The role of functional MRI images in differentiation between Cholesteatoma and recurrent otitis media with granulations

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Abstract
Background: The use of diffusion-weighted (DW) sequences to distinguish recurrent cholesteatoma from chronic otitis media with granulations has shown to be quite effective. The differential in water molecule diffusion in various biological tissues is used in DW MRI.
Objectives: The goal of this research was to evaluate the analytic exactness of DWI and the change in ADCs of the middle ear cleft cholesteatoma and non-cholesteatomatous tissue, particularly recurrent otitis media single-shot multi echo planar DW images. In the event of cholesteatoma , intraoperative findings and histological data would be used to validate the outcomes. In the event of otitis media, we will either follow up with the patients clinically to see whether their symptoms improve or if they need a CT scan.
Patients and methods: At South Valley University Hospitals, this research was performed on patients with supposed cholesteatoma (supposed clinically or by CT scan) or branded those, as well as patients with suspected recurrence of otitis media who had previously had operation or were preparing for surgery.
Results: Range of Mean ADC values of cases enrolled in this study which calculated by 3D synapse, even cholesteatoma or otitis media varies from 0.4 to 2.35 with mean average 1.028
Conclusion: DWI is a useful technique in the assessment of cholesteatoma because it distinguishes it from otitis media with high specificity, reducing needing next stare procedures in many instances.

Keywords: cholesteatoma; Diffusion-weighted; otitis media; histopathological data.

Introduction

A basic description of cholesteatoma is skin in the wrong place with keratin retention; this condition often persists and obviously corrodes the internal and internal ear lobe components. **(Bassiouni et al., 2017)**. On other hand, otitis media refers to edema fills middle ear cavity may complicate to meningitis, sinus thrombosis, epidural abscess and petrositis **(Weissleder et al., 2011)**. The diagnosis of cholesteatoma and otitis media are based on clinical findings, with otoscopy and otomicroscopy playing a key role .A polyp or granulation tissue may cover it, making it difficult to see with direct human eyesight. **(Bassiouni et al., 2017).**

High resolution computerized tomography (CT) scan is the most common technique for imaging the middle ear that hasn't been operated on, and it may be supplemented by magnetic resonance imaging (MRI).

Both imaging techniques, however, are unable to accurately differentiate residual or recurrent illness from postoperative alterations such as granulation tissue, fluid, or fibrous tissue after mastoid surgery **(Khedr et al., 2012).**The use of diffusion-weighted (DW) sequences to distinguish recurrent cholesteatoma from granulation tissue has shown to be highly accurate. Depending on that water varies in ability to diffuse within the various biological tissues molecules. Cholesteatoma water molecules are less mobile, resulting in a hyperintense signal. Water molecules are more mobile in otitis media and therefore look less intense (**Alvo et al., 2014**).

In patients with previous cholesteatoma resection, DWI may be utilized to differentiate scar tissue, granulation tissue, and inflammatory alterations from cholesteatoma, especially when CT results

are ambiguous. Small lesions may be detected using newer DWI methods with thinner section collection and less susceptibility artefacts.

The DWI method can be utilized instead of repeating the surgery, avoiding the morbidity for the patient **(Schwartz et al., 2011).** The goal of this work was to investigate the accuracy of DWI and the difference in ADCs in differentiation between middle ear cholesteatoma and non-cholesteatomatous tissue, particularly recurrent otitis media on single-shot echo planar DW images .In the event of cholesteatoma, intraoperative findings and histological data would be used to validate the results. In the event of otitis media, we will either follow up with the patients clinically to see whether their symptoms improve or if they need a CT scan.

Patients and methods

At South Valley University Hospitals, this research was performed on patients supposed to have cholesteatoma with clinical diagnosis or by ct scan or known patients or those already have recurrent otitis media surgery or well have later.

Patients were referred from the South Valley University Hospitals' otolaryngology department as well as other private clinics.

Magnetic resonance imaging was used to examine the patients (MRI).

***Inclusion Criteria*:** Age group: Any age, both sexes, Cholesteatoma, as well as patients already with recurrent otitis media, or supposed by clinical examination or by CT scanning.

***Exclusion Criteria*:** Contraindications to MR imaging in patients (e.g. pacemaker or metallic implant).

Sampling Method: This is a prospective study of 20 pre or postoperative patients who were underwent MR imaging with DWI. The radiologic findings was matched to the operative results .

Sensitivity, specificity, positive and negative predictive values was done .

Sample Size: A sample size of 40 has 80 percent power to detect a change in sensitivity from 0.5 to 0.8 and 32 percent power to detect a change in specificity from 0.5 to 0.8 using a two-sided binomial test.

The desired threshold of significance is 0.05.

***Ethical Considerations*:** before their involvement in the study, each patient gave informed consent.

***Study Tools*:** MRI was obtained using 1.5 tesla MRI scanners.

***Study Procedure*s**

The patients have: Consent taking, history taking, clinical examination, CT images (if available), detection if Patients have a to MRI contraindication , lay supine and are advised to breathe quietly and not move throughout the scan.

MRI protocol including the following

MR images of the skull base or upper neck were acquired by using a 1.5-T system with the manufacturer's head coils. The images of the selected patients were obtained in axial and coronal planes acquiring diffusion weighted images. With b factors of 0 and 1000, multi-shot fast spin-echo diffusion-weighted pictures (DW FSE) were created. s/mm2. ADC mapping was also be obtained. Additional sequences can be added per the findings such as T1 and T2 weighted images. Total imaging time: 15–20 minutes.

- Complications and how to deal with: No definite risk of complications.
- Image Interpretation: MRI images were reviewed by radiologists in our department. Cholesteatoma and recurrent otitis media were diagnosed by:- Cholesteatoma: **-** Diffusion-weighted imaging reveals high sign strength and dispersal restraint, while T2-weighted imaging reveals strong signal intensity and diffusion limitation. COM: - appears as cholesteatoma in T2WI, showing hyperintensity, although differs from cholesteatoma as no restriction in DWI.
- Calculation of the ADC value by putting ROI on image of DWI at 3D synapse application to calculate mean of ADC value, and also To rule out the existence of T2 shine finished effects, the ADC maps were utilized.

There was no picture integration amid the CT and MRI scans.

Statistical Analysis

Data was analysed statistically, and all the results was tabulated, presented graphically and will be interpreted and discussed.

Results

From the 40 cases, 20 cases (50%) underwent previous mastoid surgery while 20 cases (50%) had no previous surgical history.

Range of Mean ADC values of cases enrolled in this study which calculated by 3D synapse, even cholesteatoma or otitis media varies from 0.4 to 2.35 with mean average 1.028.

The mean ADC values of six cases that's appear Otitis media by imaging and diagnosed finally as cholesteatoma varies from 0.9 to 1.75 with average mean 0.96.

Table 1. Range and mean of ADC values of all cases included in this study

	Range	Mean ± SD
ADC values	0.4 - 2.35	1.028 ± 0.561

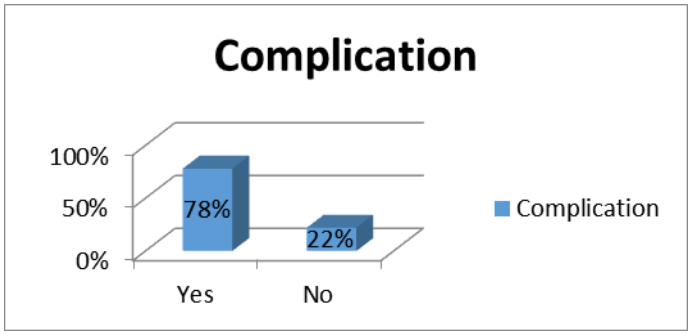


Fig.1. Complications revealed by imaging (all complications are included except bony erosion)

Intra-operative and/or follow up Data

The patients who underwent primary or second look mastoid surgery:-

All 19 cases of primary or recurrent cholesteatoma that showed intra-operative and/or histopathological evidence of cholesteatoma display restricted DWI on MRI images.

6 cases that were not visualized by DWIs showing intra-operative and/or histopathological evidence of small cholesteatomas measuring less than 4 mm.

And also other 10 cases showed inflammatory tissue with no evidence of cholesteatoma.

The patients who didn't underwent surgery after MRI imaging

5 cases of inflammatory tissue revealed significant improvement of their symptoms after 6 months of medical treatment.

Comparing MS-EPI DWIs data with intra-operative data/histopathology or follow up, the MS-EPI DWI shows the following diagnostic value:

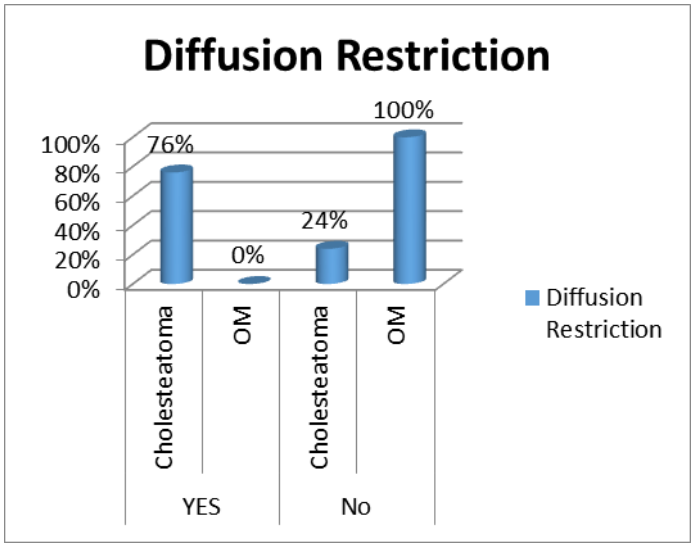


Fig.2. The diagnostic value of MS-EPI DWI comparing recurrent otitis media with cholesteatoma, depending on diffusion restriction .

Illustrative case

A 12 years old male patient, has underwent mastoid surgery 3 years ago for twice after being diagnosed with right middle ear cholesteatoma. Since 6 months ago, aggravated painless otorrhea and conductive hearing loss (CHL). Requested MRI to role out recurrent cholesteatoma.

Histopathology: recurrent cholesteatoma.

CT finding previous to the last surgery:-

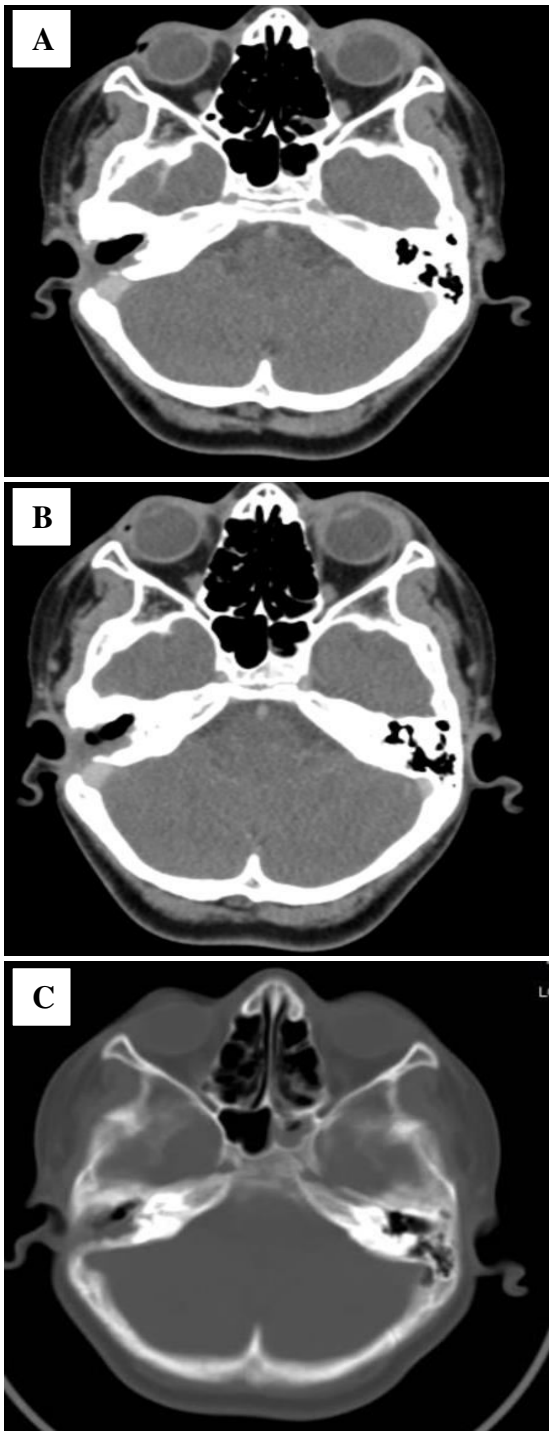


Fig.3. A, B and C axial cuts of CT images showed still detected diffuse soft tissue affecting both right external and middle ear walls.

MR finding previous to the last surgery:

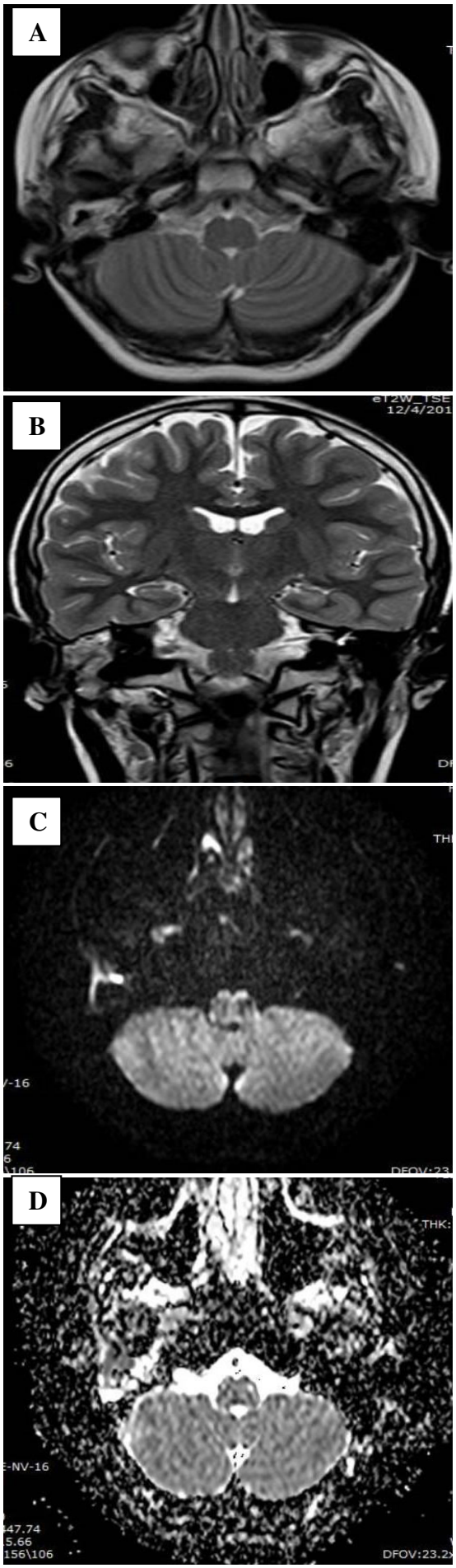
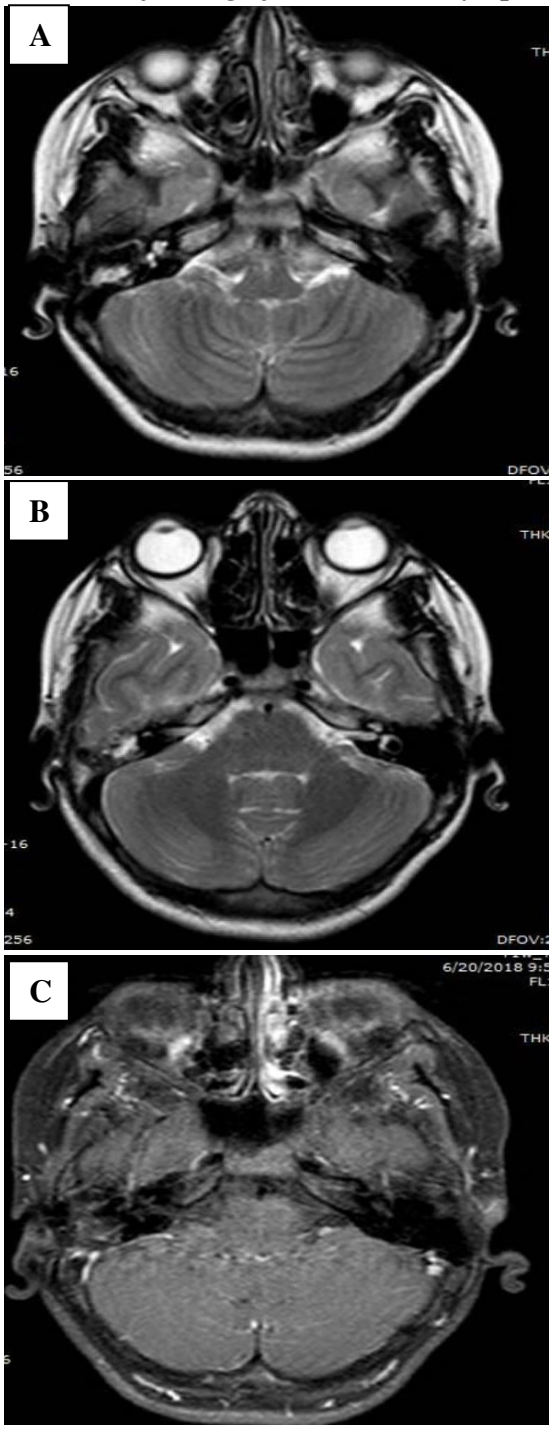


Fig.4. A and B- axial and coronal T2WIs showed diffuse T2 hyperintensity within the right middle ear cavity.
C- DWI (at b-value 1000) showing high signal intensity as a bulb light.
D- Low signal intensity is noted at mean ADC value 0.62 on ADC map image

Latest MR finding after recurrent symptoms



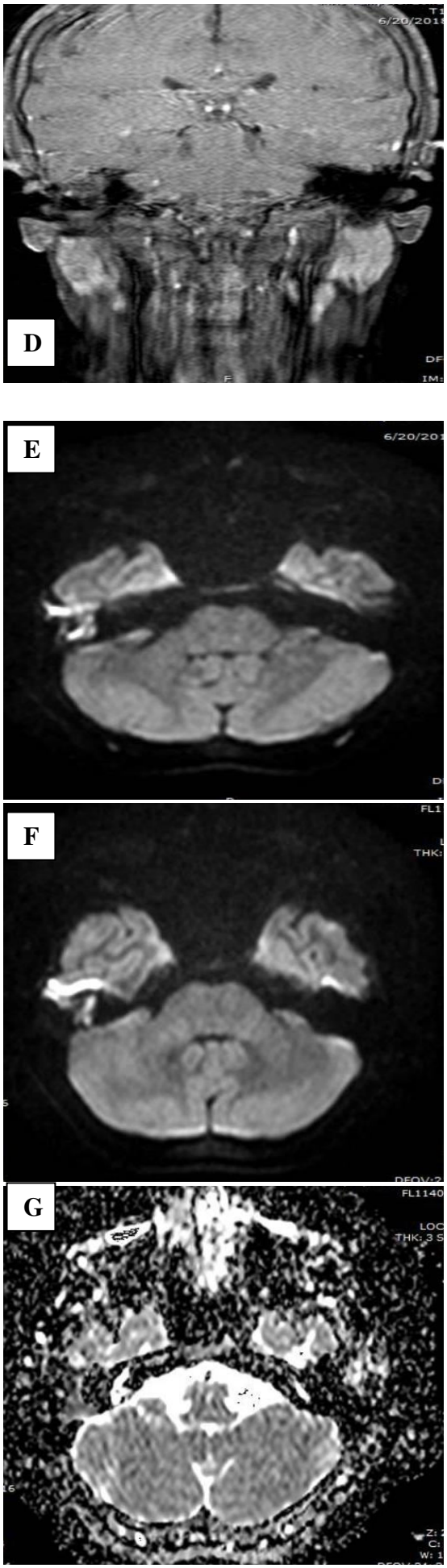


Fig.5. A and B- axial cuts of T2WIs showed right middle ear cavity diffuse T2 hyper intensity.
C and D- axial and coronal T1 showed no contrast enhancement in post contrast study.
E and F- DWI (at b-value 1000) demonstrating the lesion's high signal intensity.
G and H- ADC map picture demonstrating the lesion's low signal intensity, with a mean ADC value of 0.55.

Discussion

Cholesteatomas are acquired chronic inflammatory lesions of the middle ear and mastoid being either primary or secondary.
The erosive and damaging epithelium need total surgical removal.

Cholesteatoma's etiology, as well as the frequency and causes of residual and recurring lesions, are currently being studied. **(Louw, 2010)**
The use of post-contrast T1-weighted MRI imaging to differentiate infections, granulation tissues, or residual secretions from cholesteatoma has been recommended.

Cholesteatomas and otitis media show post-contrast enhancement for being non-vascularized, while post-contrast enhancement on delayed images are depicted on granulation tissue for being poorly vascularized.
Larger cholesteatomas may be detected with this method, but tiny residual lesions were often overlooked. **(Williams et al., 2003).**

MRI imaging has the upper hand than CT for tissue characterization and diagnosis of cholesteatoma with high diagnostic value of diffusion restriction on DWI. **(Dietrich and colleagues, 2010)**

Because of the special composition of cholesteatoma containing keratin content, eliciting high signal intensity on DWI, DWI has high sensitivity and specificity for detecting cholesteatoma. **(Elefante and colleagues, 2015)**
For differentiating cholesteatoma from inflammatory tissue in the non-surgically treated middle ear, DW EPI sequences are highly accurate as cholesteatoma exhibits high signal intensity.

Many studies have utilized DW EPI and late post-contrast T1-weighted sequences to detect pre-second-look residual cholesteatoma and postoperative recurrent cholesteatoma.
Due to susceptibility artefacts, a lower image matrix and relatively thick slices, DW EPI has a role in the characterization of large cholesteatomas that recur or relapse, while it fails to detect cholesteatomas less than 5 mm.

Recent studies have shown the effectiveness and usability of a non-EPI-based DW sequence in detecting primary middle ear cholesteatoma and postoperative recurrent cholesteatoma. **(De Foer and colleagues, 2007)**

In our study, no clear ADC values can differentiate between cholesteatoma and chronic otitis media. As calculated mean ADC values taking low ranges below 1 in all enrolled cholesteatomatous cases.

Lesions smaller than 2–3 mm may be not detected even using non-EPI DWI methods for residual disease screening. However, follow up is recommended for small lesions to detect if increasing in size. **(Migirov et al., 2009).**
Definite interval for follow up studies of small lesions is still matter of debate. However, in children close follow up is recommended for rapid growth rate. **(Plouin-Gaudon et al., 2010)**

In our study, diagnostic values of multi-shot Echo-planer DWI are compared to intra-operative and histopathological data to differentiate cholestatoma from chronic otitis media.
We used a 1.5 T. Philips MRI machine. 40 clinically and CT suspected and ENT department

referred patients of all age groups and both sexes were tested.

Using head coil, skull base images were obtained by acquiring thin cuts with multi-shot echo-planar diffusion-weighted images with b-values of 0 and 1000 s/mm2. Other additional sequences are obtained like T1, T2 and ADC maps. Total imaging time is about 15 – 20 minutes.

Obtained images were examined by radio-diagnosis department and cholesteatoma show high signal intensity on T2WIs, restricted diffusion on DWI and calculation of ADC values to exclude T2 shine through artifact.

Among our sample (40 patients), 19 patients (48%) showing restricted diffusion on DWI, suggesting cholesteatoma, either primary or recurrent. They were proved surgically and histopathologically to have cholesteatomas. The smallest lesion was about 5 mm.

Ten of the 21 patients with imaging that were negative for cholesteatoma had primary or second look mastoid surgery, with six patients (24%) revealing tiny cholesteatomas measuring less than four millimetres. (that were not visualized by imaging). The other 5 cases that didn't undergo surgery after MRI imaging were treated medically with significant improvement of their symptoms.

Sensitivity of thin cut MS-EPI in diffusion restriction of cholesteatoma according to our study was 76 % which is considerably better than other studies using SS-EPI such as **Vercruysse et al., 2006** (12.5%), **Jeunen et al., 2008** (54%) and **Venail. et al, 2008** (60%) and comparable to other studies using MS-EPI such as **Yamashita et al., 2011** (76%), and **Emonot et al., 2008** (79%). However the sensitivity of our study was less than other studies using Non-EPI DWI such as **Dubrulle et al., 2006** (100 %) and **De Foer et al., 2008** (90%). It was also relatively less than other studies using delayed post-contrast MRI such as **Ayache et al., 2005** (90%) , **Venail. et al, 2008** (90%) and **Ilica et al.,2012** (94%).

The least size of cholesteatoma detected by our study was 5 mm which is as other studies such **Vercruysse et al., 2006** (5 mm), **Jeunen et al., 2008** (5 mm) and **Aikele et al, 2003** (5 mm) but less than other studies using Non-EPI DWI such as **De Foer et al., 2008** (2 mm).

Conclusion

DWI is a valuable method in diagnosing cholesteatoma because it distinguishes it from otitis media with high specificity, reducing the necessity for another look procedures in many cases.

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