



# PROPELLER diffusion weighted imaging for diagnosis of cholesteatoma in comparison with surgical and histopathological results: emphasis on false positivity and false negativity

Aslihan Semiz-Oysu<sup>1</sup> · Cagatay Oysu<sup>2</sup> · Fatma Kulali<sup>3</sup> · Yasar Bukte<sup>3</sup>

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## Abstract

**Purpose** To investigate the role of non-echo planar diffusion weighted imaging (DWI) using “periodically rotated overlapping parallel lines with enhanced reconstruction” (PROPELLER) sequence for the diagnosis of cholesteatoma compared to surgical and histopathological results in an attempt to determine the factors causing false negative and false positive diagnoses.

**Methods** Patients who had PROPELLER DWI before ear surgery were retrospectively reviewed. The presence of a lesion with diffusion restriction on PROPELLER DWI was accepted as positive for cholesteatoma, and the results were compared to the intraoperative and histopathological findings.

**Results** A total of 112 ears in 109 patients were reviewed. On PROPELLER DWI, a lesion with diffusion restriction was found in 101 (90.2%) ears, while in 11 (9.8%) of the patients, no diffusion restriction was found. Surgery and histopathological analysis revealed a cholesteatoma in 100 (89.3%) ears, while in 12 (10.7%) ears, no cholesteatoma was found surgically. There were 96 (85.7%) true positives, 7 (6.2%) true negatives, 5 (4.5%) false positives and 4 (3.6%) false negatives. The accuracy, sensitivity, specificity, positive predictive and negative predictive values of non-echo planar DWI were calculated to be 91.96%, 96%, 58.33%, 95.05%, and 63.64%, respectively.

**Conclusion** Non-echo planar DWI using PROPELLER sequence has high accuracy, sensitivity and positive predictive value and can be used for the detection of cholesteatoma. The external auditory canal, postoperative ears and small lesions should be evaluated with caution to avoid false results.

**Keywords** Cholesteatoma · Diffusion weighted magnetic resonance imaging · Temporal bone · Diagnostic imaging · Otolgic surgical procedures

## Introduction

Cholesteatoma is a common destructive lesion of the middle ear and mastoid, consisting of keratinized squamous epithelium [1]. Cholesteatomas are categorized into two types; the acquired cholesteatomas are more commonly encountered

and associated with chronic or repeated infections, while congenital cholesteatomas are rare and already present at birth [2]. One of the most widely accepted theories for the development of acquired cholesteatomas is the formation of a retraction pocket, which is an inward pouch in the tympanic membrane towards the middle ear, caused by negative pressure due to various factors including Eustachian tube dysfunction or chronic ear infections [1, 2]. As a consequence of epithelial ingrowth and entrapment within the retraction pocket, progressive growth and accumulation of keratin debris eventually leads to the formation a cholesteatoma in the middle ear. Tendency for recidivism, identified as the residual or recurrent disease following surgical treatment, remains a significant challenge in the management of patients with cholesteatoma [3].

When there is a clinical suspicion of cholesteatoma, differentiation from other possible soft tissue lesions, such as

✉ Aslihan Semiz-Oysu  
asoysu@gmail.com

<sup>1</sup> Department of Radiology, Marmara University School of Medicine, Istanbul, Turkey

<sup>2</sup> Department of Otorhinolaryngology and Head and Neck Surgery, Marmara University School of Medicine, Istanbul, Turkey

<sup>3</sup> Department of Radiology, University of Health Sciences, Umraniye Training and Research Hospital, Istanbul, Turkey

inflammatory tissue, granulation, secretions, or cholesterol granuloma, may not be possible by physical examination alone and by routine imaging, including computed tomography (CT) and magnetic resonance imaging (MRI) [3–5]. Diffusion-weighted imaging (DWI) has been shown to be useful in cholesteatoma diagnosis and differentiation from other soft tissue lesions by revealing diffusion restriction due to its keratin content [6–8]. Although echo-planar imaging is the most commonly used DWI technique, susceptibility artifacts caused by air-bone interfaces limit its use in the temporal bone [5]. Non-echo planar DWI has improved image quality by marked reduction in susceptibility artifacts and image distortion as well as the acquisition of thinner slices to allow better spatial resolution [5, 9]. Many studies are found in the literature on the use of non-echo planar DWI in the detection of cholesteatoma; a recent meta-analysis on non-echo planar DWI reported an overall sensitivity of 92.2% (95% CI 87.3–95.3%) and specificity of 91.7% (85.2–95.5%) [6].

Nevertheless, a variety of different non-echo planar DWI sequences have been used, such as ‘half Fourier acquisition single shot turbo spin echo’ (HASTE) and ‘periodically rotated overlapping parallel lines with enhanced reconstruction’ (PROPELLER) [9–19]. The multishot turbo spin-echo (MSTSE) sequences (e.g. PROPELLER) can be acquired in a shorter time compared to single-shot turbo spin-echo (SSTSE) sequences (e.g. HASTE), and therefore are less susceptible to motion artifacts and misregistration errors in slice position [20, 21]. Because these technical differences between non-echo planar DWI sequences can affect accuracy, the role and effectiveness of each individual sequence for cholesteatoma detection must be documented. A limited number of studies have reported the diagnostic accuracy of the PROPELLER sequence thus far, however the largest study group included 54 ears, and others included less ranging between 15 and 35 patients [9–16]. There was a wide range of results for sensitivity between 75 and 100%, specificity between 60 and 100%, positive predictive value between 76 and 100%, and negative predictive value between 43 and 100% and the reason for the variation in these reported values may be the relatively small sample sizes [9–16].

The purpose of this study was to investigate whether non-echo planar DWI using the PROPELLER sequence can be used alone as a reliable technique for detection of a cholesteatoma. For this reason, we evaluated the results of PROPELLER DWI in a large cohort in comparison to surgical and histopathological results. We also aimed to document the false-positive and false-negative PROPELLER DWI results in an attempt to determine the factors causing misdiagnoses.

## Materials and methods

Patients who had a temporal bone MRI including a PROPELLER DWI with a clinical suspicion of middle ear cholesteatoma were retrospectively searched on the hospital records between 2014 and 2018. Only those who had undergone surgery and had histopathological results were included in the study. Patients who had MRIs with extensive motion artifacts to preclude evaluation were excluded. The study protocol was approved by the institutional ethical board.

Magnetic resonance imaging was performed in all patients on a 1.5 T scanner (Optima 450 W, GE Healthcare, Milwaukee, USA) using a head and neck coil with 16 channels. The PROPELLER DWI and apparent diffusion coefficient map were in the axial plane with following parameters:  $b = 0$  and 1000, repetition time/echo time 3000/85, echo train length 16, field of view 24 cm, matrix  $128 \times 128$ , slice thickness 3 mm, gap 0.5, NEX 1.5.

The MRI images were reviewed by two radiologists (one dedicated head and neck radiologist and one general radiologist with more than 10 years of experience) in consensus blinded to the surgical and histopathological results. The presence or absence of a lesion with diffusion restriction on PROPELLER DWI was noted and when present accepted as MRI positive for cholesteatoma. Diffusion restriction was defined as a markedly increased signal intensity on  $b = 1000$  images that was brighter than the neural parenchyma on the same image, with a corresponding low intensity on the apparent diffusion coefficient map. These findings were compared to the surgical and histopathological results. Intraoperative and histopathological findings were accepted as the final diagnosis for a cholesteatoma. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the PROPELLER DWI sequence were calculated.

## Results

Our search of the hospital records revealed 309 patients who had a temporal bone MRI, including PROPELLER DWI, with a clinical suspicion of cholesteatoma. Of these, a total of 112 ears in 109 patients were operated on and included in the study. The patients consisted of 42 women and 67 men whose ages ranged between 7 and 80 years (mean: 36.8 years). Thirty-one ears in 28 patients were previously operated on for a cholesteatoma and were evaluated for recidivism.

On the PROPELLER DWI sequence, a lesion with diffusion restriction was found in 101 (90.2%) ears, while

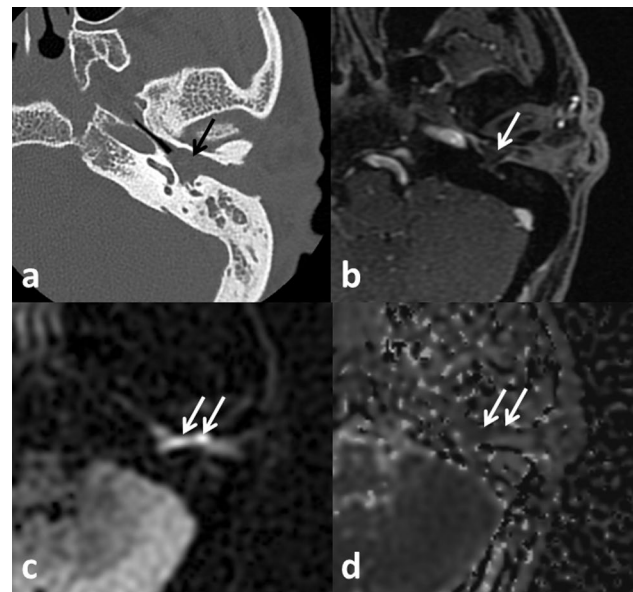
in 11 (9.8%) of the patients, no diffusion restriction was found (Figs. 1, 2). The size of the lesions varied between 4 and 39 mm (mean 13.95 mm) on MRI. The PROPELLER DWI diagnosis of cholesteatoma was confirmed by intra-operative and histopathological results in 96 (85.7%) ears. Surgery and histopathological analysis revealed a cholesteatoma in 100 (89.3%) ears, while in 12 (10.7%) ears, no cholesteatoma was found surgically and histopathologically. There was no discrepancy in surgical and histopathological findings in regard of a cholesteatoma. The alternative diagnoses in true negative ears were polyp in 2 ears, granulation tissue in 3 ears, histiocytosis in 1 ear and glomus tumor in 1 ear. There were 96 (85.7%) true positives, 7 (6.2%) true negatives, 5 (4.5%) false positives and 4 (3.6%) false negatives (Table 1). The accuracy, sensitivity, specificity, positive predictive value and negative predictive value of PROPELLER DWI were calculated to be 91.96%, 96%, 58.33%, 95.05%, and 63.64%, respectively.

There were five patients with a false positive MRI result; surgery and histopathological examination revealed polyps in three and granulation tissue in one and both polyp and granulation tissue in one. In two of these, diffusion restriction was at the external auditory canal, in three at the middle ear. One of the false positive patients had a history of trauma and none of them had a history of surgery. False negativity was present in 4 patients. One patient had a 3.5 mm lesion in the external auditory canal, and one had a lesion 2.5 mm in size in the middle ear as measured on other imaging studies, but there was no diffusion restriction on PROPELLER DWI. Another false negative patient had a history of previous mastoidectomy for cholesteatoma and showed recurrence surgically and histopathologically. The remaining false negative patient revealed retracted epithelium only at surgery instead of a frank soft tissue lesion. The features of patients with false negative and positive results on PROPELLER DWI are summarized in Table 2.

**Table 1** Diagnostic accuracy of non-echo planar diffusion weighted imaging using PROPELLER<sup>1</sup> sequence

Diagnostic accuracy	Value %	95% CI %
Sensitivity	96.00	90.07–98.90
Specificity	58.33	27.67–84.83
Disease prevalence	89.29	82.03–94.34
Positive predictive value	95.05	90.76–97.41
Negative predictive value	63.64	37.45–83.65
Accuracy	91.96	85.29–96.26

<sup>1</sup>PROPELLER: Periodically rotated overlapping parallel lines with enhanced reconstruction

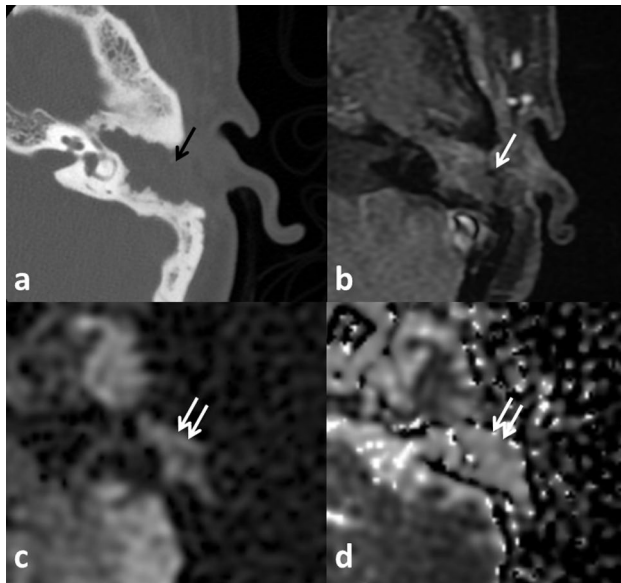


**Fig. 1** False positivity: 43 year old male with a polyp as diagnosed by surgery and histopathology **a** Axial computed tomography shows a soft tissue lesion filling the middle ear and the external auditory canal (black arrow). **b** Contrast enhanced T1-weighted fat saturated magnetic resonance image shows a soft tissue mass without contrast enhancement (white arrow). **c** PROPELLER diffusion weighted imaging demonstrates false diffusion restriction (double arrows) and **d** low signal on the corresponding apparent diffusion coefficient map (double arrows)

## Discussion

Despite the widely accepted use of non-echo planar DWI for cholesteatoma detection, there are various non-echo planar DWI sequences. The multishot turbo spin-echo (MSTSE) sequences (e.g. PROPELLER) appear to have advantages over single-shot turbo spin-echo (SSTSE) sequences (e.g. HASTE), owing to shorter acquisition time, less susceptibility to motion artifacts and less misregistration errors in slice position [20, 21]. We present a large cohort with surgically and histopathologically confirmed results in 112 ears using PROPELLER DWI. The accuracy, sensitivity, specificity, positive predictive value and negative predictive value of PROPELLER DWI are found to be 91.96%, 96%, 58.33%, 95.05%, and 63.64%, respectively.

Non-echo planar DWI has been successful for the detection of cholesteatoma recurrence after mastoidectomy and has been recommended as an alternative for second-look surgery [6]. However, bone or cartilage grafts, bone pate, silastic sheets, etc., from previous surgery were previously described to be responsible for false positivity [17, 18, 22]. One study found that recidivism detection is poor following reconstruction with autologous bony prostheses and concluded that second-look surgery may still be necessary in such patients [15]. When diffusion restriction on non-echo



**Fig. 2** False negativity: 44 year old female with a history of mastoidectomy is found to have recidivism by surgery and histopathology. **a** Axial computed tomography reveals soft tissue density (black arrow) filling the mastoidectomy cavity. **b** Contrast enhanced T1-weighted fat saturated magnetic resonance image shows a soft tissue mass without contrast enhancement (white arrow). **c** PROPELLER diffusion weighted imaging demonstrates no diffusion restriction (double arrows) and **d** high signal on the corresponding apparent diffusion coefficient map (double arrows)

planar DWI is present in postoperative patients with cartilage grafts, a decrease in the size and intensity of the suspected lesion on a follow-up scan at 6–12 months supports false positivity [22]. Another study retrospectively evaluating 11 false-positive cases suggested that DWI MRI should be used in conjunction with the patient's clinical picture and other radiological findings [23]. In our series, none of the false-positive ears had a history of mastoidectomy, however,

one patient with a previous mastoidectomy showed a false-negative diagnosis. Other causes of false positivity were reported as cholesterol granuloma, tympanosclerosis, granulation tissue, otitis media, artifacts, and keratin-containing substances such as cerumen [23]. One false-positive patient in our study had a previous history of trauma and showed false diffusion restriction in the middle ear. To the best of our knowledge, a history of trauma has not been reported before among false-positive cases.

External auditory canal appears to be another caveat of non-echo planar DWI for false diagnosis. External auditory canal lesions may have challenging appearances, and cerumen may be confused with cholesteatoma on non-echo planar DWI [11]. In the study by Kasbekar et al., it was reported that the observers detected more false-positive cholesteatomas by the use of the PROPELLER sequence, and in one patient, this could possibly be due to the difficulty in anatomical localization of the external auditory canal lesion [11]. In our study, two patients with a false-positive diagnosis had an external auditory canal lesion falsely diagnosed as cholesteatoma on PROPELLER DWI, and one patient with a false-negative diagnosis had a 3.5 mm cholesteatoma in the external auditory canal, which was missed on PROPELLER DWI. Anatomical localization problems can be overcome by evaluating non-echo planar DWI in conjunction with conventional CT and MRI images before planning surgery. It has been shown that the anatomic detail obtained via CT-DWI fusion images increased the sensitivity and specificity of PROPELLER DWI alone [16].

Non-echo planar DWI can acquire thin slices free of air-bone susceptibility artefacts and distortion; slices as thin as 2 mm by HASTE and 3 mm by PROPELLER allow detection of small cholesteatomas, however lesions without enough keratin content to generate diffusion restriction can be missed [20]. This can be either due to small size or retracted epithelium without keratin content. Previous

**Table 2** False positive and false negative results on non-echo planar DWI\*

	Age	History	Non-echo planar DWI*	Surgery and histopathology	Lesion size
False positive					
1	41	None	Diffusion restriction in middle ear	Polyp	9 mm
2	29	None	Diffusion restriction in middle ear	Granulation tissue	8 mm
3	43	None	Diffusion restriction in EAC**	Polyp	17 mm
4	33	Trauma	Diffusion restriction in middle ear	Polyp and granulation tissue	12 mm
5	26	None	Diffusion restriction in EAC**	Polyp	22 mm
False negative					
1	31	None	Negative	Retracted epithelium in middle ear	N/A***
2	80	None	Negative	Cholesteatoma in EAC**	3.5 mm
3	44	Mastoidectomy	Negative	Cholesteatoma in middle ear	N/A***
4	13	None	Negative	Cholesteatoma in middle ear	2.5 mm

\*DWI: Diffusion weighted imaging, \*\*EAC: external auditory canal, \*\*\*N/A: not available

studies reported that false negative results by non-echo planar DWI could be attributed to small (< 5 mm) cholesteatomas, retractions without soft tissue and artifacts [8, 10, 24]. Furthermore, false positive results were also found to have smaller size than true positives and it is recommended to approach cases with small DWI hyperintensity with caution to avoid unnecessary surgical interventions [25]. One pediatric study using HASTE DWI reported that the majority of lesions were correctly detected, but small cholesteatomas could not be excluded [19]. This contradicts studies reporting the detection of cholesteatomas as small as 3 or 4 mm using the PROPELLER sequence [10, 11]. In our series, we also noted diffusion restriction in cholesteatomas as small as 4 mm in the largest diameter. In our series, false negativity was found in 4 patients, and two of these were very small (< 4 mm). Additionally, one cholesteatoma showed retracted epithelium only at surgery, because of the absence of any keratinous bulk within the epithelium there was no restriction of diffusion and thus it was undetectable on PROPELLER DWI.

As per our study protocol, only the patients who had surgery were included in the study, and therefore, all of our patients had a clinical or radiological indication for surgery. Because of the lack of inclusion of all true negative patients, the specificity and negative predictive value were found to be lower than expected. However, we believe that the actual specificity of the technique should be higher. To determine the specificity and the actual true negative results of the PROPELLER DWI technique, larger studies with long-term follow-up are needed.

Our study has some limitations. First, this was a retrospective study. Prospective studies with long-term follow-up results may be more valuable to address the actual role of PROPELLER DWI in precluding unnecessary surgery. Another limitation is that diffusion restriction was evaluated visually, but apparent diffusion coefficient values were not measured. Measuring apparent diffusion coefficient values in each lesion may provide a more objective evaluation; however, this is not commonly used in daily practice, and we wanted to document the results of an easy and quick method of evaluation that could easily be applied in routine practice.

## Conclusion

Non-echo planar DWI using the PROPELLER sequence has high accuracy, sensitivity and positive predictive value and can be used for the detection of cholesteatoma. However, the external auditory canal, postoperative ears and small lesions should be evaluated with caution to avoid false results.

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**Data Availability** Available upon request.

## Declarations

**Conflict of interest** The authors have no relevant financial, non-financial or competing interests to disclose.

**Ethical approval** This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of Umranıye Training and Research Hospital approved this study and due to the retrospective nature informed consent was waived.

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