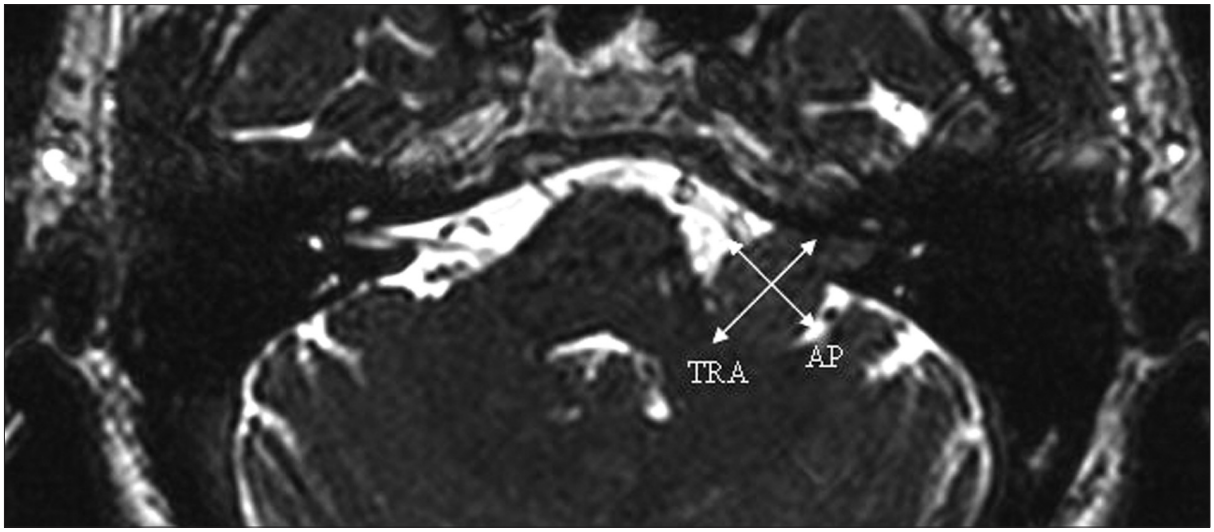

Figure 1. Axial MR image illustrating the tumor size measurements. Only the extracanalicular component was measured in tumors that had this component. The AP (anteroposterior) measurement was performed parallel to the petrous bone, and TRA (transverse) measurement was calculated perpendicular to the petrous bone in these tumors.

flip angle, 70°). Postcontrast axial and coronal T1W images were obtained after contrast media administration (gadolinium-DTPA 0.1 mmol/kg body weight i.v.).

Image analysis

Two radiologists (Observer 1 had 5 years of experience in head and neck imaging, whereas Observer 2 was a general radiologist) independently performed the measurements on the contrast-enhanced T1W images and on the corresponding CISS images. Each observer was blind to the other's MR assessments. Measurements of the axial images from both sequences from the same patients were performed on different time scales. The tumor size was measured in all scans using a digital submillimeter scale. The sizes of tumors located in the internal auditory canal (IAC) were calculated from the axial images as follows: the antero-posterior (AP) measurement was obtained along the axis of the canal, and the transverse (TRA) measurement was obtained perpendicular to the AP measurement. In tumors with a extracanalicular component, only this component was measured; the AP measurement was obtained parallel to the posterior surface of the petrous bone, and the TRA measurement was calculated perpendicular to this surface (Fig. 1). The size of the tumor was calculated as the square root of the product of the AP and TRA measurements (3). The annual growth rate (mm/year) was determined from the following formula: [change in tumor size between consecutive scans / duration of the follow up in months] x 12. A total tumor growth of >1 mm/year was considered significant radiologic growth and was referred to as tumor progression (3, 8). Contrast-enhanced T1W images were considered the gold standard to assess progression. The clinical stages of the vestibular schwannomas were determined according to the Koos classification as follows: Koos stage 1, intracanalicular tumor; Koos stage 2, tumor <20 mm in diameter; Koos stage 3, tumor >20 mm that does not compress the brain stem; and Koos stage 4, tumor that compresses the brain stem, regardless of size.

Statistical analysis

The statistical software package SPSS 17.0 (SPSS Inc., Chicago, Illinois, USA) was used to perform the statistical calculations. Bland-Altman plots were constructed using the Med Calc statistical software program to evaluate the agreement between two measurement methods. We used the student's t test and kappa statistics in the statistical evaluations. The measurements were correlated with paired t tests. The degree of interobserver agreement regarding progression was calculated using the kappa test. The value of kappa determines the strength of agreement as follows: excellent (κ = 0.93–1), very good (κ = 0.81–0.92), good (κ = 0.61–0.80), fair (κ = 0.41–0.60), slight (κ = 0.21–0.40), and poor (κ = 0.01–0.20).

Results

Tumors were located intracanalicularly in half of the patients (Koos stage 1). Two patients had cerebellopontine angle schwannomas that compressed the brain stem (Koos stage 4), and eight patients (40%) had Koos stage 2 tumors.

There were no statistically significant differences between the two observers' measurements of the anteroposterior diameters and tumor sizes from the two sequences. However, there were significant differences in the transverse measurements from both the postcontrast T1W and CISS sequences (P = 0.001 and P = 0.014, respectively). Observer 2's measurements of the transverse diameter were slightly higher than Observer 1's measurements; however, the difference in the mean measurements was less than 0.48 mm for the contrast-enhanced T1W sequence and 0.41 mm for the CISS sequence (Table 1).

Observer 2's measurements of the anteroposterior diameter and tumor size obtained from the contrast-enhanced T1W images were slightly higher than her measurements from the CISS sequences, although the difference was less than 0.40 mm. There were no significant differences between the two sequences in Observer 1's measurements of the anteroposterior diameter, transverse diameter or tumor size (Table 2).

Bland-Altman plots were constructed from the 49 MRI examinations of

the 20 patients (Figs. 2 and 3). These plots were used to determine any differences between the two sequences in two planes (transverse and anteroposterior) for each observer. The plots revealed that the differences between the two sequences were within the limits of agreement for both observers, indicating that the CISS sequence and the contrast-enhanced T1W sequence methods can be used interchangeably.

The correlations between the two observers' measurements of the linear anteroposterior diameter, transverse diameter and tumor size from the postcontrast sequence were 0.977, 0.984, and 0.987, respectively, and the correlations from the CISS sequence were 0.962, 0.980, and 0.986, respectively.

The correlations between Observer 1's measurements of the anteroposterior diameter, transverse diameter and tumor size using the two sequences were 0.964, 0.987, and 0.986, respectively, and the correlations between Observer 2's measurements using the two sequences were 0.976, 0.984, and 0.987, respectively.

The annual growth rate (mm/year) was determined by the following formula: [change in tumor size between consecutive scans / follow-up duration in months] x 12. A total tumor growth of >1 mm/year was considered significant radiologic growth and was referred to as tumor progression (3, 8). Contrast-enhanced T1W images are considered the gold standard for tumor progression assessment. Table 3 describes tumor progression detection by the two observers using the CISS sequence and the contrast-enhanced T1W sequence. On postcontrast T1W images, Observer 1 detected tumor progression in 7 studies, and observer 2 detected tumor progression in 6 studies. With the CISS, Observer 1 detected tumor progression in 6 studies, and Observer 2 detected tumor progression in 7 studies. The agreement between the observers regarding the detection of progression was very good with the CISS sequence (κ = 0.902, P = 0.0001), and agreement using the postcontrast images was good (κ = 0.706, P = 0.001). The correlations between the two observers' detections of annual progression were 0.922 for the postcontrast sequence and 0.945 for the CISS sequence.

One patient (patient number 11) exhibited a decrease in tumor size during the follow-up exam, which was detect-

Table 1. Interobserver measurement differences based on contrast enhanced T1-weighted sequence and CISS sequence

	AP		TRA		Size	
	mm	*P*	mm	*P*	mm	*P*
Post C						
Observer 1	8.47		11.40		9.74	
Observer 2	8.58		11.88		10.02	
Mean difference (SD)	-0.11 (1.0)	0.454	-0.48 (1.0)	0.001	-0.28 (0.82)	0.789
CISS						
Observer 1	8.18		11.23		9.51	
Observer 2	8.17		11.64		9.67	
Mean difference (SD)	0.01 (1.2)	0.945	-0.41 (1.1)	0.014	-0.15 (0.98)	0.874

Post C, contrast-enhanced T1-weighted sequence; CISS, constructive interference in steady state; AP, anteroposterior; TRA, transverse diameter; SD, standard deviation

Table 2. Two observers' measurements of the anteroposterior diameters and tumor size using both sequences

	AP		TRA		Size	
	mm	*P*	mm	*P*	mm	*P*
Observer 1						
CISS	8.18		11.23		9.51	
Post C	8.47		11.40		9.74	
Mean difference (SD)	0.28 (1.21)	0.106	0.16 (0.92)	0.204	0.24 (0.86)	0.064
Observer 2						
CISS	8.17		11.64		9.67	
Post C	8.58		11.88		10.02	
Mean difference (SD)	0.40 (1.06)	0.01	0.24 (1.02)	0.102	0.35 (0.81)	0.003

Post C, contrast-enhanced T1-weighted sequence; CISS, constructive interference in steady state; AP, anteroposterior; TRA, transverse diameter; SD, standard deviation

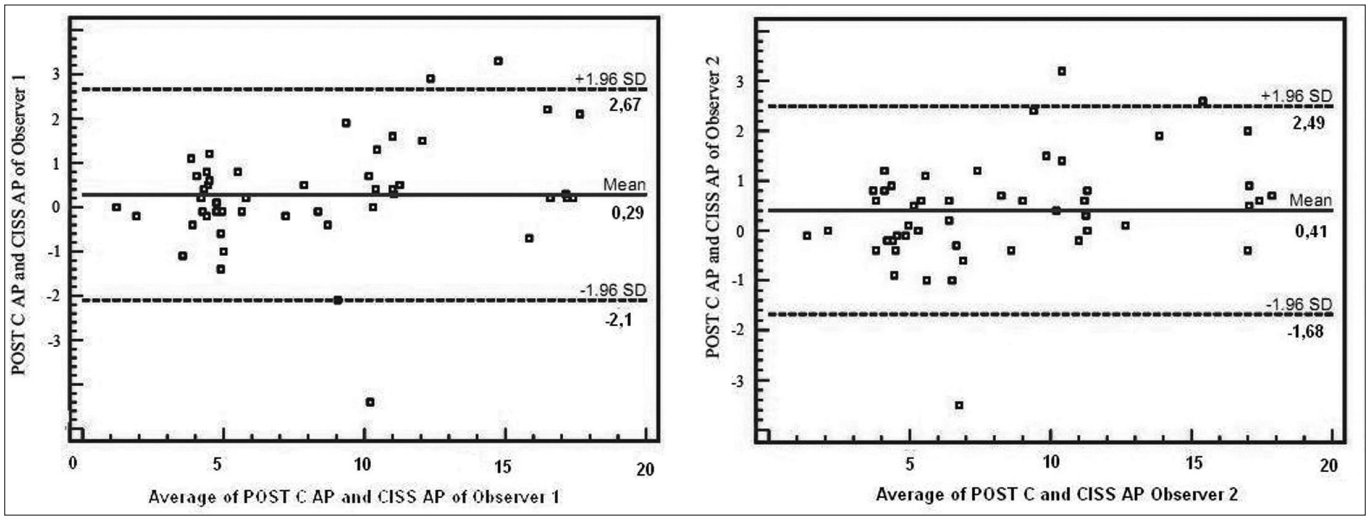

Figure 2. Bland-Altman plot of AP dimension measurements from Observer 1 and Observer 2 using the CISS and contrast-enhanced T1-weighted sequences (POST C). The values on the x-axis represent the mean of the measurements from the two sequences. The values on the y-axis represent the differences in the measurements from the two sequences and the mean difference *(unbroken line)*. Dotted lines represent 95% limits of agreement.

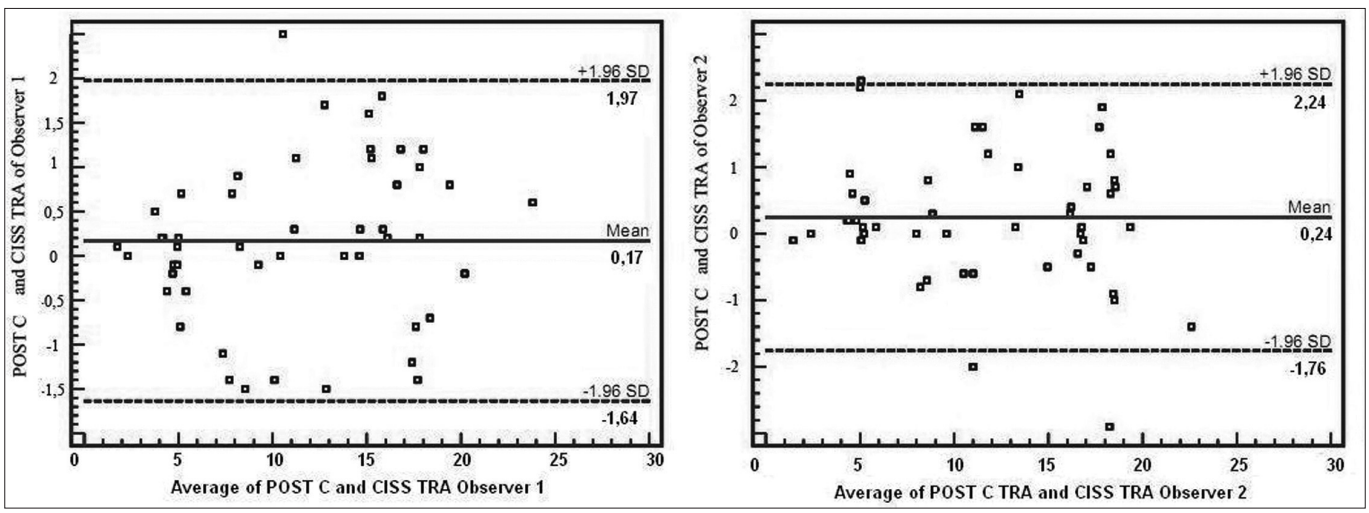

Figure 3. Bland-Altman plot of transverse (TRA) dimension measurements from Observer 1 and Observer 2 using the two sequences. POST C indicates the contrast-enhanced T1-weighted sequence.

ed with both sequences and by both observers.

The sensitivity, specificity and accuracy of the CISS sequence in the detection of progression compared with the gold standard postcontrast T1W sequence were 85.7%, 100%, 96.6%, respectively, for Observer 1 and 100%, 95.8%, 96.6%, respectively, for Observer 2.

Discussion

The incidence of clinically apparent vestibular schwannoma is 12–13 per million. However, the incidence of occult vestibular schwannomas reported on postmortem histopathological examinations is as high as 2.7% (2). This suggests that most schwannomas do not demonstrate enough growth to become clinically apparent. Studies have shown that the majority of vestibular schwannomas tend to grow slowly (38–43%) (9, 10). Conservative management of these tumors is appropriate in select cases, such as in patients with advanced age, poor general health or small tumors (3, 11).

MRI is the imaging technique used in the conservative management of vestibular schwannomas (2, 3). T1W sequences with a gadolinium-based contrast agent are the gold standard for the initial detection and follow-up examinations of these tumors (5, 7). Administration of contrast material is time consuming and costly and has serious side effects, such as NSF. To eliminate the routine use of contrast-enhanced imaging in the follow up of vestibular schwannomas, an alternative sequence that is proven to be accurate and reliable is required.

Some authors have investigated the utility of high-resolution T2W imaging (using the CISS sequence in some cases) to avoid contrast media administration in the initial detection of cerebellopontine angle masses (5, 12–14). The CISS sequence is a 3D gradient echo sequence with high spatial resolution, and lesions surrounded by cerebrospinal fluid can easily be detected with this sequence. The reported sensitivity and specificity of this sequence in the detection of cerebellopontine angle masses vary between 77–100%

and 98–94%, respectively (5, 12–14). The major challenges of this method are small lesions and tumors that are located adjacent to the brain parenchyma or the temporal lobe. Additionally, inflammatory lesions or vascular structures may mimic vestibular schwannomas on the CISS sequence and can lead to false positive findings (5). However, these challenges do not apply to our study population because the present study includes patients who have already been diagnosed with vestibular schwannomas and are undergoing follow up. In this study, we investigated the possibility of using only the CISS sequence to detect progression during follow-up examinations of vestibular schwannomas. There is only one report in the literature regarding the diagnostic accuracy of the CISS sequence in the follow up of vestibular schwannomas. Ozgen et al. (7) reported that the CISS-only MRI technique may be an alternative to routine contrast-enhanced MRI in following up lesion size in patients with vestibular schwannomas. They reported moderate interobserver agreement in evaluating progression with the CISS sequence; however, our study shows excellent interobserver agreement in evaluating progression using the CISS sequence. In our opinion, the differing degrees of interobserver agreement reported in the two studies are due to different measurement methods; we evaluated tumor growth using annual growth rate measurements in contrast to the qualitative measurements that were used in the Ozgen study (7).

Vestibular schwannoma growth can be demonstrated by volumetric studies or diameter measurements (2, 15). Studies in the literature have shown that diameter measurements can be used instead of volumetric measurements to compare tumor size (15, 16).

Table 3. Patient data and the detection of tumor progression by the two observers with the two different sequences (CISS and post C)

Patient	Age/Sex	Number of MR studies	Follow up period between MRI studies (months)	Annual progression rate Observer 1 (post C)	Annual progression rate Observer 2 (post C)	Annual progression rate Observer 1 (CISS)	Annual progression rate Observer 2 (CISS)	Koos stage
1	70/M	2	9	(+)	(+)	(+)	(+)	2
2	60/F	4	18 9 10	(-) (-) (-)	(-) (-) (-)	(-) (-) (-)	(-) (-) (-)	1
3	61/F	2	22	(-)	(-)	(-)	(-)	1
4	34/F	3	9 6	(-) (-)	(-) (-)	(-) (-)	(-) (-)	4
5	54/M	3	7 17	(-) (-)	(-) (-)	(-) (-)	(-) (-)	1
6	38/M	2	6	(+)	(+)	(+)	(+)	1
7	60/M	3	7 15	(+) (+)	(-) (+)	(+) (+)	(+) (+)	2
8	54/F	3	16 11	(-) (-)	(-) (-)	(-) (-)	(-) (-)	1
9	55/M	2	6	(-)	(-)	(-)	(-)	1
10	47/M	2	7	(+)	(-)	(-)	(-)	1
11	61/M	2	12 13	(-) (-)	(-) (-)	(-) (-)	(-) (-)	2
12	47/F	3	19 12	(-) (-)	(-) (-)	(-) (-)	(-) (-)	1
13	52/M	4	4 9 10	(-) (-) (-)	(-) (+) (-)	(-) (-) (-)	(-) (+) (-)	2
14	50/F	2	12	(-)	(-)	(-)	(-)	1
15	58/F	2	13	(-)	(-)	(-)	(-)	4
16	47/F	2	19	(-)	(-)	(-)	(-)	2
17	46/F	2	15	(-)	(-)	(-)	(-)	2
18	51/F	2	12	(-)	(-)	(-)	(-)	1
19	39/F	2	6	(+)	(+)	(+)	(+)	2
20	45/M	2	8	(+)	(+)	(+)	(+)	2

(+) indicates that the calculated increase in annual tumor size ≥1 mm
(-) indicates that the calculated increase in annual tumor size <1 mm

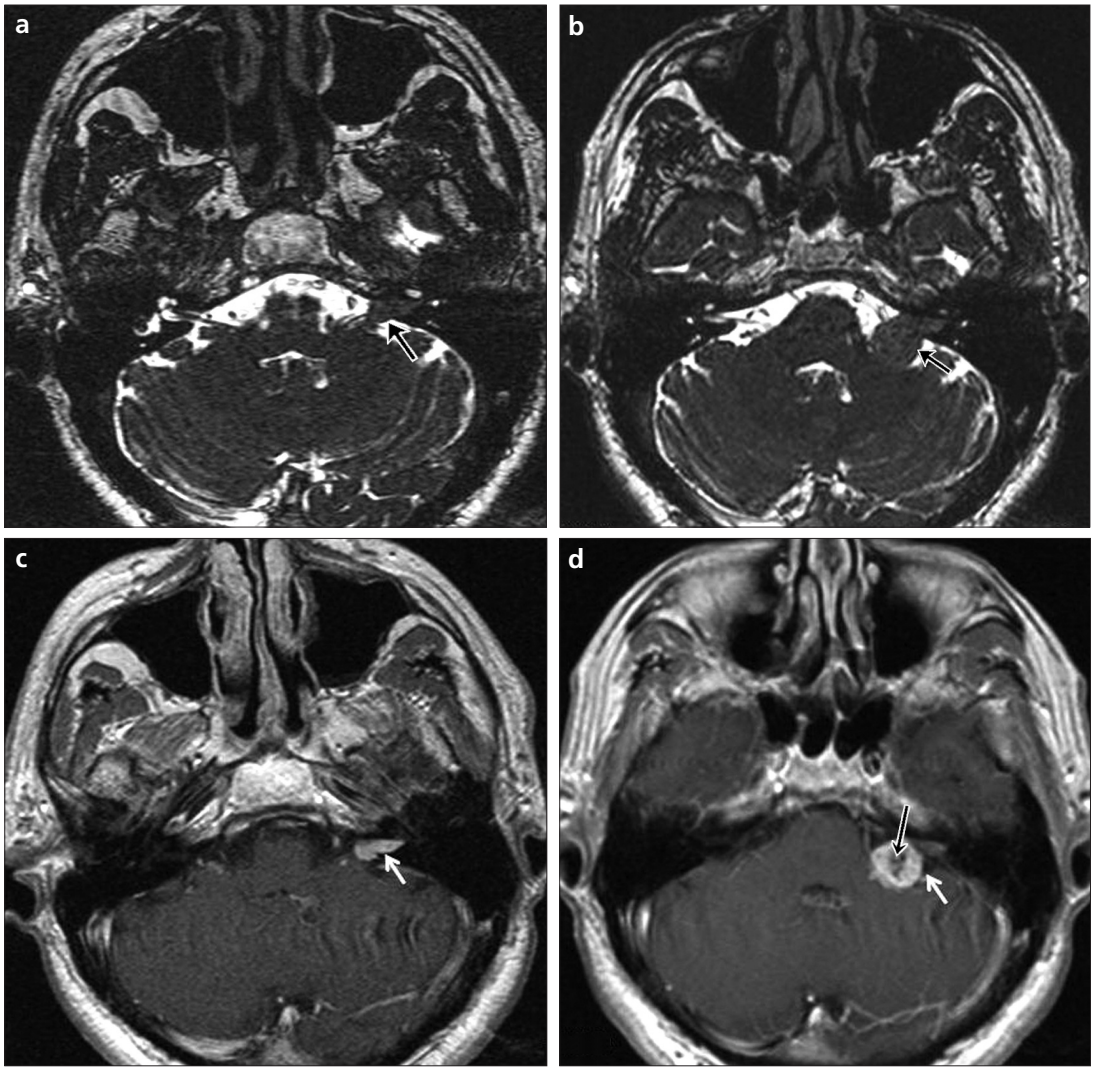

Figure 4. a–d. Axial CISS sequence **(a)** shows a vestibular schwannoma in the left internal acoustic canal *(black arrow)*. The follow-up MRI examination **(b)** 22 months later, shows that the size of the tumor has increased *(black arrow)*. Contrast-enhanced T1-weighted MRI sequences **(c, d)** demonstrate the change in size *(white arrows)*. Additionally, cystic changes that developed in the follow-up period can be detected in this sequence **(d,** *black arrow***)**. This internal structural change cannot be seen in the CISS sequence.

We used the anteroposterior and transverse diameters to assess the tumor size, and we think that this method is more practical than volumetric measurements in daily clinical practice. The annual change in tumor size is the determining factor in the detection of progression. In this study, there were no differences in the tumor size assessments between the two observers using either the CISS or contrast-enhanced T1W sequences. The correlation between observers in progression detection using the CISS sequence was even better than that of the postcontrast sequence in our study (correlation coefficient, 0.945 vs. 0.922)

Patients who had undergone surgery or gamma knife radiosurgery were not included in our study group. It has been reported that temporary tumor enlargement can occur after gamma knife radiosurgery as a biological response to radiation, and this response can complicate the interpretation of the data and might lead to false positive findings (17).

Tumors that are larger at initial presentation typically grow more than smaller tumors (18). The tumors were small in most of our patients (90% had Koos stage 1 and stage 2 tumors), and thus a small number of patients displayed tumor progression. This is a limitation of our study. However, this result was expected because conservative management is the preferred approach in patients with smaller tumors. The mean follow-up period for our patients was 15.3 months. Among the 20 patients, 13 had only one follow-up study. The short follow-up period and the limited number of follow-up studies are additional drawbacks of the study. Studies in the literature have reported that growth rate measurements during the first year of observation are predictive of growth in the following year (9, 19). Therefore, it is important to detect progression in the first follow-up study.

Intratumoral hemorrhages and cystic changes of tumors can develop during the growth of the tumor (20, 21). Cystic changes may also lead to large intratumoral hemorrhages and subarachnoid hemorrhages (22). The internal structure of vestibular schwannomas cannot be determined from the CISS sequence. In one of our patients, significant growth was observed in the follow-up examination using both the CISS and postcontrast sequences. There was also cystic degeneration within the tumor, but this internal cystic change was not apparent on the CISS sequence (Fig. 4). However, the patient group in our study was composed entirely of follow-up patients. If significant

growth is identified on a follow-up MRI examination performed without gadolinium chelate, we think that the patient can always return for a gadolinium-enhanced study if necessary, and any internal structural changes can be determined.

Our study shows that the contrast-free CISS sequence may be an option for regular follow-up examinations of vestibular schwannomas. By avoiding the routine use of gadolinium in patients undergoing a follow up of vestibular schwannomas, the additional cost and side effects of gadolinium can be eliminated.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Salzman KL, Davidson HK, Harnsberger HR, et al. Dumbbell schwannomas of the internal auditory canal. AJNR Am J Neuroradiol 2001; 22:1368–1376.
2. Langenberg R, Bondt BJ, Nelemans PJ, Baumert BG, Stokroos RJ. Follow-up assessment of vestibular schwannomas: volume quantification versus two-dimensional measurements. Neuroradiology 2009; 51:517–524.
3. Raut VV, Walsh RM, Bath AP, et al. Conservative management of vestibular schwannomas –second review of a prospective longitudinal study. Clin Otolaryngol Allied Sci 2004; 29:505–514.
4. Allen RW, Hansberger HR. Low cost high resolution fast spin echo MR of acoustic schwannoma: an alternative to enhanced conventional spin-echo MR? Am J Neuroradiol 1996; 17:1205–1210.
5. Annesley-Williams DJ, Laitt RD, Jenkins JP, Ramsden RT, Gillespie JE. Magnetic resonance imaging in the investigation of sensorineural hearing loss: is contrast enhancement still necessary? J Laryngol Otol 2001; 115:14–21.
6. Wertman R, Altun E, Martin DR, et al. Risk of nephrogenic systemic fibrosis: evaluation of gadolinium chelate contrast agents at four American universities. Radiology 2008; 248:799–806.
7. Ozgen B, Oguz B, Dolgun A. Diagnostic accuracy of the constructive interference in steady state sequence alone for follow-up imaging of vestibular schwannomas. Am J Neuroradiol 2009; 30:985–991.
8. Jorgensen BG, Pedersen CB. Acoustic Neuroma: follow up of 78 patients. Clin Otolaryngol 1994; 19:478–484.
9. Nedzelski JM, Schessel DA, Pfledderer A. Conservative management of acoustic neuromas. Otolaryngol Clin North Am 1992; 25:691–705.
10. Smouha EE, Yoo M, Mohr K, et al. Conservative treatment of acoustic neuroma: a meta–analysis and propsed treatment algorithm. Laryngoscope 2005; 115:450–454.
11. Hoistad DL, Melnik G, NamıkogluB, et al. Update on conservative management of acoustic neuroma. Otol Neurotol 2001; 22:682–685.
12. Stuckey SL, Harris AJ. Detection of acoustic schwannoma: use of constructive interference in the steady state three-dimensional MR. Am J Neuroradiol 1996; 17:1219–1225.
13. Hermans R, Van der Goten A. MRI screening for acoustic neuroma without gadolinium: value of 3DFT-CISS sequence. Neuroradiology 1997; 39:593–598.
14. Goebell E, Ries T, Kucinski T, et al. Screening for cerebellopontine angle tumors: is a CISS sufficient? Eur Radiol 2005; 15:286–291.
15. Fiirgaard B, Pedersen CB, Lundorf E. The size of acoustic neurinomas: CT and MRI. Neuroradiology 1997; 39:599–601.
16. Charabi S, Thomsen J, Mantoni M, et al. Acoustic neurinoma (vestibular schwannoma): growth and surgical and nonsurgical consequences of the wait and see policy. Otolaryngol Head Neck Surg 1995; 113:5–14.
17. Nakamura H, Jokura H, Takahashi K, Boku N, Akabane A, Yoshimoto T. Serial follow up MR imaging after gamma knife radiosurgery for vestibular schwannoma. Am J Neuroradiol 2000; 21:1540–1546.
18. Fucci MJ, Buchman CA, Brackmann DE, et al. Acoustic tumor growth: implications for teratment choices. Am J Otol 1999; 20:495–499.
19. Strasnick B, Glasscock ME, Haynes D, McMenomey SO, Minor LB. The natural history of untreated acoustic neuromas. Laryngoscope 1994; 104:1115-1119.
20. Park CK, Kim DC, Park SH, et al. Microhemorrhage, a possible mechanism for cyst formation in vestibular schwannomas. J Neurosurg 2006; 105:576–580.
21 Ohta S, Yokoyama T, Nishizawa S. Massive haemorrhage into acoustic neurinoma related to rapid growth of the tumour. Br J Neurosurg 1998; 12:455–457.
22. Misra BK, Rout D, Bhiladvala DB, et al. Spontaneous hemorrhage in acustic neurinomas. Br J Neurosurg 1995; 9:219–221.