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The Efficacy of Color Mapped Fusion Images in the Diagnosis and Treatment of Cholesteatoma Using Transcanal Endoscopic Ear Surgery

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Objective: To assess the efficacy of color mapped fusion images (CMFIs) in preoperatively evaluating the anatomic location of cholesteatomas and determining whether a patient is indicated for transcanal endoscopic ear surgery.
Study Design: Prospective case study.
Setting: A single university hospital.
Patients: Ninety-two patients scheduled for middle ear cholesteatoma surgery.
Intervention: Imaging analysis was first performed using echo planar diffusion-weighted imaging (EPI) for the first patient group with mixed results. Imaging analysis was then performed using 1-mm thin-slice non-EPI combined with magnetic resonance cisternography in a second group. The resulting image was then processed using color mapping to create a CMFI that enhanced cholesteatoma visualization. A second non-EPI was also performed on the third group, incorporating a T1-weighted image (T1WI) to reduce false-positives.
Main Outcome Measure(s): Preoperative findings from EPI, non-EPI/CMFIs, and non-EPI/T1WI-enhanced CMFIs were compared with intraoperative findings. The positive predictive value and negative predictive value were also evaluated for each group.
Results: Both the positive predictive value and negative predictive value obtained from the CMFIs were high in all areas of the middle ear, and CMFI facilitated accurate detection of the anatomic location of cholesteatomas of 3 mm or larger. The incidence of false-positives was further reduced in the final 18 patients by performing T1WI to distinguish between cholesteatomas and cholesterin granulomas.
Conclusion: CMFI combined with T1WI is a reliable diagnostic modality for evaluating the anatomic location of cholesteatomas 3 mm or larger and determining whether transcanal endoscopic ear surgery is indicated for treatment in such cases. **Key Words:** Cholesteatoma—Color mapped fusion image—Magnetic resonance cisternography—Non–echo planar diffusion-weighted imaging—T1-weighted image—Transcanal endoscopic ear surgery.

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Cholesteatomas are typically treated using conventional microscopic ear surgery (MES). Our group, however, has recently developed a new procedure incorporating the use of an endoscope that is called *transcanal endoscopic ear surgery* (TEES) (1–5). This procedure provides direct access to a cholesteatoma through the ear canal without the need for a large invasive retroauricular incision. TEES is, therefore, less invasive, provides better results, and requires a shorter period of postoperative hospitalization than MES. Moreover, TEES can be combined with powered instruments to treat cholesteatomas extending up to the antrum (1). When a cholesteatoma extends to the central mastoid, we use a dual approach using both TEES and MES with the central mastoid defined by Tos as ''the central area, which extends from the antrum down to the mastoid tip'' (6). Hence, a preoperative evaluation of the anatomic location of a cholesteatoma must be performed to determine whether a patient is indicated for TEES.

Patients are initially screened for cholesteatomas by a computed tomography (CT) scan. If the results of the CT scan suggest the presence of a cholesteatoma, a preoperative evaluation is currently performed to confirm the cholesteatoma by using diffusion-weighted imaging (DWI), a variation of conventional magnetic resonance imaging (7–15). DWI relies on the principle of Brownian

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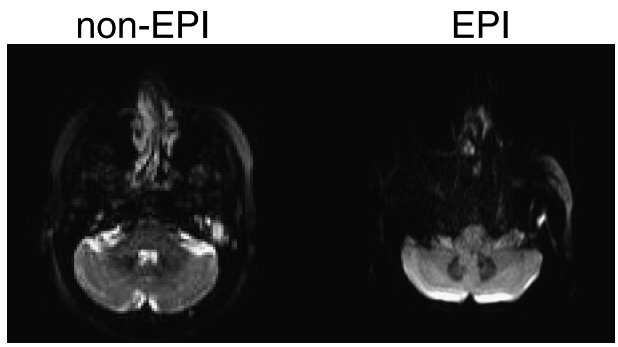

FIG. 1. Comparison of the EPI and non-EPI DWI for the same cholesteatoma patient. The high-intensity region indicates a cholesteatoma, which are more clearly visualized in non-EPI DWI than in EPI DWI.

motion as applied to water molecules. These molecules are restricted to certain pathologic tissues, such as those tissues involving tumors and/or ischemic regions (16). Two different DWI techniques are currently used in the detection of cholesteatomas: echo planar imaging (EPI) and non-EPI (Fig. 1). Although EPI has been a standard tool in diagnosing cholesteatomas, images created using EPI are frequently distorted and precise anatomic locations can be difficult to distinguish. Conversely, non-EPI has been reported to be more reliable in identifying cholesteatomas than EPI (10,11). However, non-EPI has two major drawbacks: it takes a slightly longer period to perform and, more importantly, the anatomic location is more difficult to identify because of the lower image resolution and disappearance of most of the intracranial structures.

Our dissatisfaction with EPI images leads us to conduct further research in an attempt to resolve the drawbacks associated with non-EPI and allow us to take advantage of its reliability. We first developed a two-step process designed to overcome these drawbacks and to identify the anatomic location of a cholesteatoma. The first step is to create an image of the target area by fusing a 1-mm thin-slice non-EPI with MR cisternography (MRC). The second step is to take the resulting image and apply color mapping to further enhance the visualization of the cholesteatoma (Figs. 2; 3, A and B). This final image has been dubbed a color mapped fusion image (CMFI), and the preoperative findings obtained by using a CMFI were compared with the intraoperative findings to assess the efficacy of a CMFI for the preoperative evaluation of cholesteatomas.

Although our initial results were good for CMFI alone, a number of preventable false-positives occurred. These false-positives were caused by the inability of our initial procedure to accurately distinguish between the presence of a cholesteatoma and a cholesterin granuloma. This problem was resolved by taking a T1-weighted image (T1WI) if a high-intensity red region is detected around the ear.

The aim of this study was to assess the efficacy of CMFI combined, as necessary, with T1WI in preoperatively evaluating the anatomic location of a cholesteatoma and determining whether a given patient is indicated for TEES.

METHODS

Patients were preoperatively examined with either EPI or non-EPI/MRC using a 3.0-T MR unit (Achieva, Royal Philips Electronics Inc., The Netherlands). Color mapping was applied to non-EPI/MRC alone or to non-EPI/MRC combined with T1WI to create a CMFI. The preoperative findings that were obtained using each processing method were compared with

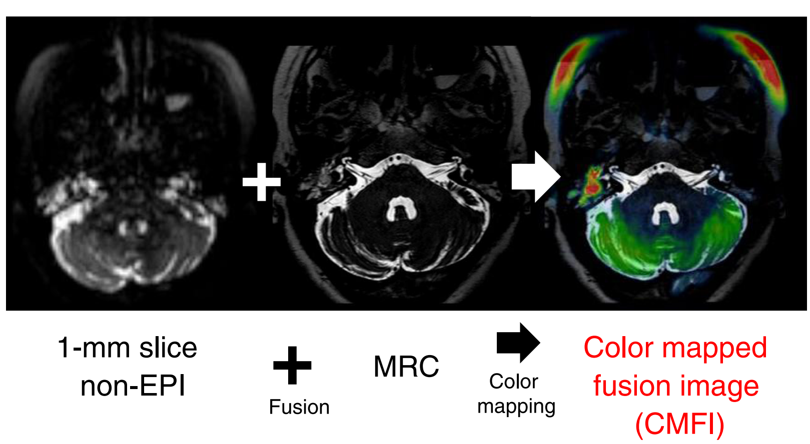

FIG. 2. Enhancing the visualization process of non-EPI. We combined the 1-mm slice non-EPI with MRC. We also performed color mapping to enhance the visualization of the cholesteatoma.

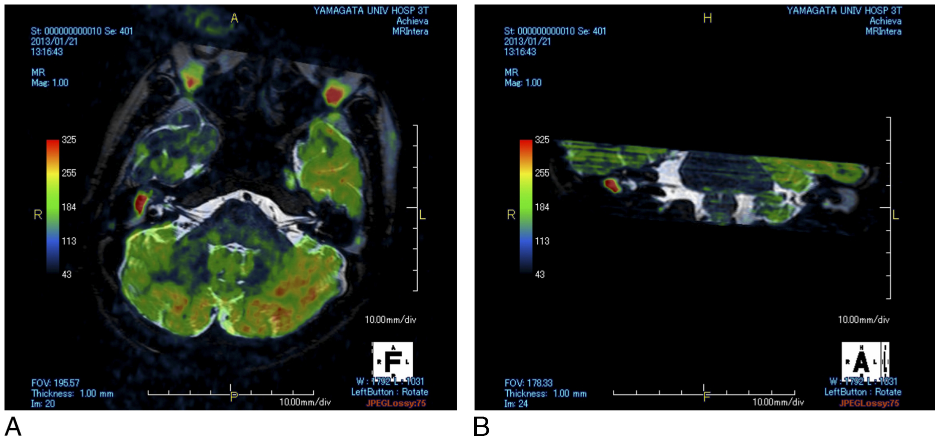

FIG. 3. An example of the resulting CMFI. *A*, Axial section. *B*, Coronal section. The *red area* indicates a cholesteatoma. The cholesteatoma extends downward beyond the lateral semicircular canal.

intraoperative findings to assess the efficacy of each method in preoperatively detecting and evaluating the anatomic location of cholesteatomas. Both the positive predictive value (PPV) and negative predictive value (NPV) were also evaluated.

Research was conducted to determine the best method for detecting cholesteatomas in three stages during the course of 20 months on a total of 92 patients. The first stage was from January to August of 2012, and 29 patients were examined using only EPI. We were dissatisfied with the images obtained and spent several months working on a better approach. The second stage was from January to August 2013, and 45 patients were examined using non-EPI combined with MRC after which color mapping was applied to create the CMFI. The preoperative findings that were obtained from EPI and non-EPI without MRC and color mapping were compared with intraoperative findings for the initial 29 patients in the first stage and 20 out of the 45 patients in the second stage. The third stage was from September to December 2013, and 18 patients were examined using the CMFI combined with T1WI. This CMFI and T1WI combination produced far superior results in comparison with the images produced in the first two stages.

EPI and Non-EPI Preoperative Findings Versus Intraoperative Findings

Table 1 compares the EPI versus the non-EPI parameters for the two groups. The slice thickness was 3 mm for both DWI methods. The total scan time was 27 seconds for EPI and 196 seconds for non-EPI. Table 2 compares the characteristics of the two groups.

CMFI Preoperative Versus Intraoperative Findings

In the second stage, we compared the preoperative findings that were obtained using CMFI with the intraoperative findings for cholesteatomas in the antrum and central mastoid. Table 1 also shows the CMFI parameters. Instead of a 3-mm slice, we first combined 1-mm slice non-EPI with MRC to clarify the anatomic location of the cholesteatoma lesions. MRC clearly reveals the lateral semicircular canal and the cochlea, and the resulting image is further enhanced by color mapping to facilitate the visualization of the cholesteatoma on a CMFI. A cholesteatoma will show up as bright red based on color mapping, and a CMFI can clearly show whether the cholesteatoma extends to the mastoid beyond the lateral semicircular canal based on the bright red area in the ear. The surrounding areas of the brain generally have a much lower intensity and will show up in the blue-green spectrum. However, some portions of the cerebellum may show up as red on a CMFI, but a cholesteatoma can be clearly distinguished from these red areas based on both anatomic location and the higher red signal of the cholesteatoma.

CMFI With T1WI Preoperative Versus Intraoperative Findings

The preoperative findings for CMFI with T1WI were compared with the intraoperative findings for cholesteatomas in the antrum and central mastoid. A CMFI/T1WI image can be used to distinguish between a cholesteatoma and cholesterin granuloma, and thus this image facilitates a more accurate preoperative diagnosis.

CMFI and Patient Breakdown

CMFI was used in the preoperative evaluation of 63 patients between January and December 2013. Table 2 also shows the characteristics of the CMFI group. The initial CT scans revealed that 48 out of the 63 patients had a soft tissue mass in the antrum, and 47 out of the 63 patients had a soft tissue mass in the central mastoid (Table 3). Five out of the 48 patients in the antrum group had a soft tissue mass only in the antrum, whereas 43 had a soft tissue mass in both the antrum and central mastoid group. Eleven patients had a soft tissue mass in the tympanic cavity and/or attic only and thus were included in the examination of CMFI efficacy. The remaining 52 patients were further examined by CMFI to

TABLE 1. *Comparison of EPI, non-EPI, and CMFI parameters*

Parameter	EPI	Non-EPI	CMFI
Field of view (mm)	240	240	240
Matrix scan	208	128	128
No. sections	12	12	32
Slice thickness (mm)	3	3	1
B-factor	1,000	800	800
Echo time (ms)	2,079	2,311	2,311
Repetition time (ms)	80	84	84
Voxel size (mm)	1.15/1.97/3.00	1.88/2.00/3.00	1.88/1.98/1.00
Total scan time (s)	27	196	480

CMFI indicates color mapped fusion image; EPI, echo planar diffusion-weighted imaging; non-EPI, non–echo planar diffusion-weighted imaging.

TABLE 2. *Breakdown of patients who underwent EPI, non-EPI, and CMFI*

	EPI	Non-EPI[a]	CMFI	
			T1WI (−)	T1 WI (+)
No. patients	29	20	63	
			45	18
Stage	Stage I January–August 2012	Stage II January–April 2013	Stage II January–August 2013	Stage III September–December 2013
Mean age (range) (yr)	46.9 (2–74)	46 (3–72)	50.5 (3–83)	
Male/female	16/13	11/9	37/26	

CMFI indicates color mapped fusion image; T1WI, T1-weighted image.
[a]Non-EPI without MR cisternography and color mapping processing.

determine the efficacy of CMFI in the detection of the anatomic location of the cholesteatoma.

RESULTS

Comparison of EPI and Non-EPI

When the preoperative findings were compared for EPI and non-EPI with a 3-mm slice thickness, the PPV was 100% for EPI versus 91.7% for non-EPI, whereas the NPV was only 27.2% for EPI versus 87.5% NPV for non-EPI (Table 4). The low NPV for EPI indicates that non-EPI is superior to EPI in detecting cholesteatomas. This finding led us to abandon EPI and use only non-EPI from the second stage of this study.

Comparison of CMFI and Intraoperative Findings

CMFI was performed on 63 patients in the second and third stages. Fifty-two of the 63 patients had soft tissue masses in the antrum and/or central mastoid, and the CMFI findings were compared with the intraoperative findings. We ultimately found that the minimum size of cholesteatomas that could be detected using CMFI was 3 mm.

We evaluated the efficacy of CMFI in preoperatively detecting and evaluating the anatomic location of cholesteatomas because performing a preoperative evaluation of the anatomic location of a cholesteatoma is crucial for determining whether a patient is indicated for TEES. This evaluation was performed by comparing the preoperative findings using non-EPI to create a CMFI and intraoperative findings. Moreover, although anatomic landmarks such as lateral semicircular canal and cochlear are visualized equally well using MRC or a CMFI, the advantage of the CMFI is that the cholesteatoma is more clearly visualized.

When the preoperative findings using CMFI were compared with the intraoperative findings, the PPV was 92.9% and the NPV was 80.0% in the antrum, whereas the PPV was 76.2% and the NPV was 96.2% in the central mastoid (Table 5).

TABLE 3. *The CT scan findings of the 63 patients in the second and third stages*

	Antrum	Central mastoid	Tympanic cavity, Attic
CT soft tissue mass (+)	43		11
	5	4	

Four false-negative cases in the antrum and one false-negative case in the central mastoid were observed in patients with cholesteatomas without debris. Two false-positive cases were detected in the antrum and five false-positive cases were detected in the central mastoid among patients with cholesterin granulomas. T1WI was also performed with CMFI to distinguish between the presence of cholesterin granulomas and cholesteatomas. When the preoperative findings using CMFI with T1WI were compared with the intraoperative findings, the PPV was 96.3% and the NPV was 80.0% in the antrum, whereas the PPV was 84.2% and the NPV was 96.2% in the central mastoid (Table 6).

DISCUSSION

A CT scan is commonly used as a presurgical diagnosis tool for cholesteatomas. However, soft tissue masses in the antrum are sometimes subject to misinterpretation and can be mistakenly diagnosed as a cholesteatoma. This problem can be clearly seen in Figure 4 where a soft tissue mass is present, but the image quality makes it nearly impossible to make an accurate diagnosis.

A CMFI is thus a useful tool to more accurately assess soft tissue masses initially found on a CT scan. Panels A and B of Figure 3 show the CMFI obtained for the same patient in Figure 4. A comparison of the three images clearly demonstrates that, although a CT scan is an excellent screening tool for possible cholesteatomas, a final diagnosis is better made based on a CMFI.

When the preoperative evaluation of cholesteatomas was compared using EPI versus non-EPI, both the PPV and

TABLE 4. *Comparison of preoperative evaluation of cholesteatomas by non-EPI and EPI*

		Intraoperative findings cholesteatoma		
Non-EPI		+	−	
DWI high	+	11	1	PPV: 91.7%
	−	1	7	NPV: 87.5%
EPI		+	−	
DWI high	+	18	0	PPV: 100%
	−	8	3	NPV: 27.2%

Both the PPV and NPV for non-EPI were high. PPV for EPI was also high; however, NPV of EPI was low.
NPV indicates negative predictive value; PPV, positive predictive value.

TABLE 5. *Preoperative evaluation for cholesteatomas by CMFI*

		Intraoperative findings cholesteatoma		
Antrum		+	−	
CMFI high (red)	+	26	2	PPV: 92.9%
	−	4	16	NPV: 80.0%
Central mastoid		+	−	
CMFI high (red)	+	16	5	PPV: 76.2%
	−	1	25	NPV: 96.2%

Both PPV and NPV were quite high in the antrum and in the central mastoid.

CMFI indicates color mapped fusion image; NPV, negative predictive value; PPV, positive predictive value.

NPV for non-EPI were high. In contrast, although the PPV for EPI was also high, the NPV for EPI was low. These results indicate that non-EPI is superior to EPI in preoperatively detecting cholesteatomas. Our results are similar to those of Jindal et al. (10) and Yamashita et al. (11), which demonstrated the effectiveness of non-EPI in detecting cholesteatomas compared with EPI. Non-EPI requires a longer period to perform compared with that required for EPI. However, non-EPI is less susceptible to developing magnetic interface artifacts than EPI, especially in the middle ear.

We thus began to use non-EPI to detect cholesteatomas in January 2013. We further created CMFIs to more accurately pinpoint the anatomic location. The 1-mm slice CMFI clearly showed the important landmarks including the lateral semicircular canal and cochlea in all 63 patients. Our study shows that CMFI results in high PPVs and NPVs in the antrum and also in the central mastoid. Thus, CMFI is a reliable diagnostic tool for evaluating the anatomic location of cholesteatomas. Such information is crucial in the determination of whether a patient is indicated for TEES.

However, two problems are associated with the detection of cholesteatomas using non-EPI. First, cholesteatomas can remain undetected. In our current study, five false-negative cases were detected among patients with cholesteatomas with a matrix without debris. Debris-free cholesteatomas may not be detected as high-intensity regions on non-EPI. Therefore, an endoscope should be used to directly access and precisely detect these lesions.

TABLE 6. *Preoperative evaluation for cholesteatomas by CMFI combined with T1WI*

		Intraoperative findings cholesteatoma		
Antrum		+	−	
CMFI high (red)	+	26	1	PPV: 96.3%
T1WI low	−	4	16	NPV: 80.0%
Central mastoid		+	−	
CMFI high (red)	+	16	3	PPV: 84.2%
T1WI low	−	1	25	NPV: 96.2%

PPVs in the antrum and in the central mastoid were better than the PPVs shown in Table 5.

CMFI indicates color mapped fusion image; NPV, negative predictive value; PPV, positive predictive value; T1WI, T1-weighted image.

Second, cholesteatomas may be indistinguishable from cholesterin granulomas. In the present study, seven false-positives (two in the antrum and five in the central mastoid) were observed for patients with cholesterin granulomas among the 63 patients in Stages II and III. The cholesteatomas in these cases could not be distinguished from cholesterin granulomas based on a CMFI because cholesterin granulomas can also appear as high-intensity regions on DWI. This problem was solved by incorporating T1WI into the magnetic resonance imaging scans because cholesteatomas exhibit a low intensity on T1 images and a high intensity on T2 images, whereas cholesterin granulomas exhibit a high intensity on both T1 and T2 images. Therefore, cholesteatomas can be distinguished from cholesterin granulomas on T1WI (9).

An additional consideration is the need for follow-up images that must be taken after surgical treatment for cholesteatomas because of the high rate of cholesteatoma recurrence. A CT scan is commonly used as a follow-up radiologic tool for assessing cholesteatomas postoperatively. However, Khemani et al. (12) have recently reported that DWI is a more reliable follow-up imaging method than a CT scan after cholesteatoma surgery. Our results support the findings of a number of researchers that non-EPI DWI can be used to accurately detect recurrent cholesteatomas for lesions larger than 3 mm in size (7,8,10,13–15).

We thus established a follow-up schedule that is designed to minimize cost while maximizing accuracy. CT scans are first taken 6 months after surgery. If soft tissue masses are not detected on the first CT scan, an additional CT scan alone

FIG. 4. The CT scan that was obtained for the same patient in Figure 3A and B. A soft tissue mass is present in the attic to the central mastoid, but the image quality makes it nearly impossible to make an accurate diagnosis.

can be used for the next 6-month follow-up and any other subsequent follow-ups. However, when the initial CT scan reveals any soft tissue masses, non-EPI DWI is performed to create a CMFI 6 months later. This CMFI is used to confirm that the mass was a postoperative change such as scarring and not a cholesteatoma. T1WI is also performed at this time to determine whether any visible mass is a cholesteatoma or a cholesterin granuloma.

CONCLUSION

CMFI combined as necessary with T1WI is a reliable diagnostic modality for detecting and evaluating the anatomic location of cholesteatomas. In addition, this modality is useful for determining whether a given cholesteatoma patient is indicated for TEES.

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