A quantitative approach in characterization of epidermoid cyst and middle ear cholesteatoma: T1 and T2 mapping

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Aims and objectives

Although intracranial epidermoid cyst is a remnant of ectodermal epithelial tissue from fetal development [1] while middle ear cholesteatoma is mostly acquired by the retraction of the tympanic membrane, [2] they are histologically identical. The cystic masses consist of a stratified squamous epithelial capsule filled with a waxy-appearing desquamated keratin debris and cholesterol crystals. [3]

Differential diagnosis of both entities is challenging. [4]

Epidermoid cyst is indistinguishable from arachnoid cyst on computed tomography (CT) and magnetic resonance imaging (MRI) due to its identical density and intensity to cerebrospinal fluid (CSF). Differential also includes craniopharyngeoma, acoustic schwannoma, dilated CSF spaces, dermoid cyst, and inflammatory cyst. [1, 5] Epidermoid cysts are slow growing, and surgical treatment is only necessary if symptomatic. However, complete resection is difficult due to adherence to surrounding cranial nerves and vessels, thus, residue and recurrence is common. [6]

On the other hand, middle ear cholesteatoma needs to be eradicated by tympanomastoid surgery to avoid severe complications. Similarly to epidermoids, residual and recurrence rate is high. Conversely, otoscopy and imaging techniques such as CT have limited ability to distinguish residual and recurrent cholesteatoma from postoperative inflammation, granulation tissue and fibrosis. Therefore, a second-look surgery is usually required, which might lead to hearing loss. [7-9]

Delayed postcontrast T1-weighted MR imaging (DPI) was the first MRI technique being able to differentiate enhancing inflammation tissue from non-enhancing cholesteatoma. Nevertheless, the examination is cumbersome due to its length and cost. [10]

Diffusion-weighted imaging (DWI) was proved to be highly specific for both cholesteatoma and epidermoid cyst due to their high keratin content. Since it is an EPI sequence, DWI is prone to susceptibility artifact especially at air-bone interfaces. This inhibits the detection of epidermoid cyst and middle ear cholesteatoma which are typically located close to the skullbase. [3, 9, 11]

Recently, the non-EPI half-Fourier acquisition single-shot turbo spin-echo diffusion weighted sequence (HASTE-DWI) has been demonstrated to identify epidermoid cyst and cholesteatoma with high specificity and sensitivity. The sequence is less prone to susceptibility artifact and has improved spatial resolution. [3, 7, 8, 12, 13]
<table>
<thead>
<tr>
<th>Method</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>gives information on the extent of the lesion and ossicular erosion</td>
<td>non-specific</td>
</tr>
<tr>
<td>conventional MRI</td>
<td>detects complications</td>
<td>non-specific</td>
</tr>
<tr>
<td>DPI</td>
<td>specific</td>
<td>expensive, lengthy</td>
</tr>
<tr>
<td>DWI</td>
<td>high specificity, high sensitivity in lesions larger than 5mm [3]</td>
<td>susceptibility artefact, low temporal resolution</td>
</tr>
<tr>
<td>HASTE-DWI</td>
<td>• high specificity and sensitivity</td>
<td>only morphological information</td>
</tr>
<tr>
<td></td>
<td>• no susceptibility artefact</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• higher temporal resolution</td>
<td></td>
</tr>
<tr>
<td>T1 and T2 mapping</td>
<td>quantitative</td>
<td>non-specific</td>
</tr>
</tbody>
</table>

Table 1. Comparison of methods in the diagnosis of cholesteatoma and epidermoid cyst

At the same time, HASTE-DWI provides only morphological, qualitative information. In the past years, quantitative MR techniques have been developing rapidly. T1 and T2 mapping are used to quantitatively measure T1 and T2 relaxation times in order to characterize the inherent properties of a tissue. This might enable to differentiate pathologies in the future by a specific T1 and T2 value. [14-16]

Consequently, the aim of the study was to quantify the T1 and T2 relaxation times of epidermoid cyst and middle ear cholesteatoma. Our further goal was to introduce a multimodal method combining HASTE-DWI, T1 and T2 mapping for the specific and quantitative characterization of epidermoid cysts and middle ear cholesteatomas. With the promotion of an accurate and reliable diagnosis, patients could avoid unnecessary second look surgeries.

**Methods and materials**

**Patients and study outline**
Our prospective study was conducted between December 2009 and November 2013. Patients with clinically suspected middle ear cholesteatoma and epidermoid cyst with no previous treatment underwent HASTE-DW, T1 and T2 mapping MR examination prior to surgery. Informed consent was signed by all patients. The MRI findings were blinded to the surgeon. Since the study aimed to validate our method, it was important to investigate patients who definitely had cholesteatoma, thus, patients with negative findings either with MRI or surgery were excluded. Further exclusion criteria were the lack of either operative or MRI data or the refusal of intervention. Out of 21 patients with middle ear cholesteatoma, 11 patients (8 male, 3 female, mean age 35.72, age range 6-62) and both of 2 patients with epidermoid cyst (2 male; mean age 38.5, age range 23-54) met the inclusion criteria. The mean time between the MR examination and surgery was 15.8 days (range: 1-48 days, SD 14.5). (Table 2. and Table 3.)

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age</th>
<th>Gender</th>
<th>Time between MR and surgery (days)</th>
<th>Localisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>male</td>
<td>1</td>
<td>4th ventricle, cisterna magna</td>
</tr>
<tr>
<td>2</td>
<td>54</td>
<td>male</td>
<td>22</td>
<td>cerebellopontine angle</td>
</tr>
</tbody>
</table>

Table 2. Patients with epidermoid cysts

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age</th>
<th>Gender</th>
<th>Type of cholesteatoma</th>
<th>Side</th>
<th>Time between MRI and surgery (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
<td>male</td>
<td>secondary acquired</td>
<td>right</td>
<td>29</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>male</td>
<td>secondary acquired</td>
<td>left</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>female</td>
<td>primary acquired</td>
<td>right</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>male</td>
<td>primary acquired</td>
<td>left</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>male</td>
<td>congenital</td>
<td>left</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>28</td>
<td>female</td>
<td>primary acquired</td>
<td>left</td>
<td>11</td>
</tr>
<tr>
<td>No.</td>
<td>Age</td>
<td>Sex</td>
<td>Side</td>
<td>Diagnosis</td>
<td>No.</td>
</tr>
<tr>
<td>-----</td>
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<td>-----</td>
</tr>
<tr>
<td>7</td>
<td>62</td>
<td>male</td>
<td>primary</td>
<td>acquired</td>
<td>13</td>
</tr>
<tr>
<td>8</td>
<td>40</td>
<td>male</td>
<td>primary</td>
<td>acquired</td>
<td>13</td>
</tr>
<tr>
<td>9</td>
<td>46</td>
<td>male</td>
<td>bilateral, right: primary acquired, left: secondary acquired</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>15</td>
<td>female</td>
<td>primary</td>
<td>acquired</td>
<td>14</td>
</tr>
<tr>
<td>11</td>
<td>36</td>
<td>male</td>
<td>primary</td>
<td>acquired</td>
<td>7</td>
</tr>
</tbody>
</table>

**Table 3. Patients with middle ear cholesteatomas**

**MR Imaging**

MR imaging was performed with a 3 T MRI scanner using a 12 channel head coil.

Conventional MR scans consisted of T1, T2, proton density weighted and FLAIR images. Additionally, axial HASTE-DW images (TR 3310ms, TE 122ms, 11 sections, slice thickness 4 mm, field of view 220 mm, matrix 192x192, flip angle 165°,15 averages, b factor 1000 s/mm²) and coronal HASTE-DW images with the same parameters (except slice number which was set 10) were acquired.

T1 map (TR 3000 ms, 8,1 TE ms,TI 100ms, 400ms, 700ms, 1100ms, 1400ms, 2000ms, 10 sections, slice thickness 3 mm, field of view 200 mm, matrix 128x128, flip angle 90°) and T2 map (TR 4500ms, TE 12,4ms, 34,8ms, 37,2ms, 49,6ms, 62ms, 74,4ms, 86,8ms, 99,2ms, 111,6ms, 124ms,15 sections, slice thickness 3 mm, field of view 210 mm, matrix 128x128, flip angle180°) were also obtained.

**Image analysis**

Images were examined by a neuroradiologist with 9 years of experience (H.K.), who was blinded to the results of surgery. Cholesteatoma or epidermoid cyst was diagnosed if the lesion had high signal intensity in comparison with brain tissue on HASTE-DW images.
Images of 2 patients with epidermoid cyst and 11 patients with middle ear cholesteatoma who showed positivity with both MRI and surgery were analyzed. Axial HASTE images were spatially coregistered to T1 and T2 maps using FSL Linear Registration Tool (FMRIB Software Library v5.0, http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). This step enabled to localize cholesteatoma and epidermoid cyst on T1 and T2 maps. 

**Fig. 1 on page 8**

**Fig. 2 on page 8**

Then, a mask was created on T1 and T2 maps where HASTE-DW indicated the lesion. T1 and T2 relaxation times were calculated by Matlab software’s curve fitting toolbox. T2 relaxation times were measured within each mask by calculating and mono-exponentially fitting the mean signal intensity to 10 echo times. **Fig. 3 on page 9** T1 relaxation times were calculated for each patient by mono-exponential fitting of the mean signal intensity to 6 inversion times. **Fig. 4 on page 9**

**References:** Department of Neurosurgery, University of Pécs, Medical School, Diagnostic Centre of Pécs - Pécs/HU
Fig. 3: The calculation of T2 relaxation time. T2 map was obtained using 10 different echo times. Afterwards, a curve was fitted to the average signal intensity values covered by the mask, thus, T2 relaxation time could be calculated.

References: Department of Neurosurgery, University of Pécs, Medical School, Diagnostic Centre of Pécs - Pécs/HU
Fig. 4: The calculation of T1 relaxation time. T1 map was obtained by using 6 different inversion times. Then, a curve was fitted to the average signal intensities covered by the mask, thus T1 relaxation time could be calculated.

References: Department of Neurosurgery, University of Pécs, Medical School, Diagnostic Centre of Pécs - Pécs/HU

Images for this section:

Fig. 1: Image registration and mask creation. A) HASTE-DW MRI of a patient with middle ear cholesteatoma B) First volume of T1 map C) Co-registration of HASTE-DWI and the first volume of T1 map D) Mask creation on co-registered images.
**Fig. 2:** Image registration and mask creation in epidermoid cyst. A) HASTE-DWI B) Third volume of T2 map C) Co-registration of HASTE-DWI and the third volume of T2 map D) Mask creation on co-registered images.

**Fig. 3:** The calculation of T2 relaxation time. T2 map was obtained using 10 different echo times. Afterwards, a curve was fitted to the average signal intensity values covered by the mask, thus, T2 relaxation time could be calculated.
Fig. 4: The calculation of T1 relaxation time. T1 map was obtained by using 6 different inversion times. Then, a curve was fitted to the average signal intensities covered by the mask, thus T1 relaxation time could be calculated.
Results

2 patients with epidermoid cyst and 11 patients with middle ear cholesteatoma met the inclusion criteria and were recruited into our study. 10 patients were subsequently excluded due to MRI negativity.

In one of the patient with epidermoid cyst, the lesion occupied the entire fourth ventricle extending into the cisterna magna. **Fig. 5** on page 13 In the other patient, the epidermoid was located in the cerebellopontine angle. **Fig. 6** on page 13

![Fig. 5: MR images of a patient with epidermoid cyst located in the fourth ventricle A) axial T1-weighted MRI B) axial T2-weighted MRI C) coronal FLAIR D) axial HASTE-DWI E) coronal HASTE-DWI](image)

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Fig. 6: MR images of a patient with epidermoid cyst located in the cerebellopontine angle A) axial T1-weighted MRI B) coronal T2-weighted MRI C) axial proton density-weighted MRI D) axial HASTE-DWI E) coronal HASTE-DWI

References: Department of Neurosurgery, University of Pécs, Medical School, Diagnostic Centre of Pécs - Pécs/HU

Among the patients with middle ear cholesteatoma, 1 patient had congenital, 7 patients had primary acquired, 2 patients had secondary acquired, and 1 patient had bilateral middle ear cholesteatoma, 1 of them was primary acquired, the other was secondary acquired.

In epidermoid cysts the mean T1 relaxation time was 2260 ms ± 361,5777 ms and the mean T2 relaxation time was 553,8 ms ± 30,42571 ms
In patients with middle ear cholesteatomas the mean T1 relaxation time was 1519.78 ms ± 201.92 ms and the mean T2 relaxation time was 169.45 ms ± 30.50 ms.

**Images for this section:**

**Fig. 5:** MR images of a patient with epidermoid cyst located in the fourth ventricle A) axial T1-weighted MRI B) axial T2-weighted MRI C) coronal FLAIR D) axial HASTE-DWI E) coronal HASTE-DWI
**Fig. 6:** MR images of a patient with epidermoid cyst located in the cerebellopontine angle
A) axial T1-weighted MRI B) coronal T2-weighted MRI C) axial proton density-weighted MRI D) axial HASTE-DWI E) coronal HASTE-DWI
Conclusion

HASTE-DW is now widely used in the diagnosis of middle ear cholesteatoma due to its high sensitivity and specificity. Restricted diffusion is one possible reason for the characteristic high signal in cholesteatoma and epidermoids on both DWI and HASTE-DWI sequences. In contrast, the diffusion of water molecules is less restricted in postsurgical conditions such as inflamed tissue, granulation tissue or fibrous tissue resulting in a hypointense signal. This enables differentiation. In addition, the other possible reason for hyperintense signal in epidermoids and cholesteatoma might be the T2 shine-through effect, which is due to the prolonged relaxation time of keratin. [4, 7, 8, 12, 13]

Our results showed relatively long T1 and T2 relaxation times in both patients groups which can be caused by the high keratin content of both epidermoid cyst and cholesteatoma. This finding supports the fact that T2-shine through effect is responsible for high signal on DWI and HASTE-DW images.

T1 and T2 relaxation times depend on the chemical and physical environments of water protons in tissue. Therefore, contrast between normal and pathologic tissue is based on differences in tissue microstructure. Thus, the knowledge of T1 and T2 relaxation times promotes understanding the inherent properties of a tissue and enables the quantitative assessment of tissue pathology. Despite of being lengthy, quantification might further increase sensitivity and specificity of measurements. Our preliminary results might be a step towards the differentiation of pathologies by specific T1 and T2 values.

In conclusion, HASTE-DW is specific and sensitive for epidermoid cyst and cholesteatoma, while T1 and T2 mapping are quantitative methods. The combination of these techniques provides objective information about the structure and inherent properties of cholesteatoma and epidermoid cyst besides being a powerful tool for the physician. As a consequence, the further development of the method may benefit patients by helping them to avoid unnecessary second-look surgery.

Personal information

References


