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Original Article

# Fusion of Diffusion-Weighted Magnetic Resonance Imaging and High-Resolution Computed Tomography Scan As a Preoperative Tool for Classification of Middle Ear Cholesteatoma

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**BACKGROUND:** The role of imaging in cholesteatoma continues to evolve with excellent bony details provided by high-resolution computed tomography and high soft tissue identification for cholesteatoma by diffusion-weighted magnetic resonance imaging. The fusion of high-resolution computed tomography and diffusion-weighted magnetic resonance imaging combines the advantages of both imaging techniques.

**METHODS:** A random sample of 40 consecutive patients with chronic suppurative otitis media with cholesteatoma was included in this study. Both high-resolution computed tomography of the petrous bone and non-echoplanar diffusion-weighted magnetic resonance imaging were performed. This was followed by their fusion. Patients were classified according to The European Academy of Otology and Neurotology, in cooperation with the Japanese Otological Society Joint Consensus Statement on the Definitions, Classification, and Staging of Middle Ear Cholesteatoma. All patients were operated, and the technique was tailored according to the data obtained from the preoperative fusion of computed tomography and diffusion-weighted magnetic resonance imaging and the intraoperative findings.

**RESULTS:** Patients were equally divided between males and females with a mean age of 26.8 years of which 52.5% were left-sided ears. The fusion of high-resolution computed tomography and diffusion-weighted magnetic resonance imaging had a 100% sensitivity and 88.9% specificity regarding The European Academy of Otology and Neurotology, in cooperation with the Japanese Otological Society classification. On the other hand, it showed 100% specificity and 100% sensitivity for all middle ear subsites except sinus tympani which obtained 55.56% sensitivity and 100% specificity. In all patients with preoperative fusion showing cholesteatoma not reaching the mastoid antrum (30%), exclusive endoscopic approach was employed, and no postauricular incision was needed.

**CONCLUSION:** The fusion of high-resolution computed tomography and diffusion-weighted magnetic resonance imaging images is an accurate tool for localizing cholesteatoma in various middle ear cleft subsites. This makes it a valuable tool for cholesteatoma classification and staging and surgical planning preoperatively.

**KEYWORDS:** Ear surgery, middle ear surgery, minimal invasive surgery, otology

## INTRODUCTION

Cholesteatoma is a cystic lesion containing accumulated keratin and squamous debris.[1] It is diagnosed mainly clinically.[2] Nevertheless, it may be obscured by a polyp or granulation tissue, making it challenging to visualize during examination.[3]

High-resolution computed tomography (HRCT) is still the most sensitive modality for the detection of middle ear (ME) cholesteatoma and its extensions. Conversely, it has poor specificity since it cannot distinguish between different types of opacifications.[4-10]

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Magnetic resonance imaging (MRI) with intravenous (IV) gadolinium permits good discrimination between granulation tissue and cholesteatoma. Though the difference remains unclear as both show no enhancement.[5,11]

Based on these disadvantages, diffusion-weighted MRI was introduced. It comprises 2 methods, namely, echoplanar diffusion-weighted (DW) MRI imaging (EPI DWI) and non-echoplanar diffusion-weighted (DW) MRI imaging (non-EPI DWI). Both methods do not need contrast injection.[5-10]

Previous studies mostly used the EPI DWI. However, later, non-EPI DWI was introduced and was proven to be less susceptible to artifacts, allowing thinner slices and higher imaging matrix. This permitted more precise detection of small-sized cholesteatoma.[12-14]

Nonetheless, non-EPI DW does not visualize the anatomical landmarks of the ME and mastoid. Therefore, the fusion of HRCT and DWMRI combines the accuracy of soft tissue recognition of diffusion-weighted images and the anatomical precision of the HRCT images.[15]

Through offering a detailed map of cholesteatoma in relation to the middle ear cleft's anatomical landmarks, fusion of HRCT and DWMRI opens the way for patients to have better counseling about their disease extent and available surgical options. For the surgeon, it provides more data allowing accurate surgical planning.[16]

The European Academy of Otology and Neurotology, in cooperation with the Japanese Otological Society (EAONO/JOS) working group, established a staging system that applies to 4 types of ME cholesteatoma: congenital cholesteatoma, pars tensa cholesteatoma, pars flaccida cholesteatoma, and cholesteatoma secondary to a tensa perforation.[1]

The staging system goes as follows:[1]

**Stage I**: Cholesteatoma in 1 site.

**Stage II**: Cholesteatoma present in 2 or more sites.

**Stage III**: Cholesteatoma plus extracranial complications.

**Stage IV**: Cholesteatoma plus intracranial complications.

## MAIN POINTS

- The fusion of high-resolution computed tomography and diffusion-weighted magnetic resonance imaging (HRCT and DWMRI) could be used as a tool for preoperative detection and localization of cholesteatoma according to The European Academy of Otology and Neurotology, in cooperation with the Japanese Otological Society classification.
- Oto-endoscopy is very valuable for intraoperative staging and looking around the corners for cholesteatoma, especially in hidden recess of the retro-tympanum.
- Cholesteatoma passing the antrum of the mastoid is beyond reach of the endoscopy and an additional incision (post-auricular or endaural) and mastoidectomy could be needed in this case.
- The fusion of HRCT and DWMRI thus could help predict a higher possibility of additional post-auricular or endaural incision and have better counseling with the patient.

**Divisions of the Middle Ear Space (STAM System)**

The middle ear and mastoid space are separated into 4 sites: tympanic cavity (T), attic (A), mastoid (M), and difficult sites (S). These difficult sites (S) include the supratubal recess (S1) and the sinus tympani (S2). The posterior limit of the attic is the posterior end of the incus short process or the fossa incudis. The mastoid represents the mastoid cells and the antrum.[5]

The present study aimed to locate cholesteatoma by the fusion of HRCT and DWMRI and to classify it preoperatively and then compare it with the intraoperative findings.

## METHODS

This was a prospective study conducted on 40 consecutive patients who presented to our outpatient clinic with chronic suppurative otitis media with cholesteatoma over the period from January 2019 to December 2020. All patients have signed informed consent for both enrolment in the study and the performance of surgery. Board of ethics approval in our institution was also obtained (serial number: 0105856). Patients without cholesteatoma (no diffusion restriction) and previous history of mastoid surgery or trauma were excluded from the study.

Non-contrast-enhanced high-resolution CT scan of the petrous bone (Canon, 64 Slices, Japan) was performed using a slice thickness of 0.5 mm and a reconstruction interval of 0.3 mm.

Non-echoplanar diffusion-weighted MRI was used (Siemens Avanto, Germany). Axial and coronal views using a 1.5T closed magnet were performed using a slice thickness of 2.3 mm. Coronal T2W and axial T1W sequences were added to help anatomical localization.

The fusion of CT and non-echoplanar diffusion-weighted MRI was conducted using Osirix MD DICOM viewer version 3 using the image fusion function with the help of anatomical landmarks for co-registration.

Patients were classified according to EAONO/JOS Joint Consensus Statement on the Definitions, Classification, and Staging of Middle Ear Cholesteatoma.[1]

In all patients, tympanoplasty with or without mastoidectomy was performed. Surgery was either totally endoscopic (TEES, total endoscopic ear surgery) or microscopic-assisted endoscopic ear surgery.

Endoscopes used were 0°, 30°, and 45° lenses of 3-mm-diameter (Karl Storz, Tuttlingen, Germany). The video equipment consisted of Image 1S camera (Karl Storz) and a high-definition monitor. Microscope used was OPMI (S7) Sensera, Carl Zeiss, Jena, Germany.

Depending on data from the preoperative fusion of HRCT and DWMRI and intraoperative findings, if cholesteatoma was not reaching the antrum or beyond the lateral semi-circular canal (LSCC), decision was taken to perform surgery exclusively endoscopic (TEES). On the other hand, if cholesteatoma was reaching the antrum or beyond the LSCC, surgery was done by endoscopic-assisted microscopic ear surgery performing a retro-auricular incision and mastoidectomy (Figure 1A and B).

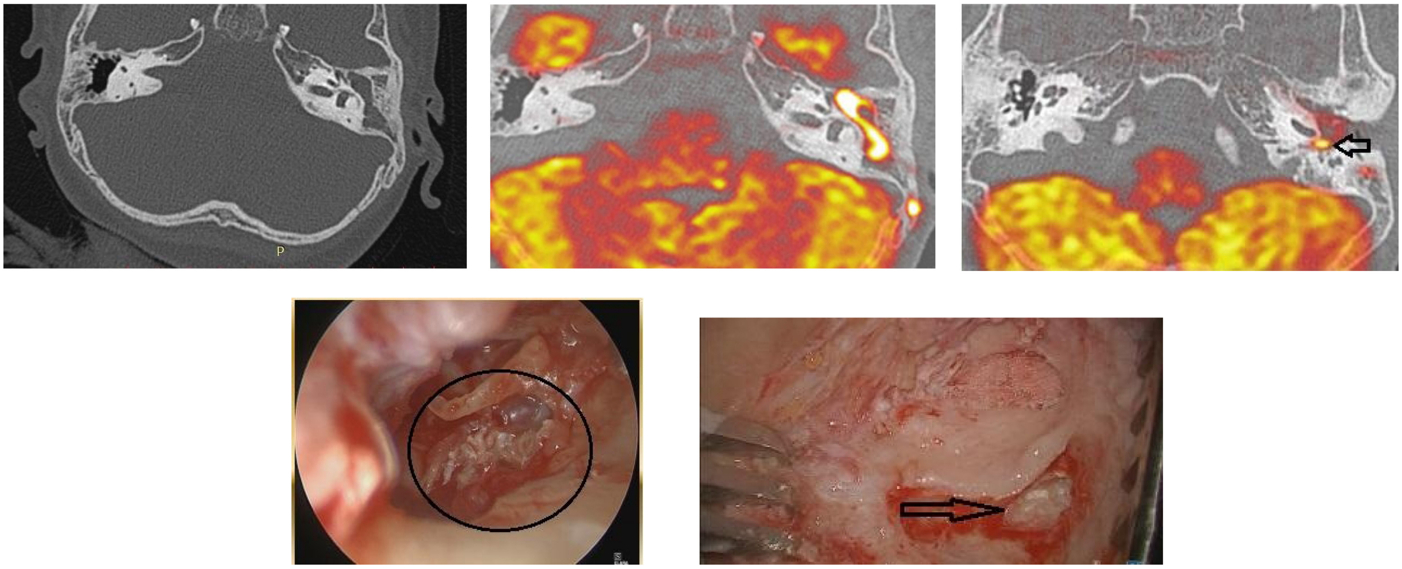

**Figure 1.(** A). HRCT showing opacification of all left ME compartments and the mastoid cavity (stage II); (B) fusion of HRCT and DWMRI showing diffusion restriction in the ME and mastoid cavity; (C) fusion showing restriction in sinus tympani (arrow); (D) endoscopic view showing left middle ear cholesteatoma spreading to the retro-tympanum; (E) intraoperatively, cholesteatoma was extending to the mastoid cavity. HRCT, high-resolution computed tomography; ME, middle ear; DWMRI, diffusion-weighted magnetic resonance imaging.

The following parameters were evaluated intraoperatively:

- the presence or absence of cholesteatoma in the following sites: attic, tympanic cavity, supratubal recess, sinus tympani, and mastoid and whether it passed into the antrum and needed postauricular incision,
- intraoperative staging of cholesteatoma.

**Statistical Analysis of the Data**

Data were fed to the computer and analyzed using International Business Machines Statistical Package for the Social Sciences software package version 20.0. (IBM SPSS Corp.; Armonk, NY, USA). The Kolmogorov–Smirnov test was used to verify the normality of distribution of variables, and comparisons between groups for categorical variables were assessed using chi-square test (Monte Carlo). Receiver operating characteristic curve was used to determine the diagnostic performance of the markers. Area more than 50% gives acceptable performance and area of about 100% is the best performance for the test. Significance of the obtained results was judged at the 5% level.

## RESULTS

The study included 40 patients; 20 were males (50%) and 20 were females (50%). The mean age was 26.8 $\pm$ 14.1 years in the range of 6-54 years old. Regarding sides, 52.5% were left-sided ears and the rest were right.

**Preoperative Localization**

Preoperatively combined HRCT and DWMRI showed that the attic was the most frequently affected site in 32/40 patients (80%), followed by the mastoid cavity in 28/40 patients (70%), and then tympanic and supratubal recess (S1) which were present each in 20/40 patients (50%) and lastly sinus tympani (S2) in 10/40 patients (25%).

**Operative Findings**

Attic involvement was the most frequently affected site present in 32/40 patients (80%), followed by the mastoid cavity in 28/40 patients (70%), and then the tympanic cavity and the supratubal recess (S1) which were present each in 20/40 patients (50%) and lastly sinus tympani (S2) in 18/40 patients (45%). Consequently, our study showed 100% specificity and 100% sensitivity for all sites except sinus tympani which resulted in 55.56% sensitivity and 100% specificity. (Table 1)

Figures 1C and D show an example demonstrating accurate preoperative localization of HRCT and DWMRI fusion in the retrotympanum when matched with intra-operative findings.

**Table 1.** Agreement (Sensitivity, Specificity) for Comparison of HRCT and DWMRI Fusion in Relation with Operative Findings Regarding Subsites Affection

| Combined CT and DWMRI | AUC | *P* | 95% CI | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|
| Attic | 1.000* | <.001* | 1.000-1.000 | 100.0 | 100.0 | 100.0 | 100.0 |
| Mastoid | 1.000* | <.001* | 1.000-1.000 | 100.0 | 100.0 | 100.0 | 100.0 |
| Tympanic | 1.000* | <.001* | 1.000-1.000 | 100.0 | 100.0 | 100.0 | 100.0 |
| S1 | 1.000* | <.001* | 1.000-1.000 | 100.0 | 100.0 | 100.0 | 100.0 |
| S2 | 0.778* | .003* | 0.621-0.934 | 55.56 | 100.0 | 100.0 | 73.3 |

*Statistically significant at $P \le .05$.

AUC, area under a curve; NPV, negative predictive value; PPV, positive predictive value; CT and DWMRI, computed tomography and diffusion-weighted magnetic resonance imaging.

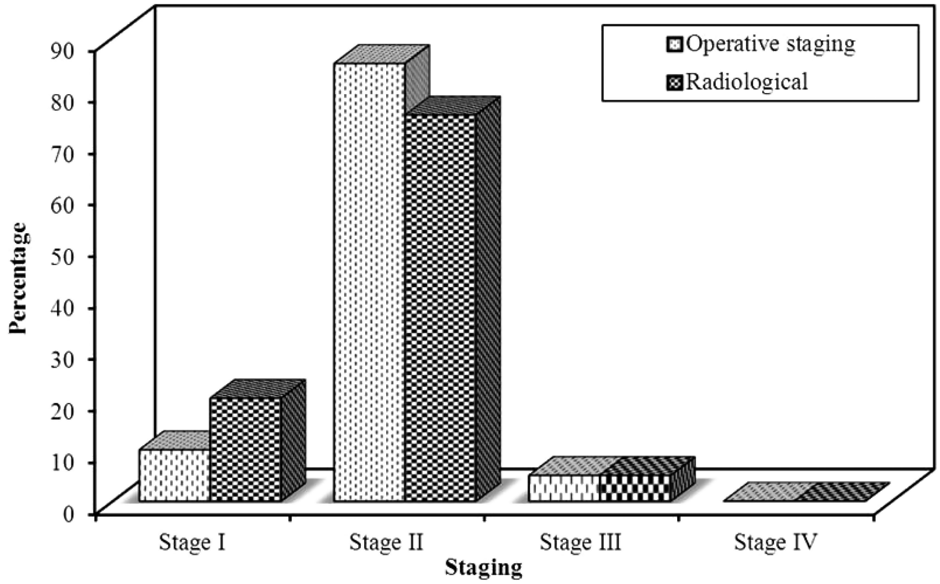


**Figure 2.** Graph showing comparison between radiological staging and operative staging.

**The European Academy of Otology and Neurotology, in Cooperation with the Japanese Otological Society Classification**

- Preoperative combined HRCT and DWMRI showed 4 cases (10%) in stage I, 34 cases (85%) in stage II, 2 cases (5%) in stage III, and none in stage IV (Figure 2).
- Operative staging showed 8 cases (20%) in stage I, 30 cases in stage II (75%), 2 cases (5%) in stage III, and none in stage IV (Figure 2).

The fusion of HRCT and DWMRI had 100% sensitivity and 88.9% specificity in predicting the intraoperative classification of the cholesteatoma (Table 2).

Our study showed 12/40 cases (30%) of cholesteatoma not passing to the antrum and were done by a TEES without the need for mastoidectomy or postauricular incision. On the other hand, in all cases passing to the antrum on imaging, mastoidectomy had to be performed for complete eradication of the disease. Therefore, 12/40 patients (30%) were managed via TEES and the rest 28/40 patients (70%) were managed via combined approach. Figure 1B and E show a patient with a cholesteatoma that passed into the antrum and needed retroauricular incision and mastoidectomy.

High-resolution computed tomography in the present study showed false-positive results in 8/40 cases (20%) in the attic, 10/40 cases (25%) in the mastoid, and 16/40 cases (40%) in both supratubal recess and sinus tympani. Stated differently, the above-mentioned cases showed opacities on HRCT scans that did not prove to harbor cholesteatoma in those specific sites based on DWMRI or intraoperative findings.

**DISCUSSION**

The DWMRI has become increasingly used in clinical practice for the diagnosis of cholesteatoma.[5-10]

One of the significant drawbacks of non-EPI DWMRI is the difficulty of visualizing the anatomical landmarks of the middle ear and mastoid. Fusion of HRCT and DWMRI has been reported to improve the accuracy of the diffusion-weighted images and increase the anatomical precision of the CT images.[15] In the present study, we obtained false-positive results on CT with opacification and no cholesteatoma on neither DWMRI nor intraoperatively in all subsites ranging from 20% to 40%.

Our work aimed to study the role of fusion of non-echoplanar DWMRI and HRCT using combined images as a preoperative tool for the classification of middle ear cholesteatoma. In the present study, we used EAONO/JOS staging system.[1]

The main benefit of HRCT and DWMRI fusion is that it makes it possible to superimpose MR hyperintense cholesteatoma onto bony details provided by CT imaging. This is a post-processing phase; thus, no more imaging is required. Therefore, there is neither added risk for exposure to radiation nor contrast injection. A fusion of HRCT and DWMRI is quite straightforward, requiring some more time post-acquisition (mean time was about 15 minutes in the present study) for both automatic and manual image processing. Nevertheless, with advances in digital technology and learning curve, this method could be even quicker and simpler.[16]

The HRCT and DWMRI fusion can locate cholesteatoma related nearby bony structures like the facial nerve canal and ossicles.[17,18] It is also

**Table 2.** Agreement (Sensitivity, Specificity) for Operative and Radiological Patient's Staging

| | AUC | *P* | 95% CI | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|---|
| Radiological staging | 0.944* | .004* | 0.873-1.016 | 100.0 | 88.89 | 50.0 | 100.0 |

*Statistically significant at $P \leq .05$.
AUC, area under a curve;NPV, negative predictive value; PPV, positive predictive value.

useful to detect the relation of disease to the ossicles, which could prevent unnecessary removal of the ossicles if there is no medial disease, consequently improving postoperative hearing results.[16]

The fusion of HRCT and DWMRI has the additional advantage of choosing the approach before the operation. The postauricular incision could be avoided if the cholesteatoma is not reaching the antrum. To be noted, the mastoid cavity was opacified on CT and found free on DWMRI in 25% of our cases. This means that all these cases would have been expected to have an unnecessary postauricular or endaural incision and mastoidectomy if CT was used alone as preoperative imaging tool.

In the present study, preoperative mapping of cholesteatoma was done, thus guiding the surgeon to plan surgery either by total endoscopic (TEES) or combined endoscopic/microscopic approach. Twelve of our patients were managed exclusively endoscopically. The surgeon made his decision before the operation, depending on the data from combined HRCT and DWMRI, showing that cholesteatoma was not passing beyond the LSCC or reaching the antrum. No additional incision was needed.

We performed the rest of the cases by a combined approach using a retro-auricular incision because cholesteatoma bypassed the line of the LSCC and reached the antrum. The decision to operate either by total endoscopic (TEES) or by a combined endoscopic/microscop ic approach was not changed during operation in any of our cases. Other centers may apply endaural incision or other alternative endoscopic techniques. However, this is our center's preferred strategy.

Regarding cholesteatoma subsites, in the present study, we were able to confirm the preoperative radiological findings with the intraoperative ones, except in 8 cases in relation to the sinus tympani, with a 55.56% sensitivity and 100% specificity. This was attributed to minor image slice misregistration in the process of fusion. Also, the sinus tympani is a very small recess and thus the contained cholesteatoma could be very small. Previous studies have identified similar limitations of non-EPI DWMRI in the identification of small-sized cholesteatoma of less than 2-3 mm.[17,19] Our study revealed that this drawback in the sensitivity could be present in the performance of fusion of HRCT and DWMRI. The sensitivity and the specificity for the rest of the subsites were 100%. False-negative results were present only with sinus tympani. The accuracy of this location could be enhanced by practice and improvements in fusion technology. Nevertheless, this limitation in sinus tympani did not affect the decision-making intraoperatively.

It is worth mentioning that the sinus tympani has 3 radiological degrees of depth. Type C is the deepest type that goes medial and posterior to the mastoid segment of facial nerve. This type is uncontrollable by endoscopes and only controllable by a microscopic post auricular retro-facial approach.[20] This type, however, was not encountered in any of our patients.

In our series, we obtained a 100% sensitivity and 88.9% specificity regarding staging of the cholesteatoma. Consequently, our study has demonstrated that fusion of HRCT and DWMRI has high accuracy for localizing cholesteatoma in the middle ear cleft. It concurs with a previously published study on 12 patients, which demonstrated an accurate correlation between HRCT and DWMRI fusion and surgery for location and extent of cholesteatoma.[21] An additional work studied the accuracy of each imaging technique to diagnose cholesteatoma and localize it through 6 different temporal bone locations. It revealed that the accuracy for DWMRI was 0.83 and for HRCT and DWMRI fusion was 0.90, which matches well with our results.[22]

TEES continues to gather momentum due to improved visualization and less soft tissue dissection and unnecessary mastoidectomy in contrast to the open approach for surgical management of cholesteatoma.[23,24] The minimally invasive endoscopic surgery necessitates a precise preoperative assessment of the site and extent of cholesteatoma. Combining HRCT and DWMRI could provide these data.

While the restriction of water molecules is essential for the generation of high signal on DWMRI, a "T2 shine-through" effect has been suggested as a theory for the high signal.[25] Some materials have prolonged T2 relaxation potential and might produce false-positive results, such as inflammation, proteinaceous fluid, cerumen, cartilage grafts, and silastic sheets.[25,26] None of these materials were encountered in our cases.

By performing a prospective study, as well as using the surgical findings as the gold standard for the anatomical localization of cholesteatoma, we could reinforce the reliability of our study. Limitations of this study include lack of inter and intra observer variability assessment because it was performed by a single expert radiologist. In addition, the possible intra-observer errors of any manual reconstruction is to be considered. We stress the importance of high level of expertise needed to perform precise fusion images in order to obtain accurate and valid information.

Our study demonstrated that the HRCT and DWMRI fusion technique could be used as a preoperative tool for the staging of ME cholesteatoma. Also, it provided favorable outcome supporting increased localization accuracy. This could help the surgeon foreplan the appropriate surgical approach. Yet, the increase in the accuracy must be balanced against the added cost of acquiring DWMRI imaging, particularly when there is strong clinical evidence of cholesteatoma.

It should be noted that all recesses and subsites of the middle ear should be routinely inspected with angled endoscopes at the conclusion of surgery even if the preoperative HRCT and DWMRI fusion was highly suggestive of no disease. This is of special value in hidden recesses such as the sinus tympani.[27] The need for postauricular or endaural incision (according to each center's preference) also must be consented to for every patient in case there was a false-negative result and cholesteatoma was found to be reaching the antrum.

## CONCLUSION

The fusion of HRCT and DWMRI could be considered an accurate tool for localizing cholesteatoma to various middle ear subsites and choosing the appropriate surgical approach (TEES vs. combined endoscopic/microscopic surgery). It provides a promising tool to classify middle ear cholesteatoma preoperatively according to the EANO/JOS classification. This accurate localization could be accomplished by combining the bony details of HRCT with the soft tissue detection ability of non-EPI DWMRI.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee of Alexandria University Faculty of Medicine (Approval no: 0105856).

**Informed Consent:** Written informed consent was obtained from all participants who participated in this study.

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**Author Contributions:** Concept – M.B., A.O.; Design – M.B., M.E., A.O.; Supervision – M.B., A.O.; Materials – M.El., M.E.; Data Collection and/or Processing – M.El., M.E.; Analysis and/or Interpretation – M.E., A.G.; Literature Review – M.El., A.G.; Writing – M.El., A.G.; Critical Review – M.B., A.O., A.G.

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