**University of
Zurich^{UZH}**

**Zurich Open Repository and
Archive**

University of Zurich
University Library
Strickhofstrasse 39
CH-8057 Zurich
www.zora.uzh.ch

Year: 2012

Magnetic resonance imaging features of large endolymphatic sac compartments: audiological and clinical correlates

Connor, S E J ; Siddiqui, A ; O'Gorman, R ; Tysome, J R ; Lee, A ; Jiang, D ; Fitzgerald-O'Connor, A

Abstract: **OBJECTIVES:** (1) To study the prevalence and characteristics of large endolymphatic sac internal compartments on thin-section T2- and T2*-weighted magnetic resonance imaging, and to relate these to other large endolymphatic sac magnetic resonance imaging features, and (2) to correlate the compartment imaging features, endolymphatic sac size and labyrinthine anomalies with the patients' clinical and audiological data. **METHOD:** Magnetic resonance imaging studies for 38 patients with large endolymphatic sac anomalies were retrospectively reviewed in a tertiary referral centre. Endolymphatic sac compartment presence, morphology and imaging signal were assessed. Endolymphatic sac size and labyrinthine anomalies were also recorded. Endolymphatic sac compartments and other imaging features were correlated with clinical and audiological data. **RESULTS:** Compartments were present in 57 per cent of the imaged endolymphatic sacs, but their presence alone did not correlate with other imaging features or clinical data. The endolymphatic sac : internal auditory meatus signal ratio was associated with a history of sudden or fluctuating hearing loss. Hearing loss correlated with opercular and extraosseous endolymphatic sac size measurements. A larger midpoint intraosseous endolymphatic sac size was associated with clear fluid loss at cochlear implantation. **CONCLUSION:** The magnetic resonance imaging characteristics of large endolymphatic sac compartments have been defined. The endolymphatic sac size and distal compartment signal should be recorded, as these provide prognostic information and assist the planning of appropriate interventions.

DOI: <https://doi.org/10.1017/S0022215112000606>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-64839>

Journal Article

Accepted Version

Originally published at:

Connor, S E J; Siddiqui, A; O'Gorman, R; Tysome, J R; Lee, A; Jiang, D; Fitzgerald-O'Connor, A (2012). Magnetic resonance imaging features of large endolymphatic sac compartments: audiological and clinical correlates. *Journal of Laryngology and Otology*, 126(6):586-593.

DOI: <https://doi.org/10.1017/S0022215112000606>

Large endolymphatic sac compartments and associated magnetic resonance imaging features: a study of their audiological and clinical correlates

S.E.J. Connor, A. Siddiqui, R.O’Gorman, J.R. Tysome, A. Lee, D. Jiang, A. Fitzgerald
O’Connor

Large endolymphatic sac compartments and associated magnetic resonance imaging features: a study of their audiological and clinical correlates

S.E.J. Connor^{1,2}, A. Siddiqui^{1,2}, R.O’Gorman^{2,3}, J.R. Tysome⁴, A. Lee⁴, D. Jiang⁴, A. Fitzgerald- O’Connor⁴

¹Department of Radiology, Guy’s and St Thomas’ Hospital, London

²Department of Neuroradiology, King’s College Hospital, London

³MR-Center, University Children's Hospital, Zurich

⁴Ear Nose and Throat Department and Auditory Implantation Centre, Guy’s and St Thomas’ Hospital, London

Corresponding author:

Dr S.E.J. Connor,

Neuroradiology department,

Ruskin Wing,

Kings College Hospital,

Denmark Hill,

London

United Kingdom

SE5 9RS

tel. +44 (0)203 299 9000

e mail steve.connor@nhs.mail

Abstract

Objective: To study the prevalence and characteristics of large endolymphatic sac internal compartments on thin section T2/T2*-w MRI and to relate them to other MRI morphological features of the large endolymphatic sac anomaly. To correlate the presence, morphology and signal of the compartments, endolymphatic sac size and labyrinthine anomalies with clinical and audiological data.

Method: MRI studies for 38 patients with large endolymphatic sac anomalies were retrospectively reviewed in a tertiary referral centre. Endolymphatic sac compartment presence, morphology and signal were assessed on MRI studies. Endolymphatic sac size measurements and labyrinthine anomalies were recorded. Endolymphatic sac compartments and other MRI features were correlated with clinical and audiological data (patterns of hearing loss, presence of gusher ears, and mean pure tone audiograms).

Results: Compartments within the large endolymphatic sac anomalies were present in 57% of MRI studies, but their presence alone did not correlate with other MRI features or clinical data. The endolymphatic sac / internal auditory meatus signal ratio was associated with a history of sudden or fluctuating hearing loss. Hearing loss correlated with opercular and extraosseous endolymphatic sac size measurements. Larger midpoint intraosseous endolymphatic sac size was associated with a oozer/gusher at cochlear implantation.

Conclusion: The MRI characteristics of large endolymphatic sac compartments have been defined. The endolymphatic sac size measurements and the signal of any distal compartment should be recorded, since this will provide prognostic information and help plan appropriate interventions.

Keywords :magnetic resonance imaging, hearing loss; hearing disorders; labyrinth diseases; otolaryngology; large vestibular aqueduct; large endolymphatic sac syndrome

Introduction

Large endolymphatic sac anomaly is a congenital abnormality with acquired hearing loss and is one of the most frequent malformations of the inner ear recognisable on imaging studies ¹⁻³. The pathophysiology of hearing loss is unconfirmed. It has been postulated that hyperosmolar fluid from the large endolymphatic sac may reflux into the cochlea and damage the hair cells ⁴ or that cerebrospinal fluid pressure fluctuations are transmitted to the inner ear by the patent endolymphatic sac, resulting in endolymphatic hydrops, perilymphatic fistula or rupture of the cochlear membranes^{1,5}. Alternatively it has been proposed that that cerebrospinal fluid pressure is transmitted into the labyrinth through an associated deficient modiolus⁶, or that hearing loss is due to such concurrent inner ear anomalies^{5,7}. There have been attempts to correlate specific anatomical features such as endolymphatic sac size, the endolymphatic sac T2-weighted signal and associated labyrinthine anomalies with the audiological findings, although there have been inconsistent outcomes^{4,5,8,9}. There have also been limited reports of internal compartments demonstrated in the endolymphatic sacs on MRI of patients with large endolymphatic sac anomaly^{4,10,11}, however their significance and impact on our understanding of the hearing loss has not been systematically explored. We aimed :

- 1) To document the prevalence of internal compartments demonstrated by MRI in large endolymphatic sac anomaly subjects.
- 2) To record the location and morphology of these compartments together with the signal characteristics of individual fluid compartments.

- 3) To correlate the presence and MRI characteristics of the compartments, and their interfaces, with the presence of other large endolymphatic sac anomaly imaging features (endolymphatic sac size, associated labyrinthine anomalies and large endolymphatic sac anomaly fluid signal) together with clinico-audiological data.
- 4) To correlate the additional large endolymphatic sac anomaly imaging features (endolymphatic sac size, associated labyrinthine anomalies and large endolymphatic sac anomaly fluid signal) with clinico-audiological data.

Method

Patients with a diagnosis of large endolymphatic sac anomaly were retrospectively identified from a search of the radiology management system and the cochlear implant program database. The study was reviewed by the local National Health Service Research and Ethics committee and informed consent was not considered to be required for this retrospective study. MR imaging with thin section T2/T2*-w sequences was available in digital form for 40 patients (imaging performed between 2002-9) however two of these were excluded from the study due to adjacent pathology or incomplete volume coverage. The remaining 38 patients (mean age=16.9, age range=1-65, SD=15.2, 24 female, 14 male) were reviewed for the study. There were 7 cases of unilateral large endolymphatic sac anomaly and 31 cases of bilateral large endolymphatic sac anomaly, in accordance with previously defined criteria^{8,12}, so a total of 69 inner ears underwent imaging analysis. Comprehensive clinical data was obtained in 33/38 patients and audiometric data (performed within one year of the MRI study, mean 3.9 months, SD 3.2 months) was present for 62 ears in 31/38 patients (in 18/38 patients performed within 3 months of the MRI study). MRI was performed on 1.5 Tesla systems, however in view of the retrospective nature of the study, a variety of thin section T2/T2*-w sequences were utilised: driven equilibrium radiofrequency reset pulse (DRIVE) n=22, constructive interference in steady state (CISS) n=8, sampling perfection with application-optimized contrasts using different flip angle evolutions (SPACE) n=3, turbo spin echo (TSE) n=5

Radiological analysis

MRI digital data was reviewed on a GE Centricity PACS workstation (GE Medical Systems, Milwaukee, Wisconsin) by two independent neuroradiology observers. Axial images only were assessed. A series of endolymphatic sac size measurements, and assessments of labyrinthine morphology and endolymphatic sac compartment interface anatomy (when present) were performed. For the purposes of measuring endolymphatic sac size, the midpoint measurement required an initial delineation of the vestibular plane (a horizontal plane at the level of the dorsal common crus as it arises from the vestibule) (fig 1a) and the opercular plane (a horizontal plane at the level of the superior opercular lip) (fig 1b). The midpoint plane was defined as halfway between the vestibular and opercular planes (fig 1c)^{8,12}. The midpoint measurement bisected the midpoint plane in the angle of the endolymphatic sac trajectory (fig 2a). The operculum measurement was the maximum perpendicular endolymphatic sac width at the level of the operculum (fig 2b). Extraosseous long measurement and extraosseous short measurements represented the maximum longitudinal and short axis dimensions perpendicular to the petrous ridge (fig 2c). Labyrinthine morphology was recorded for the modiolus (normal/deficient/absent), the cochlear segmentation (normal/abnormal) and vestibular-semicircular canal (normal/mild/severe). Endolymphatic sac compartments were defined as visually apparent areas of differing signal within the endolymphatic sac with a clear interface. The MRI features of the compartments and the interfaces between compartments recorded were: angle of interface, orientation of interface, location of lower signal compartment and proportion of endolymphatic sac filled by the lower signal compartment (fig 3). Regions of interest were

placed within the endolymphatic sacs (including separate compartments) and within the internal auditory meati (fig 3).

Clinical and audiometric analysis

Clinical records were reviewed. Pure tone audiograms , with or without conductive thresholds, were documented at 250,500,1000, 2500 and 4000Hz and the mean was calculated. A conductive or mixed component to the hearing loss was defined if the air bone gap was >10dB at one or more frequencies in the presence of a normal tympanogram, however some data (12/62 ears) was incomplete due to the audiometry being performed unmasked. The course of the hearing loss was recorded as constant or progressive from the clinical history and progressive hearing loss was supported by pure tone audiometry showing >10dB increase in pure tone audiometry over more than a 3 month follow up period ¹⁴. Episodes of sudden or fluctuating hearing loss and associated precipitating factors were assessed. Family history, additional systemic syndromic associations and, when available, the results of Pendred gene analysis and perchlorate discharge testing were recorded. We recorded whether an “ooze” or "gush" of fluid was seen at cochlear implant surgery when entering the cochlea.

Statistical analysis

Interobserver reproducibility was assessed for MRI measurements of endolymphatic sac size and endolymphatic sac/internal auditory meatus signal ratios with Pearson's correlation coefficient, difference/mean and absolute difference/mean. Combined mean values were used for subsequent analysis.

Audiological data (pure tone audiometry and patterns of hearing loss), was compared with endolymphatic sac size measurements and the lowest endolymphatic sac/internal auditory meatus signal ratios using a 2-tailed Pearson correlation. Audiological data (pure tone audiometry and patterns of hearing loss), endolymphatic sac size measurements and the lowest endolymphatic sac / internal auditory meatus signal ratios were also compared with the presence of compartments and other labyrinthine abnormalities using a 2-tailed Mann Whitney U or Kruskal-Wallis test, (depending on whether the labyrinthine abnormalities included two or more categorical values). The same comparisons were also performed for only those ears without other labyrinthine abnormalities.

Further correlations between the categorical labyrinthine abnormalities were tested with 2-tailed Mann-Whitney or Kruskal Wallis tests.

For endolymphatic sacs in which compartments were present, the orientation of the interface between compartments, proportion of endolymphatic sac filled by low signal compartment and endolymphatic sac signal ratio measurements in proximal/distal compartments were compared with pure tone audiometry and patterns of hearing loss.

t-tests were used to compare the endolymphatic sac/ internal auditory meatus signal ratio in the endolymphatic sacs without compartments with the endolymphatic sac/ internal auditory meatus signal ratio in the proximal and distal compartments of those with compartments.

The presence of a gusher at surgery was compared with the endolymphatic sac size measurements and the presence of modiolar deficiency with a Mann Whitney U test.

Results and analysis

Clinical and audiological data

There was progressive hearing loss in 46% and sudden or fluctuating hearing loss in 30% of patients (n=33) when comprehensive clinical and audiometric data was available. There was mixed or conductive hearing loss in 76% of the ears (n=50) when comprehensive clinical and audiometric data was available. There were no patients who had experienced episodes of vertigo. Systemic associations were present in 27% of patients (distal renal tubular acidosis in 9%, Pendred's syndrome in 12% and others in 6%). Hearing loss was categorised as normal (2%), mild 30-49 dB (3%), moderate 50-59dB (3%), severe 60-79dB (16%), near deafness >80 dB (24%) and deafness (54%). Of those patients who underwent cochlear implantation (n=15), there was oozing or a gusher ear in 6 patients (40%).

MRI data

Compartments were present in 39/69 ears (57%) and were clearly demonstrated in 28/39 of cases. When compartments were present, the lower signal compartment was always distal (posterolateral). The proportion of the endolymphatic sac occupied by the low signal compartment was 0-25% (10%), 25-50% (21%), 50-75% (31%) and 75-100% (38%). Hence it was the dominant compartment in 69% of ears. The interfaces were always straight (38%) or bowing away from the labyrinthine aspect (68%) in orientation.

The mean (SD) endolymphatic sac / internal auditory meatus signal ratios were 0.914 (0.09) for the proximal septated compartment , 0.489 (0.16) for the distal septated compartment and 0.881 (0.12) for endolymphatic sacs without compartments. The endolymphatic sac / internal auditory meatus signal ratio in the distal compartment of those with compartments was significantly lower than the endolymphatic sac/ internal auditory meatus signal ratio in endolymphatic sacs without compartments ($p < 0.001$).

The mean (and SD) for size measures were: midpoint measurement 1.99 (0.70) mm, opercular measurement 2.63(0.91) mm, extraosseous long measurement 13.5 (6.4) mm and extraosseous short measurement 3.36 (3.1) mm. The modiolus was deficient in 38% of cases and absent in 4% of large endolymphatic sac anomalies, the cochlear segmentation was abnormal in 51% of large endolymphatic sac anomalies, and there was vestibular dysplasia in 41% of large endolymphatic sac anomalies (35% mild; 6% severe).

The interobserver reproducibility was excellent for all continuous data (endolymphatic sac size measures and endolymphatic sac / internal auditory meatus signal ratio) with Pearson's R 0.9-0.99.

Correlation of clinical and audiometric data with MRI data

The presence of compartments was significantly associated with larger extraosseous long measurements ($p = 0.000$).

Subjects with sudden or fluctuating hearing loss had significantly larger extraosseous dimensions when only including those ears without labyrinthine anomalies ($p = 0.034$ for extraosseous long measure and 0.043 for extraosseous short measure). Sudden or fluctuating

hearing loss was also associated with a lower endolymphatic sac / internal auditory meatus signal ratio in the distal compartment ($p=0.009$).

A concave interface demonstrated a trend to progressive hearing loss ($p=0.071$) when including only those ears without labyrinthine anomalies.

Pure tone audiometry was lower in ears with larger opercular measurements ($p=0.022$) and extraosseous measurements ($p=0.003$ for extraosseous long measure, $p=0.004$ for extraosseous short measure). These associations remained significant in ears without labyrinthine abnormalities.

The presence of a gusher at surgery (in the 15 ears implanted) was significantly associated with midpoint measurement ($p=0.05$) but not with modiolar deficiency nor any other endolymphatic size measurement (all $p>0.1$).

Discussion

The normal intraosseous endolymphatic sac contains only a few large folds and rugae, however a multitubular appearance (termed the pars rugosa or multilobular portion) becomes more conspicuous within its extraosseous portion, distal to the confines of the bony vestibular aqueduct (fig 3c)¹⁴. The contents of the lumen are heterogeneous and it varies in its degree of staining with haematoxylin and eosin. The more distal areas, related to the pars rugosa, have been shown to be composed of mucopolysaccharide and hyaluronic acid, which are of unknown function, but which may relate to inner ear fluid haemostasis¹⁵. There is limited pathological data concerning the histopathology of large endolymphatic sac anomaly. The appearance of an archived case of Pendred's syndrome with bilateral large endolymphatic sac anomaly demonstrated a prominent pars rugosa on one side whereas it was completely replaced on the other side¹⁶. Another case of an enlarged endolymphatic sac in the setting of a Mondini defect, revealed replacement of the perisac connective tissue stroma.¹⁷

Imaging studies have demonstrated that the entire endolymphatic sac may be of differing MRI signal or CT density to the cerebrospinal fluid or labyrinthine fluid^{4,18} and it has been postulated that this is a consequence of increased protein concentration. Normally the endolymphatic sac is filled with endolymph which resembles intracellular fluid² with hyperosmolar protein concentrations of 1000-3000mg/dl. In cases of large endolymphatic sac anomaly sampled at surgery, the protein concentration is reported as 335-660 mg/dl^{1,19}. It has been suggested that there may be abnormal bidirectional fluid flows between the large endolymphatic sac and the cochleovestibular organ leading to mixing and chronic contamination

of the protein poor cochleovestibular endolymph¹⁹. This mixing may be responsible for the reduced protein concentration relative to the normal endolymphatic sac. Such a scenario implies that protein concentration may vary over time and varying signal has also been noted on serial MRI²⁰.

Previous authors have also recognised that the distal (posterolateral) endolymphatic sac alone may return lower T2/T2*-w signal than the cerebrospinal fluid or labyrinthine fluid⁴ and this feature has been illustrated in other reports^{9,11} although its significance has not been explored. It has been proposed that this differing signal within the compartments represents the subepithelial connective tissue or multitubular tissue of the pars rugosa rather than the hyperosmolar proteinaceous contents^{11,14}. The morphology of the low signal compartments with their well defined interfaces, the known variation in endolymphatic sac signal with time²⁰ and the impressive erosion of bone around the endolymphatic sac¹⁷ consistent with hydraulic pressure, would be more indicative of a fluid containing compartment than solid tissue. The paucity of pars rugosa and connective tissue in the majority of previous pathological correlates, and the frequent extension of the low signal compartment into the intraosseous endolymphatic sac away from the pars rugosa, would also argue against connective tissue or pars rugosa being responsible for this observation. We postulate that, since the low signal compartment equates to the position of the pars rugosa, that it may correspond to mucopolysaccharide or hyaluronic acid secretion into the endolymph at this site, with separation from the proximal endolymphatic compartment by a rugal fold or septation. A dysfunctional enlarged endolymphatic sac may not be able to adequately remove such metabolites, particularly if they are compartmentalised. Such a concentration of metabolites may explain why lower signal was observed in the distal

compartments of septated large endolymphatic sac anomalies than in large endolymphatic sac anomalies without compartments. It is appreciated that this remains speculation in the absence of any pathological correlation, and alternative explanations include haemorrhage or reduced signal due to fluid pulsatility within the distal compartment.

The presence of the septations provides another potential anatomical correlate with the audiovestibular phenotype and this represents the largest study correlating any large endolymphatic sac anomalies MRI features with audiological findings. We speculated that bowing of the septation may provide an insight into differing compartment pressure or the direction of endolymph flow and that both this and the proportion of the endolymphatic sac occupied by the low T2/T2* signal compartment may correlate with degree and progression of hearing loss. Apart from a trend to progressive hearing loss with a concave septation, these hypotheses were not supported by our results. Indeed, the presence of septations overall was not significantly associated with the degree of hearing loss or any pattern of hearing loss.

There is some evidence that intralabyrinthine reflux of the low T2/T2* signal fluid may be implicated in hearing loss. A case report describes a patient scanned soon after hearing deterioration, in whom 3T MRI revealed low 3D CISS signal within the endolymphatic space of the labyrinth²¹. Our data concurs with previous studies in which measures of signal intensity within the endolymphatic sacs have not shown a correlation with the degree of hearing loss⁵. We were particularly interested in the possibility that the presence and occasional rupture of a compartment with reflux of accumulated debris and metabolites, would be associated with the

well described episodes of sudden or fluctuating hearing loss and vertigo. Sudden hearing loss may be triggered by coryzal illness, trauma, exercise and plane travel⁵ and associated variations in pressure could result in septation rupture and leakage. Endolymphatic sac signal measurement in the distal compartment was indeed associated with sudden hearing loss. We did not document episodes of vertigo in our patient group. Cases have been observed in which abnormal caloric responses has been related to low T2* signal within the intraosseous endolymphatic sac²². Additional audiovestibular findings such as a conductive component or mixed hearing loss^{1,5,9,23} may be described in the setting of large endolymphatic sac anomaly. The potential causes of a conductive component include increased cochlear fluid pressure, a third window effect or stapes fixation. We showed no relationship between the presence of septations or other MRI features and the presence of a conductive or mixed hearing loss.

Perilymphatic gushers at the time of cochlear implant surgery have been encountered previously in patients with large endolymphatic sac anomaly²⁴ and these were recorded in 6/15 of our cases undergoing cochlear implantation. It has been previously suggested that this may result from either transmission of fluid through the enlarged endolymphatic sac or the cochlear aperture in the presence of a deficient modiolus. We demonstrated a significant relationship between the presence of “gushers” and the midpoint measurement (generally the narrowest part of the endolymphatic sac and hence a potential “bottleneck”) but not modiolar deficiency, hence favouring the former mechanism.

Although not the main focus, our data allowed us to analyse the relationship between ES size and audiological findings. We showed that all four of our endolymphatic sac measurements, and in particular the extraosseous measurements, could be performed with excellent reproducibility on MRI. Previous series have failed to demonstrate any association between the endolymphatic sac size (at the midpoint measurement, opercular measurement^{5,9,10} or extraosseous measures^{5,10}) and the severity of hearing loss although there has been a documented association with the progression of hearing loss⁸. The size measurements were related to pure tone audiometry (significant in the case of the opercular measurement and extraosseous measurements) and there was an additional relationship between extraosseous endolymphatic sac measurements and a history of sudden hearing loss, when patients without other labyrinthine abnormalities were studied alone.

Conclusion

1) Compartments within the large endolymphatic sac anomalies were documented in 57% of thin section T2/T2*-w MRI studies, but their presence did not correlate with clinical and audiological data.

2) Septations were particularly frequent in the larger extraosseous large endolymphatic sac anomalies and were either straight or bowed towards the labyrinth. The distal compartment was usually larger, and was always of lower signal on T2/T2* images.

3) The endolymphatic sac / internal auditory meatus signal ratio within the distal compartment was lower than in those endolymphatic sacs without compartments, and the lower signal was associated with a history of sudden or fluctuating hearing loss.

4) Pure tone audiometry was lower in ears with larger opercular measurement and extraosseous measurements. Midpoint endolymphatic sac measurement, but not modiolar deficiency, was associated with a “gusher” at the time of cochlear implantation.

Summary

- We showed that large endolymphatic sac anomalies demonstrate compartments of differing signal abnormality on 57% of thin section T2/T2*-w MRI studies however their presence alone does not correlate with clinical and audiological data
- Decreased T2/T2*-w signal within the distal compartment is associated with a history of sudden or fluctuating hearing loss
- Larger extraosseous and opercular dimension endolymphatic sacs are associated with lower pure tone audiometry
- Larger intraosseous sacs (at their midpoint dimension) are associated with an “oozer” or “gusher” at the time of cochlear implantation
- These MRI features should be emphasised since they may provide prognostic information and help plan appropriate interventions.

References

- 1) Jackler RK, De La Cruz A. The large vestibular aqueduct syndrome. *Laryngoscope* 1989; 99: 1238-1243
- 2) Mafee MF, Charlette D, Kumar A, Belmont H. Large vestibular aqueduct and congenital sensorineural hearing loss. *AJNR Am J Neuroradiol* 1992; 13: 805-819
- 3) Valvassori GE, Clemis JD. The large vestibular aqueduct syndrome. *Am J Otol* 1985; 6: 387-415
- 4) Naganawa S, Koshikawa T, Iwayama , Fukatsu H, Ishiguchi T, Ishigaki T et al. MR imaging of the enlarged endolymphatic duct and sac syndrome by use of a 3D fast asymmetric spin-echo sequence: Volume and signal-intensity measurement of the endolymphatic duct and sac and area measurement of the cochlear modiolus. *AJNR Am J Neuroradiol* 2000; 21: 1664-1669
- 5) Colvin I, Beale T, Harrop-Griffiths K. Long term follow up of hearing loss in children and young adults with enlarged vestibular aqueducts: Relationship to radiologic findings and Pendred syndrome diagnosis. *The Laryngoscope* 2006; 116: 2027-2036
- 6) Lemmerling MM, Mancuso AA, Antonelli PJ, Kubilis PS. Normal modiolus: CT appearance in patients with a large vestibular aqueduct. *Radiology* 1997; 204: 213-219

7)Hirsch BE, Weissman JL, Curtin H, Kameron DB. Magnetic resonance imaging of the large vestibular aqueduct. Arch Otolaryngol Head Neck Surg 1992; 118:124-1127

8)Boston M, Halsted M, Meinzen-Derr J, Bean J, Vijayasakaren S, Arjmand E et al. The large vestibular aqueduct: A new definition based on audiologic and computed tomography correlation. Otolaryngol Head Neck Surg 2007; 136: 972-977

9)Koesling S, Rsainski C, Amaya B. Imaging and clinical findings in large endolymphatic duct and sac syndrome. Eur J Radiol 2006; 57: 54-62

10)Naganawa S, Ito T, Iwayama E. MR imaging of the cochlear modiolus: Area measurement in healthy subjects and in patients with a large endolymphatic duct and sac. Radiology 1999; 213: 819-823

11)Romo LV, Casselman JW, Robson CD. Temporal bone: Congenital anomalies. In: Som PS, Curtin HD eds. Head and Neck Imaging 4th ed. Vol 2. St Louis: CV Mosby; 2003: 1109-1171

12)Vijayasekaren S, Halsted MJ, Boston M, Meinzen-Derr J, Bardo DME, Greinwald J, Benton C. When is the vestibular aqueduct enlarged?A statistical analysis of the normative distribution of vestibular aqueduct size. AJNR Am J Neuroradiol 28: 1133-1138

- 13) Davidson HC, Harnsberger HR, Lemmerling MM, Mancuso AA, White DK, Tong KA et al. MR evaluation of vestibulocochlear anomalies associated with large endolymphatic duct and sac. AJNR Am J Neuroradiol 1999; 20: 1435-1441
- 14) Bagger-Sjoberg D, Jansson B, Friberg U, Rask-Anderson H. Three dimensional anatomy of the human endolymphatic sac. Arch Otolaryngol Head Neck Surg 1990; 116: 345-349
- 15) Danckwardt-Lilliestrom N, Laurent C, Hellstrom S, Friberg U, Kinnefors A, Rask-Andersen H. Localisation of hyaluronan in the human endolymphatic sac. Acta Otolaryngol 1994; 114: 382-386
- 16) Gill H, Michaels L, Phelps PD, Reardon W. Histopathological findings suggest the diagnosis in an atypical case of Pendred syndrome. Clin Otolaryngol 1999; 24:523-526
- 17) Gussen R. The endolymphatic sac in Mondini disorder. Eur Arch Otorhinolaryngol 1985; 242: 71-76
- 18) Okamoto K, Ito J, Furusawa T, Sakai K, Tokiguchi S. Large vestibular aqueduct syndrome with high CT density and high MR signal intensity. AJNR Am J Neuroradiol 1997; 18: 482-484

- 19) Couloigner V, Grayeli AB, Sterkers O, Ferrary E. Composition of endolymphatic sac luminal fluid in a patient with Mondini dysplasia. *Ann Otol Rhinol Laryngol* 2008; 117: 123-126
- 20) Naganawa S, Koskikawa T, Fukatsu H, Ishigaki T, Nukashima T. Serial MR imaging studies in enlarged endolymphatic duct and sac syndrome. *Eur Radiol* 2002;12: 114-117
- 21) Naganawa S, Sone M, Otake H, Kakashima T. Endolymphatic hydrops of the labyrinth visualized on noncontrast MR imaging: a case report. *Magn Reson Med Sci* 2009; 8: 43-46
- 22) Oh SH, Choi BY, Son KR, Lee KJ, Chang SO, Kim CS. Can magnetic resonance imaging provide cues to the inner ear functional status of enlarged vestibular aqueduct subjects with PDS mutation? *Otol Neurotol* 2008; 29: 593-600
- 23)Antonelli PJ, Nall AV, Lemmerling MM, Mancuso AA, Kubilis PC. Hearing loss with cochlear modiolar defects and large vestibular aqueducts. *Am J Otol* 1998; 19: 306-312
- 24) Au G, Gibson W. Cochlear implantation in children with large vestibular aqueduct syndrome. *Otol Neurotol* 1999; 20: 183-1

Legends and figures

Fig 1. T2 DRIVE axial MR images demonstrating the vestibular, opercular and midpoint planes in a patient with bilateral large endolymphatic sac anomaly but no septations. A) Line corresponds to the vestibular plane defined by the horizontal plane at the level of the dorsal common crus as it arises from the vestibule (indicated by arrowhead on contralateral side). B) Line corresponds to the opercular plane defined by the horizontal plane at the level of the superior opercular lip (indicated by arrowhead on contralateral side). C) . Line corresponds to the midpoint plane, defined as halfway anteroposteriorly between the vestibular and opercular planes.

FIG 1a

FIG 1b

FIG 1c

Fig 2.T2 DRIVE axial MR images demonstrating the endolymphatic sac size measurements. A) T2 DRIVE axial MR images cropped to the large endolymphatic sac anomaly. The midpoint measurement is demonstrated bisecting the midpoint plane in the angle of the endolymphatic sac trajectory such that the measurement forms an equal angle with the lateral and medial walls of the endolymphatic sac . B) T2 DRIVE axial MR image demonstrating bilateral large endolymphatic sac anomaly with septations and small proximal compartments.The opercular measurements are shown on either side as the maximum endolymphatic sac widths at the level of the opercula. They extend perpendicular to the lateral wall of the endolymphatic sac.C) T2 DRIVE axial MR image shows the extraosseous endolymphatic sac measurements of the extraosseous short measurement and extraosseous long measurement

FIG 2a

FIG 2b

FIG 2c

Fig 3. T2 DRIVE axial MR images demonstrating imaging septation anatomy, labyrinthine anomalies and ROI placement. A) T2 DRIVE axial MR image demonstrating bilateral large endolymphatic sac anomaly . The right sided distal lower signal compartment comprised 50-75% of the volume (on scrolling through adjacent images) whilst that on the left comprised 75-100%. There is a right sided concave (with 60-90% angle) and left sided straight (with 30-60% angle) septation. B) T2 DRIVE axial MR image demonstrating bilateral large endolymphatic sac anomaly, abnormal cochlear segmentation and vestibular dysplasia. Regions of interest s are shown for the two left sided endolymphatic sac compartments. The distal lower signal compartment occupies 75-100% of the endolymphatic sac and there is a concave septation. C) T2 DRIVE axial MR images cropped to the enlarged right endolymphatic sac. Regions of interest are shown for the internal auditory meatus , proximal and distal endolymphatic sac compartments. The region of interest corresponding to the distal compartment would include the region of the pars rugosa. Note the separate high signal “bubble” within the distal compartment. 75-100% of the endolymphatic sac is filled by the lower signal distal compartment and the septation is concave.

FIG 3a

FIG 3b

FIG 3c