



## ORIGINAL ARTICLE

# Non-Echo-Planar Versus Multishot Echo-Planar Diffusion-Weighted Imaging in Diagnosis of Suspected Cholesteatoma

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## ABSTRACT

**Background:** Cholesteatoma is a destructive middle ear lesion that can cause serious complications if not accurately detected and treated. Diffusion-weighted imaging (DWI) has become the standard noninvasive tool for diagnosis. This study aimed to compare the diagnostic performance of non-echo-planar (non-EPI) DWI and multishot echo-planar (EPI) DWI in patients with suspected cholesteatoma, using histopathology as the gold standard.

**Methods:** This cross-sectional study included 18 patients with clinically suspected cholesteatoma referred for MRI between January and December 2024. All patients underwent both non-EPI and multishot EPI DWI sequences on a 1.5T scanner. Two blinded neuroradiologists independently assessed images, and results were compared with intraoperative and histopathological findings.

**Results:** The mean lesion size was  $108.1 \pm 110.3$  mm<sup>2</sup> with an average maximal diameter of 13.5 mm. Offensive otorrhea was the most frequent symptom (61.1%), followed by loss of balance (50%) and tinnitus (50%). Non-EPI DWI detected 14/16 histopathology-proven cholesteatomas (sensitivity 87.5%) and falsely classified 2/2 histopathology-negative cases as positive (specificity 0%); overall accuracy 77.8% and PPV 87.5% ( $p = 0.01$ ). Median lesion size detected was 36.5 mm<sup>2</sup> (range 6–105). Interobserver agreement was moderate ( $\kappa = 0.52$ ). Multishot EPI DWI classified 3/18 cases as positive; relative to histopathology this yielded 3 true positives, 0 false positives, and 13 false negatives (2 true negatives): sensitivity = 18.8% (3/16), specificity = 100% (2/2), PPV = 100% (3/3), NPV = 13.3% (2/15), accuracy = 27.8% (5/18) ( $p = 0.50$ , not significant). Median lesion size was 45 mm<sup>2</sup> (range 30–60). The agreement with histopathology was poor ( $\kappa = 0.05$ ). The difference in lesion size detection between techniques was statistically significant ( $p = 0.04$ ), favoring non-EPI DWI.

**Conclusions:** The present pilot study suggests that non-EPI DWI may offer superior sensitivity and diagnostic accuracy compared with multishot EPI DWI in diagnosing middle ear cholesteatoma, particularly for small lesions.

**Keywords:** Non-Echo-Planar; Multishot Echo-Planar; Diffusion-Weighted Imaging; Cholesteatoma

## INTRODUCTION

Cholesteatoma of the middle ear is an abnormal growth of keratinizing

squamous epithelium that can arise congenitally or, less frequently, as an acquired condition. As the lesion expands, it

progressively erodes adjacent osseous structures including the ossicles, labyrinth, fallopian canal, and the bony plate of the middle cranial fossa [1].

A second-look surgery is often considered about one year after the initial operation, depending on the intraoperative findings and disease extent, to evaluate residual disease and to reconstruct the ossicular chain when necessary. Radiological imaging plays a critical role in both initial diagnosis and postoperative surveillance, and in some cases may reduce the need for repeated surgical exploration [2].

Over the years, diffusion-weighted imaging (DWI) has become the key non-invasive tool for detecting cholesteatoma. Conventional single-shot echo-planar imaging (EPI) is limited by susceptibility artifacts and difficulty detecting lesions smaller than 4–5 mm. To overcome these issues, non-echo-planar (non-EPI) DWI was developed, capable of depicting lesions as small as 2 mm with fewer artifacts. Multishot EPI techniques such as readout-segmented EPI (RESOLVE) have also emerged, aiming to reduce distortion while retaining reasonable scan times. However, few studies have directly compared non-EPI DWI with modern multishot EPI in a controlled clinical setting[4]. To overcome these limitations, non-EPI DWI methods were developed, capable of detecting lesions as small as 2 mm while minimizing artifacts and geometric distortion. Multishot (MS) EPI has also been investigated, offering reduced image distortion at the expense of longer scan times, although classic single-shot EPI is no longer favored for this indication [5].

Despite the growing evidence on advanced DWI techniques, there remains debate regarding which approach provides the most reliable balance between diagnostic accuracy, image quality, and clinical practicality in suspected cholesteatoma.

Most available studies have evaluated non-EPI DWI in comparison to single-shot EPI, while fewer have directly compared non-EPI with multishot EPI in a controlled clinical setting. Therefore, additional evidence is required to clarify whether non-EPI or multishot EPI DWI should be considered the superior standard in preoperative and postoperative assessment of cholesteatoma. Therefore, the aim of this research was to compare the accuracy of non-EPI DWI versus multishot EPI DWI in the diagnosis of cholesteatoma.

## METHODS

This cross-sectional study was conducted at the Radiodiagnosis Department, of our University Hospitals, within the MRI unit, over a period of one year from January 2024 to December 2024. Patients who were clinically suspected of having middle ear cholesteatoma and were referred for MRI evaluation were considered for inclusion. Out of the total 24 patients initially recruited, 6 were excluded due to either poor image quality or not meeting inclusion criteria, leaving 18 patients for final analysis. Eight of these patients had prior temporal bone CT examinations, which were reviewed to complement MRI assessment.

The sample size was based on the number of eligible patients referred during the 12-month study period; no formal power calculation was performed because this was designed as a pilot study aimed at generating preliminary data for future larger trials.

The study protocol was approved by the Institutional Review Board of Zagazig University (ZU-IRB#342/7-May-2024). Written informed consent was obtained from all participants before enrollment. All procedures were performed in accordance with the Declaration of Helsinki and patient confidentiality was maintained throughout the study.

Patients of all ages and both sexes were eligible if they demonstrated specific

otoscopic/endoscopic findings highly suggestive of cholesteatoma, including a keratin-filled retraction pocket, persistent foul-smelling otorrhea, and/or crust in external auditory canal or polypoid mass in the middle ear on otoscopy/endoscopy, in accordance with established clinical diagnostic criteria[4]. Exclusion criteria involved poor-quality MRI scans significantly degraded by artifacts such as motion; patients with known malignancy; and cases with contraindications to MRI, such as pacemakers or cochlear implants.

#### **Imaging Technique:**

MRI examinations were performed using a 1.5 tesla American GE creator (closed MRI) with a dedicated head coil. Both non-echo-planar DWI (non-EPI DWI) and multishot echo-planar DWI were obtained for each patient prior to surgery. The multishot EPI protocol was a readout-segmented echo-planar imaging (RESOLVE) DWI sequence performed on a 1.5 T GE scanner using parallel imaging (ASSET) to minimize distortion. Sequence-specific parameters for both non-EPI and RESOLVE DWI are detailed in **Supplementary Table 1**. Standard T1-weighted and T2-weighted sequences were also performed for anatomical correlation.

For the Non EPI diffusion-weighted imaging sequences, acquisition was performed using thin contiguous slices with a thickness of 3–4 mm and no interslice gap, providing adequate spatial resolution. The imaging matrix was set at  $128 \times 128$ , ensuring a balance between resolution and acquisition time. Repetition and echo times were optimized for each sequence, typically within a TR of 3000–4000 ms and TE of 80–100 ms. A field of view of  $180 \times 180$  mm was applied, maintaining appropriate coverage of the region of interest. Diffusion sensitivity was achieved using two b-values (0 and 1000 s/mm<sup>2</sup>), allowing for both

baseline and diffusion-weighted contrast assessment.

#### **Image Interpretation:**

All imaging datasets were independently reviewed by two experienced neuroradiologists with more than 10 years of expertise in head and neck imaging. The radiologists were blinded to each other's findings and to the surgical/histopathology results at the time of review.

Interpretation was standardized as follows: lesions were considered positive for cholesteatoma when they demonstrated marked hyperintensity on DWI with corresponding low ADC values. Lesions isointense or hypointense without diffusion restriction were considered negative [4].

#### **Reference Standard:**

All imaging findings were compared with intraoperative and histopathological results, which served as the diagnostic gold standard.

#### **Data Analysis:**

Diagnostic performance of each technique (non-EPI vs. MS-EPI DWI) was assessed by calculating sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy. Agreement between the two radiologists was measured using Cohen's kappa statistic.

#### **Statistical analysis:**

Data were analyzed using descriptive statistics, with quantitative variables presented as mean  $\pm$  SD, median, and range, and qualitative variables as frequencies and percentages. The Lesion size between non-EPI and EPI was compared using the paired Wilcoxon test, while paired comparisons of sensitivity and specificity between non-EPI and multishot EPI sequences were performed using Crohn's Kappa agreement test. Statistical significance was set at  $p < 0.05$ . All statistical analyses were performed using SPSS version 22.

RESULTS

This cross-sectional pilot study included 18 cases—6 males and 12 females—who were clinically suspected to have cholesteatoma, age of the studied cases ranged from 8 to 50 years with mean 29.83 years. Regarding sex, 66.7% were females, all cases had unilateral lesion, 55.6% of the cases had in left side while 44.4% had in right side. Lesion size ranged from 17 to 338 mm<sup>2</sup> with a median of 73 mm<sup>2</sup>. Most frequent clinical findings among the studied cases were offensive discharge (61.1%) followed by loss of balance (50%) and tinnitus in ear (50%). Sensation of ear fullness, crust n EAC and unhealthy mucosa of middle ear all were reported in 33.3% of the cases while unhealthy and perforation of tympanic membrane were found in 27.8% of the cases. Decrease hearing accuracy founded in 16.7% of them and tenderness behind ear in 11.1% (**Table 1**).

Non-EPI DWI demonstrated a wider range of detectable lesion sizes (6–105 mm; median 36.5 mm) compared to EPI DWI (30–60 mm; median 45 mm). The difference was statistically significant (p = 0.04), highlighting the superior sensitivity of non-EPI DWI, particularly in identifying smaller cholesteatomas that may be overlooked on EPI sequences (**Table 2**).

Table 3 shows that by non-EPI DWI, 88.9 % of cases demonstrated restricted diffusion, whereas by multishot EPI DWI only 16.7 % of cases did so, with a non-statistically significant agreement between the two

techniques (**Table 3**). As detailed in Table 4, of the 16 patients with positive non-EPI DWI findings, 14 were confirmed to have cholesteatoma (true positives) while 2 did not (false positives).

Histopathological evaluation confirmed cholesteatoma in most cases, with keratin detected in 88.9% of specimens, whereas only 11.1% revealed granulation tissue. the two patients without cholesteatoma, histopathology demonstrated granulation tissue with inflammatory changes.

When compared with histopathology as the gold standard, non-EPI DWI demonstrated markedly higher diagnostic performance than EPI. Non-EPI achieved a sensitivity of 87.5% and accuracy of 77.8%, with a significant agreement (K = 0.52, p = 0.01), though specificity was 0% due to false positives. In contrast, EPI showed limited diagnostic utility, with sensitivity of only 18.8% and accuracy of 27.8%, despite a specificity of 100% and perfect PPV, but with poor overall agreement (K = 0.05, p = 0.50). Multishot EPI DWI classified 3/18 cases as positive; relative to histopathology this yielded 3 true positives, 0 false positives, and 13 false negatives (2 true negatives): sensitivity = 18.8% (3/16), specificity = 100% (2/2), PPV = 100% (3/3), NPV = 13.3% (2/15), accuracy = 27.8% (5/18) (p = 0.50, not significant). (**Table 4**).

Representative cases highlighting the superior visualization of cholesteatoma on non-EPI DWI compared with multishot EPI DWI are shown in **Figures 1–3**.

**Table (1):** Demographic data, Side, size of lesion, and Clinical findings of the studied cases (n=18)

| Variable     |         | (n=18)      |      |
|--------------|---------|-------------|------|
| Age: (years) | Mean±SD | 29.83±14.07 |      |
|              | Median  | 30          |      |
|              | Range   | 8-50        |      |
| Variable     |         | Number      | %    |
| Sex:         | Male    | 6           | 33.3 |
|              | Female  | 12          | 66.7 |

| Variable                          |                            | (n=18)                        |              |
|-----------------------------------|----------------------------|-------------------------------|--------------|
| Side:                             | Right<br>Left              | 8<br>10                       | 44.4<br>55.6 |
| Size: (mm <sup>2</sup> )          | Mean±SD<br>Median<br>Range | 108.06±110.26<br>73<br>17-338 |              |
| Variable                          |                            | Number                        | %            |
| Offensive discharge:              | No<br>Yes                  | 7<br>11                       | 38.9<br>61.1 |
| Loss of balance:                  | No<br>Yes                  | 9<br>9                        | 50<br>50     |
| Sensation of ear fullness:        | No<br>Yes                  | 12<br>6                       | 66.7<br>33.3 |
| Decreasing hearing accuracy       | No<br>Yes                  | 15<br>3                       | 83.3<br>16.7 |
| Tinnitus:                         | No<br>Yes                  | 9<br>9                        | 50<br>50     |
| Crust n EAC:                      | No<br>Yes                  | 12<br>6                       | 66.7<br>33.3 |
| Unhealthy mucosa of middle ear:   | No<br>Yes                  | 12<br>6                       | 66.7<br>33.3 |
| Unhealthy tympanic membrane:      | No<br>Yes                  | 13<br>5                       | 72.2<br>27.8 |
| Perforation of tympanic membrane: | No<br>Yes                  | 13<br>5                       | 72.2<br>27.8 |
| Tenderness behind ear:            | No<br>Yes                  | 16<br>2                       | 88.9<br>11.1 |

SD: Standard deviation

**Table (2):** Size in non-EPI& EPI among the studied cases

| Variable                   |                 |                          |
|----------------------------|-----------------|--------------------------|
| Non-EPI (mm <sup>2</sup> ) | Median<br>Range | (n=16#)<br>36.5<br>6-105 |
| EPI (mm <sup>2</sup> )     | Median<br>Range | (n=3#)<br>45<br>30-60    |
| Paired Wilcoxon            |                 | 2.01                     |
| P                          |                 | 0.04*                    |

Sizes summarized among cases classified positive on each sequence (Non-EPI n = 16; EPI n = 3).NS: non significant (P>0.05)

**Table (3):** Signal intensity in non-EPI& EPI among the studied cases (n=18)

| Variable |                      | (n=18)  |      |
|----------|----------------------|---------|------|
|          |                      | No      | %    |
| Non-EPI: | No restriction       | 2       | 11.1 |
|          | Restricted diffusion | 16      | 88.9 |
| EPI:     | No restriction       | 15      | 83.3 |
|          | Restricted diffusion | 3       | 16.7 |
| K        |                      | 0.05    |      |
| P        |                      | 0.50 NS |      |

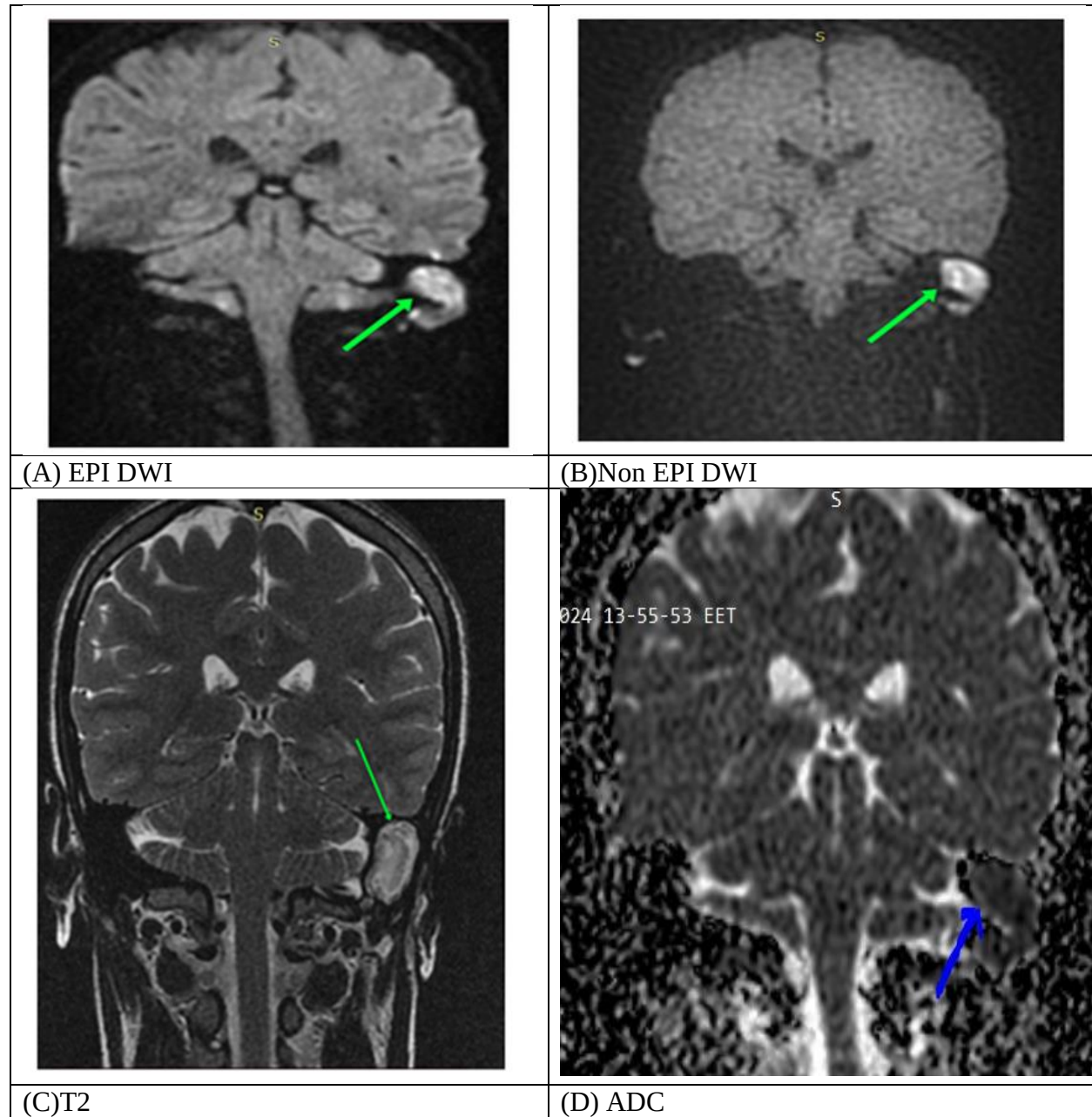
K: Crohn's Kappa agreement test, NS: non-significant (P>0.05)

**Table (4):** Validity of Non-EPI and EPI in diagnosis of Cholesteatoma in comparison to histopathology as a gold standard among the studied case (n=18)

| Non-EPI      |                     |                                                                    |                     |                      |      |            |
|--------------|---------------------|--------------------------------------------------------------------|---------------------|----------------------|------|------------|
| Variable     |                     | Histopathology                                                     |                     | Total<br>(n=18)      | K    | P          |
|              |                     | Cholesteatoma                                                      | No<br>Cholesteatoma |                      |      |            |
| Non-<br>EPI: | Cholesteatoma       | 14                                                                 | 2                   | 16                   | 0.52 | 0.01*      |
|              | No<br>Cholesteatoma | 2                                                                  | 0                   | 2                    |      |            |
| Total        |                     | 16                                                                 | 2                   | 18                   |      |            |
|              |                     | Sensitivity= 87.5%<br>0%<br>PPV= 87.5%<br>0%<br>Accuracy=77.8%     |                     | Specificity=<br>NPV= |      |            |
| EPI          |                     |                                                                    |                     |                      |      |            |
| Variable     |                     | Histopathology                                                     |                     | Total<br>(n=18)      | K    | P          |
|              |                     | Cholesteatoma                                                      | No<br>Cholesteatoma |                      |      |            |
| EPI:         | Cholesteatoma       | 3                                                                  | 0                   | 3                    | 0.05 | 0.50<br>NS |
|              | No Cholesteatoma    | 13                                                                 | 2                   | 15                   |      |            |
| Total        |                     | 16                                                                 | 2                   | 18                   |      |            |
|              |                     | Sensitivity= 18.8%<br>100%<br>PPV= 100%<br>13.3%<br>Accuracy=27.8% |                     | Specificity=<br>NPV= |      |            |

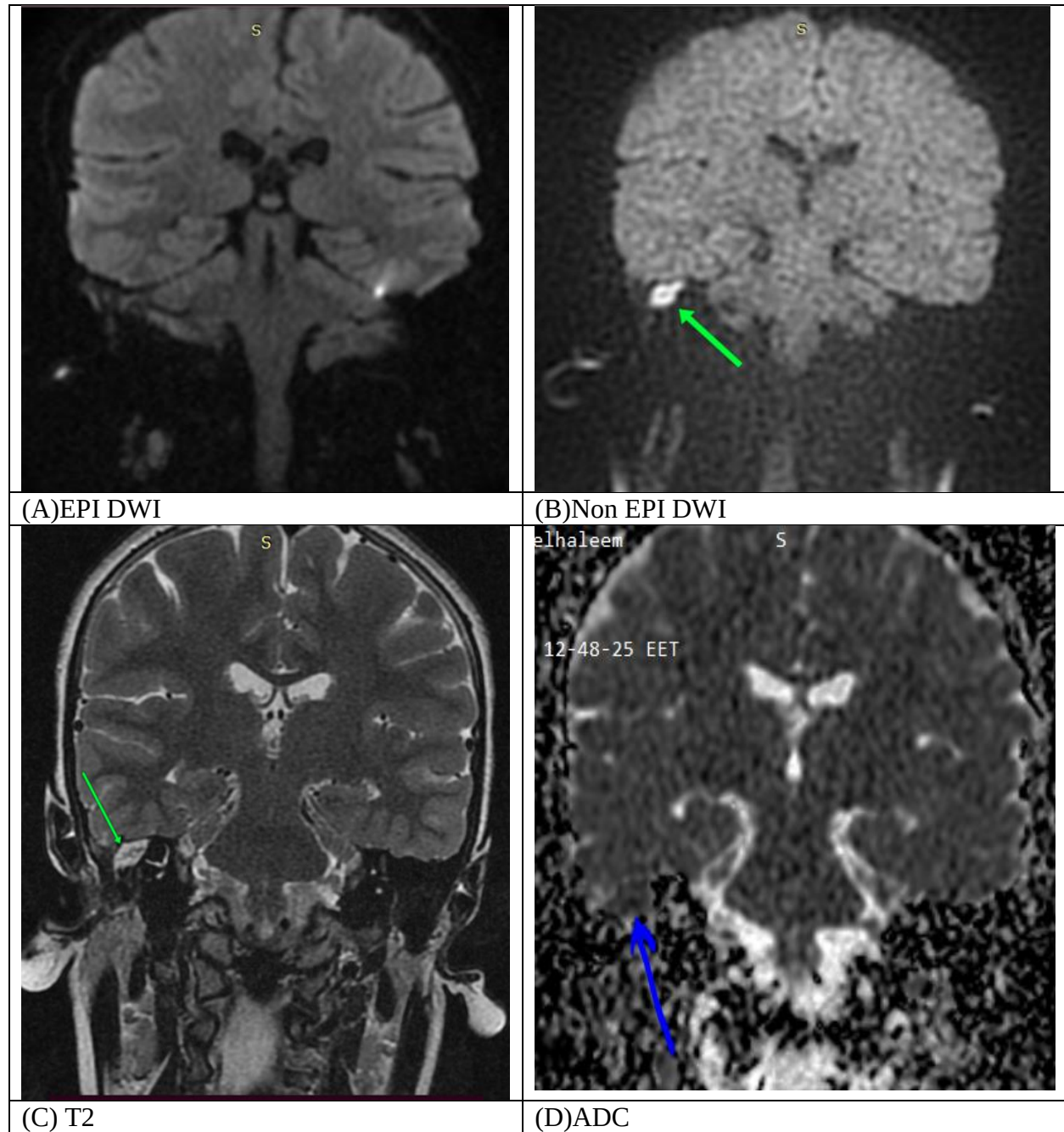
K: Crohn's Kappa agreement test, \*: Significant (P<0.05), PPV: Positive predicted value, NPV: Negative predicted value.





**Figure 1:** Female patient 30 years old had Cholesteatoma (A): EPI DWI: there is a lesion of increased signal intensity measuring 10x3mm on EPI- DWI and decreased signal intensity in ADC in left middle ear, (B): Non-EPI DWI: there is lesion of increased signal intensity measuring 8x3mm in Non-EPI DWI and decreased signal intensity in ADC in the left

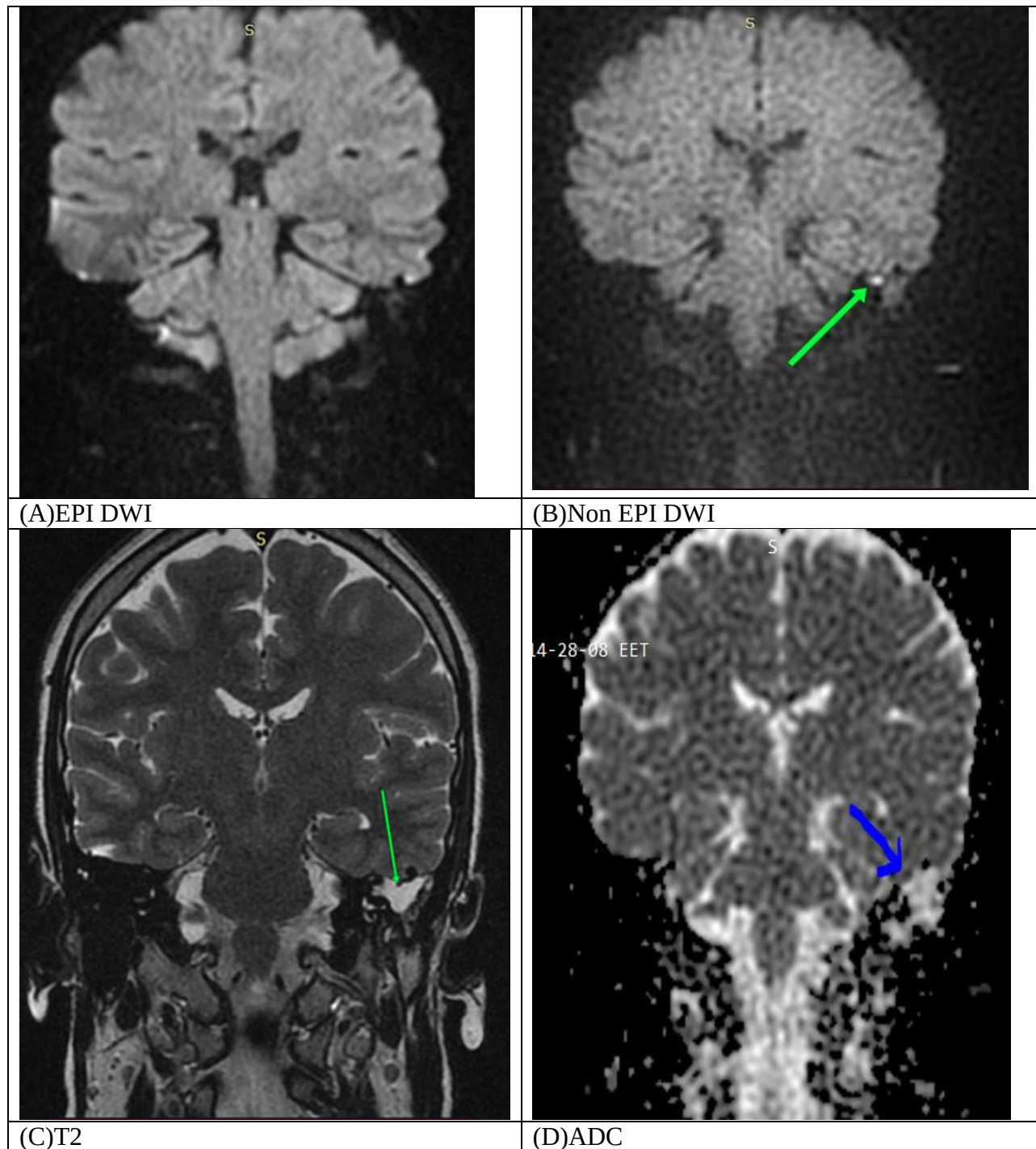
middle ear, (C): MRI:T2: abnormal high signal intensity lesion seen in left middle ear cavity measuring 12x4mm. Histopathological examination confirmed cholesteatoma. (D): Coronal ADC map demonstrating a focal area of low signal intensity (restricted diffusion) in the left middle ear (blue arrow) measuring 10x3mm.



**Figure 2:**Female patient 8 years old had cholesteatoma (A): EPI DWI: lesion cannot properly visualized (no diffusion restriction), (B): Non-EPI DWI: there is a well-defined lesion in right middle ear measuring 13x7mm of increased signal intensity in Non-EPI DWI and decreased signal intensity in ADC, (C): MRI:T2: abnormal increased signal intensity lesion in

right middle ear measuring 14x7mm. Histopathological examination confirmed cholesteatoma, (D): Coronal ADC map showing a lesion with low signal intensity (restricted diffusion) measuring 13x7mm in the right middle ear (blue arrow), .





**Figure 3:** Female patient 27 years old had cholesteatoma (A): EPI DWI: lesion cannot properly visualized (no diffusion restriction). (B): NON-EPI DWI: there is well defined lesion measuring 3x0.5mm of increased signal intensity in Non-EPI DWI and low signal intensity in ADC in left middle ear, (C): MRI:T2: abnormal

increased signal intensity lesion in left middle ear cavity measuring 17x1mm. Histopathological examination confirmed cholesteatoma, (D): Coronal ADC map showing lesion of low signal intensity (restricted diffusion) measuring 3x0.5mm in the left middle ear (blue arrow)..

## DISCUSSION

In the present study, the mean age of patients with cholesteatoma was  $29.8 \pm 14.1$  years (range, 8–50 years), which is consistent with Rosito et al. [6], who noted that while the disease may occur at any age, it is most frequently diagnosed in adults, particularly those in their third and fourth decades of life.

A female predominance was observed in the current study (66.7% vs. 33.3% males). This finding contrasts with the large-scale UK Biobank analysis by Wilson et al. [7], who reported a slight male predominance (odds ratio = 1.33) among nearly 490,000 participants. However, Keita et al. [8] reported a more balanced sex distribution, with some cohorts even showing female predominance. Such variability may be related to demographic differences, referral patterns, or healthcare accessibility across populations.

Lesion size in the current research was relatively large, with an average size of 108 mm<sup>2</sup> on T2-weighted imaging and a median diameter of 13.5 mm. This is clinically important, as Song et al. [9] demonstrated that cholesteatomas  $\geq 4$  mm were associated with worse prognosis and more extensive disease. The predominance of larger lesions in this study may reflect late clinical presentation, which is common in developing countries.

Regarding clinical presentation, 61.1% of patients in the present study presented with foul-smelling ear discharge, which was the most frequent complaint. This aligns with Rutkowska et al. [10], who emphasized that persistent, offensive otorrhea is typically the earliest and most common manifestation of cholesteatoma. Other symptoms in our series included loss of balance (50%), tinnitus (50%), ear fullness (33.3%), and hearing loss (16.7%). Less frequent features included tympanic membrane perforation (27.8%), unhealthy mucosa (33.3%), and

postauricular tenderness (11.1%). These findings collectively support the notion that cholesteatoma presents with a wide clinical spectrum, though otorrhea and progressive conductive hearing loss remain the hallmark features.

From a diagnostic perspective, the present study demonstrated that non-EPI DWI achieved a sensitivity of 87.5% and an overall accuracy of 77.8%, with a statistically significant agreement with histopathology ( $p = 0.01$ ). In contrast, multishot EPI DWI showed a markedly lower sensitivity of 18.8% and an overall accuracy of only 27.8%, despite achieving a specificity of 100% ( $p = 0.50$ , not significant). Notably, the median lesion size detected by non-EPI DWI was 36.5 mm<sup>2</sup>, compared to 45 mm<sup>2</sup> for EPI, with a significant difference ( $p = 0.04$ ). These findings underscore the superior diagnostic performance of non-EPI sequences, particularly in identifying smaller lesions that are often missed by multishot EPI.

An important limitation is the 0% specificity of non-EPI DWI in our series, as both histopathology-negative cases were falsely interpreted as positive. This likely reflects postoperative or inflammatory changes that can mimic restricted diffusion. Such false positives underscore the need to interpret non-EPI DWI in conjunction with clinical and operative findings to avoid unnecessary re-exploration. This low specificity inevitably downgrades the clinical utility of non-EPI DWI when used in isolation, as false-positive interpretations could lead to unwarranted surgical exploration. Therefore, non-EPI findings should be correlated with otoscopic, clinical, and operative data before recommending re-intervention.

While our findings confirm the superior sensitivity of non-EPI DWI, the specificity in our cohort (0 %) differs markedly from the high values reported by Romano et al. (100 %) and Díaz Zufiaurre et al. (96.4 %)

[11,12]. This discrepancy likely reflects the small sample size and the presence of two histopathology-negative cases interpreted as positive, possibly due to postoperative or inflammatory changes mimicking cholesteatoma. Consequently, our specificity estimate should be viewed as preliminary and underscores the need for larger, multicenter studies to accurately define the diagnostic performance of non-EPI DWI.

A focused review of the two histopathology-negative cases revealed that both specimens contained granulation tissue with inflammatory changes and keratin debris, without evidence of cholesteatoma. Each lesion exhibited high signal on non-EPI DWI and low ADC values, imaging features that can mimic true cholesteatoma. Similar false-positive diffusion restriction has been attributed to inflammatory or proteinaceous material and postoperative changes in prior reports. These findings reinforce the importance of correlating diffusion imaging with clinical and operative findings to avoid unnecessary surgical exploration.

Although non-EPI DWI offers superior sensitivity and spatial resolution, several well-recognized pitfalls limit its specificity. Postoperative changes, cholesterol granuloma, proteinaceous effusion, and inflammatory granulation tissue can all exhibit high signal intensity and low ADC values, closely mimicking cholesteatoma and leading to false-positive interpretations[12]. Such factors were likely responsible for the false positives in our cohort. These limitations underscore the necessity of integrating non-EPI findings with detailed clinical assessment, otoscopic examination, and surgical correlation before recommending re-exploration.

The current research findings are supported by Díaz Zufiaurre et al. [12], who conducted a retrospective cohort study including 63 post-mastoidectomy patients with a mean age of 41 years, and demonstrated that non-

EPI DWI achieved excellent diagnostic performance with 100% sensitivity and 96.4% specificity. Similarly, in the present study, non-EPI DWI yielded a high sensitivity of 87.5% and an overall accuracy of 77.8%, confirming its value as a reliable diagnostic tool when compared with histopathology. In contrast, multi-shot EPI DWI in our series demonstrated poor sensitivity (18.8%) and limited accuracy (27.8%), with non-significant correlation to histopathology ( $p = 0.50$ ), indicating its limited clinical utility.

Our findings are in line with Piekarek et al. [13], who assessed 32 suspected cases of cholesteatoma and reported that EPI sequences misdiagnosed between 27–31% of cases, showing poor agreement with histopathology. In the same study, non-EPI DWI successfully detected all cases, achieving perfect concordance with surgical findings. This highlights the superior diagnostic capability of non-EPI over EPI techniques, particularly in smaller lesions that are easily overlooked.

Dudau et al. [14] also provided supportive evidence, reviewing 358 MRI examinations in 285 patients. Their comparison revealed that non-EPI DWI had superior predictive values compared to EPI, with PPV and NPV of 94% and 80%, respectively, versus 93% and 70% for EPI. This again underscores the higher reliability of non-EPI for both detection and exclusion of disease.

In agreement with these observations, Benson et al. [15] demonstrated that non-EPI DWI outperformed multi-shot EPI in both primary and recurrent cholesteatoma detection, accurately identifying all cases. Multi-shot EPI, however, produced equivocal results in over 20% of cases and missed two cholesteatomas entirely. Importantly, Benson et al. [15] also noted that smaller lesions were disproportionately missed on EPI, while non-EPI consistently depicted lesions more accurately and with

larger measured dimensions. This finding is consistent with the established detection threshold of approximately 2 mm for non-EPI DWI, a threshold that provides significant clinical value in early disease recognition.

Similarly, Bazzi et al. [16] conducted a systematic review and meta-analysis in children, confirming that non-EPI DWI achieves very high sensitivity and specificity, frequently exceeding 90%. This level of accuracy translates into reduced reliance on invasive second-look procedures and greater confidence in longitudinal follow-up. High interobserver agreement was also observed, supporting the reproducibility of non-EPI as a robust diagnostic technique in clinical practice.

In contrast, EPI DWI sequences including single-shot and multishot techniques such as RS-EPI have repeatedly been shown to exhibit lower sensitivity and higher false-negative rates, particularly for lesions under 4–5 mm. Lingam et al. [17] emphasized that despite technical improvements, EPI remains more vulnerable to susceptibility artifacts and geometric distortion at the skull base, ultimately reducing diagnostic confidence. In comparison, non-EPI offers superior image quality, higher negative predictive values, and greater overall accuracy, making it the preferred imaging sequence for the reliable detection of cholesteatoma and guiding clinical decision-making.

This study offers several strengths, notably its comprehensive head-to-head comparison of non-EPI and multishot EPI DWI for the diagnosis of cholesteatoma, with histopathology serving as the reference standard. The design minimized inter-patient variability and incorporated blinded review by two experienced neuroradiologists, which reduced interpretation bias. The study also provides well-structured clinical data, including analysis of symptomatology and

lesion size, adding valuable clinical context to the imaging findings. Importantly, the results are interpreted in light of current literature, reinforcing the established superiority of non-EPI in terms of sensitivity, diagnostic accuracy, and artifact reduction.

The relatively small sample size, dictated by the low referral rate and stringent inclusion criteria during the study period, inherently limits statistical power and external generalizability. Future multicenter studies with larger cohorts are warranted to confirm and expand upon these findings. In addition, the lack of long-term follow-up restricts assessment of recurrence or delayed disease detection. Variations in lesion size, patient demographics, and imaging protocols across published studies also challenge direct comparisons with external data. Furthermore, the single-center design may introduce referral bias, and interobserver variability although moderate for non-EPI remains a consideration in clinical interpretation.

Larger multicenter prospective studies are warranted to validate these results, establish standardized imaging protocols, and identify imaging characteristics on non-EPI DWI that help differentiate cholesteatoma from other diffusion-restricting pathologies such as granulation tissue, cholesterol granuloma, or post-operative changes. Such work will be essential to improve specificity while maintaining the high sensitivity demonstrated in the current pilot study.

## CONCLUSIONS

The present pilot study suggests that non-EPI DWI may offer superior sensitivity and diagnostic accuracy compared with multishot EPI DWI in diagnosing middle ear cholesteatoma, particularly for small lesions. These preliminary findings warrant confirmation in larger, multicenter cohorts before definitive clinical recommendations can be made.



### Conflict of Interest & Funding Statement:

This work was completed independently, with no external funding, and the authors report no competing interests.

**Data Availability:** Requests for access to the underlying data that substantiate the results of this study may be directed to the corresponding author, who will consider providing them in accordance with institutional policies and applicable ethical guidelines.

**Author contribution:** Z.A. contributed significantly to the formulation of the research hypothesis and provided key insights during the planning and interpretation phases. H.F.A.T. offered critical revisions and strategic guidance throughout the study. M.H.S. supported the technical execution of imaging analysis and ensured methodological consistency. A.Y.A.Y. conducted patient data collection, organized imaging sessions, performed statistical analysis, and drafted the manuscript. All authors reviewed and validated the final draft. A.Y.A.Y. acting for managing communications and submission logistics.

**Supplementary material:** Table supplementary 1 (S1)

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### Supplementary material:

#### Table supplementary 1 (S1): MRI DWI Parameters Comparison

| Parameter                 | Non-EPI DWI                              | EPI DWI                                                               |
|---------------------------|------------------------------------------|-----------------------------------------------------------------------|
| Slice thickness           | 3 mm                                     | 3 mm                                                                  |
| Inter-slice gap           | None                                     | None                                                                  |
| Matrix size               | 128 × 128                                | 128 × 128                                                             |
| TR (repetition time)      | 3000–4000 ms                             | 7000–9000 ms                                                          |
| TE (echo time)            | 8–100 ms                                 | 80–120 ms                                                             |
| b-values                  | 2 values (0 and 1000 s/mm <sup>2</sup> ) | 1000 s/mm <sup>2</sup>                                                |
| FOV (field of view)       | 180 × 180 mm                             | 220 × 260 mm                                                          |
| NEX                       | 4                                        | 2                                                                     |
| Bandwidth                 | Moderate (100–200 kHz)                   | High (200–300 kHz)                                                    |
| SNR                       | Lower                                    | Higher                                                                |
| Artifact / susceptibility | Minimal susceptibility distortion        | Significant susceptibility distortion (esp. near air–bone interfaces) |
| Scan time                 | Moderate/long (≈3–6 min)                 | Short (≈30–60 sec)                                                    |

DWI: Diffusion-Weighted Imaging, EPI: Echo-Planar Imaging, TR: Repetition Time, TE: Echo Time, FOV: Field of View, NEX: Number of Excitations, SNR: Signal-to-Noise Ratio

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