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The value of diffusion-weighted MR imaging in the diagnosis of primary acquired and residual cholesteatoma: a surgical verified study of 100 patients

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Abstract Our goal was to determine the value of echo-planar diffusion-weighted MR imaging in detecting the presence of primary acquired and residual cholesteatoma. One hundred patients were evaluated by preoperative magnetic resonance (MR) imaging with diffusion-weighted MR imaging. The patient population consisted of a first group of 55 patients evaluated in order to detect the presence of a primary acquired cholesteatoma. In the second group, 45 patients were evaluated for the presence of a residual cholesteatoma 8–18 months after cholesteatoma surgery, prior to second-look surgery. Surgical findings were compared with preoperative findings on diffusion-weighted imaging (DWI). The sensitivity, specificity, positive and negative predictive values of both groups was assessed. In the group of primary surgery patients, hyperintense signal compatible with cholesteatoma was found in 89% of cases with a sensitivity, specificity, positive and negative predictive value for DWI of 81, 100, 100 and 40%, respectively. In the group of second-look surgery patients, only one of seven surgically verified residual cases was correctly diagnosed using DWI, with a sensitivity, specificity, positive and negative predictive values of 12.5, 100, 100 and 72%, respectively. These results confirm the value of DWI in detecting primary cholesteatoma, but show the poor capability of DWI in detecting small residual cholesteatoma.

Keywords Cholesteatoma · Diffusion · EPI-DWI

Introduction

The detection of a primary or residual cholesteatoma with the use of imaging techniques remains challenging. The diagnosis of a primary cholesteatoma is mainly based on clinical suspicion (otoscopic findings, conductive or mixed hearing loss and otorrhea). Imaging can provide additional information concerning extension and ossicular and bony erosion on high-resolution computed tomography (CT). Magnetic resonance (MR) imaging is useful in selected cases for further characterisation of soft tissues and description of possible complications.

The detection of residual cholesteatoma after cholesteatoma surgery with the use of CT and MR imaging techniques has been shown to be inaccurate, due to poor sensitivity of high-resolution CT [1–3] and MR [4–6] imaging. Recent reports, however, suggested the improvement in the MR imaging technique in diagnosing cholesteatoma with the use of delayed contrast-enhanced T1-weighted imaging [7, 8] and echo-planar diffusion-weighted MR imaging [9–14]. The purpose of this study was to evaluate the value of echo-planar diffusion-weighted MR imaging (DWI) using 3 mm thick slices in detecting primary or residual cholesteatoma in a large serie of surgically verified cases.

Materials and methods

Between the 5th March 2001 and the 14th March 2005, MR imaging with DWI was performed on 100 patients suspected to have a middle ear cholesteatoma. Two separate groups were formed based upon the type of performed surgery.

In the first group, 55 patients were referred for MR imaging for a clinically suspected acquired cholesteatoma. In the second group, 45 patients were referred for MR imaging before a planned second stage surgery within 8–18 months after primary cholesteatoma surgery. The primary and second stage cholesteatoma surgery was performed by two

experienced surgeons. Our series consisted of 77 male and 33 female patients with an average age of 28.4 years (median: 23.9 years, range: 5.5–66.5 years). Thirty-one patients of the reported cases were children (≤16 years). All patients underwent MR imaging at an average of 15 days (median: 11 days, range: 1–57 days) prior to second look surgery.

MR imaging

MR imaging was performed with a superconductive 1.5 Tesla machine (Echospeed Horizon, GE Milwaukee, USA), using a circularly polarised head coil. The examination was centred—for all sequences but the 3D FSE T2-weighted images and the diffusion-weighted images—(B0 and B1000) on the affected ear in a small field of view (14 cm) with a saturation band on the contralateral ear.

Coronal FSE T1-weighted images (TR/TE, 475/14; slice thickness 3 mm, spacing 0; matrix, 256×224; 2 NEX; field of view 140×140 mm) and T2- weighted images, (TR/TE, 3,000/102; slice thickness 3 mm, spacing 0; matrix, 256×224; 5 NEX field of view 140×140 cm) axial 3D FSE T2-weighted images (TR/TE,4,000/180:slice thickness 0.8 mm; matrix, 256×256; 2 NEX) and coronal diffusion-weighted images (TR/TE,10,000/88 ms; slice thickness 3 mm; matrix 128×128; *b* value, 0 and 1,000 s/mm; scan time, 40 s) were performed before injection of gadolinium. Parallel imaging techniques were not used, because they were not available on our MR. After injection of gadolinium in a dosage of 0.1 mmol/kg body weight coronal and axial T1-weighted images were obtained.

Radiological interpretation

All DWI images were analysed in consensus by two radiologists with long-standing experience in head and neck radiology. The identity of patients, clinical data and operative results were blinded for the observers. Standard MR sequences were evaluated looking for a moderate hyperintense lesion on T2-weighted images, the characteristic peripheral enhancing cholesteatoma matrix and the central non-enhancing cholesteatoma on T1-weighted images. Cholesteatoma was diagnosed on DWI as a marked hyperintense signal in comparison with brain tissue (B1000). All cases were classified as positive or negative, according to the above-described signal characteristics. The sensitivity, specificity and positive and negative predictive values were assessed.

Results

In the first group of presumed primary acquired cholesteatoma (*n*=55), we found cholesteatoma in 89% (*n*=49). Apparent diffusion coefficient (ADC) values could be evaluated in 20 out of 49 cholesteatomas. Mean ADC values for cholesteatomas and grey matter were 0.844 and 0.837 (10^{-3} mm^2/s), respectively (Table 1). A correct diagnosis was made in 84% (*n*=46) with 40 patients diagnosed as true positives and six patients as true negatives. In nine patients, DWI failed in diagnosing surgically verified cholesteatoma (i.e. false negatives). The size of the primary acquired cholesteatomas ranged from 5 to 21 mm. An additional evaluation of standard MR sequences revealed the detection of two supplementary cholesteatomas in this group of false negatives by identifying a characteristic region of non-enhancing cholesteatoma on gadolinium-enhanced T1-weighted images surrounding by enhancing cholesteatoma matrix. The surgical findings of false negatives cases revealed atelectatic retraction cholesteatoma or partially evacuated cholesteatoma with limited keratin accumulation. No false positives were seen in this group. The sensitivity, specificity, positive and negative predictive values were 81, 100, 100 and 40%, respectively.

In the second group of patients during second look surgery (*n*=45), residual cholesteatoma was found in 17% (*n*=7). In this group, ADC values could not be calculated due the small volume of the lesions (Table 2). A correct diagnosis using DWI was made only in one patient with a residual pearl with a shortest diameter of 6 mm. All other residual pearls detected during the second stage surgery were ≤4 mm. No false positives as well were seen in the second group. The sensitivity, specificity, positive and negative predictive values were 12.5, 100, 100 and 84%, respectively.

Discussion

The detection of primary or residual cholesteatoma with the use of imaging techniques remains challenging for the head and neck radiologist. The primary examination tool for the evaluation of a suspected primary acquired cholesteatoma is still high-resolution CT, as it provides good information on cholesteatoma delineation and extension, delineation of the tympanic segment of the facial nerve, bony erosion and anatomical features such as the delineation of the tegmen and bony labyrinth. MR imaging offers the possibility of using different types of sequences—including diffusion-weighted sequences and post gadolinium T1-weighted images—and different imaging planes. However, after primary surgery, eventual soft tissue extension in the middle ear and mastoidectomy cavity cannot be differentiated by using high-resolution CT [1–3].

MR imaging has been shown to be able to differentiate granulation tissue from cholesteatomatous tissue [15]. Cholesteatoma (congenital, acquired or residual) has been reported to have,in comparison with brain tissue, moderately hyperintense signal intensity on T2-weighted images and an isointense signal intensity on T1-weighted images without or

Table 1 Detailed description of the first study group (n=55) [*m* male, *f* female, *NA* not applicable (absence of cholesteatoma), *X* data not available]

Patients	Gender	Age (years)	Surgical results[a]	DWI[b]	ADC in grey matter (10^{-3} mm^2/s)	ADC in cholesteatoma (10^{-3} mm^2/s)	Enhancement T1 + gadolinium	Cholesteatoma dimension (mm)
1	m	47	+	+	X	X	Peripheral	9
2	f	63	+	+	X	X	Peripheral	13
3	f	14	+	+	X	X	Peripheral	10
4	f	14	+	+	X	X	Peripheral	6
5	f	22	+	+	0.947	0.817	Peripheral	8
6	m	64	+	+	0.82	0.832	Peripheral	14
7	m	43	+	+	0.827	1.07	Peripheral	8
8	f	55	+	+	X	X	Peripheral	8
9	m	58	+	+	0.775	0.703	Peripheral	9
10	m	48	+	+	0.83	0.664	Peripheral	15
11	m	49	+	+	X	X	Peripheral	12
12	m	9	–	–	NA	NA	Complete	NA
13	f	33	+	+	0.859	0.763	Peripheral	17
14	m	71	+	+	X	X	Peripheral	16
15	m	6	+	–	X	X	Peripheral	5
16	m	48	+	+	0.855	1.07	Peripheral	16
17	m	54	+	+	X	X	Peripheral	9
18	m	37	–	–	NA	NA	Complete	NA
19	m	41	+	+	X	X	Peripheral	9
20	m	12	+	–	X	X	Partial	Retraction cholesteatoma
21	m	47	+	+	0.873	1.107	Peripheral	8
22	m	57	–	–	NA	NA	Complete	NA
23	m	50	+	–	X	X	Partial	Partially evacuated cholesteatoma
24	m	21	+	–	X	X	Absent	Retraction cholesteatoma
25	f	46	+	–	0.978	0.74	Peripheral	21
26	f	6	+	+	X	X	Peripheral	8
27	m	49	+	+	X	X	Peripheral	15
28	f	57	–	–	NA	NA	Complete	NA
29	m	8	+	+	X	X	Peripheral	13
30	m	39	+	+	0.849	1.09	Peripheral	13
31	m	32	+	+	0.686	0.992	Peripheral	11
32	f	45	+	–	X	X	Partial	Partially evacuated cholesteatoma
33	f	12	+	–	X	X	Absent	Partially evacuated cholesteatoma
34	m	13	+	+	X	X	Peripheral	13
35	f	51	+	+	0.935	0.783	Peripheral	10
36	m	48	+	+	0.907	0.723	Peripheral	18
37	f	17	+	+	X	X	Peripheral	17
38	m	26	–	–	NA	NA	Complete	NA
39	m	6	+	+	X	X	Peripheral	9
40	m	37	+	+	0.714	0.703	Peripheral	19
41	m	27	+	+	0.989	0.939	Peripheral	15
42	m	37	+	+	0.717	0.89	Peripheral	12
43	f	36	+	+	0.7	0.686	Peripheral	15
44	m	53	–	–	NA	NA	Complete	NA

Table 1 (continued)

Patients	Gender	Age (years)	Surgical results[a]	DWI[b]	ADC in grey matter (10^{-3} mm^2/s)	ADC in cholesteatoma (10^{-3} mm^2/s)	Enhancement T1 + gadolinium	Cholesteatoma dimension (mm)
45	m	4	+	+	X	X	Peripheral	13
46	m	24	+	+	X	X	Partial	8
47	f	8	+	+	X	X	Peripheral	13
48	m	16	+	–	X	X	Peripheral	6
49	f	43	+	+	X	X	Peripheral	10
50	f	51	+	+	0.858	0.688	Peripheral	18
51	f	60	+	+	0.835	0.809	Peripheral	9
52	m	40	+	+	X	X	Peripheral	14
53	m	16	+	–	X	X	Partial	Partially evacuated cholesteatoma
54	m	11	+	–	X	X	Peripheral	5
55	f	49	+	+	0.782	0.811	Peripheral	8

[a]Presence (+) or absence (–) of cholesteatoma
[b]Positive (+) or negative (–) DWI evaluation

with moderate peripheral enhancement after i.v. gadolinium administration [16, 17]. Several reports have shown that standard MR imaging sequences are not able to detect residual cholesteatoma prior to second stage surgery [4–6]. Spin-echo diffusion-weighted MR imaging has primarily been used for the diagnosis of ischemic brain infarction [18], but has recently been described as an additional diagnostic tool in detecting congenital, acquired and residual cholesteatoma [9–14]. Congenital, acquired and residual cholesteatoma appear to have a high signal on diffusion-weighted images. The combination of restricted water diffusion and a T2 shine-through effect is thought to be responsible for high signal intensity on DWI [9, 10]. In our study, calculated ADC values revealed that there was no clear diffusion restriction (Table 1). This supports the hypothesis that a T2 shine-through effect is predominantly responsible for the hyperintensity on DWI. A known additional problem using spin-echo DWI imaging are the artefacts caused by susceptibility disturbances at air-bone interfaces at the skull base. Artefacts appear rim-shaped and are situated preferentially at the position of the tegmen. Furthermore hyperintense signals on spin-echo DWI have a somewhat distorted shape [10]. The use of parallel imaging is able to reduce these artefacts [19].

In our study, a high sensitivity of 81.6% (40/49) and specificity of 100% was obtained when detecting primary acquired cholesteatoma (Fig. 1a,b). These results were very similar to previous results reported by Fitzek et al. [10], supporting the additional value of DWI in detecting presumed primary cholesteatomas. Analysis of our surgical results revealed in the false negative cases (n=9), the presence of an atelectatic retraction cholesteatoma and/or partially

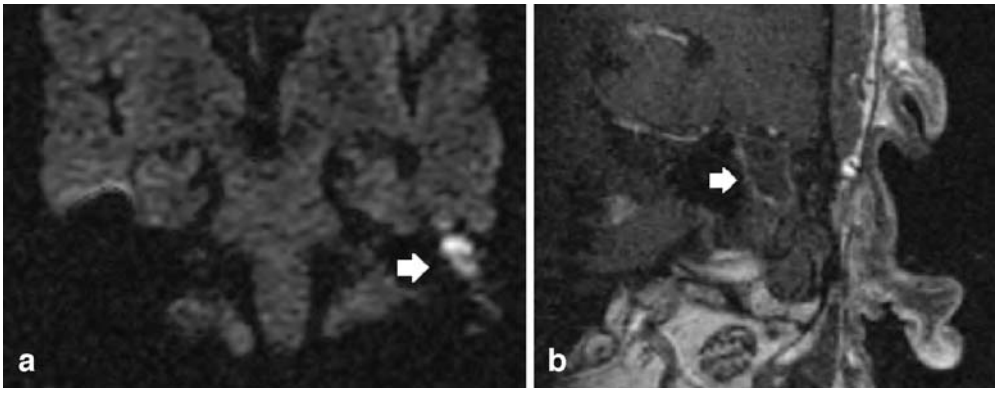

Fig. 1 **a** A 60-year-old male suspected of having a primary acquired middle ear cholesteatoma. Coronal echo-planar DWI shows a clear hyperintens lesion in the left mastoid region under the tegmen (*arrow*). **b** Same patient as in **a**. Corresponding coronal T1-weighted image after gadolinium administration shows a non-enhancing cholesteatoma with peripheral enhancing cholesteatoma matrix (*arrow*). Surgery revealed the presence of a large mastoid cholesteatoma corresponding with MR findings on echo-panar DWI and contrast-enhanced T1-weighted MR images

Table 2 Detailed description of the second study group (n=45) [*m* male, *f* female, *NA* not applicable (absence of cholesteatoma), *NM* ADC not measureable]

Patients	Gender	Age (years)	Surgical results[a]	DWI[b]	ADC Grey matter (10^{-3} mm^2/s)	ADC cholesteatoma (10^{-3} mm^2/s)	Enhancement T1 + gadolinium	Cholesteatoma dimensions (mm)
1	m	6	+	–	NM	NM	Partial	2
2	m	62	–	–	NA	NA	Complete	NA
3	f	18	+	–	NM	NM	Peripheral	3
4	f	7	–	–	NA	NA	Complete	NA
5	m	26	–	–	NA	NA	Complete	NA
6	f	39	–	–	NA	NA	Partial	NA
7	m	47	–	–	NA	NA	Complete	NA
8	m	10	–	–	NA	NA	Complete	NA
9	f	24	–	–	NA	NA	Partial	NA
10	m	45	+	–	NM	NM	Peripheral	4
11	m	17	+	–	NM	NM	Partial	2
12	m	66	–	–	NA	NA	Complete	NA
13	m	10	–	–	NA	NA	Complete	NA
14	f	46	–	–	NA	NA	Peripheral	NA
15	m	50	–	–	NA	NA	Partial	NA
16	m	59	–	–	NA	NA	Complete	NA
17	f	43	–	–	NA	NA	Complete	NA
18	m	8	–	–	NA	NA	Complete	NA
19	m	7	–	–	NA	NA	Complete	NA
20	m	8	–	–	NA	NA	Absent	NA
21	m	17	–	–	NA	NA	Complete	NA
22	m	50	–	–	NA	NA	Complete	NA
23	f	13	–	–	NA	NA	Partial	NA
24	f	34	–	–	NA	NA	Complete	NA
25	m	52	–	–	NA	NA	Partial	NA
26	m	53	–	–	NA	NA	Complete	NA
27	m	5	+	–	NM	NM	Partial	3
28	m	21	–	–	NA	NA	Complete	NA
29	m	11	+	–	NM	NM	Partial	3
30	m	50	–	–	NA	NA	Complete	NA
31	m	11	–	–	NA	NA	Complete	NA
32	m	12	–	–	NA	NA	Complete	NA
33	m	45	–	–	NA	NA	Complete	NA
34	f	8	+	–	NM	NM	Partial	2
35	f	35	–	–	NA	NA	Partial	NA
36	f	13	–	–	NA	NA	Complete	NA
37	m	8	–	–	NA	NA	Partial	NA
38	f	28	–	–	NA	NA	Partial	NA
39	m	40	–	–	NA	NA	Partial	NA
40	m	51	+	+	NM	NM	Peripheral	5
41	f	34	–	–	NA	NA	Partial	NA
42	m	13	–	–	NA	NA	Complete	NA
43	m	24	–	–	NA	NA	Complete	NA
44	m	6	–	–	NA	NA	Partial	NA
45	f	41	–	–	NA	NA	Complete	NA

[a]Presence (+) or absence (–) of cholesteatoma
[b]Positive (+) or negative (–) DWI evaluation

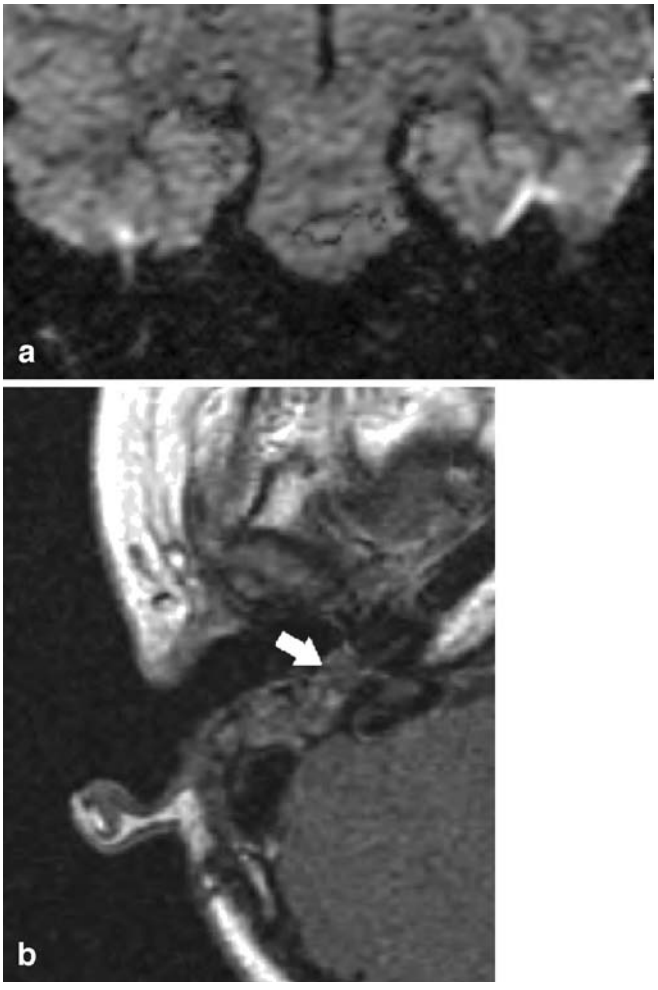

Fig. 2 **a** A 10-year-old boy suspected of having a primary acquired cholesteatoma. Previous MR imaging shows a large curvilinear artefact under the tegmen and middle fossa on both sides on echo-planar DWI. A clear hyperintensity, suggestive for a cholesteatoma was not seen on echo-planar DWI. **b** Same patient as in **a**. Note the hypointense non-enhancing nodular lesion in the retrotympanum on axial contrast-enhanced T1-weighted images suggestive of a cholesteatoma (*arrow*). Surgery revealed the presence of a cholesteatoma in the retrotympanum with a diameter of 5 mm

evacuated cholesteatoma, with limited keratin accumulation, which was similar to the results reported by Fitzek et al. [10].

Additional evaluation of standard MR sequences revealed the detection of two supplementary cholesteatomas in the group of false negatives by visualisation of a non-enhancement on gadolinium enhanced T1-weighted images of the cholesteatoma matrix (Fig. 2a,b). This suggests that the combination of standard MR imaging sequences and diffusion-weighted sequences appears to have a higher sensitivity in detecting middle ear cholesteatoma [13].

In the second group of patients, only one of seven residual cholesteatoma pearls was correctly diagnosed using DWI, with a diameter of 6 mm (Fig. 3a,b). All other residual pearls detected during the second stage surgery were ≤4 mm.

In recent literature, Aikele et al. [9] reported a sensitivity of 77% (10/13) in detecting residual or recurrent cholesteatoma using the combination of standard MR imaging sequences and DWI missing three small residual cholesteatoma pearls (<5 mm). Specificity, positive and negative predictive values of 100%, 100% and 75% were reported [9]. Another recent report by Stasolla et al. [14] reported a sensitivity of 86% (6/7) detecting recurrent cholesteatoma using echo-planar DWI. In their series only one small cholesteatoma of 2 mm was missed, while the size of the other cholesteatomas varied from 4 to 14 mm. Specificity, positive and negative predictive values of 100%, 100% and 92% were reported [14]. In both studies, included patients were clinically suspected of having residual of recurrent cholesteatoma. In comparison, our findings differ signifi-

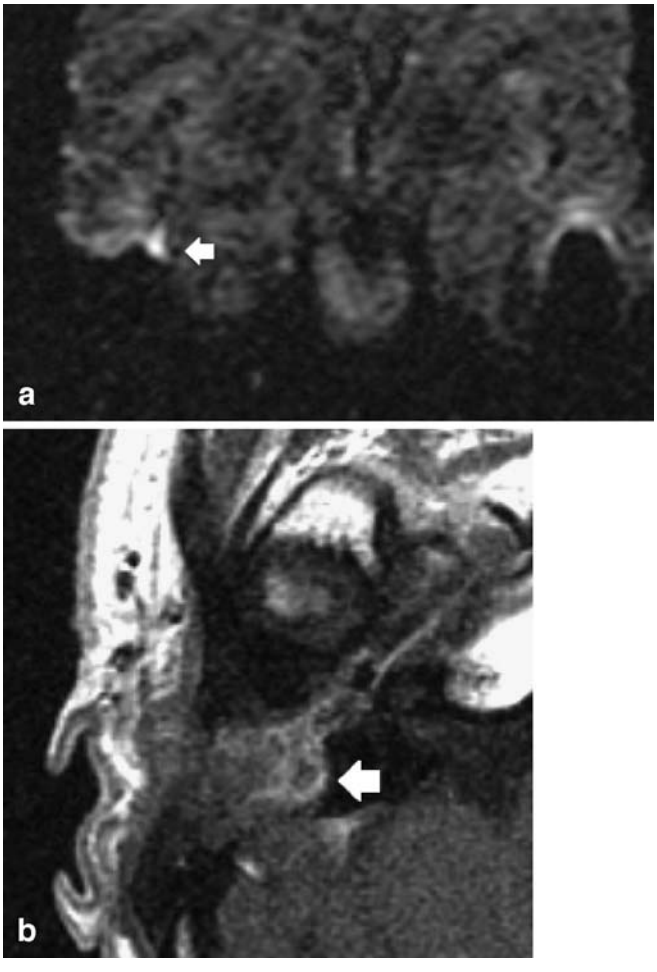

Fig. 3 **a** A 51-year-old male planned for second look surgery. MR imaging prior to second-look surgery shows a nodular hyperintense lesion under the tegmen on echo-panar DWI imaging (*arrow*). **b** Same patient as in **a**. Axial contrast-enhanced T1-weighted MR image shows a peripheral enhancing nodular lesion, suggestive of cholesteatoma. Surgery revealed the presence of a residual cholesteatoma with a diameter of 6 mm

cantly from these studies. In order to exactly evaluate the capability of DWI to detect residual cholesteatoma, we planned 45 consecutive patients for second stage surgery 8–18 months after primary surgery. In this group no recurrent cholesteatoma was suspected. The reason for the higher sensitivity in those two previously reported studies is probably caused by larger size of the recurrent cholesteatoma in these clinically suspected patients. On the basis of these results, we think that the major limitations for detecting cholesteatoma on diffusion-weighted sequences is definitely the size of the lesion (4–5 mm), combined with the low spatial resolution, the relative thick slices and the air-bone artefacts.

Conclusion

On the base of our results, we conclude that DWI has an important role in the evaluation of primary acquired middle ear cholesteatoma. Its sensitivity can be augmented when associated with standard MR imaging sequences. Our results do not confirm the high sensitivity of DWI of previous reports detecting residual cholesteatoma due to the fact that in our study we did not select patients on a clinical basis. We think that at the present time DWI has a limited role in the detection of residual cholesteatoma after primary surgery due to the small size of residual cholesteatoma, the air-bone artefact of DWI at the tegmen, the low resolution and relative thick slices of DWI. With current MRimaging techniques (standard MR imaging sequences and spin-echo echo-planar DWI sequences) second look cannot be replaced by MR imaging. The development of newer non-echo-planar diffusion-weighted sequences with a higher resolution and less susceptibility artefacts in combination with late post contrast T1 images remains to be evaluated in detecting residual cholesteatoma.

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