lek. Emilia Wnuk

Ocena aktualnych kryteriów radiologicznych w badaniu rezonansu magnetycznego u pacjentów z chorobą Ménière'a

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu

w dyscyplinie nauki medyczne

Promotor: Prof. dr hab. n. med. Magdalena Lachowska

Promotor pomocniczy: Dr n. med. Edyta Maj

II Zakład Radiologii Klinicznej Warszawskiego Uniwersytetu Medycznego

Katedra i Klinika Otorynolaryngologii, Chirurgii Głowy i Szyi

Warszawskiego Uniwersytetu Medycznego

Obrona rozprawy doktorskiej przed Radą Dyscypliny Nauk Medycznych

Warszawskiego Uniwersytetu Medycznego

Warszawa 2023 r.

Słowa kluczowe w języku polskim

Choroba Ménière'a

Wodniak endolimfatyczny

Wodniak śródchłonki

Rezonans magnetyczny

Sekwencja 3D-FLAIR

Skala Barath

Skala Bernaerts

Słowa kluczowe w języku angielskim *(keywords)*

Ménière's disease

Endolymphatic hydrops

Magnetic resonance imaging

3D-FLAIR sequence

Barath's scale

Bernaerts' scale

Wykaz publikacji stanowiących pracę doktorską

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Pol J Radiol. 2022; 87: e354–e362. MEiN **70 pkt**

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023; 12(1): 202. MEiN **140 pkt,** IF **4,964**

Łączna punktacja MEiN: **210 pkt**

Łączny Impact Factor: **4,964**

Spis treści

Wykaz stosowanych skrótów (w kolejności alfabetycznej)

3D-FLAIR	trójwymiarowa sekwencja powrotu inwersji z supresją płynu (*three dimensional-fluid-attenuated inversion recovery sequence*)
3D-REAL IR	trójwymiarowa rzeczywista sekwencja powrotu inwersji (*three dimensional-real inversion recovery sequence*)
AAO-HNS	Amerykańska Akademia Otorynolaryngologii, Chirurgii Głowy i Szyi (*American Academy of Otorhinolaryngology, Head and Neck Surgery*)
CoEH	wodniak endolimfatyczny ślimaka (*cochlear endolymphatic hydrops*)
EH	wodniak endolimfatyczny (*endolymphatic hydrops*)
MD	choroba Ménière'a (*Ménière's disease*)
MR	badanie rezonansu magnetycznego (*magnetic resonance imaging*)
PE	wzmocnienie struktur perylimfatycznych (*perilymphatic structures enhancement*)
VEH	wodniak endolimfatyczny przedsionka (*vestibular endolymphatic hydrops*)

Streszczenie w języku polskim

Wstęp

Choroba Ménière'a (MD) jest chorobą ucha wewnętrznego charakteryzującą się zawrotami głowy, fluktuującym niedosłuchem w zakresie niskich częstotliwości, szumami usznymi i uczuciem pełności w uchu. Na podstawie wyników badań sekcyjnych publikowanych w literaturze uważa się, że u jej podłoża leży poszerzenie struktur śródchłonki ucha wewnętrznego tzw. wodniak endolimfatyczny (EH). Przez lata brakowało możliwego do łatwej oceny biomarkera tej choroby, a diagnostyka choroby Ménière'a oparta była na obrazie klinicznym, wynikach badań dodatkowych i była diagnozą z tzw. wykluczenia innych przyczyn obserwowanych dolegliwości. Z rozwojem techniki rezonansu magnetycznego (MR) oraz odkryciem, że struktury perylimfatyczne wzmacniają się po podaniu kontrastu, a endolimfatyczne pozostają niezakontrastowane, uwidocznienie wodniaka endolimfatycznego *in vivo* stało się możliwe. Istnieje jednak kilka możliwych sposobów uwidoczniania EH w MR, dodatkowo powstało kilka sposobów oceny EH. W rezultacie aktualnie występują rozbieżności w wynikach publikowanych badań. Większość badaczy zgadza się, że EH towarzyszy chorobie Ménière'a, ale bywa też obecny w innych podobnych do choroby Ménière'a patologiach ucha wewnętrznego, a nawet u osób zdrowych. Poszukiwane są zatem dodatkowe cechy diagnostyczne, m.in. ocenia się stopień wzmocnienia kontrastowego struktur perylimfatycznych ucha wewnętrznego (PE), które mogłyby stać się biomarkerem choroby. Ponieważ jest to nowa metoda diagnostyki, wiele kwestii wymaga jeszcze wyjaśnienia i ustalenia standardów co do sposobu wykonywania badań MR, jak i ich analizy.

Przedstawiana rozprawa doktorska składa się z cyklu publikacji, w której prezentuję wyniki badań po raz pierwszy wprowadzonych w Polsce do diagnostyki radiologicznej w chorobie Ménière'a. Jednocześnie wszystkie pochodzące z Polski publikacje na ten temat (przytoczone w rozprawie jako „spoza cyklu" pochodzą z ośrodka, w którym pracuję, tj. II Zakładu Radiologii Klinicznej Warszawskiego Uniwersytetu Medycznego, a także z Katedry i Kliniki Otorynolaryngologii, Chirurgii Głowy i Szyi Warszawskiego Uniwersytetu Medycznego, z którą współpracuję w tym zakresie.

Publikacja nr 1 wchodząca w skład cyklu rozprawy doktorskiej

Wnuk E*, Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology*

and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971

W artykule szczegółowo przedstawiony został protokół badawczy z dokładnym opisem metodologii badania i szczegółowym objaśnieniem zasad oceny obrazów rezonansu magnetycznego struktur ucha wewnętrznego, zaprezentowany na przykładach siedmiu pacjentów z klinicznie zdefiniowaną jednostronną chorobą Ménière'a. Opisane zostały używane w protokole sekwencje, ich parametry, cewka odbiorcza, sposób i ilość podania środka kontrastowego. Szczegółowo przedstawiona i wyjaśniona została skala oceny EH, zarówno dla ślimaka jak i przedsionka, według metody opisanej przez Barath i wsp., a także modyfikacja tej skali przez Bernaerts i wsp. Opisy uzupełnione zostały drobiazgowo oznaczonymi obrazami skanów MR, aby ułatwić zrozumienie tej metody oceny. Ponadto, zawarty został przegląd literatury na temat obrazowania EH. Praca ta może stanowić instrukcję opisującą w jaki sposób stworzyć i wprowadzić protokół diagnostyki dla pacjentów z chorobą Ménière'a, a następnie jak powstałe badania należy interpretować w świetle aktualnej wiedzy.

Publikacja nr 2 wchodząca w skład cyklu rozprawy doktorskiej

Wnuk E*, Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023, 12(1), 202. DOI. 10.3390/jcm12010202*

W pracy oceniano obrazy MR, 110 pacjentów z podejrzeniem choroby Ménière'a, uzyskane z zastosowaniem trójwymiarowej sekwencji powrotu inwersji z supresją płynu (3D-FLAIR) w fazie opóźnionej po kontraście. Skany oceniały niezależnie trzy badaczki, które w czasie oceniania obrazów MR nie były świadome statusu klinicznego pacjentów. Dwie z nich były radiologami z wieloletnim doświadczeniem, jedna była otolaryngologiem, nauczonym metody oceny w trakcie krótkiego szkolenia w tym zakresie. W sumie oceniono 220 uszu pod kątem czterech parametrów: wodniaka endolimfatycznego ślimaka (CoEH) w trójstopniowej skali zaproponowanej przez Barath i wsp., wodniaka endolimfatycznego przedsionka (VEH) w trójstopniowej skali zaproponowanej przez Barath i wsp., i w czterostopniowej skali zaproponowanej przez Bernaerts i wsp., oraz wzmocnienia struktur perylimfatycznych ucha wewnętrznego.

Celem pracy było sprawdzenie na ile ocena poszczególnych, wyżej wspomnianych, parametrów jest powtarzalna pomiędzy badaczami w badaniach wykonanych z użyciem sekwencji 3D-FLAIR i czy jest łatwa do nauczenia. Dodatkowo praca przedstawia analizy

częstości występowania wodniaka endolimfatycznego w uszach pacjentów z chorobą Ménière'a, w porównaniu z uszami z innymi objawami imitującymi chorobę Ménière'a oraz w uszach bez objawów.

Analizując obecność wodniaka w uszach objawowych pacjentów z chorobą Ménière'a, obecność CoEH stwierdzono w 76-80% uszu (zależnie od badacza), VEH w skali Barath w 74,7% uszu, VEH w skali Bernaerts w 81,3% uszu, zaś PE było obecne w 58,7-62,7% uszu objawowych. Natomiast w uszach bezobjawowych częstość występowania tych kryteriów były znacząco niższa, CoEH był obecny w 2,7-8,2% uszu, VEH w skali Barath w 2,7%, VEH w skali Bernaerts w 11%, PE w 2,7-5,5%. Obecność wodniaka była też niska w uszach z innymi objawami przypominającymi chorobę Ménière'a, stanowiąc kolejno 4,5-6%, 4,5%, 7,5% oraz 13,4%. Traktując te kryteria łącznie dało to wysoką czułość 0.84-0.87 i swoistość 0.82-0.88 tej metody oceny dla uszu z MD.

Jednocześnie zaobserwowano duże różnice pomiędzy badaczami dla oceny parametru CoEH. Parametr ten był zwłaszcza trudny do oceny dla badacza bez doświadczenia w ocenie MR (różnice między radiologami i badaczem niedoświadczonym 8% i 13%), ale również pomiędzy radiologami różnice były duże (5%). Okazało się jednak, że problemem nie było odróżnienie ślimaka z patologią od zdrowego, ale poprawne przypisanie stopnia zaawansowania EH. W przypadku oceny VEH w obu skalach doświadczeni badacze oceniali parametr dokładnie tak samo dla 220 obserwacji, zaś nieco odbiegały jedynie oceny niedoświadczonego badacza, ale i tak zgodność wszystkich badaczy dla tego parametru była wysoka. Podobnie było z ostatnim kryterium.

Podsumowanie

Przedstawione wyniki prac stanowiących cykl publikacji tworzących rozprawę doktorską dowodzą, że wizualizacja w MR struktur endolimfatycznych i perylimfatycznych ucha wewnętrznego jest możliwa. Pokazują, że istnieją cechy radiologiczne (EH i PE), które występują znacznie częściej w uszach z objawami choroby Ménière'a niż w uszach bezobjawowych, czy patologiach o objawach podobnych do choroby Ménière'a. W efekcie mogą być one obrazowym biomarkerem tej choroby, wspierającym rozpoznanie zwłaszcza w nietypowych i wczesnych przypadkach, nie spełniających jeszcze pełnych klinicznych kryteriów rozpoznania.

Ocena struktur endolimfatycznych przedsionka w badaniach z użyciem sekwencji 3D-FLAIR jest łatwa do nauczenia i powtarzalna, co przedstawiono w prezentowanych

publikacjach tworzących cykl rozprawy doktorskiej. Trudniejsza jest ocena struktur śródchłonki ślimaka; z tym, że samo zdiagnozowanie CoEH nie jest trudne, to jego stopniowanie stwarza trudności i jest mniej powtarzalne nawet dla doświadczonych badaczy. Wydaje się, że dla monitorowania stopnia nasilenia patologii należy szukać innej metody diagnostyki (być może innej sekwencji MR).

Streszczenie w języku angielskim *(Abstract)*

Evaluation of currently used radiological criteria in the diagnostics of Ménière's disease

Introduction

Ménière's disease (MD) is an inner ear disorder characterized by vertigo episodes, fluctuating low-frequency hearing loss, tinnitus, and aural fullness. The hydropic dilatation of endolymphatic structures (EH) was found in post-mortem studies of temporal bone specimens of patients with MD and is claimed to be a cause of disease.

For many years, the *in vivo* assessment of the EH was not possible. The diagnosis of MD was based on the patient's symptoms, clinical findings, and functional test and was the diagnosis of exclusion.

With the development of magnetic resonance imaging (MR) and the discovery that the intravenously administered contrast moves into perilymphatic spaces of the inner ear, whereas not to the endolymphatic structures, visualization of endolymphatic structures has become possible.

The two principal sequences applied to EH imaging using MR exist, and several scales of EH assessment were proposed in the literature. It results in a discrepancy in the reported frequency of EH, potentially due to the radiological criteria used. Most researchers agree that EH accompanies MD, but it is sometimes present in healthy individuals and in other MD-like pathologies of the inner ear. Additional radiological features are sought, including the degree of enhancement of inner ear structures (PE), which could become a biomarker of disease. Since this is a new method in diagnostics, many issues still need to be clarified and standards established regarding the methodology of MR and evaluation of images.

My doctoral dissertation consists of a series of published manuscripts presenting the results of MR studies for the first time introduced in Poland into radiological diagnostics in Ménière's disease. At the same time, all Polish publications on this subject (cited at the end of this dissertation as "outside the series" come from the center where I work, which is the 2nd Department of Clinical Radiology of the Medical University of Warsaw and the Department of Otorhinolaryngology, Head and Neck Surgery of the Medical University of Warsaw, with which I cooperate in this regard.

Manuscript #1 in the dissertation series

***Wnuk E**, Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971*

The manuscript presents the research protocol with a detailed description of the methodology and a detailed explanation of magnetic resonance images evaluation of the structures of the inner ear, presented on the examples of seven patients with clinically defined unilateral Ménière's disease. All applied MR sequences, their parameters, used receive coil, method, and amount of administrated contrast agent were presented. The EH assessment scale for both the cochlea and the vestibule, according to the method described by Barath et al. and its modification by Bernaerts et al., was explained in detail. The descriptions were supplemented with MR scans, which makes this method easier to understand. Furthermore, a review of the literature on EH imaging is included. This manuscript may be an instruction on creating and implementing a diagnostic protocol for patients with MD and how the results should be interpreted according to current knowledge.

Manuscript #2 in the dissertation series

***Wnuk E**, Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023, 12(1), 202. DOI. 10.3390/jcm12010202*

The study evaluated MR images obtained using the contrast-delayed three dimensional-fluid-attenuated inversion recovery sequence (3D-FLAIR) of 110 patients with suspected MD. The images were assessed independently by three researchers who were unaware of the patients' clinical status. Two of them were radiologists with many years of experience, and one was an otorhinolaryngologist who was taught the MR assessment method during a short training in this field. In total, 220 ears were evaluated using four parameters: cochlear endolymphatic hydrops (CoEH) in a three-point scale proposed by Barath et al., vestibular endolymphatic hydrops (VEH) in a three-point scale proposed by Barath et al. and on a four-point scale proposed by Bernaerts et al., and enhancement of the inner ear structures.

The study aimed to evaluate if the qualitative assessment of the 3D-FLAIR sequence using the above mentioned criteria is consistent between the observers and whether it is easy

to learn. In addition, all the MR assessed endolymphatic hydrops features were analyzed to calculate the sensitivity and specificity of the method.

When analyzing the presence of hydrops in the symptomatic MD ears, CoEH was found in 76-80% (depending on the observer), Barath VEH in 74.7%, Bernaerts VEH in 81.3-82.7%, and PE was present in 58.7-62.7% of symptomatic ears. However, in asymptomatic ears, the prevalence of these criteria was significantly lower. CoEH was present in 2.7-8.2% of ears, Barath VEH in 2.7%, Bernaerts VEH in 11%, and PE in 2.7-5.5%. It was also low in ears with other MD-like symptoms, 4.5-6%, 4.5%, 7.5%, and 13.4%, respectively. Analyzing these above mentioned features together gives a high sensitivity of 0.84-0.87 and a specificity of 0.82-0.88 for this assessment method for ears with MD.

At the same time, significant inter-observer differences in assessing the CoEH parameter were observed. This parameter was more complicated to grade for the observer after a short training in MR evaluation (differences between radiologists and unexperienced observer 8% and 13%). However, even between radiologists, the differences in the CoEH parameter evaluation were significant (5%). However, after a more detailed analysis of the obtained results, it turned out that the problem was not to distinguish a pathologically changed cochlea from a normal cochlea but to correctly assign the severity of the pathology. In VEH staging using both scales, experienced observers were consistent in their assessment of 220 ears. Only the unexperienced observer's assessments differed slightly. However, still, the agreement of all researchers for this parameter was high. Same with the last criterion – increased perilymphatic enhancement.

Conclusions

The results of presented studies constituting the series of publications of my doctoral dissertation prove that MR visualization of endolymphatic and perilymphatic structures of the inner ear is possible. They show that radiological criteria of EH and PE occur much more often in ears with MD symptoms than in asymptomatic ears or ears with MD-like symptoms. Therefore they might be a biomarker of MD, supporting the diagnosis, especially in atypical and early cases of MD. Evaluation of MR scans of vestibular endolymphatic structures using 3D-FLAIR is easy to learn and repeatable. The evaluation of cochlear endolymphatic structures might be more complicated; however, the diagnosis of CoEH itself using MR is not complicated, and its gradation is, even for experienced observers. It seems that another diagnostic method of CoEH (perhaps a different MR sequence) should be sought to monitor the severity of the pathology.

Rozprawa doktorska – cykl publikacji

Ocena aktualnych kryteriów radiologicznych w badaniu rezonansu magnetycznego u pacjentów z chorobą Ménière'a

Wstęp

Choroba Ménière'a (MD) jest przewlekłą chorobą ucha wewnętrznego charakteryzującą się grupą objawów takich jak zawroty głowy pochodzenia błędnikowego, fluktuujący niedosłuch w zakresie niskich częstotliwości, szumy uszne i uczucie pełności w uchu. Na podstawie wyników badań sekcyjnych publikowanych w literaturze uważa się, że u jej podłoża leży poszerzenie struktur śródchłonki ucha wewnętrznego, tzw. wodniak endolimfatyczny (EH). Do tej pory brakowało jednak możliwości obserwacji takich zmian *in vivo*. Toteż rozpoznanie choroby Ménière'a oparte była na wywiadzie, obrazie klinicznym oraz wynikach badań audiologicznych i otoneurologicznych, i było niejako diagnozą z wykluczenia innych przyczyn powstałych objawów. Dopiero z rozwojem techniki obrazowania metodą rezonansu magnetycznego (MR) odkryto, że po dożylnym podaniu kontrastu struktury perylimfatyczne ucha wewnętrznego ulegają zakontrastowaniu (są widoczne w badaniu jako jasne obszary), a endolimfatyczne pozostają niezakontrastowane (pozostają ciemne na tle wzmacniających się struktur perylimfatycznych), tym samym przyżyciowe uwidocznienie wodniaka śródchłonki (EH) stało się możliwe.

Aby uzyskać wspomniany obraz w badaniu MR, wykonuje się ponownie badanie MR po 4 godzinach od podania gadolinowego środka kontrastowego (tzw. faza opóźniona), stosując zmodyfikowane sekwencje trójwymiarowe powrotu inwersji z supresją płynu (3D-FLAIR) i/lub rzeczywistą powrotu inwersji (3D-REAL IR). Następnie powstałe w badaniu MR obrazy oceniane są pod kątem poszerzania struktur śródchłonki. W literaturze opisanych zostało kilka metod analizy radiologicznej, każda z nich ocenia osobno struktury endolimfatyczne ślimaka i przedsionka. Są to następujące metody: półilościowa - scharakteryzowana przez Naganawę i wsp. tzw. skala z Nagoya, objętościowa - opublikowana m.in. przez Gürkova i wsp. oraz jakościowa - opisana przez Barath i wsp. Dodatkowo Attye i wsp. zaobserwowali, że w wodniaku śródchłonki zmienia się szerokość struktur endolimfatycznych przedsionka, tj. woreczka i łagiewki, i na tej podstawie określony został tzw. wskaźnik wymiaru woreczka do łagiewki. Bazując na tych obserwacjach, Bernaerts i wsp. zmodyfikowali skalę oceny przedsionka zaproponowaną przez Barath i wsp., dodając jeden dodatkowy stopień - bardzo niskiego stopnia wodniak przedsionka (*extra low-grade vestibular hydrops*).

Biorąc pod uwagę fakt, że metoda radiologicznej oceny wodniaka endolimfatycznego jest nowa (obecna dopiero od kilku lat), a w różnych ośrodkach stosowane są zróżnicowane protokoły badania MR oraz skale do oceny stopnia EH, toteż panuje występują rozbieżności

w wynikach publikowanych badań. Większość badaczy zgadza się, że EH towarzyszy chorobie Ménière'a, ale zaobserwowano, że bywa obecny też u osób zdrowych i w innych patologiach o objawach podobnych do choroby Ménière'a. Podawane dane liczbowe różnią się jednak pomiędzy publikacjami. Dodatkowo znajdowane są inne cechy radiologiczne mogące być istotnymi, kryteriami diagnostycznymi u pacjentów z chorobą Ménière'a, m.in. ocenia się stopień wzmocnienia struktur ucha wewnętrznego (PE). Te cechy łącznie prawdopodobnie mogłyby być obrazowym biomarkerem choroby, ale kwestie metodologii wykonywania badania MR (tj. stosowania odpowiednich sekwencji i wybór właściwych parametrów) oraz oceny tego badania wymagają jeszcze wyjaśnienia i ustalenia standardów. Zwłaszcza, że wydaje się, iż ta nowa metoda, która jest szczegółowo zaprezentowana w publikacjach stanowiących rozprawę doktorską, pozwalając na diagnostykę patologii jaką jest wodniak endolimfatyczny, będzie wspierać i ułatwiać diagnozę kliniczną choroby Ménière'a. Umożliwi także zrozumienie procesów patologicznych leżących u jej podłoża i w dalszej perspektywie ułatwi optymalny wybór leczenia i monitorowanie efektów terapii.

Prezentowane publikacje stanowiące rozprawę doktorską traktują o zastosowaniu MR w diagnostyce patologii ucha wewnętrznego u pacjentów z klinicznym rozpoznaniem choroby Ménière'a oraz szczegółowo analizują stosowane radiologiczne kryteria oceny wodniaka endolimfatycznego.

Zgodnie z moją wiedzą, jestem pierwszą badaczką w Polsce, która wprowadziła i dostosowała parametry badania tej metody diagnostyki radiologicznej, tak, że stała się dostępna na szeroką skalę. Dodatkowo, wszystkie pochodzące z Polski publikacje na ten temat, których znaczna część jest opublikowana w czasopismach zagranicznych, pochodzą z ośrodka w którym pracuję, tj. II Zakładu Radiologii Klinicznej Warszawskiego Uniwersytetu Medycznego oraz z Katedry i Kliniki Otolaryngologii, Chirurgii Głowy i Szyi Warszawskiego Uniwersytetu Medycznego, z której Zespołem współpracuję.

Pierwszą pracę cyklu rozprawy doktorskiej (***Wnuk E***, *Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971)* stanowi artykuł, w którym przedstawiony został protokół badawczy z dokładnym opisem metodologii badania i szczegółowym objaśnieniem zasad oceny obrazów rezonansu magnetycznego struktur ucha wewnętrznego zaprezentowany na przykładach siedmiu pacjentów z klinicznie zdefiniowaną

jednostronną chorobą Ménière'a, zgodnie z kryteriami Amerykańskiej Akademii Otorynolaryngologii, Chirurgii Głowy i Szyi (AAO-HNS).

W artykule tym szczegółowo opisany został protokół badawczy diagnostyki radiologicznej badaniem MR, stosowany w ocenie struktur ucha wewnętrznego u pacjentów z chorobą Ménière'a. Zaprezentowane zostały używane w protokole sekwencje MR, ich parametry, stosowana cewka odbiorcza, sposób podania i dawka środka kontrastowego. Precyzyjnie opisana została kluczowa dla diagnostyki wodniaka sekwencja 3D-FLAIR wykonywana w fazie opóźnionej po podaniu środka kontrastowego. Ponadto przedstawiona i wyjaśniona została skala oceny EH - zarówno dla ślimaka, jak i przedsionka, według metody opisanej przez Barath i wsp, a także modyfikacja tej skali przez Bernaerts i wsp. Opisy uzupełnione zostały drobiazgowo oznaczonymi obrazami skanów MR, aby ułatwić zrozumienie tej metody oceny. Ponadto w dyskusji artykułu zawarto przegląd aktualnej literatury na temat obrazowania wodniaka endolimfatycznego.

Praca ta może stanowić instrukcję opisującą w jaki sposób stworzyć i wprowadzić protokół diagnostyki dla pacjentów z chorobą Ménière'a, a następnie jak powstałe w badaniu obrazy MR należy interpretować w świetle aktualnej wiedzy.

Drugą pracą cyklu rozprawy doktorskiej (***Wnuk E***, *Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023, 12(1), 202. DOI. 10.3390/jcm12010202*) jest artykuł w którym dokonano analizy obrazów MR 110 pacjentów z podejrzeniem choroby Ménière'a. Skany uzyskane z zastosowaniem sekwencji 3D-FLAIR w fazie opóźnionej po kontraście, zostały ocenione niezależnie przez trzy badaczki, które w czasie oceniania obrazów MR nie były świadome statusu klinicznego pacjentów. Dodatkowo dwie z nich były radiologami z wieloletnim doświadczeniem w ocenie badań MR, jedna była otolaryngologiem, przeszkolonym w krótkim czasie w zakresie metody oceny wodniaka. W sumie oceniono 220 uszu pod kątem czterech parametrów (kryteriów):

1. wodniaka endolimfatycznego ślimaka (CoEH) w trójstopniowej skali zaproponowanej przez Barath i wsp.,
2. wodniaka endolimfatycznego przedsionka (VEH) w trójstopniowej skali zaproponowanej przez Barath i wsp.,
3. wodniaka endolimfatycznego przedsionka (VEH) w czterostopniowej skali zaproponowanej przez Bernaerts i wsp.,
4. wzmocnienia struktur perylimfatycznych ucha wewnętrznego.

Celem pracy było sprawdzenie na ile ocena poszczególnych kryteriów jest powtarzalna pomiędzy badaczami i czy jest łatwa do nauczenia, nawet dla początkującego, niedoświadczonego badacza. Dodatkowo praca przedstawia analizy częstości występowania wodniaka endolimfatycznego w uszach pacjentów z chorobą Ménière'a, w porównaniu z uszami z innymi objawami imitującymi chorobę Ménière'a oraz w uszach bez objawów.

Założenia i cel pracy

Celem przeprowadzonych badań było sprawdzenie:

1. Czy uwidocznienie wodniaka endolimfatycznego w badaniu MR jest możliwe.
2. Jak często w grupie uszu z objawami choroby Ménière'a występuje wodniak endolimfatyczny oraz intensywniejsze wzmocnienie kontrastowe struktur perylimfatycznych w porównaniu z grupą uszu bezobjawowych oraz z uszami z objawami przypominającymi chorobę Ménière'a .
3. Na ile, ocena stopnia nasilenia wodniaka struktur endolimfatycznych, przy użyciu skal Barath i wsp. oraz modyfikacji zaproponowanej przez Bernaerts i wsp. oraz stopnia wzmocnienia struktur perylimfatycznych ucha środkowego jest powtarzalna pomiędzy badaczami, w badaniach MR wykonanych z użyciem sekwencji 3D-FLAIR, i czy jest łatwa do nauczenia, nawet dla początkującego badacza.

Ponadto, opisując szczegółowo metodologię wykonywania badań i ich oceny w „Polskim Przeglądzie Radiologicznym" („*Polish Journal of Radiology"*), chciałam spopularyzować i ułatwić rozpoczęcie wykonywania tych badań w innych ośrodkach w naszym kraju.

Kopie opublikowanych prac

© Pol J Radiol 2022; 87: e354-e362
DOI: https://doi.org/10.5114/pjr.2022.117971

Received: 04.05.2021
Accepted: 07.02.2022
Published: 30.06.2022

Polish Journal of Radiology

http://www.polradiol.com

Original paper

Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series

Emilia Wnuk[1,A,B,D,E,F], Magdalena Lachowska[2,A,D,E,F], Agnieszka Jasińska-Nowacka[2,B,D,E], Edyta Maj[1,D,E], Olgierd Rowiński[1,D,E], Kazimierz Niemczyk[2,A,E]

[1]2nd Department of Clinical Radiology, Medical University of Warsaw, Poland
[2]Department of Otorhinolaryngology, Head and Neck Surgery, Medical University of Warsaw, Poland

Abstract

Purpose: The study aimed to describe the methodology and detailed interpretation of magnetic resonance imaging (MRI) in patients with Ménière's disease (MD).

Material and methods: MRIs were performed on a 3T scanner. The three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) sequence 4 hours after a double dose of intravenous contrast was added to the standard MRI protocol in patients with clinically diagnosed MD. MRI findings of 7 patients with unilateral MD were analysed using 2 qualitative grading systems by Barath and Bernaerts.

Results: In MRI, the following changes in the group of patients with MD were observed: lack of endolymphatic hydrops (cases #1 and #7), various grades of cochlear hydrops (cases #2 and #3), various grades of vestibular hydrops (cases #4, #5, and #6), endolymphatic hydrops herniation into the semi-circular canal (case #6), and more robust perilymphatic enhancement (case #7).

Conclusions: In patients with MD, endolymphatic hydrops can be studied on MRI using 3D-FLAIR delayed post-contrast images. The qualitative grading system may be easily used in endolymphatic hydrops assessment. Recently described new radiological signs of MD such as increased perilymphatic enhancement of the cochlea and an extra low-grade VH may increase MD diagnosis sensitivity. MRI not only supports the clinical diagnosis of MD but also may help to understand its pathophysiology.

Key words: Ménière's disease, endolymphatic hydrops, inner ear, magnetic resonance imaging, 3D-FLAIR.

Introduction

Ménière's disease (MD) is a chronic inner ear disorder characterized by spontaneous vertigo episodes, fluctuating low-frequency hearing loss, tinnitus, and fullness in the ear [1]. In 1861 Prosper Ménière was the first to report that the inner ear disease might be a source of symptoms typical for this disease [2]. About 80 years later, Hallpike and Cairns [3] in England and Yamakawa [4] in Japan independently described the dilatation of endolymphatic structures in post-mortem temporal bone sections of patients with MD. For many years, the possibility of *in vivo* assessment of the endolymphatic hydrops (EH) did not exist. The diagnosis of MD was based on the patient's symptoms, clinical findings, and functional tests. Guidelines for MD diagnosis were formulated in 1995 by the American Academy of Otolaryngology-Head and Neck Surgery [5]. According to these criteria, a definite MD could be recognized only post-mortem. In 2015 this scale was simplified by the Barany society [1,6]; definite MD is recognized when the combination of symptoms and audiometrically proved sensorineural hearing loss is present and no other underlying vestibular pathology exists (Table 1); thus, it is a diagnosis of exclusion.

Correspondence address:
Prof. Magdalena Lachowska, MD, PhD, Department of Otorhinolaryngology, Head and Neck Surgery, Medical University of Warsaw, 1a Banacha St., 02-097 Warsaw, Poland, phone: +48 22 599 25 21, e-mail: mlachowska@wum.edu.pl

Authors' contribution:
A Study design · **B** Data collection · **C** Statistical analysis · **D** Data interpretation · **E** Manuscript preparation · **F** Literature search · **G** Funds collection

Table 1. American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) criteria for the diagnosis of Ménière's disease (MD) described in 2015 [1,5]

Definite MD	• Two or more spontaneous episodes of vertigo, each lasting 20 min to 12 h • Audiometrically documented low- to mid-frequency sensorineural hearing loss in one ear, defining the affected ear on at least one occasion before, during, or after one of the episodes of vertigo • Fluctuating aural symptoms (hearing, tinnitus, or fullness) in the affected ear • Not better accounted for by another vestibular diagnosis
Probable MD	• Two or more episodes of vertigo or dizziness, each lasting 20 min to 24 h • Fluctuating aural symptoms (hearing, tinnitus, or fullness) in the affected ear • Not better accounted for by another vestibular diagnosis

Consequently, radiology's role was to rule out other pathologies that might cause symptoms similar to those of MD. With the development of the magnetic resonance imaging (MRI) technique, especially very high-field scanners (3 Tesla), the visualization of endolymphatic structures has become possible. Nakashima and Naganawa [7] intratympanically administered contrast, which moved into the perilymphatic space of the inner ear so that non-contrasted endolymphatic structures were clearly visible on three-dimensional fluid-attenuated inversion recovery T2 (3D-FLAIR) sequence. A few years later, they improved this method using a double dose of intravenously administered contrast [8]. Once this method became more accessible, a great perspective of inner ear research opened up. Several scales of EH assessment were proposed: first, semi-quantitative described by Nakashima *et al.* [9], next volumetric by Gürkov *et al.* [10], a qualitative system by Barath *et al.* [11], followed by a saccular morphology-based method by Attye *et al.* [12], and a four-grade staging system recently published by Bernaerts *et al.* [13].

Our study aimed to describe the methodology and detailed interpretation of MRI findings in patients with MD.

Material and methods

The local Ethics Committee reviewed and approved the study protocol at the institution where the study was conducted (KB/110/2019). The project conforms to the Code of Ethics of the World Medical Association (Declaration of Helsinki). All patients gave their written informed consent for participation in the study.

In this study, the presented patients were included as examples to illustrate the methodology and detailed interpretation of MRI results. All the included patients were diagnosed with MD according to AAO-HNS criteria [1]. Seven patients (4 females and 3 males) with definite unilateral MD at different EH stages were enrolled in this study. The mean age at the time of the examination was 50.7 years (34-68 range).

All patients underwent an MRI study using a 3 Tesla MR scanner (Signa Architect, GE Healthcare, Milwaukee, USA) with a 16-channel phased array flex coil (GEM Flex Large coil, Neocoil, Pewaukee, USA). The examination was carried out in a supine position. Care was taken to tighten the coil as much as possible, considering patients' comfort and achieving the best image quality. The imaging protocol for MD included the following sequences: T2, T2 fluid-attenuated inversion recovery (T2 FLAIR), three-dimensional – fast-inflow steady-state acquisition (3D-FIESTA), three-dimensional – T1 (3D-T1), and three-dimensional fluid-attenuated inversion recovery T2 (3D-FLAIR). Post-contrast images were obtained shortly after administering a double dose (0.2 ml/kg) of gadobutrol (Gadavist; Bayer Schering Pharma AG, Berlin, Germany; 1.0 mmol/ml) using 3D-T1 sequence, and delayed post-contrast images were acquired 4 hours after contrast injection using 3D-FLAIR T2 sequence. The last sequence of 3D-FLAIR T2 with a double dose of contrast media was crucial for EH visualization and assessment. The detailed scan parameters are described in Table 2.

The MRI scans were analysed by 2 head and neck radiologists (the first and fourth authors) and by an otolaryngologist (the third author) using commercial imaging software (AW Server 3.2, GE Healthcare, Milwaukee, USA). EH was categorized using 2 grading systems: Barath [11] and Bernaerts [13] (Table 3). The assessment of the cochlear hydrops (CH) was performed at the level of the mid-modiolar area and the vestibular hydrops (VH)

Table 2. Detailed magnetic resonance sequence parameters of imaging protocol for Ménière's disease

Sequence	Plane	TR (ms)	TE (ms)	NEX	Matrix (mm)
T2	Axial and coronal	5385	120	2.0	416 × 416
T2 FLAIR	Axial	12 000	143	1.0	260 × 200
3D-FIESTA	Axial	9.3	3.0	1.0	480 × 480
3D-T1	Sagittal	6.9	2.8	1.0	256 × 256
3D-T2 FLAIR	Axial	7602	170	2.0	232 × 232

FLAIR – fluid-attenuated inversion recovery, 3D – three-dimensional, FIESTA – fast-inflow steady-state acquisition.

Table 3. Magnetic resonance imaging grading qualitative scales proposed by Barath [11] and modified by Bernaerts [13] for evaluation of the cochlear and vestibular endolymphatic hydrops

Severity of hydrops	Barath scale	Bernaerts scale
Cochlear endolymphatic hydrops (grade)		
Normal	0 – Barely visible/Invisible cochlear duct in enhancing scala vestibuli	
Mild	1 – Partial obstruction of scala vestibuli by dilated cochlear duct	
Severe	2 – Total obliteration of scala vestibuli by enlarged cochlear duct	
Vestibular endolymphatic hydrops		
Normal	0 – The saccule and utricle are separated, and the saccule is smaller than the utricle.	
Extra-low		1 – The saccule is equal or larger than the utricle but is not confluent with the utricle
Mild	1 – A confluence of saccule and utricle, a circular rim of perilymphatic space is visible	2 – A confluence of saccule and utricle, a circular rim of perilymphatic space is visible
Severe	2 – Total obliteration of the vestibular perilymphatic space by dilated endolymphatic structures	3 – Total obliteration of the vestibular perilymphatic space by dilated endolymphatic structures

at the level of the inferior part of the vestibule (below the mid-modiolar level). Furthermore, the degree of cochlear perilymphatic enhancement (PE) was evaluated in comparison to the contralateral (unaffected) side.

Results

Patients' demographics and clinical characteristics are presented in Table 4.

In the first example (patient #1), a 60-year-old female with right-sided MD, on post-contrast 3D-FLAIR, a non-enhancing endolymphatic cochlear duct was invisible within the enhancing perilymphatic scala vestibuli and scala tympani – no CH was observed. Moreover, the vestibular structures, saccule and utricle, were clearly separated from each other. These images were interpreted as normal, meaning grade 0 CH and grade 0 VH in the Barath scale (Figure 1). Moreover, the saccule was smaller than the utricle, which was also graded 0 VH on the Bernaerts scale (Figure 2).

In the second example (patient #2), a 34-year-old female with right-sided MD, MRI revealed a cochlear duct partially pushed away, enhancing the vestibular duct. It was classified as grade 1 CH (Figure 3). The vestibular structures were widened and confluent, but the vestibule's enhancing rim was still visible, corresponding with grade 1 of VH in the Barath scale and grade 2 in the Bernaerts scale. In addition, the more robust enhancement of the basal turn of the cochlea was present on the affected side (Figure 4).

In the third example (patient #3), a 53-year-old female with right-sided MD, MRI revealed a significant cochlear EH. The enlarged scala media completely obstructed the scala vestibuli corresponding to grade 2 CH in Barath classifications; in addition, the more pronounced enhancement of the cochlea was observed (Figure 5). Moreover, VH grade 1 in the Barath scale was present, which corresponds with grade 2 in the Bernaerts scale.

In the fourth example (patient #4), a 36-year-old male with right-sided MD, the only abnormality observed on MRI was an enlarged saccule. This structure was bigger than the utricle but not yet confluent with it. According to the Barath criteria, this finding is considered normal grade 0 VH, but in the grading system proposed by Bern-

Table 4. Patients' demographics and clinical characteristics of the study population [1,5]

Case No.	Gender	Age (years)	MD duration (years)	Affected ear	Hearing level (dB)	Hearing fluctuation (Y – Yes/N – No)	Tinnitus – Arenberg's scale (0-6)	Vertigo attacks (in the last 6 months)	AAO-HNS classification (definite/probable)
1	F	60	6	Right	20.00	Y	2	0	Definite
2	F	34	19	Right	32.50	Y	3	6.33	Definite
3	F	53	13	Right	70.00	N	4	7.17	Definite
4	M	36	14	Right	18.75	Y	5	0.33	Definite
5	F	59	3	Right	43.75	N	3	4	Definite
6	M	45	5	Right	72.50	N	5	4	Definite
7	M	68	5	Right	61.25	Y	0	1	Definite

AAO-HNS – American Academy of Otolaryngology-Head and Neck Surgery

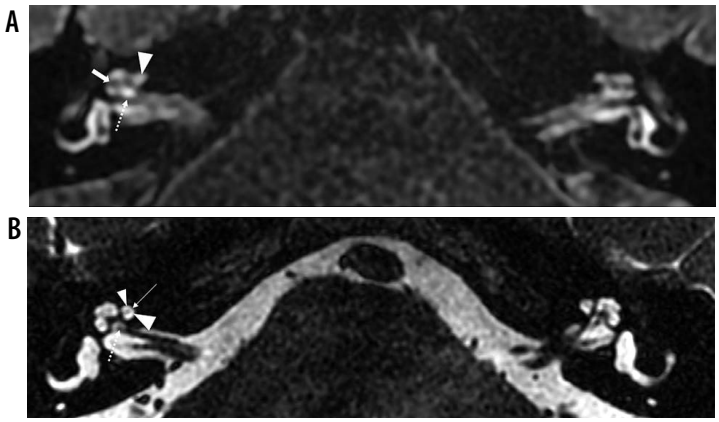


Figure 1. Magnetic resonance images of a 60-year-old female (patient #1) with right-sided clinically defined Ménière's disease. According to the Barath classification [11], the example case of the normal cochlea classified as grade 0 cochlear hydrops (CH). **A)** Delayed-postcontrast three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) T2 axial image of both ears at the level of cochlear modiolus (marked with a dotted arrow). A non-enhancing cochlear duct is invisible in the enhanced scala vestibuli and scala tympani (marked with an arrowhead) – no signs of CH, the inter-scalar septum visible between the cochlear turns (marked with a thick arrow). **B)** Three-dimensional fast-inflow steady-state acquisition (3D-FIESTA) axial image of both ears demonstrates the normal anatomy of the inner ear structures at the cochlear modiolus level (marked with a dotted arrow). Osseus spiral lamina (marked with a thin arrow) separates scala vestibuli (marked with an arrowhead) from scala tympani (marked with a small arrowhead)

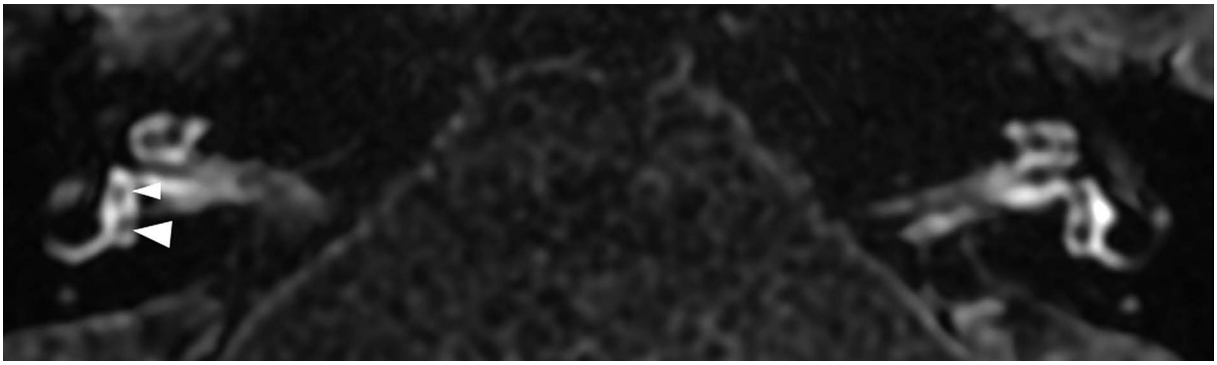


Figure 2. Magnetic resonance images of a 60-year-old female (patient #1) with right-sided clinically defined Ménière's disease. According to the Barath [11] and Bernaerts [13] classification, the example case of a normal vestibule classified as grade 0 vestibular hydrops. Delayed-postcontrast 3D-FLAIR T2 axial image of both ears below the level of modiolum (inferior part of the vestibule). The saccule (marked with a small arrowhead) and utricle (marked with an arrowhead) are well visualized. The saccule is smaller than the utricle, and endolymphatic structures encompass less than 50% of the vestibular area

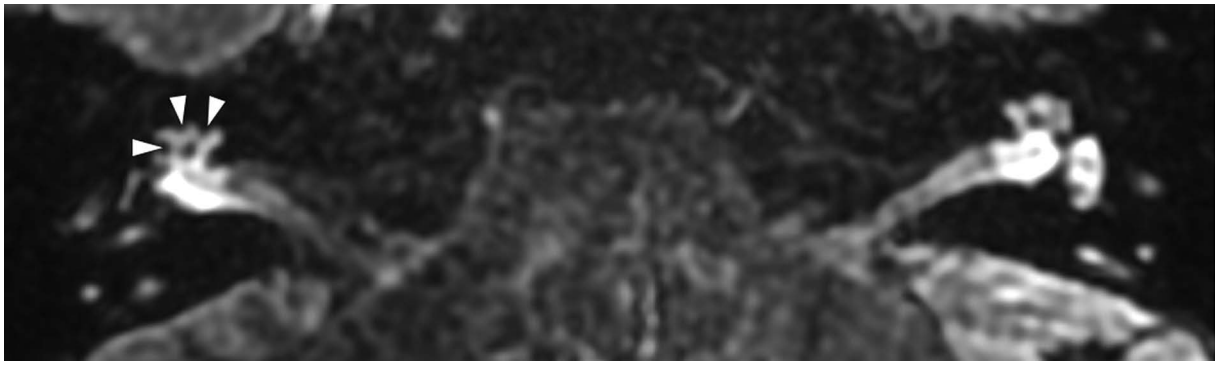


Figure 3. Magnetic resonance image of a 34-year-old female (patient #2) with right-sided clinically defined Ménière's disease. According to the Barath classification [11], it is an example case of grade 1 cochlear hydrops. Delayed-postcontrast 3D-FLAIR T2 axial image of both ears at the level of the cochlear modiolus. On the right side, a non-enhancing cochlear duct is visible as small dark nodules (marked with arrowheads) in the enhancing scala vestibuli; on the left side, normal left inner ear anatomy is presented for comparison

aerts, it was regarded as abnormal grade 1 VH (Figure 6). The CH or asymmetric PE was absent.

In the fifth example (patient #5), a 59-year-old female with right-sided MD, on MRI, vestibular endolymphatic structures were enlarged and confluent, but circular perilymphatic space was still visible. It corresponded with grade 1 VH in the Barath scale and grade 2 in Bernaerts modification (Figure 7). Furthermore, in this patient,

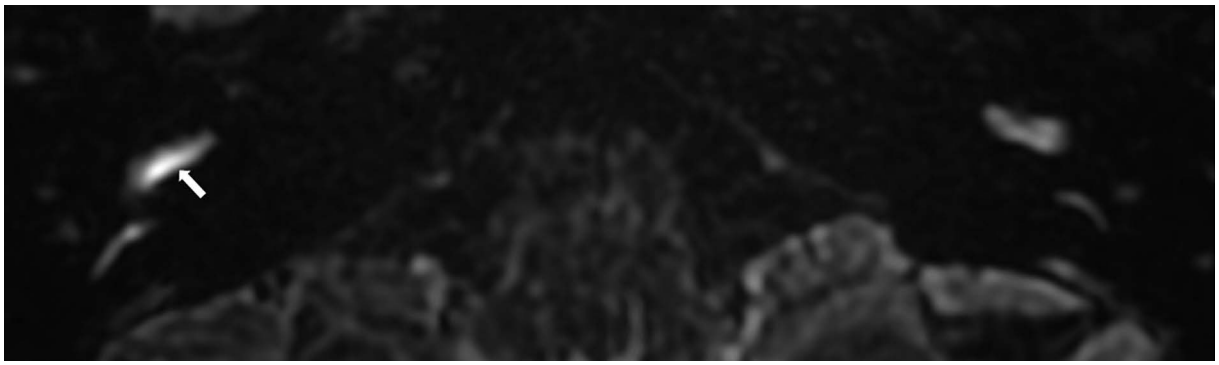


Figure 4. Magnetic resonance image of a 34-year-old female (patient #2) with right-sided clinically defined Ménière's disease. Delayed-postcontrast 3D-FLAIR T2 axial image of both ears at the level of the basal turn of the cochlea. The more robust enhancement of the basal cochlear turn on the affected right side (marked with an arrow) compared with normal perilymphatic enhancement on the left side

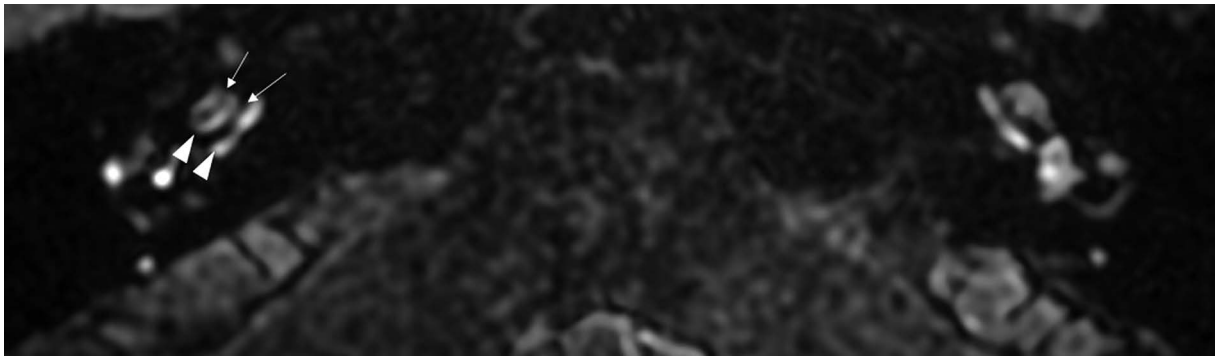


Figure 5. Magnetic resonance image of a 53-year-old female (patient #3) with right-sided clinically defined Ménière's disease. According to the Barath classification [11], it is an example case of grade 2 cochlear hydrops. Delayed-postcontrast 3D-FLAIR T2 axial image of both ears at the level of the cochlear modiolus. On the right side, a non-enhancing widened cochlear duct (marked with arrows) completely obstructs scala vestibuli, enhancing scala tympani (marked with arrowheads) resembling stripes

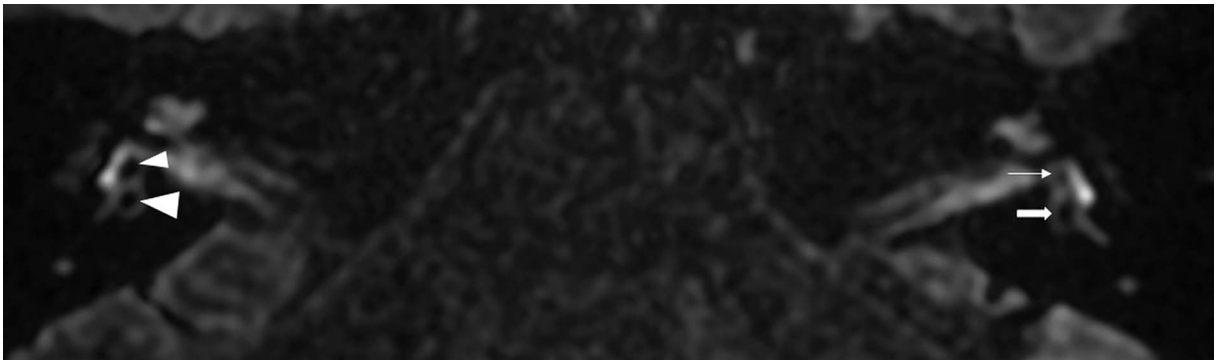


Figure 6. Magnetic resonance image of a 36-year-old male (patient #4) with right-sided clinically defined Ménière's disease. According to the Bernaerts classification [13], it is an example case of grade 1 (extra-low) vestibular hydrops. On the Barath scale [11], it is grade 0, presenting no signs of VH. Delayed-postcontrast 3D-FLAIR T2 axial image of both ears below the mid-modiolar level (inferior part of the vestibule). The right saccule (small arrowhead) is slightly bigger than the utricle (marked with an arrowhead), but the vestibular structures are still separated. Compared with a left unaffected side, the saccule (marked with a thin arrow) is smaller than the utricle (marked with a thick arrow)

grade 1 CH in the Barath classification and a more robust enhancement of the cochlea were present.

In the sixth example (patient #6), a 45-year-old male with right-sided MD, the dilated confluent saccule and utricle pushed away the perilymphatic space, and no surrounding contrast structure was seen around them (Figure 8A). Using the Barath classification, it was classified as grade 2 VH and as grade 3 in the Bernaerts modification. The widening of endolymphatic vestibular structures was so significant that they herniate into the posterior crus of the lateral semi-circular canal (Figure 8B). Moreover, CH grade 2 in the Barath classification with more robust PE was present.

In the seventh example (patient #7), a 68-year-old male with right-sided MD, on post-contrast 3D-FLAIR images no cochlear or vestibular EH was present, meaning grade 0 CH and grade 0 VH in both classifications, Barath and Bernaerts. Still, a robust PE of the cochlea was observed on the affected (right) side (Figure 9).

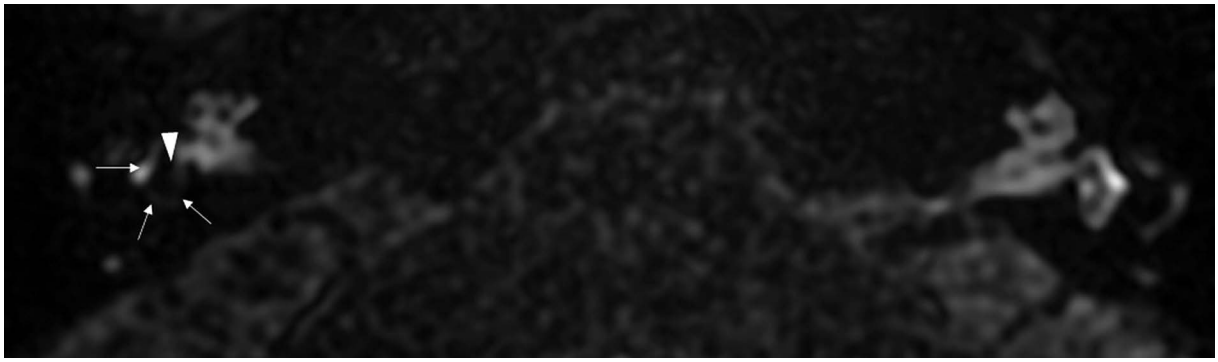


Figure 7. Magnetic resonance image of a 59-year-old female (patient #5) with right-sided clinically defined Ménière's disease. The example case of the mild vestibular hydrops – grade 2 in the Bernaerts scale [13] and grade 1 in the Barath grading system [11]. Delayed-postcontrast 3D-FLAIR T2 axial image of both ears below the mid-modiolar level (inferior part of the vestibule). On the right side, the saccule and utricle are enlarged and fused (arrowhead), but the enhancing rim of the vestibule's perilymphatic space is still visible (marked with arrows)

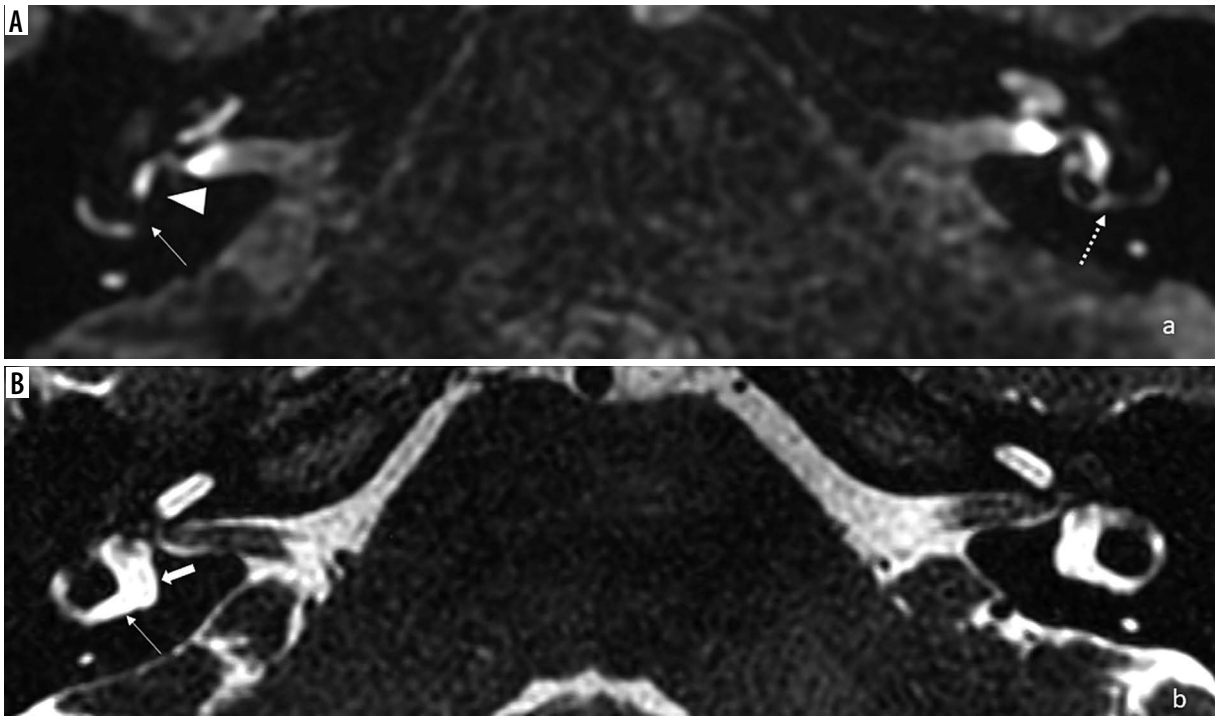


Figure 8. Magnetic resonance images of a 45-year-old male (patient #6) with right-sided clinically defined Ménière's disease. The example case of grade 2 vestibular hydrops according to the Barath classification [11] and grade 3 in the Bernaerts scale [13]. **A**) Delayed-postcontrast 3D-FLAIR T2 axial image of both ears below the mid-modiolar level (inferior part of the vestibule). No enhancing perilymphatic vestibular space is seen on the right. It is entirely encompassed by the widened, confluent endolymphatic saccule and utricle (marked with arrowhead). The endolymphatic hydrops herniation into the lateral semi-circular canal's posterior crus is visible (marked with an arrow). On the left side, the non-affected ear, the lateral semi-circular canal is preserved (marked with a dotted arrow). **B**) 3D-FIESTA axial image of both ears. Normal anatomy of the fluid-filled inner ear structures is visualized. The vestibule is marked with a thick arrow, posterior crus of the lateral semi-circular canal is marked with a thin arrow

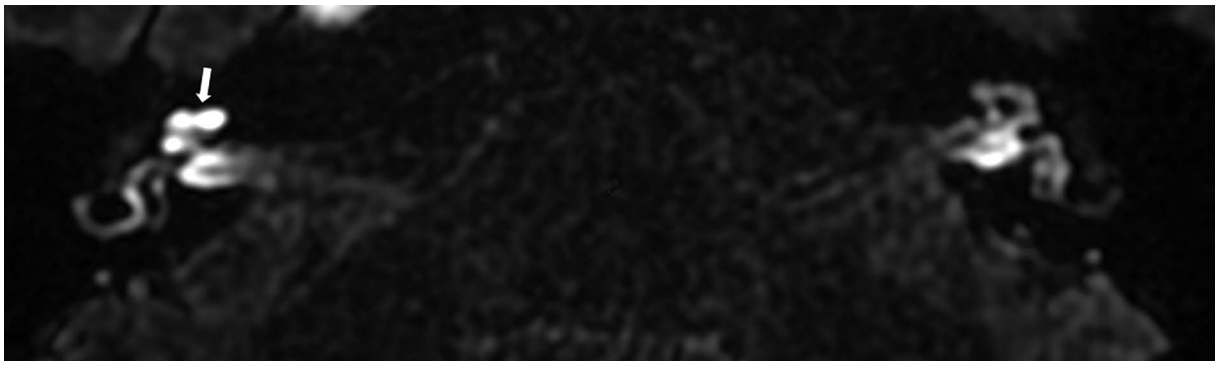


Figure 9. Magnetic resonance images of a 68-year-old male (patient #7) with right-sided clinically defined Ménière's disease. According to the Barath [11] and Bernaerts [13] classification, no signs of cochlear or vestibular endolymphatic hydrops are visible, classified as grade 0 in both scales. Delayed-postcontrast 3D-FLAIR T2 axial image of both ears at the mid-modiolar level revealed a more robust perilymphatic enhancement of cochlea on the affected (right) side (marked with an arrow)

Table 5. Magnetic resonance imaging findings in a group of patients with Ménière's disease. A cochlear hydrops was assessed using the Barath scale [11]. Vestibular hydrops was evaluated using the Barath [11] and Bernaerts [13] grading systems (VH grading in these 2 systems differ from each other, see Table 2). The degree of perilymphatic cochlear enhancement is presented

Case No.	Barath classification cochlea (grade 0, 1, or 2)	Barath classification vestibule (grade 0, 1, or 2)	Bernaerts classification vestibule (grade 0, 1, 2, or 3	Degree of perilymphatic cochlear enhancement (equal/stronger)
1	0	0	0	Equal
2	1	1	2	Stronger
3	2	1	2	Stronger
4	0	0	1	Equal
5	1	1	2	Stronger
6	2	2	3	Stronger
7	0	0	0	Stronger

All the above-described imaging findings are summarized in Table 5.

Discussion

In our study, the usefulness of the well-known Barath scale [11] and a four-stage vestibular grading system recently described by Bernaerts [13] was illustrated in 7 example cases to present all possible MRI findings. It shows that MRI is a valuable and accurate EH visualization method that supports the MD's clinical diagnosis. The delayed post-contrast 3D-FLAIR sequence allows for the visualization of endolymphatic structures.

The first example patient with definite MD had no signs of any EH and no signs of increased PE of inner ear structures. Although EH is thought to be a hallmark of MD [3,4,11], controversies exist about whether the EH is a cause of MD or a result of an underlying pathology that leads to MD development [14-16]. Many postmortem studies of temporal bones reported the presence of asymptomatic EH [15-19] as well as cases of MD without the EH [20-22]. These results are comparable with MRI studies. According to the literature [13,23,24], MRI does not reveal EH in 0-31% of patients with clinically diagnosed unilateral definite MD. Seo *et al.* [23] reported only one case without any EH within the group of 26 patients with MD (0.04%). In the Barath *et al.* [11] study, EH was not found in 5% (2/43) of affected ears, and in the Pakdaman *et al.* [24] study, EH was absent in 31% (10/32). These discrepancies might result from different EH assessment methods; some scientists used the semi-quantitative system proposed by Nakashima *et al.* [9], while others used the qualitative Barath system [11]. Furthermore, the MD duration in our first presented patient was not very long (6 years). The symptoms were mild; only weak vestibular symptoms were present, and the hearing was well preserved, which might explain the lack of visible changes within the inner ear. The impact of MD duration, the severity of symptoms, and the fluctuating character of MD in the presence of EH were analysed by Sepahdari *et al.* [25] and Bernaerts *et al.* [13]. They reported the influence of MD duration on the grade of EH.

The next controversial issue is the pattern of EH development. In his meta-analysis of 184 temporal bone reports with EH, Pender [26] found that EH starts in the cochlear apex and then encompasses the saccule, utricle, ampullae, and canals. Other observations from MRI studies [11,27,28] questioned this theory because many studies found a higher prevalence of vestibular rather than CH in MD patients. Attye *et al.* [12] found that comparing vestibular structures to each other (saccule to utricle) increased the specificity of MD detection on MRI. Bernaerts *et al.* [13] confirmed that adding a saccule evaluation increases the sensitivity without loss of specificity for the diagnosis of definitive MD, and cochlear EH does not improve diagnostic accuracy. In addition, studies on the use of heavily T2-weighted images evaluate only VH [29,30]. Those MRI findings support saccular [12,31] rather than cochleacentric theory for MD development.

A fourth example patient from our presented series is in line with the saccular theory. In this patient with normal hearing thresholds, no cochlear EH was present. However, the saccule was distended but was still separated from the utricle. On the Barath scales [11], this patient was classified as grade 0, which means no vestibular EH signs. By contrast, using the saccule-to-utricle ratio by Attye *et al.* [12] or four-stage VH by Bernaerts *et al.* [13], this case would be interpreted as abnormal, i.e. grade 1 VH on Bernaerts classification.

In our study, in the sixth example patient with severe VH, widened endolymphatic structures from the vestibulum herniated into the posterior, non-ampullated crus of the lateral semi-circular canal. A similar finding was described by Okuno and Sando [32] in MD patients' temporal bone specimens. Using MRI, the presence of this lesion was first reported by Gürkov *et al.* [33], who discovered that it correlates with an impaired caloric test. Recently, Sugimoto *et al.* [34] noticed that unilateral herniation is connected with EH progression.

Most of the patients in our group (5 of 7) had stronger PE of cochlea on the affected side. Two patients had equal PE on both sides; simultaneously, they did not have any CH signs. The first example patient had no signs of EH at all. The fourth example case had only VH. The increased inner-ear PE in MD was previously noted in various studies [11,24,35-37]. It is postulated that increased PE is related to increased blood-labyrinth barrier permeability [35,36]. Tagaya *et al.* [36] showed that the blood-labyrinth barrier is impaired in MD and that there is a correlation between EH and PE. In their study, all diseased ears presented stronger PE. Barath *et al.* [11] reported that the more robust contrast uptake was present in 90% of patients with EH. Conversely, Pakdaman *et al.* [24] compared blood-perilymph barrier permeability in MD patients with idiopathic sudden sensorineural hearing loss patients and found it to be higher in the MD group. They suggested that it might be a biomarker of MD. Recently, the value of cochlear PE in MD was proven by Bernaerts *et al.* [13]. They showed that PE assessment has high specificity and supports the diagnosis of MD. Furthermore, they proposed the diagnostic algorithm for unilateral MD. If the PE is more robust in the symptomatic ear, the ear can be classified as the MD ear, regardless of the presence of EH. The authors proved that this single factor has a higher inter-reader agreement than the clinical evaluation (0.79 vs. 0.66). In this context, our last patient (case example #7) is extremely interesting, with no EH signs but only with the cochlea's stronger PE on the symptomatic side. In this patient the dominating symptom was severe hearing loss, and the vestibular symptoms were not severe. In the literature, more robust PE enhancement was also described in patients with sudden deafness [38,39] and idiopathic sudden sensorineural hearing loss [24].

The main limitation of our study is the small number of patients; however, this is a pilot study, and we aimed to present the methodology and the most characteristic findings in a case series. Further studies with a larger group of patients are required. The second concern is the lack of a control group of healthy subjects. In our study, to evaluate endolymphatic hydrops, we chose the qualitative scale where each ear is assessed separately; therefore, there was no need to compare them to healthy controls. According to the Bernaerts criteria [13], each patient's affected ears and the contralateral ears were evaluated when assessing the perilymphatic enhancement of the cochlea as it is included in the criteria. Still, it does not mean that the contralateral ears were considered entirely healthy. The contralateral ears in our patients were asymptomatic and presented normal test results. However, it should be kept in mind that endolymphatic hydrops can develop for years in the contralateral ear in patients with unilateral MD before clinical symptoms from that ear start [24,40]. Moreover, using a double dose of contrast media in healthy volunteers might be ethically controversial, and there was no Ethics Committee approval for that.

Conclusions

In patients with MD, endolymphatic hydrops can be studied on MRI using 3D-FLAIR delayed post-contrast images. The qualitative Barath [11] grading system may be easily used in EH assessment. Bernaerts *et al.* [13] recently described new radiological signs of MD, such as increased perilymphatic enhancement of the cochlea, and an extra low-grade VH would be worth adding to the MRI assessment of EH. It might increase the diagnosis sensitivity of MD. MRI supports not only the clinical diagnosis of MD but also helps to understand its pathophysiology.

Statement of ethics

The local Ethics Committee reviewed and approved the study protocol at the institution where the study was conducted (KB/110/2019). The project conforms to the Code of Ethics of the World Medical Association (Declaration of Helsinki). All patients gave their written informed consent for participation in the study.

Conflict of interest

The authors report no conflict of interest.

References

1. Goebel JA. 2015 Equilibrium Committee amendment to the 1995 AAO-HNS guidelines for the definition of Meniere's disease. Otolaryngol Head Neck Surg 2016; 154: 403-404.
2. Meniere P. Maladies de l'oreille interne offrant les symptoms de la congestion cerebrale apoplectiforme. Gaz Med Paris 1861; 16: 88-89.
3. Hallpike CS, Cairns H. Observations on the pathology of Ménière's syndrome. Proc R Soc Med 1938; 31: 1317-1336.
4. Yamakawa K. Über die pathologische Veränderung bei einem Ménière-Kranken. J Otorhinolaryngol Soc Jpn 1938; 4: 2310-2312.
5. Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Menière's disease. American Academy of Otolaryngology-Head and Neck Foundation, Inc. Otolaryngol Head Neck Surg 1995; 113: 181-185.
6. Lopez-Escamez JA, Carey J, Chung WH, et al. Diagnostic criteria for Menière's disease. J Vestib Res 2015; 25: 1-7.
7. Nakashima T, Naganawa S, Sugiura M, et al. Visualization of endolymphatic hydrops in patients with Meniere's disease. Laryngoscope 2007; 117: 415-420.

8. Nakashima T, Naganawa S, Teranishi M, et al. Endolymphatic hydrops revealed by intravenous gadolinium injection in patients with Ménière's disease. Acta Otolaryngol 2010; 130: 338-343.
9. Nakashima T, Naganawa S, Pyykko I, et al. Grading of endolymphatic hydrops using magnetic resonance imaging. Acta Otolaryngol Suppl 2009; (560): 5-8.
10. Gurkov R, Berman A, Dietrich O, et al. MR volumetric assessment of endolymphatic hydrops. Eur Radiol 2015; 25: 585-595.
11. Barath K, Schuknecht B, Naldi AM, et al. Detection and grading of endolymphatic hydrops in Menière disease using MR imaging. AJNR Am J Neuroradiol 2014; 35: 1387-1392.
12. Attye A, Eliezer M, Boudiaf N, et al. MRI of endolymphatic hydrops in patients with Meniere's disease: a case-controlled study with a simplified classification based on saccular morphology. Eur Radiol 2017; 27: 3138-3146.
13. Bernaerts A, Vanspauwen R, Blaivie C, et al. The value of four stage vestibular hydrops grading and asymmetric perilymphatic enhancement in the diagnosis of Menière's disease on MRI. Neuroradiology 2019; 61: 421-429.
14. Rauch SD, Merchant SN, Thedinger BA. Meniere's syndrome and endolymphatic hydrops. Double-blind temporal bone study. Ann Otol Rhinol Laryngol 1989; 98: 873-883.
15. Merchant SN, Adams JC, Nadol JB Jr. Pathophysiology of Meniere's syndrome: are symptoms caused by endolymphatic hydrops? Otol Neurotol 2005; 26: 74-81.
16. Foster CA, Breeze RE. Endolymphatic hydrops in Ménière's disease: cause, consequence, or epiphenomenon? Otol Neurotol 2013; 34: 1210-1214.
17. Schuknecht HF, Gulya AJ. Endolymphatic hydrops. An overview and classification. Ann Otol Rhinol Laryngol Suppl 1983; 106: 1-20.
18. Vasama JP, Linthicum FH Jr. Meniere's disease and endolymphatic hydrops without Meniere's symptoms: temporal bone histopathology. Acta Otolaryngol 1999; 119: 297-301.
19. Belal A Jr, Antunez JC. Pathology of endolymphatic hydrops. J Laryngol Otol 1980; 94: 1231-1240.
20. Arnvig J. Histological findings in a case of Ménière's disease with remarks on the pathologic-anatomic basis of this lesion. Acta Otolaryngol 1947; 35: 453-466.
21. Belal A, Ylikoski J. Pathologic significance of Ménière's symptom complex: a histopathologic and electron microscopic study. Am J Otolaryngol 1980; 1: 275-284.
22. Fraysse BG, Alonso A, House WF. Menière's disease and endolymphatic hydrops: clinical-histopathological correlations. Ann Otol Rhinol Laryngol Suppl 1980; 89 (6 Pt 3): 2-22.
23. Seo YJ, Kim J, Choi JY, Lee WS. Visualization of endolymphatic hydrops and correlation with audio-vestibular functional testing in patients with definite Meniere's disease. Auris Nasus Larynx 2013; 40: 167-172.
24. Pakdaman MN, Ishiyama G, Ishiyama A, et al. Blood-labyrinth barrier permeability in Menière disease and idiopathic sudden sensorineural hearing loss: findings on delayed postcontrast 3D-FLAIR MRI. AJNR Am J Neuroradiol 2016; 37: 1903-1908.
25. Sepahdari AR, Ishiyama G, Vorasubin N, et al. Delayed intravenous contrast-enhanced 3D FLAIR MRI in Meniere's disease: correlation of quantitative measures of endolymphatic hydrops with hearing. Clin Imaging 2015; 39: 26-31.
26. Pender DJ. Endolymphatic hydrops and Ménière's disease: a lesion meta-analysis. J Laryngol Otol 2014; 128: 859-865.
27. Pyykko I, Nakashima T, Yoshida T, et al. Meniere's disease: a reappraisal supported by a variable latency of symptoms and the MRI visualisation of endolymphatic hydrops. BMJ Open 2013; 3: e001555.
28. Attye A, Dumas G, Tropres I, et al. Recurrent peripheral vestibulopathy: is MRI useful for the diagnosis of endolymphatic hydrops in clinical practice? Eur Radiol 2015; 25: 3043-3049.
29. Venkatasamy A, Veillon F, Fleury A, et al. Imaging of the saccule for the diagnosis of endolymphatic hydrops in Meniere disease, using a three-dimensional T2-weighted steady state free precession sequence: accurate, fast, and without contrast material intravenous injection. Eur Radiol Exp 2017; 1: 14.
30. Simon F, Guichard JP, Kania R, et al. Saccular measurements in routine MRI can predict hydrops in Menière's disease. Eur Arch Otorhinolaryngol 2017; 274: 4113-4120.
31. Morita N, Kariya S, Farajzadeh Deroee A, et al. Membranous labyrinth volumes in normal ears and Ménière disease: a three-dimensional reconstruction study. Laryngoscope 2009; 119: 2216-2220.
32. Okuno T, Sando I. Localization, frequency, and severity of endolymphatic hydrops and the pathology of the labyrinthine membrane in Menière's disease. Ann Otol Rhinol Laryngol 1987; 96: 438-445.
33. Gurkov R, Flatz W, Louza J, et al. Herniation of the membranous labyrinth into the horizontal semicircular canal is correlated with impaired caloric response in Ménière's disease. Otol Neurotol 2012; 33: 1375-1379.
34. Sugimoto S, Yoshida T, Teranishi M, et al. Significance of endolymphatic hydrops herniation into the semicircular canals detected on MRI. Otol Neurotol 2018; 39: 1229-1234.
35. Zou J, Poe D, Bjelke B, Pyykko I. Visualization of inner ear disorders with MRI in vivo: from animal models to human application. Acta Otolaryngol Suppl 2009 (560): 22-31.
36. Tagaya M, Yamazaki M, Teranishi M, et al. Endolymphatic hydrops and blood-labyrinth barrier in Ménière's disease. Acta Otolaryngol 2011; 131: 474-479.
37. Yamazaki M, Naganawa S, Tagaya M, et al. Comparison of contrast effect on the cochlear perilymph after intratympanic and intravenous gadolinium injection. AJNR Am J Neuroradiol 2012; 33: 773-778.
38. Tagaya M, Teranishi M, Naganawa S, et al. 3 Tesla magnetic resonance imaging obtained 4 hours after intravenous gadolinium injection in patients with sudden deafness. Acta Otolaryngol 2010; 130: 665-669.
39. Lee HY, Jung SY, Park MS, et al. Feasibility of three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging as a prognostic factor in patients with sudden hearing loss. Eur Arch Otorhinolaryngol 2012; 269: 1885-1891.
40. Balkany TJ, Sires B, Arenberg IK. Bilateral aspects of Meniere's disease: an underestimated clinical entity. Otolaryngol Clin North Am 1980; 13: 603-609.

Journal of
Clinical Medicine

MDPI

Article

Reliability of Endolymphatic Hydrops Qualitative Assessment in Magnetic Resonance Imaging

Emilia Wnuk [1], Magdalena Lachowska [2,*], Agnieszka Jasińska-Nowacka [2], Edyta Maj [1] and Kazimierz Niemczyk [2]

[1] 2nd Department of Clinical Radiology, Medical University of Warsaw, 02-097 Warsaw, Poland
[2] Department of Otorhinolaryngology Head and Neck Surgery, Medical University of Warsaw, 02-097 Warsaw, Poland
* Correspondence: magdalena.lachowska@wum.edu.pl; Tel.: +48-225992521

Abstract: The study aimed to compare the consistency of MRI interpretation of endolymphatic hydrops qualitative assessment of inner ear structures performed by independent observers. MRI with a delayed post-contrast 3D-FLAIR sequence was performed to visualize EH in patients suspected of having or diagnosed with MD. The scans were analyzed independently by three observers. In total, 220 ears were evaluated and, of these, 75 had definite MD, five probable MD, 67 with other Menieriform symptoms, and 73 were asymptomatic. Significant differences in cochlear endolymphatic hydrops (CoEH) grading between all observers were observed. On the Barath scale of vestibular endolymphatic hydrops (VEH), differences were found between the radiologists and otorhinolaryngologist in grading. No differences were noted in VEH on the Bernaerts scale and increased perilymphatic enhancement. Our study showed that evaluation of vestibular endolymphatic hydrops is repeatable between observers and easy to learn. It proved that Bernaerts' modification increased the sensitivity of EH diagnosis. Both parameters, CoEH and VEH, may serve as a differentiation method of EH from normal ears. The distinction between normal and hydropic ears is much easier to perform than EH grading. Therefore, it may be used to diagnose MD rather than EH staging.

Keywords: endolymphatic hydrops; inner ear; magnetic resonance imaging; Ménière's disease; vertigo; 3D-FLAIR

Citation: Wnuk, E.; Lachowska, M.; Jasińska-Nowacka, A.; Maj, E.; Niemczyk, K. Reliability of Endolymphatic Hydrops Qualitative Assessment in Magnetic Resonance Imaging. *J. Clin. Med.* **2023**, *12*, 202. https://doi.org/10.3390/jcm12010202

Academic Editor: Dong-Hee Lee

Received: 18 November 2022
Revised: 21 December 2022
Accepted: 25 December 2022
Published: 27 December 2022

1. Introduction

Ménière's disease (MD) is a chronic disorder of the inner ear characterized by spontaneous attacks of vertigo, fluctuating sensorineural hearing loss, tinnitus, and aural fullness [1,2].

The MD diagnosis depends on the patient's symptoms, medical history, and functional inner ear test results. Since the symptoms of MD are heterogenous and it takes time to develop from monosymptomatic to fully symptomatic disease, diagnosing early stages of MD or atypical forms of the disease is often complicated.

Therefore, scientists have been searching for a distinct characteristic of this disease. Approximately 80 years ago, a hydropic enlargement of the endolymphatic structures (cochlear duct within cochlea, utricle, and saccule of the vestibule) in temporal bone specimens of patients with MD was observed [3]. Even though it was an important discovery, its usefulness was limited, as it was impossible to visualize inner ear structures in vivo. Consequently, the diagnosis of MD has been based on the patient's symptoms, clinical findings, and functional inner ear test results. The only role of radiology was to exclude other pathologies with symptoms similar to MD [1,2]. With the breakthrough discovery of Nakshima and Naganawa that, in magnetic resonance imaging (MRI) using the delayed post-gadolinium contrast sequences, perilymphatic structures enhance and endolymphatic structures do not, visualizing endolymphatic hydrops (EH) became possible [4]. Since then, many studies have been performed to evaluate if an endolymphatic hydrops is a

biomarker of MD or if there are any other imaging features characteristic of this disease. A few imaging methods for the assessment of EH have been described in the literature, as follows: semiquantitative scale [5], qualitative [6], comparison of the size of saccule and utricle [7], and a modification of the qualitative scale by adding an extra-low vestibular hydrops grade [8].

Furthermore, a more robust enhancement of the affected inner ear structures has been reported in MD ears as a sign of blood–labyrinth barrier breakdown [8]. Many studies have described the presence of EH and increased perilymphatic enhancement in MD patients. However, a discrepancy in the reported frequency of EH exists, potentially due to the radiological criteria used.

One of the critical features of imaging in medicine is its reliability concerning image reading. It should be reliable regardless of the observers involved. In clinical settings, usually, it is one expert observer who studies a large number of images (cases), rather than multiple observers studying each case and comparing their results to determine the final image result. In the outpatient department setting, an otolaryngologist takes patients' history and examines and reads the MRI scans bought to the visit by the patient (sometimes without a result written by a radiologist).

The described frequency of endolymphatic hydrops differs among studies, as mentioned above. Some authors described the presence of endolymphatic hydrops also in healthy patients. It is not clear if endolymphatic hydrops is present only in Ménière's disease ears or might be present also in other inner ear diseases. This is similar to the asymmetry of perilymphatic enhancement. The debate is still going on, as to whether endolymphatic hydrops and increased perilymphatic enhancement can be biomarkers of Ménière's disease. From a clinical point of view, it is interesting and important to investigate if the differences between studies presented in the literature might result from MRI scan interpretation by different observers.

This study aimed to evaluate the qualitative assessment of inner ear hydrops to verify if it is consistent between observers and easy to learn from a practical clinical point of view for the needs of the daily work of a radiologist and otolaryngologist in clinical and outpatient department settings. In addition, all the MRI-assessed endolymphatic hydrops features were analyzed to calculate the sensitivity and specificity of the method.

In this study, we performed an MRI interpretation of endolymphatic hydrops qualitative assessment of inner ear structures by independent observers and compared the consistency of their MRI interpretation. We wanted to perform this investigation mimicking real clinical and outpatient department settings; that is, each of the observers interpreted the MRI scan once, and their results were compared. For that reason, three observers were engaged in this study, two radiologists and one otorhinolaryngologist. In addition, engaging an otorhinolaryngologist aimed to check if the evaluated method of endolymphatic hydrops assessment was easy to learn after reasonably short training, so that an ENT specialist (otorhinolaryngologist) in the outpatient department could read inner ear MRI scans by themselves during a patient's visit.

2. Materials and Methods

2.1. Ethical Consideration

This prospective study protocol was reviewed and approved by the Institutional Ethics Committee, where the study was conducted (KB/110/2019). All patients gave their written informed consent for participation in the study. The project conforms to The Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2. Study Group Description

Between June 2018 and December 2020, 120 consecutive patients suspected of having or diagnosed with MD according to AAO–HNS and Barany Society criteria [1,2] underwent MRI with delayed post-gadolinium 3D-FLAIR sequence. Furthermore, out of this group, ten patients were excluded due to insufficient clinical information (n = 4), insufficient MRI

quality (n = 3), or previous inner ear surgery (n = 3). Eventually, 110 patients were enrolled in this study and underwent a detailed analysis.

2.3. Magnetic Resonance Imaging Procedure and Analysis

The patients' MRI scans were performed using a 3 Tesla MR scanner (Signa Architect, GE Healthcare, Milwaukee, WI, USA) with a 16-channel phased array flex coil (GEM Flex Large coil, Neocoil, Pewaukee, WI, USA). This coil was used to minimize the distance between the inner ear structures and the coil. The examination was carried out in a supine position. A four hours delayed post-contrast axial 3D-FLAIR sequence was added to the standard MRI protocol of the posterior cranial fossa to visualize the inner ear structures. The following parameters characterized the sequence: 3D-FLAIR with a fat-suppression, acquired on an axial plane, covering the posterior cranial fossa; time of repetition 7602 ms, time of echo 170 ms, time of inversion 1897 ms, NEX 2.0, the field of view 18, slice thickness 0.8 mm, variable flip angle. A double dose (0.2 mL/kg) of intravenously injected gadobutrol (Gadovist; Bayer Schering Pharma AG, Berlin, Germany; 1.0 mmol/mL) was used to achieve optimal perilymphatic enhancement [4,6,9]. The posterior cranial fossa protocol also consisted of a three-dimensional fast inflow steady-state acquisition (3D-FIESTA) sequence to visualize the inner ear fluid space.

The MRI scans were analyzed independently by two (head and neck and neuro-) radiologists—(Rad 1 and Rad 2) and an otorhinolaryngologist in training (Oto), who was taught for a short time how to read the inner ear structures on MRI scans. All of them interpreted MRIs independently from one another, and all were blinded to the patients' clinical status and other diagnostics test results. The goal was to check if the method is repeatable between the different observers and if it is easy to learn.

The following radiological features were assessed in four steps:

1. Cochlear endolymphatic hydrops (CoEH) in a three-stage grading system by Barath [6]
2. Vestibular endolymphatic hydrops (VEH) in a three-stage grading system by Barath [6]
3. VEH in a modified four-stage scale by Bernaerts [8]
4. Enhancement of the inner ear structures [8].

The assessment of the CoEH was performed at the mid-modiolar level, and the VEH was evaluated at the level of the inferior part of the vestibule as described previously [6]. The signal intensity of perilymphatic structures enhancement (PE) was evaluated visually, and any asymmetry between two inner ear structures was reported. Each of the four radiological features was presented on an ordinal scale.

Cochlear endolymphatic hydrops in the three-stage grading system by Barath [6] was defined as either 0 as normal, 1 or 2 as pathology (Figure 1). Normal indicates a situation where the cochlear duct is faintly visible between the enhancing scala tympani and scala vestibuli. Grade 1 is a moderate cochlear duct enlargement and narrowed scala vestibuli. Grade 2 indicates a significantly enlarged cochlear duct that entirely obliterates scala vestibuli (virtually obstructing scala vestibuli).

Vestibular endolymphatic hydrops on the Barath scale, like cochlear endolymphatic hydrops, have been defined with a three-point scale (Figure 2). Grade 0—normal—means that the saccule and utricle are visible as nonenhanced structures within an enhanced vestibule. Grade 1 means some enlargement of the saccule and utricle, meaning that those structures are confluent and only the enhancing boundaries of the vestibule are still visible. Grade 2 indicates a significant enlargement of the saccule and utricle, so that the vestibule is obliterated.

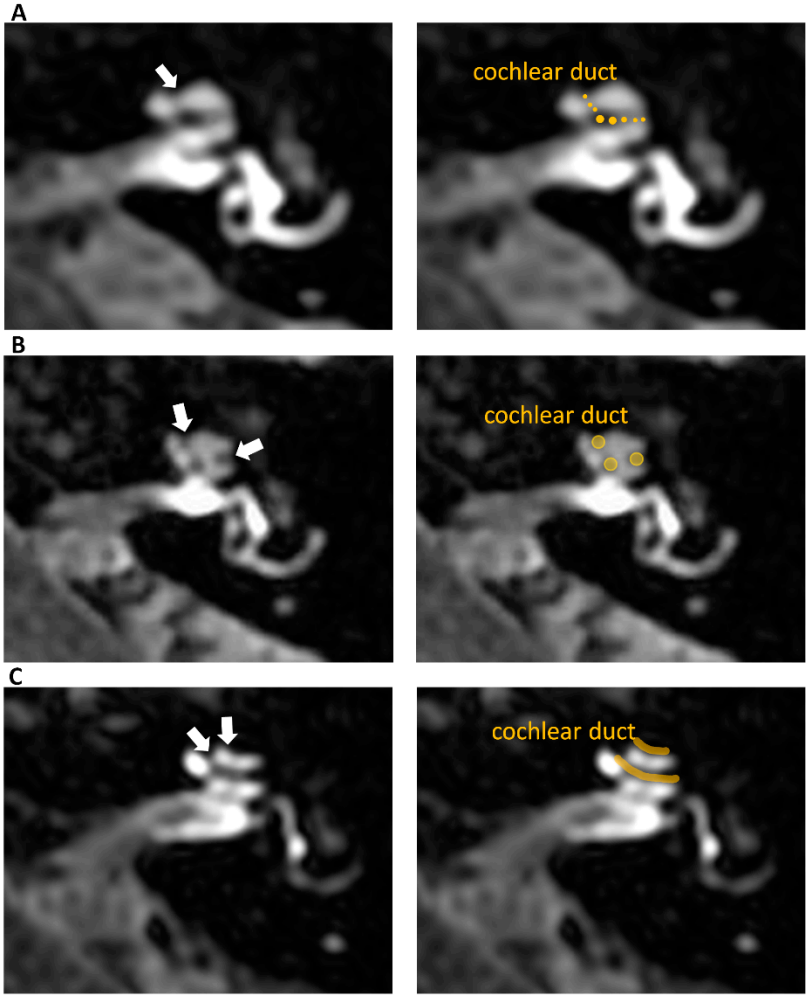


Figure 1. Delayed post-contrast 3D-FLAIR axial images of the left ears at the level of the cochlear modiolus. Right side images on panels (**A**–**C**) show the same images as the left ones in respective panels but in the form of companion scans with some line art applied to define specific anatomical structures for easier identification of observed pathologies. Panel (**A**) presents normal cochlea—grade 0 according to Barath classification, where a non-enhancing cochlear duct is barely visible between the enhancing scala vestibuli and scala tympani (arrow), and no signs of cochlear endolymphatic hydrops are detectable. Panel (**B**) shows grade 1 cochlear endolymphatic hydrops with partial obstruction of the scala vestibuli by a mildly dilated cochlear duct. The scan shows the nodular non-enhancing regions visible at the margins of the cochlea (arrows). Panel (**C**) presents grade 2 cochlear endolymphatic hydrops where the cochlear duct is significantly enlarged and obstructs scala vestibuli. The scan shows the non-enhancing stripes within the enhancing scala tympani (arrows).

In *vestibular endolymphatic hydrops in Bernaerts' modification* of the Barath scale [8], a new grade, 1, was added, making the scale a four-point, from 0 to 3 (Figure 2). In the Bernaerts' modification scale, grade 1 indicates small vestibular hydrops where the saccule is larger than the utricle but is still visually separated. Adding the new grade 1 means that grade 1 of the Barath scale becomes grade 2 and grade 2 becomes grade 3 in the modified Bernaerts scale.

Perilymphatic enhancement describes the enhancement of the inner ear structures. In MD, it has been observed that perilymphatic enhancement is more robust on the affected side than on the healthy side [8–10] (Figure 3). The scale, in this case, consists of 2 stages, from 0 to 1, with 1 indicating a more robust enhancement, while 0 describes a regular enhancement.

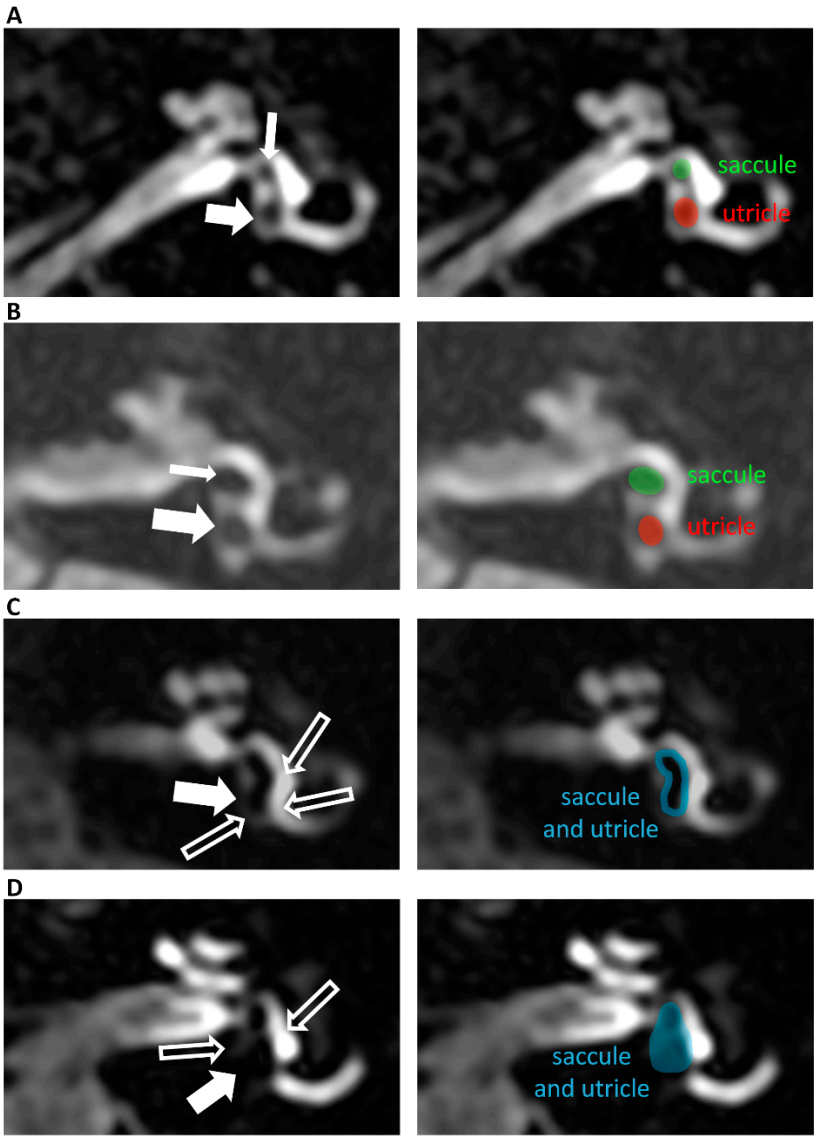


Figure 2. Delayed post-contrast 3D-FLAIR axial images of left ears below the mid-modiolar level (inferior part of the vestibule). The right side images on panel (**A**–**D**) show the same images as the left ones in respective panels but in the form of companion scans with some line art applied to define specific anatomical structures for easier identification of observed pathologies. Panel (**A**) presents a normal vestibule—grade 0 where non-enhancing the saccule (thin arrow) and utricle (thick arrow) are easily visible in the enhancing vestibule. The saccule is smaller than the utricle. Panel (**B**) presents extra low-grade, that is, grade 1 vestibular endolymphatic hydrops on Bearnaerts scale (but still grade 0 on Barath scale) where the saccule (thin arrow) and utricle (thick arrow) are well separated; however, the saccule is larger than the utricle, and the enhancing vestibule is seen around them. Panel (**C**) shows grade 2 vestibular endolymphatic hydrops on Bearnaerts scale (grade 1 on Barath scale) where the saccule and utricle are enlarged and confluent (thick arrow); however, thin enhancing boundaries of the vestibule are seen around them (long "empty" arrows). Panel (**D**) shows grade 3 vestibular endolymphatic hydrops on the Bearnaerts scale (grade 2 on the Barath scale), where significant enlargement of the saccule and utricle is so pronounced that the vestibule is almost totally obliterated (thin "empty" arrow). The saccule and utricle are enlarged and confluent (thick arrow); however, thin enhancing boundaries of the vestibule are seen around them (thin "empty" arrows).

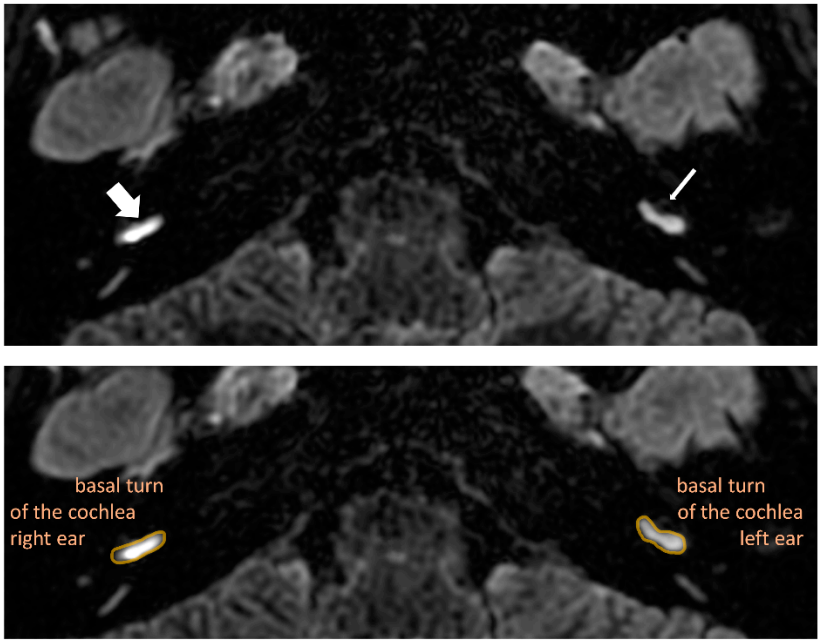


Figure 3. Delayed post-contrast 3D-FLAIR axial image of both ears at the level of the basal turn of the cochlea. In the top image, there is more robust enhancement of the basal cochlear turn on the affected right side (thick arrow), compared with normal perilymphatic enhancement on the left side (thin arrow). The bottom image is the same as the top one but in the form of a companion scan with some line art applied to define specific anatomical structures for easier identification of observed pathologies.

Furthermore, the four features were analyzed in detail. The sensitivity and specificity of each feature to identify Ménière's disease on MRI were calculated separately. Then the features mentioned above were combined to calculate the method's overall sensitivity and specificity.

2.4. Statistical Analysis

Statistical analysis was carried out in STATISTICA software (StatSoft, Inc. 2017 analysis software system, version 13.3). The data were tested for normality, parametric and non-parametric criteria. Detailed statistical analysis was performed with the following tests: Friedman analysis of variance (ANOVA), Kendall's concordance coefficient (Kendall's W), and Wilcoxon signed rank. The level of statistical significance was set at $p = 0.05$.

3. Results

3.1. Results

3.1.1. Patients' Characteristics

The mean age of the patients at the time of MRI evaluation was 47.65 years old (range 20–84). There was a slight female predominance, with 64 females and 46 males.

Out of 110 patients, 72 were diagnosed with definite MD, 5 with probable MD, and 33 with other diseases and symptoms that do not fulfill the diagnostic criteria for MD. Of the patients with definite MD, 69 presented unilateral disease, and three bilateral (which equalled made 75 definite MD ears). Furthermore, among patients with unilateral definite MD, 15 had unspecified symptoms from the contralateral ear that do not fulfill diagnostic AAO–HNS criteria for MD. A total of 220 ears were evaluated in this study, of which 75 were definite MD ears, five probable MD ears, 67 ears with other Menieriform symptoms, and 73 were asymptomatic ears (Table 1).

Table 1. The frequency of endolymphatic hydrops and increased perilymphatic enhancement of the inner ear structures in analyzed ears evaluated by three observers (two radiologists and an otorhinolaryngologist in training).

		CoEH Number of Ears (Percentage)			VEH Barath Number of Ears (Percentage)			VEH Bernaerts Number of Ears (Percentage)			PE Number of Ears (Percentage)		
Clinical diagnosis	**Number of ears** (total 220)	Rad1	Rad2	Oto	Rad1	Rad2	Oto	Rad1	Rad2	Oto	Rad1	Rad2	Oto
Definite MD	75	58 (77%)	60 (80%)	57 (76%)		56 (74.7%)			61 (81.3%)	62 (82.7%)	47 (62.7%)	46 (61.3%)	44 (58.7%)
Probable MD	5					0 (0%)						1 (20%)	
Other diseases	67	4 (6%)	4 (6%)	3 (4.5%)		3 (4.5%)			5 (7.5%)			9 (13.4%)	
Asymptomatic	73	4 (5.5%)	6 (8.2%)	2 (2.7%)		2 (2.7%)			8 (11%)		4 (5.5%)	2 (2.7%)	

CoEH—cochlear endolymphatic hydrops (grades 1, 2 together); VEH Barath—vestibular endolymphatic hydrops in scale proposed by Barath; VEH Bernaerts—vestibular endolymphatic hydrops in Bernaerts' modification of the Barath scale; PE—increased perilymphatic enhancement; MD—Ménière's disease; Rad1—radiologist #1; Rad2—radiologist #2; Oto—otorhinolaryngologist in training.

3.1.2. MRI Findings—Radiological Features Analysis

Cochlear endolymphatic hydrops. Within the group of definite MD ears, CoEH was present in 76–80% of ears, depending on the observer (Table 1). The sensitivity and specificity for CoEH diagnosis ranged between 0.76–0.8 and 0.92–0.97, respectively. In probable MD ears, CoEH was not observed. In patients with other Menieriform symptoms, CoEH was observed in 4.5–6%. CoEH was reported in 2.7–8.2% of asymptomatic ears, depending on the observer. The differences in CoEH grading are presented in Figure 4. The difference in observations was 5% between the two radiologists and 8% and 13% between radiologists (Rad1 and Rad2) and the otorhinolaryngologist, respectively. Multiple comparisons indicated significant differences between all three observers, confirmed by the low agreement value of Kendall's W test (Table 2). Pairs of observers' comparison showed significant differences, with a more considerable difference between the pairs of radiologists and otorhinolaryngologist. The main inconsistency was in the proper grading of CoEH, not in assessing the presence of any hydrops within the cochlea.

Vestibular endolymphatic hydrops on Barath scale. Using the qualitative Barath scale, VEH was observed in 75% of definite MD ears for all observers (Table 1). In asymptomatic ears, VEH was present in 2.7% of ears of patients with definite MD. The sensitivity for VEH was good at 0.75, and the specificity was very high at 0.97. In probable MD ears, VEH was not observed. In patients with other types of vertigo, EH was present in 4.5%. The differences in VEH grading are shown in Figure 4. The assessment of VEH on the Barath scale, comparing both radiologists, was precisely the same, and the only statistically significant differences were present between the pair of radiologists and the otorhinolaryngologist (Table 2). The main inconsistency was in the proper grading of VEH, not in assessing the presence of any hydrops within the vestibule.

Vestibular endolymphatic hydrops in Bernaerts' modification of Barath scale. Adding one grade (extra-low VEH) to the Barath scale increased the frequency of VEH diagnosis in MD ears to 81.3–82.7% and in asymptomatic ears to 11% (Table 1). Consequently, it improved the sensitivity to 0.81–0.83 but slightly decreased the specificity to 0.89. In probable MD ears, VEH was not observed. In patients with other types of vertigo, VEH was present in 9% of ears. The differences in VEH grading are summarized in Figure 4 and Table 2.

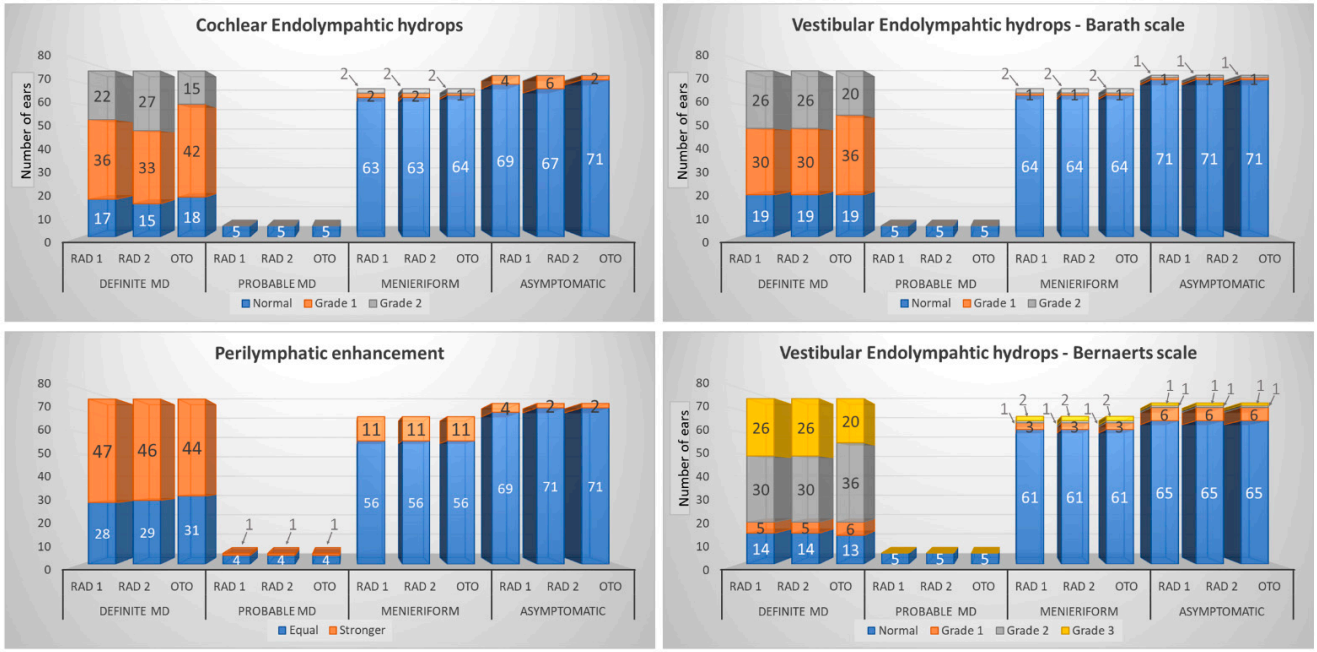


Figure 4. Stacked bar chart presenting differences of cochlear endolymphatic hydrops grading, vestibular endolymphatic hydrops grading on Barath scale, vestibular endolymphatic hydrops grading on Bernaerts modification, and perilymphatic enhancement assessment in each group of analyzed ears (definite Ménière's, probable Ménière's, ears with Menieriform symptoms, asymptomatic ears) performed by three observers (two radiologists and one otorhinolaryngologist in training; Rad1, Rad2, and Oto, respectively).

Table 2. Statistical dependencies (*p*-values) of ANOVA Friedman test, Kendall's concordance coefficient, and Wilcoxon signed-rank test—evaluation of each analyzed MRI hydrops feature differences across three observers (two experienced radiologists and otorhinolaryngologist in training) to assess inter-judge reliability.

Radiological Feature	Friedman ANOVA *p*-Value	Kendall's Concordance Coefficient	Pairs of Observers Compared	Number of Different Observations	Wilcoxon Test Results *p*-Value	ANOVA Test Results *p*-Value
CoEH	**0.0000 ***	0.0456	Rad1 vs. Rad2	11	0.0164	**0.0067 ***
			Rad1 vs. Oto	19	0.0269	**0.0116 ***
			Rad2 vs. Oto	30	0.0014	**0.0003 ***
VEH Barath	**0.0111 ***	0.0205	Rad1 vs. Rad2	0	–	–
			Rad1 vs. Oto	8	0.0587	**0.0339 ***
			Rad2 vs. Oto	8	0.0587	**0.0339 ***
VEH Bernaerts	0.1030	0.0103	Rad1 vs. Rad2	0	–	
			Rad1 vs. Oto	11	0.1823	0.1317
			Rad2 vs. Oto	11	0.1823	0.1317
PE	0.2053	0.0072	Rad1 vs. Rad2	7	0.3105	0.2568
			Rad1 vs. Oto	11	0.1823	0.1317
			Rad2 vs. Oto	6	0.4631	0.4142

The asterisk (*) and bold font were used to mark statistically significant differences ($p < 0.05$). CoEH—cochlear endolymphatic hydrops (grades 1, 2 together); VEH Barath—vestibular endolymphatic hydrops in scale proposed by Barath; VEH Bernaerts—vestibular endolymphatic hydrops in Bernaerts' modification of the Barath scale; PE—increased perilymphatic enhancement; Rad1—radiologist #1; Rad2—radiologist #2; Oto—otorhinolaryngologist in training.

Perilymphatic enhancement. An increased PE was observed in 58.7–62.7% of definite MD ears, 20% of probable MD ears, 16.4% of ears with other Menieriform symptoms, and 2.7–5.5% of asymptomatic ears (Table 1). The differences in perilymphatic enhancement assessment are shown in Figure 4. The ANOVA Friedman test showed no significant differences for this parameter between the assessment of all three observers and between the pairs of observers (Table 2).

The above-mentioned combined features to identify Ménière's disease on MRI (endolymphatic hydrops (both cochlear and vestibular) and increased perilymphatic enhancement) gave a sensitivity ranging between 0.84 and 0.87 and specificity of 0.82–0.88.

4. Discussion

In the last few years many MRI studies have been performed on MD but, still, there is a lack of a gold standard for MRI protocols and assessment methods. Different protocols of examinations (both methods of contrast administration and sequences employed on MRI), various scales, and biomarkers are used in radiological diagnosis. Some researchers have used intratympanic [4,11–17], others intravenous administration of gadolinium-based contrast-agent [6,8,18–21]. Yamazaki et al. [22] compared two methods of contrast injection and suggested that the intratympanic contrast administration provides better perilymphatic enhancement than intravenous and probably should be used in unilateral MD. However, the intratympanic method is invasive, allows for unilateral examination only, is off-label GBCA use, and requires 24-h waiting time [18,23], so the intravenous method is widely used as more feasible and comfortable for the patient. Furthermore, this method of contrast administration allows the assessment of EH and blood–perilymph barrier permeability.

The two principal sequences applied to EH imaging are 3D-FLAIR and 3D-REAL IR, compared visually with the heavily T2 cisternography sequence for anatomical reference. Furthermore, Naganawa et al. developed a series of subtraction sequences such as HYDROPS [23], HYDROPS2 [24], and Hydrops-Mi2 [25], but those techniques are still used as clinical research methods and are not commonly available. Moreover, there are two main EH grading methods, and each evaluates cochlear and vestibular EH separately. Some researchers have used the semiquantitative scale proposed by Nakashima [5], while others have used the qualitative scale described by Barath et al. [6]. In addition, the latter has been recently modified by adding a grade to the VEH evaluation [8]. Each of the factors mentioned above can affect image quality and final assessment.

Furthermore, in some studies, the diagnosis of EH was made by one author [26], or if more observers were involved, the diagnosis of EH was made by consensus [4,23,27,28] or there is a lack of information about the observers' agreement [29–32]. Consequently, the reported frequency of EH in MD and asymptomatic ears varies in the literature, and debate still exists if the EH, especially CoEH, is a valuable biomarker of MD [7].

Our study aimed to evaluate if the discrepancy in the prevalence of EH in MD might result from the radiological criteria used. We wanted to investigate if the criteria, such as assessment of the presence of EH in the Barath scale and Bernaerts' modification of this scale and increased perilymphatic enhancement, are repeatable and easy to evaluate. For this purpose, the assessment of MRI examinations of all the ears in our group was made by two experienced radiologists and one otorhinolaryngologist in training.

Our study showed that the frequency of cochlear endolymphatic hydrops in definite MD ears was 76–80%. This type of endolymphatic hydrops was more often detected by experienced observers (Rad 1 and 2) than by the observer in training (Oto). Our results can be compared with other studies based on the same MRI sequence—delayed post-contrast 3D-FLAIR. In Barath et al.'s [6] study, this type of hydrops was described in 86.9% of MD ears, van Steekelenburg et al. [21] reported the presence of CoEH in 85% of definite MD ears, and Pai et al. [30] recognized CoEH in 100% of MD ears. In authors that used other MRI sequences (most often three dimension inversion recovery sequence—3D-IR), the frequency of CoEH in MD patients was 90% in Shi et al. [33], while Ito et al. [28] reported this biomarker in 62% of MD ears, and Yoshida et al. [34] observed CoEH in

87% of MD ears. Suárez Vega et al. [27] compared 3D-FLAIR and 3D-IR and found CoEH in 75% of definite MD ears. In our study, in a group of ears without a diagnosis of MD, CoEH was rare, ranging from 4.5 to 6% for ears with Menieriform symptoms and 2.7–8.2% for asymptomatic contralateral ears in MD patients. Similar results were described by van Steekelenburg et al. [21]. They observed CoEH in 3.1% of ears with Menieriform symptoms and 2% of asymptomatic ears MD patients. Ito et al. [28] observed this in 6.3% of asymptomatic ears.

In our study, all the observers detected vestibular endolymphatic hydrops using the Barath scale in 74.7% of definite MD ears. Referring to other studies that used the 3D-FLAIR sequence, our results are similar to those reported by Paskoniene et al. [29], who revealed VEH in 76.4% of MD ears, and lower than results obtained in studies by Barath et al. [6] (92%), van Steekelenburg [21] (89%) and by Pai et al. [30] (86%). Similar results were obtained with other MRI sequences, as follows: Shi et al. [33] described VEH in 88% of MD ears, Ito et al. [28] in 66%, and Yoshida et al. [34] in 94%. Suárez Vega et al. [27] described VEH in 92% of MD ears. In our study, for ears with other symptoms that do not fulfil the criteria for MD but presented some symptoms, VEH was assessed only in 4.5%, and similarly in asymptomatic contralateral ears in 2.7%.

In our study, adding one grade to Barath's classification of vestibular endolymphatic hydrops, as was described by Bernaerts, changed the frequency of VEH identification in definite MD ears to 81–83%, depending on the observer. However, this criterion changed the frequency of recognizing VEH in ears with Menieriform symptoms to 7.5% and 11% in asymptomatic ears. Consequently, the sensitivity increased, but the specificity decreased. Similarly, in Bernaerts et al.'s study [8], this feature increased the sensitivity of VEH from 79.5% to 85%, and in the study of Jasinska et al. [10], from 82% to 92%. It is worth emphasizing the extra low VEH in asymptomatic ears of six patients diagnosed with unilateral definite MD and two with sudden deafness. This finding might be explained by the fact that MD is often a bilateral disease with different onset in each ear, and dilation of the saccule might be an early sign of MD before symptoms appear [10,35,36].

In the literature, increased perilymphatic enhancement of the inner ear structures as a sign of blood–perilymph barrier impairment was described as the next probable biomarker of MD [6,8,21,22,37–39]. Our study observed it in 59–63% of definite MD patients, in the group of ears with other symptoms in 13%, and only 2.7% in asymptomatic ears. In Bernaerts et al.'s [8] study, 67.9% of MD patients had increased PE on the affected side. Van Steekelenburg et al. [21] observed increased PE in 82.6% of MD, 9.4% of Menieriform symptoms, and 3.4% of asymptomatic ears. However, this parameter should probably be combined with the EH because it may also be present in other ear diseases, such as sudden sensorineural hearing loss or vestibular neuritis [21,40].

Ménière's disease is a complex disease with heterogeneous symptoms. Moreover, it is chronic and gradually progresses from monosymptomatic to fully symptomatic. The actual diagnostic criteria (AAO–HNS) for diagnosing MD include patients with advanced-stage disease. Therefore, the diagnosis of this disease is often difficult. According to the literature, in 20% of patients, it takes more than five years to diagnose MD [41]. Additionally, it was discovered that the presence of EH may precede symptoms in MD patients [8,41], can progress with the disease duration, and is correlated with clinical symptoms [10,42–48]. Therefore, it can serve as a method of early detection and support the diagnosis in clinically atypical cases, help to choose proper treatment, and potentially monitor therapeutic effects [39,47,49,50].

In our study, when assessing the radiological features, the highest differences between the observers occurred for the evaluation of cochlear endolymphatic hydrops. A significant difference was found between all pairs of observers, with a more considerable difference between the pairs of radiologists and otorhinolaryngologist. Earlier studies suggest that the assessment of CoEH on delayed post-contrast 3D-FLAIR sequence might be interpreted variably [27,51,52]. Our study confirmed this finding; however, it also showed 96% inter-observer agreement for the differentiation of hydropic and normal ears. Consequently, it

showed that it is much easier to classify ears as normal or hydropic than to choose the proper grade of endolymphatic hydrops.

The assessment of vestibular endolymphatic hydrops in both Barath and Bernaerts scales, comparing both radiologists, was precisely the same. The only differences were present between radiologists and otorhinolaryngologist when assessing the VEH on the Barath scale, not on the Bernaerts scale. However, like with CoEH, the main non-accordance was in the proper grading of hydropic ears, not in assessing the presence of any hydrops. All observers differentiated normal and hydropic ears almost the same way. When comparing interobserver agreement, our results slightly differ from the literature. Most researchers showed a higher concordance coefficient for CoEH than VEH recognition, as follows: Barath et al. [6], 0.97 for CoEH and 0.94 for VEH grading, van Steekelenburg et al. [21], 0.93 for CoEH and 0.92 for VEH, Bernaerts et al. [8], 0.83 for CoEH and 0.81 for VEH. However, Suárez Vega et al. [27] reported that degree of concordance was higher for VEH (0.66) than for CoEH (0.39) using the 3D-FLAIR sequence. Moreover, they also found that the concordance coefficient was higher (0.82) when diagnosing any EH than scoring it. The latter is similar to our findings.

As for the perilymphatic enhancement of the inner ear structures, there were no significant differences between the three observers and the pairs of observers for this parameter, which is in line with the literature [8,21].

In our study, three observers evaluated MRI scans independently to evaluate if the assessment method was repeatable. By engaging a less experienced MRI observer (otorhinolaryngologist) who was trained with a few cases of MRI scans of inner ears, the study aimed to evaluate if the method was easy to learn. It showed that the assessment of vestibular endolymphatic hydrops is easy to learn and repeatable. For experienced radiologists, the readings for 220 ears were the same, whereas, for the otolaryngologist, the number of different observations was very low. Typically, the saccule and utricle are easily identified in the vestibule's inferior part as two "black dots" surrounded by a bright (enhancing) rim of perilymph. Furthermore, the saccule is smaller than the utricle. Even for an untrained observer, it is not difficult to find that this configuration is changed. That is probably the reason for such high agreement in assessing this parameter.

Similarly, with the perilymphatic enhancement qualitative assessment, it is not difficult to visually compare two sides and find an asymmetry.

When it comes to cochlear endolymphatic hydrops assessment using a 3D-FLAIR MRI sequence, this is more complicated. In this sequence, differentiating endolymphatic structures from surrounding bone is impossible because both have low signals [27]. First, changes in the contours of the cochlea should be found and compared with the FIESTA sequence as an anatomic reference. Second, how much outlines are changed should be evaluated, and then CoEH should be graded. Evaluation of this parameter is more complicated, which is probably why it is so difficult to properly stage EH, even for experienced users. According to existing literature, the solution to this problem might be using a post-contrast 3D-IR inversion recovery sequence [23,24,27,53]; however, this sequence is not widely available, takes longer, and is more prone to motion artifacts. The repeatability of CoEH assessment using different sequences needs to be confirmed in further studies.

5. Conclusions

Our study confirmed that endolymphatic hydrops and robust perilymphatic enhancement are much more often present in MD ears than in other inner ear diseases. Both cochlear and vestibular endolymphatic hydrops parameters may serve as a method of differentiation of MD from normal ears. It showed that evaluation of vestibular endolymphatic hydrops is repeatable between observers and easy to learn. Furthermore, it proved that Bernaerts' modification increased the sensitivity of endolymphatic hydrops diagnosis. It also confirmed the recent opinion that it is more challenging to assess cochlear than vestibular endolymphatic hydrops using an MRI 3D-FLAIR sequence. The interpretation of MRI is more consistent when evaluated by radiologists in the case of cochlear hydrops.

In addition, when assessing cochlear hydrops, distinguishing between normal and hydropic ears is much easier to perform than EH grading. Therefore, it may be used to diagnose MD rather than EH staging. These observations could shed new light on the usefulness of MRI 3D-FLAIR in diagnosing cochlear endolymphatic hydrops.

The method of EH diagnosis using MRI scans described above is not difficult to perform, and it may be included in the diagnostic protocol of MD to support the diagnosis of MD in clinical settings.

In conclusion, the most important findings of this study for otolaryngologists are as follows:

1. Visualization of endolymphatic structures is possible.
2. Endolymphatic hydrops is present more often in Ménière's disease ears than in other inner diseases and much more frequent than in asymptomatic ears, so it might be used as a diagnostic criterion to support the diagnosis of Ménière's disease for clinically unclear cases.
3. Increased perilymphatic enhancement is not difficult to assess and is present more often in Ménière's disease than in other inner ear pathologies.
4. Quick diagnosis of endolymphatic hydrops on MRI is not difficult, even for quickly trained observers, that is, otorhinolaryngologists after a short period of training.

In conclusion, the most important findings of this study for radiologists are as follows:

1. The assessment of vestibular hydrops on the two scales mentioned above is easy to learn. The modified scale increases the sensitivity and specificity of the method to diagnose Ménière's disease ears, so it can be used for diagnosing and staging vestibular endolymphatic hydrops.
2. Evaluation of cochlear hydrops is more complicated than vestibular. However, the main concern is not to diagnose pathology but to grade it properly (which means to answer the question "is it 1st or 2nd grade endolymphatic hydrops?") rather than to diagnose it ("is it normal = 0 or abnormal = 1st or 2nd grade?"). Therefore, it should be used for the diagnosis of endolymphatic hydrops, not for grading it.

Author Contributions: Conceptualization: M.L., K.N.; Methodology: E.W., M.L.; Formal Analysis: E.W., M.L., A.J.-N., E.M.; Investigation: E.W., A.J.-N., E.M.; Data Curation: E.W., M.L.; Writing—Original Draft Preparation: E.W., M.L., A.J.-N., Writing—Review and Editing: M.L., K.N.; Visualization: E.W., M.L., A.J.-N.; Supervision: M.L., K.N. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Ethics Committee of the Medical University of Warsaw (KB/110/2019).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Lopez-Escamez, J.A.; Carey, J.; Chung, W.H.; Goebel, J.A.; Magnusson, M.; Mandala, M.; Newman-Toker, D.E.; Strupp, M.; Suzuki, M.; Trabalzini, F.; et al. Diagnostic criteria for Meniere's disease. *J. Vestib. Res.* **2015**, *25*, 1–7. [CrossRef] [PubMed]
2. Goebel, J.A. 2015 Equilibrium Committee Amendment to the 1995 AAO-HNS Guidelines for the Definition of Meniere's Disease. *Otolaryngol. Head Neck. Surg.* **2016**, *154*, 403–404. [CrossRef] [PubMed]
3. Hallpike, C.S.; Cairns, H. Observations on the Pathology of Meniere's Syndrome: (Section of Otology). *Proc. R. Soc. Med.* **1938**, *31*, 1317–1336.
4. Nakashima, T.; Naganawa, S.; Sugiura, M.; Teranishi, M.; Sone, M.; Hayashi, H.; Nakata, S.; Katayama, N.; Ishida, I.M. Visualization of endolymphatic hydrops in patients with Meniere's disease. *Laryngoscope* **2007**, *117*, 415–420. [CrossRef]

5. Nakashima, T.; Naganawa, S.; Pyykko, I.; Gibson, W.P.; Sone, M.; Nakata, S.; Teranishi, M. Grading of endolymphatic hydrops using magnetic resonance imaging. *Acta Otolaryngol. Suppl.* **2009**, *129*, 5–8. [CrossRef]
6. Barath, K.; Schuknecht, B.; Naldi, A.M.; Schrepfer, T.; Bockisch, C.J.; Hegemann, S.C. Detection and grading of endolymphatic hydrops in Meniere disease using MR imaging. *AJNR Am. J. Neuroradiol.* **2014**, *35*, 1387–1392. [CrossRef]
7. Attye, A.; Eliezer, M.; Boudiaf, N.; Tropres, I.; Chechin, D.; Schmerber, S.; Dumas, G.; Krainik, A. MRI of endolymphatic hydrops in patients with Meniere's disease: A case-controlled study with a simplified classification based on saccular morphology. *Eur. Radiol.* **2017**, *27*, 3138–3146. [CrossRef]
8. Bernaerts, A.; Vanspauwen, R.; Blaivie, C.; van Dinther, J.; Zarowski, A.; Wuyts, F.L.; Vanden Bossche, S.; Offeciers, E.; Casselman, J.W.; De Foer, B. The value of four stage vestibular hydrops grading and asymmetric perilymphatic enhancement in the diagnosis of Meniere's disease on MRI. *Neuroradiology* **2019**, *61*, 421–429. [CrossRef]
9. Naganawa, S.; Kawai, H.; Sone, M.; Nakashima, T. Increased sensitivity to low concentration gadolinium contrast by optimized heavily T2-weighted 3D-FLAIR to visualize endolymphatic space. *Magn. Reson. Med. Sci.* **2010**, *9*, 73–80. [CrossRef]
10. Jasinska, A.; Lachowska, M.; Wnuk, E.; Pierchala, K.; Rowinski, O.; Niemczyk, K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Meniere's disease. *Auris Nasus Larynx* **2022**, *49*, 34–45. [CrossRef]
11. Hornibrook, J.; Flook, E.; Greig, S.; Babbage, M.; Goh, T.; Coates, M.; Care, R.; Bird, P. MRI Inner Ear Imaging and Tone Burst Electrocochleography in the Diagnosis of Meniere's Disease. *Otol. Neurotol.* **2015**, *36*, 1109–1114. [CrossRef] [PubMed]
12. Jerin, C.; Floerke, S.; Maxwell, R.; Gurkov, R. Relationship Between the Extent of Endolymphatic Hydrops and the Severity and Fluctuation of Audiovestibular Symptoms in Patients with Meniere's Disease and MRI Evidence of Hydrops. *Otol. Neurotol.* **2018**, *39*, e123–e130. [CrossRef] [PubMed]
13. Fukuoka, H.; Takumi, Y.; Tsukada, K.; Miyagawa, M.; Oguchi, T.; Ueda, H.; Kadoya, M.; Usami, S. Comparison of the diagnostic value of 3 T MRI after intratympanic injection of GBCA, electrocochleography, and the glycerol test in patients with Meniere's disease. *Acta Otolaryngol.* **2012**, *132*, 141–145. [CrossRef] [PubMed]
14. Wu, Q.; Dai, C.; Zhao, M.; Sha, Y. The correlation between symptoms of definite Meniere's disease and endolymphatic hydrops visualized by magnetic resonance imaging. *Laryngoscope* **2016**, *126*, 974–979. [CrossRef]
15. Yamazaki, M.; Naganawa, S.; Kawai, H.; Nihashi, T.; Nakashima, T. Signal alteration of the cochlear perilymph on 3 different sequences after intratympanic Gd-DTPA administration at 3 tesla: Comparison of 3D-FLAIR, 3D-T1-weighted imaging, and 3D-CISS. *Magn. Reson. Med. Sci.* **2010**, *9*, 65–71. [CrossRef]
16. Bykowski, J.; Harris, J.P.; Miller, M.; Du, J.; Mafee, M.F. Intratympanic Contrast in the Evaluation of Meniere Disease: Understanding the Limits. *AJNR Am. J. Neuroradiol.* **2015**, *36*, 1326–1332. [CrossRef]
17. Fang, Z.M.; Chen, X.; Gu, X.; Liu, Y.; Zhang, R.; Cao, D.R.; He, H.G. A new magnetic resonance imaging scoring system for perilymphatic space appearance after intratympanic gadolinium injection, and its clinical application. *J. Laryngol. Otol.* **2012**, *126*, 454–459. [CrossRef]
18. Nakashima, T.; Naganawa, S.; Teranishi, M.; Tagaya, M.; Nakata, S.; Sone, M.; Otake, H.; Kato, K.; Iwata, T.; Nishio, N. Endolymphatic hydrops revealed by intravenous gadolinium injection in patients with Meniere's disease. *Acta Otolaryngol.* **2010**, *130*, 338–343. [CrossRef]
19. Sepahdari, A.R.; Ishiyama, G.; Vorasubin, N.; Peng, K.A.; Linetsky, M.; Ishiyama, A. Delayed intravenous contrast-enhanced 3D FLAIR MRI in Meniere's disease: Correlation of quantitative measures of endolymphatic hydrops with hearing. *Clin. Imaging* **2015**, *39*, 26–31. [CrossRef]
20. Sano, R.; Teranishi, M.; Yamazaki, M.; Isoda, H.; Naganawa, S.; Sone, M.; Hiramatsu, M.; Yoshida, T.; Suzuki, H.; Nakashima, T. Contrast enhancement of the inner ear in magnetic resonance images taken at 10 minutes or 4 hours after intravenous gadolinium injection. *Acta Otolaryngol.* **2012**, *132*, 241–246. [CrossRef]
21. Van Steekelenburg, J.M.; van Weijnen, A.; de Pont, L.M.H.; Vijlbrief, O.D.; Bommelje, C.C.; Koopman, J.P.; Verbist, B.M.; Blom, H.M.; Hammer, S. Value of Endolymphatic Hydrops and Perilymph Signal Intensity in Suspected Meniere Disease. *AJNR Am. J. Neuroradiol.* **2020**, *41*, 529–534. [CrossRef] [PubMed]
22. Yamazaki, M.; Naganawa, S.; Tagaya, M.; Kawai, H.; Ikeda, M.; Sone, M.; Teranishi, M.; Suzuki, H.; Nakashima, T. Comparison of contrast effect on the cochlear perilymph after intratympanic and intravenous gadolinium injection. *AJNR Am. J. Neuroradiol.* **2012**, *33*, 773–778. [CrossRef] [PubMed]
23. Naganawa, S.; Yamazaki, M.; Kawai, H.; Bokura, K.; Sone, M.; Nakashima, T. Imaging of Meniere's disease after intravenous administration of single-dose gadodiamide: Utility of subtraction images with different inversion time. *Magn. Reson. Med. Sci.* **2012**, *11*, 213–219. [CrossRef]
24. Naganawa, S.; Yamazaki, M.; Kawai, H.; Bokura, K.; Sone, M.; Nakashima, T. Imaging of Meniere's disease by subtraction of MR cisternography from positive perilymph image. *Magn. Reson. Med. Sci.* **2012**, *11*, 303–309. [CrossRef] [PubMed]
25. Naganawa, S.; Suzuki, K.; Nakamichi, R.; Bokura, K.; Yoshida, T.; Sone, M.; Homann, G.; Nakashima, T.; Ikeda, M. Semi-quantification of endolymphatic size on MR imaging after intravenous injection of single-dose gadodiamide: Comparison between two types of processing strategies. *Magn. Reson. Med. Sci.* **2013**, *12*, 261–269. [CrossRef] [PubMed]
26. Li, X.; Wu, Q.; Sha, Y.; Dai, C.; Zhang, R. Gadolinium-enhanced MRI reveals dynamic development of endolymphatic hydrops in Meniere's disease. *Braz. J. Otorhinolaryngol.* **2020**, *86*, 165–173. [CrossRef] [PubMed]

27. Suarez Vega, V.M.; Dominguez, P.; Caballeros Lam, F.M.; Leal, J.I.; Perez-Fernandez, N. Comparison between high-resolution 3D-IR with real reconstruction and 3D-flair sequences in the assessment of endolymphatic hydrops in 3 tesla. *Acta Otolaryngol.* **2020**, *140*, 883–888. [CrossRef]
28. Ito, T.; Kitahara, T.; Inui, H.; Miyasaka, T.; Kichikawa, K.; Ota, I.; Nario, K.; Matsumura, Y.; Yamanaka, T. Endolymphatic space size in patients with Meniere's disease and healthy controls. *Acta Otolaryngol.* **2016**, *136*, 879–882. [CrossRef]
29. Paskoniene, A.; Baltagalviene, R.; Lengvenis, G.; Beleskiene, V.; Ivaska, J.; Markeviciute, V.; Mickeviciene, V.; Lesinskas, E. The Importance of the Temporal Bone 3T MR Imaging in the Diagnosis of Meniere's Disease. *Otol. Neurotol.* **2020**, *41*, 235–241. [CrossRef]
30. Pai, I.; Mendis, S.; Murdin, L.; Touska, P.; Connor, S. Magnetic resonance imaging of Meniere's disease: Early clinical experience in a UK centre. *J. Laryngol. Otol.* **2020**, *134*, 302–310. [CrossRef]
31. Quatre, R.; Attye, A.; Karkas, A.; Job, A.; Dumas, G.; Schmerber, S. Relationship between Audio-Vestibular Functional Tests and Inner Ear MRI in Meniere's Disease. *Ear. Hear* **2019**, *40*, 168–176. [CrossRef] [PubMed]
32. Shi, S.; Zhou, F.; Wang, W. 3D-real IR MRI of Meniere's disease with partial endolymphatic hydrops. *Am. J. Otolaryngol.* **2019**, *40*, 589–593. [CrossRef] [PubMed]
33. Shi, S.; Guo, P.; Wang, W. Magnetic Resonance Imaging of Meniere's Disease After Intravenous Administration of Gadolinium. *Ann. Otol. Rhinol. Laryngol.* **2018**, *127*, 777–782. [CrossRef] [PubMed]
34. Yoshida, T.; Sugimoto, S.; Teranishi, M.; Otake, H.; Yamazaki, M.; Naganawa, S.; Nakashima, T.; Sone, M. Imaging of the endolymphatic space in patients with Meniere's disease. *Auris Nasus Larynx* **2018**, *45*, 33–38. [CrossRef] [PubMed]
35. Conlon, B.J.; Gibson, W.P. Meniere's disease: The incidence of hydrops in the contralateral asymptomatic ear. *Laryngoscope* **1999**, *109*, 1800–1802. [CrossRef]
36. Perez-Carpena, P.; Lopez-Escamez, J.A. Current Understanding and Clinical Management of Meniere's Disease: A Systematic Review. *Semin Neurol* **2020**, *40*, 138–150. [CrossRef]
37. Tagaya, M.; Yamazaki, M.; Teranishi, M.; Naganawa, S.; Yoshida, T.; Otake, H.; Nakata, S.; Sone, M.; Nakashima, T. Endolymphatic hydrops and blood-labyrinth barrier in Meniere's disease. *Acta Otolaryngol.* **2011**, *131*, 474–479. [CrossRef]
38. Pakdaman, M.N.; Ishiyama, G.; Ishiyama, A.; Peng, K.A.; Kim, H.J.; Pope, W.B.; Sepahdari, A.R. Blood-Labyrinth Barrier Permeability in Meniere Disease and Idiopathic Sudden Sensorineural Hearing Loss: Findings on Delayed Postcontrast 3D-FLAIR MRI. *AJNR Am. J. Neuroradiol.* **2016**, *37*, 1903–1908. [CrossRef]
39. Jasinska-Nowacka, A.; Lachowska, M.; Wnuk, E.; Niemczyk, K. Changes in endolymphatic hydrops after vestibular neurectomy observed in magnetic resonance imaging—A pilot study. *Auris Nasus Larynx* **2022**, *49*, 584–592. [CrossRef]
40. Kim, T.Y.; Park, D.W.; Lee, Y.J.; Lee, J.Y.; Lee, S.H.; Chung, J.H.; Lee, S. Comparison of Inner Ear Contrast Enhancement among Patients with Unilateral Inner Ear Symptoms in MR Images Obtained 10 Minutes and 4 Hours after Gadolinium Injection. *AJNR Am. J. Neuroradiol.* **2015**, *36*, 2367–2372. [CrossRef]
41. Pyykko, I.; Nakashima, T.; Yoshida, T.; Zou, J.; Naganawa, S. Meniere's disease: A reappraisal supported by a variable latency of symptoms and the MRI visualisation of endolymphatic hydrops. *BMJ Open* **2013**, *3*, e001555. [CrossRef] [PubMed]
42. Gurkov, R.; Flatz, W.; Louza, J.; Strupp, M.; Krause, E. In vivo visualization of endolyphatic hydrops in patients with Meniere's disease: Correlation with audiovestibular function. *Eur. Arch. Otorhinolaryngol.* **2011**, *268*, 1743–1748. [CrossRef]
43. Naganawa, S.; Nakashima, T. Visualization of endolymphatic hydrops with MR imaging in patients with Meniere's disease and related pathologies: Current status of its methods and clinical significance. *Jpn. J. Radiol.* **2014**, *32*, 191–204. [CrossRef] [PubMed]
44. Kahn, L.; Hautefort, C.; Guichard, J.P.; Toupet, M.; Jourdaine, C.; Vitaux, H.; Herman, P.; Kania, R.; Houdart, E.; Attye, A.; et al. Relationship between video head impulse test, ocular and cervical vestibular evoked myogenic potentials, and compartmental magnetic resonance imaging classification in meniere's disease. *Laryngoscope* **2020**, *130*, E444–E452. [CrossRef]
45. Kato, K.; Yoshida, T.; Teranishi, M.; Sano, R.; Otake, H.; Sone, M.; Naganawa, S.; Nakashima, T. Peak width in multifrequency tympanometry and endolymphatic hydrops revealed by magnetic resonance imaging. *Otol. Neurotol.* **2012**, *33*, 912–915. [CrossRef]
46. Katayama, N.; Yamamoto, M.; Teranishi, M.; Naganawa, S.; Nakata, S.; Sone, M.; Nakashima, T. Relationship between endolymphatic hydrops and vestibular-evoked myogenic potential. *Acta Otolaryngol.* **2010**, *130*, 917–923. [CrossRef]
47. Gurkov, R.; Flatz, W.; Keeser, D.; Strupp, M.; Ertl-Wagner, B.; Krause, E. Effect of standard-dose Betahistine on endolymphatic hydrops: An MRI pilot study. *Eur. Arch. Otorhinolaryngol.* **2013**, *270*, 1231–1235. [CrossRef]
48. Gurkov, R.; Flatz, W.; Ertl-Wagner, B.; Krause, E. Endolymphatic hydrops in the horizontal semicircular canal: A morphologic correlate for canal paresis in Meniere's disease. *Laryngoscope* **2013**, *123*, 503–506. [CrossRef] [PubMed]
49. Uno, A.; Imai, T.; Watanabe, Y.; Tanaka, H.; Kitahara, T.; Horii, A.; Kamakura, T.; Takimoto, Y.; Osaki, Y.; Nishiike, S.; et al. Changes in endolymphatic hydrops after sac surgery examined by Gd-enhanced MRI. *Acta Otolaryngol.* **2013**, *133*, 924–929. [CrossRef]
50. Miyagawa, M.; Fukuoka, H.; Tsukada, K.; Oguchi, T.; Takumi, Y.; Sugiura, M.; Ueda, H.; Kadoya, M.; Usami, S. Endolymphatic hydrops and therapeutic effects are visualized in 'atypical' Meniere's disease. *Acta Otolaryngol.* **2009**, *129*, 1326–1329. [CrossRef]
51. Connor, S.E.J.; Pai, I. Endolymphatic hydrops magnetic resonance imaging in Meniere's disease. *Clin. Radiol.* **2021**, *76*, 76.e1–76.e19. [CrossRef] [PubMed]

52. Eliezer, M.; Gillibert, A.; Tropres, I.; Krainik, A.; Attye, A. Influence of inversion time on endolymphatic hydrops evaluation in 3D-FLAIR imaging. *J. Neuroradiol.* **2017**, *44*, 339–343. [CrossRef] [PubMed]
53. Naganawa, S.; Satake, H.; Kawamura, M.; Fukatsu, H.; Sone, M.; Nakashima, T. Separate visualization of endolymphatic space, perilymphatic space and bone by a single pulse sequence; 3D-inversion recovery imaging utilizing real reconstruction after intratympanic Gd-DTPA administration at 3 Tesla. *Eur. Radiol.* **2008**, *18*, 920–924. [CrossRef] [PubMed]

Podsumowanie i wnioski

Przedstawione prace stanowiące cykl rozprawy doktorskiej dowodzą, że:

1. Wizualizacja w MR struktur endolimfatycznych i perylimfatycznych ucha wewnętrznego *in vivo* jest możliwa.
2. Opisane kryteria radiologiczne wskazujące na wodniaka endolimfatycznego występują znacząco częściej w uszach objawowych pacjentów z MD, niż w uszach pacjentów z innymi patologiami i uszach bezobjawowych. Kryteria te mogłyby zatem być biomarkerem choroby Ménière'a, wspierającym rozpoznanie tej choroby, zwłaszcza w nietypowych i wczesnych jej przypadkach.
3. Ocena wodniaka endolimfatycznego przedsionka na obrazach uzyskanych w MR za pomocą sekwencji 3D-FLAIR jest łatwa do nauczenia i powtarzalna. Natomiast dla oceny wodniaka endolimfatycznego ślimaka łatwa i powtarzalna jest identyfikacja patologii, ale ocena jej stopnia nasilenia jest trudniejsza, nawet dla doświadczonych badaczy. Wydaje się, że dla monitorowania stopnia nasilenia wodniaka ślimaka należy szukać innej metody diagnostyki.

Publikacje poza cyklem dotyczące tematyki rozprawy doktorskiej

Dodatkowo, poza cyklem stanowiącym moją rozprawę doktorską, jestem współautorką czterech prac na temat obrazowania MR zmian w uchu wewnętrznym u pacjentów z chorobą Ménière'a powstałych w ramach projektu prowadzonych przeze mnie badań.

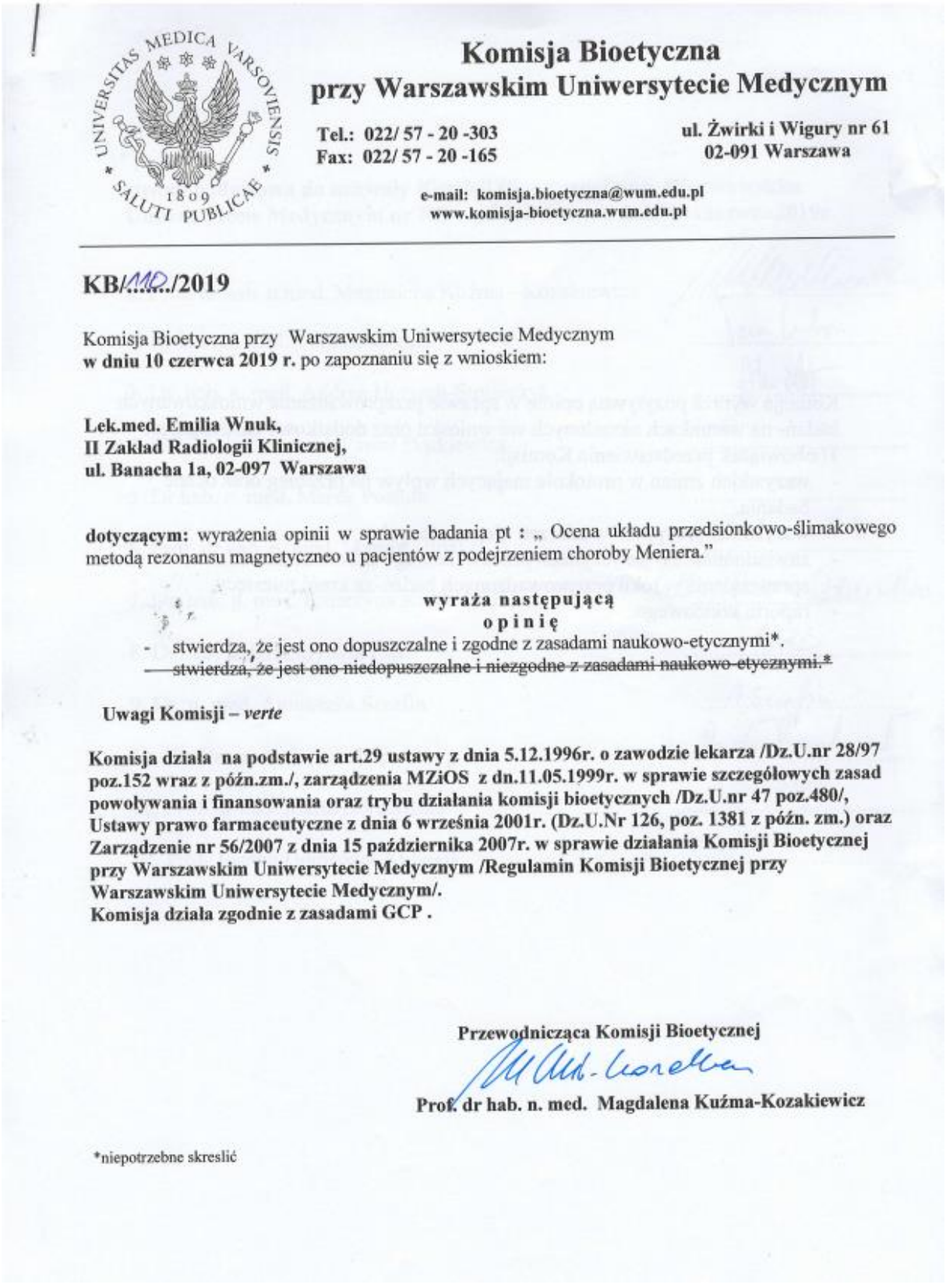
Pierwsza z nich (*Jasińska A, Lachowska M, **Wnuk E**,Niemczyk K. Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease. Otorynolaryngologia Polska 2021:75(2):1-8. DOI: 10.5604/01.3001.0014.6176)* jest pierwszym w polskiej literaturze doniesieniem o zastosowaniu MR w diagnostyce wodniaka endolimfatycznego u pacjentów z chorobą Ménière'a. Prezentuje sposób oceny wodniaka w MR, zilustrowana jest skanami MR z naszych badań oraz zawiera przegląd aktualnej literatury.

Druga opublikowana praca (*Jasińska A, **Wnuk E**, Pierchała K, Niemczyk K. Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a. Polski Przegląd Otorynolaryngologiczny 2019;8(3):20-23)* stanowi opis dwóch przypadków pacjentów zarówno w zakresie obrazu klinicznego, jak i radiologicznego. Zaprezentowani zostali pacjenci z chorobą Ménière'a z różnymi objawami, o różnym czasie trwania choroby, u których w MR zaobserwowano poszerzenie struktur endolimfatycznych ucha wewnętrznego.

Trzecia praca (*Jasińska A, Lachowska M, **Wnuk E**, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx. DOI: 10.1016/j.anl.2021.03.027)* to artykuł oryginalny, będący oceną korelacji zaawansowania wodniaka endolimfatycznego w MR z obrazem klinicznym i wynikami badań diagnostycznych. W grupie 38 pacjentów ze zdefiniowaną, jednostronną chorobą Ménière'a oceniony został związek między stopniem zaawansowania wodniaka endolimfatycznego w MR (w skalach opisanej przez Barath i wsp. oraz jej modyfikacji Bernaerts i wsp.) z wynikami badań audiologicznych, otoneurologicznych i nasileniem objawów. Zaobserwowano, że zaawansowanie wodniaka endolimfatycznego koreluje z poziomem niedosłuchu w audiometrii tonalnej. Dodatkowo zauważono związek między zaawansowaniem wodniaka przedsionka (VEH) a stosunkiem amplitudy potencjału czynnościowego (SP/AP) w badaniu elektrokochleografii transtympanalnej. Te wyniki przemawiają za wpływem poszerzenia przestrzeni endolimfatycznych na stopień uszkodzenia słuchu w chorobie Ménière'a. Nie zaobserwowano natomiast korelacji z czasem trwania choroby i stopniem nasilenia odczuwanych przez pacjentów objawów.

Czwarta praca (*Jasińska-Nowacka A, Lachowska M, **Wnuk E**, Niemczyk K. Changes in endolymphatic hydrops after vestibular neurectomy observed in magnetic resonance imaging - A pilot study. Auris Nasus Larynx. 2022: 49(4):584-592. DOI: 10.1016/j.anl.2021.12.001)* jest analizą stopnia nasilenia objawów, wyników testów audiologicznych i otoneurologicznych oraz obrazu MR struktur ucha wewnętrznego czterech pacjentów z chorobą Ménière'a. Badania MR wykonano w tej grupie przed oraz osiem miesięcy po zabiegu neurektomii przedsionkowej. Zaobserwowano, że klinicznie u wszystkich badanych pacjentów wycofały się zawroty głowy i poprawiło się funkcjonowanie. W badaniu MR u jednego pacjenta zaobserwowano zmniejszenie intensywności wzmocnienia kontrastowego struktur ucha wewnętrznego po operacji, natomiast nie zaobserwowano wycofania wodniaka endolimfatycznego. Prawdopodobnie obraz ten częściowo wynikał ze zbyt wczesnej kontroli pooperacyjnej – nadal intensywnie kontynuujemy badania w tym zakresie.

Opinia Komisji Bioetycznej



Komisja Bioetyczna
przy Warszawskim Uniwersytecie Medycznym

Tel.: 022/ 57 - 20 -303
Fax: 022/ 57 - 20 -165

ul. Żwirki i Wigury nr 61
02-091 Warszawa

e-mail: komisja.bioetyczna@wum.edu.pl
www.komisja-bioetyczna.wum.edu.pl

KB/110/2019

Komisja Bioetyczna przy Warszawskim Uniwersytecie Medycznym
w dniu 10 czerwca 2019 r. po zapoznaniu się z wnioskiem:

Lek.med. Emilia Wnuk,
II Zakład Radiologii Klinicznej,
ul. Banacha 1a, 02-097 Warszawa

dotyczącym: wyrażenia opinii w sprawie badania pt : „ Ocena układu przedsionkowo-ślimakowego metodą rezonansu magnetyczneo u pacjentów z podejrzeniem choroby Meniera."

wyraża następującą
opinię

- stwierdza, że jest ono dopuszczalne i zgodne z zasadami naukowo-etycznymi*.
- ~~stwierdza, że jest ono niedopuszczalne i niezgodne z zasadami naukowo-etycznymi.*~~

Uwagi Komisji – *verte*

Komisja działa na podstawie art.29 ustawy z dnia 5.12.1996r. o zawodzie lekarza /Dz.U.nr 28/97 poz.152 wraz z późn.zm./, zarządzenia MZiOS z dn.11.05.1999r. w sprawie szczegółowych zasad powoływania i finansowania oraz trybu działania komisji bioetycznych /Dz.U.nr 47 poz.480/, Ustawy prawo farmaceutyczne z dnia 6 września 2001r. (Dz.U.Nr 126, poz. 1381 z późn. zm.) oraz Zarządzenie nr 56/2007 z dnia 15 października 2007r. w sprawie działania Komisji Bioetycznej przy Warszawskim Uniwersytecie Medycznym /Regulamin Komisji Bioetycznej przy Warszawskim Uniwersytecie Medycznym/.
Komisja działa zgodnie z zasadami GCP .

Przewodnicząca Komisji Bioetycznej
Prof. dr hab. n. med. Magdalena Kuźma-Kozakiewicz

*niepotrzebne skreślić

Oświadczenia wszystkich współautorów cyklu publikacji stanowiących rozprawę doktorską, określające ich indywidualny wkład

Oświadczenia pierwszego autora publikacji stanowiącej rozprawę doktorską

Lek. **Emilia Wnuk** (II Zakład Radiologii Klinicznej, Warszawski Uniwersytet Medyczny) – stworzenie protokołu badawczego, projektu badań, opracowanie metodologii, wykonanie badań, analiza i interpretacja wyników, częściowo analiza statystyczna, przegląd literatury, pisanie artykułów stanowiących cykl publikacji, pierwsza autorka publikacji stanowiących cykl.

Wnuk E. *Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971)*

Mój udział procentowy w przygotowaniu publikacji określam jako **72%**

Wnuk E. *Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023, 12(1), 202. DOI. 10.3390/jcm12010202*)

Mój udział procentowy w przygotowaniu publikacji określam jako **64%**

Emilia Wnuk

Oświadczenia współautora publikacji stanowiącej rozprawę doktorską

Prof. dr hab. n. med. **Magdalena Lachowska** (Katedra i Klinika Otolaryngologii, Chirurgii Głowy i Szyi, Warszawski Uniwersytet Medyczny) – nadzór merytoryczny nad prowadzeniem badania i wyborem grupy badawczej, współtworzenie projektu cyklu, wykonanie analiz statystycznych, nadzór nad interpretacją otrzymanych wyników badań, pisanie artykułów stanowiących cykl publikacji, autor korespondencyjny artykułów stanowiących cykl.

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971)

Mój udział procentowy w przygotowaniu publikacji określam jako 20%.

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023, 12(1), 202. DOI. 10.3390/jcm12010202)

Mój udział procentowy w przygotowaniu publikacji określam jako 20%.

Wyrażam zgodę na wykorzystanie w/w prac jako część rozprawy doktorskiej lek. Emilii Wnuk.

Prof. dr hab. n. med.
MAGDALENA LACHOWSKA
specjalista audiolog foniatra
1559289

Oświadczenia współautora publikacji stanowiącej rozprawę doktorską.

Dr n. med. **Edyta Maj** (II Zakład Radiologii Klinicznej, Warszawski Uniwersytet Medyczny) – wsparcie w stworzeniu protokołu badawczego, udostępnienie miejsca i sprzętu do przeprowadzenia badań, wykonanie analiz radiologicznych, interpretacja otrzymanych wyników badań, współtworzenie projektu cyklu, przygotowanie manuskryptów.

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971)

Mój udział procentowy w przygotowaniu publikacji określam jako 2%

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023, 12(1), 202. DOI. 10.3390/jcm12010202)

Mój udział procentowy w przygotowaniu publikacji określam jako 7%

Wyrażam zgodę na wykorzystanie w/w prac jako część rozprawy doktorskiej lek. Emilii Wnuk.

lek. Edyta Maj
spec. radiolog

Oświadczenia współautora publikacji stanowiącej rozprawę doktorską.

Dr n. med. i. n. o zdr. **Agnieszka Jasińska-Nowacka** (Katedra i Klinika Otolaryngologii, Chirurgii Głowy i Szyi, Warszawski Uniwersytet Medyczny) – współtworzenie projektu badań, opieka nad grupą badawczą, interpretacja wyników badań, przygotowanie manuskryptów.

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971)

Mój udział procentowy w przygotowaniu publikacji określam jako 4%

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023, 12(1), 202. DOI. 10.3390/jcm12010202)

Mój udział procentowy w przygotowaniu publikacji określam jako 7%

Wyrażam zgodę na wykorzystanie w/w prac jako część rozprawy doktorskiej lek. Emilii Wnuk.

Oświadczenia współautora publikacji stanowiącej rozprawę doktorską.

Prof. dr hab. n. med. **Kazimierz Niemczyk** (Katedra i Klinika Otolaryngologii, Chirurgii Głowy i Szyi, Warszawski Uniwersytet Medyczny) – nadzór merytoryczny nad wyborem grupy badawczej, udostępnienie miejsca i sprzętu do przeprowadzenia badań otolaryngologicznych, nadzór nad pisaniem manuskryptów

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971)

Mój udział procentowy w przygotowaniu publikacji określam jako 1%

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Niemczyk K. Reliability of endolymphatic hydrops qualitative assessment in magnetic resonance imaging. J. Clin. Med. 2023, 12(1), 202. DOI. 10.3390/jcm12010202)

Mój udział procentowy w przygotowaniu publikacji określam jako 1%

Wyrażam zgodę na wykorzystanie w/w prac jako część rozprawy doktorskiej lek. Emilii Wnuk.

KIEROWNIK
Katedry i Kliniki Otorynolaryngologii,
Chirurgii Głowy i Szyi
prof. dr hab. n.med. Kazimierz Niemczyk

Oświadczenia współautora publikacji stanowiącej rozprawę doktorską.

Prof. dr hab. n. med. **Olgierd Rowiński** (II Zakład Radiologii Klinicznej, Warszawski Uniwersytet Medyczny) – udostępnienie miejsca i sprzętu do przeprowadzenia badań, nadzór nad przygotowaniem manuskryptu.

Wnuk E, Lachowska M, Jasińska-Nowacka A, Maj E, Rowiński O, Niemczyk K. Detailed insight into magnetic resonance assessment of Ménière's disease – description of methodology and imaging findings in a case series. Polish Journal of Radiology. 2022; 87: e354–e362. DOI: 10.5114/pjr.2022.117971)

Mój udział procentowy w przygotowaniu publikacji określam jako 1%

Wyrażam zgodę na wykorzystanie w/w pracy jako części rozprawy doktorskiej lek. Emilii Wnuk.

Uniwersyteckie Centrum Kliniczne
Warszawskiego Uniwersytetu Medycznego
Centralny Szpital Kliniczny
II Zakład Radiologii Klinicznej
02-097 Warszawa, ul. S. Banacha 1a
NIP 522-00-02-529, REGON 000288975-00030
tel. 22 599 23 00, fax: 22 599 23 02

KIEROWNIK
II Zakładu Radiologii Klinicznej
Prof. nadzw. dr hab. n. med.
Olgierd Rowiński